The development and evaluation of a self-monitoring and patient-initiated follow-up service for people with rheumatoid or psoriatic arthritis on methotrexate

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for the degree of
PhD in Health Psychology

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June, 2014

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ACKNOWLEDGEMENTS

There are a many people I would like to thank for their advice, support and encouragement during the course of this thesis.

Firstly my supervisors Professor Stan Newman and Dr Shashi Hirani, who have shown great trust and belief in me throughout this process, more than I had for myself. I have been given so many new opportunities throughout this period and I will forever be grateful for your generosity and encouragement. I would like to acknowledge the contributions and support of the following: all participants who took part in the trial; my collaborators at UCLH especially Consultant Rheumatologist Dr Michael Shipley without whom this project and thesis would not have been possible, and Clinical Nurse Specialists Ms. Abigail Olaleye, Ms. Samantha Moore and Ms. Nicola Daly for facilitating our patient recruitment and assisting in the running of the intervention. You have all been wonderful to work with, and I hope we can again in the future. The UCLH Charities fund, specifically the Otto Beit Fund and Shipley Rudge Fund for supporting this study, and members of the Centre for Health Services Research at City University London for their assistance in the systematic review and qualitative study.

To Sophie, Justine, Tara and Nadine thank you for showing me that there was light at the end of the tunnel, for the inspiration and advice, but most importantly the wine. I must also say a huge thank you to Kathleen who has shown me huge support, particularly in these last few months, I could not have asked for a more supportive colleague.

To my husband Ian, the only one who knows the real sacrifices we have both had to make to get me through this journey. You have been my rock, and at times the only sane person in our household. You have held me together when I've been at my lowest and been there to celebrate at the good times. I thank you from the bottom of my heart for supporting me, wiping my tears and bringing me endless cups of tea and hugs. I could not have accomplished this without you. Now let's get back living!

DEDICATION

To my Mum and Dad, you have shown me boundless encouragement, support and love. You have never questioned my ability and always encouraged me to pursue everything I do with tenacity and drive. I dedicate this thesis to you.

DECLARATION

I, Hayley McBain, confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm this has been indicated in this thesis.

ABSTRACT

This thesis describes the development and evaluation of a self-monitoring and patient-initiated follow-up service for people with rheumatoid arthritis (RA) or psoriatic arthritis (PsA) on methotrexate. Using a mixed methods approach including a randomised controlled trial (RCT) and qualitative semi-structured interviews.

The overall aims of this thesis were to design an alternative model of care which could be delivered in rheumatology outpatients by clinical nurse specialists (CNS) in order to reduce the burden of established patients in clinic. This is followed by an evaluation of intervention effectiveness and safety, along with an exploration of the mechanisms of action and patient acceptability.

One hundred patients from University College Hospital London (UCLH) with either RA or PsA on methotrexate were recruited into the trial and were followed for six consecutive blood tests. Patients randomised to the intervention group were required to monitor their symptoms, side effects and laboratory results and use this information to initiate care from the CNS. The results indicated that patients were able to accurately initiate a consultation with their nurse on approximately 75% of occasions. The intervention led to 55% fewer appointments with the CNS (p<0.0001) and 39% fewer GP appointments (p=0.07) compared to usual care, with tentative evidence to suggest cost savings. There were no significant differences in clinical or psychosocial well-being, including function, pain, quality of life and mood. Intervention participants were positive about the new model of care, valuing its efficiency and tailored approach. The service allowed patients to gain new knowledge and use this information along with the skills they obtained to take control of their health and arthritis.

This model of care may, therefore, be a viable alternative for established RA and PsA patients on methotrexate in order to reduce healthcare utilisation without compromising clinical or psychosocial well-being.

ABBREVIATIONS

ACR - American College of Rheumatology
AIC - Akaike's Information Criterion
ALP - Alkaline Phosphatase
ALT - Alanine Transferase
AMSTAR - Assessment of Multiple Systematic Reviews
ANCOVA - Analysis of Covariance
ANOVA - Analysis of Variance
anti-TNF – Anti-Tumour Necrosis Factor
ARA - American Rheumatology Association
ARMA - Arthritis Musculoskeletal Alliance
ASMP - Arthritis Self-management Programme
ATH - Aggressive Treatment in a Hospital Setting
BCTT - Behaviour Change Technique Taxonomy
BDOC – Bed Days Of Care
BG – Blood Glucose
BMQ - Beliefs about Medicines Questionnaires
BP – Blood Pressure
CAD – Coronary Artery Disease
CASPAR - Classification Criteria for Psoriatic Arthritis
CATS - Clinical Assessment And Treatment Services
CCA - Corrected Cover Area
CCG - Clinical Commissioning Group
CDSMP - Chronic Disease Self-Management Programme
CHF – Chronic Heart Failure
CI – Confidence Interval
CNS – Clinical Nurse Specialist
CONSORT - Consolidated Standards of Reporting Trials
CRP – C-Reactive Protein
DAS - Disease Activity Score
DBP – Diastolic Blood Pressure
df – degrees of freedom
DMARDS - Disease Modifying Anti-Rheumatic Drugs
DV - Dependant Variable
ECG – Electrocardiogram
ED – Emergency Department
ER – Emergency Room
ESR - Erythrocyte Sedimentation Rate
EULAR - European League Against Rheumatism
FBG – Fasting Blood Glucose
GLM - Generalized Linear Models
GLMM - General Linear Mixed Model
GSES - General Self-Efficacy Scale
HAQ - Health Assessment Question
HeiQ - Health Education Impact Questionnaire
HF- Heart Failure
HTA - Health Technology Assessment

HTM – Telemonitoring
IBD - Irritable Bowel Disease
ICC - intra-class correlations
INR - International Normalized Ratio
IPA - Interpretative Phenomenological Analysis
IPQ - Illness Perceptions Questionnaire
ITT – Intention-To-Treat
IV - Independent Variable
LVEF – Left Ventricle Injection Fraction
MA – Meta-Analysis
MCAR - Missing Completely At Random
MCS - Mental Component Summary
MeiQ - Medication Education Impact Questionnaire
MHRA - Medicines and Healthcare Products Regulatory Agency
MLM - Multilevel Modelling
MRC - Medical Research Council
MSF - Musculoskeletal Services Framework
NHS - National Health Service
NICE - National Institute for Health and Care Excellence
NIDDM/NID – Non-Insulin Dependent (Diabetes Mellitus)
NR – Not Reported
NSAIDS - Non-Steroidal Anti-Inflammatory Drugs
NYHA – New York Heart Association
OR – Odds Ratio
PCA - Principal Component Analysis
PCS - Physical Component Summary
PRISMA - Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PROMS - patient reported outcome measures
PsA - Psoriatic Arthritis
PsARC - Psoriatic Arthritis Response Criteria
PSM – Patient Self-Management
PST- Patient Self-Testing
QoL – Quality of Life
RA - Rheumatoid Arthritis
RCT - Randomized Controlled Trial
RD – Risk Difference
REML - Restricted Estimate Maximum Likelihood
RF – Rheumatoid Factor
RR – Relative Risk
SBP – Systolic Blood Pressure
SCSC - Symptom Control and Shared Care
SD – Standard Deviation
SF-12v1® - Short-Form Health Survey 12-item
SMBG - Self-Monitoring of Blood Glucose
SR – Systematic Review
STROBE - Strengthening the Reporting of Observational studies in Epidemiology
T2DM – Type 2 Diabetes Mellitus
TIDieR - Template For Intervention Description and Replication
UCLH - University College Hospital London

VIF - Variance Inflation Factor
WBC - White Blood Cells
WMD – Weighted Mean Difference

CHAPTER 1 - INTRODUCTION TO RHEUMATOID AND PSORIATIC ARTHRITIS

1.1 PROLOGUE

The intention of this thesis is to develop and evaluate the effectiveness and acceptability of a self-monitoring and patient-initiated service for patients with rheumatoid arthritis (RA) or psoriatic arthritis (PsA) from the patient perspective. The specific aims of this thesis were:

- To establish the current evidence for patient-initiated services in rheumatology in comparison to other models of care.
- To understand the benefits, to healthcare utilisation and psychosocial well-being, of formal self-monitoring across a range of long-term conditions.
- To design a self-monitoring and patient-initiated service that could be delivered in rheumatology outpatients by Clinical Nurse Specialists (CNS).
- To evaluate the effectiveness and safety of this intervention in relation to usual care.
- To identify the mediators and moderators of intervention effectiveness.
- To establish patient acceptability and the value placed on this model of care.

This introductory chapter will, therefore, provide an overview of the clinical features of both RA and PsA, including diagnostic criteria, the possible causes and risk factors of disease onset, prevalence and incidence rates, mortality and co-morbidities, pharmacological management and the disease and treatment monitoring requirements. It concluded with an assessment of the financial impact of these two conditions on the UK National Health Service (NHS).

1.2 DEFINITION

RA and PsA are both classified as chronic inflammatory arthritis that primarily affect the joints. Both conditions are described as “autoimmune” meaning that certain cells of the body attack other healthy cells and tissues. The synovial tissue, which maintains the nutrition and lubrication of the joints becomes swollen and inflamed and causes

pain, stiffness and disability (Husted, Gladman, Farewell, & Cook, 2001). Both RA and PsA have a wide clinical spectrum, from mild joint symptoms to severe inflammation and damage but in some cases sustained remission is possible (Gladman, Hing, Schentag, & Cook, 2001; Svensson *et al.,* 2013) (Figure 1.1).

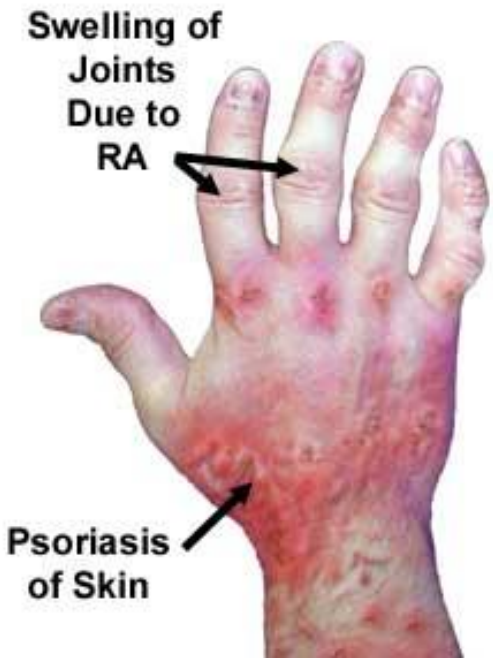


Figure 1.1. Photograph of the effects of RA and PsA

RA typically affects the small joints of the hands and feet symmetrically, although any synovial joints can be involved. Other organs can also be affected including the lungs, blood vessels and the haematopoietic system. Many autoimmune diseases also involve the skin; the most prevalent in rheumatology is PsA, which is arthritis in association with psoriasis. In contrast to RA, PsA not only affects the joints but also the surrounding structures such as tendons and ligaments, particularly the enthesis – the point where a ligament or tendon joins bone, as well as the skin and nails. Joint involvement is asymmetrical and the distal interphalangeal joints of the hands and feet are more frequently affected than in RA. Most patients with PsA have mild to moderate psoriasis, and there is some evidence to suggest a correlation between total joint involvement and the extent of skin disease (Elkayam, Ophir, Yaron, & Caspi, 2000; Serarslan, Güler, & Karazincir, 2007). For some the arthritis predates the skin disease but can be diagnosed by a family history of psoriasis or PsA (Cantini *et al.,* 2010).

1.3 DIAGNOSIS

There is no single diagnostic test for either RA or PsA; diagnosis involves a series of clinical and laboratory observations. In the early stage this relies heavily on the history and examination of the patient, with blood and imaging tests helping to confirm the most likely diagnosis. The American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR) (Aletaha *et al.,* 2010) classification are now the most applied criteria for RA (Table 1.1).

Table 1.1.ACR/EULAR 2010 classification criteria for RA

Criterion	Definition	Score
A. Joint involvement (swollen or tender)		
• 1 large joint	• Large refers to shoulders, elbows, hips, knees & ankles.	0
• 2-10 large joints		1
• 1-3 small joints (with or without involvement of large joints)	• Small refers to the joints of the hands & feet.	2
• 4-10 small joints (with or without involvement of large joints)		3
• >10 joints (at least 1 small joint)		5
B. Serology (at least 1 test result is needed for classification)		
• Negative RF *and* negative ACPA tests		0
• Low-positive RF *or* low-positive ACPA		2
• High-positive RF *or* high-positive ACPA		3
C. Acute-phase reactants (at least 1 test result is needed for classification)		
• Normal CRP *and* normal ESR	• Normal/abnormal is determined by local laboratory standards	0
• Abnormal CRP *or* abnormal ESR		1
D. Duration of symptoms (self-report)		
• <6 weeks		0
• ≥6 weeks		1

RF – Rheumatoid Factor; ACPA – Anti-Citrullinated Protein Antibody; CRP – C-Reactive Protein; ESR – Erythrocyte Sedimentation Rate

These criteria are applied if the patient has at least 1 joint with definite clinical synovitis that cannot be better explained by another disease. A total score of ≥6 is

needed for classification of definite RA. Although patients with a score of <6 are not classifiable as having RA, their status can be reassessed to determine if the criteria may be fulfilled at a later date.

PsA was first recognised as a distinct condition in 1964 by the American Rheumatology Association (ARA) (Blumberg, Bunim, Calmns, Pirani, & Zvaifler, 1964). Diagnosis of PsA is primarily established through the presence of signs and symptoms associated with both skin and joint involvement and by eliminating other forms of inflammatory arthritis including RA. There is, however, clinical overlap between RA and PsA and, therefore, diagnosis is easier if psoriasis is present. In some patients with PsA the pattern of joint involvement is very similar to that of RA but the rheumatoid factor, the antibody directed against the body's own tissue, is usually negative whilst in RA it is normally positive. The Classification Criteria for PsA (CASPAR) (Taylor *et al.,* 2006) has been shown to be highly sensitive to the diagnosis of PsA (Figure 1.2).

- Inflammatory articular disease (joint, spine or enthesis)
- AND at least 3 points from the following:
    - Current psoriasis (2 points), a personal history of psoriasis (1 point), or a family history of psoriasis (1 point)
    - Typical nail dystrophy (1 point): onycholysis, pitting, hyperkeratosis
    - Negative RF (1 point): ELISA or pephelometry preferred
    - Dactylitis (1 point): current dactylitis or a previous episode noted by a rheumatologist
    - Juxta-articular new bone formation (1 point): on hand or foot radiograph.

RF – Rheumatoid Factor; ELISA – Enzyme-Linked Immunosorbent Assay

Figure 1.2. Classification criteria for PsA

1.4 PREVALENCE AND INCIDENCE

It has been almost 50 years since the first age and sex-specific estimates of RA prevalence were published in the UK. Using the ARA 1958 criteria, 2.1% of males and 5.2% of females had probable or definite RA. Rising with age in both sexes, reaching a maximum of 6% in males aged 75 years and over and 16% in females aged 65 to 74 years (Lawrence, 1961). Applying the subsequent 1987 ACR criteria Symmons *et al.,*

(2002) were able to capture those who were in remission but had some accumulated damage as a result of their RA. In this two stage process Symmons *et al.,* (2002) used a screening questionnaire and clinical examination of positive responders, classified as participants who reported ever having had swelling of two or more joints (excluding the ankles) lasting for 4 or more weeks, or who had ever been told by a doctor that they had RA. Although the classification criteria used were different from those in the study conducted by Lawrence (1961), there appears to be some change in prevalence rates in the last 50 years. A fall in numbers was reported in all women except those over the age of 75 for whom there was an 8% increase. This reduction in prevalence rates for women has been observed in other studies (Doran, Crowson, O'Fallon, & Gabriel, 2004), notably since the 1960s, and has been attributed to the protective effect of the oral contraceptive pill. In contrast the prevalence in males had risen by 27-30% for those aged 45 and older in the study by Doran *et al.,* (2004). A number of studies have estimated the prevalence of PsA to be between 1 and 420 cases per 100,000, depending on the country of the study (Cantini *et al.,* 2010). There are, however, currently no accurate figures for the UK.

Several papers have been published over the last 20 years estimating the incidence rates of RA in the UK. The most recent study by Humphreys *et al.,* (2012), utilising the 2010 criteria, reported incidence rates as 40 per 100,000; 54 per 100,000 for women and 25 per 100,000 for men. In women the peak age of incidence was younger than in men, with highest rates between the ages of 45 and 74 years. In men incidence appeared to increase with age, with highest rates in men over 65 years old. A systematic review by Alamanos, Voulgari and Drosos (2006) identified 28 studies reporting either the incidence and/or prevalence of RA worldwide. Whereas, incidence rates in the UK were comparable to other countries for both men and women, prevalence estimates were considerably higher in the UK.

The systematic review of PsA by Cantini *et al.,* (2010) found that incidence rates ranged between 3 and 23.1 cases per 100,000; however, the review did not include any studies from the UK. Harrison, Silman, Barrett, Scott and Symmons (1997) did find that in the UK incidence rates for PsA were 3.6 for males and 3.4 for females per 100,000, less than in other European countries (Alamanos, Voulgari, & Drosos, 2008).

In contrast to RA, equal numbers of males and females are affected by PsA and the mean age of onset is between 30 and 55 years (Cantini *et al.,* 2010). For approximately 70% of patients psoriasis develops before the onset of arthritis, for 15% the two conditions occur within 12 months of each other and in the remainder arthritis precedes the onset of psoriasis by more than 1 year (Cantini *et al.,* 2010).

1.5 AETIOLOGY

Both RA and PsA are diseases of unknown cause. A number of risk factors have been identified to help explain the development, persistence and outcome of these conditions. The general consensus is that they are multi-factorial diseases that occur as a result of a combination of genetic and environmental factors. The primary causes will now be discussed; however, this is not an exhaustive list.

1.5.1 Genetic

There is a lack of consensus on the role of genetics in the development of RA. Whilst MacGregor *et al.,* (2000) estimated that the genetic contribution to RA susceptibility is around 60%, recent research has suggested that genes are of lesser importance and in fact environmental effects may be more important in the development of the condition than previously thought (Svendsen *et al.,* 2002). Being able to determine the impact of genetics in the development of PsA is complicated by the difficulty in discerning whether a genetic marker is specifically associated with skin disease, joint disease, or both. Due to the polygenic nature of the disease a number of genes may be contributing small effects resulting in the wide range of symptoms. Research has suggested that PsA is highly heritable, with heritability far higher than that of psoriasis alone and also in comparison to RA (Gladman, Farewell, Pellett, Schentag, & Rahman, 2003; Bhalerao & Bowcock, 1998; Myers, Kay, Lynch, & Walker, 2005; Rahman & Elder, 2005). The development of the PsA classification criteria should help to improve our understanding of the genetic factors contributing to this condition by having a clear definition of what constitutes a case of PsA.

1.5.2 Hormones

As noted previously RA is more common in women than men, suggesting that reproductive and hormonal factors may play a role in the development of the disease.

A large number of studies have identified that the oral contraceptive pill has a protective effect, most likely postponing disease onset rather than preventing the disease (Silman & Pearson, 2002). In addition, pregnancy can reduce disease activity by 50-75% and disease onset by 70%. This then increases, however, more than fivefold in the first 3 months postpartum (Silman, Kay, & Brennan, 1992). This increase has been associated with elevated secretion of the pro-inflammatory hormone prolactin whilst breastfeeding. Similarly, pregnancy in the 2 years prior to onset of psoriasis is associated with a decreased risk of developing PsA, even after adjusting for the influence of age, duration of psoriasis and corticosteroid use (Thumboo *et al.,* 2002). Exposure to the oral contraceptive pill or hormone replacement therapy, and menopause were, however, not linked to the development of PsA (Thumboo *et al.,* 2002).

1.5.3 Smoking

Smoking has been linked to both the development and course of RA and PsA, but in differing ways. In a recent meta-analysis of observational studies Sugiyama *et al.,* (2010) concluded that males who had ever smoked were 1.89 times more likely to develop RA compared to non-smokers and for females 1.27 times. Smoking 20 or more packets a year posed a similar risk for both males and female, with odd ratios of 2.31 and 1.75 respectively. The review also showed that the risk of developing seropositive RA in smokers is greater than the risk of developing seronegative RA (Sugiyama *et al.,* 2010). Smoking, psoriasis, and PsA have an interesting relationship. Smoking is a risk factor for the development of psoriasis on its own (Setty, Curhan, & Choi, 2007) but the time to development of PsA decreases with smoking prior to psoriasis onset and increases with smoking after psoriasis onset (Rakkhit *et al.,* 2007).

1.5.4 Socio-economic status

Although there is no evidence to suggest a link between socio-economic status and onset of RA, it does appear to have an impact on the course and outcome of the disease. A number of authors have reviewed the literature in this area and patients with RA who live in socially deprived areas have been found to experience worse physical function and higher mortality rates (Symmons, 2002). Lower formal education has also been associated with increased mortality, morbidity, physical function, tender

and swollen joint count and more x-ray damage in RA (Symmons, 2003). It is unclear, however, why these differences exist; it may in part be due to the lower rates of medication adherence in these groups or due to late presentation of symptoms and diagnosis. There has been little research exploring the relationship between socio-economic status and PsA and these potential associations remain to be explored.

1.5.5 Infection

There has been a vast amount of interest in the role of infections as the initiators of the inflammatory process in RA and PsA. It has been suggested that infection could trigger the development of these conditions in a genetically susceptible group. Although a number of infections have been implicated, including post-streptococcal tonsillitis, parvovirus, rubella, Epstein-Barr virus and Borrelia burgdorferi, there is no epidemiological evidence that suggests these infections could explain a significant number of cases in either condition (Symmons *et al.,* 1997; Cantini *et al.,* 2010).

1.5.6 Diet

In a recent review of 14 studies Pattison, Harrison and Symmons (2004) concluded that consumption of olive oil and fish oil were associated with protective effects against RA onset, particularly for seropositive RA. A mixed picture was presented for both caffeine and alcohol, with some studies reporting an association between increased risk of RA and higher consumption and others reporting no significant difference. There was more convincing evidence that eating more fruit, cooked vegetables and cruciferous vegetables (e.g. cabbage, broccoli, and cauliflower) was associated with a lower risk of developing RA. There has been little research exploring the impact of diet on the development and course of PsA; however, a generally healthy diet and supplementary fish oils have been recommended for psoriasis (Raychaudhuri & Farber, 2001; Raychaudhuri & Gross, 2000).

1.6 MORTALITY

A number of studies have shown that patients with RA and PsA have an increased risk of death compared to the general population. These studies vary in their diagnosis criteria, exclusion and inclusion criteria, length of follow-up, duration of disease before

recruitment, methods of statistical analysis and the causes of death. Overall, however, the findings are consistent.

In the most recent systematic review and meta-analysis of mortality in RA Dadoun *et al.,* (2013) synthesized 11 longitudinal studies representing 51,819 patients. The review looked at studies pre 1970, from 1970 to 1983 and after 1983, which corresponds to the introduction of methotrexate. The meta-analysis suggested a significant decrease in incident mortality rates over the 3 periods, starting at 4.7 per 100 person-years for studies before 1970, 3 per 100 person-years from 1970 to 1983 and 2 per 100 person-years for those studies conducted after 1983. A significant decrease in incidence the mortality rate of 2.84% per year was found over time. These rates were significantly higher than in the general population, with higher mortality rates associated with older age at diagnosis and longer length of follow-up.

There is some discordance when looking at mortality rates in PsA. Some studies have shown no increase in mortality (Shbeeb, Uramoto, Gibson, O'Fallon, & Gabriel, 2000; Wilson *et al.,* 2009) whilst others show rates similar to that of the RA population (Wong *et al.,* 1997). A UK study found that the leading causes of death in PsA were cardiovascular disease (38%), diseases of the respiratory system (27%), and malignancy (14%) (Buckley *et al.,* 2010). Mortality was not significantly different from the general UK population. This is supported by a more recent systematic review that found no increased risk of cardiovascular mortality for patients with PsA (Horreau *et al.,* 2013). In a cohort sample of patients with PsA followed prospectively over close to 20 years the risk for premature death was related to previously active and severe disease, the level of medication and the presence of erosive disease (Gladman, Farewell, Wong, & Husted, 1998). It remains to be seen whether modern treatments, such as biological agents, will alter these findings in PsA or RA.

1.7 CO-MORBIDITIES

1.7.1 Cardiovascular disease

The prevalence of ischemic heart disease, atherosclerosis, peripheral vascular disease, congestive heart failure, cerebrovascular disease, hyperlipidaemia, hypertension,

myocardial infarction, stroke, coronary artery disease, along with type II diabetes, are significantly higher in patients with RA and PsA than in the general population (Han *et al.,* 2006; Horreau *et al.,* 2013). There is however, some evidence to suggest that the introduction of methotrexate is associated with a reduced risk of cardiovascular disease in patients with RA and PsA, as a result of reduced inflammation (Westlake *et al.,* 2010; Horreau *et al.,* 2013).

1.7.2 Lung problems

The inflammatory process characteristic of arthritis can affect the membrane lining the lungs (the pleura), leading to pleurisy and fluid collection around the lungs. This can result in problems such as collapsed lung, coughing up blood, infection, or pleural effusion – the accumulation of fluid between the lung and the chest cavity. Rheumatoid nodules can also form in the lungs, although in most cases these are harmless. Interstitial lung diseases rarely develop as a complication of RA and respiratory problems are not generally a feature of PsA. Treatments for both conditions can however, cause interstitial lung disease, characterized by shortness of breath, cough and fever. These symptoms tend to improve when the drugs are stopped.

1.7.3 Eye complications

RA and PsA can affect the eyes in several ways. Inflammation of the episclera, the thin membrane that covers the sclera is a common complication of RA. It is usually mild, but the eye can become red and painful. Scleritis, inflammation of the white of the eye, is more serious and can lead to vision loss. Having RA also puts the individual at risk of Sjogren's syndrome (Ramos-Casals, Brito-Zerón, & Font, 2007), a condition in which the immune system attacks the lacrimal glands, which produce tears. This causes the eyes to feel gritty and dry. If not treated, dryness can lead to infection and scarring of the conjunctiva (the membrane that covers the eye) and to corneal ulceration. Eye involvement in RA and PsA occurs in between 2 and 25% of cases (Cantini *et al.,* 2010; Matsuo *et al.,* 1997).

1.8 PHARMACOLOGICAL MANAGEMENT

There is no known cure for either RA or PsA; therefore, treatment aims to reduce the impact of the disease by limiting the symptoms of pain, stiffness and fatigue. Reducing inflammation and the consequent irreversible joint damage that leads to disability, maintains or improves quality of life (Pollard, Choy, & Scott, 2005).

Aggressive treatment early in the disease course normally involves a combination of drugs. Drug treatment can be broken down into three types. The first is for the relief of symptoms, with pain relief being the number one priority for patients. The second aims to slow or halt the disease process to prevent progressive functional impairment. The latter are often called disease modifying anti-rheumatic drugs (DMARDs). The third are the new class of biologic agents which are often used in combination with DMARDS.

1.8.1 Non-steroidal anti-inflammatory drugs

Non-steroidal Anti-inflammatory Drugs (NSAIDS) have analgesic and fever reducing effects, as well as anti-inflammatory properties. NSAIDS are used for symptomatic relief only and will not alter the course of the disease in RA or PsA. As these drugs have been associated with a number of adverse drug reactions including gastrointestinal and renal effects clinicians are cautious in ensuring that there are no contra-indications and that the lowest dose is prescribed for the shortest period of time. The success of disease modifying anti-rheumatic drugs (DMARDS) has enabled the use of NSAIDS to be reduced significantly. If a patient continues to need high doses of NSAIDS for symptomatic relief this may reflect inadequate disease control.

1.8.2 Analgesics

Analgesics such as paracetamol and codeine, or combinations of these two drugs help to control pain and are used by most patients with arthritis at some point in the course of their disease. Weak opioids, however, such as codeine, dextropropoxyphene and tramadol, despite having short-term benefits for pain management, can cause adverse effects that may outweigh the benefits. Therefore, an alternative non-opioid analgesic should be considered first (Whittle, Richards, & Buchbinder, 2013).

1.8.3 Disease modifying anti-rheumatic drugs

Any anti-rheumatic drug that reduces radiographic joint damage is known as "disease-modifying". The most commonly used DMARDS include methotrexate, sulphasalazine, leflunomide and hydroxychloroquine. In the past the care pathway in the UK for a patient with RA involved the introduction of DMARDS at a point when there was evidence of radiological erosions. It has, however, been argued that these criteria often failed to identify recent onset RA as erosions are usually seen on X-rays relatively late in the disease and reflect existing and usually irreversible damage. Radiographic damage and disease activity are independent contributors to impaired physical function in both early and late RA (Ødegård *et al.,* 2006) which has led to the view that DMARD therapy should not be delayed but used early in patients with persistent synovitis, exhibited by joint swelling and raised inflammatory markers in the blood (National Institute for Health and Care Excellence, 2013b). Clinically, the aim of any therapeutic intervention is to reduce disease activity to the lowest level possible in the shortest period of time. Research suggests that for symptoms, joint damage, function and quality of life, any delay in introducing DMARDs is inferior to early commencement (Nell *et al.,* 2004). The benefits experienced as a result of this early DMARD therapy have been shown to persist for up for 5 years after the drug is introduced when compared with a delayed start (Finckh, Liang, van Herckenrode, & de Pablo, 2006).

DMARDS can be used as a monotherapy, but also in combination regimens that include one or more DMARDS, usually methotrexate plus another and sometimes with glucocorticoids and/or a biologic agent (see section 1.8.4, page 36). Evidence suggests that these combination therapies can prolong the period during which patients are in remission and do not compromise tolerability (e.g. Breedvald *et al.,* 2006). Current UK guidelines for treating RA recommend that methotrexate should be initiated as the first DMARD therapy, either as a monotherapy or as part of a combination of other drugs, including another DMARD (sulphasalazine or hydroxychloroquine) plus short-term glucocorticoids (National Institute for Health and Care Excellence, 2013b). Ideally this therapy should be within 3 months of the onset of persistent symptoms. Prior to this it is important to use NSAIDs and analgesics to control symptoms. Once satisfactory disease control has been achieved the number of drugs can be reduced,

often stopping corticosteroids first, and the doses of the other drugs reducing to a level where disease control is maintained. If a patient fails to respond to at least two conventional DMARDS (including methotrexate), in the UK under National Institute for Health and Care Excellence (NICE) guidelines, they may be considered for anti-tumour necrosis factor (anti-TNF) therapies or other biologic therapies (National Institute for Health and Care Excellence, 2013b) (see section 1.8.4, page 36).

Methotrexate is considered to be the gold standard treatment for patients with RA, it is also used extensively in patients with PsA and is the most widely used drug in patient's naïve to DMARDs (Coates L *et al.,* 2012; National Institute for Health and Care Excellence, 2013b). Methotrexate is most commonly administered orally and starts as a weekly dose of between 7.5 and 15mg, depending on age and the presence of co-morbidities or co-medication. If disease activity remains unsatisfactory the dose can be increased up to a maximum of 25mg over a period of 1-3 months. It can take 6-8 weeks before the benefits of methotrexate are first seen. As with all drugs any potential benefits have to be weighed against the potential for side effects. Adverse reactions to methotrexate occur in half of treated patients, but tend to be minor and can often be managed without cessation of the drug; these include nausea and vomiting, oral ulcers and elevation of liver enzymes (Espinoza *et al.,* 1992; Emery, Sebba, & Huizinga, 2013). Rarer but more serious side effects include an effect on the bone marrow to lower platelets or neutrophils in the blood. Methotrexate is usually prescribed in combination with folic acid or antiemetic drug to reduce gastrointestinal, mucosal and haematological side effects (Emery *et al.,* 2013).

As with any medications that suppress the immune system, methotrexate poses some increased risk of the body's vulnerability to infections and other diseases. As a consequence before commencing methotrexate, patients are assessed for any evidence of tuberculosis. An anti-flu and anti-pneumococcal pneumonia vaccination is also given before starting the drug. As a consequence patients should not receive live vaccinations whilst taking the drugs and are asked to seek immediate medical attention if they develop persistent fever or unexplained symptoms. If an infection does develop and patients are required to take antibiotics, methotrexate is stopped.

1.8.4 Biologic agents

In the last decade, there have been significant advances in treating RA and PsA, especially for patients whose arthritis does not respond to traditional DMARDs. The most important improvement for these patients has been the development of a group of drugs called biologic response modifiers or biologic agents. Biologics work by blocking specific chemical triggers of inflammation and target specific proteins (cytokines) in the immune system known to increase inflammation and cause damage in arthritis. By blocking these cytokines these drugs reduce inflammation and have relatively few side effects. These agents block the pro-inflammatory cytokine tumour necrosis factor (TNF) alpha and are used when a patient has "failed" or not responded adequately to traditional DMARDs. These anti-TNF agents are often used in combination with traditional DMARDs, usually methotrexate, for greater effectiveness. This may need to be varied for individual patients because of differences in the method of administration and treatment schedules. The self-injecting anti-TNF drugs etanercept (trade name Enbrel) and adalimumab (trade name Humira) in combination with methotrexate have been found to reduce disease activity and the number of swollen and painful joints with a consequent reduction of pain, morning stiffness and fatigue (Klareskog *et al.,* 2004; Breedveld *et al.,* 2006). They also lower the blood markers of inflammation and in the longer term damage and disability are also reduced.

Current NICE guidelines (National Collaborating Centre for Chronic Conditions, 2009) recommend that anti-TNF agents are used for patients with active RA, defined as a disease activity score (DAS) (Prevoo *et al.,* 1995) greater than 5.1 on at least two occasions (1 month apart) and have undergone trials of two DMARDs including methotrexate (for at least 6 months) with 2 months at a standard dose. The DAS is a measure of disease activity, see section 1.9.2 (page 42) for more detail. According to NICE, treatment with anti-TNF agents should only be continued if there is an improvement in the DAS28 score of 1.2 or more, 6 months after initiation of treatment.

Recent NICE guidelines for the use of etanercept and adalimumab in PsA (National Institute for Health and Clinical Excellence, 2010) recommend that these drugs are introduced when a person has peripheral arthritis (i.e. arthritis in the extremities), with three or more tender joints and three or more swollen joints, and they have not responded to adequate trials of at least two standard DMARDs, administered either individually or in combination. It is recommended that these medications should be discontinued in people whose joints do not respond according to the PsARC response criteria (Clegg *et al.,* 1996), 12 weeks after the drug is introduced. If the psoriatic skin disease responds to treatment at 12 weeks, but PsARC response does not justify continuation of treatment the patient should be assessed by a dermatologist to determine whether continuing treatment is appropriate on the basis of their skin response.

Patients are usually taught to give their own injections of etanercept and adalimumab. They are administered under the skin (subcutaneously) once or twice a week (etanercept) or once a fortnight (adalimumab). If patients are unwilling or unable to inject themselves a family member or caregiver who has been trained may also give the injection. Preloaded syringes are available as self-injectable click-pens. In addition to pain and inflammation at the injection site, the most common side effects are an increased risk of infection, including upper respiratory infections like colds or chest infections. These are usually minor but as with methotrexate patients with pre-existing lung problems must be carefully assessed and vaccinations should be undertaken prior to commencement. Since biologic therapy is in its relatively early stages of use, some of the long-term effects of using these medications are not known, prompting regular monitoring. Varieties of newer biological agents are also available, for example infliximab which is delivered via infusion, and offer hope to those who fail to respond to etanercept and adalimumab.

1.9 DISEASE AND TREATMENT MONITORING

Monitoring of disease activity in RA and PsA involves the sharing of information between patient and healthcare professional about symptoms and side effects, along with physical examinations and laboratory tests. Symptoms may indicate a flare of arthritis or infection and include pain, swelling and tenderness, length of morning

stiffness, fever and weight loss or gain. In addition to this, laboratory tests (see section 1.9.3, page 44) act as objective measures of the level of inflammation and of some of the drug induced side effects before they are apparent clinically, for example any early effect on liver function or bone marrow.

For some drugs and drug combinations the adverse effects can be serious and, therefore, monitoring using blood tests is required in order to ensure treatment is effective and to identify any adverse effects early and before they become serious. Guidelines have been established for the prescribing and monitoring of methotrexate in NHS Camden (Pang & Malhotra, 2009), the health authority in which this thesis is sited and are described in more detail in section 2.6 (page 93).

1.9.1 Symptoms and side effects

There are a number of primary symptoms which need to be monitored as part of the care of someone with RA or PsA. These symptoms may be directly related to the inflammatory process or to drug induced side effects. Reporting of these experiences during the consultation process is essential in order for the patient and healthcare professional to have a full understanding of disease activity and treatment response. The symptoms and side effects described below are not an exhaustive list but are the most characteristic and frequently reported by someone with either RA or PsA.

1.9.1.1 Pain

Pain is described by people with arthritis as the most important symptom, particularly early in the disease (Carr *et al.,* 2003). Despite this patients feel that clinicians focus more on disease control rather than pain relief (Breivik, Collett, Ventafridda, Cohen, & Gallacher, 2006). In a survey of over 11,000 people with a rheumatic condition over 60% reported severe pain and irritation. Of these almost half said that pain limited their daily activities, a large number also reported that the ability to lead a normal life was affected because they were always in pain. The proportions were higher for those with RA compared with unspecified arthritis, with half of RA patients reporting that they were always in pain (Badley & Tennant, 1993).

The impact of pain however, goes beyond the sensation and is associated with frequent use of health services (Waltz, 2000) and analgesic use (Blamey, Jolly,

Greenfield, & Jobanputra, 2009), with work disability (Wolfe & Hawley, 1998; Wallenius *et al.,* 2009), and increased current (Dickens, McGowan, Clark-Carter, & Creed, 2002) and future depression (Sharpe, Sensky, & Allard, 2001; Husted, Tom, Farewell, & Gladman, 2012) in both RA and PsA. In a recent longitudinal study of over 15,000 patients with RA Courvoisier *et al.,* (2012) found that pain was the single most important predictor of increased quality of life, more important than disease activity and functional disability. This suggests that anti-rheumatic drugs are having an insufficient effect on pain relief. These results corroborate other studies which suggest that two-thirds of people with RA experience inadequate pain relief despite their disease being considered well-controlled (Taylor *et al.,* 2010).

1.9.1.2 Fatigue

The varying definitions and instruments used to measure fatigue are likely to be responsible for the variation in the rates of fatigue found in RA and PsA. Moderate to severe fatigue is reported by between 42% and 80% of patients with RA or PsA (Belza, 1995; Belza, Henke, Yelin, Epstein, & Gilliss, 1993; Wolfe, Hawley, & Wilson, 1996; Husted, Tom, Schentag, Farewell, & Gladman, 2009). Despite this potentially high proportion and confirmation from patients that it is an important problem (Kirwan *et al.,* 2007), the clinical mechanisms that cause or exacerbate fatigue are poorly understood and are rarely measured in clinical practice. A number of variables have been associated with increased fatigue; these include greater disease activity, physical limitations, pain and poorer quality of life (Husted *et al.,* 2009); along with depression (Huyser *et al.,* 1998), disability (Repping-Wuts, Fransen, van Achterberg, Bleijenberg, & van Riel, 2007; Wallenius *et al.,* 2009) and anxiety (Mancuso, Rincon, Sayles, & Paget, 2006).

1.9.1.3 Synovitis

Synovitis is inflammation of the joint lining and is usually characterised by pain, tenderness and stiffness making movement problematic. Joint swelling is part of the DAS28 assessment and examination of joint swelling is achieved through observation and palpation; with the examiner looking for soft tissue swelling not bony swelling or deformity. Swelling and tenderness of small joints are associated with radiological damage (Boers, Kostense, Verhoeven, & Van Der Linden, 2001; Klarenbeek *et al.,* 2010). In addition an 8 year follow-up of patients with RA found that concomitant joint

swelling and tenderness at least once in the first 2 years of diagnosis was independently associated with damage in the large joints, as was swelling without tenderness. This damage was associated with greater functional disability, as compared to those without large joint damage (van den Broek *et al.,* 2013). The manifestation may however, be different in patients with RA compared to PsA. People with PsA tend to have more tender than swollen joints whereas those with RA have more swollen than tender joints (Harty *et al.,* 2012).

1.9.1.4 Joint stiffness

Joint stiffness, and particularly morning joint stiffness, is a common and clinically important complaint for people with arthritis. It is caused by the inflammation found around a joint which causes tightness. Although not included in more recent classification guidelines, early diagnostic criteria for RA included information on duration and location of stiffness (Arnett *et al.,* 1988). It was removed as the criteria failed to discriminate between different types of arthritis as morning stiffness was found to be present in over 70% of people with PsA, 48% with lupus and 31% with gout (Sierakowski & Cutolo, 2011). It seems that morning stiffness, however, may capture elements of disease activity not included in the DAS28. Morning stiffness is independently associated with pain, patient global assessment, shorter disease duration, and younger age (Yazici, Pincus, Kautiainen, & Sokka, 2004). Furthermore, in patients with low disease activity, the presence of morning stiffness may indicate clinically active disease (Khan *et al.,* 2009) and rheumatologists often use the duration of early morning stiffness as one of the primary considerations when changing medications in RA (Kirwan, De Saintonge, Joyce, & Currey, 1984; Soubrier *et al.,* 2006).

1.9.1.5 Skin conditions

Along with psoriatic plaques and damage to nails, PsA is also characterised by dactylitis, also known as “sausage” finger, where the skin, nail, tendon sheathes and joints are inflamed. Approximately 5.6-53% of people with PsA during the course of their illness will experience dactylitis and this most commonly involves one or two digits at a time, with the feet more often affected than the hands (Cantini *et al.,* 2010). Patients can also experience enthesitis which is an inflammatory lesion at the insertion of a tendon or ligament into bone. The most common site is the Achilles tendon, which

presents as a swelling at the back of the heel. Enthesitis is reported in approximately 25-78% of patients with PsA (Sakkas, Alexiou, Simopoulou, & Vlychou, 2013).

Patients with RA may have rheumatoid nodules – swellings which can occur anywhere but are normally found in the dermis around sites of pressure, particularly on the elbows, forearms, heels, or fingers. They can develop gradually or appear suddenly. Around a 20-30% of patients with RA are affected by these nodules and they are more common in men, Caucasians and those who test positive for rheumatoid factor (Kaye, Kaye, & Bobrove, 1984). These nodules, although sometimes unsightly, generally do not cause the patient any problems and, therefore, do not usually need specific treatment unless they ulcerate. Certain DMARDS can shrink rheumatoid nodules (Sayah & English, 2005). If they are large and interfere with function, for example nodules on the feet can restrict walking, some experts recommend injection with a corticosteroid to shrink them. Surgery may also be required if the nodule is causing problems such as nerve pain, an open sore or are having a major impact on physical functioning.

1.9.1.6 Gastrointestinal problems and oral health

The gastrointestinal problems reported by patients with RA and PsA are primarily drug induced side effects caused by both NSAIDS and DMARDS and, therefore, need monitoring to prevent them developing into serious complications. Use of NSAIDS is associated with a significant increase in the risk of gastrointestinal clinical events such as bleeding, perforation, obstruction and symptomatic ulcers and increase dramatically with risk factors such as *a priori* event, older age and severe RA (Laine *et al.,* 2002). In RA 29% of patients experience nausea and 12% diarrhoea, as a result of taking methotrexate (Bathon *et al.,* 2000). Research in PsA also indicates that gastrointestinal side effects are the most commonly reported adverse effects for patients taking methotrexate. Eighty-four percent of patients with PsA reported nausea (41%), vomiting (8%), diarrhoea (7%), constipation (3%) or gastritis (25%) (Wollina, Ständer, & Barta, 2001).

Present on the palate, underside of the lips or inside of the cheek, oral ulcers or mouth sores are a common side effects of drugs such as NSAIDS and methotrexate. Research

suggests that 14% of patients with RA who take methotrexate experience mouth ulcers (Bathon *et al.,* 2000). This may be due to a lack of folic acid or possibly over dosing due to confusion regarding the treatment regimen (Deeming, Collingwood, & Pemberton, 2005).

1.9.2 Disease activity and treatment response

The monitoring of disease activity and treatment response is essential in both RA and PsA. The composite scores reported below are now part of routine practice and guidelines in RA recommend they are measured monthly until treatment has controlled the disease (National Institute for Health and Care Excellence, 2013b).

In RA the DAS (Prevoo *et al.,* 1995) is a combined index designed to measure disease activity. It has been extensively validated for use in clinical trials and is now widely used in clinical practice to collect valuable information about the condition and treatment response. The DAS measures the total number of swollen and tender joints out of a total of 44 and the DAS28 is a simplified version (i.e. 28 joints). The joints of the shoulders, elbows, wrists, metacarpophalangeal joints, proximal interphalangeal joints and the knees are examined for tenderness and swelling and this count is then combined with either the ESR or C-Reactive Protein (CRP) and patient reported global health on a scale of 0 (best) to 10 (worst). The DAS28 scores is interpreted as follows (Radboud University Nijmegen, 2014):

- Remission: DAS28 ≤ 2.6.
- Low Disease activity: 2.6 < DAS28 ≤ 3.2.
- Moderate Disease Activity: 3.2 < DAS28 ≤ 5.1.
- High Disease Activity: DAS28 >5.1.

The DAS28 provides a cross-sectional assessment of disease activity. In order to assess how patients with RA change over time two widely applied response criteria have been developed by ACR, and EULAR. The ACR criteria (Felson *et al.,* 1995) are referred to as the ACR 20, 50 and 70 response criteria, depending on the required percentage of improvement (i.e. 20%, 50% or 70%). The EULAR criteria (van Gestel *et al.,* 1996) are

based on the DAS or DAS28 and response is defined as none, moderate or good (Table 1.2).

Table 1.2. EULAR treatment response criteria for RA

	Improvement in DAS28 from baseline		
DAS28 at end point	**>1.2**	**>0.6 and ≤ 1.2**	**≤ 0.6**
≤ 3.2	Good	Moderate	None
>3.2 and ≤ 5.1	Moderate	Moderate	None
>5.1	Moderate	None	None

DAS – Disease Activity Score

Unlike the EULAR criteria, the ARC criteria are based on a percentage change only and patients are classified as either responders or non-responders (Figure 1.3).

20% improvement in:

- Tender joint count.
- Swollen joint count.

And in three of the following:

- Patient pain.
- Patient global assessment (on a 0–5 Likert scale, with improvement defined as a decrease by at least one unit, and worsening defined as an increase by at least one unit).
- Assessor global assessment (on a 0–5 Likert scale, with improvement defined as a decrease by at least one unit, and worsening defined as an increase by at least one unit).
- Disability.
- Acute phase response.

Figure 1.3. ACR improvement criteria

There is no single point disease activity score in PsA only response criteria. The Psoriatic Arthritis Response Criteria (PsARC) (Clegg *et al.,* 1996) is a combination of percentage change and global improvement rated by the patient and doctor (Figure 1.4). The criteria are currently undergoing validation and further development.

Achieve two of the following with no worsening of any

- Tender joint count improvement of at least 30%.
- Swollen joint count improvement of at least 30%.
- Patient global improvement by one point on a 5-point Likert scale.
- Doctor global improvement by one point on a 5-point Likert scale.

Figure 1.4. PsA Response Criteria (PsARC)

1.9.3 Blood tests

NICE guidelines suggest that markers of inflammation need to be checked via blood tests every month until treatment has controlled the disease to a level previously agreed with the patient (National Collaborating Centre for Chronic Conditions, 2009). BSR/BHPR in collaboration with the British Association of Dermatologists (Chakravarty *et al.,* 2008) state that patients should also be encouraged to take part in self-management education so that they can monitor their own therapy. The monitoring schedule for methotrexate should include full blood count, urea and electrolytes and liver function every 2 weeks until the dose of methotrexate and monitoring is stable for 6 weeks and thereafter monthly until the dose and disease is stable for 1 year. The monitoring may then be reduced in frequency, based on clinical judgement with due consideration for risk factors including age, co-morbidity and renal impairment, when monthly monitoring is to continue. The following tests are included;

1.9.3.1 Haemoglobin

Haemoglobin is the oxygen carrying pigment found in red blood cells. A below normal level of haemoglobin is known as anaemia. Anaemia can be a temporary condition, a consequence of other health conditions, or it can be a chronic problem. People with active RA and PsA can develop anaemia, which may cause symptoms such as fatigue, rapid heartbeat, shortness of breath, dizziness, leg cramps and insomnia. There are a number of reasons why a person with arthritis may experience anaemia. One cause is joint inflammation which can have an effect on iron metabolism, bone marrow, and erythropoietin production by the kidneys (a hormone that controls production of red blood cells). The other is iron deficiency which could be caused by digestive tract bleeding a side effect of some arthritis medications. By monitoring haemoglobin levels these can be detected early before they become serious.

1.9.3.2 White blood cell count and neutrophils

White blood cells (WBC) are cells of the immune system defending the body against both infectious disease and foreign materials. Neutrophils (a sub-set of white cells) are the most abundant type of WBC. They are normally found in the blood stream during the acute phase of inflammation and are recruited to the site of injury within minutes following trauma. Through blood tests, WBC and neutrophil counts are monitored as indicators of possible inflammation in arthritis. As people with RA and PsA are also more prone to infections, which may be related to the underlying disease or to the immune-suppressant medications used to treat them, regular monitoring of WBC is required. DMARD therapy can lead to neutropenia, a deficiency in WBC, which can lead to an increased susceptibility to infection. In addition treatment with biologic agents may greatly increase the risk of serious infections in people with arthritis by inducing a certain extent of immunosuppression (Galloway *et al.,* 2011).

1.9.3.3 Platelets

Platelets or thrombocytes are irregularly-shaped, colourless bodies that are present in blood. Their sticky surface lets them, along with other substances, form clots to stop bleeding. If platelet levels are too low, excessive bleeding can occur. High platelet levels increase the risk of thrombosis, which may result in events such as a stroke, heart attack, pulmonary embolism or the blockage of blood vessels to other parts of the body, such as the extremities of the arms or legs. Platelets are often elevated in active arthritis as a result of enhanced local inflammation; therefore, monitoring of platelets, via blood tests, acts as an indicator of possible inflammation. There is also accumulating evidence to suggest that DMARD therapy is associated with a possible suppression of platelet production in the bone marrow (Gasparyan, Stavropoulos-Kalinoglou, Mikhailidis, Douglas, & Kitas, 2011); therefore, increasing susceptibility to bleeding.

1.9.3.4 Liver function

The alkaline phosphatase (ALP) test is used to help detect liver disease (or some bone disorders). Damaged liver cells release increased amounts of ALP into the blood. A raised alanine transferase (ALT) can also reveal liver damage. Although it is probably the most specific test for liver damage, it does not reveal the severity of the liver damage as the amount of dead liver tissue does not correspond to higher ALT levels. In

addition, patients with normal or declining ALP levels may experience serious liver damage without an increase in ALT. Lower levels of ALT may indicate any kind of liver disease, whereas higher levels generally indicate extensive liver damage from toxins or drugs, viral hepatitis, or a lack of oxygen (usually resulting from very low blood pressure or a heart attack). Hepatotoxicity is one of the most feared side effects of methotrexate. A meta-analysis by Whiting-O'Keefe, Fye and Sack (1991) reported a prevalence of advanced histological changes of 2.7% after 4 years on methotrexate. This has been associated with cumulative methotrexate dose, duration of treatment, drugs or chemicals, such as alcohol; being older; presence of hepatitis B and C virus; and a family history of liver disease (Dávila-Fajardo, Swen, Barrera, & Guchelaar, 2013). It is important to detect these changes early before irreversible liver damage has developed.

1.9.3.5 Markers of inflammation

ESR and CRP are both markers of inflammation. Generally, ESR does not change as rapidly as CRP, either at the start of inflammation or as it goes away. CRP is not affected by as many factors as ESR, making it a better marker of inflammation. As ESR, however, is an easily performed test, many doctors use ESR as an initial test when they think a patient has inflammation. CRP is produced in the liver and is present during episodes of acute inflammation or infection. Hence, a high result serves as a general indication of acute inflammation. In arthritis changing levels of CRP or ESR can be used to assess the effectiveness of treatment and monitor periods of disease flare. Both ESR and CRP are, however, non-specific and can rise with any viral or bacterial infection, not just arthritis-related inflammation.

1.10 ECONOMIC IMPACT

Due to advances in the treatment of RA and PsA, the need for this extensive and ongoing monitoring and the potential for long-term damage and disability it is unsurprising that the economic impact of arthritis is substantial. The cost of illness is said to consist of direct and indirect costs. Direct costs are those for which actual payments are made these include treatment costs, social services and private expenditure. Indirect costs are those for which no direct payment is made but for which resources are lost, for example loss of productivity, earnings or tax revenue.

NHS expenditure on musculoskeletal disorders was £5.06 billion in 2010/11, an increase of almost 20% since 2008-2009 (Department of Health, 2012a). This is 4.7% of the overall NHS budget and is the fifth highest area of spend in the NHS. This represents an increase per patient from £80.58 in 2007/2008 to £96.62 in 2010/2011 (Department of Health, 2012a). Using incidence and prevalence rates the National Audit Office estimates that RA costs the NHS in England £557 million annually in healthcare costs and an additional £1.8 billion a year on the wider cost to the economy including sick leave and work-related disability (National Audit Office, 2009b) this equates to £960 per person per year.

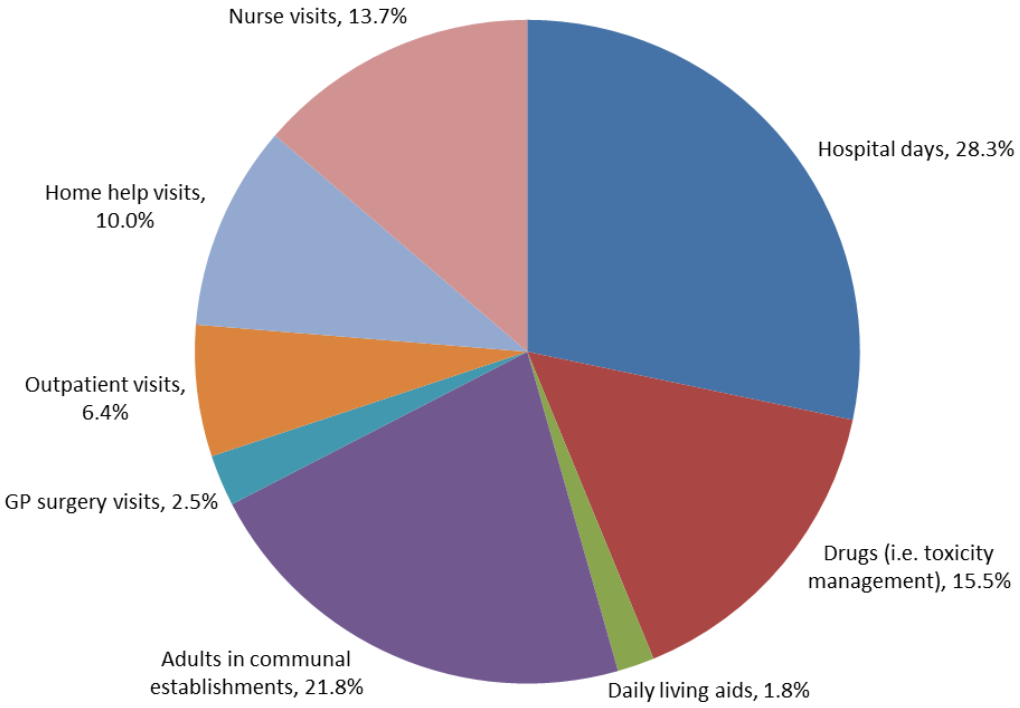
McIntosh (1996) conducted one of the most comprehensive surveys in the England and found that RA imposed a £1.256 billion burden in 1992. Direct costs accounted for £604.6 million and indirect costs £651.5 million. Table 1.3 summarizes the mean annual service utilization estimate and annual costs of these services.

Table 1.3. Summary of the mean annual service utilization estimates for RA (£) in 1992

	Service utilization estimates		
Service	**16-64 years**	**65 years +**	**Annual cost**
GP visits	9.6 (p/a)	8.3 (p/a)	14,917,512
Hospital Days	5.8 (p/a)	6.2 (p/a)	170,752,014
Specialist outpatient visits	8.6 (p/a)	4.3 (p/a)	38,901,997
Nurse visits	0.4 (p/w)	0.8 (p/w)	83,203,184
Home-help visits	0.2 (p/w)	1.0 (p/w)	60,426,688
Total			368,201,395

GP – General Practitioner; p/a – per annum; p/w – per week

Most of the ambulatory visits consisted of GP attendance (at £7.46 per surgery visit) and of the £38.9 million cost for specialist outpatient services, the majority of this was for visits to the rheumatology unit, which were estimated at £108.75 per person per year. This was equivalent to three 20 minute appointments with a rheumatologist. Interestingly, the costs of nurse visits were almost double; however, it is unclear what percentage of this was specific to nurse specialists in rheumatology, if any.



Adapted from (McIntosh, 1996)
Figure 1.5.The direct costs of RA in the UK in 1992

A majority of the costs associated with RA were hospital days and adults in communal establishments (Figure 1.5). The total cost of NSAIDs, DMARDs and steroids was £35.5, daily livings aids £10.8 million and laboratory tests for the management of toxicity £56.7 million (Table 1.4). The morbidity costs resulting from productivity loss were higher in females (£474.3 million) compared to males (£172.2 million), due to the higher prevalence rates in women. Although McIntosh's analysis was conducted prior to the introduction of biologics, which are associated with substantially higher costs than those of traditional DMARDS, these figures do reflect more recent international estimates (Lundkvist, Kastang, & Kobelt, 2008; Franke, Ament, Laar, Boonen, & Severens, 2009).

Table 1.4. Summary of the costs for laboratory tests for the management of toxicity in RA (£) in 1992

Test	Times per year	Cost per test	Total annual cost
Full blood count	12	8.81	19,027,975
ESR	12	8.81	19,027,975
Urea and electrolytes	3	4.89	2,642,774

Test	Times per year	Cost per test	Total annual cost
Liver function test	12	4.89	10,571,097
Urinalysis	12	0.06	126,853
X-ray hands and feet	1	29.35	5,285,548
Total			56,682,222

ESR – Erythrocyte Sedimentation Rate

Using the most comparable sub-components of McIntosh's analysis and combining these with the National Audit Office figures the average direct care costs per person with RA in the UK are estimated to be £2,065 per year or £861 million per annum in total (Oxford Economics, 2010).

The economic burden associated with PsA may be even greater than RA (Poole, Lebmeier, Ara, Rafia & Currie, 2010) found that the total annual health care costs for biologic-naïve patients with PsA in the UK ranged from £11 to £20,782, with a mean of £1446 per person (SD=£1756). Prescription costs and secondary care episodes accounted for more than one-third of the total cost. The average annual cost of prescribed medications per person per year was £544 and for secondary care episode £497. Consultations with the GP cost on average £226 per year, while the mean annual cost of clinical investigations was £135. Costs were significantly higher in people aged over 50 years and those experiencing greater disability.

1.11 SUMMARY

Chronic inflammatory conditions like RA and PsA are highly prevalent in the UK. Both can lead to significant impairments in daily living including pain and fatigue, along with potentially debilitating complications to the eyes, lungs, skin, liver, immunological and cardiac system and most importantly mortality. Intensive treatment regimens have been introduced over recent years in order to ensure tight control of disease activity; these include new therapeutic agents and new treatment strategies. Due to the potential toxicity of these drugs, however, patients require close monitoring. This monitoring is achieved through a combination of patient reported symptoms and side effects along with a clinical assessment of disease activity and regular laboratory tests to ensure any adverse effects are detected early before they become serious and

irreversible. The economic burden of both blood monitoring and regular outpatient care is clear. The next chapter will review how the monitoring of patients with RA and PsA is undertaken in accordance with UK guidelines and then introduce potential alternative methods of managing and monitoring patients with RA and PsA, including nurse, community and patient-led services.

CHAPTER 2 - UK SERVICE DELIVERY IN RHEUMATOLOGY

2.1 PROLOGUE

The previous chapter described some of the clinical features of RA and PsA including the monitoring requirements of a person receiving DMARD therapy. This chapter will begin with a general overview of current UK policy regarding the management of long-term conditions and the key targets and indicators of success. This will be followed by a discussion of the relevance of these policies to patients with arthritis and the arthritis-specific policies and guidelines which are now in place, both for the disease and also the monitoring of DMARD therapy.

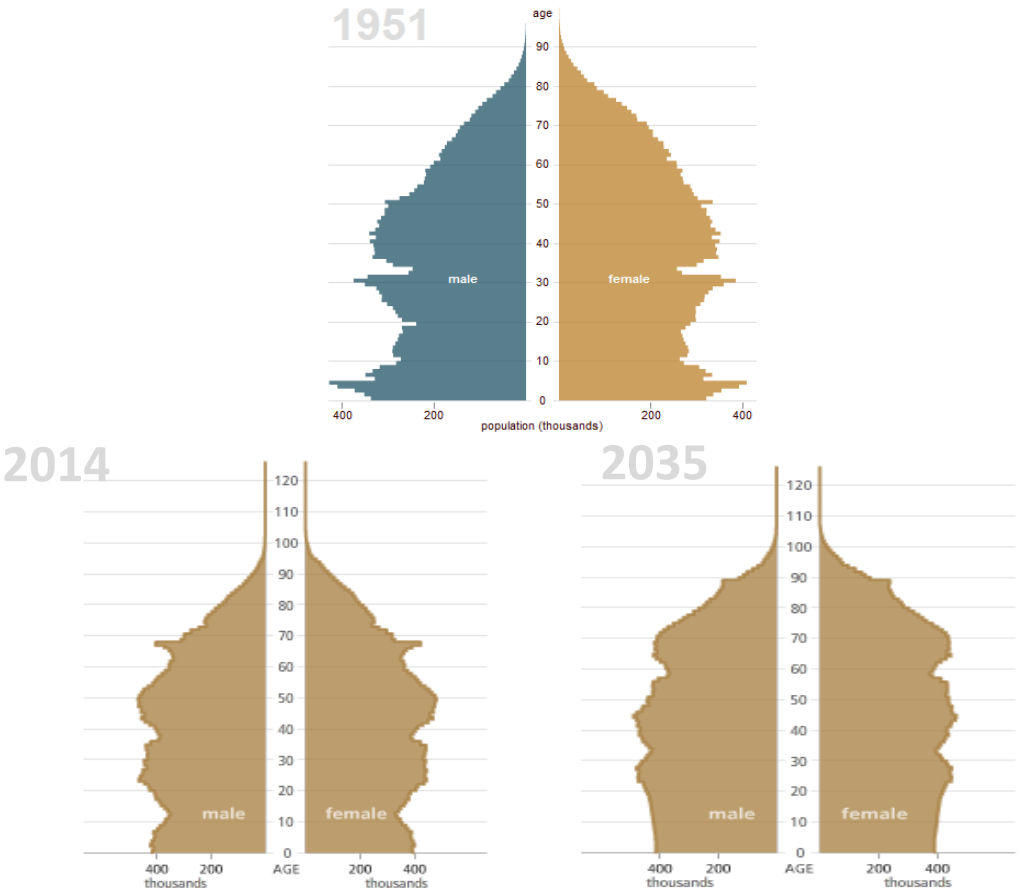
The second part of this chapter will then present data on the current state of musculoskeletal outpatient services for established patients in the UK, along with the different models of follow-up care that have been implemented and evaluated. This includes the evidence relating to consultant-led, nurse-led, community-led and patient-led services, as well as telephone consultations. The chapter will then conclude with a proposal of how patient-initiated services could be extended to include patients taking on a more active role in the monitoring of their conditions leading to a new and innovative model of care for managing patients with established arthritis on DMARD therapy. Data will then be presented on how University College Hospital London (UCLH) and NHS Camden Clinical Commissioning Group (CCG), the local site of this thesis, have performed in relation to quality indicators along with the model of care adopted by UCLH at the start of this research.

2.2 MANAGEMENT OF LONG-TERM CONDITIONS IN THE UK

As a result of the baby boom post Second World War, a reduction in fertility rates, the elimination of many acute and occupational illnesses and the success of modern treatments, the world's population is aging as life expectancy continues to rise. The consequence has been that the focus of healthcare has shifted to the burden of long-term conditions, which increase in prevalence with age. One such condition is arthritis for which the prevalence rate in those over the age of 75 has increased by 8% over the last 50 years (Symmons *et al.,* 2002). In addition more than half of older adults are now

living with three or more long-term conditions (American Geriatrics Society Expert Panel on the Care of Older Adults with Multimorbidity, 2012).

In parallel with this the UK population is projected to increase by 3.1 million to 67.2 million by 2020, which is equivalent to an average annual rate of growth of 0.8%. Based on past trends this growth will continue, reaching 72.6 million by 2035. Figure 2.1 illustrates the projected age structure of the population and shows the disproportionate growth of those aged over 60 years. This is underlined by the projected rise in average age from 39.7 years in 2010 to 39.9 years in 2020 and 42.2 years by 2035 (Office for National Statistics, 2012).



Source. Office of National Statistics

Figure 2.1. Estimated and projected age structure of the UK population, 1951, mid-2011 and mid-2035.

Although the impact on health and social care is hard to predict, the aging population is likely to lead to an increase in the demand on GPs, accident and emergency (A&E) and hospital in- and out-patient services and, consequently, the annual costs of health

and social care. Figures from 2007/2008 already suggest that retired households cost the NHS twice as much (£5,200) as non-retired households (£2,800) (House of Commons Library Research, 2010). This is not surprising given the costs associated with managing a long-term condition such as arthritis, as highlighted in section 1.10 (page 46). The NHS has, therefore, had to shift its focus in recent years to provide outpatient services that are able to cope with increased demands but at the same time achieve this with limited resources.

As a result of these population changes government policy has increasingly focused on the needs of those living with one or more long-term conditions. Since 2010 the UK Government has introduced a number of key changes to the structure of the NHS and the commissioning processes, which aim to meet these demands. In 2010 the White Paper 'Equality and Excellence: Liberating the NHS' (Department of Health, 2010a) outlined the current Coalition Government's long-term vision for the future of the NHS. This White Paper proposed the abolition of Primary Care Trusts (PCTs) and the formation of GP consortia, known as Clinical Commissioning Groups (CCGs), which would take over the responsibility of commissioning NHS services in England. The premise being that decision making about the allocation of resources should take place locally so that services reflect the needs of patients in the local community and the clinicians who support them. In addition there should be greater integration of services across primary and secondary care. Since 2010 the Department of Health has enshrined these principles in the Health and Social Care Act 2012 and published a number of national policy documents which add operational detail to these proposed changes.

In November 2013 the Department of Health published the NHS Mandate for 2013-2015 (Department of Health, 2013e) and accompanying 2014/15 NHS Outcomes Framework (Department of Health, 2013f). The purpose of the NHS Mandate and Outcomes Framework is to provide a national level overview of how well the NHS is performing and an accountability mechanism between the Secretary of State and NHS England, previously known as the NHS Commissioning Board. From 2013 the Secretary of State holds NHS England to account on the basis of the Mandate and NHS England holds the CCGs to account for their performance.

This framework builds on the three previous frameworks (Department of Health, 2010c; Department of Health, 2011b; Department of Health, 2012b) and contains measures, known as indicators, to help the health system focus on measuring health outcomes as opposed to process targets. Indicators within the NHS Outcomes Framework are grouped around five domains and set out the high-level national outcomes which the NHS should be aiming to improve. Within each domain there are a small number of overarching indicators and several improvement domains. The NHS Mandate is structured around these five domains and, as such, progress against the objectives laid out in the Mandate will be assessed using the NHS Outcomes Framework. The most relevant domains to musculoskeletal outpatient services are domain 2 and domain 4.

Domain 2 – 'Enhancing the quality of life of people with long-term conditions' acknowledges that patient empowerment and support for people with a long-term condition, such as arthritis, is vital to enabling them to manage their illness and treatment without needing to go into hospital. By March 2015 the Department of Health expects NHS England to have made progress in relation to four key areas within this domain, one of which is involving people in their own care. Their objective is to ensure that the NHS becomes better at involving patients and empowering them to manage and make decisions about their own care and treatment in order to improve their quality of life. Achieving this objective would mean that by 2015 more people with arthritis will have developed the knowledge, skills and confidence to manage their own health, so they can live their lives to the full. The Department of Health also wants to see improvements in the way that care is coordinated around the needs, convenience and choices of patients rather than the interests of organisations that provide care. The indicator that is being used to assess the success of this domain is the proportion of people who feel supported to manage their condition and is measured in the GP patient survey at a general practice level and then aggregated up to CCG level (Department of Health, 2013b).

Domain 4 – 'Ensuring that people have a positive experience of care'. As 80% of hospital care is delivered in outpatients, improving the experience for patients was identified as a key improvement area in the 2011/12 NHS Outcomes Framework (Department of Health, 2010c). The indicator being "patient experience of outpatient

services". Success will be derived from the Outpatient Survey last conducted in 2011 and to be completed again in 2014. This survey consists of questions about patients' experiences prior to attending clinic, waiting on the day of the appointment, the hospital environment and facilities, tests and treatments, seeing the doctor and other professionals, the overall appointment, leaving the outpatients department and the patient's overall impression.

NHS England is now supporting CCGs to develop and deliver these indicators and includes amongst its members a National Clinical Director for Musculoskeletal Disorders who will work closely with patients and clinicians to support improvements in health outcomes for people with a musculoskeletal condition (Arthritis UK, 2012). Figure 2.2 outlines how these national policy documents are linked to arthritis specific guidelines, which will reviewed in the following section.

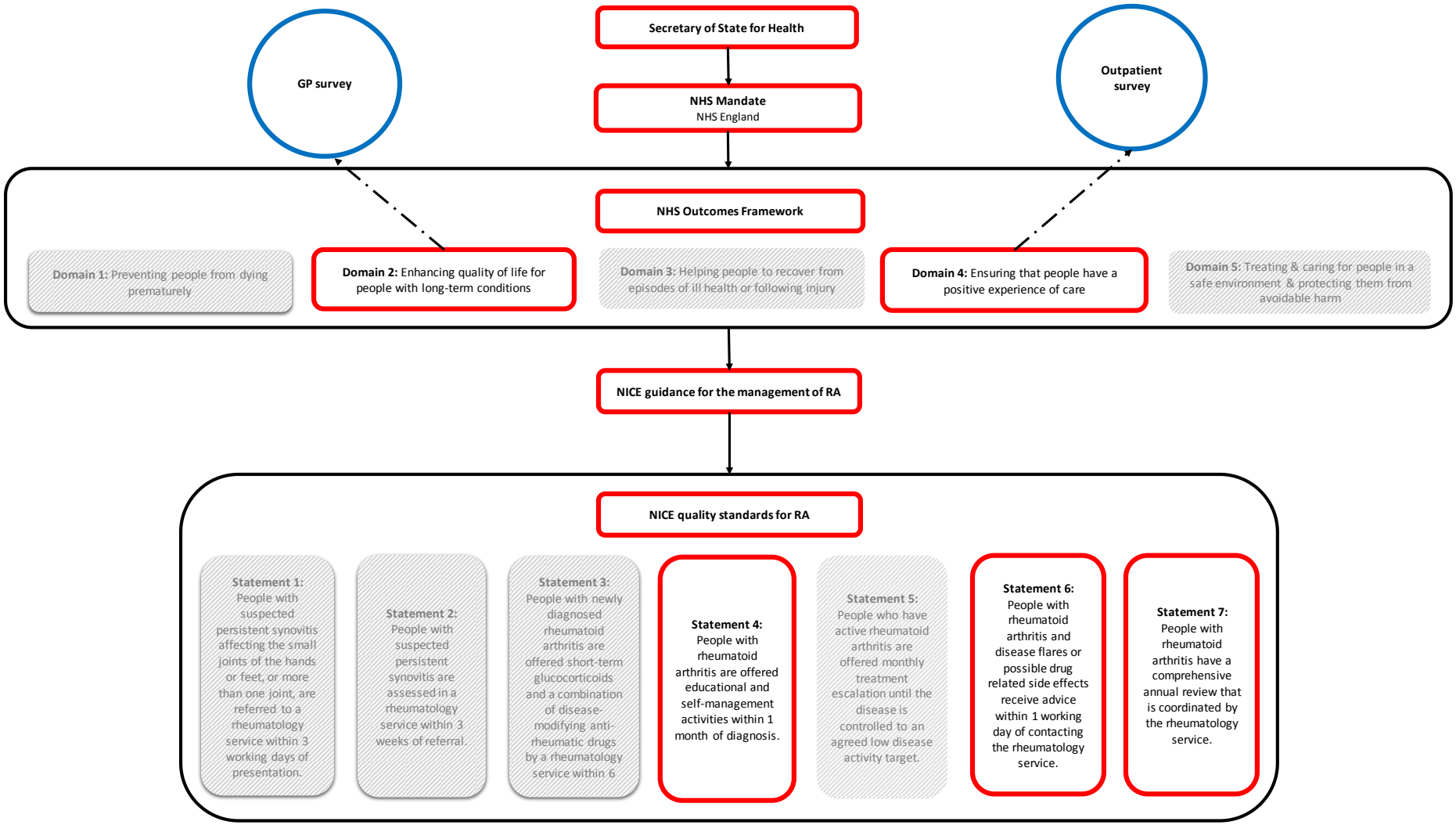


Figure 2.2. Connection between UK government policy and arthritis-specific guidelines

2.3 UK ARTHRITIS GUIDELINES

The NHS Outcomes Framework is supported by a suite of NICE clinical guidelines which provide recommendations on what high-quality care should look like for a particular condition or treatment. According to NICE (National Institute for Health and Care Excellence, 2013c) their guidance for the management of RA (National Institute for Health and Care Excellence, 2013b) can be linked directly to domain 2 of the NHS Outcomes Framework; therefore, supporting people to manage their RA should be integral to the decision to commission musculoskeletal services throughout England.

NICE guidance for the management of RA were issued in 2009, with minor updates in 2013 (National Institute for Health and Care Excellence, 2013b). The guidance offers best practice advice which is underpinned by the premise of person-centred care. It states that a person with RA should have the opportunity to make informed decisions about their care and treatment in partnership with healthcare professionals; supported by evidence and using information which is tailored to their needs. The guidelines indicate that measuring CRP and other key components of disease activity, such as the DAS28 should be undertaken monthly for recent-onset patients but once treatment has controlled the disease to a level previously agreed with the patient this monitoring should be done "regularly", although "regularly" is not defined. The frequency and location of appointments can then be organised according to the needs and demands of the patient. When a disease flare occurs, patients should have additional visits and know when and how to get rapid access to specialist care. An annual review should be offered to all people with RA to assess disease activity, function and damage, monitor co-morbidities and refer on to other services. Those who have a desire to know more about their condition should also be offered the opportunity to attend education sessions including self-management.

Full guidelines for managing and treating RA were also published in 2009 (National Collaborating Centre for Chronic Conditions, 2009) and recommend that verbal and written information need to be provided to patients in order to improve their understanding of the condition and its management, and counter any misconceptions patients may have. People with RA who wish to know more about their disease and its

management should also be offered the opportunity to take part in existing educational activities, including self-management programmes. The guidelines also state that there is a lack of consistent evidence relating to the most effective frequency and location of follow-up appointments for established patients (i.e. primary or secondary care). It was noted that no one approach would be suitable for all and, therefore, for those in whom patient-initiated follow-up appointments are appropriate this method should be offered rather than regular routine reviews. These patients, however, need to be well educated about their disease and know about how and when to access services, whilst routine drug monitoring continues to take place. The guideline reports that in the absence of any evidence, annual reviews are a reasonable method to address the disease, complications and co-morbidities. There are currently no guidelines for the management of PsA, but in practice the above recommendations would be considered appropriate.

NICE has since published the quality standard for RA (National Institute for Health and Care Excellence, 2013a), which includes seven quality statements that are aimed at high priority areas of health. These are specific, concise and measurable statements that act as markers of high-quality, cost-effective patient care. These standards contribute to the improvements outlined in the NHS Outcomes Framework 2013/14 and map directly onto domain 2 (enhancing quality of life for people with long-term conditions) and domain 4 (ensuring that people have a positive experience of care). The quality statements most relevant to established patients with RA are Quality Statements 4, 6 and 7 (Figure 2.2). This includes an offer of self-management education within 1 month of diagnosis, receipt of advice within 1 working day of a report of disease flare or side effects and the provision of comprehensive annual reviews.

2.4 RHEUMATOLOGY OUTPATIENT SERVICES IN THE UK

The monitoring requirements of arthritis and DMARD therapy are traditionally and most frequently achieved by attending for blood tests either at the local hospital or GP practice followed by regular appointments with a rheumatologist and/or a CNS in the outpatient setting (Kay & Lapworth, 2004). This means that planned follow-up appointments account for approximately 75% of the rheumatologist's workload

(Kirwan & Snow, 1991) and although exact figures are not available similar estimates have been reported for nurses working in rheumatology (Royal College of Nurse Rheumatology Forum, 2009). Between 1988 and 2000 however, the number of follow-up cases seen in rheumatology outpatients increased by 58.3%, an average of 4.9% per year and this was dominated by patients with RA (Kirwan *et al.,* 2003a). These follow-up appointments are not only costly to the NHS, as described in Chapter 1, but are also potentially inconvenient and costly for patients as well, particularly for those in employment (Gignac, Cao, Lacaille, Anis, & Badley, 2008). These prescheduled appointments, which take up the bulk of outpatient time, reduce the flexibility of the NHS by increasing waiting times for new referrals and reduce the ability of the rheumatology team to respond rapidly to new and urgent cases. Despite this pressure on outpatients, follow-up appointments for patients with arthritis who are feeling well often result in little or no intervention (Mitchell, 2000). In fact 30% of rheumatologist outpatient appointments result in no investigations or other actions (Hehir *et al.,* 2001). When rheumatologists were asked about the appropriateness of these appointments, 10% could have been dealt with by a GP, in 35% of appointments patients had no problems and 55% required specialist rheumatology review. Overall 42% of all visits were deemed completely unnecessary. It is, therefore, likely that a considerable amount of time and resources are wasted in rheumatology outpatient clinics and unsurprisingly alternative models of care are now being considered.

In order to ensure that everyone receives high quality care in outpatients and to support the improvement of services for people of all ages with a musculoskeletal condition the Department of Health published the Musculoskeletal Services Framework (MSF) (Department of Health, 2006). This was part of the then government's strategy for long-term conditions, which included 'Supporting people with long-term conditions: Improving care, improving lives' (Department of Health, 2005a) and the 'The National Service Framework for long-term conditions' (Department of Health, 2005b). As opposed to the clinical guidelines published by NICE (National Institute for Health and Care Excellence, 2013b), BSR/BHPR (Coates *et al.,* 2013; Chakravarty *et al.,* 2008) and EULAR (Smolen *et al.,* 2013) the MSF focuses on delivery of services. The MSF sought to address the fragmented and incoherent services offered in musculoskeletal care by promoting a redesign. This included the

introduction of the 18 week referral-to-treatment target and the need to review all patients regularly. It detailed the provision of nurse-led monitoring clinics, support for self-management and the use of telephone advice lines. Despite a change in government and, therefore, vision for the NHS the MSF remains an important document for clinicians and allied health professionals with an interest in rheumatology as the NHS Outcomes Framework (Department of Health, 2013f) does not make specific reference to rheumatology services.

In 2009 the Arthritis Musculoskeletal Alliance (ARMA) conducted an audit of the implementation of the MSF and found a worrying difference between UK trusts in the monitoring of follow-up waiting times for patients with RA (Arthritis and Musculoskeletal Alliance, 2009). Eighty-nine percent of trusts had not made an assessment of the average waiting time for a follow-up appointment, citing the 18 week referral-to-treatment target as the reason for not doing so. This audit validated the Kings Fund report from the Rheumatology Futures Group (The King's Fund, 2009), which highlighted that although services had addressed the delays found in referral-to-treatment time they had lost sight of how they monitored established patients. In parallel to the NICE guidance for management of RA (National Institute for Health and Care Excellence, 2013b), ARMA suggested that annual reviews should take place to ensure that all aspects of the condition, including the physical, psychological and educational needs of the patient are addressed.

ARMA then conducted an update of the audit in 2011 to ascertain whether any progress had been made since 2009 (Arthritis and Musculoskeletal Alliance, 2012). The updated audit found that musculoskeletal services continued to suffer from large-scale variation in the way they were delivered. In fact an even worse situation was found in regards to a number of the MSF's recommendations, including the assessment of average waiting times for a follow-up RA appointments, which only 9% of trusts had achieved, a drop from 11% in 2009 (Arthritis and Musculoskeletal Alliance, 2009). Therefore, this indicated that there was a continued focus on initial waiting times for treatment rather than the care of established patients.

In parallel with ARMA's 2009 audit the National Audit Office (2009b) published a report on the services provided for people with RA, which aimed to examine the potential for improving the delivery of services. It included a census of all NHS trusts with a rheumatology department between November 2008 and January 2009 (National Audit Office, 2009a), of which 95% of trusts responded. A majority reported an increase in the number of new patients with RA, compared to figures from the previous financial year and on average 50% of all outpatient appointments were for those with RA. In the case of a flare a majority of trusts advised their patients to call the nurse telephone advice line or contact their consultant directly. However, 66% of trusts did not have the capacity to offer all RA patients who needed them follow-up appointments on a timely basis. Sixty-three per cent were able to offer an annual review for established patients and only 40% could offer monthly reviews for patients with active disease. The primary barriers to not providing these services were lack of outpatient capacity, emphasis on referral-to-treatment targets and lack of staffing. The report concluded that patients with well-controlled RA should be offered review appointments at a frequency and location suitable to their needs but in order to address the gap between need and capacity it recommended that services should develop new models of delivery.

The following section will now review these new models of care along with the traditional service of rheumatologist-led clinics in order to establish possible methods via which these issues could be addressed.

2.5 MODELS OF CARE FOR ESTABLISHED PATIENTS IN RHEUMATOLOGY

2.5.1 Introduction

At the time of the MSF being published the Department of Health was also focused on the improvement of services more widely and suggested that a reduction in how unnecessary new and follow-up outpatient appointments and do not attends (DNAs) could substantially reduce costs and streamline services (National Health Service Institute for Innovation and Improvement, 2006). Since then a number of strategies have been developed with the aim of increasing capacity in rheumatology services whilst attempting to maintain high quality care. A report published by Li *et al.,* (2008)

synthesized these strategies in order to develop an integrated service delivery framework in rheumatology. The authors reviewed the literature in relation to the delays found in the various stages of the care pathway, from identification of symptoms by the patient and the delay in seeking help, through to referral for orthopaedic consultations. Forty-eight articles were found each of which focused on one of five potential times of delay in the: community, primary care, secondary care, follow-up and referral for orthopaedic review. The evidence in relation to secondary care supported the role of allied healthcare professionals in reducing delay, including nurses, physiotherapists and occupational therapists in providing tailored education and non-pharmacological treatments such as performing musculoskeletal examinations, monitoring and recommending changes to medications. The authors also recognised the role of patient-centred care in follow-up services and proposed that patient-initiated care could be integrated into the framework. Central to all of these strategies, however, was the aim to improve the care and management of RA and PsA to ensure that the appropriate patients are seen by an appropriate person in an appropriate setting and in a timely manner (Hay & Adebajo, 2005). The following sections consider each of the models of follow-up care in more detail.

2.5.2 Consultant-led care

Rheumatologists are seen as central to the treatment and management of inflammatory arthritis (Badley & Davis, 2012; Smolen *et al.,* 2013). Regular reviews are ingrained in medical practice (Spence, 2013) and particularly so in rheumatology where patients are required to attend ongoing reviews with a rheumatologist and nurse. These appointments are customarily managed within a scheduling system that arranges appointments well in advance. The frequency of visits does vary but are normally scheduled for every 3-6 months (Li *et al.,* 2008) and last for between 10 and 15 minutes (Royal College of Physicians, 2011). These reviews will customarily include an assessment of disease status, damage, function, co-morbidities and a review of current needs including medication, education, psychosocial support and referral to other services.

As with most other long-term conditions, the delivery of musculoskeletal services is within the organisational framework of the local healthcare system and is a balance

between not only need and demand but also the availability of resources. As a result a decision to follow a patient with arthritis up, or the timeframe in which to do this, is based not only on the severity and volatility of the condition but also the availability of clinic slots (Bukhari, Bamji, & Deighton, 2007). This advanced booking system may, therefore, mean that some patients are followed-up by their rheumatologist at a time when no help is required, whereas others may not be able to access the rheumatologist when they are in most need. The result is that rheumatologist-led follow-up appointments for patients with arthritis who are feeling well often result in little or no intervention (Mitchell, 2000; Hehir *et al.,* 2001) as previously stated (section 2.4, page 58).

The organisation and frequency of outpatient visits to the rheumatologist may also be influenced by the 'Payment by Results' system implemented by the Department of Health (2013c). This payment system implemented in England sees commissioners pay healthcare providers for each patient seen or treated; with the amount dependant on the complexity of the patient's healthcare needs. 'Payment by results' incentivises hospitals for outpatient attendance. The tariff offered for a new patient in rheumatology is more than twice of that of a follow-up patient, £214 versus £100 (Department of Health, 2013d). This disparity could in part explain why rheumatologists are now being driven to reduce their new to follow-up ratios (i.e. more new and fewer follow-up patients) or work to fixed ratios that are lower than their usual practice. A recent survey of rheumatologists found that 35% had been asked to work to a set new to follow-up ratio and this on average was 3.1:1 (Bukhari, Dixey, & Deighton, 2011). As noted earlier figures in 1991 suggested that planned follow-up appointments accounted for approximately 75% of the rheumatologist's workload (Kirwan & Snow, 1991). These more recent data, therefore, suggest an attempt to reverse these proportions. This drive to review new patients quickly is justified given the evidence for early intervention and tight disease control (Strand & Singh, 2007; Grigor *et al.,* 2004; Tanaka *et al.,* 2008) however, a clear and appropriate care pathway for established patients would need to be implemented in order to meet the needs of this population as well. The findings of Bukhari *et al.,* (2011) sparked debate about the influence of the CNS on these new to follow-up ratios and the

potential for DMARD monitoring clinics to be run by these nurse, along with moving activity out in to the community.

Early evidence suggested that access to specialist rheumatology input resulted in better patient outcomes than management by non-rheumatologists alone (Yelin, Such, Criswell, & Epstein, 1998; Criswell, Such, & Yelin, 1997). This was attributed to earlier intervention with DMARD therapy. The effectiveness of rheumatologist-led services has not, in itself, been evaluated in recent years most likely because this is the traditional and most established method of reviewing and monitoring patients with arthritis. However, it is often employed as a comparator group in trials of what are considered more contemporary models of care including nurse-led clinics, rheumatology clinics in primary care and patient-initiated services, all of which will be reviewed in the following section. This will provide an understanding of how consultant-led services compare with more recent developments in service delivery.

As a result of current government policy there is now a significant focus on the community and a shift of some hospital-based rheumatology services into primary care. This could be achieved either by introducing GP-led services (as reviewed in section 2.5.4, page 74) or by moving rheumatologist or CNSs out into the community. The former may explain why the number of consultant physicians in rheumatology has expanded in the UK by only 3.1% from 2003 to 2011 compared with 5.2% across all other general medical specialities (Royal College of Physicians, 2013). The latter may explain why the proportion of rheumatology consultants with sessions in primary care has increased from 9% in 2007 to 15% in 2009 (Harrison, Lee, Deighton, & Symmons, 2011). There has also been a growth in the number of musculoskeletal services being run in conjunction with clinical assessment and treatment services in England, which provide patients with quick and accessible assessment, diagnostics and treatment services under one roof, from 13% in 2007 to 17% in 2009 (Harrison *et al.,* 2011). These services are, however, yet to be evaluated and BSR has expressed anxiety about these changes and the impact they are having on the rheumatology workforce (Royal College of Physicians, 2013).

Evaluation of these so called outpost clinics, whereby specialist services are run in the community by rheumatologists suggests that patients are highly satisfied with the service they receive. This is probably due to the proximity and more scheduled time with the consultant due to a more rigid booking system. However, this makes the community setting less "efficient", defined as the number of patients seen per clinic, as hospital based systems allow for overbooking. Although the community clinic has been found to be cheaper with regard to total staff costs (£114 versus £262), estate costs, travel and the higher consultation rate meant that the overall cost per patient in the hospital setting was lower (£10.35/patient versus £15.93/patient) (Helliwell, 1996).

2.5.3 Nurse-led care

2.5.3.1 Face-to-face care

The introduction of the rheumatology CNS in the 1980's heralded an important step towards developing a multidisciplinary team in the care of patients with arthritis. Initially activities included basic disease management and patient education but more recently the role of the CNS in rheumatology has been extended to incorporate activities traditionally undertaken by the consultant and nurses now lead their own clinics separate to that of the rheumatologist (Vliet Vlieland, 2004). A survey conducted by the Royal College of Nurse Rheumatology Forum (2009) found that rheumatology nurses hold on average 4-5 clinics per week, consisting of 4-10 follow-up patients per clinic session and 1-2 emergency patients, with an average slot of 30 minutes per follow-up appointment, double that of a rheumatologist. For over 70% of nurses these clinics consist primarily of patients with RA or PsA. The survey also revealed that 44% of rheumatology nurses had been asked to change their usual work pattern or take on extra work within the previous 18 months. This was primarily in relation to extra clinics and changes in their role or service, described by the nurses themselves as "increased activity without increased resources". For over 80% of the sample monitoring patients on DMARDs and educating patients about their disease and its management were a major, or significant part of their role (Royal College of Nurse Rheumatology Forum, 2009).

In the UK nurse-led rheumatology clinics are now a well-established method for following up stable patients and reviewing new patients with possible arthritis. As

highlighted by the Royal College of Nurse Rheumatology Forum (2009) rheumatology nurses play an important role in addressing the unmet needs of patients with arthritis. Research both with fellow rheumatology healthcare professionals (Cottrell *et al.,* 2012) and patients with arthritis (van Eijk-Hustings *et al.,* 2013) indicate that disease and drug monitoring, education, self-management support, emotional support and well organised care are essential parts of the rheumatology nurse role. It appears that 80% of CNSs in rheumatology are already routinely performing these activities (Goh, Samanta, & Samanta, 2006).

Until recently, however, the evidence for the effectiveness of rheumatology nurse-led clinics was not robust. A systematic review published by Ndosi, Vinall, Hale, Bird and Hill (2011) aimed to analyse the clinical effectiveness of nurse-led rheumatology services for people with RA. Seven randomized controlled trials (RCTs) (Hill, Thorpe, & Bird, 2003; Hill, Bird, Harmer, Wright, & Lawton, 1994; Hill, 1997; Tijhuis *et al.,* 2002; Tijhuis, Zwinderman, Hazes, Breedveld, & Vlieland, 2003; Tijhuis *et al.,* 2003; Ryan, Hassell, Lewis, & Farrell, 2006) were found, four of which were conducted in the UK (Hill *et al.,* 2003; Hill *et al.,* 1994; Hill, 1997; Ryan *et al.,* 2006). Pooled effects in the meta-analyses suggested equivalence between nurse-led care and usual care, which tended to be a consultant-led service, with regard to pain, morning stiffness, DAS28 scores, plasma viscosity, physical or psychosocial functioning. The nurse-led follow-up service did, however, lead to significant improvements in joint tenderness, knowledge and satisfaction. But as there were so few studies the authors of the review concluded that good quality RCTs were still required in order to provide evidence for the effectiveness of nurse-led care for people with RA. In addition the review did not include the cost-effectiveness analysis reported in the study by Van den Hout, Tijhuis, Hazes, Breedveld and Vlieland (2003). This study indicated that although compared with inpatient and day patient team care, CNS care led to equivalent quality of life, the nurse-led clinic was associated with lower societal and hospital costs.

Since this systematic review a number of good quality RCTs have been conducted. This includes a UK based multi-centre pragmatic RCT conducted by the authors of the systematic review (Ndosi *et al.,* 2013). In this trial patients with RA had five follow-up visits over a 12 month period either in a nurse-led or rheumatologist-led clinic. The

nurse-led consultations covered a combination of pain control, medication and dosage changes, intra-articular or intra-muscular steroid injections, provision of patient education and psychosocial support, prescription of splints, non-protocol blood tests or radiographic examination and referrals. The rheumatologist provided "usual care", although exact details were not provided. The analysis indicated that the nurse-led clinic was equivalent to a clinic led by a rheumatologist with regards to disease activity and in fact led to significant improvements in satisfaction, pain and physical function compared with the rheumatologist-led clinic. There was, however, a significant worsening in patient fatigue, stiffness and mood in the nurse-led service compared to slight improvements in the rheumatologist-led group. Definitive conclusions with regards to cost-effectiveness were difficult as the analysis suggested cost benefits when disease activity was considered, but when quality-adjusted life-years were used the intention to treat (ITT) analyses indicated no significant cost benefits for the nurse-led clinic.

A number of trials have also been conducted in inflammatory arthritis outside of the UK (Koksvik *et al.,* 2013; Larsson, Fridlund, Arvidsson, Teleman, & Bergman, 2013; Koksvik *et al.,* 2013; Larsson *et al.,* 2013; Primdahl, Sørensen, Horn, Petersen, & Hørslev-Petersen, 2014). In an RCT conducted by Koksvik *et al.,* (2013) in Norway a nurse specialist-led clinic was compared to follow-up by a medical doctor for patients with inflammatory arthritis who had just started DMARD therapy. The nurse service consisted of assessment of disease activity, co-morbidities, medication use, function and psychosocial well-being; the content of the doctor's clinic was not described other than being usual practice. At 21 months post-implementation participants in the nurse-led service were significantly more satisfied with their care, with the provision of information, felt that the service was more empathic and technically competent and were more positive about the clinician's attitude towards them, the access they had and the continuity of care. There were also no significant differences in disease activity, pain or quality of life suggesting at least equivalence in symptoms and psychosocial well-being between the two services.

Similar findings were also been reported in an RCT by Larsson *et al.,* (2013) who evaluated an exclusive rheumatologist-led follow-up service with a system which

alternated between a rheumatologist-led appointment and a person-centred nurse-led clinic for patients with chronic inflammatory arthritis treated with biological therapy. In the exclusive rheumatologist-led service patients had a 30 minute appointment every 6 months for an assessment of disease activity and medication side effects. Patients were also able to contact the rheumatology clinic between these scheduled follow-up visits. In comparison participants in the other arm of the trial alternated between the nurse-led clinic and a rheumatologist-led appointment. These nurse-led appointments were person-centred whereby patients were given the opportunity to talk about their illness openly in order to build collaboration between the patient and the nurse. Disease activity was also assessed and laboratory tests evaluated the same as in the rheumatologist-led clinic. The service aimed to empower patients to take an active role in their treatment and find solutions to any problems they encountered; however, exact details about how this was achieved was unclear. Over the 12 month evaluation there were no statistically significant differences in changes in disease activity, tender and swollen joints, pain, disability, satisfaction or confidence in the system between the two groups. Qualitative interviews with those in the nurse-led service found that patients felt that the nurse was added value and indicated that the service made the care pathway more complete (Larsson, Bergman, Fridlund, & Arvidsson, 2012).

In a three arm trial conducted in Denmark, Primdahl *et al.,* (2014) compared a control group which included consultations with the rheumatologist every 3-12months, with a "shared care" group (discussed further in section 2.5.6.1, page 82) and a nursing group, which included 30 minute appointments with a specialist nurse every 3 months covering medication monitoring, clinical assessment and self-management issues. At the 2 year follow-up the nursing group had significantly greater self-efficacy along more confidence and satisfaction in the care they received compared with the rheumatologist group. There were also no significant differences between nursing care and the control group on any of the patient safety measures, including adherence to blood monitoring, out-of-range blood tests and the number of side effects. Further analysis of this study found that reduced disease activity, a shorter disease duration and less fatigue and functional disability at baseline were associated with greater improvements in self-efficacy at 3 months (Primdahl, Wagner, Holst, & Hørslev-

Petersen, 2012). A subsequent qualitative study was undertaken which aimed to compare the experiences of patients in each of these three groups (Primdahl, Wagner, & Hørslev-Petersen, 2011b). The data indicated that patients valued the continuity of care, that their relationship with their nurse was more holistic than with the rheumatologist and all patients felt able to contact the service for additional advice if they felt it necessary.

A Rheumatology Monitoring Clinic jointly run by Advanced Practice Nurses or pharmacists, under the supervision of a rheumatologist has also been implemented in Singapore (Chew & Yee, 2013; Chew *et al.,* 2012). These clinics were for established patients on a stable dose of DMARDs and inactive or stable disease activity. Monitoring of disease activity and side effects were undertaken along with issuing repeat prescriptions. In the event of a flare or medication-related complications the rheumatologist was approached for their specialist input (Chew & Yee, 2013). Over a 1 year period 200 patients were seen in the service, a random sample of these patients were audited, which indicated that patients remained largely stable (although the definition of stability was not provided). Ten percent of sample required either an increment, reduction or discontinuation of their DMARD therapy. According to the authors these patients were detected early and were seen by a rheumatologist in a "timely manner". Satisfaction was measured via a survey of 97 patients seen within the clinic over a 6 month period, 84% of whom had RA (Chew *et al.,* 2012). An overwhelming majority of the sample felt more confident in their ability to take their medication and adhere to treatment after their appointment. Patients also felt that the therapist provided clear and detailed information about their disease and medication and hence they had a better understanding of their disease and medication and knew what to look out for if their condition deteriorated or if they developed side effects. They also felt that their therapist was professional and knowledgeable and were willing to come back for follow-up assessment in the clinic. Seven rheumatologists and six professionals running the clinic also completed questionnaires and all were satisfied with the patients' management and control of their disease. The rheumatologists all agreed that the therapists were professional, knowledgeable and capable in providing this service and 80% agreed that the clinic freed up time for them to see more complex cases. Those running the clinic felt that the referrals were

appropriate and workflow was acceptable. This study, however, was not an RCT but an internal audit conducted by the team one year after implementation of the service. The findings, therefore, cannot be assumed to be attributable to the new model of care.

In addition to these quantitative trials a number of qualitative studies have been undertaken to explore the impact of nurse-led rheumatology clinics from the patient perspective. Arvidsson *et al.,* (2006) interviewed 16 patients with RA who had been treated with DMARD therapy in a nurse-led rheumatology clinic. The clinic was found to have an impact on the empowerment of patients by teaching them about their condition and treatment options along with how to adapt their activities and daily life in order to live with arthritis. Regular reviews with the same nurse gave patients a sense of security and comfort. In these visits the approach was more holistic and as a result patients felt respected and listened to. Similarly, Bala *et al.,* (2012) interviewed 18 people also with RA who had experience of a nurse-led rheumatology clinic and found that their experience was one of a person-centred, holistic approach to care.

There is an ongoing RCT being conducted in Sweden (Bergsten, 2014) comparing a nurse-led clinic including person-centred care and tight control with usual care in patients with RA and moderate or high disease activity. Usual care is described as visits to physician every 6 months, whereas the nurse-led clinic will be visits every 6 weeks, with structured person-centred care and evaluation of disease activity. If disease remission is not reached in the nurse-led group, pharmacological treatment including both short-term (intra-articular and oral steroids) and long-term alterations (DMARDs and biologics) will be made according to a predefined algorithm. The study will recruit 120 patients and compare disease activity, quality of life, pain, fatigue, self-management skills, beliefs about medicines and satisfaction with care over a 6 month period. The study is due to complete in 2015 and will provide further evidence either for or against the use of nurse-led rheumatology services.

As a result of these studies EULAR (van Eijk-Hustings *et al.,* 2012) have outlined 10 recommendations for the role of the nurse in the management of chronic inflammatory arthritis' including RA and PsA (Figure 2.3). In the development of these

recommendations, the role and capabilities of the nurse in rheumatology services were found to vary quite significantly between countries. The recommendations acknowledged that the value of a rheumatology nurse was most prominent and important in disease monitoring as well as in support for patients across a range for chronic inflammatory arthritis'. The recommendations also recognised that high-quality studies, with clear descriptions of nursing roles and interventions needed to be conducted as the role of the nurse in care is currently often not clearly stated in many studies.

1. Patients should have access to a nurse for education to improve knowledge of chronic inflammatory arthritis and its management throughout the course of their disease.
2. Patients should have access to nurse consultations in order to experience improved communication, continuity and satisfaction with care.
3. Patients should have access to nurse-led telephone services to enhance continuity of care and to provide ongoing support.
4. Nurses should participate in comprehensive disease management to control disease activity, to reduce symptoms and to improve patient-preferred outcomes.
5. Nurses should identify, assess and address psychosocial issues to minimise the chance of patients' anxiety and depression.
6. Nurses should promote self-management skills in order that patients might achieve a greater sense of control, self-efficacy and empowerment.
7. Nurses should provide care that is based on protocols and guidelines according to national and local contexts.
8. Nurses should have access to and undertake continuous education in order to improve and maintain knowledge and skills.
9. Nurses should be encouraged to undertake extended roles after specialised training and according to national regulations.
10. Nurses should carry out interventions and monitoring as part of comprehensive disease management in order to achieve cost savings.

Figure 2.3. EULAR recommendations for rheumatology nursing management of chronic inflammatory arthritis

In summary, the literature suggests that nurse-led follow-up clinics for patients with chronic inflammatory arthritis are at the very least equal to, if not superior to rheumatologist-led clinics, in relation to disease activity, symptoms and psychosocial outcomes. Despite the evidence regarding the role of nurse-led clinics, problems still persist in many services regarding limited access for established patients with acute problems, high "no show" rates, and the routine scheduling of follow-up visits often well in advance for no defined purpose, all of which are indications of sub-optimal and inefficient care (Newman & Harrington, 2007). The development of telephone clinics have gone someway to addressing these issues and will be reviewed in section 2.5.3.3 (page 72).

2.5.3.2 Community

Community based nurse-led rheumatology services have also been implemented in the UK, although evaluations are extremely scare. These services tend to involve management of arthritis in the home for people who are housebound. In an audit of such a service Douglas *et al.,* (2009) found that over a 3 month period 1510 patient contacts were made by the nurse team, which would have been traditionally seen by a rheumatologist in clinic. Four percent of patients required a home visit from the nurse, 11% urgent contact visits (i.e. joint injections), 31% clinic visits and 53% a telephone contact. The service, however, was not formally evaluated and it was unclear how decisions were made with regards to who entered the service, who was subsequently seen and via what method (i.e. at home or in clinic). The evidence for community based rheumatology nursing is, therefore, lacking.

2.5.3.3 Telephone care

Nurse-led telephone clinics are becoming increasingly more popular as an alternative to face-to-face clinic visits as they address some of the concerns highlighted by Newman and Harrington (2007). Unlike a nurse-led telephone help-line, appointments are scheduled like a standard face-to-face visit for the nurse to review and monitor the patient. The feasibility and acceptability of this mode of follow-up has been found to vary. Whilst Hawley and Quilty (2009) report that only 12% of rheumatology patients could be followed-up using a telephone review due to the stage of their illness and treatment, Pal (1997) found that 80% of patients would be willing to accept a telephone follow-up appointment. This suggests a difference between what clinicians

feel is feasible and what patients find acceptable. Pal (1998) reported the results of a pilot study that followed rheumatology patients up by telephone rather than face-to-face. These calls included a review of progress, changes in the disease and its treatment, and feedback from test results. Ninety per cent of patients were satisfied or very satisfied with the service and most patients felt that the advantages of saving time and money, less stress and fewer problems with transport, outweighed the disadvantages of telephone clinics being impersonal, the potential for misunderstandings and problems that might occur as a result of hearing and language issues.

Hennell, Spark, Wood and George (2005) evaluated a nurse-led telephone clinic, aided by a consultation proforma which reflected a traditional outpatient consultation, covering diagnosis, current medication, monitoring attendance and blood test results. Patients were also asked to report any current joint swelling and/or tenderness. At the end of the consultation the content was summarized for the patient and the plan of action confirmed. During the first month 71 patients who were on the follow-up waiting list were allocated a nurse-led telephone appointment, three patients were not in or did not answer the telephone. Of the 68 patients surveyed 72% were very happy with their consultation and would be happy to use the service again, those that were not happy (8%) preferred to see the nurse in person in the future. This telephone clinic enabled nurses to review more patients and, therefore, helped reduce follow-up wait times by 2 months, down to the recommended 3 monthly interval.

In both studies however, the quality of the methodology and reporting of the intervention content and exclusion/inclusion criteria were poor. It is assumed in both studies that telephone calls were a replacement for standard face-to-face contact although the authors do not clearly state this. There was also no comparison group and hence no randomisation of participants, or no details on what clinical care and from whom the patients continued to receive. Failure to collect data on clinical outcomes makes it difficult to establish if this form of contact had any detrimental impact on health and well-being. These studies suggest tentative evidence for nurse-led telephone consultations in regards to patient acceptability; however, more robust

trials need to be undertaken to establish whether this mode of delivery is in any clinically or psychologically detrimental to patient well-being.

2.5.4 GP-led care

As reported earlier, there is little evidence to support either rheumatologist or CNS-led primary care services. Therefore, much of the published literature on rheumatology community services focuses on the role of GPs in the management of patients with arthritis early in the disease course, either alone or in collaboration with rheumatologists, the premise being that this will free up specialist services for those with more complex needs such as those with RA and PsA who require DMARD therapy.

This shift is occurring despite the fact that there is little evidence to suggest that GP-led monitoring of patients with arthritis on DMARD therapy is effective. In fact concerns have been raised about the impact that discharging patients with chronic inflammatory arthritis back to primary care will have on GP workload (Bukhari *et al.,* 2011). There are also concerns about the inadequacy of rheumatology education in the primary care setting (Wise & Isaacs, 2005). The knowledge of the treating healthcare professional is considered by rheumatology patients as one of the most important aspects of care (Jacobi, Boshuizen, Rupp, Dinant, & Van Den Bos, 2004). However, 27% of patients surveyed by Jacobi *et al.,* (2004) felt that their GP's knowledge was inadequate for specialist rheumatology care.

Musculoskeletal disorders make up approximately 18% of a GP's perceived workload (Roberts, Adebajo, & Long, 2002). In this survey of 240 GPs in the UK over one third were confident that with advice from a rheumatologist they could manage a patient with early RA (Figure 2.4). A further 34% were confident to make a diagnosis but would prefer to refer long-term monitoring and management to a rheumatologist (Roberts *et al.,* 2002). This lack of confidence may prove problematic as it may generate reluctance to provide rheumatological care (Mann, 2006).

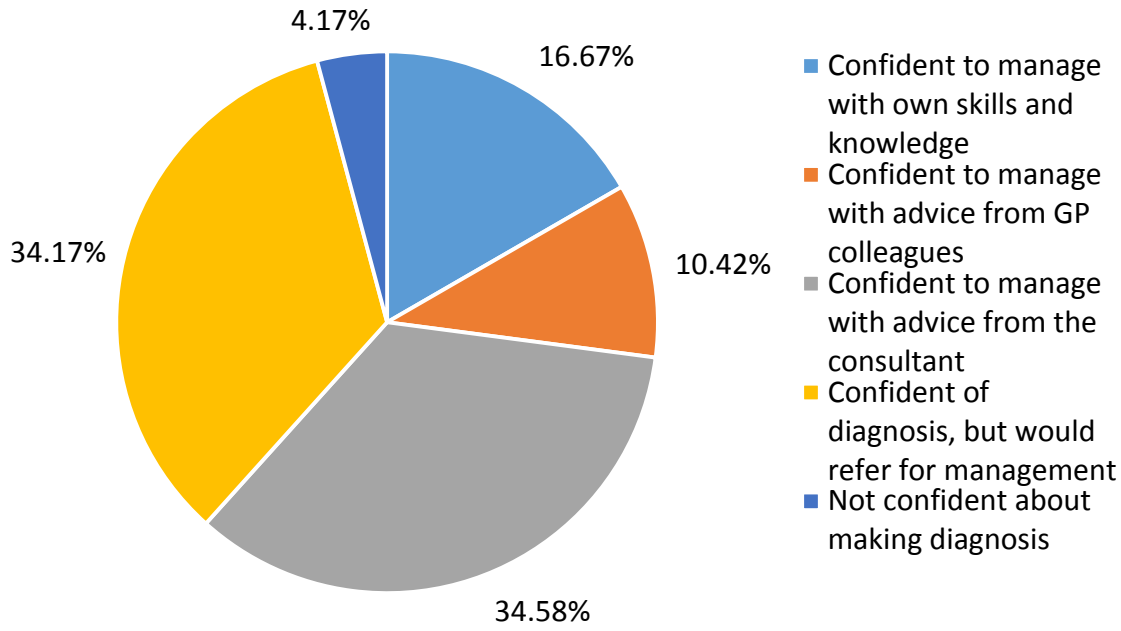


Figure 2.4. Level of GP self-confidence in managing early RA

In addition population based studies in Canada show that patients with RA managed predominantly by primary care physicians are less likely to be prescribed DMARDs (Lacaille, Anis, Guh, & Esdaile, 2005; Shipton, Glazier, Guan, & Badley, 2004). Similar findings from a UK survey comparing a primary care-led rheumatology service with secondary care found that fewer patients with RA or unspecified inflammatory arthritis managed in primary care were taking a DMARD compared to those in secondary care (Hetthen & Helliwell, 1999). These studies suggest that GPs not only lack confidence in their ability to manage established patients with arthritis but the provision of DMARD therapy in primary care is poor and in direct contrast to the guidelines which recommend treatment to be started as early as possible in order to obtain tight control of the condition (National Institute for Health and Care Excellence, 2013b). Evaluations of GP-led rheumatology services have been conducted. Schulpen *et al.,* (2003) explored the feasibility of referring patients with arthritis back to their GP for management. If considered eligible by the rheumatologist, although it was unclear what the eligibility criteria were, consenting participants were randomized to either remain under the care of their rheumatologist or referred back to the GP. Those randomised to referral back to their GP were presented during a joint consultation clinic where the rheumatologist explained to the GP how their follow-up care should proceed. From that moment on follow-up care was provided by the GP with the

opportunity to consult the rheumatologist at any subsequent joint consultation clinic. At the start of the study 276 patients were identified as having been originally referred from one of the 17 participating GP practices. Of these 276 patients, 45% had been subsequently discharged from secondary care without the need for any additional medical follow-up, and 32% were deemed to require specialist follow-up. Overall in only 10% of cases was it deemed appropriate to refer their care back to the GP suggesting that community-led services may not be an acceptable model of care from the specialist perspective. This may in part be due to the lack of faith rheumatologists had in the ability of the GPs to manage established arthritis and as a result classified the patient as needing specialist services. It is unclear, however, what the composition of this population was as authors failed to detail the diagnostic status of participants and how many patients had chronic inflammatory arthritis. It could be that those remaining in specialist services were not established on their treatment or were experiencing a period of flare which meant the rheumatologist wanted to review the patient more closely. Schuplen *et al.,* (2003) concluded that moving follow-up services to primary care does not appear to be the solution as the gap in specialist knowledge between rheumatologists and GP is too wide.

Other evaluations of GP-led follow-up clinics from the clinical and patient perspective have been undertaken (Hetthen & Helliwell, 1999; Arthur & Clifford, 2004b; Arthur & Clifford, 2004a) however, the quality of these studies suggests that there is a lack of methodologically robust evaluations within the published literature.

Hetthen and Helliwell (1999) compared 100 patients, with different rheumatological diagnosis, seen at a GP-led rheumatology service and 100 patients, seen at a hospital-based rheumatology outpatient service on both clinical and patient reported outcomes (PROMS). Two GP services were commissioned to deliver specialist rheumatology care in general practice whilst at the same time acting as clinical assistants in the rheumatology outpatient department, working alongside the rheumatologists to increase their knowledge and skills. Patients seen in primary care had a median waiting time of 0 days compared with 37.5 in secondary care. A majority of patients was satisfied with the convenience and length of their appointment and this was similar across both groups. Utilisation of support services such as blood tests, radiography,

physiotherapy, occupational therapy and podiatry were, however, greater in secondary care, as was provision of written information to the patient. Although levels of disability were much greater in secondary care, this was likely to reflect the greater proportion of patients with established disease attending these clinics. The number of patients with RA or inflammatory arthritis on DMARDs was also substantially lower in the primary care group (22%) compared with secondary care (69%). This suggests either that the GP-led service was being utilised as a substitute for early referral rather than for ongoing monitoring and management of established patients who remained in secondary care, or established patients in primary were being under prescribed DMARDs. This latter hypothesis supports previous findings (Lacaille *et al.,* 2005; Shipton *et al.,* 2004) but as the authors failed to describe the sample adequately it is not possible to establish the reasons for these discrepancies. In addition the authors failed to report the inclusion and exclusion criteria for patients being referred into either service.

Arthur and Clifford (2004b) conducted a qualitative study of 10 rheumatology patients all taking DMARDs; five being followed up by their GP in primary care and five by a rheumatology nurse in a secondary care nurse-led clinic. Participants were asked what they expected when they attended their drug monitoring appointment and what they would you like to happen in an ideal world. Both groups of participants gave varying responses, but those in secondary care tended to provide more examples and spoke more about feeling empowered and the psychological care offered by the rheumatology nurse whilst those in primary care focused more on the technical aspects such as tests. Those cared for in the hospital setting were sceptical about the ability of GPs to provide specialist care and knowledge; praising the quality and quantity of the information given to them by their nurse as compared to previous experiences with their GP.

The same authors also conducted a quantitative assessment of patient satisfaction between two cohorts of patients with RA on DMARD therapy (Arthur & Clifford, 2004a). The first was a group of patients whose drug monitoring was undertaken by the GP supplemented by 4 monthly follow-up appointments with the consultant rheumatologist in the outpatient department (primary care route). The other group of

patients were referred to the rheumatology nurse and attended nurse-led clinics in the outpatient department for monitoring, along with 4-6 monthly appointments with their rheumatologist (secondary care route). Levels of satisfaction were high in both groups but in contrast to the study by Hetthen and Helliwell (1999) who found no difference, satisfaction was significantly higher in secondary care across all six dimensions of satisfaction (general satisfaction, information provision, empathy, technical quality, attitude to patient, continuity of care and overall satisfaction). Those managed in secondary care were also more likely to have received information about their disease. It was, however, unclear from the published article how patients were selected for referral into the primary or secondary care route. The use of a non-randomized convenience sample also means that these participants may not be representative of the larger population and hence the findings cannot be generalised.

A number of trials have evaluated a "shared-care service" (Hewlett *et al.,* 2000; Kirwan *et al.,* 2003b; Hewlett *et al.,* 2005b; Primdahl *et al.,* 2012; Primdahl *et al.,* 2014) in which GPs monitor DMARD therapy but care, either from the GP or rheumatology team is initiated by the patient with no regular scheduled appointments. This model of care will be reviewed in section 2.5.6.1 (page 82).

Although GPs with a specific clinical interest such as rheumatology are not new, there is now recognition of a new "breed" of GP: "a GP with a specialist interest" (Hay & Adebajo, 2005) and there are now recognised services delivered in primary care by these clinicians (Roberts, Dolman, Adebajo, & Underwood, 2003) and associated accreditation for the role (Royal College of General Practitioners, 2014). A competency framework has also been published specifically for GPs with a special interest in musculoskeletal/rheumatology practice (Hay, Campbell, Linney, & Wise, 2007) but as yet there is little information or evidence to understand how these new roles are impacting on the experience of patients or on the health service. Robust evaluations will be required to assess the clinical effectiveness, cost-effectiveness, acceptability and sustainability of such services.

Glazier (1996) proposed that rather than waging a "war over turf", rheumatologists should take the lead on working with GPs to provide expert training and support to

ensure that patients receive high quality specialist care, irrespective of whether that is delivered in the community or hospital setting. These studies suggest that there is little robust evidence to indicate that either patients or the healthcare system would benefit from such a radical change in service delivery particularly in the case of patients with established arthritis on DMARD therapy.

2.5.5 Multidisciplinary teams

A multidisciplinary team approach which incorporates various healthcare professions is often used in the management of patients with arthritis. The composition of the team may vary between centres but their general approach aims to bring together the skills and knowledge of different disciplines, for both the assessment and management of the disease.

Guidelines however, seem to have differing views on the benefits of the multidisciplinary team. EULAR recommendations for the management of RA patients on DMARDs states that the primary responsibility of caring for a patient should lie with the rheumatologist, but a multidisciplinary team approach may sometimes be needed when dealing with co-morbidities such as cardiovascular disease, or complications of applied therapies, such as serious infections (Smolen *et al.,* 2013). This approach fails to acknowledge other members of the rheumatology team, such as specialist nurses, physiotherapists and occupational therapists all of whom are cited as key members of the rheumatology multidisciplinary team (Cherry, Crossland, Field, Ainsworth, & Edwards, 2014). In contrast NICE guidelines for RA state that patients should have access to a multidisciplinary team who can provide knowledge and skills to complement that of the rheumatologist. These guidelines recommend that people with RA should have access to a named member of the multidisciplinary team, for example the specialist nurse, who is responsible for coordinating their care. These recommendations are, however, made “despite the lack of demonstrated benefit” (National Institute for Health and Care Excellence, 2013b).

A systematic review of multidisciplinary team care programs both in outpatient and inpatient services for patients with RA by Vliet Vlieland and Hazes (1997) identified 42 papers reporting on 35 clinical trials. The impact of a multidisciplinary team outpatient

care approach was evaluated in two uncontrolled trials and six controlled trials in which it was compared with usual outpatient care. The controlled trials found that the multidisciplinary team approach was associated with greater improvements in physical and social functioning, overall health, disease activity and psychosocial well-being. The uncontrolled studies also report significant improvements in disease activity, functional status and general health over time. Many of these studies, however, were methodologically flawed and in all but one of the controlled studies, multidisciplinary team care led to more medical visits. The intensity of other treatment modalities, such as the use of NSAIDs, the number of orthopaedic consultations, and hospitalizations, appeared similar across groups. Vliet Vlieland (2004) published another review 10 years later including only controlled clinical trials. The evidence at this time supported the role of the CNS in coordinating the multidisciplinary team.

A recent systematic review by Cherry *et al.,* (2014) aimed to identify and synthesise the literature relating to the clinical importance of multidisciplinary team working in musculoskeletal healthcare. A total of 63 articles were found but only 11 were RCTs. Over 80% of these RCTs reported significant clinical benefits for multidisciplinary team working compared to minimal team intervention and the remaining reported no effect on clinical outcomes. These findings are, however, reported in conference proceedings with the full review yet to be published. It is, therefore, not possible to determine the quality of these primary research papers, the type of patients included or the exact clinical benefits. There does, however, appear to be some positive outcomes in relation to this approach.

2.5.6 Patient-led care

The models of care described so far in this chapter have sought to redirect care either within secondary care or from secondary to primary care. The focus has now begun to move towards reducing unnecessary outpatient appointments and follow-up appointments altogether (National Health Service Institute for Innovation and Improvement, 2006) through the introduction of patient-led services.

The provision of patient-led services in rheumatology is a result of not only the need to streamline services but reflects the shift away from a paternalistic model of healthcare

where the patient is seen as a passive recipient of care and the clinician in a position of dominance and authority. The term patient-led refers to "reshaping how the service delivers care, based on what patients need and want" (Fitzpatrick, 2005). Patients are now encouraged to take an active role in knowing and managing their health, in expressing their concerns and preferences and participating in medical decisions. This is especially important in chronic diseases such as arthritis where the reality of living with the condition is demanding, and successful management requires increased responsibility on the part of the patient.

A vast body of literature both before and after publication of the NHS White Paper 'Equity and excellence: liberating the NHS' (Department of Health, 2010a) which stressed "no decision about me without me" has explored the role of patient involvement in rheumatology. This research emphasises the need for an ongoing exchange of information between the clinician and patient, understanding and agreement about treatment priorities and objectives and shared decision making around future treatment plans (Neame, Hammond, & Deighton, 2005; Renzi, Di, & Tabolli, 2011; Garfield, Smith, Francis, & Chalmers, 2007; Ishikawa, Hashimoto, & Yano, 2006).

Research suggests that people with arthritis have a desire to make their own decisions about their health. Neame *et al.,* (2005) found that 78% of patients with RA agreed or strongly agreed that they should be free to make decisions about everyday medical problems. However, 52% agreed or strongly agreed that if hospitalised they should *not* be making decisions about their own care and 79.5% felt if their illness was to become worse they would want the doctor to take greater control. This suggests that when patients are well they want to make more autonomous decisions and when unwell more collaborative decisions. In a smaller survey of 33 people with PsA only 28% of patients preferred to leave treatment decisions entirely to their doctor, whereas 69% wanted some level of involvement (Renzi *et al.,* 2011). The desire to participate has been linked to a number of factors including being younger, female and of higher educational status or social class (Neame *et al.,* 2005; Garfield *et al.,* 2007; Ishikawa *et al.,* 2006).

Despite this desire, in practice many people with arthritis report only some level of involvement and most would like greater collaboration. In a sample of 223 patients with RA only 32% felt they had some impact on treatment decisions (Cunha-Miranda, Costa, & Ribeiro, 2010). In addition a number of surveys have found that approximately 30% of patients with arthritis are not involved in decisions about treatment, despite being given the opportunity to ask questions, suggesting that involvement is more than just being able to ask questions (Brekke, Hjortdahl, & Kvien, 2001; Lim, Ellis, Brooksby, & Gaffney, 2007; Kjeken *et al.,* 2006). In comparison, the level of involvement in PsA is even lower with only 8.7% of patients actively involved in medical decision-making and 76.7% having no participation at all (Leung *et al.,* 2009), this could be associated with duality of their condition (i.e. arthritis and psoriasis). Actual involvement has been linked to patient characteristics including being female, a patient's age (being younger in RA and older in PsA) and a higher level of formal education (Kjeken *et al.,* 2006; Brekke *et al.,* 2001; Leung *et al.,* 2009; Ishikawa *et al.,* 2006).

Although the direction of causality is unclear there may be potential benefits to having greater involvement including higher levels of satisfaction with care (Leung *et al.,* 2009; Brekke *et al.,* 2001; Kjeken *et al.,* 2006), a more positive attitude about arthritis and the impact of treatment, increased adherence to medications (Martin & Johnson, 2011), better mental health and greater self-efficacy (Brekke *et al.,* 2001). Given that patients with RA and PsA have in general a desire for greater involvement more recent research has gone beyond involving patients in decisions about treatment and care towards patient-led outpatient services; allowing people to take active control of initiating aspects of their own care.

2.5.6.1 Patient-initiated services

The traditional rheumatology system assumes that patients need to be seen on a regular basis by a healthcare professional and, when they are seen decisions are made by clinicians rather than the patient themselves. Nevertheless, over 40% of patients receiving rheumatology services feel they should be able to decide how frequently they need a check-up (Neame *et al.,* 2005) and take responsibility for organizing their own DMARD monitoring appointments (Kay & Lapworth, 2004), suggesting that

patient-initiated services may be acceptable to patients. In fact 30% of outpatient appointments result in no investigation or other actions and 42% of all visits are deemed completely unnecessary (Hehir *et al.,* 2001) providing further endorsement for this model of care.

A number of rheumatology services have been successful in involving patients in initiating their own care, much like we all do in primary care. These models include varying degrees of patient involvement and involve patients directing their needs to either primary or secondary care, or a combination of these services. This section will now review the content of these interventions and synthesise the evidence in relation to patient-initiated follow-up services in rheumatology. It is important to highlight that these services have been labelled differently, some are described as direct access others shared care and also patient-initiated. In this section the label given by the authors will be used. The common thread throughout these services is that patients either alone or in combination with their primary care physicians are able to initiate their own arthritis-related reviews, which take place either within primary or secondary care.

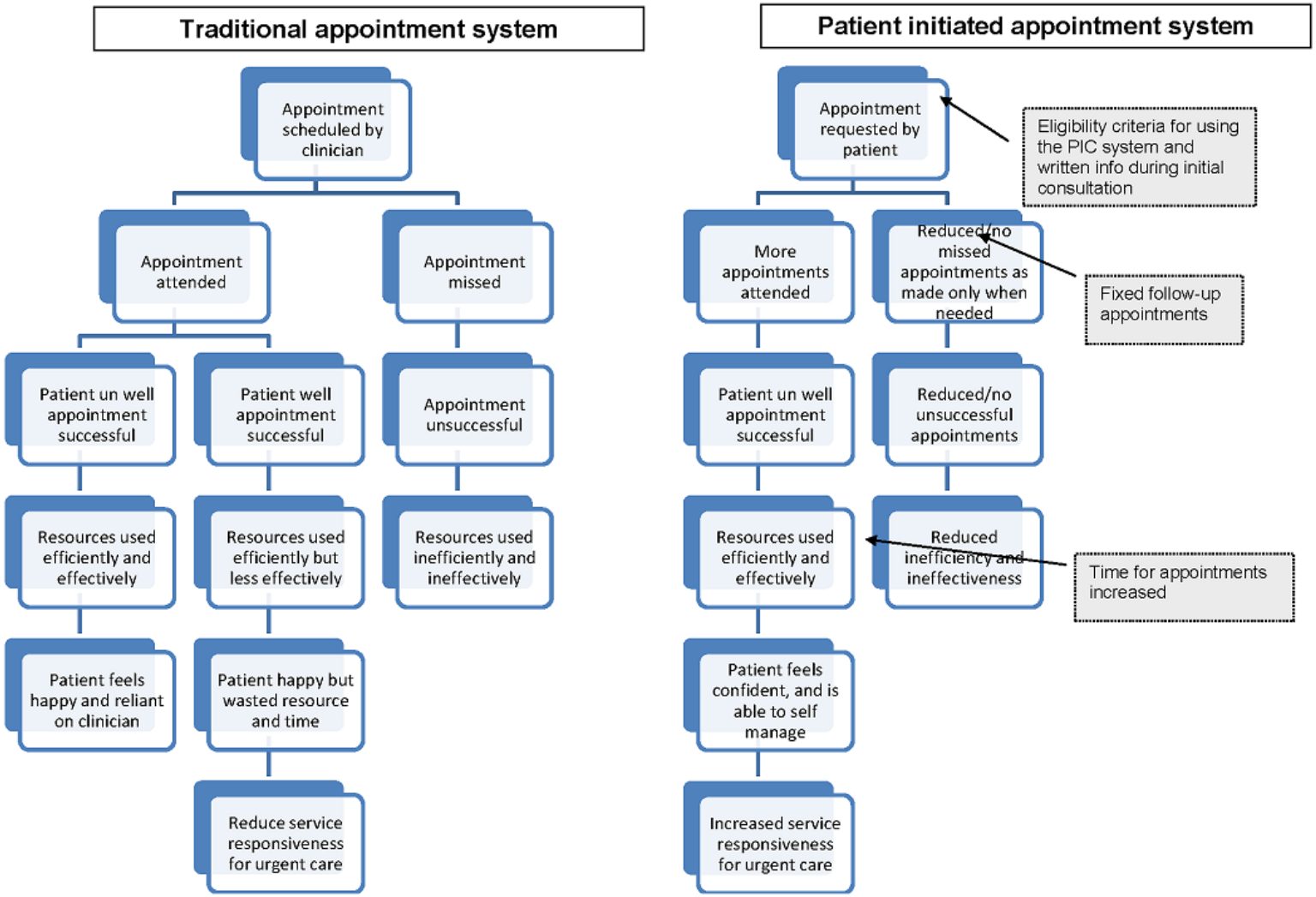
A priority briefing exercise was undertaken between October 2009 and February 2010 by the Collaboration for Leadership in Applied Health Research and Care for the South West Peninsula (PenCLAHRC, 2010a) in order to guide stakeholders in prioritising topics for research. One of the 12 questions of interest was 'How can patient-initiated clinics be implemented for RA given the demonstration of the acceptability, effectiveness and cost-effectiveness of such service organisation?' (PenCLAHRC, 2010b). As a result of this exercise a systematic review was undertaken by Whear *et al.,* (2013) synthesising the clinical effectiveness of patient-initiated clinics for patients with chronic or recurrent conditions managed in secondary care.

Whear *et al.,* (2013) identified 10 articles describing eight individual studies; seven were RCTs and one a retrospective audit. These studies included a total of 1927 participants, across three conditions, breast cancer (n=3), irritable bowel disease (IBD) (n=3) and RA (n=2). All were conducted in the UK and participants were followed-up for between 12 and 72 months. The patient-initiated clinics in each of these studies

were broadly similar, with the primary access point a telephone helpline through which patients could request clinical advice and if necessary arrange an outpatient appointment. In three RCTs, two in breast cancer and one in patients with IBD were also given written information about how to self-manage their condition and the symptoms or events that should initiate the need for a consultation. An initial consultation was offered in three RCTs in breast cancer and IBD and an annual review in all studies. A broad range of clinical outcomes was measured across studies and indicated that patient-initiated clinics do not have a significant detrimental impact on relapse in breast cancer and IBD or clinical outcomes over time for patients with RA. There was evidence to suggest that the frequency of meaningful medical interventions such as change in medications or further investigations for patients with RA was greater in those who participated in the patient-initiated clinics. The review also suggested savings in relation to healthcare resource use, healthcare costs and reductions in clinician time as a result of patient-initiated clinics. The authors concluded that UK policy is eager for patient-initiated services, which are evidence-based, to be implemented and evaluated so that the time of both the patient and the healthcare professional is not wasted and costs are minimised without compromising clinical or psychosocial well-being. It is important to note, however, that although the quality of these studies did vary those in RA had less potential for bias in their results than those in breast cancer and IBD as they met more of the quality criteria guidelines outlined by the Centre for Reviews and Dissemination (2009). This included specification of eligibility criteria, a power calculation, details of the sample at baseline, descriptions of co-interventions, they accounted for all participants and conclusions were supported by their results.

The authors of this systematic review proposed a logic model for the theory behind both traditional and patient-initiated clinic appointments systems (Figure 2.5). The model suggests that the traditional review system is more likely to lead to inefficient and ineffective use of resources due to people who DNA and because stable, well patients are being seen in clinic. Although this may lead to a happier patient in the short-term it could lead also to services being less responsive to urgent cases, whereas a patient-initiated service would mean unwell patients could be seen more frequently and a reduction in DNAs because stable patients are not required to attend

unnecessarily. Therefore, resources are being used more efficiently and effectively. The model however, does fail to acknowledge the possibility that patient-initiated services may lead to unwell patients going unnoticed by the service as they do not make contact with the rheumatology team or GP and hence deteriorate further, leading to concerns about patient well-being both clinically and psychologically.



Source Whear *et al.,* (2013)

Figure 2.5. Logic model of traditional and patient-initiated clinic systems

Examining in more detail the two studies in RA, within Whear *et al*'s (2013) systematic review, may shed further light on this issue and provide further evidence in relation to the current thesis. Of these two studies, one was a 6 year RCT (Hewlett *et al.,* 2000; Kirwan *et al.,* 2003b; Hewlett *et al.,* 2005b) and the other a retrospective audit conducted by Chattopadhyay and Hickey (2008).

The long-term follow-up RCT undertaken by Hewlett *et al.,* (2000, 2005b) and Kirwan *et al.,* (2003b) compared what authors initially called "a direct access group", then "shared care" and later a "patient-initiated service" with rheumatologist-initiated care. Participants in the patient-initiated service could arrange reviews with a rheumatologist, physiotherapist, or occupational therapist through a nurse-led telephone helpline. The GPs of patients in this group were already monitoring DMARD therapy in this locality, but were also given information to support the day-to-day management of patient care and could also initiate reviews with the rheumatology team. The control group received traditional routine hospital reviews with their rheumatologist every three to six months. Analysis of the self-referrals at the end of year one indicated that participants given open outpatient appointments were able to appropriately self-refer. There remained a risk, however, that a small percentage of patients were not using the system when needed (Hogg, Hewlett, & Kirwan, 1997). Comparisons between those who requested a hospital review and those that didn't up to 2 years post-implementation indicated that those who did self-refer were significantly worse, both physically and psychologically at the start and throughout the trial than those who did not self-refer, again confirming the patient's ability to initiate care from their rheumatology team appropriately (Hewlett, Mitchell, & Kirwan, 1999). Comparison between the intervention and control group on disease deterioration confirmed that there was no difference between the two groups (Mitchell, Hewlett, & Kirwan, 1999).

Analysis comparing the patient-initiated group with the control group 2 years after the implementation of the programme suggested a 43.8% difference in consultant reviews, with the patient-initiated service resulting in fewer visits (Hewlett *et al.,* 2000). Despite this, levels of pain were significantly lower in the patient-initiated group at 24 months, self-efficacy was also significantly greater in this group at 6, 15, 18 and 21 months into

the trial and increases in pain were significantly lower (+0.4) compared to control participants (+1.6). There were, however, no significant differences between groups on changes in disability, anxiety or depression, although there were trends in favour of the patient-initiated group. Participants were also more satisfied with the service when asked to look back over the previous 2 years and more confident in the system than those in the control group (Hewlett *et al.,* 2000). At 4 and 6 years post-intervention patient satisfaction with outpatient care declined in the control group but improved significantly in the patient-initiated group. A similar pattern was exhibited for patient confidence in the service (Kirwan *et al.,* 2003b; Hewlett *et al.,* 2005b) and after 6 years, satisfaction with and confidence in care were significantly greater in the patient-initiated group, which also had 38% fewer hospital appointments. Importantly there were no differences between the traditional review and patient-initiated service on either clinical or psychological outcomes, suggesting that this responsive model of care is not clinically detrimental and, therefore, warrants further consideration in the management of patients with arthritis (Hewlett, 2005). This new system seems to be running efficiently as part of standard care for patients with RA at Bristol Royal Infirmary and is managed by the existing nurses. This has enabled the system to reduce any unnecessary outpatient appointments and fast-track urgent ones. Patients also report feeling more empowered to manage their problems for longer at home as they know rapid help is available if necessary (Pope, Tipler, Kirwan, & Hewlett, 2005). It is unclear, however, how much contact and initiation of services was driven by the patient and what was initiated by the GP.

The second study in RA included in Whear *et al*'s. (2013) systematic review was an audit of one UK hospital in which patient-initiated clinics were standard care. Data were compared to that of another hospital which utilized a traditional review system (Chattopadhyay & Hickey, 2008). The records of 173 outpatient follow-up appointments were reviewed, 113 were traditional reviews and 60 patient-initiated appointments. A majority of patients had inflammatory arthritis (61.8%). The patient-initiated clinic was associated with a significantly higher rate of overall medical interventions – 96.7% compared to 52.2%, and higher rates of "meaningful" intervention – 66.7% compared to 30.1%. Time between appointments did not differ significantly between the two groups and the authors report no inappropriate

accessing of services in the patient-initiated clinic. The authors calculated that the patient-initiated service lead to an increase of approximately 25% more new patient throughput. This however, was a conference abstract and it is, therefore, unclear what the patient-initiated service consisted of. Also, selection bias introduced by comparing two hospital settings with potentially very different patient populations and care guidelines introduces the possibility that confounding variables may account for these differences.

In addition to the articles identified in Whear's systematic review, there are three additional studies which have since been published (Adams & Sands, 2009; Sands & Adams, 2009; Primdahl *et al.,* 2014; Primdahl *et al.,* 2012; Primdahl *et al.,* 2011b; Symmons *et al.,* 2005; Symmons *et al.,* 2006). These articles evaluated three different types of patient-initiated services. Both Primdahl *et al.,* (2014) and Symmons *et al.,* (2005; 2006) trialled a shared care service similar to that of Hewlett *et al.,* (2000, 2003b, 2006b), in which both patients and GPs were able to initiate reviews with the rheumatology team and GPs monitored medications according to guidelines written by their respective rheumatology departments. Although the description of the service is not entirely clear the study by Adams and Sands (2009), appears to be the only true patient-initiated service, as only patients are described as being able to initiate reviews with their rheumatology team, with no mention of primary care involvement.

The trial conducted by the British Rheumatoid Outcome Study Group compared a symptom control and shared care (SCSC) intervention with aggressive treatment in a hospital setting (ATH) (Symmons *et al.,* 2006; Symmons *et al.,* 2005). SCSC was managed in primary care with the goal of controlling joint pain, stiffness and related symptoms from the patient's perspective. The patient had no regular scheduled appointment but was "encouraged" to visit the GP if they developed new or deteriorating symptoms at which point the GP used an algorithm to guide their treatment decisions and were asked to contact the rheumatologist if they felt that a change in DMARD or steroid therapy was indicated. DMARD therapy was monitored by the GP using current guidelines for each centre. The ATH arm was managed predominantly in the hospital setting and monitoring of the DMARD therapy continued as usual. The patient attended the hospital clinic at least once every 4 months where

ESR, CRP and the number of swollen joints were measured. Of the 404 participants randomised at baseline, 3 years after implementation there were no significant differences between the patient-initiated service and the more aggressive hospital based system on levels of disability, disease status, pain, quality of life or patient satisfaction. An assessment of healthcare utilisation and cost-effectiveness, however, found that SCSC lead to fewer outpatient appointments and GP visits. The differences were, however, extremely small and it was unclear if they were statistically significant. Despite this SCSC was likely to be more cost-effective than ATH in 60–90% of cases, (Davies *et al.,* 2007), suggesting that even this small reduction in healthcare utilisation impacted on the cost of care.

As described in section 2.5.3.1 (page 65) Primdahl *et al.,* (2014) compared a rheumatologist-led care (n=92) with a nurse-led (n=90) and shared-care service (n=94) in a three arm RCT. Shared-care involved no planned consultations with the rheumatology team, the GP monitored blood tests and the patient could contact either the GP or CNS when required. The GP could also make contact with the rheumatology department and use the nurse-led telephone helpline for advice or specialist reviews. Comparisons between the rheumatologist and nurse-led service are discussed in section 2.5.3.1 (page 65); no comparisons were made between the nurse-led service and shared-care. Analysis at the end of the 2 year follow-up period found no significant differences in disease activity, self-efficacy, satisfaction or confidence in the service between rheumatologist-led and shared care over time. Although significantly fewer patients in the shared-care service had their blood tests taken at the planned intervals compared to the rheumatologist-led group, there was no difference in the number of out-of-range blood tests or alerts, defined as significant changes in RA disease activity or functional disability, or any other patient safety measure including death, number of telephone consultations and initiation of biological treatments. This suggests that shared-care and rheumatologist-led services were equal in regards to psychosocial and a majority of clinical outcomes, but there may be concerns about attendance for blood tests.

A comparative pragmatic mixed methods study of a patient- versus physician-initiated review service that had been running for 4 years was also evaluated by Adams and Sands (Adams & Sands, 2009; Sands & Adams, 2009). Retrospective questionnaire data

were collected from 88 patients with RA who were referred into the service, along with qualitative data from 12 additional patients. Data from these patients were then compared to those receiving conventional follow-up at the same rheumatology unit. Participants had only experienced the system from which they were recruited and this depended on which rheumatologist was responsible for their care. Comparisons between the two groups indicated no significant difference in well-being, mood, satisfaction or confidence in the services. Participants in the physician-initiated service saw the doctor almost twice as often as those in the patient-initiated group; however, it is unclear which doctor the authors are referring to, the GP or rheumatologist. The design of this trial, however, introduced significant bias as there was no randomisation and hence the variation in the care received from the rheumatologist may have significantly affected the results of the trial. The lack of measurement prior to the service starting also means that it is unclear whether any changes occurred over time or if there were groups differed at baseline which could explain the lack of difference found at follow-up. Analysis of the semi-structured interviews, however, suggested that patients initiating their own follow-up felt that their appointments were less rushed and they were more satisfied with the continuity of their care.

A larger implementation trial is currently being undertaken by Paudyal, Perry, Child and Gericke (2012) at Plymouth Hospitals NHS Trust using a stepped-wedge design. Researchers are randomising 380 patients who have had RA for more than 2 years and are able to initiate telephone contact if needed, to either a patient-initiated service or to a regular clinician-initiated review group. The patient-initiated service will include patient education about the system prior to their enrolment in the service and patients will not have routine clinical reviews with their consultant rheumatologist. Their GP will be informed about this and sent a short summary of managing the common problems experienced by people with established RA. Clinical advice and requests for a review will be managed via a nurse-led telephone advice line. The evaluation will compare the groups on patient satisfaction, clinical outcomes and healthcare utilisation over a 12 month period, at which point all patients in the control arm will be transferred to the patient-initiated service. This will provide further evidence either for or against the use of patient-led rheumatology services.

Although the quality of the studies evaluating patient-initiated services are mixed, good quality RCTs indicated at least equality, if not significant benefits to patient-initiated services compared with standard consultant-led care. In support of Whear *et al.,* (2013), although UK policy may be eager to implement patient-initiated services, robust evaluations are still needed in order to provide an quality evidence base for this model of care so that the time of both patients and healthcare professional is used efficiently and effectively without compromising clinical care or psychological well-being.

There are, however, a number of important issues which should be highlighted in relation to the "patient-initiated" services described above. With the exception of Adams and Sands (2009), all of these interventions were a combination of both patients and GPs initiating rheumatology services and were not wholly patient-initiated. In addition an important element of any patient-initiated service is the information participants are given about the symptoms or events that should trigger contact with the clinical team. An implicit or explicit assumption is made within all of these trials that patients will use their experience of symptoms and side effects as triggers for contacting a healthcare professional. These triggers are vital given that their sensitivity could lead to over utilization of services or a potentially dangerous situation where a patient does not contact a healthcare professional when they are seriously unwell. In some trials more detail is provided about these triggers than others; however, most are not described in sufficient detail to be evaluated. Pope *et al.,* (2005) reported that after a period of running the patient-initiated service evaluated by Hewlett *et al.,* (2000, 2003b, 2006b), a patient education session was deemed necessary for those joining the service. A 90 minute session was, therefore, developed which sought to address a number of key objectives including understanding how and when to request an appointment with the CNS or doctor. This included "recognising the obvious and less obvious reasons why they may request a clinic appointment" which the authors describe as recognising and managing an inflammatory flare of RA. This is likely to include the self-monitoring of symptoms and side effects which are persistent and unmanageable, indications of a possible disease flare (Hewlett *et al.,* 2012). The service currently being evaluated by Paudyal *et al.,* (2012) is also using this approach. Primdahl *et al.,* (2014) delivered a short course to

participants in all three arms of their trial, prior to randomisation. This consisted of two sessions of 3 hours delivered by a multidisciplinary team. The course aimed to enhance patient self-efficacy to manage disease-related problems in everyday life and to know when and how to seek help from healthcare professionals. Topics included how to detect a flare-up, the medical treatment including how to manage it and possible side effects, how to self-manage common problems like pain, fatigue, joint stiffness and poor sleep. Details about the remaining studies are unclear.

It is important to describe the active content of any intervention in order to aid replicability and identify the active ingredients that bring about a desired change in behaviour (Craig *et al.,* 2008). Therefore, future trials of patient-initiated initiated services should describe in greater detail the content of any additional education sessions or materials along with the specific triggers which patients are required to follow when initiating their care.

2.6 LOCAL SERVICE PROVISION

At the start of this thesis there were 450 patients with RA or PsA on DMARD therapy at UCLH. These patients were managed via a combination of CNS and rheumatologist-led appointments with a small number of patients also being monitored by their GP. The frequency or combination (i.e. alternate visits to the CNS and rheumatologist) of appointments was dependant on the rheumatologist and/or CNS the patient was being managed by, but was driven by a combination of clinical need and capacity. A vast majority of methotrexate monitoring was undertaken in the CNS-led DMARD monitoring clinics. This was despite NHS Camden's published shared care guidelines for methotrexate (Pang & Malhotra, 2009) which invites GPs to participate in these activities.

These shared care guidelines are for patients being treated for moderate to severely active RA or for the treatment of severe psoriasis and were established in order to clarify responsibilities between the specialist team and GP for managing the prescribing and monitoring of methotrexate. The guidelines cover:

1. Who will prescribe methotrexate;

2. Who will monitor;
3. How often blood tests will be conducted and in which location;
4. Which clinician will be responsible for receipt and review of the results;
5. Who will communicate any necessary changes in dose to the patient and the GP;
6. Who will record test results in the Patient-Held Monitoring and Dosage Record booklet

GPs are invited to participate, but if the GP is not confident to undertake these roles, total clinical responsibility for the patient remains with the specialist team at UCLH. The document is also clear about the importance of patients being consulted about the monitoring and treatment plan. The roles and responsibilities for all stakeholders are in summarised in (Figure 2.6), the full shared-care guidelines can be found in Appendix A.

Consultant and CNS

1. Perform baseline tests (FBC, LFTs, U&Es, creatinine, chest X-ray).
2. Initiate and stabilise treatment with methotrexate.
3. Educate patients about methotrexate.
4. Invite GP to participate in shared care.
5. Inform GP of test results, frequency of monitoring, recommended dose and changes to treatment
6. Periodically review the patient's condition and evaluate adverse effects
7. Ensure that clear backup arrangements exist for GPs to obtain advice and support.

General Practitioner

1. Reply to the request for shared care.
2. Monitor patient's overall health and wellbeing.
3. Prescribe methotrexate at the dose recommended.
4. Ensure that the patient understands dose and adverse effects.
5. Monitor blood counts, hepatic and renal function at recommended frequencies as described, and inform consultant if abnormal.
6. Offer annual influenza vaccination to the patient.

Patient

1. Report to the specialist or GP if he or she does not have a clear understanding of the treatment.
2. Share any concerns in relation to treatment with methotrexate.
3. Inform specialist or GP of any other medication being taken, including over-the-counter products.
4. Report any adverse effects or warning symptoms to the specialist or GP.

Primary Care Trust

1. To support GPs to decide whether or not to accept clinical responsibility for prescribing.
2. To support Trusts in resolving issues that may arise as a result of shared care

Figure 2.6. NHS Camden Shared Care Guideline for methotrexate – roles and responsibilities

These shared care guidelines state that regular monitoring should take place in accordance with the BSR/BHPR clinical guidelines for monitoring methotrexate (Chakravarty *et al.,* 2008). This includes full blood count, urea, electrolytes and liver function tests monitored fortnightly until the dose of methotrexate and monitoring is stable for 6 weeks, then monthly thereafter until the dose and disease is stable for 1 year. The monitoring may then be reduced in frequency to every 2 to 3 months, based on clinical judgement with due consideration for risk factors for example age, comorbidity and renal impairment. The frequency of monitoring advised by the specialist to the GP may vary from the above recommendations depending on patient factors.

Despite this shared care approach at the start of this research a very small proportion of the GP practices in Camden PCT had taken on the role of monitoring. As GPs were reluctant to take on the monitoring and/or the prescribing of methotrexate these activities remained in the CNS-led DMARD monitoring clinics based at UCLH. The capacity of these DMARD monitoring clinics continued to be stretched and alternative models of care, therefore, needed to be considered to meet the needs of patients. As a patient-initiated service is the only model of care designed to reduce overall contact with healthcare professionals rather than redirect patients to other services this was deemed a viable option which required further exploration.

The most recent evaluation of the local services was provided by the GP patient survey conducted between July 2012 and March 2013 (NHS England 2013) and the 2012 Outpatient Survey (Care Quality Commission, 2012). Fifteen percent of responders to the GP survey (NHS England 2013) in NHS Camden CCG had arthritis or other long-term joint problem. Of these, 53% felt fairly confident that they could manage their own health (compared to 50% at a national level) and 62% had in the last 6 months received enough support from local services/organisations to help manage their long-term conditions (compared to 65% at a national level). Although the local rates appear to reflect the national picture, there was clearly a need to either develop new services or improve signposting to relevant local organisations in order for a significant proportion of patients with arthritis to feel confident in their ability to manage their condition, both locally and nationally.

The outpatient survey undertaken at UCLH (Care Quality Commission, 2012) indicated that the Trust fell within the worse performing 20% of trusts for: clinic waiting times, providing information on a patient's condition and treatment, allowing patients to find out the results of any tests, the purpose of the medications they were taking, the reasons for any changes in medication, as well as receiving contradictory advice from different healthcare professionals, and not being treated with respect or dignity. The Trust also scored poorly on explaining: the risks and benefits of treatments, the result of any tests, who could be contacted if the patient was worried about their condition or treatment, any danger signs the patient should watch out for. Confidence and trust in the clinical team, sufficient time for the patient to discuss their health and overall

satisfaction with their appointment was also poor. Although these results are not specific to the rheumatology department they suggest that UCLH were potentially not meeting NICE guidelines for RA which state that patients should be offered the opportunity to attend education sessions including self-management (National Institute for Health and Care Excellence, 2013). Steps, therefore, needed to be taken in order to improve the service that was being delivered in outpatients. Only 43% of patients who visited outpatients at UCLH in 2011, however, completed the questionnaire, this may suggest a possible bias towards those responding who had the worst experience. Given these results it is not surprising that one of NHS Camden CCG's key interests is to review the experience of people in outpatients and ensure that patients are seen in the appropriate setting of their choice in a timely manner whilst ensuring that best value for money is achieved (Camden Clinical Commissioning Group, 2013).

A major part of the CNS-led rheumatology run clinics at UCLH at the start of this thesis was the reviewing of blood test results, along with the symptoms and side effects patients were experiencing or had experienced since their last appointment. This supported the findings of Goh *et al.,* (2006) who found that 82.1% of surveyed nurses were frequently undertaking drug monitoring. This raised the question about whether patients could be involved in monitoring their own blood tests and use this information along with their symptoms and side effects as triggers for initiating care from their CNS. This was a way in which the rheumatology service could be more responsive to the needs of established patients and offered an opportunity to make the services more effective and efficient for all.

As stated above the patient-initiated services outlined in section 2.5.6.1 (page 82) used patients' experiences of symptoms and side effects as triggers for initiating care. This thesis would, therefore, be the first trial of patients with arthritis formally monitoring their own blood test results and symptoms and using this information to initiate their own care. As well as being described as patient-initiated services these interventions could also be thought of as patient self-monitoring interventions. In concept analyses of self-monitoring in chronic illness both Song and Lipman (2008) and Wilde and Garvin (2007) identified three closely related components of self-monitoring (i) awareness, (ii)

interpretation and (iii) response. In the context of this thesis a self-monitoring and patient-initiated service would increase a person's awareness of a disease flare, provide them with the knowledge required to understand and interpret these indications and allow patients to respond to changes in their health by taking the necessary steps to initiate care from their rheumatology team. The transfer of monitoring laboratory tests from CNS to patient may seem like a radical step for patients with arthritis; however, the use of formal self-monitoring in chronic illness is widely implemented in other conditions including diabetes and anti-coagulation therapy. A broader synthesis of the literature in relation to formal chronic disease self-monitoring would establish the potential outcomes of the proposed intervention, the results of which are presented in Chapter 3.

2.7 SUMMARY

An assessment of the current state of rheumatology services has identified significant deficits in the provision of care for patients with arthritis. This includes possible unnecessary appointments for those who are feeling well and substantial delays or lack of capacity for those who are feeling worse and need faster attention. This has led to the development of contemporary models of rheumatology care including patient-initiated services. These services reflect the move away from the paternalistic model of healthcare to one which puts the patient at its centre and are integral to rheumatology guidelines. To date this model of care has focused on reducing unnecessary visits to the rheumatologist however; since a majority of DMARD monitoring is now performed by the CNS an alternative model could look to focus on reducing the demand in these clinics. These DMARD monitoring clinics primarily consist of patients with RA and PsA for monitoring of symptoms and side effects as well as blood tests, therefore, if these subjective and objective markers could be used as triggers for a patient-initiated service this would allow established patients to self-monitor at home rather than attend for regular monitoring appointments with their CNS. As formal self-monitoring is not a technique that has been used extensively in rheumatology the next chapter will present a review of the effectiveness of self-monitoring across a range of long-term conditions with regards to healthcare utilisation, psychosocial well-being and clinical outcomes.

CHAPTER 3 - THE IMPACT OF SELF-MONITORING ON HEALTHCARE UTILISATION AND PATIENT REPORTED OUTCOMES ACROSS LONG-TERM CONDITIONS: AN OVERVIEW OF REVIEWS.

3.1 PROLOGUE

The first chapter in this thesis described the clinical features and treatment monitoring requirements of patients with established RA or PsA who are receiving DMARD therapy, along with financial impact of these two conditions on the UK economy. Chapter 2 then went on to explore how current UK government policy has influenced the delivery of services in rheumatology and how patients with arthritis are involved in the care and treatment they receive. These patient-initiated services have been successful in reducing the demand placed on outpatient clinics without compromising clinical and psychological well-being but currently use informal indicators of disease flare as triggers for initiating care. These effects could be enhanced by integrating patients formally self-monitoring their symptoms and side effects along with their blood test results in order to reduce the demand of established patients with RA or PsA on methotrexate in the CNS-led DMARD monitoring clinics. This chapter will present the rationale, methods and results of an overview of reviews exploring the benefits of formal self-monitoring across a range of long-term conditions in order to establish the potential benefits of the proposed service in relation to healthcare utilisation, psychosocial well-being and clinical outcomes.

3.2 BACKGROUND

3.2.1 Self-monitoring in long-term conditions

Monitoring of a long-term physical health condition involves the periodic collection of data which are used to guide the management of the illness and can be done by clinicians, patients or both. Such checks require decisions to be made about what needs to be monitored and when and how to adjust treatment. Poor choices in each of these can lead to poor disease control, poor use of time and dangerous adjustments to treatment (Glasziou, Irwig, & Mant, 2005). The data monitored as part of a long-term

health condition may include clinical tests, physiological signs and symptoms, behaviour and/or emotions. Patients can now be actively involved in monitoring all types of data, enabled by more open access to their own clinical data and the introduction of technology.

Self-monitoring is part of best practice in many long-term conditions. The most established is that of blood glucose self-monitoring (SMBG) in diabetes. To improve glycaemic control patients are advised to undertake regular blood tests and use this information to manage their illness effectively, either by changing their lifestyle, treatment regimen or seeking help from a healthcare professional. SMBG is now part of usual care and is recommended in NICE guidance for the management of type 1 (National Institute for Clinical Excellence, 2010) and type 2 diabetes (National Collaborating Centre for Chronic Conditions, 2008). These recommendations follow meta-analysis suggesting significant reductions in HbA1c as a result of SMBG (Sarol Jr, Nicodemus Jr, Tan, & Grava, 2005; Welschen *et al.,* 2005b; Allemann, Houriet, Diem, & Stettler, 2009; Poolsup, Suksomboon, & Jiamsathit, 2008; Poolsup, Suksomboon, & Rattanasookchit, 2009). The involvement of patients in the monitoring of their illness is also becoming more widespread in other long-term conditions including respiratory conditions such as asthma and COPD, hypertension and in treatments such as anticoagulation therapy. As a result of significant reductions in blood pressure (Cappuccio, Kerry, Forbes, & Donald, 2004; Bray, Holder, Mant, & McManus, 2010; Verberk, Kessels, & Thien, 2011), mortality and severe complications (Christensen, Johnsen, Hjortdal, & Hasenkam, 2007).

3.2.2 Self-monitoring in arthritis

As outlined in section 1.9 (page 37) DMARD therapy in RA and PsA requires monitoring of blood tests, symptoms and side effects. This is commonly undertaken during a nurse-led or consultant-led clinic using a combination of patient self-report and clinical tests. Together these are interpreted by a healthcare professional and when necessary lead to adjustments in treatment, lifestyle or monitoring schedules. However, 30 to 42% of outpatient visits lead to no adjustments to treatment (Mitchell, 2000; Hehir *et al.,* 2001). Consequently, a large proportion of regular monitoring appointments could be eliminated to allow greater capacity for new patients and those with established

arthritis who are in need of an urgent appointment. This could be achieved by empowering patients to take a more active and formal role in the monitoring of their DMARD therapy. This is yet to be implemented in arthritis and hence it is important to establish what the benefits are in relation to healthcare utilisation and psychosocial well-being across other long-term conditions.

3.3 AIMS AND OBJECTIVES

The primary aim of this review was to assess the impact of formal self-monitoring on healthcare utilisation and psychosocial outcomes, with a secondary aim of summarising the effects on clinical well-being. The primary research questions addressed were:

- Do interventions that include self-monitoring reduce healthcare utilisation for patients with a long-term condition?
- Do interventions that include self-monitoring improve patient reported outcomes for patients with a long-term condition?
- To establish whether self-monitoring of blood test results would have any additional benefits or harms in comparison to interventions which included patients monitoring just their symptoms or side effects.

3.4 RATIONALE FOR METHODOLOGY

Due to the amount of literature exploring the effectiveness of self-monitoring in long-term conditions a number of systematic reviews and meta-analyses have been conducted. Therefore, in order to establish whether self-monitoring is associated with significant reductions in healthcare utilisation and improvements in patient reported outcomes across a range of long-term conditions this review will synthesise the evidence from published systematic reviews and meta-analyses, rather than primary research studies.

An overview of reviews is a logical and appropriate next step to a systematic review or meta-analysis, as it allows the findings of separate reviews to be compared and contrasted. The York Centre for Reviews and Dissemination defines an overview of reviews as “a systematic review that includes only other systematic reviews” (Centre

for Reviews and Dissemination, 2009). This report states that the systematic reviews included in the review should have covered most of the primary studies available and are particularly helpful when a review question is very broad and a number of systematic reviews have already been conducted in the area, as is the case for the current review. These overviews aim to provide a summary of evidence from more than one systematic review at a variety of different levels, including the combination of different interventions, different outcomes, different conditions, problems or populations, or the provision of a summary of evidence on the adverse effects of an intervention.

The different inclusion criteria adopted by the various reviews can, however, make their synthesis problematic. Secondary analysis is beset with inherent limitations, the quality of this review will be heavily dependent on the quality of not only the reviews themselves and hence quality assessment will be performed, but also the quality of reporting. In addition individual primary research studies that appear in several of the included reviews will mean that some of the same evidence is included more than once. Despite these possible biases, however, a synthesis of this nature in relation to these specific outcomes will provide a general overview of the benefits of self-monitoring across a range of long-term conditions. If found beneficial this would suggest that formal self-monitoring merits further investigation for people with arthritis.

3.5 METHODOLOGY

3.5.1 Terminology

To clarify, use of the term **primary research study** refers to the individual studies found within each of the included systematic reviews and meta-analyses. **Article** refers to the systematic review or meta-analysis being reviewed within this overview.

3.5.2 Synthesis

This overview follows the methodological guidelines outlined by Smith, Devane, Begley and Clarke (2011) which reflect that of a standard systematic review. The included articles were combined in a systematic review, no statistical analyses or meta-analysis were undertaken. Synthesising the results of all reviews in an area could result in

incorrect conclusions as many of the primary research studies will be included in more than one article potentially biasing the results. In order to measure the degree of overlap the Corrected Cover Area (CCA) (Pieper, Antoine, Mathes, Neugebauer, & Eikermann, 2014) was calculated. This calculation accounts for articles that include a large number of primary research studies and also allows accurate calculation of overlap when different articles include completely different primary research studies. A CCA of 0-5 is considered slight overlap, 6-10 moderate, 11-15 high and >15 very high (Pieper *et al.,* 2014).

A description of the articles is presented, followed by details about the interventions evaluated and their effectiveness. In accordance with reporting guidelines for systematic reviews, a Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist (Moher, Liberati, Tetzlaff, & Altman, 2009) can be found in Appendix B.

3.5.3 Search strategy

The following databases were searched in September 2012 and updated in February 2014. The overall conclusions of the review completed in 2012 did not differ on completion of the update in 2014 and, therefore, what is included here is a synthesis of the most recent publications.

- Via EBSCOHost:
    - CINAHL Plus® full text (1937 to 2014)
    - MEDLINE with Full Text (1948 to February 5, 2014)
    - PsycINFO (from 1806 to 2014)
- Via OVID Online:
    - EMBASE (1996 to 2014 Week 06)
    - Allied and Complementary Medicine (1985 to February 2014)
    - Evidence Based Medicine Reviews (All)[1]
    - Health Management Information Consortium (1979 to November 2013)

[1] ACP Journal Club 1991 to January 2014; Cochrane Register of Controlled Trials January 2014; Cochrane Database of Systematic Reviews 2005 to December 2013, Cochrane Methodology Register 3rd Quarter 2012, Database of Abstracts of Reviews of Effects 1st Quarter 2014, Health Technology Assessment 1st Quarter 2014; NHS Economic Evaluation Database 1st Quarter 2014

The basic search terms used are given in Figure 3.1, with the detailed search strategies for each database in Appendix C.

[self-care **OR** self monitor* **OR** self administer* **OR** self examin **OR** self medicat* **OR** self inject* **OR** self evaluat* **OR** self test* **OR** self adjust* **OR** self measure* **OR** patient participation **OR** patient monitor* **OR** patient manage* **OR** patient adjust* **OR** patient administer* **OR** patient control* **OR** patient cent?d **OR** tele* **OR** home monit**OR***]

[meta-analys* **OR** systematic review **OR** overview **OR** narrative review]

1 **AND** 2

Figure 3.1. Basic search strategy

3.5.4 Inclusion and exclusion criteria

3.5.4.1 Publishing

Articles must have been published in an academic peer reviewed journal or database with an established reporting system (i.e. Cochrane or Health Technology Assessment (HTA)). The article must have been written in English. When either a Cochrane or HTA review also had an accompanying peer reviewed journal article, only the peer reviewed journal article was included unless additional material (i.e. a meta-analysis) was provided in which case only the publication with the additional material was included.

3.5.4.2 Study design

Included articles were either a systematic review or meta-analysis which included primary research studies only. If these articles contained summaries of qualitative studies or secondary data (i.e. other systematic reviews or meta-analyses) this content was not extracted. The article had to have a defined research question and show that reasonable effort was made to identify all relevant literature.

3.5.4.3 Participants

All participants were aged 18 and over exclusively and living with a long-term physical health condition. Defined as “a [physical] condition that cannot, at present be cured; but can be controlled by medication and other therapies” (Department of Health,

2010b). Articles which included more than one long-term physical health condition were excluded in order for data to be summarised within a long-term condition.

3.5.4.4 Interventions

The article had to include interventions where patient self-monitoring was the focus of the review or be an element of all interventions by virtue of the nature of that intervention (i.e. telemonitoring). "Self" refers to patient, not carer or healthcare professional. Self-monitoring was defined as the patient undertaking one or more of the following, using the components identified within the concept analyses by Song and Lipman (2008) and Wilde and Garvin (2007):

- **Awareness**: Measurement of vital signs, symptoms, behaviour or psychological well-being, with the implicit or explicit function of interpreting that data in order to adjust medication, treatment, lifestyle or help-seeking behaviour by either a healthcare professional or the patient.
- **Interpretation**: Interpretation of vital signs, symptoms, behaviour or psychological well-being.
- **Response**: Adjustment of medication, treatment, lifestyle or help-seeking behaviour as a result of awareness and/or interpretation.

Interventions that included the testing of a monitoring device or comparing for example home to office blood pressure monitoring were excluded as these reviews tended to focus on accuracy of the monitored data or performance of technology, which although important was not the focus of this review.

3.5.4.5 Outcomes

The article had to report findings for either healthcare utilisation or a patient reported outcomes, for example quality of life, mood, satisfaction or acceptability. Articles that only included clinical outcomes, cost effectiveness or feasibility outcomes were excluded from this review. Articles that included both clinical outcomes, economic or feasibility and either patient reported or healthcare utilisation were included in this review but the economic and feasibility data were not extracted. Data for clinical outcomes were extracted in order to provide an overview of the evidence and a context in which the primary outcomes could be discussed. This is because any

benefits in relation to healthcare utilisation or psychosocial well-being should be balanced against any potential deterioration in clinical outcomes.

3.5.5 Procedure

3.5.5.1 Initial assessment

After the removal of duplicates and articles not published in English, one reviewer assessed all titles for relevance. Those clearly not related to the research question or inclusion and exclusion criteria were immediately disregarded. Full articles thought to be of relevance were retrieved for review. The retrieved articles were assessed for inclusion by one reviewer and then those judged to be relevant assessed by a second reviewer according to the outlined criteria. Any disagreements were then discussed with a third person and resolved by consensus.

In addition to the above literature search the reference lists of all included articles were examined for relevant titles and the full articles obtained for inspection. The process of second reviewing was then repeated. References were managed in Reference Manager 12.

3.5.5.2 Data extraction

A data extraction form (Appendix D) was designed by the author to assess the following characteristics of the article: illness or disease type, level of self-monitoring (i.e. awareness/interpretation/response), search strategy, inclusion and exclusion criteria, quality assessment, data extraction procedure, total number of studies and participants, author's conclusions and interpretations. The relevant data were extracted and recorded by one reviewer; independent data extraction was also performed on 20% of articles by a second reviewer. Any disagreements were then discussed with a third person and resolved by consensus. The following criteria were applied when data were extracted:

- Quantitative pooling (i.e. meta-analysis) was regarded as possessing greater validity than qualitative synthesis.

- If results were reported inconsistently in different sections of the review, the effects were extracted from the main result section or tables, depending on which was perceived as being more comprehensive and coherent.

3.5.5.3 Review quality

The Assessment of Multiple Systematic Reviews (AMSTAR) checklist was used to assess the quality of the included articles (Shea *et al.,* 2007). This is a systematically developed 11-item measurement tool (Appendix E) which possesses satisfactory inter-observer agreement, reliability, construct validity and feasibility (Shea *et al.,* 2007; Shea *et al.,* 2009). For each criterion, the response is either yes (1 point), no (0 points), can't answer (0 points) or not applicable (0 points). The quality score is the total number of points awarded and, therefore, ranges from 0 (lowest) to 12 (highest). The quality of all articles in this review were assessed by one reviewer and 20% of articles (a different set of articles than the data extraction) were checked by a second reviewer. Any discrepancies were discussed and resolved by consensus with a third reviewer.

3.6 RESULTS

3.6.1 Identified papers

Using the search strategy detailed in Appendix C, a total of 2114 references were retrieved. Figure 3.2 illustrates the selection of articles at each stage of the search strategy. After exclusions based on title alone 320 full articles were then retrieved and after screening 25 were selected for possible inclusion. A total of 25 individual articles were identified in the search, detailing 23 different systematic reviews or meta-analyses. Two reviews had been published twice, both as Cochrane reviews and again as peer reviewed journal articles (Welschen *et al.,* 2005b; Welschen *et al.,* 2005a; McLean *et al.,* 2011; McLean *et al.,* 2012). The papers published by McLean *et al.,* (2011; 2012) contained the same data with no additional material in either publication, therefore, the peer reviewed article (McLean *et al.,* 2011) was selected. The papers by Welschen *et al.,* (2005a; 2005b) did differ as the peer reviewed journal article included a meta-analysis and, therefore, this publication (Welschen *et al.,* 2005b) was retained. Four additional articles were identified as a result of reference list searches, therefore,

a total of 27 articles were included in this overview. Details of the studies excluded and reasons can be found in Appendix F.

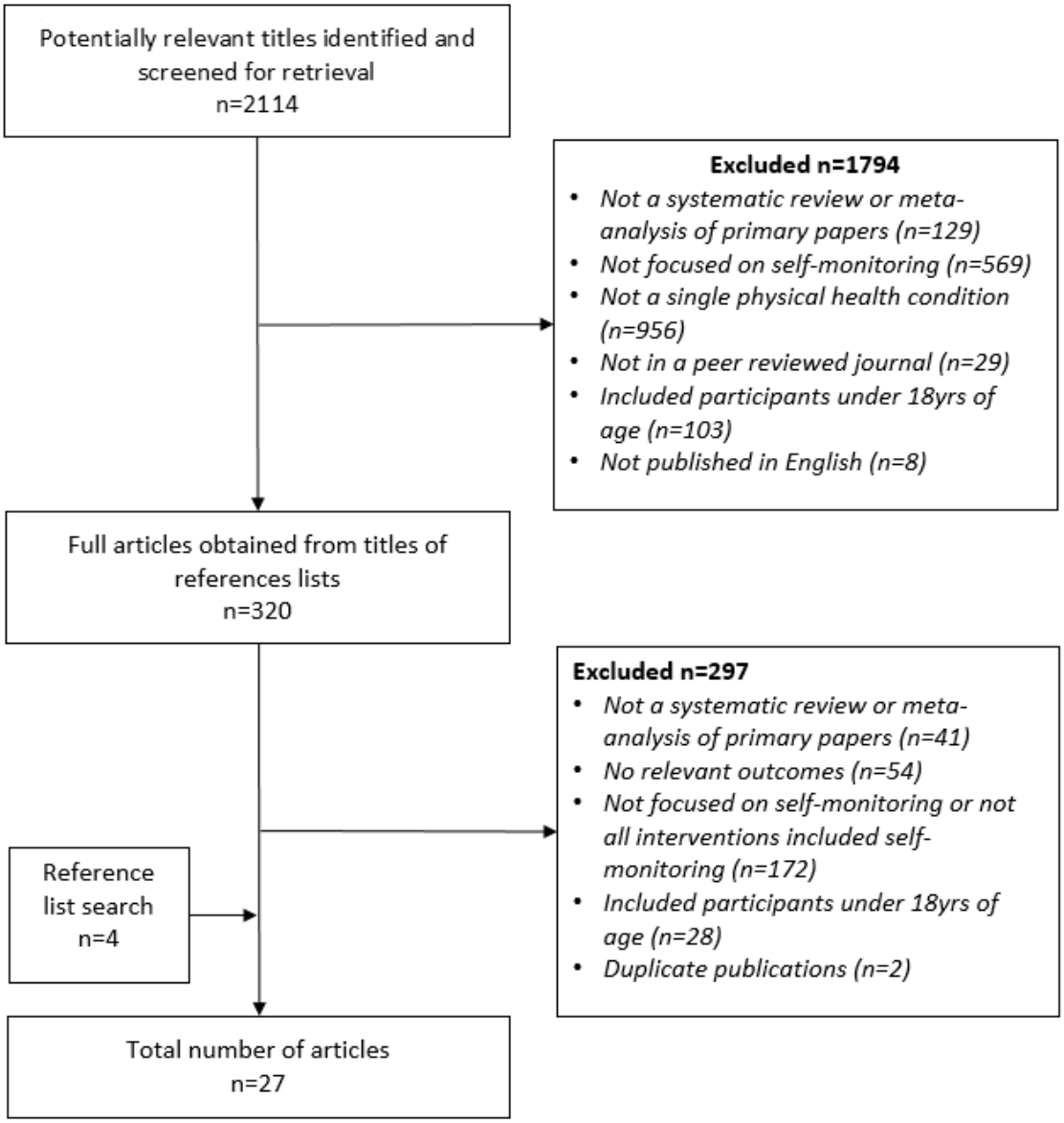


Figure 3.2. Flow chart of article selection

3.6.2 Article characteristics

All article characteristics can be found in Table 3.1.

Table 3.1. Article characteristics – systematic review

Authors, year	Type of review	Aim	Period searched	Inclusion/Exclusion criteria	n primary research studies(n participants)	Primary outcome/s	Quality assessment tool	AMSTAR score
Hypertension								
Jaana, Pare, & Sicotte (2007)	SR	Evaluate the evidence for the effectiveness of hypertension TM.	1966 to 2006	Design: Experimental or quasi-experimental Participants: Chronic hypertension Intervention: Home TM	14(1119)	BP	None	4
AbuDagga, Resnick, & Alwan (2010)	SR & MA	What is the impact of BP TM technologies on clinical, patient-centred outcomes, healthcare utilization & cost?	1995 to September 2009	Design: RCT, single group, quasi-experimental Participants: Established diagnosis of uncontrolled hypertension Intervention: TM	15(3192)	BP	None	4

Authors, year	Type of review	Aim	Period searched	Inclusion/Exclusion criteria	n primary research studies(n participants)	Primary outcome/s	Quality assessment tool	AMSTAR score
COPD								
Turnock, Walters, Walters, & Wood-Baker (2005)	SR & MA	Determine whether action plans alone, or as part of a broader self-management intervention, are an effective way to manage COPD exacerbations.	Not stated	Design: RCT Participants: Diagnosed primary COPD Intervention: Action planning	3(367)	Hospital admissions	Jadad scale & Cochrane	4
McLean *et al.,* (2012)	SR & MA	To review the effectiveness of telehealthcare for COPD compared with face-to-face usual care in improving quality of life & reducing accident & emergency department visits & hospitalisations.	Inception to January 2010	Design: RCT Participants: Diagnosed COPD Intervention: Telehealthcare	10(1307)	Quality of life, healthcare utilisation	Cochrane risk of bias	6

Authors, year	Type of review	Aim	Period searched	Inclusion/Exclusion criteria	n primary research studies(n participants)	Primary outcome/s	Quality assessment tool	AMSTAR score
Heart failure								
Louis, Turner, Gretton, Baksh, & Cleland (2003)	SR	To present the current evidence on TM as a means of reducing hospitalisations in HF.	1996 to 2002	Design: NR Participants: Diagnosed HF Intervention: TM	24(3643)	Acceptability, hospital admissions	None	4
Jovicic, Jolroyd-Leduc, & Straus (2006)	SR & MA	Determine the effectiveness of self-management interventions on hospital readmission rates, mortality & QoL in patients diagnosed with HF.	1966 to Nov 2005	Design: RCT Participants: Hospitalised with diagnosed HF Intervention: Self-management	6(857)	Readmissions, mortality	Author designed	7
Martinez, Everss, Rojo-Alvarez, Pascual, & Garcia-Alberola (2006)	SR	To assess the value of home monitoring for HF patients.	1966 to April 2004	Design: Experimental studies Participants: Not stated Intervention: Home monitoring	42(2303)	Patient acceptability	Jovell & Navarro-Rubio scale	6

Authors, year	Type of review	Aim	Period searched	Inclusion/Exclusion criteria	n primary research studies(n participants)	Primary outcome/s	Quality assessment tool	AMSTAR score
Chaudhry *et al.,* (2007)	SR	In-depth examination of a wide range of TM interventions in HF to find out which components are effective.	1966 to August 2006	Design: Randomized study design Participants: Adults with HF Intervention: Home monitoring	9(3582)	Hospitalization, mortality	Juni *et al* & York Centre for Reviews & Dissemination	5
Clark, Inglis, McAlister, Cleland, & Stewart (2007)	SR & MA	To determine whether remote monitoring without regular clinic or home visits improves outcomes for patients with CHF.	Jan 2002 to May 2006	Design: RCT Participants: HF, living at home Intervention: Remote monitoring	14(4264)	Hospitalization, mortality	Cochrane	8
Dang, Dimmick, & Kelkar (2009)	SR	Examine the evidence base for home telehealth & remote monitoring interventions in the management of HF.	1966 to April 2009	Design: RCT Participants: HF Intervention: Home telehealth & remote monitoring	9(2017)	Hospitalization, mortality	Adapted Hailey *et al* which was adapted from Jovell & Navarro-Rubio scale	5

Authors, year	Type of review	Aim	Period searched	Inclusion/Exclusion criteria	n primary research studies(n participants)	Primary outcome/s	Quality assessment tool	AMSTAR score
Klersy, De Silvestri, Gabutti, Regoli, & Auricchio (2009)	SR & MA	Assess the effect of remote patient monitoring on the outcome of CHF patients.	Jan 2000 to October 2008	Design: RCT, OB cohort studies Participants: CHF, living at home Intervention: Remote patient monitoring	32(8612)	Hospitalization, mortality	CONSORT & STROBE	6
Maric, Kaan, Ignaszewski, & Lear (2009)	SR	Review studies conducted in HF TM, which are not telephone based, but utilize the concept of patient self-monitoring in HF.	Inception to August 2007	Design: Any Participants: HF Intervention: Use of technology or device to assist in self-monitoring	56(NR)	Hospitalization	None	2
Polisena *et al.,* (2010)	SR & MA	Conduct a SR & MA to look at clinical outcomes, patient QoL & the use of healthcare services for home TM compared to usual care for patients with CHF.	1998 to 2008	Design: RCT, OB Participants: CHF Intervention: Home TM	22(3028)	Hospitalization, mortality	Adapted version Jovell & Navarro-Rubio scale	5

Authors, year	Type of review	Aim	Period searched	Inclusion/Exclusion criteria	n primary research studies(n participants)	Primary outcome/s	Quality assessment tool	AMSTAR score
Inglis *et al.,* (2010)	SR & MA	To review RCTs of STS or TM compared to standard practice for patients with CHF.	From 2006 onwards	Design: RCT Participants: CHF, within the community Intervention: STS or TM	30(10490)	Hospitalization, mortality	Author designed	9
Clarke, Shah, & Sharma (2011)	MA	To assess the effectiveness of TM on primary & secondary outcomes.	From January 1969 to October 2009	Design: RCT Participants: CHF Intervention: TM	13(NR)	Hospitalization, mortality	None	5
Ciere, Cartwright, & Newman (2012)	SR	To examine whether the introduction of telehealth leads to an increase in self-care behaviour or potential precursors of self-care behaviour (i.e. knowledge, self-efficacy) in CHF patients.	Inception to August 2010	Design: RCT, cohort, case controlled trial Participants: CHF Intervention: Telehealth	12(943)	Knowledge, self-efficacy, self-care	Adapted version of the Effective Public Health Practice Project's Quality Assessment Tool for Quantitative Studies & additional items from Downs & Black's checklist	6

Authors, year	Type of review	Aim	Period searched	Inclusion/Exclusion criteria	n primary research studies(n participants)	Primary outcome/s	Quality assessment tool	AMSTAR score
Giamouzis *et al.,* (2012)	SR	To assess whether TM provides any substantial benefit in patients with HF.	Inception to November 2011	Design: RCT Participants: CHF Intervention: TM	12(3877)	Mortality, healthcare utilisation	None	3
Pandor *et al.,* (2013)	SR & MA	To determine whether remote monitoring strategies improve outcomes for adults who have been recently discharged (<28 days) following an unplanned admission due to HF.	2008 to January 2012 (plus papers from 2 earlier reviews)	Design: RCT, OB cohort studies Participants: Adults, HF, discharged from hospital with <28days Intervention: Remote monitoring	21(6317)	All-cause mortality	Criteria based on The Delphi list & The Newcastle-Ottawa Scale	6
Thrombophilia								
Siebenhofer, Berghold, & Sawicki (2004)	SR	Conduct a SR of controlled & RCTs, comparing self-managed patients to patients under routine care provided by GPs or a special haemostasis care unit.	1966 to Jan 2003	Design: RCT Participants: Those taking oral anticoagulants Intervention: Self-management	4(1547)	Haemorrhage & thromboembolic events	Adapted version of Cochrane & Jadad & Schulz	6

Authors, year	Type of review	Aim	Period searched	Inclusion/Exclusion criteria	n primary research studies(n participants)	Primary outcome/s	Quality assessment tool	AMSTAR score
Connock *et al.,* (2007)	SR & MA	To examine the clinical effectiveness & cost-effectiveness of self-testing & self-management of oral anticoagulation treatment compared with clinic-based monitoring.	1966 to September 2005	Design: RCT & non-RCT Participants: Not stated Intervention: Patient self-testing & self-management	24(5567)	Haemorrhage & thromboembolic events	Authored designed for RCTs, Khan *et al.,* (2001) for non-RCTs	6
Garcia-Alamino *et al.,* (2010)	SR & MA	To evaluate the effects of self-monitoring or self-management of oral anti-coagulation therapy compared to standard monitoring.	1966 to Nov 2007	Design: RCT & cross-over trials Participants: On oral anticoagulation therapy Intervention: Self-monitoring or self-management	18(4723)	Haemorrhage & thromboembolic events	Cochrane & GRADE scale	10

Authors, year	Type of review	Aim	Period searched	Inclusion/Exclusion criteria	n primary research studies(n participants)	Primary outcome/s	Quality assessment tool	AMSTAR score
Bloomfield *et al.,* (2011)	SR & MA	To determine whether patient self-testing, alone or in combination with self-management is more effective & safer than usual care.	2005 to 2010 (+ references from a pre 2005 review)	Design: RCT Participants: Adult outpatients receiving long-term (>3 months) oral anticoagulation therapy Intervention: Self-testing	29(8413)	Mortality, haemorrhage & thromboembolic events	Schulz *et al.,* 1997	8
Diabetes								
Welschen *et al.,* (2005b)	SR & MA	To assess the effects of SMBG relative to usual care without SMBG on glycaemic control, QoL & well-being, patient satisfaction & hypoglycaemic episodes in patients with NID T2DM.	Inception to Sept 2004	Design: RCT Participants: NID T2DM Intervention: SMBG	6(1285)	HbA1c	Maastricht-Amsterdam score list	8
McGeoch, Derry, & Moore (2007)	SR	Is there evidence to support a clinical algorithm for identifying T2DM patients who will benefit from SMBG?	Jan 1990 to Nov 2006	Design: RCT (lasting at least 6 months), OB Participants: NID T2DM Intervention: SMBG	17(81901)	HbA1c	Author designed	5

Authors, year	Type of review	Aim	Period searched	Inclusion/Exclusion criteria	n primary research studies(n participants)	Primary outcome/s	Quality assessment tool	AMSTAR score
Kleefstra *et al.,* (2009)	SR	Review trials investigating the effects of SMBG in NID T2DM patients on glycaemic control, QoL & satisfaction.	Inception to June 2009	Design: RCT Participants: NID T2DM Intervention: SMBG	9(2532)	HbA1c	Maastricht-Amsterdam score list	6
Clar, Barnard, Cummins, Royle, & Waugh (2010)	SR & MA	To examine whether or not SMBG is worthwhile, in terms of glycaemic control, hypoglycaemia & QoL in patients with T2DM who are not treated with insulin or who were on basal insulin combination with oral agents.	1996 to April 2009	Design: OB Participants: Adults, T2DM Intervention: Self-testing of BG	66(146148)	HbA1c	QUOROM & CONSORT statements	5
Malanda *et al.,* (2012)	SR & MA	To assess the effects of SMBG in patients with NID T2DM.	Inception to July 2011	Design: RCT Participants: NID T2DM Intervention: SMBG	12(3170)	HbA1c	Cochrane	7

AMSTAR – Assessing the Methodological Quality of Systematic Reviews; BP – Blood Pressure; CHF - Chronic Heart Failure; CONSORT - Consolidated Standards of Reporting Trials; COPD - Chronic Obstructive Pulmonary Disease; HF- Heart Failure; MA – Meta-Analysis; NID – Non-Insulin Dependent; NR – Not Reported; OB – observational; QoL – Quality of Life; RCT – Randomised Controlled Trial; SMBG – Self-Monitoring Blood Glucose; SR – Systematic Review; STROBE - Strengthening the Reporting of Observational studies in Epidemiology; STS – structured telephone support; T2DM – Type 2 Diabetes Mellitus; TM – telemonitoring; QUOROM - Quality of Reporting of Meta-analyses; RM – remote monitoring

3.6.2.1 Content and structure

Eleven of the 27 articles were a systematic review only and 16 included a meta-analysis. The articles were published between 2003 and 2013 and the primary research studies between 1986 and 2011.

The articles reviewed interventions in five long-term conditions; heart failure (n=14), diabetes (n=5), thrombophilia (n=4), COPD (n=2) and hypertension (n=2). Three hundred and twenty-one primary research studies were reviewed across all five conditions, within each condition the total number of primary research studies ranged from 15 in COPD to 162 in heart failure (Table 3.2). There was no significant correlation (p>0.20) between year of publication and number of primary research studies either when looking at all articles together or within each long-term condition.

The overall CCA across all five long-term conditions was 2.66%, which represented slight overlap. There was variation within each long-term condition. Articles in thrombophilia and hypertension had a very high level of overlap according to Pieper *et al*'s. (2014) criteria, in heart failure the overlap was moderate and in diabetes high. The articles in COPD had no duplicate primary research studies as one article was a review of action planning and the other telehealthcare (Table 3.2).

Table 3.2. Summary of included systematic reviews and meta-analyses

Condition	Articles	Total n of primary research studies	Intervention	Primary outcomes	Monitored data	CCA
Hypertension	2	26	Home blood pressure monitoring	BP	BP	15.38%
COPD	2	15	Action planning & telehealthcare	Hospitalisation	Symptoms	0%
Heart failure	14	162	Telemonitoring	Hospitalisation	Symptoms, weight	6.55%
Thrombophilia	4	38	Self-management	Haemorrhage & thromboembolic events	INR	31.58%
Diabetes	5	80	Self-monitoring	HbA1c	Glucose	13.75%

BP – Blood Pressure; CCA - Corrected Cover Area; COPD – Chronic Obstructive Pulmonary Disease; FEV - Forced Expiratory Volume; HbA1c - Glycated Haemoglobin; INR - International Normalized Ratio

3.6.2.2 Study designs

Fifteen articles included only RCTs, the remaining articles included a combination of study designs including RCTs, experimental or quasi-experimental designs, single group, observational and cohort studies and case controlled trials. One article did not report study designs (Louis *et al.,* 2003).

3.6.2.3 Outcome measures

Healthcare utilisation was reported in 17 articles and included a combination of data on overall and disease-specific hospital admissions, length of hospital stay, A&E visits, GP and outpatient appointments. PROMS such as patient satisfaction, quality of life, acceptability and mood were reported in 22 articles. All articles also reported on at least one clinical outcome as well.

3.6.3 Participant characteristics

The total number of participants included in each article was not always clearly reported and due to poor reporting in some cases could not be calculated from the sample sizes of each primary research study. From the data that could be extracted, within each condition the total number of included participants ranged from 367-1307 in COPD to 1285-146148 in diabetes. Articles focusing on diabetes and those which included a range of study designs tended to include more participants (Table 3.1).

Within each condition there was diagnostic consistency in the type of patients included. In hypertension participants were those diagnosed with high blood pressure; however, the definition of high blood pressure did differ between primary research studies. Articles in heart failure and COPD focused on those with a clinical diagnosis. In diabetes, on the whole articles included only patients with non-insulin dependent type 2 diabetes. In the thrombophilia the participant inclusion criteria were more diverse often including patients with any indication, but primarily mechanical heart valve and atrial fibrillation. The reporting of participant characteristics, such as the age, gender and prescribed medication or treatment was inconsistent across all five long-term conditions and in many cases not reported at all.

3.6.4 Intervention characteristics

3.6.4.1 Eligibility and completion rates

Fifteen articles provided detail on the proportion of patients eligible to take part in the primary research studies (n=1) and/or the number who completed the studies or withdrew (n=12) and two reported both. The proportion of patients eligible to take part in these trials were relatively high, as were completion rates (Table 3.3).

Table 3.3. Primary research study eligibility and completion rates

First author, year	Intervention	n papers (n participants)	Follow-up time	Results
Hypertension				
Jaana, 2007	BP TM	14(1119)	Study duration ranged from 5 days to 12 months	• 1 study reported a withdrawal rate of 15% in the intervention and 8% in control group. In another 50% of the patients were willing to stay in the trial to the end of the year.
COPD				
Turnock, 2005	Action planning	3(367)	6 months & 1 year	• 87% completed the studies. • Dropout rate ranged from 4.4% to 18.8%
McLean, 2011	Telehealthcare	10(1307)	3, 6 and 12 months	• In 1 RCT only 57% of patients finished the intervention arm at 12 months.
Heart failure				
Clark, 2007	TM or STS	14(4264)	Range 2 months - 400 days	• % lost to follow-up ranged from 0-11%
Polisena, 2010	TM	22(3028)	Ranged 30 days - 1 year	• The number of patients who withdraw from the studies ranged from 0 to 29%
Inglis, 2010	STS or TM	30(10490)	Range 3-18 months	• Mean % lost to f/u was 7.6% (range 0 to 26%)

First author, year	Intervention	n papers (n participants)	Follow-up time	Results
Thrombophilia				
Connock, 2007	PST or PSM	24(5135)	Range 2-43.6 months	• More patients dropped out of the PSM/PST group (2-42%) than in the control group (0-10%) in 10 of the 11 trials that compared PSM/PST with usual care. • Patients who withdraw during or after training for self-testing tended to be older and female.
Garcia-Alamino, 2010	PST or PSM	26(4723)	Duration of study 3-19 months	• The average % of people that could or would not take part in the trials was 68% (range 31-88%). • 24.9% (range 0-57.3%) of the intervention group did not complete. • Main reasons for drop-out were: problems with the device, physical limitations preventing self-testing and problems attending the training assessments or failing the assessment.

First author, year	Intervention	n papers (n participants)	Follow-up time	Results
Bloomfield, 2011	PST or PSM	29(8413)	Duration of follow-up was less than 12 months in 13 studies	• The % of patients who were screened and met preliminary eligibility criteria, who successfully completed the training and agreed to be randomly assigned, was less than 20% in 4 studies, between 20-50% in 7 studies and greater than 50% in 3 studies. 8 studies did not report this information. • Among participants who were randomly assigned, the % continuing the intervention ranged from 64-98%.
Diabetes				
Welschen, 2005b	SMBG	6(1285)	Range 6 months-44 weeks	• 5 studies had an "acceptable" withdrawal/dropout rates. • 1 study reported a drop-out rate of >40% which was considered non-acceptable
Kleefstra, 2009	SMBG	9(2532)	Study duration range 6-12 months	• Rated as acceptable in 8 RCTs
Clar, 2010)	SMBG	85(169919)	Range 12 weeks-30 months	• Ranged from 0-45% in RCTs

First author, year	Intervention	n papers (n participants)	Follow-up time	Results
Malanda, 2012	SMBG	16(2795)	Study duration 26 weeks-12 months	• Drop-out was rated as low risk of biasing the results for 11 articles, high for 3 and unclear in 2.

BP – Blood Pressure; COPD – Chronic Obstructive Pulmonary Disease; PSM – Patient Self-Management; PST- Patient Self-Testing; RCT – Randomised Controlled Trial; SMBG –Self-Monitoring of Blood Glucose; STS – Structured Telephone Support; TM - Telemonitoring

3.6.4.2 Type of intervention

Characteristics of the interventions can be found in Table 3.4. Articles in hypertension explored the effects of home-based blood pressure monitoring, all five diabetes articles explored the use of blood and/or urine glucose self-monitoring and in thrombophilia interventions were either self-testing or self-management. In the former patients perform the International Normalized Ratio (INR) test, which is a test of how well a particular dose of the anticoagulants are working. If the INR is too high, blood clots will not form quickly enough and the patient may experience bruising or be at increased risk of bleeding. In this case, the dose of anticoagulants may need to be reduced. If the INR is too low, the anticoagulant is not working sufficiently, which means that clots could still form unnecessarily and block a blood vessel. In this case, the dose of anticoagulants may need to be increased. Self-testing involves patients performing the test then any dose adjustments are made by a healthcare professional, whereas in self-management the patient makes all dose changes. In COPD one article focused on self-management and another on action planning. Similarly, in heart failure some articles focused on self-management and others on telemonitoring.

3.6.4.3 Mode of monitoring

Sixteen of the 27 articles focused specifically on technology to enable patients to monitor and transmit data to a healthcare professional. These interventions were labelled as telemonitoring, telehealth, telehealthcare, structured telephone support, remote monitoring and telephone support. Although the labels varied these interventions were either device based monitoring where patients entered data into electronic equipment (e.g. mobile phone, personal digital assistant or computer) and sent it via telephone line to a monitoring station where it was viewed by a healthcare professional; or by using a telephone to either enter data using the touch pad or speaking to a healthcare professional on the telephone to report data. Video consultations in combination with transmitted data were also used. The remaining articles did not state whether data were monitored and recorded using paper based formats or other methods.

Table 3.4. Intervention characteristics

First author, year	Type of intervention	Level of patient involvement	Recommended frequency of monitoring	Behaviour/s monitored	Follow-up time
Hypertension					
Jaana, 2007	BP TM	Data was given to a HCP. No information on what these readings were used for.	Range 6 a day to weekly	BP, heart rate, symptoms, medication adherence, stress, ECG, weight, sleep quality.	Study duration range 5 days-12 months
AbuDagga, 2010	TM	Self-measurement & self-transmission of BP. Typically, when BP values exceeded predetermined parameters, an alarm message was automatically generated & sent to a nurse or pharmacist, who contacted patients with disease management tips &/or contacted primary care providers for action. In other cases, the alarm message was sent directly to patients with instructions to contact their physicians.	Range once a week to a few times a day	BP (in some studies titration decisions, side effects).	Study duration range 8 weeks-24 months
COPD					
Turnock, 2005	Action planning	All studies included patients using an action plan to interpret symptoms & make adjustments to their medications or seeking HCP advice.	NR	Symptoms.	6 months & 1 year

First author, year	Type of intervention	Level of patient involvement	Recommended frequency of monitoring	Behaviour/s monitored	Follow-up time
McLean, 2012	Telehealthcare	In all studies patients were required to transmit data to HCP for personalised feedback. In some studies patients were trained to make changes to their medication according to an action plan.	NR	NR	3, 6 & 12 months
Heart failure					
Louis, 2003	TM	NR	NR	Weight, BP, HR, ECG, respiratory rate, body temperature, extracellular fluid, weight, O^2 saturation.	Range post intervention-12 months
Jovicic, 2006	Self-management	Patients were taught to recognise when to seek medical assistance.	NR	Sign, symptoms, weight.	Range 3 months-1 year
Martinez-Everss, 2006	Home monitoring	Data were given to a HCP. There is no information on what these readings were used for.	NR	ECG, weight, BP, symptoms.	Range 3-12 months
Chaudhry, 2007	TM	Data were given to a HCP & was used by a nurse or clinician to adjust medication.	Range twice daily to being determined by patient status	Symptoms, weight, physiologic measures.	Range 60 days-12 months

First author, year	Type of intervention	Level of patient involvement	Recommended frequency of monitoring	Behaviour/s monitored	Follow-up time
Clark, 2007	TM or STS	Data were given to a HCP. There is no information on what these readings were used for.	Range daily to being determined by patient status	Symptoms, weight, pulse, BP, electrocardiographic data.	Range 2 months-400 days
Dang, 2009	Home telehealth remote monitoring	Data were given to a HCP. There is no information on what these readings were used for.	Range twice daily to weekly	Weight, BP, HR, O^2 saturation, symptoms, ECG, pulse, steps/day, medication, pedal oedema, respiratory effort, facial expressions, ankle circumference.	Range 3-12 months
Klersy, 2009	Remote monitoring	NR	NR	Symptoms, weight, BP, physical activity, HR, ECG, arrhythmias, O^2 saturation, RV pressure.	RCT: Median 6 months (range 2-18 months) Cohort studies: Median 12 months (range 2-17 months)

First author, year	Type of intervention	Level of patient involvement	Recommended frequency of monitoring	Behaviour/s monitored	Follow-up time
Maric, 2009	TM	Authors report that changes in weight & symptoms were interpreted by a HCP & appropriate action taken. But fail to report what happened in each trial.	NR	Signs, symptoms, weight, medication, BP, CAD risk factors, HR, O^2 saturation, QoL, blood test results, pulse, ECG, steps per day.	Range 3 months-1 year
Polinsena, 2010	TM	Authors discuss patients being "encouraged to assume a more active role in their disease management". But fail to report what happened in each trial.	NR	NR	Ranged 30 days-1 year
Inglis, 2010	STS or TM	It is unclear what happened to the data in a majority of studies. In many cases, data were sent to a HCP for review but it is unclear what happened as a result.	Range twice daily to weekly	Symptoms, adherence, BP, HR, weight, 24hr urine output.	Range 3-18 months
Clarke, 2011	TM	It is unclear what the data was used for in each trial. 10 studies included physiological monitoring & data were transmitted to HCP to determine if any action was required.	Daily	Weight, heart rate. BP, ECG, HF symptoms.	NR

First author, year	Type of intervention	Level of patient involvement	Recommended frequency of monitoring	Behaviour/s monitored	Follow-up time
Ciere, 2012	Telehealth	In all studies patients monitored aspects of the disease & transmitted this data. In 4 studies it was unclear what the transmitted data were used for, in 7 studies the data were reviewed by a HCP & feedback was given to the participant on adjustments to either medication (adherence or dose) &/or lifestyle.	NR	Symptoms, medication adherence, BP, HR, weight, 24hr urine output, hear rate, O^2 saturation, self-care practices.	Range 2-12 months
Giamouzis, 2012	TM	NR	NR	Weight, BP, heart rate, medication dose, dyspnoea, asthenia or oedema score, blood results, changes in therapy, pulse oximetry, symptoms, 24hr urine output, ECG.	Range 6-26 months

First author, year	Type of intervention	Level of patient involvement	Recommended frequency of monitoring	Behaviour/s monitored	Follow-up time
Pandor, 2013	Remote monitoring	NR	Ranged daily to being determined by patient status	Signs & symptoms, current medication, weight, BP, HR, ECG, fluid retention, dyspnoea, ankle circumference, 24hr urine output, O^2 saturation.	Study duration range 3-15 months
Thrombophilia					
Siebenhofer, 2004	PSM	In all studies patients monitored their INR values, interpreted the results & made adjustments to medication.	Ranged once a week to once a month	INR.	Mean 3 months
Connock, 2007	PST or PSM	5 RCTs looked at monitoring only & 9 monitoring with the addition of interpreting & adjusting medication. 1 study looked at both. Of the 8 non-randomised controlled studies, 1 study compared monitoring, interpretation & adjustment with just monitoring. The remaining studies looked at monitoring, interpretation & adjustment.	Range 0.5 to 4 per week in the intervention group & from 1 to 4 in the control group.	INR.	Range 2-43.6 months

First author, year	Type of intervention	Level of patient involvement	Recommended frequency of monitoring	Behaviour/s monitored	Follow-up time
Garcia-Alamino, 2010	PST or PSM	In 11 trials patients monitored INR levels, interpreted the results & made adjustments to their medication. In the remaining 6 trials patients just monitored their results. 2 reported information on both.	Range weekly to "guided by patient status"	INR.	Study duration range 3-19 months
Bloomfield, 2011	PST or PSM	In 19 trials patients monitored INR, interpreted the results & made adjustments to their medication. In 5 trials patients just monitored their results & dose adjustment was made by the clinic. In 2 studies it was unclear what was taking place. 3 studies compared the 2 methods.	Range 3 times a week to at the patients discretion	INR.	Duration of follow-up was less than 12 months in 13 studies
Diabetes					
Welschen, 2005b	SMBG	In 3 trials no standard instructions were provided to patients to adjust their behaviour or change their lifestyle & medication. No details were provided for the 3 other studies.	Range 6 times a day to 6 times per week	BG.	Range 6 months-44 weeks

First author, year	Type of intervention	Level of patient involvement	Recommended frequency of monitoring	Behaviour/s monitored	Follow-up time
McGeoch, 2007	SMBG	2 RCTs encouraged active modification of behaviour based on SMBG readings. 1 of these also used a clear management algorithm for changing diabetes-related medication. There were no details for the other studies.	Range 6 times a day to twice every other day	BG	Range 6 months-6.5 years
Kleefstra, 2009	SMBG	Glucose values were used for HCP to give advice on lifestyle responses. In 4 studies strict algorithms were used to adjust BG lowering therapy. But it is unclear if this was done by the patient or HCP. 5 studies were not clear on whether therapy was adjusted.	Range 6 to 42 times per week	BG	Study duration range 6-12 months
Clar, 2010	SMBG/SMUG	In 7 RCTs it was unclear if treatment adjustment took place. In 2 studies adjustment did not take place at all, in 11 trials adjustment was done by a HCP, by the patient in 4 trials or a combination. In 2 further studies adjustment did take place but it did not state who did it.	Range at the patient convenience to 36 times a week	BG, UG	Range 12 weeks-30 months
Malanda, 2012	SMBG	NR	Range 6/week to 6/day	BG	Range 26 weeks-12 months

BG – Blood Glucose; BP – Blood Pressure; CAD – Coronary Artery Disease; ECG – electrocardiogram; HCP – healthcare professional; HR – heart rate; HF – heart failure; INR – international normalized ratio; NR – not reported; PST – patient self-testing; PSM – patient self-management; SMBG – self-monitoring of blood glucose; SMUG – self-monitoring of urine glucose; STS – structured telephone support; TM – telemonitoring; UG – urine glucose; RV – right ventricle

3.6.4.1 Level of patient involvement

It was important to understand whether all three elements of self-monitoring were taking place (i.e. awareness, interpretation, response) according to the concept analysis undertaken by Song and Lipman (2008) and Wilde and Garvin (2007). There was considerable variation both within and between long-term conditions in the degree of involvement patients had in adjusting their behaviour (Table 3.4). In some articles participants only undertook the awareness step and data were then passed to a healthcare professional or automated system to be interpreted and feedback provided on any recommended adjustments to treatment or lifestyle. Other articles included participants monitoring, along with interpreting and using this information to adjust their treatment regimens, lifestyle and help-seeking behaviour.

In anticoagulation therapy the level of patient involvement differed between articles. In all primary research studies patients performed their own INR test. One article in this review included only primary research studies in which all intervention participants performed an INR test, interpreted the results and adjusted their own dose of anticoagulants (Siebenhofer *et al.,* 2004). In the three remaining articles not all primary research studies included this level of patient involvement, some only required patients to take an INR measurement and then inform a healthcare professional of the result for them to decide on the necessary dose adjustment (Connock *et al.,* 2007; Garcia-Alamino *et al.,* 2010; Bloomfield *et al.,* 2011).

In both hypertension articles, measurement of blood pressure was undertaken by the patient. In the article by Jaana *et al.,* (2007) data were transmitted to a healthcare professional but it was unclear what the information was used for. AbuDagga *et al.,* (2010) stated that when blood pressure levels were outside of predetermined parameters either a healthcare professional would contact the patient or the patient received an automated message to contact their healthcare team but it was not explicitly clear in all primary research studies.

The article focusing on action planning in COPD involved patients monitoring their symptoms and using their action plan to alter their medication regime and/or access

relevant medical assistance (Turnock *et al.,* 2005). In the review of telehealthcare by McLean *et al.,* (2012) patients were required to transmit data to their healthcare professional for personalised feedback or were trained to make their own medication changes according to a pre-agreed action plan.

In heart failure four articles failed to report any details on what the monitored data were used for and by whom (Giamouzis *et al.,* 2012; Klersy *et al.,* 2009; Louis *et al.,* 2003; Pandor *et al.,* 2013). Participants appeared to play a more active role in their disease management in three articles (Jovicic *et al.,* 2006; Maric *et al.,* 2009; Polinsena *et al.,* 2010). Jovicic *et al.,* (2006) included primary research studies that involved teaching patients to monitor aspects of their condition and to recognise when to seek medical assistance. Maric *et al.,* (2009) reported that patients interpreted changes in their weight and symptoms and took "appropriate action" and Polinsena *et al.,* (2010) stated that patients were "encouraged to assume a more active role in their disease management". Both Polinsena *et al.,* (2010) and Maric *et al.,* (2009), however, failed to report the level of involvement participants had in each of the primary research studies.

In heart failure five articles clearly stated that the monitored data were shared with a healthcare professional (Chaudhry *et al.,* 2007; Ciere *et al.,* 2012; Clark *et al.,* 2007; Dang *et al.,* 2009; Martinez *et al.,* 2006). Martinez *et al.,* (2006), Clark *et al.,* (2007) and Dang *et al.,* (2009), however, provided no information on what the monitored data were used for. Chaudhry *et al.,* (2007) stated that a healthcare professional used the data to alter treatment in all primary research studies. Ciere *et al.,* (2012) combined primary research studies in which it was unclear what the data were used for, with studies in which data were reviewed by a healthcare professional and feedback provided to the participant about adjustments to either medication and/or lifestyle. In the remaining articles reporting was inconsistent and definite transmission of data to a healthcare professional was reported for only a selection of the primary research studies (Clarke *et al.,* 2011; Inglis *et al.,* 2010). Although Inglis *et al.,* (2010) failed to detail what the data were used for, Clarke *et al.,* (2011) reported that in a majority of the primary research studies physiological monitoring and data were transmitted to healthcare professional to determine if any action was required.

Despite SMBG being part of standard care in diabetes the level of involvement patients had in the interpretation and adjustment of their lifestyle and treatment was poorly reported. Malanda *et al.,* (2012) failed to include any information on the level of involvement participants had. The four remaining articles included some primary research studies that specified the level of patient involvement but in other articles it was unclear (Clar *et al.,* 2010; Kleefstra *et al.,* 2009; McGeoch *et al.,* 2007; Welschen *et al.,* 2005b).

It is worth noting that use of technology was not associated with patients being more actively involved in interpreting and responding to their monitored data. In fact the reverse was true. In only one article did authors state that patients were "encouraged to assume a more active role in their disease management". No detail was, however, provided in how this manifested in the intervention (Polinsena *et al.,* 2010).

3.6.4.2 Behaviour monitored

The data monitored by participants was in the main consistent within each condition. Glucose and INR blood test results were monitored in diabetes and thrombophilia respectively. The remaining articles involved monitoring of various symptoms and side effects depending on the population. Two articles failed to outline what data patients were required to transmit as part of telemonitoring (McLean *et al.,* 2012; Polinsena *et al.,* 2010).

3.6.4.3 Additional behaviour change techniques

In addition to patients self-monitoring many of the primary research studies included additional behaviour change components within education and healthcare professional feedback. In a majority of cases, however, these details were poorly reported and articles either failed to document the specific components or were unable to make any conclusions about the effectiveness of these additional techniques due to high heterogeneity or too few primary research studies.

3.6.4.4 Control groups

On the whole the articles that included studies with a control group generally provided a poor description of the content. Two articles failed to detail the content of any control groups (Chaudhry *et al.,* 2007; Jaana *et al.,* 2007). For a majority there was no consistency in what the intervention group was compared to and were a mixture of

usual care and/or an active control group. In most cases however, the definition of usual or standard care was either not described or was not consistent across primary research studies.

3.6.5 Assessment of review quality

The methodological quality of the 27 articles varied (Figure 3.3), but was generally good (median score = 6). The most common methodological problems were not reporting any conflicts of interest either for the authors of the articles or for the primary research studies, potential bias in the selection of primary research studies, ensuring that there was a search for grey literature and that reports were not excluded based on their publication status or language. Appendix G provides detailed scores for the AMSTAR checklist for each article.

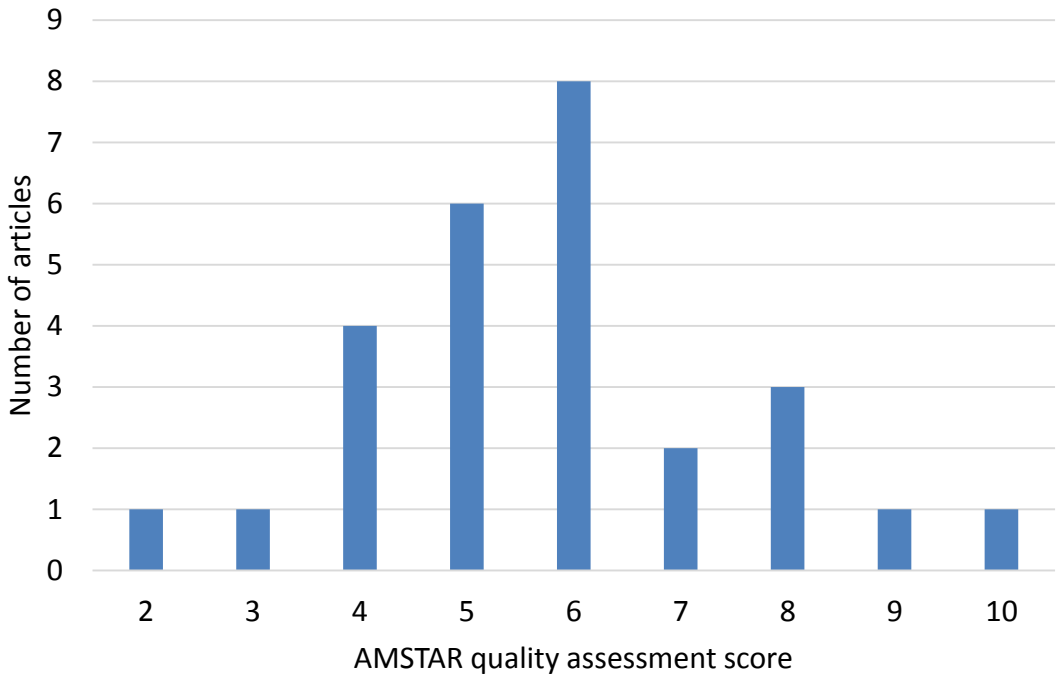


Figure 3.3. Distribution plot of the quality of review articles

3.6.6 Intervention effectiveness

3.6.6.1 Healthcare utilisation

Healthcare utilisation was reported in 17 articles; 13 in heart failure, 2 in hypertension and 2 in COPD (Appendix H). The most frequently reported outcomes were disease-specific and all-cause hospitalisation. In all but three of these articles did the

intervention consist of self-monitoring aided by technology. In summary, five articles failed to find any effect on healthcare utilisation, three found a definite positive impact, in three articles it was unclear due to poor reporting and in seven articles the results were mixed with a combination of positive effects on some specific outcomes and no effect on other aspects of healthcare utilisation.

3.6.6.1.1 Hospitalisation

Of these 17 articles, 13 reported the effects of telemonitoring or action planning on disease-specific and/or all-cause hospitalisation, 11 in heart failure and 2 in COPD. The two meta-analyse both in **COPD** report conflicting results, whereas Turnock *et al.,* (2005) found no significant impact on rates of hospitalisation for action planning, in which patients were actively involved in adjusting their treatment or seeking medical advice. The meta-analysis by McLean *et al.,* (2012) suggested that the number of patients with one or more hospital admissions over a 12 month period was significantly greater in the control group compared to telehealthcare in which patients used an action plan in only a small proportion of studies.

Of the 11 articles in **heart failure** six were a meta-analysis of telemonitoring and/or structured telephone support and five a systematic review. The level of involvement patients had in interpreting and responding to their monitoring data was unclear in all these articles. The meta-analyses indicated that telemonitoring and structured telephone support were associated with 23% fewer patients being hospitalised for any cause (Polisena *et al.,* 2010) and up to 27% fewer total all-cause or disease-specific hospitalisations (Pandor *et al.,* 2013; Inglis *et al.,* 2010; Clarke *et al.,* 2011; Klersy *et al.,* 2009; Clark *et al.,* 2007).

Subgroup analyses were conducted in two of these meta-analyses and suggested that telemonitoring with medical support available only during office hours was associated with a greater reduction in hospitalisations than when medical support was available 24/7 (Pandor *et al.,* 2013). Pandor *et al.,* (2013) also found that human-to-human structured telephone support led to a 23% reduction in heart failure-related hospitalisations, although human-to-machine structured telephone support failed to have any effect on either disease specific or all-cause hospitalisation. Klersy *et al.,*

(2009) replicated their findings in a subgroup analysis of both low and high quality studies and at short- and long-term follow-ups.

Five further systematic reviews included a combination of primary research studies that found significant reductions in all-cause and disease-specific hospitalisation rates as a result of telemonitoring along with studies that found no significant differences between groups (Chaudhry *et al.,* 2007; Dang *et al.,* 2009; Giamouzis *et al.,* 2012; Louis *et al.,* 2003; Maric *et al.,* 2009). Te overall conclusions, however, from each of these articles suggested a positive trend for a reduction in healthcare utilisation in favour of telemonitoring.

3.6.6.1.2 Readmissions

One meta-analysis and three systematic reviews all in **heart failure** reported outcomes in relation to readmission rates. The meta-analysis found that self-management, in which patients were taught to seek medical assistance in response to symptoms, reduced the odds of all-cause and disease-specific readmission by up to 54% of what they were in usual care (Jovicic *et al.,* 2006). A majority of the included primary research studies in the three systematic reviews reported an association between telemonitoring and fewer readmissions to hospital (Louis *et al.,* 2003; Maric *et al.,* 2009; Martinez *et al.,* 2006). In all three articles, however, it was unclear whether the patient or HCP was responding to the monitored data.

3.6.6.1.3 Length of hospital stay

The number of days spent in hospital was summarised in eight **heart failure** systematic reviews. The overall findings were mixed, telemonitoring was associated with a reduction in the length of hospital stay in many of the primary research studies; both within the intervention group over time and when compared to a control group (Louis *et al.,* 2003; Maric *et al.,* 2009; Martinez *et al.,* 2006). In many of these studies, however, it was unclear if these reductions were statistically significant. The remaining articles found that a majority of the included primary research studies failed to associate telemonitoring with any reduction in time spent in hospital (Clarke *et al.,* 2011; Dang *et al.,* 2009; Inglis *et al.,* 2010; Pandor *et al.,* 2013; Polinsena *et al.,* 2010). In a majority of these articles it was unclear who was interpreting and responding to monitored data.

3.6.6.1.4 Accident and emergency attendance

Seven articles; three meta-analyses and four systematic reviews reported the effects of self-monitoring on A&E attendance. The three meta-analyses in **COPD** and **heart failure** reported conflicting results. Action planning, which involved patients with COPD adjusting their own treatment or seeking medical assistance, did not have any significant effect on visits to A&E (Turnock *et al.,* 2005). Nor did telemonitoring in heart failure, where data were transmitted to a HCP to determine if any action was required (Clarke *et al.,* 2011). Telehealthcare in COPD was associated with less attendance at A&E compared to the control group; however, the level of patients' involvement in responding to data did vary (McLean *et al.,* 2012). A majority of the primary research studies in the four heart failure systematic reviews did find that telemonitoring resulted in fewer visits to A&E for both all-cause and heart failure-related attendance (Dang *et al.,* 2009; Louis *et al.,* 2003; Maric *et al.,* 2009; Polinsena *et al.,* 2010). It was not possible to examine whether level of patient involvement had an impact on this outcome due to poor reporting.

3.6.6.1.5 Outpatient visits

Polinsena *et al.,* (2010) included two observational studies, in their systematic review of telemonitoring in **heart failure,** which reported fewer outpatient visits in the intervention compared to usual care and two RCTs that found telemonitoring to be associated with more outpatient visits. It is unclear, however, if these differences were significant and although patients were "encouraged to assume a more active role in their disease management" it was unclear to what degree this was.

3.6.6.1.6 GP visits

The impact of self-monitoring on the frequency of GP visits was reported in three articles, one meta-analysis and two systematic reviews. The meta-analyses in **COPD** found no significant difference in scheduled or unscheduled GP visits between action planning, in which patients made adjustments to their medications and sort medical help when required, and usual care (Turnock *et al.,* 2005). These findings were substantiated in systematic reviews by Jaana *et al.,* (2007) and AbuDagga *et al.,* (2010) in **hypertension**. In both articles data were transferred to a healthcare professional which, in many cases, triggered feedback to the patient.

3.6.6.1.7 Home visits

Two systematic reviews in **heart failure** report weak and inconsistent effects for telemonitoring on the frequency of home visits. One article described a single primary research study that found a reduction in home visits from pre- to post-intervention (Maric *et al.,* 2009). The second systematic review, however, described two primary research studies that found an increase in home care visits in the intervention group compared to usual care (Polinsena *et al.,* 2010). But both articles failed to report if these changes were statistically significant and it was not possible to determine who interpreted and responded to the monitoring, data due to poor reporting.

3.6.6.2 Patient reported outcomes

Overall the impact of self-monitoring on PROMs was diverse. As a result of incomplete reporting it proved difficult to tease out specific findings and hence make overall conclusions. This was largely due to the heterogeneity in concept definitions, scales and the overall lack of primary research studies which meant only two articles were able to perform a meta-analysis (McLean *et al.,* 2012; Turnock *et al.,* 2005), both in COPD.

Reporting was particularly poor in regards to detailing the type of measures used, the rationale for grouping measures together (e.g. satisfaction combined with anxiety), the reporting of significance tests and whether analysis was within or between groups. Outcomes for 17 PROMS were summarised in 22 articles (Appendix I). Due to the number of outcomes this overview focuses on the most frequently reported and relevant variables. Due to the heterogeneity in how terms were grouped within an article, data were extracted at primary research study level, where possible. Where results for individual primary research studies were not available results are reported for each of the outcomes according to the label within the article. In summary, four articles found a definite positive impact for self-monitoring on PROMS, three found no significant effect, in four article it was unclear primarily due to poor reporting and 11 articles found positive effects in relation to some PROMS and no significant effect for other measures.

3.6.6.2.1 Quality of life

Quality of life was the most frequently described PROM and was reported in 18 systematic reviews; two in COPD, two in hypertension, three in thrombophilia, four in

diabetes and eight in heart failure. Quality of life was measured in several ways including validated measures such as the COPD specific St George's Respiratory Questionnaire (Jones, Quirk, & Baveystock, 1991) and Minnesota Heart Failure Quality of Life (Rector, Kubo, & Cohn, 1987) questionnaire but also using author developed questionnaires.

In **COPD**, the meta-analysis by Turnock *et al.,* (2005) found no significant difference in quality of life when patients with COPD undertook self-monitoring and medication adjustment based on a pre-agreed action plan, compared to usual care at either the 6 or 12 month follow-up. Although the meta-analysis of telehealthcare by McLean *et al.,* (2012) validated this non-significant result, the mean difference between the intervention and control group was greater than the minimally important clinical difference on the COPD-specific St George's Respiratory Questionnaire (Jones *et al.,* 1991). This indicates a clinically significant improvement in quality of life as a result of telehealthcare, in which patients changed their medications according to an action plan in some of the primary research papers.

In, **hypertension**, **diabetes** and **heart failure** the systematic reviews either found no significant impact of quality of life as a result of blood pressure or blood glucose monitoring (Clar *et al.,* 2010; Kleefstra *et al.,* 2009; Malanda *et al.,* 2012; Jovicic *et al.,* 2006) or a combination of primary research studies reporting positive results in favour of self-monitoring and others that failed to find any significant impact on quality of life (Jaana *et al.,* 2007; AbuDagga *et al.,* 2010; Welschen *et al.,* 2005b; Clark *et al.,* 2007; Inglis *et al.,* 2010; Louis *et al.,* 2003; Maric *et al.,* 2009; Martinez *et al.,* 2006; Pandor *et al.,* 2013; Polinsena *et al.,* 2010). In the hypertension articles the intervention involved data being transferred to a healthcare professional; however, it was not always clear what response was taken. In heart failure it was not clear what level of involvement patients had in interpreting their monitored data and making the adjustments, whereas SMBG was performed by the patient in diabetes; however, it was unclear in a majority of cases who was interpreting and responding to the data.

When self-management in **thrombophilia** was compared to usual care in the article by Siebenhofer *et al.,* (2004) two RCTs reported significant differences in quality of life in

favour of self-management. These interventions included patients being trained to perform an INR test and adjust their dose of anticoagulants. Conversely when primary research studies in which dose adjustment was undertaken by either the patient or healthcare professional were combined, the results were less clear. Connock *et al.,* (2007) and Bloomfield *et al.,* (2011) present a combination of studies that found the intervention led to improvements in quality of life and other studies which fail to find any significant effects.

3.6.6.2.2 Mood

Outcomes in relation to anxiety and depression were synthesised in eight systematic reviews; one in COPD, three in diabetes and four in heart failure. In the only article in which patients with **COPD** were taught to interpret their symptoms and make adjustments to their medications or seek medical assistance there were no significant between group differences in either anxiety or depression (Turnock *et al.,* 2005). The systematic reviews in **diabetes** and **heart failure** were inconclusive, with some primary research studies suggesting significant improvements in mood as a result of self-monitoring and other primary research studies that found no significant effects for anxiety or depression (Clar *et al.,* 2010; Kleefstra *et al.,* 2009; Malanda *et al.,* 2012; Clark *et al.,* 2007; Inglis *et al.,* 2010; Maric *et al.,* 2009; Martinez *et al.,* 2006). It is of note that one primary research study found a significant increase in depression as a result of SMBG (Clar *et al.,* 2010; Malanda *et al.,* 2012). In both diabetes and heart failure the level of involvement patients had in adjusting was unclear.

3.6.6.2.3 Satisfaction, acceptability and ease of use

Fifteen systematic reviews reported on patient satisfaction, acceptability of the intervention or, when the article focused on telemonitoring, how easy the technology was to use. Of these 15 articles, one was in COPD, two in hypertension, two in thrombophilia, four in diabetes and six in heart failure.

Jaana *et al.,* (2007) described two primary research studies in **hypertension** that assessed how easy the technology was to use but failed to report any results and two other primary research studies in which satisfaction was high. Anecdotal data from AbuDagga *et al.,* (2010) suggested high rates of technology acceptance among participants. In both articles data were transferred to either an automated system or

healthcare professional, the patient did not have any involvement in interpreting the data they monitored.

A majority of the primary research studies in **thrombophilia** and **heart failure** articles reported high levels of satisfaction, both general- and treatment-specific, in the intervention group compared to usual care (Bloomfield *et al.,* 2011; Garcia-Alamino *et al.,* 2010; Clark *et al.,* 2007; Inglis *et al.,* 2010; Louis *et al.,* 2003; Martinez *et al.,* 2006; Pandor *et al.,* 2013; Polinsena *et al.,* 2010). The interventions in both thrombophilia articles included a combination of self-testing and self-management. Due to poor reporting the heart failure articles can only be assumed to involve patients monitoring their symptoms, with no patient interpretation or response to data. There were, however, no between group differences in patient or treatment satisfaction when SMBG was compared with controls in any of the **diabetes** systematic reviews (Kleefstra *et al.,* 2009; Malanda *et al.,* 2012; McGeoch *et al.,* 2007; Welschen *et al.,* 2005b).

3.6.6.3 Clinical outcomes

Twenty-six of the 27 articles reported clinical outcomes. The range of clinical outcomes was vast and included 25 different variables. Some were disease-specific such as HbA1c, in diabetes and thromboembolic events in thrombophilia. In contrast other outcomes were reported across conditions such as mortality, blood pressure, weight and adherence. In many cases a meta-analysis was not possible because of too few primary research studies and high heterogeneity. Due to the large number of clinical outcomes this will review will focus on the most frequently reported and relevant. For details of all outcomes see Appendix J. Overall the results were generally positive with 7 of 26 articles finding positive clinical implications as a result of self-monitoring and the remaining articles describing a combination of positive effects for some clinical variables and no significant effects on other outcomes.

3.6.6.3.1 Generic outcomes

Mortality

Twenty articles synthesised the evidence on mortality; two in COPD, two in diabetes, three in thrombophilia and 13 in heart failure.

Whilst meta-analyses in **COPD** (McLean *et al.,* 2012; Turnock *et al.,* 2005) and an earlier meta-analysis in **heart failure** found no significant effects on mortality (Jovicic *et al.,* 2006) the meta-analyses in **thrombophilia** and later meta-analyses in **heart failure** found significant reductions in mortality in favour of self-monitoring (Bloomfield *et al.,* 2011; Connock *et al.,* 2007; Garcia-Alamino *et al.,* 2010; Clark *et al.,* 2007; Inglis *et al.,* 2010; Klersy *et al.,* 2009; Pandor *et al.,* 2013; Polinsena *et al.,* 2010). In all articles the level of patient involvement in interpreting and responding to data was not consistent. These significant results were maintained across disease indications (Connock *et al.,* 2007), when self-monitoring was compared to GP and secondary care (Connock *et al.,* 2007; Garcia-Alamino *et al.,* 2010), when studies were restricted to RCTs only (Polinsena *et al.,* 2010), those of high quality (Klersy *et al.,* 2009) and at long and short-term follow-up (Inglis *et al.,* 2010; Klersy *et al.,* 2009). Clark *et al.,* (2007), however, found that there was no difference in all-cause mortality when structured telephone support was compared to telemonitoring in a subgroup analysis. Pandor *et al.,* (2013) found that whereas telemonitoring supported either by office hours or 24/7 medical advice had a statistically significant effect on mortality, structured telephone support was only effective in reducing mortality rates when the support was human-to-human as opposed to human-to-machine.

One primary research study was reported in two **diabetes** systematic reviews. This longitudinal observational study found significant reductions in mortality in those that self-monitored despite significantly worse initial fasting glucose and HbA1c (Clar *et al.,* 2010; McGeoch *et al.,* 2007). A second observational study reported in one of these systematic reviews found no change in mortality overtime (Clar *et al.,* 2010). In all cases it was unclear who if anyone made changes to treatment.

Blood pressure

Four articles reported outcomes in relation to blood pressure (e.g. systolic, diastolic, ambulatory, blood pressure within a recommended target range); one in diabetes, one in heart failure and two in hypertension. The systematic review in **diabetes** (Clar *et al.,* 2010) and another in **heart failure** (Maric *et al.,* 2009) suggested either no effect or very weak evidence to suggest that self-monitoring improved blood pressure. The evidence in **hypertension** was more convincing a majority of the primary research

studies found significant reductions in blood pressure when participants were required to measure their blood pressure and transmit these readings to a healthcare professional (AbuDagga *et al.,* 2007). AbuDagga *et al.,* (2007) suggested that greater reductions in blood pressure were found when rates of compliance with telemonitoring and self-titration were higher. This, however, was only found in one single group study. In a majority of cases patients were not involved in adjusting their treatment or lifestyle and data were transferred to a healthcare professional for action to be decided upon.

Weight

Three articles, one in hypertension and two in heart failure report limited evidence for telemonitoring reducing weight. A single primary research study in **hypertension** found significant improvements in weight from pre- to post-intervention (Jaana *et al.,* 2007). Similarly, both systematic reviews in **heart failure** report the results of a single primary research study that found self-monitoring to significantly improve weight over time (Inglis *et al.,* 2010; Maric *et al.,* 2009). In all cases data were transferred to a healthcare professional for review.

Adherence

Five systematic reviews, two in hypertension and three in heart failure reported outcomes in relation to either adherence to medication or lifestyle recommendations. Overall the results were inconclusive. Systematic reviews in both **hypertension** and **heart failure** reported primary research studies that found significant improvements in medication adherence and dietary and exercise recommendations as a result of self-monitoring whilst other primary research studies found no significant difference either within an intervention over time or between intervention and control groups (AbuDagga *et al.,* 2007; Inglis *et al.,* 2010; Jaana *et al.,* 2007; Jovicic *et al.,* 2006; Maric *et al.,* 2009). Only in the article by Jovicic *et al.,* (2006) were patients taught to recognise when medical advice was needed.

3.6.6.3.2 Disease-specific outcomes

HbA1c

All five articles in type 2 **diabetes** compared the effects of SMBG on HbA1c, primarily for non-insulin dependent patients. The results were inconclusive in the two

systematic reviews (Kleefstra *et al.,* 2009; McGeoch *et al.,* 2007). Two meta-analyses, however, concluded that SMBG significantly reduced HbA1c compared to no self-monitoring, with a weighted mean difference of between -0.21% and -0.39% (Clar *et al.,* 2010; Welschen *et al.,* 2005b). These significant results remained when SMBG was undertaken less frequently and for participants who started the trial with HbA1c greater than ≥8% the reduction in HbA1c across the trial was greater (Clar *et al.,* 2010). When SMBG with an additional educational or feedback component was compared with SMBG alone there were no significant differences. In comparison to no SMBG, however, this enhanced intervention led to a greater reduction HbA1c (Clar *et al.,* 2010). In a third meta-analysis Malanda *et al.,* (2012) explored the impact of length of follow-up in combination with disease duration. For those who had been living with diabetes for more than 1 year SMBG led to a statistically significant decrease in HbA1c of 0.3% compared with controls at short-term follow-up (up to 6 months) but there were no significant differences at the longer term follow-up (between 6 and 12 months). For newly diagnosed participants pooled analysis for short term follow-up was not possible due to high heterogeneity; however, at the medium-term follow-up there was a statistically significant decrease in HbA1c of 0.5%. None of these articles explored the impact of level of patient involvement. Welschen *et al.,* (2005b), Clar *et al.,* (2010) and McGeoch *et al.,* (2007) included a number of primary research studies in which patients adjusted their lifestyle and medication in order to modify their glucose values.

Hypoglycaemia

The results for hypoglycaemic events were inconsistent, although there was a suggestion that occurrence of mild or moderate hypoglycaemia was increased with more frequent self-monitoring (Clar *et al.,* 2010).

Fasting blood glucose

There were no significant effects for SMBG on fasting blood glucose (Welschen *et al.,* 2005b).

Thromboembolic and haemorrhage events

All four articles in thrombophilia synthesised the effects of self-monitoring on thromboembolic and haemorrhage events. Three meta-analyses reported significantly

fewer thromboembolic events in the intervention compared to control group, but no differences in major haemorrhage events (Bloomfield *et al.,* 2011; Connock *et al.,* 2007; Garcia-Alamino *et al.,* 2010). A majority of the primary research studies in the systematic review by Siebenhofer *et al.,* (2004) reported too few thromboembolic and haemorrhage events to draw any conclusions. Connock *et al.,* (2007) also found that trials conducted outside of the UK had a greater effect on thromboembolic events than those conducted inside the UK (Connock *et al.,* 2007). The type of control group the intervention was compared to (i.e. family physician care or anticoagulation clinic) did not affect these outcomes (Connock *et al.,* 2007; Garcia-Alamino *et al.,* 2010). Connock *et al.,* (2007) also found that there was no difference between patient self-testing and patient self-management on thromboembolic events. Garcia-Alamino *et al.,* (2010), however, found that patient self-management led to significantly fewer haemorrhage events and the relative risk of experiencing a thromboembolic event was also lower than in the group that self-monitored. Although the latter finding was not a statistically significant interaction. Conversely Connock *et al.,* (2007) found that self-management led to significantly more haemorrhage events than patient self-testing.

International normalized ratio

The impact of self-monitoring on INR values was reported in four articles, one meta-analysis and three systematic reviews, either as the percentage of time participants spent within the recommended INR range or as the proportion of INR tests within the recommended range. One was a meta-analyses and the others systematic reviews. The meta-analysis found that self-monitoring, where medication adjustment was undertaken by either the patient or healthcare professional, failed to have any significant effect on the percentage of time spent within the therapeutic range or the percentage of INR tests within range (Bloomfield *et al.,* 2011). Two primary research studies in this article compared self-monitoring with self-management and found no significant difference in percentage of time in the therapeutic range between the two interventions. Two systematic reviews, described primary research studies that found significant benefits for self-monitoring on INR values and other studies which failed to find any significant effects (Garcia-Alamino *et al.,* 2010; Siebenhofer *et al.,* 2004). Whilst another systematic review pooled estimates and found that intervention participants spent a greater proportion of time within the recommended INR range

compared to control group participants in both RCTs and non-RCTs, no statistical comparisons were made (Connock *et al.,* 2007).

3.7 DISCUSSION

This overview of systematic reviews and meta-analyses has for the first time examined the effectiveness of interventions that include patients self-monitoring their long-term condition, on healthcare utilisation, PROMS and clinical variables. It is based on a systematic and extensive literature search, combined with an assessment of quality. A total of 27 articles were reviewed across five long-term conditions: COPD, hypertension, thrombophilia, heart failure and diabetes.

3.7.1 Healthcare utilisation

Seventeen of the 27 articles included in this review synthesised the evidence in relation to healthcare utilisation, principally in heart failure, COPD and hypertension. The results indicated that interventions which involved self-monitoring can lead to significant reductions in healthcare usage, with little evidence to indicate an increase in healthcare utilisation.

Although the results present a mixed picture in regards to attendance at A&E, admission to hospital decreased significantly in patients with heart failure and COPD. These findings principally focused on interventions using telemonitoring and structured telephone support and suggested that self-monitoring facilitated by technology led to significant reductions in both disease-specific and all-cause hospitalisation and readmissions. This indicates that in certain long-term conditions self-monitoring can impact upon not only on healthcare utilisation relevant to the targeted long-term condition but also other areas of health. Both human-to-human structured telephone support and telemonitoring interventions that were accompanied by office hour's medical support were found to be additionally advantageous, and in the long- as well as short-term. This suggests that communication with another person rather than automated feedback may be additionally advantageous. This could be due to the immediate action that can be taken or the additional social support offered. Once hospitalised however, the picture was mixed in regards to the number of days patients spent in hospital with some

reviews suggesting a significant reduction in days both between groups and overtime and others that failed to associate self-monitoring with any reduction in time spent in hospital. In light of the fall found in hospital admissions, a failure to find a significant change in GP attendance is encouraging as this suggests that patients are not diverting healthcare usage from secondary to primary care.

The lack of primary research studies exploring the impact of self-monitoring on outpatient attendance means that further work is needed in order to establish whether the reductions found in other aspects of healthcare usage can be replicated in outpatient services. Rather than outpatient attendance not being an important outcome for the interventions synthesised within this overview, it was more likely that inpatient attendance was a more critical outcome for these patient groups and hence a reduction in outpatient attendance was not targeted in these interventions. This does, however, remain an important outcome for patients with arthritis who may be less likely to be hospitalised than those with heart failure or COPD.

3.7.2 Patient reported outcomes

Despite PROMS being synthesised in 22 of the 27 articles, psychosocial well-being and patient satisfaction were the most poorly described of all outcomes. This inadequate reporting along with heterogeneous measurement tools and concept definitions and the limited number of primary research studies made it difficult to draw definitive conclusions about the effects of self-monitoring on the patient experience. Overall the impact of self-monitoring suggested no detrimental effects on patient well-being or satisfaction with care. In fact patients were highly satisfied with self-monitoring when investigated within the intervention group, but when compared to usual care many articles found no difference in overall or treatment-specific satisfaction. Patient acceptability of technology assisted self-monitoring was also high in both hypertension and heart failure with very little evidence of rejection.

There was tentative evidence to indicate a possible improvement in quality of life. Whilst two meta-analyses reported a statistically non-significant effect on quality of life, the actual difference between the intervention and control was clinically significant in one article and indicated an improvement in quality of life as a result of

self-monitoring in COPD (McLean *et al.,* 2012). In addition both Siebenhofer *et al.,* (2004) and Connock *et al.,* (2007) concluded that patient self-management in thrombophilia enhanced quality of life, although in these reviews the authors included a combination of primary research studies that did find benefits and others that did not, suggesting the these findings are not conclusive. The literature was less persuasive for mood, with most systematic reviews reporting a combination of primary research studies that failed to find any impact on anxiety or depression, other studies which found significant improvements and one primary research study which found a significant increase in depression as a result of SMBG in type 2 diabetes. These articles did not report the hypotheses of the primary research studies in relation to mood; therefore, it is unclear whether improvements or equivalence were expected. An intervention designed to promote self-monitoring would not necessarily be aimed at reducing levels of anxiety and depression, but no detrimental effects or no difference between groups could be taken as a positive result.

An increase in any aspect of healthcare utilisation would be particularly important in relation to mood as concerns have been raised about the impact that self-monitoring may have on levels of anxiety. For instance in diabetes patients have been found to feel anxious if blood glucose readings are high and they are unable to understand why (Peel, Parry, Douglas, & Lawton, 2004). Intuitively, it may then be expected that someone with a long-term physical illness who is more anxious will also exhibit greater health-seeking behaviours. There is evidence to suggest that persistently high anxiety scores do predict greater hospitalisation (Moser *et al.,* 2011). Implementation of any intervention that includes self-monitoring should, therefore, be mindful as to whether anxiety could manifest or be exacerbated by self-monitoring and how this could be prevented or combated by providing information and guidance on how to interpret monitored data and take appropriate action.

3.7.3 Clinical outcomes

A wide range of clinical outcomes were measured across reviews reflecting the overall aims of the articles and range of long-term conditions. As the aim of this review were to explore the evidence in relation to healthcare utilisation and patient reported outcomes, many published articles that focused on synthesising the effects of clinical

outcomes only were excluded from this review. Despite this there are several important conclusions that can be drawn from the findings of this overview which mirror other published work, in relation to both general and disease-specific outcomes.

Self-monitoring was associated with a significant reduction in mortality, of between 17 and 52%, primarily in thrombophilia and heart failure. These results support the earlier meta-analyses by Heneghan *et al.,* (2006) and Christensen *et al.,* (2007), which found significant reductions in mortality in favour of self-monitoring in thrombophilia. A more detailed meta-analyses by Heneghan *et al.,* (2011) using individual patient data did not see the same reduction in mortality as these previous reviews or the current findings, but did find a trend towards significance and a significant effect for those aged over the age of 85. This lack of effect is likely due to the larger number of participants needed to find a reliable and conclusive treatment effect when conducting a review with individual patient data.

With regards to disease-specific measures, blood pressure improved significantly as a result of home-based monitoring and HbA1c reduced significantly as a result of SMBG, supporting previous meta-analyses in hypertension (Verberk *et al.,* 2011; Cappuccio *et al.,* 2004; Bray *et al.,* 2010) and diabetes (Sarol Jr *et al.,* 2005; Allemann *et al.,* 2009; Poolsup *et al.,* 2008; Poolsup *et al.,* 2009; Towfigh *et al.,* 2008). Long-term follow-up of SMBG was also found to be more beneficial for new-onset patients and for participants who began SMBG with poorer glycaemic control, confirming previous meta-analyses (Allemann *et al.,* 2009; Jansen, 2006; Poolsup *et al.,* 2009). Self-monitoring and self-management are also likely to prevent thromboembolic events for patients on anticoagulation therapy. Two meta-analyses however, found conflicting results in relation to anticoagulation control but this is likely to reflect the additional benefits of patients adjusting their own anticoagulant dose as opposed to adjustment by a healthcare professional.

3.7.4 The implementation of self-monitoring

The manner in which self-monitoring was implemented within each of the interventions differed between long-term conditions but was on the whole consistent

within each condition likely owing to specific monitoring and treatment requirements. In hypertension interventions were home-based blood pressure monitoring, in diabetes self-monitoring of blood glucose and in thrombophilia home-based INR monitoring. In heart failure and COPD the interventions were more diverse and included a combination of self-management which incorporated self-monitoring and telemonitoring. Across all conditions participants were required to monitor different aspects of disease status, encompassing symptoms and side effects, active use of technology to monitor for instance blood pressure or oxygen saturation, along with home testing of blood and urine samples to measure glucose levels and INR blood testing in anticoagulation therapy. These activities varied from being aspects of disease management that are customary in the standard care of any physical health condition i.e. reporting of symptoms, to more novel and complex tasks that were likely to require skills training and monitoring schedules such as INR testing. Although as discussed later in this section, the reporting of the additional behaviour change techniques which accompanied self-monitoring were poorly described.

Irrespective of what data patients were required to monitor the integral part of any intervention that includes self-monitoring is who has access to the monitored data and what the data were used for. The clinical objectives of self-monitoring were in fact similar across long-term conditions, those being to help identify early signs of deterioration and allow for timely changes to treatment, lifestyle or help-seeking behaviour. Although self-monitoring was being used as a tool to aid patient behaviour change these objectives were achieved by a decision making process led either by a healthcare professional or the patient. By scrutinising the content of these interventions, this review has enabled the development of a schematic representation of self-monitoring across long-term conditions (Figure 3.4).

The interventions included in this review, involved monitored data either being retained by the patient for interpretation and clinical adjustment or transferred to a health professional or automated system for review. In this latter case self-monitoring was used purely as a tool for clinical monitoring, where the patient was active in gathering the data but not in the interpretation of that data or in the decision to adjust treatment or lifestyle behaviours, fulfilling only the awareness stage of self-monitoring

(Song & Lipman, 2008; Wilde & Garvin, 2007). In the former, which represents chronic disease self-management, interventions empowered patients to adjust and hence enabled them to manage the consequences of living with their long-term condition (Barlow, Wright, Sheasby, Turner, & Hainsworth, 2002). This involved patients interpreting their data and adjusting their lifestyle and medication behaviours in order to maintain or improve outcomes. These outcomes included clinical and/or psychosocial well-being, as well as healthcare utilisation. Other self-monitoring interventions, including the one evaluated within this thesis, lie somewhere in the middle of these two approaches, whereby patients use their monitored data to make decisions about help-seeking in accordance with pre-defined clinical criteria. Healthcare professionals then adjust treatment plans or lifestyle behaviours and assume that patients then implement these recommended changes.

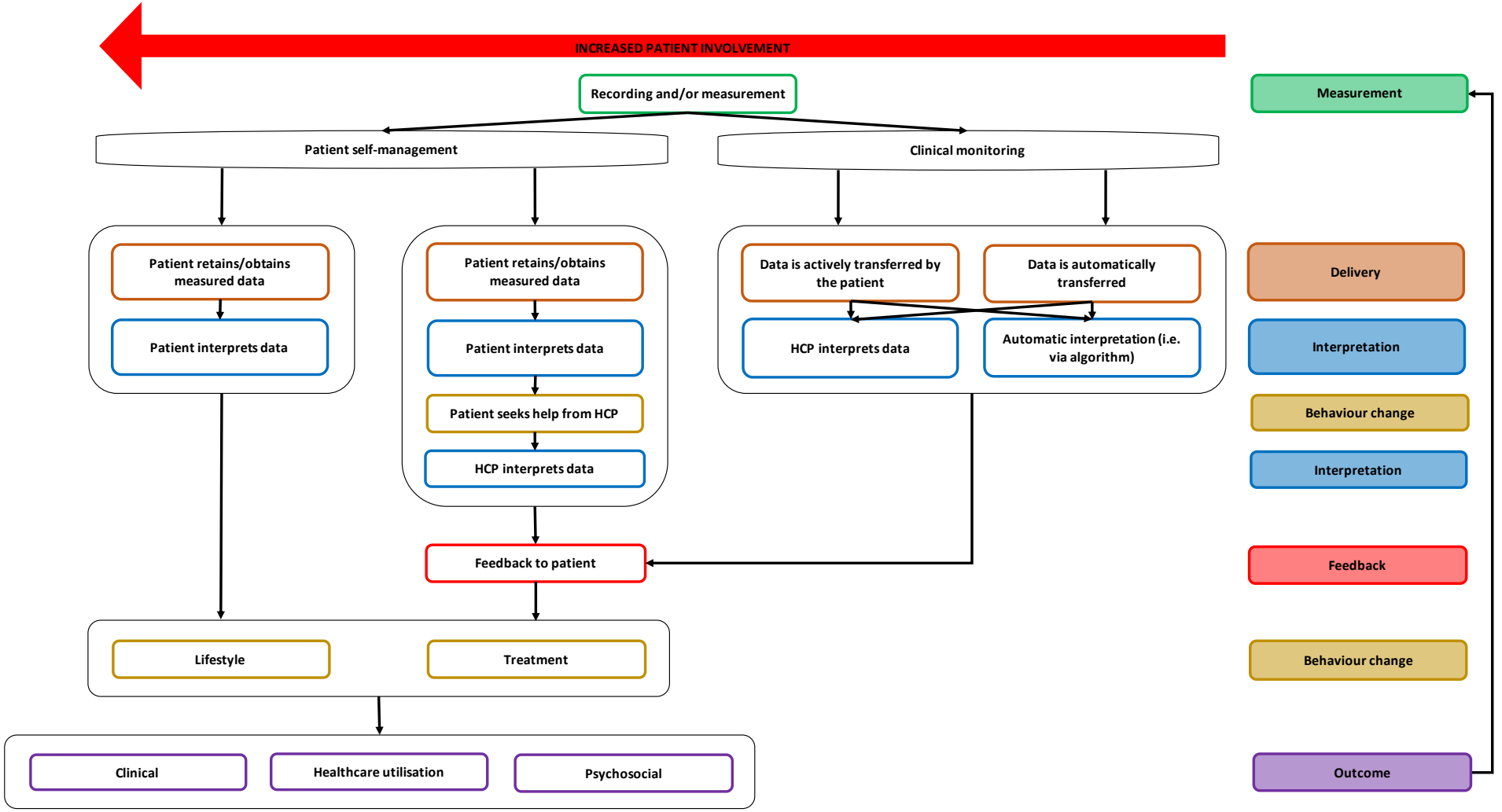


Figure 3.4. A diagrammatic representation of self-monitoring in long-term conditions

As the articles included in this review suffered from poor reporting it was not always possible to establish whether self-monitoring was taking place in the context of chronic disease self-management or purely as a tool for clinical monitoring. Allowing patients with a long-term condition to make decisions about necessary treatment and lifestyle adjustments may engage and empower patients to make changes to their health-related behaviour. In contrast adjustment decisions made by a healthcare professional may allow for a more passive patient and lead to comparatively poorer outcomes due to a lack of awareness between behaviour and outcome. Lack of studies and poor reporting, however, made it difficult to provide robust evidence to examine this hypothesis. Only in anticoagulation therapy were direct comparisons made between interventions that included patients adjusting as opposed to healthcare professionals. The results were, however, contradictory with evidence to suggest no difference in clinical outcomes, a detrimental effect for patients taking control of adjusting and also beneficial effects. Inconsistent clinical benefits for patients as opposed to healthcare professionals adjusting have also been reported elsewhere in the literature. Whereas an early review by Heneghan *et al.,* (2006) failed to find any advantage to patients adjusting their own medication in regards to mortality, thromboembolic and haemorrhage events, the author's more recent review found significantly fewer thromboembolic and haemorrhage events for patients who self-managed as opposed to just testing (Heneghan *et al.,* 2011).

Two additional articles in this review that only included interventions in which patients made adjustments to their medication or help-seeking behaviour, found either a significant decrease in healthcare utilisation and improvements in quality of life (Siebenhofer *et al.,* 2004) or no change in healthcare usage (Turnock *et al.,* 2005). The interventions in this more recent article would however, fall within the middle ground between patient's self-management and clinical monitoring as patients were required to seek help in respond to abnormal symptoms.

Further investigation and analysis of the primary research studies is needed so that definitive conclusions can be made about the additional benefits of patients using their monitored data to adjust their own medication, lifestyle and help-seeking behaviours. A recently published Cochrane protocol indicates that this is currently being explored

in type 2 diabetes (Ng, Liew, Vethakkan, Abdullah, & Teng, 2013). Authors will be comparing patient-adjusted versus healthcare professional-adjusted insulin dosing, in order to explore whether patient-adjusted insulin dosing is more empowering for the patient, leads to better glycaemic control due to a quicker response to high or low blood glucose levels and is more cost-effective as fewer contacts with healthcare-professionals are needed or whether healthcare professional-adjusted insulin is safer. As recognised by Clar *et al.,* (2010) in diabetes, but also applicable across other long-term conditions, self-monitoring is often treated as a diagnostic tool, as an intervention in its own right, without acknowledging that in order to change patient outcomes self-monitoring needs to include the appropriate education, feedback and behavioural adjustment. This could be achieved by returning to the original 321 primary research studies, classifying them according to level of patient involvement in interpreting and responding to data and exploring how this impacts upon study outcomes. This was however, outside of the scope of this overview.

Due to poor reporting and study heterogeneity it was not possible to systematically extract data on whether additional behaviour change techniques were part of the delivered interventions. In the context of self-monitoring it is likely that other behaviour change techniques were implemented but this information was often missing in the articles and primary research papers; therefore, making it difficult to have an accurate and detailed understanding of the intervention delivered. An intervention designed to enable participants to monitor and use this information to seek help or adjust medication or lifestyle behaviours is likely to include an educational and possibly skills training component and it is these additional components that could explain the variability found in intervention effectiveness. Lack of detail is common in the description of complex interventions and it is, therefore, not surprising that there was an absence of detail in the articles included in this overview. This however, constrains scientific replication and limits the subsequent introduction of successful interventions (Michie, Fixsen, Grimshaw, & Eccles, 2009) because even when significant effects are found it is not possible to determine which behaviour change techniques were responsible for these observed changes. This review assumes that self-monitoring was the integral component of all of the interventions however, without a detailed description of the other behaviour change techniques it is not

possibly to say unequivocally that this was the key behavioural component. Systematic reviews conducted within the general population and in those with a long-term illness have however, demonstrated the importance of self-monitoring in behaviour change and the significance of combining it with other behaviour change components (Dombrowski *et al.,* 2010; Michie, Abraham, Whittington, McAteer, & Gupta, 2009; Knittle, Maes, & de Gucht, 2010; Bray *et al.,* 2010). Future work would benefit from coding intervention descriptions using the recently developed Behaviour Change Technique Taxonomy (BCTTv1) (Michie, Johnston, Abraham, Francis, & Eccles, 2013) which enables a detailed description of intervention content according 93 hierarchically structured behaviour change techniques all derived from theory. This would establish the exact content of the intervention and control groups and evaluate the impact the content is having on effectiveness.

A majority of the articles in this review evaluated the effectiveness of various point-of-care technologies to monitor a patient's physiological status and health condition, known as telehealth. In the context of this review telehealth involved patients monitoring and transmitting their data via telephone or computer, to either receive an automated message about any necessary action to take or reviewed by a healthcare professional and in some cases feedback provided. The primary advantage to self-monitoring supported by technology is that it allows patients and healthcare professionals to be connected in real time and has become a popular method via which self-monitoring is facilitated. There was no consistent evidence within this overview that the use of technology was more advantageous than interventions that did not use technology nor were there any differences between telemonitoring and structured telephone support.

The evaluation of telehealth outside of this review has revealed a complex picture. In 2006, the Department of Health established three 'Whole Systems Demonstrators' which recruited over 3,000 patients with diabetes, heart failure or COPD into a large RCT (Bower *et al.,* 2011). The results of this trial indicated that telehealth patients were less likely to die and needed fewer hospital admissions and bed days in hospital than patients receiving usual care, but unexpected patterns that appeared among usual care patients suggested that the differences might not be attributable to telehealth

but to the detection of unmet need in the intervention group (Steventon *et al.,* 2012). There were also no discernable benefits for quality of life or psychosocial outcomes (Cartwright *et al.,* 2012). The model of self-monitoring proposed in Figure 3.4 suggests that a majority of telehealth is undertaken for clinical monitoring purposes and not chronic disease self-management, as in many cases adjustments were made either by an automated system or healthcare professional and fed back to the patient for implementation. How chronic disease self-management is integrated into telehealth is yet to be explored and despite many of these interventions explicitly stating that the intervention is one of self-management or aimed to enable self-management patients were rarely involved in responding to the data. In fact there is evidence to suggest that these interventions may lead to over dependency on technology with negative consequences such as an assumption that a healthcare professional is "watching over" them leading to a lack of response to monitored data (Radhakrishnan, Jacelon, & Roche, 2012; Ure *et al.,* 2012). As has been underlined in the article by Ciere *et al.,* (2012) the mechanisms at work in telehealth interventions have rarely been investigated and, therefore, there is little evidence available on which behaviour change techniques are included and how they affect outcomes, similarly true of the wider self-monitoring literature.

In the context of the current thesis one of the aims of this overview was to establish whether self-monitoring of blood test results would have any additional benefits or harms, in comparison to interventions which included patients monitoring just their symptoms or side effects. It is interesting to highlight that the articles that explored the impact of blood test self-monitoring (i.e. in thrombophilia and diabetes) failed to explore the impact of the interventions on healthcare utilisation and focused only patient reported outcomes and clinical well-being, whilst the articles in heart failure, COPD and hypertension all included healthcare utilisation and were focused solely on symptoms and side effect monitoring. Where comparisons can be made, there appears to be no consistent evidence that blood test monitoring is no more beneficial to clinical and psychosocial well-being than symptom monitoring, or detrimental.

3.7.5 Strengths and weaknesses of this review

Reviews of reviews bring together all of the systematic reviews and meta-analyses in the area in order to provide an overview of the evidence. By bringing together a large number of primary research studies, clinical groups and settings this review provides a comprehensive and evidence-based overview of self-monitoring across a range of long-term physical health conditions. There are however, several limitations that should be acknowledged.

As with any overview of secondary data, this review relies on the quality of the reporting found in not only the articles but also the primary research studies. Reporting was particularly poor in regards to the content of the intervention and control groups, the type of analysis undertaken within the primary research studies and in many cases whether between or within group differences were statistically significant. It was unclear if some of these reporting issues were due to poor reporting within the primary papers or as a result of word limit restrictions placed on the articles themselves; although many articles were able to provide this information, as exhibited in a number of high quality scores on the AMSTAR checklist.

The overall quality of the systematic reviews and meta-analyses were good, but with significant variation with some scoring the minimum possible quality score to some with a maximum score. The potential bias introduced by not reporting the sources of support and funding for both the review and primary research papers was of particular concern, as was the selection of studies for inclusion; by not searching grey literature many primary research studies may have been missed. Furthermore, the quality checks performed in this review assessed the quality of the article as a whole rather than the synthesis performed for each outcome within each article. This is particularly problematic for articles which combined a high quality meta-analysis of RCTs with a systematic review of varying study designs. For instance data may have only been aggregated or publication bias explored for some outcomes within a review and were hence given a lower score according to the AMSTAR quality assessment tool. Assessing the quality of evidence for each outcome would overcome this but was beyond the scope of this review. Despite the quality of the reviews themselves being good, a high

quality review may contain poor quality evidence, or even limited evidence, because that it all that is available. Therefore, assessment of quality within each article was vital however, integration of study quality into conclusions and recommendations was undertaken in less than half of all articles.

The inclusion of some primary research studies in more than one systematic review or meta-analyses may have unduly influenced the overall conclusions of this review. It is however, unlikely given that there was only slight overlap across the review (Pieper *et al.,* 2014). This however, did vary quite significantly between long-term conditions with no overlap in COPD and a very high level of overlap in thrombophilia. A high degree of overlap may reflect an unnecessary duplication of reviews (Pieper *et al.,* 2014). A systematic review should only really be performed in the case of an out-of-date review or a significantly different research objective. It is however, reassuring that reviews appear to reach broadly the same conclusion; that self-monitoring on the whole does not have a negative impact on health, psychological well-being or healthcare usage and in many cases it is at least, if not more effective in improving these outcomes than usual care.

The searches attempted to be comprehensive up to February 2014; however, as this is a rapidly evolving field, several primary research papers will have been published since the searches were undertaken and the articles may currently be being updated or new reviews undertaken. In addition for every review, primary studies will be missed. In this paper we have presented brief summaries of all the reviews in the tables, since our data extraction was limited to what was contained within the systematic review and not the original studies, it is possible that not all minor outcomes were captured. Primary or major outcomes for each disease were, however, available in all reviews.

In addition the current review included only articles published in English and those that were peer-reviewed. Applying language restrictions is not recommended (Smith *et al.,* 2011); but was unavoidable due to lack of access to translation services and funds to pay for these. Only eight articles, however, were excluded on this basis; therefore, suggesting low risk of bias. Although the recommendations encourage the inclusion of unpublished studies, the current review did not search grey literature and many of the

articles themselves also failed to search these sources. Data suggests that published trials generally include more participants and may show an overall greater treatment effect than studies published in the grey literature (Hopewell, McDonald, Clarke, & Egger, 2007; McAuley, Pham, Tugwell, & Moher, 2000). Therefore, potentially biasing the results towards a more positive effect.

A pragmatic decision was taken to structure the overview by outcome measure and then by long-term condition. This was due to the amount of data and to ensure a coherence to the results. Inevitably an overview of this kind can provide only a summary of the major points and conclusions about the reviews. It is, therefore, strongly encouraged that readers refer to the original reviews for additional information.

3.8 CONCLUSION

Despite the limitations of this overview of reviews, it is innovative in that it attempts to integrate conclusions across a number of long-term conditions, synthesises both systematic reviews and meta-analyses and examines a range of outcomes. The findings of this review need to be considered in light of the overall quality of the reviews, which varied quite significantly. Nonetheless it provides a useful synthesis of findings on the role of self-monitoring in long-term illness.

In summary, self-monitoring can have significant benefits including reductions in hospitalisation and readmission to hospital hence reducing the pressure placed on the healthcare system whilst at the same time improving, albeit in some cases small changes, in mortality, blood pressure, quality of life and adverse events. The impact of self-monitoring on outpatient services, GP attendance and other patients reported outcomes, however, remains unclear and requires further exploration. Due to heterogeneity in concept definitions, utilized scales and an overall low number of primary research studies definite conclusions are difficult to make but in the main suggest equivalence across all other outcomes. The role of patients in using the self-monitored data to adjust medication or lifestyle behaviours or seeking help is potentially crucial to the outcome of such interventions and requires further investigation.

3.9 POTENTIAL FOR SELF-MONITORING IN RA AND PSA

The preceding chapters have described the clinical implications of RA and PsA along with the therapeutic regimens and the associated economic burden of both blood monitoring and regular outpatient care (Chapter 1). Despite these requirements the current state of rheumatology services suggests there are significant deficits in the provision of care for patients with RA and PsA. This includes possibly unnecessary appointments for those who are feeling well and substantial delays or lack of capacity for those who are feeling worse. This has led to the development of patient-initiated services which have been shown to be both acceptable to patients and effective in increasing capacity without compromising the physical and psychological well-being of patients. Nevertheless, the literature recognises the need for further quantitative and qualitative research in order to provide a quality evidence base for this model of care (Chapter 2).

The potential of formal self-monitoring to reduce healthcare utilisation whilst maintaining and in some cases improving quality of life and clinical outcomes suggests that integration of these models of care for patients with arthritis could be a suitable substitute for usual care but is yet to be trialled (Chapter 2). An intervention of this nature would aim to teach patients how to formally self-monitor their symptoms, side effects and the blood tests undertaken for DMARD monitoring and provide them with the opportunity to use data to initiate their own contact with their CNS. This offers a possible avenue to develop a patient-led rheumatology service which is more responsive to the needs of established patients and offers an opportunity for more effective and efficient care in the CNS-led DMARD monitoring clinics at UCLH. Its feasibility and effectiveness would, however, need to be evaluated in order to establish effectiveness and acceptability. Therefore, the aim of this thesis is to answer these research questions. The following chapter will go on to describe the theoretical underpinnings of these types of intervention.

CHAPTER 4 - THEORETICAL UNDERPINNINGS

4.4 PROLOGUE

Chapters 1 to 3 have outlined the context in which this thesis is taking place along with the evidence for self-monitoring in long-term conditions and patient-initiated services in rheumatology. This chapter will now describe the theoretical underpinnings for these interventions, and the applicability of these theories to patients with arthritis.

4.5 COMPLEX INTERVENTIONS

Patient-initiated services and self-monitoring interventions can be described as complex, as in they consist of a number of interacting components and target a number of behaviours which vary in their level of difficulty (Craig *et al.,* 2008). These interacting components are the active ingredients that make the intervention "work" i.e. bring about the desired change in behaviour.

Patient-initiated services and self-monitoring interventions can be placed under the umbrella of "self-management". Self-management has been defined by Barlow *et al.,* (2002) as an individual's ability to manage the clinical and psychosocial consequences, along with the lifestyle changes inherent in living with a chronic condition. By enabling patients to manage their own DMARD monitoring appointments and access to rheumatology services, self-monitoring and patient-initiated services empower patients to manage the consequences of living with arthritis, which includes regularly attending hospital. Due to this broad definition the content and complexity of self-management interventions varies quite significantly, not only in terms of their aims and the behaviour/s they target, but also in terms of the behaviour change techniques they use and their theoretical underpinnings.

4.6 SELF-MANAGEMENT IN ARTHRITIS

In response to patients desire for greater involvement in their care and treatment decisions, along with the shift in control from clinician to patient, the last 25 years has seen a huge growth in self-management interventions particularly in the field of rheumatology. This is unsurprising given that arthritis requires daily management

outside of the contact had with healthcare professionals. Self-management interventions in arthritis aim to facilitate the learning of various behavioural and cognitive techniques in order to help patients manage their condition. This could be how to deal with pain and fatigue, how to monitor symptoms and side effects, how to manage access to healthcare or cope with the emotional and social adjustments required.

Guidelines for the management of RA suggest that self-management training is essential in order for patients to manage their illness effectively (National Audit Office, 2009b; National Collaborating Centre for Chronic Conditions, 2009; National Institute for Health and Care Excellence, 2013b). The Arthritis Self-management Programme (ASMP) developed by Lorig, Lubeck, Kraines, Seleznick and Holman (1985) is by far the most well-known program and has undergone extensive evaluation in multiple arthritis populations and in different settings. This programme differs from many others in that it is community based and delivered by trained lay leaders who themselves have arthritis. The ASMP combines elements of patient education and cognitive behavioural techniques, such as educating patients about their arthritis and the importance of self-care, whilst engaging them in goal setting, action planning and self-monitoring, as well as other self-management strategies. A majority of other interventions have been designed for a single rheumatic disease but ASMP groups can include people with different types of arthritis. In a 12 year review of the programme improved behaviour, self-efficacy and aspects of health status were reported (Lorig & Holman, 1993). Subsequent research in the UK suggested benefits of up to 12 months post-intervention in terms of mood, self-efficacy and pain for both patients with osteoarthritis or RA (Barlow, Turner, & Wright, 2000). Cost-effectiveness analysis of the ASMP has also revealed significant savings as a result of decreased physician visits (Kruger, Helmick, Callahan, & Haddix, 1998); therefore, suggesting that self-management interventions should have role in the standard care of patients with arthritis.

Due to the vast number of trials evaluating the effectiveness of self-management interventions in arthritis there are now a number of systematic reviews and meta-analyses that have synthesised the evidence. Although the content, delivery and

intensity of these interventions differs, there is some consistency in regards to the short-term benefits including improvements in pain, functional disability, knowledge, coping and psychosocial well-being (Riemsma, Taal, Kirwan, & Rasker, 2004; Niedermann, Fransen, Knols, & Uebelhart, 2004; Astin, Beckner, Soeken, Hochberg, & Berman, 2002; Knittle *et al.,* 2010; Warsi, LaValley, Wang, Avorn, & Solomon, 2003). Although the long-term effects have been questioned by Riemsma *et al.,* (2004), there is some evidence to suggest positive benefits in terms of physical activity, pain, disability, tender joints, psychological status and coping up to 14 months post-intervention and across different types of arthritis (Astin *et al.,* 2002; Knittle *et al.,* 2010; Iversen, Hammond, & Betteridge, 2010).

Although the content of the intervention developed and evaluated within this thesis differs to these other self-management interventions in regards to the behaviours targeted there is likely to be some consistency in the behaviour change techniques adopted within these interventions as a result of the similarities in their theoretical underpinnings.

4.6.1 Theories of self-management

Whilst a number of theories have informed the move towards and development of self-management interventions there is no one theory that encapsulates and dominates self-management (Serlachius & Sutton, 2009). A number of theories have been proposed by Serlachius and Sutton (2009) and these can be used to inform the content of an intervention as well as the framework used to evaluate it, by identifying theoretical constructs that could be targeted to change or explain a change in behaviour. Within the self-management literature two key theories have been discussed and utilised more extensively in people with arthritis: social cognitive theory (Bandura, 1986; Bandura, 1997) and self-regulation theory (Leventhal, Meyer, & Nerenz, 1980). It important to highlight that the intervention evaluated within this thesis was not developed to test a particular theory. Nevertheless, the behaviour change techniques which have been employed within the intervention and which are described in section 5.8.1.1 (page 204) can be linked to both of these theories. These theories were also used to select the psychological constructs measured within the evaluation of the intervention and to formulate the hypotheses relating to the

mechanisms of effectiveness. These two theories will now be presented alongside their applicability to patients with RA or PsA.

4.6.1.1 Social cognitive theory

Social cognitive theory has become one of the most influential social cognitive models in the field of self-management. It proposes that behaviour is determined by an interaction between personal factors, environmental influences and behaviour (Bandura, 1986). The basic premise is that people learn through a combination of their own experiences and by observing the behaviour of others and the consequences of those actions (MacAlister, Perry, & Parcel, 2008). There are nine key constructs within social cognitive theory (Table 4.1) which can be grouped into five categories (i) psychological determinants of behaviour, (ii) observational learning, (iii) environmental determinants of behaviour (iv) self-regulation and (v) moral disengagement.

Table 4.1. Constructs of social cognitive theory

Concept	**Definition**
Outcome expectations	Beliefs about the likelihood and value of the consequences of behavioural choices
Self-efficacy	Beliefs about the person's ability to perform behaviours that bring about desired outcomes
Collective efficacy	Beliefs about the ability of a group to performed concerted actions that bring about desired outcomes
Observational learning	Learning to perform new behaviours by exposure to interpersonal or media displays of them, particularly through peer modelling
Reciprocal determinism	Environmental factors influence individuals and groups, but individuals and groups can also influence their environments and regulate their own behaviour
Incentive motivation	The use and misuse of rewards and punishments to modify behaviour
Facilitation	Providing tools, resources, or environmental changes that make new behaviours easier to perform

Concept	Definition
Self-regulation	Controlling ones-self through self- monitoring, reward & instruction, goal setting, feedback & enlistment of social support
Moral disengagement	Ways of thinking about moral behaviours and the people who harmed that make infliction of suffering acceptable, by dis-engaging moral self-regulatory moral standards

Adapted from (MacAlister *et al.,* 2008), p.171

The psychological determinants of behaviour include outcome expectancies which are defined as the beliefs a person holds about the outcomes of performing a behaviour and the perceived value of these outcomes. These may be expectations about the physical, social or personal outcomes. In the context of the current thesis physical outcome expectations could be the perceived pleasant or unpleasant clinical consequences of performing self-monitoring, such as poorer control of inflammation as a result of not seeing the CNS face-to-face. Social outcomes expectancies might include the anticipated reaction of others and the social consequences of contacting the CNS for help, whereas personal outcome expectations refer to the anticipated feelings a person may have after performing a behaviour, such as a greater sense of control. This assumes that people will act to maximise the benefits and minimise the costs and work towards distant goals whilst ignoring the immediate costs and short-term benefits of performing alternative behaviours.

Self-efficacy defined as the confidence a person has about their ability to perform a behaviour (Bandura, 1997) is the concept for which social learning theory is most widely known and is particularly important when the behaviour is complex or difficult to perform. Social learning theory has identified four ways in which self-efficacy can be developed (i) mastery experience (ii) social modelling (iii) improving physical and emotional states and (iv) verbal persuasion (Table 4.2). Numerous studies have found that the performance of a behaviour is determined by both outcome expectancies and self-efficacy. Bandura (1997) suggests that people who doubt their self-efficacy will not attempt a behaviour, regardless of outcome expectancies.

Table 4.2. Methods of increasing self-efficacy

Concept	**Method**
Mastery experience	Enabling the person to succeed in attainable but increasingly challenging behaviours. The experience of performance mastery is the strongest influence on self-efficacy belief.
Social modelling	Showing the person that others like themselves can do it. This should include detailed demonstrations of the small steps taken in the attainment of a complex objective.
Improving physical and emotional states	Making sure people are well-rested and relaxed before attempting a new behaviour. This can include efforts to reduce stress and depression while building positive emotions—as when "fear" is re-labelled as "excitement".
Verbal persuasion	Telling the person that he or she can do it. Strong encouragement can boost confidence enough to induce the first efforts toward behaviour change.

Adapted from (MacAlister *et al.,* 2008), p.171

Although social cognitive theory includes other constructs, a majority of the empirical applications of this theory focus on self-efficacy and the concept has been employed extensively in rheumatology research. A recent literature review found 74 studies that had either reported the association between self-efficacy and arthritis-related disease variables or had included self-efficacy as the outcome of a behavioural intervention for patients with arthritis. Lower levels of self-efficacy were linked to greater physical disability, pain, fatigue and disease duration. The authors were also able to conclude that interventions that led to improvements in self-efficacy tended to have a positive impact on disease-related variables (Primdahl, Wagner, & Hørslev-Petersen, 2011a).

Poor self-efficacy has also been linked to higher levels of anxiety and depression in RA (Lowe *et al.,* 2008; Wright *et al.,* 1996). Very little research has been undertaken to explore the role of self-efficacy in PsA. Early work suggests, however, that lower self-efficacy is related to the use of catastrophizing as a coping strategy (Stewart & Knight, 1991) and more recently self-management interventions which have included patients with PsA have led to improvements in self-efficacy (Grønning, Skomsvoll, Rannestad, & Steinsbekk, 2012).

Observational learning draws on both outcome expectancies and self-efficacy. According to Bandura there are four key process which govern observational learning (Bandura, 1986) (i) attention (ii) retention (iii) production and (iv) motivation. People will tend to focus on and observe a behaviour which they feel has significant benefits. Retention of the behaviour will depend on intellectual capabilities. Performing or learning to perform that behaviour will then depend on a person's self-efficacy and motivation will also be influenced by outcome expectancies.

However, no matter how much observational learning takes place unless the observer's environment will support the behaviour or the person is able to influence their environment, the behaviour is unlikely to be performed. One basic environmental influence on behaviour is reinforcement or punishment, the other is facilitation in which the provision of new structures or resources are introduced in order for the new behaviour to be performed or to make it easier to be performed.

Self-regulation or self-control refers to a person's ability to endure short-term negative outcomes in anticipation of long-term positive outcomes. This is achieved through the acquisition of skills in order to self-manage. Bandura (1997) identified six ways in which self-regulation can be achieved (i) self-monitoring of one's own behaviour (ii) goal setting (iii) feedback on the quality of performance and how it can be improved (iv) self-reward (v) self-instruction by talking oneself through a behaviour and (vi) social support (Table 4.3). These strategies are both similar to and overlap with the techniques used to increase self-efficacy (MacAlister *et al.,* 2008) and are the most widely used when social cognitive theory is used to develop behaviour change interventions.

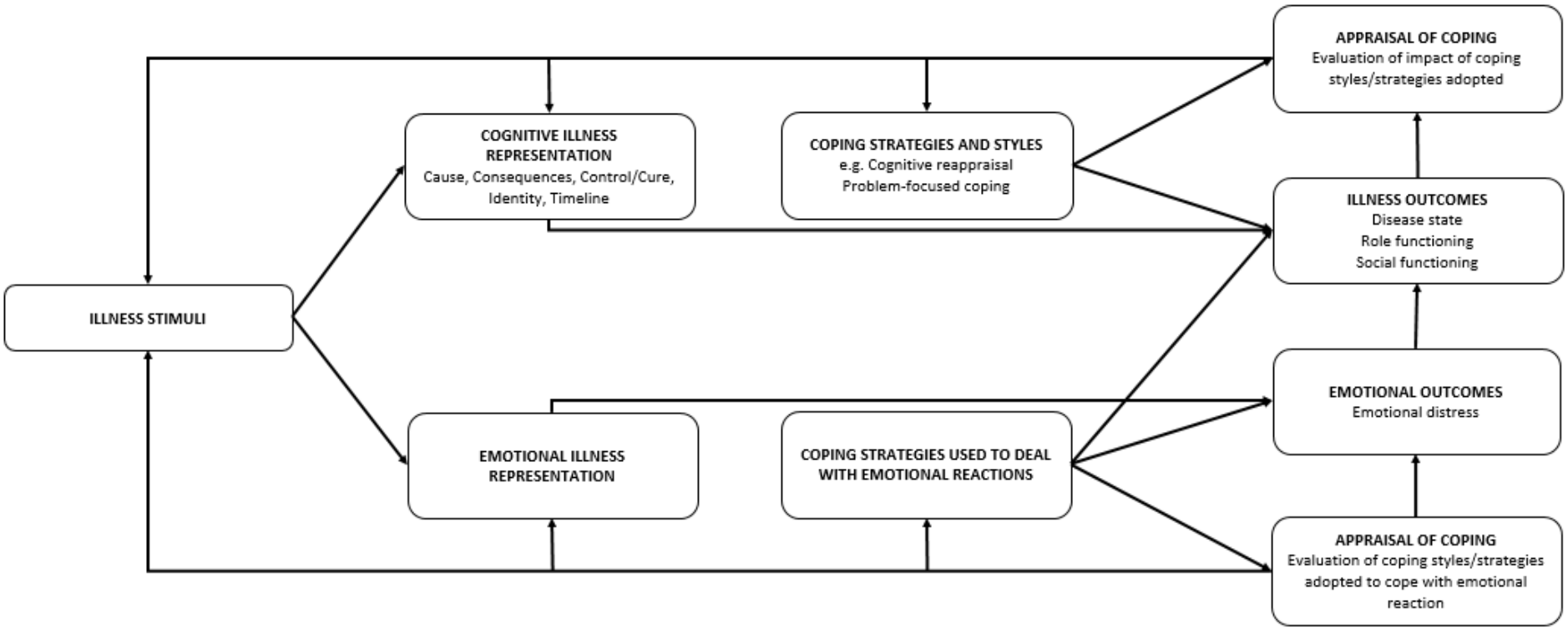
Table 4.3. Methods of achieving self-regulation

Concept	**Method**
Self-monitoring	The systematic observation of one's own behaviour—includes observing and recording both the behaviour itself and the context and cues or events accompanying the behaviour.
Goal setting	This is planned behaviour in which intentions are formulated in terms of both long-term and short-term goals that will bring people closer to the changes they desire. Gradual steps are needed to achieve the successes which will then increase self-efficacy.
Feedback	Feedback consists of information about the quantity and quality of the behaviour, either provided by others or from the person's own observations.
Self-reward	Short-term and frequent rewards that people give themselves may be more effective than rewards that may occur in the distant future.
Self-instruction	Effective self-instruction involves speaking to oneself about each subtask in a complex series of tasks.

4.6.1.2 Self-regulatory theory

Also known as the illness perceptions or common sense-model (Leventhal *et al.,* 1980), self-regulatory theory acknowledges that the cognitive determinants of self-regulation are important but also proposes that bottom-up processes like the experience of health and illness also play an integral role. Health-related behaviours are said to be the result of an interaction between cognitions (top-down information) and physiological experiences (bottom-up information). Social regulation theory suggests

that people develop representations of their condition following five key domains: identity, timeline, consequences, cause and control. Identity relates to the symptoms or label that an illness is given and timeline is the beliefs about how long the illness will last (i.e. acute, chronic or cyclical). Consequences, cause and control related to the perceived consequences of living with arthritis, the perceived causes and how much a person can influence the outcome of their arthritis. Each of these five components are related to both the cognitive and emotional processing of illness information which impact upon the type of coping strategies. This in turn influences outcomes, which could be emotional or illness-related. The final stage then involves an appraisal of the chosen coping strategy and a decision to either continue or chose another strategy, this can be achieved either directly or via a change in illness representations (Figure 4.1).



Source: adapted from Hagger and Orbell (2003)

Figure 4.1. The self-regulation model of illness representations

The five domains of illness representations have been explored extensively in RA and PsA and have been found to relate to a number of important outcomes, including physical and social functioning, quality of life, depression, functional disability, anxiety and pain (Sharpe *et al.,* 2001; Groarke, Curtis, Coughlan, & Gsel, 2005; Carlisle, John, Fife-Schaw, & Lloyd, 2005; Scharloo *et al.,* 1998; Graves, Scott, Lempp, & Weinman, 2009; Murphy, Dickens, Creed, & Bernstein, 1999; van Os, Norton, Hughes, & Chilcot, 2012; Kotsis *et al.,* 2012). Recent work has also sought to group patients with RA according to similarities in their beliefs. Longitudinal data from 227 patients suggested that there are two groups of individuals, one that is characterised by a negative representation of their arthritis who attributes more symptoms to their condition and reports stronger perceptions of the consequences, chronicity and cyclicality of their condition, and less control compared to a positive group. Membership of the negative representation group was associated with reports of greater pain, functional disability and distress, both cross-sectionally and over time (Norton *et al.,* 2013).

A systematic review and meta-analysis of psychological interventions for RA that included behaviour change techniques derived from self-regulation theory found 27 trials. The meta-analysis found positive effects in favour of the interventions based on self-regulation theory for outcomes such as mood, physical activity, pain and disability immediately post-intervention. At final follow-up, these differences remained significant for physical activity, pain, disability and depression. The authors found that interventions that included more self-regulation techniques reduced depressive symptoms and anxiety significantly more than interventions utilizing fewer self-regulation techniques (Knittle *et al.,* 2010). This provides further support for this theory in the development and evaluation of interventions for patients with arthritis.

A recent extension to self-regulation theory, the Necessity-Concern Framework (Horne, 2003; Horne, Weinman, & Hankins, 1999), acknowledges the importance of illness representations, but also recognises the importance of treatment beliefs. The proponents of the framework suggest that people's beliefs about their prescribed medication can be categorized into perceptions about the necessity of taking the drugs and concerns about taking them. As well as having beliefs about specific medications, people also have views about medications in general and their harm and overuse.

These beliefs have been explored in RA and suggest that concerns about taking DMARDS, having a poor understanding of the necessity of DMARDS and a belief that medications are harmful and overused are associated with poor adherence to DMARD therapy (Neame & Hammond, 2005; Treharne *et al.,* 2005) and more self-reported side effects (Nestoriuc, Orav, Liang, Horne, & Barsky, 2010). Research however, has not been conducted in PsA.

CHAPTER 5 - TRIAL METHODOLOGY

5.1 PROLOGUE

This chapter describes the aims and objectives of the RCT along with a description of the methodology. This will include information about study design, recruitment, inclusion and exclusion criteria for participants and a detailed description of procedures. The intervention is reported in line with the Template for Intervention Description and Replication (TIDieR) guidelines (Hoffmann *et al.,* 2014). This is followed by a description for each of the quantitative measures and their psychometric properties, concluding with the analysis plan.

5.2 AIMS AND OBJECTIVES OF THE TRIAL

- To assess whether patients with RA or PsA on DMARD therapy can safely self-monitor their symptoms, side-effects and blood test results and use data to safely initiate a telephone consultation with their CNS.
- Identify the factors which may impact upon a patient's ability to safely self-monitor and initiate care.
- To establish whether a patient-initiated and self-monitoring service for patients with RA or PsA has an effect on healthcare utilisation, psychosocial and clinical outcomes in comparison to usual care.
- To explore the mechanisms through which the intervention affects healthcare utilization and quality of life (mediation).
- To explore which baseline variables alter the strength of the relationship between trial arm and healthcare utilization and quality of life (moderation).

5.3 HYPOTHESIS

These predictions are based on the findings of previous literature outlined in Chapters 2 and 3, and the theoretical basis of the study outlined in Chapter 4.

- Participants in the intervention group will attend for fewer CNS outpatient visits than those in the control group over the trial period.

- There will be equivalence between the intervention and control group on visits to the rheumatologist and arthritis-related GP appointments.
- Participants in the intervention group will report greater improvements in their quality of life and mood than those in the control group.
- There will be equivalence between the intervention and control group on clinical outcomes.
- Participants in the intervention group will report greater improvements in the components of social cognitive theory (Bandura, 1986; Bandura, 1997) and self-regulation theory (Leventhal *et al.,* 1980) than those in the control group.
- The components of social cognitive theory (Bandura, 1986; Bandura, 1997) and self-regulation theory (Leventhal *et al.,* 1980), will be significant mediators and moderators of intervention effectiveness.

5.4 ETHICS APPROVAL

The study received full ethics approval from Camden and Islington Community Local Research Ethics Committee (Ref. 09/H0722/91).

5.5 STUDY DESIGN

This study was a parallel-group, explanatory, superiority RCT designed to assess the effectiveness of a self-monitoring and patient-initiated follow-up service in comparison to a usual care control group. Figure 5.1 represents the flow of participants in the trial. As in many trials of non-pharmacological interventions, participants could not be blind to group allocation. In order to obtain the rheumatologists agreement to recruit, each rheumatologist was informed when one of their patients were recruited into the trial and which arm they had been allocated to. Therefore, treating clinicians were also not blind. All psychosocial assessments were self-report and clinical assessments were undertaken by either the rheumatologist running the intervention or treating CNS who was also aware of group allocation. The final analysis was undertaken by the researcher managing the overall trial, who also co-facilitated the training sessions and, therefore, was also not blind to group allocation.

Figure 5.1. Flow chart of trial procedure

5.6 PROCEDURE

5.6.1 Study site

Participants were recruited from three hospital-based CNS-led DMARD monitoring clinics run in the Centre for Rheumatology at UCLH between February 2010 and July 2011.

5.6.2 Inclusion and exclusion criteria

At the beginning of 2010 UCLH had approximately 450 patients with RA or PsA who were receiving oral methotrexate either with or without the self-injecting anti-TNF agent's adalimumab or etanercept. These patients were selected for inclusion in the trial as they formed a majority of the monitoring appointments at UCLH and are treatments that do not require administration by a healthcare professional, as opposed to drugs such as infliximab which require attendance in outpatients for regular infusions.

5.6.2.1 Inclusion criteria

- All patients with RA or PsA (according to ACR/EULAR/CASPAR criteria) (Aletaha *et al.,* 2010; Taylor *et al.,* 2006).
- Attending a hospital-based CNS-led DMARD monitoring clinic appointment in the Centre for Rheumatology at UCLH.
- Aged 18 years or over.
- Fluent in written and spoken English.
- Patients whose treatment was classified as stable defined as disease management with methotrexate for at least 6 months, plus a further 3 months if patient were receiving one of two self-injected anti-TNF agents, adalimumab or etanercept.

5.6.2.2 Exclusion criteria

- Patients with psychosis or dementia, identified by the CNS via electronic patient records.
- Patients with significant co-morbidity (i.e. their predominant treatment was for another illness).
- Patients for whom blood tests and monitoring was undertaken by their GP.

- Patients whose treatment was classified as unstable. Defined as disease management with methotrexate for less than 6 months, or receiving one of two self-injected anti-TNF agents, adalimumab or etanercept for less than 3 months.
- Patients prescribed infliximab.

5.6.3 Identification of participants

Patients who met the inclusion and exclusion criteria were identified from clinic lists by the CNS on a monthly basis. Those identified as eligible were sent an information sheet (Appendix K) and consent form (Appendix L) two weeks prior to their outpatient appointment, where they were invited to talk further about the study with the CNS and/or researcher.

5.6.4 Consent and randomization procedure

At the outpatients appointment the CNS enquired about the patient's interest in participating and introduced them to the researcher who gave a full explanation of the study, including what would be involved in each arm of the trial. It was clearly explained that each participant would have a 50% chance of being in either the intervention or control group. Participants who consented to take part in the study were immediately randomised to one of two arms (i) the intervention or (ii) usual care.

Randomization took place using a randomization plan generator (Dallall, 2010). Randomly permuted blocks of 10 participants were used; this ensured that for every 10 participants entering into the study, five were randomized to the control and five to the intervention group. This prevented serious imbalance should the study have been terminated prematurely.

5.6.5 Assessment procedure

Participants were required to complete a questionnaire booklet on three occasions, immediately following randomisation and then again after phase one and then phase two of the trial (see section 5.8.1, page 199) for intervention participants and after the 3rd and 6th blood test for control participants. Each administration took approximately 30-40 minutes to complete.

Control group participants took the questionnaire away with them on the day of randomisation and were asked to return it in the freepost envelope provided. The intervention group could either do the same or bring the completed questionnaire along to the intervention training session. All subsequent questionnaires were sent via post and returned in a freepost envelope. Those who had not returned their questionnaire within 2 weeks of either randomisation or posting (if a follow-up questionnaire) received a telephone reminder and then another questionnaire. Thereafter, if no response was received, the participant was deemed lost to follow-up in regards to the psychosocial variables. Clinical measures and healthcare utilisation continued to be collected from the electronic patient records unless the participants requested otherwise.

5.7 MEASURES

In the evaluation of any complex interventions it is essential to select appropriate outcome measures (Medical Research Council, 2000). As health is multi-dimensional several different aspects may be relevant to assess the impact of a complex intervention. Nevertheless, because of errors that may arise from multiple statistical testing, and also because of participant burden and study costs, it is essential that investigators make an explicit and strategically considered choice of outcome measures (Medical Research Council, 2000).

As the theoretical underpinnings of the intervention lay within social cognitive (Bandura, 1986; Bandura, 1997) and self-regulation theory (Leventhal *et al.,* 1980) the evaluation framework and selection of measures were, therefore, based on these theories. In the UK, the Medical Research Council's (MRC) framework for complex interventions places theory at the centre of any evaluation (Craig, Dieppe, Macintyre, Michie, Nazareth, & Petticrew 2008). Ideas for complex interventions emerge from various sources, including: past practice, existing evidence, theory, an investigator, policy makers or practitioners, new technology, or commercial interests (Craig *et al.,* 2008). As the aim of this intervention was to enable patients to self-monitor their symptoms, side effects and blood test results at home and use this information to initiate care from their CNS, the content of the intervention was developed in order to address gaps in patient knowledge and skills. So although the aim of the current study

was not to test a particular theory, the content of the intervention, the selection of psychological constructs to measure and the formulation of hypotheses about the mechanisms of effectiveness were based on these two theories. The following measures were, therefore, selected on the basis that either the intervention would have an impact on the variable, or the variable would mediate or moderate the effects of the intervention; at the same time considering participant burden (Figure 5.2). A copy of the questionnaires can be found in Appendix M.

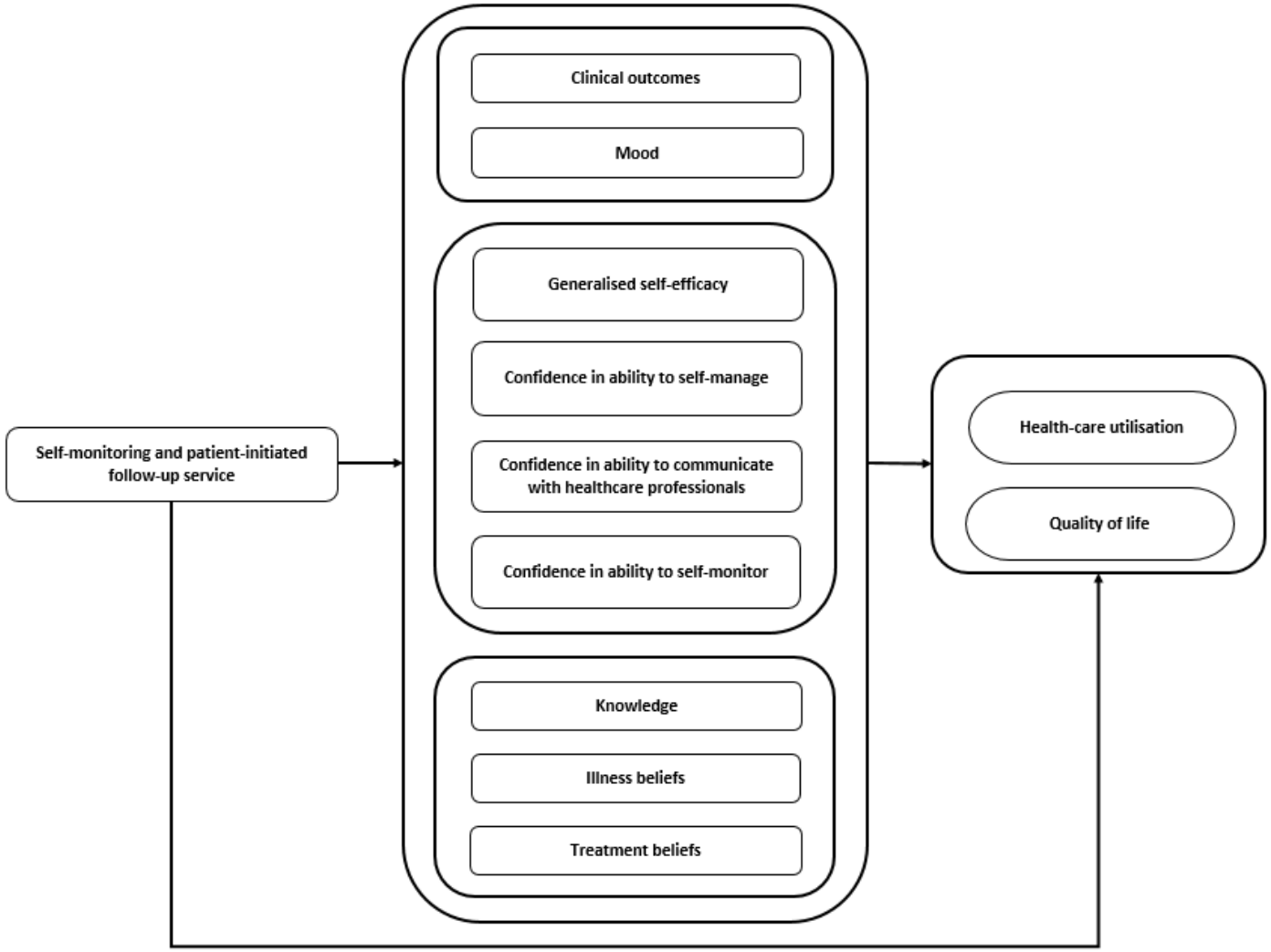


Figure 5.2. Evaluation framework

5.7.1 Demographic characteristics

Details of the participant's sex, age, living status (married/living with partner, living alone or living with relatives/friends) and ethnic background (Bangladeshi, Black-African, Black-Caribbean, Chinese, Indian, Pakistani, White or other) were self-reported.

5.7.2 Clinical variables

Participants provided information on their year of diagnosis and the date methotrexate was started; this was checked against electronic patient records. Clinical records were taken as more accurate, when the information could not be found in the clinical notes participant self-report was referred to. The dose of methotrexate administered at the start of the trial was extracted from the electronic patient records.

5.7.2.1 Response to treatment

As there is no single-point disease activity score for PsA, a response to treatment score was calculated for all participants. For patients with RA the EULAR response criteria (Fransen & van Riel, 2005) was used. These criteria are based on the DAS28 (Prevoo *et al.,* 1995), a measure of disease activity which incorporates the number of swollen and tender joints, ESR levels and patient's global overall well-being. To be classified as a responder to treatment, there needs to be a significant change in the DAS28 score and also low current disease activity. The three categories of good, moderate and non-responders are based on absolute improvement and the level of disease activity achieved (Table 5.1).

Table 5.1. EULAR disease activity criteria for rheumatoid arthritis

	Improvement in DAS28 from baseline		
DAS28 at end point	**>1.2**	**>0.6 and ≤ 1.2**	**≤ 0.6**
≤ 3.2	Good	Moderate	None
> 3.2 and ≤ 5.1	Moderate	Moderate	None
> 5.1	Moderate	None	None

DAS - Disease Activity Score

For patients with PsA the Psoriatic Arthritis Response Criteria (PsARC; (Clegg *et al.,* 1996)) was used. The criterion includes measurement of the following at baseline and again after treatment has commenced:

- Physician global assessment (0-5 scale) – response: reduction by one.
- Patient global assessment (0-5 scale) – response: reduction by one.
- Tender joint account (76 or 68) – response: reduction of > 30%.
- Swollen joint count (76 or 68) – response: reduction of > 30%.

Overall response is defined as improvement in two of the four items, one of which must be a joint count and there must not be worsening in any of the four items.

A new variable was then created in order to combine the results of the EULAR criteria and PsARC. The EULAR response criteria of moderate and good were recoded as a response; and none as no response in order to correspond to the categories within the PsARC. Individual items on the DAS28 and PsARC were also retained for analyses.

5.7.2.2 Blood test results

The blood tests outlined in section 1.9.3 (page 44) were performed as part of the routine monitoring of methotrexate and disease activity in RA and PsA for all trial participants.

5.7.2.3 Functional disability

Version 2 of the Health Assessment Question (HAQ-II; (Wolfe, Michaud, & Pincus, 2004)) is one of the most widely used questionnaires of functional disability in rheumatology. The questions ask about the ability of the individual to undertake certain activities (e.g. lift heavy objects) over the past week. This 10-item scale has responses from without any difficulty (1) to unable to do (4). The scale score ranges from 0-3 after appropriate item score reversals and scale adjustments; higher scores represent greater levels of functional disability. The HAQ-II possess satisfactory reliability (Cronbach's alpha = 0.88), correlates well with the full version of the HAQ (Fries, Spitz, Kraines, & Holman, 1980), quality of life and clinical outcomes (Maska, Anderson, & Michaud, 2011) but test–retest reliability is yet to be investigated.

5.7.2.4 Pain and fatigue

To reduce participant burden pain and fatigue were measured using a visual numeric scale. Participants were asked how much they were affected by pain and fatigue using two separate histogram visual numeric scale (see Figure 5.3 as an example). These modified scales are easier for participants and result in less missing data and unclear responses (Ritter, Gonzalez, Laurent, & Lorig, 2006). The histograms become larger in size and darker in colour as the severity of the pain or fatigue increases (from left to right). Circling the number below the histogram described the pain or fatigue the participant had experienced in the past 2 weeks. Scores ranged from 0 to 10, with the higher scores indicating more pain or fatigue.

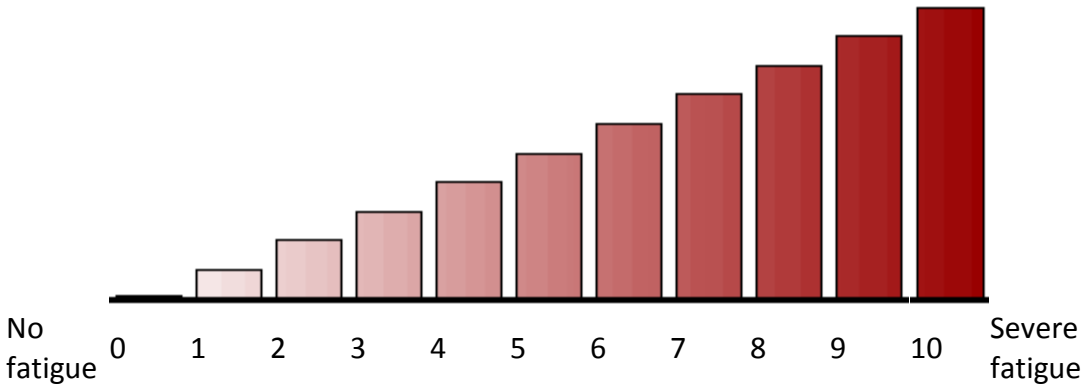


Figure 5.3. Histogram of visual numeric scale for fatigue

5.7.3 Primary outcome

5.7.3.1 Healthcare utilisation

The primary outcome was healthcare utilisation. This included outpatient visits to the CNS, rheumatologist and arthritis-related GP visits. Data on outpatient visits were taken from electronic patients records at the end of the trial period and recorded as a cumulative frequency. Data on GP visits were provided by participants at each of the assessment points and a cumulative frequency was calculated.

5.7.4 Psychosocial outcome variables

The following variables were measured at baseline, after phase one and phase two for the intervention group and after the 3rd and 6th blood test for the control group.

5.7.4.1 Quality of life

Health-related quality of life was the other primary outcome measure and was measured using the 12-item Short-Form Health Survey (SF-12v1®) (Ware Jr, Kosinski, & Keller, 1996) which is a shortened version of the 36-item SF-36® (McHorney, Ware Jr, & Raczek, 1993; Ware Jr & Sherbourne, 1992). Designed to measure quality of life across two component summary scales the Physical Component Summary (SF-12v1® PCS) and the Mental Component Summary (SF-12v1® MCS). This 12-item version was chosen as opposed to the SF-36® to reduce participant burden. After item aggregation and transformation, total scores range from 0-100 with higher scores representing better quality of life.

The psychometric properties of the SF-12v1® have been compared to the SF-36® in a sample of British patients with RA (Hurst, Ruta, & Kind, 1998). Moderate and strong correlations were found between the two component scales. Both SF-12v1® component scores were also found to be responsive to change over a 3 month period and ICC suggested good test-retest reliability (SF-12v1® MCS = 0.71, SF-12v1® PCS = 0.75).

5.7.4.2 Mood

As well as each being important outcomes in their own right, anxiety and depression were also considered psychosocial process variables and were measured using the Hospital Anxiety & Depression Scale (HADS; Zigmond & Snaith 1983). The HADS is a 14-item self-screening questionnaire for depression and anxiety in patients with physical health problems. The two 7-item subscales, measure how a person has been feeling in the past week. The scale scores range from 0-21, with higher scores indicating greater levels of anxious or depressed mood. A score of 0–7 on either subscale is regarded as being in the normal range, a score of 8–10 is suggestive of the presence of moderate levels of anxiety or depression, and a score of 11 or above indicates caseness, a high likelihood that a person would be diagnosed with clinical anxiety or clinical depression. A systematic review of the HADS has confirmed the factor structure, found the cut-off points to be valid against clinical interviews, reports excellent internal consistency (Cronbach's alpha: anxiety 0.68-0.93; depression 0.67-0.90) and appropriate correlations between the scales and other commonly used questionnaires (Bjelland *et*

al., 2002). High test-retest reliability has also been reported (*r*=0.86-0.89) (Spinhoven *et al.,* 1997).

5.7.5 Psychosocial process variables

The following variables were measured at baseline, after phase one and phase two for the intervention group and after the 3rd and 6th blood test for the control group.

5.7.5.1 Self-efficacy

5.7.5.1.1 Generalised self-efficacy

Self-efficacy is person's belief in their ability to perform a task. There are a number of measures of self-efficacy which have been published and utilized within the rheumatology literature, some of which are specific to arthritis and others generic. A generalised measure of self-efficacy was selected rather than an arthritis-specific measure such as the Arthritis Self-Efficacy Scale (ASES) (Lorig, Chastain, Ung, Shorr, & Holman, 1989) or Rheumatoid Arthritis Self-Efficacy scale (RASE) (Hewlett, Cockshott, Barrett, Stamp, & Haslock, 2001). These measures specify behaviours which were not related to the content of the current intervention, such as self-efficacy for pain and function, and, therefore, a validated generalized measure of self-efficacy was deemed more appropriate to both the intervention and control group.

In a review of three generalised self-efficacy measures (Scherbaum, Cohen-Charash, & Kern, 2006) only the General Self-Efficacy Scale (GSES) has been assessed for comprehensibility, reliability and validity in patients with arthritis (Barlow, Williams, & Wright, 2005). Therefore, the 10 item GSES (Schwarzer & Jerusalem, 1995) was selected, which assesses the belief that one can perform a novel or difficult task, or cope with adversity in various domains.

Responses are on a 4-point Likert scale from 1 (not at all true) to 4 (exactly true). Total scores range from 10-40. Higher scores on this measure indicate higher levels of generalised self-efficacy. The scale has been confirmed to be one-dimensional, to possess good reliability with Cronbach's alpha ranging from 0.88 to 0.91, test-retest reliability in people with arthritis (*r*=0.63) and correlates well with other clinical and psychosocial variables and in the expected directions (Barlow *et al.,* 2005). These

findings have been replicated in a systematic review of the measure in a variety of populations and countries (Scholz, Doña, Sud, & Schwarzer, 2002).

5.7.5.1.1 Behaviour-specific confidence

The Health Education Impact Questionnaire (HeiQ™; Osborne, Elsworth, & Whitfield, 2007) and the Medication Education Impact Questionnaire (MeiQ™; Ciciriello, Buchbinder, Wicks, & Osborne, 2010) have been developed to assess the impact of health education and self-management programs in relation to medication use. The HeiQ™ v3.0 is a shortened version of the original HeiQ™ v1.2 and is organised into a set of eight constructs. Similarly the MeiQ™ (Ciciriello *et al.,* 2010) consists of 29 items making up six constructs (Figure 5.4). The constructs can be administered independently; however, item order must be preserved.

In order to assess a person's confidence in their ability to monitor and manage their arthritis and communicate with healthcare professionals the self-monitoring and insight construct was selected from the HeiQ™ and the active communication and self-management ability constructs from the MeiQ™ (Figure 5.4). Responses for the self-monitoring and insight construct of the HeiQ™ are on a 4-point Likert scale from 1 (strongly disagree) to 4 (strongly agree), with a total score ranging from 1-4. Responses for the two MeiQ™ constructs are on a 6-point Likert scale ranging from 1 (disagree strongly) to 6 (agree strongly), with total scale scores ranging from 1-6. Higher scores on all scales indicate stronger beliefs in the concepts represented by the scale.

The original 51-item HeiQ™ v1.2 was developed and validated in a sample of 592 people with a wide range of chronic diseases and demographic characteristics (Osborne *et al.,* 2007). The results suggest that the HeiQ™ v1.2 is a reliable and sensitive measure for assessing the benefits of a broad range of health education programs. The authors report Cronbach's alphas of 0.70 for the self-monitoring and insight subscale and an intra-class correlation (ICC) of 0.63 which indicates good test-retest reliability (Schuler *et al.,* 2012). The authors have also demonstrated good internal consistency for the MeiQ™ constructs, with Cronbach's alphas ≥0.7. The test-retest reliability also suggests good stability and reliability over time, with ICCs ranging from 0.68 to 0.87 (Ciciriello *et al.,* 2010).

Domain 4 - Self-monitoring and insight – HeiQ™

This construct captures the individuals' ability to monitor their condition, and their physical and/or emotional responses that lead to insight and appropriate actions to self-manage. An important component of this construct is the individuals' acknowledgment of realistic disease-related limitations, and the ability and confidence to adhere to these limits. This may also relate to the monitoring of specific sub-clinical indicators of disease status.

Domain 2 - Active Communication - MeiQ™

This scale measures the capacity of health consumers to communicate effectively with health professionals. Active communication includes the ability to understand what the health professional is saying, the capacity and confidence to feedback beliefs and experiences and discuss the information provided. It also requires the confidence and capacity to ask questions clarifying the information given, and to gather further information if it is required.

Domain 4 - Self-management ability- MeiQ™

This scale measures health consumers' confidence and ability to perform self-management tasks. These include the ability to actively participate in decision-making and perform self-management tasks related to their condition and medication.

Figure 5.4. HeiQ™ and MeiQ™ included construct definitions

5.7.5.2 Illness and treatment beliefs

5.7.5.2.1 Illness beliefs

Illness perceptions are cognitive representations or beliefs that a patient has about their illness. These perceptions have been shown to determine not only behaviour but have also been associated with a number of arthritis-related outcomes including function, depression, psychiatric morbidity and quality of life (Maas, Van Der Linden, & Boonen, 2009). Based on self-regulation theory (Leventhal *et al.,* 1980), the original Illness Perceptions Questionnaire (IPQ; Weinman, Petrie, Moss-Morris, & Horne, 1996) was developed to provide a quantitative assessment of Leventhal's illness representation component of the self-regulatory model (Leventhal *et al.,* 1980).

A revised version of the IPQ, the IPQ-R (Moss-Morris *et al.,* 2002) was developed to address the internal consistency problems identified in some of the IPQ subscales. The questionnaire assesses each of the components of illness representation: identity, time (acute/chronic), consequences, personal control, treatment control, illness coherence, timeline cyclical and emotional representations. Table 5.2 provides definitions for the five subscales utilised within this trial. Selection of these subscales was based on suitability for the study population and the possible mechanisms through which the intervention was hypothesised to impact on healthcare utilisation and quality of life.

Table 5.2. Definitions of the IPQ-R subscales

Subscale	**A belief…..**
Identity	…about the number of symptoms attributable to their arthritis
Consequences	…that their arthritis will have serious consequences
Personal control	…in one's ability to personally influence the outcome of their arthritis
Treatment control	…that medical treatments will be effective in controlling their arthritis
Illness coherence	…that arthritis "makes sense"

IPQ-R – Illness Perceptions Questionnaire-Revised

The IPQ-R is divided into three sections, with the identity presented first as a list of 12 commonly experienced symptoms. Respondents are asked to indicate whether they have experienced any of these symptoms since starting treatment for their arthritis and to subsequently judge whether the symptom is related to their arthritis. The sum of this latter question forms the illness identity subscale, with yes scoring 1 and no 0, total scores range from 0-12. The remaining subscales are measured by a total of 22 items. Responses are rated on a 5-point Likert scale, from 1 (strongly disagree) to 5 (strongly disagree). After the relevant reverse scoring, total scale scores range from 6-30 for consequences and personal control and 5-25 for treatment control and illness coherence. High scores on the identity and consequences dimensions represent strongly held beliefs about the number of symptoms attributed to their arthritis and the negative consequences of arthritis. High scores on the personal control, treatment

control and coherence dimensions represent positive beliefs about the controllability of their arthritis and its treatment and a personal understanding of the condition.

The psychometric properties of the IPQ-R have been evaluated in eight illness groups including a sample of 76 patients with RA (Moss-Morris *et al.,* 2002). Principal Component Analysis (PCA) confirmed the structure of the measures and Cronbach's alphas ranged from 0.75 to 0.89 indicated good internal consistency. The validity of the identity subscale was evaluated using an independent samples t-test which found a significant difference between those symptoms experienced versus those participants associated with their illness, in addition all the symptoms were endorsed by a percentage of the patients, confirming the validity of the range of symptoms included in the identity subscale. The 6 month test-retest reliability also confirmed that the IPQ-R had acceptable consistency overtime (ICC=0.46-0.88). The IPQ-R has been specified in this trial, with the questions stating RA or PsA rather than "the illness". This specified measure has been used successfully in a number of studies with Cronbach's alpha ranging from 0.68 to 0.88 on each of the subscales (Sterba *et al.,* 2008; Graves *et al.,* 2009).

5.7.5.2.2 Treatment beliefs

In addition to the IPQ-R treatment control subscale, beliefs about methotrexate were measured using the Beliefs about Medicines Questionnaires (BMQ) (Horne *et al.,* 1999). The specific concern and specific necessity subscales were selected. Each subscale consists of five items assessing concerns about the potential adverse consequences of taking methotrexate and the necessity of methotrexate. The scales are measured using a 5-point Likert scale from 1 (strongly disagree) to 5 (strongly agree). Sum scores range from 5-25 with higher scores suggesting more concerns about the adverse consequences of taking methotrexate and viewing methotrexate as necessary. The subscales possess acceptable internal consistency for patients with RA with reported Cronbach's alphas of between 0.81-0.88 for specific necessity and 0.56-0.66 for specific concern (Treharne, Lyons, & Kitas, 2004; Van De Bemt *et al.,* 2009). The authors of the measure also report good test-retest reliability (0.60 to 0.78) and correlations between the subscale and other measures of illness and medication beliefs and adherence in the expected directions (Horne *et al.,* 1999).

An item was also developed to assessment perceived treatment burden. Participants were asked to rate how burdensome their treatment had been so far, from 1 (not burdensome) to 5 (extremely burdensome).

5.7.5.2.3 Knowledge about methotrexate

In addition to the IPQ-R illness coherence subscale which measures a person's overall understanding of their arthritis, the Methotrexate in Rheumatoid Arthritis Knowledge (MiRAK) (Ciciriello, Wicks, Osborne, & Buchbinder, 2010) and the adapted Methotrexate in Psoriatic Arthritis Knowledge (MiPAK) tests were used to assess patients overall knowledge of methotrexate in relation to their illness. The MiRAK was adapted for the purposes of this thesis, for use in people with PsA. This adaption was undertaken by a rheumatologist, two CNSs and the MiRAK authors who include a rheumatologist and an epidemiologist/health services researcher. Forty-two of the questions remained the same, for 16 questions RA was replaced with PsA and the remaining items were deemed inappropriate for patients with PsA. The questions "Having untreated RA increases your chance of having a heart attack" and "Methotrexate is often combined with other medications that treat RA" were removed. The items "Methotrexate stops most fingernail problems in people with psoriatic arthritis" and "Methotrexate can be used to control skin diseases" were added. Both scales consist of 60-items with responses either true, false or don't know. Total scale scores range from 8-57, with greater scores indicating greater knowledge. The authors report excellent internal consistency (0.84) and test-retest reliability (ICC=0.894) for the MiRAK (Ciciriello *et al.,* 2010)

5.7.6 Safety of decision-making[2]

The safety with which participants made decisions about the need for a telephone consultation with their CNS was recorded within the intervention group after each blood test, as either "safe" or "unsafe". A decision was deemed "unsafe" when the participant did not initiate a telephone consultation when either a blood test result had significantly changed or was outside the normal range, or there was a new or worsening symptom or side effect. A decision was deemed "safe" either because:

[2] Assessed in the intervention group only

a. The participant did not initiate a telephone consultation when either a blood test result had remained the same and was within the normal range, or there was no new or change in symptoms or side effects, or
b. The participant initiated a telephone consultation when either a blood test result had significantly changed or was outside the normal range, or there was a new or worsening symptom or side effect, or
c. The participant initiated a telephone consultation when either a blood test result had remained the same and was within the normal range, or there was no new or change in symptoms or side effects.

It was important to distinguish between safe or unsafe decision making as opposed to correct or incorrect decision making. The former classification differs from the latter, as patients may have made a decision that was incorrect but was not unsafe i.e. contacting the CNS when blood tests were normal and there was no new or worsening symptoms or side effects. The former could be detrimental to tight disease control and well-being.

5.8 INTERVENTION GROUP

Figure 5.5 provides a diagrammatic representation of the intervention.

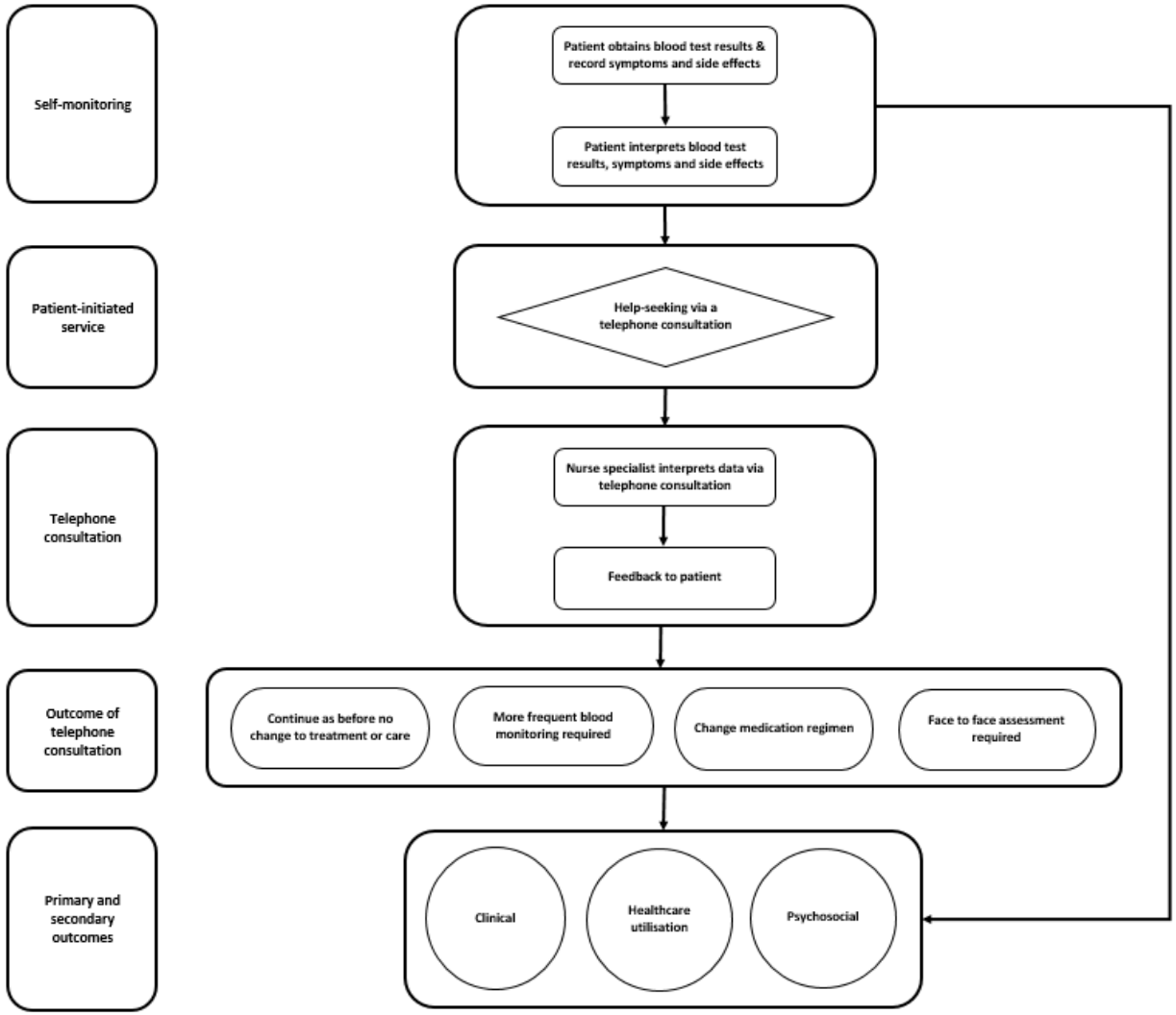


Figure 5.5. A diagrammatic representation of the intervention.

5.8.1 Intervention procedures

All participants randomised to the intervention group took part in a training session to provide them with the knowledge, skills and resources required to monitor their own blood test results, symptoms and side effects and initiate care. This one-off 2 hour training session was delivered by a rheumatologist and the researcher with a group of between 2-6 participants. These groups were held in the day and evening at UCLH, in order to increase participation. The content of this training session was established in collaboration with the supervisory team and the CNSs at UCLH. The rheumatologist delivering the intervention is an experienced clinician, with a specific interest in the social and psychological impact of living with a rheumatic disease. The researcher was a Trainee Health Psychologist, with an interest in chronic disease self-management and who had received training in how to facilitate and deliver self-management interventions. Both were supervised by Professor Stanton Newman an expert in designing and delivering self-management interventions. A CNS was also present either at the beginning or end of the session to take clinical measurements.

The training session introduced the research team, the purpose and aims of the intervention and the rationale for participants' selection in the study. The rheumatologist then provided detailed clinical information covering the following areas;

- The cause and symptoms of RA and PsA.
- The pharmacological treatment options and their potential side effects.
- Information about the blood tests, symptoms and side-effects that would need to be monitored.
- How to initiate care from the CNS.

Participants were then trained how to identify normal or "safe" ranges of blood levels, side effects and symptoms and decide if any action was necessary. After a short break participants were guided through an example blood test scenario and then practiced interpreting example blood test results, symptoms and side effects. The results of these practice tasks were then reviewed within the group in a discussion led by the

rheumatologist. This enabled the group facilitators to provide tailored feedback to each participant in order for them to understand why they had made any errors and the potential implication of that error in the real world, highlighting the importance of safety and being conservative in their decision making.

The rheumatologist then reviewed, in collaboration with the respective participant, the results of their last five blood tests. This enabled the rheumatologist and patient to understand and obtain normative ranges. The standard normal ranges applied to most participants however, for those whom these ranges were deemed unacceptable personalised ranges were set by the rheumatologist. The researcher then guided participants through the study documentation and instruction on what would happen next. Participants were given the following materials:

- A file to store all study documentation.
- A copy of the training slides (Appendix N).
- A table indicating the triggers for patient action (Appendix O).
- Contact details for all members of the research team (Appendix P).
- A blood record sheet (Appendix Q).
- Practice documentation (Appendix R).

The date of the participant's next blood test was noted at the training session to allow the researcher to monitor the patients' attendance and check results. The participant was asked to inform the researcher when any subsequent blood tests had been undertaken. The blood test results the participants were expected to assess were markers of inflammation (CRP and ESR), plus haemoglobin, WBC, liver function tests (ALP and ALT), platelets and neutrophils.

Table 5.3 highlights the normal range and definition of significant change for each of the eight tests. These ranges and significant changes were developed and agreed by the clinical team at UCLH. From this point on participants in the intervention group received routine care from their rheumatologist, defined as outpatient appointments every 6 months, and had access to the emergency CNS helpline if requested. All

participants attended the hospital for their blood tests every 4-6 weeks depending on their dose of methotrexate, as per usual care.

Table 5.3. Normative ranges by blood test

Test	**Normal Range**	**Definition of significant change**
Haemoglobin	12.0 - 17.0	Fall of more than 1.0
WBC	3.0 - 10.0	Two readings in a row each with a fall of more than 1.0
Neutrophils	2.0 - 7.5	A fall of more than 2
Platelets	150 - 400	Two readings in a row with falls of more than 50
ALP	40 - 129	A result which doubles from the previous blood test or rises 258
ALT	10 - 50	A results which doubles from the previous blood test or rises above 100
ESR	0 - 20	A rise of more than 20 from the previous blood test results
CRP	0 - 5	A rise of more than 20 from the previous blood test results

WBC - White Blood Count; ALP - Alkaline Phosphatase; ALT - Alanine Transaminase; ESR - Erythrocyte Sedimentation Rate; CRP - C-Reactive Protein

The intervention arm consisted of two phases:

Phase One: This phase encompassed the participants' first three blood tests. Twenty-four hours after each blood test, participants were sent a copy of their results either via email or post, depending on the patient's preference. Included were the patient's previous blood test results (Appendix S), to enable calculation of change scores by the participant. The form required participants to record if the current result was out-of-range or a significant change had occurred since their last blood test and if any further advice was needed. This structured approach allowed participants to work through the results methodically. Participants also recorded, using a 17-item checklist, the side effects and symptoms they had experienced since their last blood test, indicating if they were any new or continuing symptoms. For continuing symptoms participants also had to indicate if the symptom had become worse, better or remained the same

since their last blood test. The final questions asked participants to record whether based on these blood test results, symptoms or side effects if a telephone consultation with the CNS was required using the following criteria:

- A blood test result was outside of the normal range.
- A blood test result had changed significantly since their last blood test.
- A new symptom or side effect had appeared since their last blood test.
- A continuing symptom or side effect had become worse since their last blood test.

In between blood tests participants were asked to take immediate action, by contacting the CNS helpline, upon the appearance of any of the situations listed in Table 5.4.

Table 5.4. Symptoms and side effects to be monitored between blood tests

Symptom	**Contact the CNS if….**
Vomiting	persists over 24 hours
Diarrhoea	persists over 48 hours
Mouth ulcers	symptoms, causing discomfort and interference with normal eating
Skin problems	unexplained rash or itching occurs
Bruising	unexplained bruising occurs
Bleeding	frequent nose bleeds or excessive bleeding following minor injury
Sore throat	if episodes requiring treatment occur within a 4 week period
Fever	if fever persist for over 24 hours
Breathlessness	if breathlessness occurs in the absence of physical exertion
Dry cough	unexplained dry cough
Chicken pox/shingles	if been exposed to the chicken pox or shingles virus
Pregnancy	if pregnancy is suspected

The researcher contacted the participant within 48 hours of receiving their results to go through the completed documentation and provide feedback on whether they had made the appropriate decision. If any errors were made these were reviewed and feedback was provided as to why they were incorrect. This was to ensure that the patient fully understood the implications of their decisions and the consequences of not reporting this information to their CNS.

If any of the triggers for patient action were present participants contacted the CNS for a telephone consultation in order to evaluate whether the issue could be resolved remotely. If during this consultation the CNS felt that there was a need for a face-to-face outpatient appointment an emergency appointment was booked for within the subsequent 7 days.

Progression onto Phase Two: If after the 3rd blood test participants had correctly identified the need for contact with the CNS on at least two of the three blood tests they were able to move onto phase two of the trial. Those who did not meet these criteria continued on in phase one until they correctly interpreted two consecutive blood tests. If after the fifth blood test a participant had not been able to successfully identify when an outpatient appointment was needed, they were removed from the trial and returned to usual care as they were deemed unable to self-monitor safely.

Before progression onto phase two of the trial, intervention participants completed a follow-up questionnaire, a repetition of the baseline questionnaire, without demographic data.

Phase Two: The second phase of the trial encompassed blood tests 4 to 6. As in phase one after each blood test the participant was sent their results via post or email depending on their preference, along with the same questionnaire. Participants were asked to complete the questionnaire on receipt of the results and send it back in the freepost envelope provided. Participants did not receive a telephone call from the researcher, as this part of the study was to evaluate how participants did when interpreting and initiating contact with their CNS independently. By removing the additional support provided by the researcher the second phase of the trial aimed to

assess the effectiveness of the intervention without attention as a confounder. Patients were asked to call or email their CNS using the same criteria described on page 201. After the final blood test a third follow-up questionnaire was then completed.

5.8.1.1 Behaviour change techniques

A complex intervention, such as the one evaluated within this trial, is defined by several interacting components known as the "active ingredients" (Medical Research Council, 2000). As the aim of this intervention was to enable patients to self-monitor aspects of their disease at home and use this information to initiate care from their CNS, the content of the intervention was developed in order to address gaps in patient knowledge and skills, using a number of well-established behaviour change techniques. By defining the current intervention in terms of behaviour change techniques this not only allows replication and implementation it also provides a link with theory. The recently updated BCTTv1 (Michie *et al.,* 2013) contains 93 hierarchically clustered techniques many of which can be linked to the published theories of self-management described in Chapter 4. A retrospective assessment of the intervention using the BCTTv1 was undertaken and Table 5.5 outlines the results of this process. Prior to any coding of BCTs it is important to specify the target behaviour/s and target population. In the case of this intervention the targeted behaviours were (i) self-monitoring – including recording and interpretation and (ii) initiating care (help-seeking). The target population were patients with RA or PsA on DMARD therapy. A total of 13 BCTs were identified in the intervention. These 13 behaviour change techniques can be linked to both social cognitive theory (Bandura, 1997) and self-regulation theory (Leventhal *et al.,* 1980) described in Chapter 4 and were used to guide the selection of outcome measures for the trial evaluation, as described in section 5.7.5 (page 191).

Table 5.5. Behaviour change technique and implementation in the RCT

Behaviour change technique	**Definition of the technique**	**Implementation**
Behaviour practice or rehearsal	Prompt practice or rehearsal of the performance of the behaviour one or more times in a context or at a time when the performance may or may not be necessary, in order to increase habit and skill.	Participants were asked to practice the monitoring of blood tests (four separate scenarios) within the training session.
Credible source	Present verbal or visual communication from a credible source in favour of or against the behaviour.	The training session was delivered by the rheumatologist and researcher who provided information on the benefits of undertaking self-monitoring and initiating their own care.
Demonstration of the behaviour	Provide an observable sample of the performance of the behaviour, directly in person or indirectly e.g. via film, pictures, for the person to aspire to or imitate.	Participants were shown during the training session an example scenario of how blood test results should be interpreted.

Behaviour change technique	Definition of the technique	Implementation
Discrepancy between current behaviour and goal	Draw attention to discrepancies between a person's current behaviour (in terms of the form, frequency, duration, or intensity of that behaviour) and the person's previously set outcome goals, behavioural goals or action plans (goes beyond self-monitoring of behaviour).	At each of the telephone calls for blood tests 1-3 the researcher highlighted any discrepancies between the participant's current ability to safely self-monitor and initiate care and the goal of the intervention.
Feedback on behaviour	Monitor and provide feedback on performance of the behaviour (e.g. form, frequency, duration, intensity).	At each of the telephone calls for blood tests 1-3 the researcher monitored and provided feedback on the participant's decision making. Paying particular attention to unsafe help-seeking.

Behaviour change technique	Definition of the technique	Implementation
Framing/reframing	Suggest the deliberate adoption of a perspective or new perspective on behaviour (e.g. its purpose) in order to change cognitions or emotions about performing the behaviour.	If participants made an unsafe decision the researcher elicited the patient's beliefs about the need for contact with the CNS and their understanding of the principles of the intervention. Together attempts were made to reframe these beliefs and address why their response was incorrect.
Goal setting (behaviour)	Set or agree a goal defined in terms of the behaviour to be achieved.	During the training session the goal of the intervention was defined and agreed with each of the participants.
Information about social and environmental consequences	Provide information (e.g. written, verbal, visual) about social and environmental consequences of performing the behaviour.	During the training session information was provided on the benefits of performing the behaviour and the potential reduction in hospital visits.

Behaviour change technique	Definition of the technique	Implementation
Instruction on how to perform the behaviour	Advise or agree on how to perform the behaviour.	The training session and supporting documentation provided instruction on how to interpret their symptom, side effects and blood test results and how to initiate care from the rheumatology team.
Self-monitoring of behaviour	Establish a method for the person to monitor and record their behaviour(s) as part of a behaviour change strategy.	Participants were provided with documentation to record and monitor their blood test results, symptoms and side effects as well as whether they needed to initiate care.
Social comparison	Draw attention to others' performance to allow comparison with the person's own performance.	Attention was drawn to the performance of other participants after practice of the behaviour in the education session.

Behaviour change technique	Definition of the technique	Implementation
Social reward	Arrange verbal or non-verbal reward if and only if there has been effort and/or progress in performing the behaviour	Participants were congratulated and encouraged when they interpreted their symptoms, side effects and blood tests safely and made safe decisions to initiate care.
Social support (unspecified)	Advise on, arrange or provide social support (e.g. from friends, relatives, colleagues, "buddies" or staff) or non-contingent praise or reward for performance of the behaviour. It includes encouragement and counselling, but only when it is directed at the behaviour.	Encouragement was given to all participants by the researcher to support self-monitoring and the initiation of care.

DMARD – Disease Modifying Anti-Rheumatic Drug

5.9 CONTROL GROUP

Participants in the control group received standard care this typically consisted of a blood test every 4-6 weeks, outpatient appointments with the CNS every 3 months and rheumatologist every 6 months. Advice was also freely available via the CNS emergency helpline when requested.

5.10 PARTICIPANT SAFETY

The safety of participants both in the intervention and control groups were of the utmost priority to the research team. Phase one of the study was developed in order to establish that participants could correctly and safely interpret their blood test results, symptoms and side effects with support from the research and clinical team. The blood tests of all intervention participants were reviewed both by the researcher and CNS independently of the patient. Any serious concerns about the health and care of these patients were acted upon immediately. If the participant had any concerns about any aspect of their healthcare within the study period they were able to contact any member of the research team by email or telephone. This included the CNS helpline or their consultant's secretary, where patients were responded to within 24-48 hours.

5.11 STATISTICAL ANALYSIS

All analyses were undertaken in IBM SPSS Statistics Version 21.0.

5.11.1 Sample size calculation

An *a priori* power calculation was conducted using G-Power 3.1 (Faul, Erdfelder, Lang, & Buchner, 2007). An initial power calculation was performed using data from Hewlett *et al.,* (2005b). This study reported a median of 8 (range 5-13) appointments with the consultant rheumatologist in the patient-initiated service and 13 (range 11-17) appointments in the control group. These medians and ranges were converted into mean and standard deviations using online software (Lowry, 2014) based on calculations derived from Hozo, Djulbegovic, & Hozo (2005). This generated a mean and standard deviation of 8.5(2.31) and 13.5(1.73) respectively. To conduct an independent samples Mann-Whitney U test (two groups), a total sample size of 10 participants would be required at 80% power (α=0.05), with an effect size of 2.45. The

magnitude of the effect size and hence sample size were deemed inappropriate for a trial of effectiveness and, therefore, a generic sample size calculation was conducted with an estimate medium effect size of 0.50, 80% power and α=0.05. This required a total sample of 134 participants.

5.11.2 Missing data

The authors of the MeiQ™ and HeiQ™ specify mean item replacement as the method by which missing data should be dealt with; this was undertaken when calculating scale scores. No other scales specify a method for imputing missing data.

Across the entire dataset there was 3.65% missing data and no participant had more than 50% missing data (the a *priori* cut off for exclusion from the analyses). Appendix T provides greater detail of missing data levels with indication of which variables had the highest amounts of missing data. At baseline the component scores of the SF-12v1® had the most missing data (n=30, 30%), at first follow-up the knowledge about methotrexate scale had the most missing data (n=10, 11.9%) and at final follow-up the DAS28 had the most missing data (n=31, 48.4%). At baseline the missing SF-12v1® data was as a result of an administrative error which meant that the questionnaire was distributed with a missing page, the knowledge questionnaire is particularly long and the poor response at first follow-up may have been a result of questionnaire fatigue although the measure was in the middle of the questionnaire booklet and was completed at baseline and final follow-up with no problems. At final follow-up due to organisational issues difficulty was experienced in gathering disease response data. No individual variables had more than 50% missing data (the *a priori* cut off for exclusion from the analyses).

The pattern of missing data was evaluated using the IBM SPSS version 21.0 missing data function. Little's Missing Completely At Random (MCAR) test was conducted to check if there was any systematic differences between the missing values and the observed values. A non-significant result (p=0.53) indicated that data was MCAR and as the overall dataset had less than 5% missing data multiple imputation methods were used. This minimizes the bias found in any further analyses.

Missing data was imputed at scale level, but not for an entire time point (i.e. when a participant was lost to follow-up). Imputation was performed separately for the dataset which included intervention only variables (i.e. data specific to the interpretation of symptoms, side effects and blood test results) after imputation of the variables which were applicable for both trial arms. Constraints and rounding were used to ensure that the imputed scale level data was meaningful and corresponded to possible values. Ten scale-level imputation iterations were used to eliminate bias; it has been suggested that between three and ten imputations are sufficient, particularly for datasets with minimal missing data (Rubin, 2009). All analyses, unless otherwise stated, were performed on each of these 10 datasets and then pooled for multiple imputation to give a final combined result.

The multiple imputed dataset was, therefore, used for the analysis of baseline differences between trial arms, intervention effectiveness in relation to healthcare utilisation and the associated economic evaluation. The analysis exploring changes over time in the psychosocial variables was undertaken using multi-level modelling (MLM) (described in more detail in section 5.11.9.3, page 223) which can be undertaken on datasets with missing data. Therefore, these analyses were conducted on the original dataset. The analyses of the mediators and moderators of intervention effectiveness were conducted using the PROCESS macro developed by Hayes (2013), this macro cannot be implemented on multiply imputed datasets; therefore, the 1st imputation was analysed. Although this is not ideal as fewer imputations lead to less precise confidence intervals and p-values, Bodner (2008) recommends having as many imputations as the percentage of missing data which in this case is not far from this estimate.

5.11.3 Internal reliability and validity

Cronbach's alphas were calculated to assess the internal reliability of each of the psychosocial measures at each of the three time points. Cronbach's alpha of >0.70 were considered acceptable (Cronbach, 1951); variables with Cronbach's alpha <0.70 were explored further and recalculated on removal of each item. An item was permanently removed from a scale, across all time points, if the Cronbach's alpha improved sufficiently to justify its exclusion.

The authors of the IPQ-R suggest two methods for assessing the validity and internal validity of the identity subscale (Moss-Morris *et al.,* 2002). Firstly, a paired-samples t-test was conducted comparing participant's scores on the symptoms experienced subscale and the identity subscale. A significant difference between the symptoms patients experienced versus those they associated with their arthritis, would suggest a conceptual difference between somatisation and identity and, therefore, validated the measure. Secondly, the frequencies with which different symptoms were endorsed as part of patients' illness identity were calculated. Because the IPQ-R identity subscale consists of disparate symptoms and a certain number of these symptoms are more relevant to arthritis than others, the internal consistency is less relevant than in the other subscales. Nevertheless, Cronbach's alphas were also calculated for each time point.

5.11.4 Normality and outliers

Distributions of responses were examined using histograms and by performing the Shapiro-Wilk test ($p \leq 0.01$). As data transformations can hinder interpretation of the results (Osborne, 2002) non-parametric statistics were conducted on variables that failed to meet the assumptions of normality.

Scatterplots were inspected for outliers, defined as standardised scores in excess of ±3.29 (Tabachnick & Fidell, 2013). Mahalanobis D^2 ($p<0.001$) was also calculated, values above or below the critical chi squared value (corresponding to the number of included independent variables) identified any multivariate outliers. Cook's distance indicated if these cases were having any undue influence on the results. Values above one were of concern and cases were removed and the analyses rerun by means of a sensitivity analysis. Any outliers remained in the analysis, as these were viewed as legitimate data points that may contain valuable information on the relationships between variables (Orr, Sackett, & Dubois, 1991).

The regressions performed as part of this analysis took the form of a Poisson distribution and were, therefore, undertaken within the Generalized Linear Models (GLM) function in IBM SPSS version 21.0 (further details in section 5.11.8.3, page 218). GLM procedures within IBM SPSS version 21.0 do not generate any output in relation

to multicolinearity between IVs; therefore, the final regression models were rerun using the standard multiple linear regression function within SPSS to obtain the tolerance and Variance Inflation Factor (VIF) measures of multicolinearity. Tolerance is an indicator of how much of the variability of the specified Independent Variable (IV) is not explained by the other IVs in the model, values <0.10 are of concern as this may indicate that correlations between the IV are high. The VIF is an inverse of the tolerance value and values above 10 would be of concern (Pallant, 2007). The normal probability plots (P-P) of the regression standardised residuals were also inspected to ensure that the points laid in a reasonable straight diagonal line from bottom left to top right. In the scatterplot of the standardised residuals, the residuals should be in roughly a rectangular distribution, with most of the scores concentrated in the centre, along the 0 y-axis.

5.11.5 Intention-to-treat analysis

For those participants who did not complete the first and/or final follow-up questionnaires blood test and healthcare utilisation data continued to be collected from the electronic patient records. This allowed a comprehensive ITT analysis to be performed on these outcomes. ITT is deemed the most suitable way of analysing RCTs and compares participants in the groups they were originally assigned irrespective of whether they received the intervention or not (i.e. dropped out and returned to usual care). A full ITT analysis was not possible for PROMS because if a participant were lost to follow-up they had no data to analyse, they did however, remain within the group they were allocated to. In order to test the robustness of the findings sensitivity analyses were performed for complete (i.e. all three administrations of the questionnaire) (n=79) and available case cohorts (n=100).

5.11.6 Significance level

A significance level of $p<0.01$ was set, unless otherwise stated, this was due to the large number of tests performed and hence the risk of obtaining a false-positive result i.e. rejecting the null hypothesis when it is in fact true (Type 1 error).

5.11.7 Comparison between trial arms at baseline

Differences between the intervention and control group on normally distributed continuous variables were explored using independent samples t-tests. Equality of

variances were checked using Levene's test, if significant the variances of the two groups differed and the assumption of equality of variance was violated; the adjusted values were then used. Effect sizes were calculated using eta squared (η^2), which ranges from 0 to 1 and are interpreted as Cohen's d (Cohen, 1988), whereby 0.01 is a small effect, 0.06 moderate and 0.14 large. Differences on non-parametric continuous data were explored using the Mann-Whitney U test and the associated median values and inter-quartile range for the ranked data were calculated. Effect sizes were reported using *r* and interpreted using Cohen's (1988) criteria as described above.

In order to explore the relationship between categorical variables a chi squared test for independence were performed, with Yates' Continuity Correction which compensates for the overestimate of the chi squared value in a 2 by 2 design. Cell frequencies were checked to ensure that at least 80% of cells had an expected frequency of five or more, and if it was a 2 by 2 design a frequency of 10 or more. If a 2 by 2 table violated this assumption the Fisher's Exact Probability Test was employed. In designs where any cell contained a frequency of 0, groups were collapsed appropriately. Phi (ϕ) was used as the effect size for 2 by 2 tables, using Cohen's (1988) criteria as described above. For tables larger than 2 by 2, Cramer's V was reported as the effect size, as this takes into account the degrees of freedom (*df*). The criteria for a small, medium and large effect differs depending on the size of the table. One is subtracted from the number of categories in the row variables (R-1) and column variable (C-1) and whichever of these values is smaller is the effect size and is evaluated using the following criteria:

- For R-1 or C-1 equal to 1 (two categories): small = 0.01, medium = 0.30, large = 0.50.
- For R-1 or C-1 equal to 2 (three categories): small = 0.07, medium = 0.21, large = 0.35.
- For R-1 or C-1 equal to 3 (four categories): small = 0.06, medium = 0.17, large = 0.29.

In order to explore whether there were any differences in demographic and clinical data between trial arms, between those who did and did not receive their allocated

group and the interaction between trial arm and receipt of allocation a series of factorial analysis of variances (ANOVA), for continuous variables, and factorial logistic regressions, for categorical variables, were performed. For the factorial ANOVAs homogeneity of variances were checked using Levene's test as described above.

5.11.8 Safety of initiating care

5.11.8.1 Were intervention participants able to safely initiate contact with their CNS?

Safety of decision making was modelled as the percentage of intervention participants who made a safe decision to initiate care at each of the assessment points and also as the percentage of safe decisions made by each participant. Percentages rather than frequencies are reported as not all participants were in the trial for six blood tests. Assessments in relation to blood test results were deemed objective triggers and symptoms and side effects subjective triggers.

5.11.8.2 Did safety improve over time?

In order to assess whether safety improved over time multilevel models were run within the general linear mixed model (GLMM) function of IBM SPSS version 21.0. MLM, also known as random-coefficient, mixed-effect, hierarchical linear and multilevel regression models, deal with nested data – that is, where observations are clustered within successive levels of a data hierarchy (Heck, Thomas, & Tabata, 2013). In this trial decision making was nested within participants and GLMM provides a means of incorporating this categorical repeated measures outcome (i.e. safe or unsafe) in situations where there are clustered data structures. Changes in decision making over time, as the dichotomous categorical dependant variable were modelled as a function of time nested in participant, as illustrated in Figure 5.6. In which safe or unsafe decision making was the binomial dependant variable, time was a fixed effect and participant identification number a random effect.

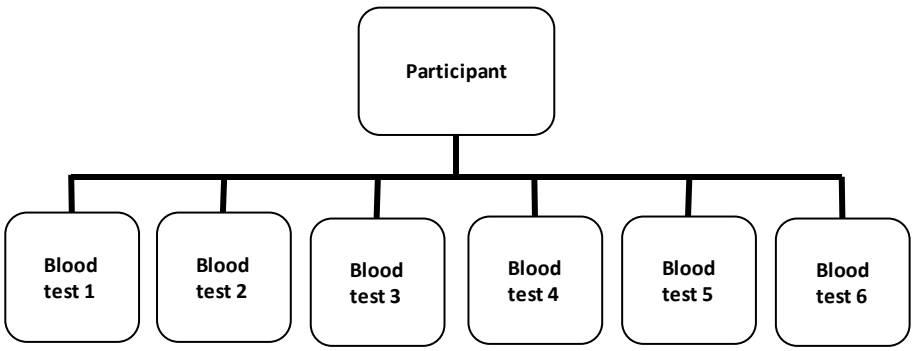


Figure 5.6. Data structure of the RCT – decision-making

MLM is a relatively new statistical technique within psychology but is gaining popularity (Marques & Hamilton, 2014). This is because in comparison to more traditional methods of analysis such as ANOVA, it allows the hierarchical structure of the data to be taken into account, it is able to include all data despite missingness and has the ability to calculate random intercepts and slopes for each participant rather at a group level; therefore, enabling a more accurate modelling of the data. The dataset was restructured in IBM SPSS Statistics Version 21.0 from a wide to a long format so that each variable was represented as a single column. Each participant, therefore, had multiple rows of data, one for each longitudinal measurement occasion.

In order to check the assumption that scores within a participant were highly correlated the first MLM included no predictors and a scaled identity covariance type for both level one and level two in order to calculate the ICC. An ICC of 0.1 are classified as small, 0.2 medium and 0.3 large (Maas & Hox, 2005). A large ICC suggests that scores within a participant are more similar than between participants; therefore, the assumption of independence is violated. In this situation the use of traditional analysis methods, such as ANOVA, may lead to biased results as the sample size becomes artificially inflated which could lead to overestimate of the effect. ICC for safe/unsafe initiation of care based on blood test results was r=0.40 and symptoms and side effects r=0.43; therefore, indicating the value of nesting time (first-level unit) within participant (second–level unit).

5.11.8.3 What were the baseline predictors of safe initiation of care?

In order to explore whether any of the demographic, clinical or psychosocial variables measured at baseline predicted a person's ability to safely self-monitor and initiate care a series of Poisson regressions were performed. Poisson rather than standard hierarchical multiple linear regressions were undertaken as the DV (number of correct decisions over the trial period) was count data, a positive integer and on the whole negatively skewed with many cases of 0 (Figure 5.7).

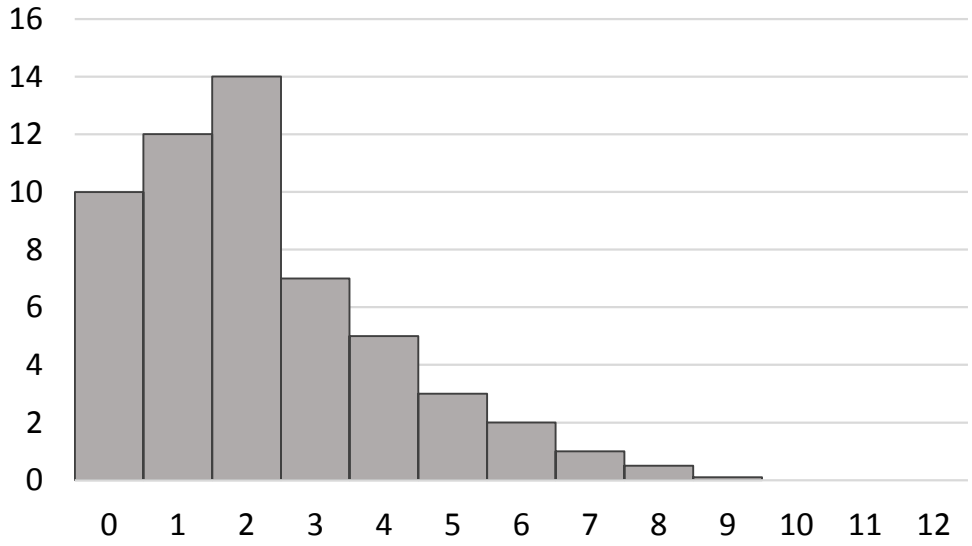


Figure 5.7. Example of a Poisson distribution

These analyses were performed using the GLM function in IBM SPSS version 21.0. Modelling the raw cell counts however, can be misleading because each participant had a varying number of blood tests within the trial. Variables of this nature are handled within the GLM as offset variables.

In a study with many predictor variables, such as this, it is desirable to reduce the number of variables whilst preserving the usefulness of the predictions and power. In a traditional multiple linear regression this is achieved through well-known methods such as stepwise, forward and backward regressions. These methods are, however, not easily implemented when performing a Poisson regression within IBM SPSS version 21.0. The forward selection algorithm method has, therefore, been proposed and is found to be superior to transforming the dependant variable to no longer fit a Poisson distribution (Famoye & Rothe, 2003). The method involves running univariate

regressions for each IV, selecting the IV with the smallest Akaike's Information Criterion (AIC) value, which indicates the best fitting model. If $p>0.05$ the variable is disregarded and the next lowest AIC value is selected and so on. When the first significant ($p<0.05$) IV is found this variable is retained and another Poisson regression is performed which incorporates the significant IV with all other IVs. This stepped process is continued until there are no remaining significant variables.

In a Poisson regression the β coefficient can be interpreted for continuous IVs as the amount that a one-unit change in that IV increases or decreases the DV, holding all other IVs in the model constant. For categorical IVs the β coefficient represents an increase or decrease in the DV when comparing all groups to the reference group. The Exponentiated β Coefficients (Exp(β)) is interpreted as is an incident rate ratio, so that Exp(β)>1 indicate more safe decisions and Exp(β)<1 fewer safe decisions.

5.11.9 Intervention effectiveness

5.11.9.1 Effects of the intervention on healthcare utilisation

As healthcare utilisation was a cumulative frequency across the trial period, univariate Poisson regressions were performed using the GLM function in IBM SPSS version 21.0, as described above. Trial arm was the IV and healthcare utilisation (CNS, rheumatologist, GP and total) the DV.

5.11.9.2 Effects of the intervention on healthcare costs

The analyses of cost effectiveness was unplanned *a priori* and was only considered important in light of the results found in relation to healthcare utilisation. Post-hoc tests are often considered to be data dredging and, therefore, inferior to *a priori* comparisons (Rothwell, 2005). These additional tests greatly inflated the total number of statistical tests performed; therefore, the *p*-value was adjusted to 0.001 to compensate for these additional comparisons. Caution should however, remain when interpreting these results. The cost-effectiveness analyses was performed for two different models of care:

Model One: The intervention and control group as implemented including the CNS -led telephone consultations.

Model Two: The intervention and control group as implemented not including the CNS -led telephone consultations - replicating the analysis performed by Hewlett *et al.,* (2000). This model assumes that the additional telephone contact generated by the intervention could be managed by the existing CNSs.

Each of these models was costed using the national average unit cost as well as the upper and lower quartiles provided by the Department of Health reference costs for 2010-2011 (Department of Health, 2011a) and 2012-13 (Department of Health, 2013a) and the published Unit costs of Health and Social Care 2012 (Curtis, 2012) (Table 5.6). The analysis of cost effectiveness was conducted with all three estimates (upper, average and lower) in order to provide a sensitivity analysis, this was followed by the analysis of complete cases only.

Table 5.6.Source of unit costs

Usage	Source	Description in source	Average cost
Face-to-face rheumatology nurse outpatient appointment	Department of Health (2013a) Reference costs for 2012-13	Non-consultant led, non-admitted, face-to-face, follow-up outpatient appointment in rheumatology	£89 (Lower quartile £52, upper quartile £105)
Telephone consultation with rheumatology nurse	Department of Health (2013a) Reference costs for 2012-13	Non-consultant led, non-admitted, non-face to face, follow-up outpatient appointment in rheumatology	£80 (Lower quartile £52, upper quartile £112)
Face-to-face consultant rheumatologist outpatient appointment	Department of Health (2013a) Reference costs for 2012-13	Consultant-led, non-admitted, face-to-face, follow up outpatient appointment in rheumatology	£133 (Lower quartile £105, upper quartile £150)
GP appointment	Unit costs of Health and Social Care 2012 (Curtis, 2012)	11.7 minute consultation	£43 including direct staff costs & staff training £36 including direct staff costs but without training (average £39.50)

Usage	Source	Description in source	Average cost
Education training session†	Unit Costs of Health and Social Care 2012 (Curtis, 2012)	One hour of patient contact with a senior staff nurse costs £105 excluding qualifications and £121 including qualifications. The training session was 2hrs long and included 5-6 patients per session‡	Lower £35 per patient (5 people attending) Upper £48.40 per patient (6 people attending)
Travel to an outpatient appointment	Department of Health (2011a) Reference costs for 2010-2011	Travel to an outpatient appointment	£18
Travel to services other than outpatients	Department of Health (2011a) Reference costs for 2010-2011	Travel to services other than outpatients	£5
Blood tests	Local costs	Full blood count=£10.33 ALP & ALT=£7.26 ESR=£7.26 CRP=£7.26	£32.11

GP – General Practitioner; ALP - Alkaline Phosphatase; ALT - Alanine Transaminase; ESR - Erythrocyte Sedimentation Rate; CRP - C-Reactive Protein

† Intervention participants only

‡ The cost of running the expert patient programme, a chronic disease self-management programme is £298 per patient. This 6 week programme which runs for 2½ hours a week and, therefore, equates to £19.87 per patient per hour

5.11.9.3 Effects of the intervention on clinical and psychosocial outcomes

As DAS were collected only at baseline and final follow-up exploration of significant group by time interaction effects were explored using mixed between-within subjects ANOVA rather than MLM. MLM is not recommended for nested data that consists of ≤2 time points as there is only one observable change (Hoffman, 2010). Homogeneity of variances were checked using Levene's test which indicated p-values of greater than 0.05 and, therefore, the variances for the two trial arms were equal. In addition to homogeneity of variances a mixed between-within subjects ANOVA assumes homogeneity of inter-correlations. Therefore, for each level of the between-subjects variables, the pattern of inter-correlations among the levels of the within-subjects variable should be the same. This assumption was tested using Box's Test of equality of covariance matrices which indicated at the recommended $p<0.001$ level that the assumption was not violated. In order to explore whether there were any differences between the intervention and control group on response to treatment, using the EULAR treatment response criteria for RA and the PsARC response scale, chi squared for independence with Yate's continuity correction for a 2 x 2 table, were used.

In order to explore changes overtime on blood test results and psychosocial variables MLM was undertaken using the GLMM function in IBM SPSS statistics version 21.0. The data collected were nested within participant and hence the dataset was restructured from a wide to a long format so that each variable was represented as a single column. Each participant, therefore, had multiple rows of data, one for each longitudinal measurement occasion.

In order to check the assumption that scores within a participant were highly correlated the first MLM included no predictors and a scaled identity covariance type for both level one and level two in order to calculate the ICC. ICCs were medium for CRP blood tests ($r=0.21$) and large for all remaining variables ($r>0.40$); therefore, indicating the value of nesting time (first-level unit) within participant (second–level unit). The complete case analysis replicated the magnitude of the ICCs found in the whole cohort.

Trial arm (0=control, 1= intervention), time (0, 1, 2) and the interaction between trial arm and time were entered as fixed effects in each model, with participant identification number as a random effect. Models were fitted with a first order autoregressive (AR1) covariance structure. This covariance structure assumes a type of dependence between adjacent observations which dies out between observations further apart (Snijders & Bosker, 2012). Restricted Estimate Maximum Likelihood (REML) methods were used as these are preferred for small samples (Bryk & Raudenbush, 1992).

A significant interaction term was interpreted as evidence for differential treatment effectives. The main effects of group and time are reported but were not relevant to the primary research question and, therefore, have not been interpreted. Standardized adjusted effect sizes for group differences at each time point were calculated using Hedges g along with 99% confidence intervals (as $p<0.01$) using the formula provided by Turner and Bernard (2006). Hedges g includes a correction factor for small samples which, if absent, may lead to a less accurate and upwardly biased effect size. These effect sizes are interpreted in the same way as Cohen's *d* (1988) (small=0.20, medium=0.50, large=0.80).

5.11.10 Mechanisms of effectiveness

The mechanisms via which the intervention was hypothesised to work are outlined in Table 13.

Table 5.7. Hypothesised mechanisms of action

Measure	Mechanism of action	Outcome
Clinical variables (i.e. pain, fatigue, disease activity)	Deterioration in health	↓ Quality of life ↑ Healthcare utilisation
Mood	Increased anxiety and depression	↓ Quality of life ↑ Healthcare utilisation
Self-efficacy	Increased self-efficacy	↑ Quality of life ↓ Healthcare utilisation

Measure	Mechanism of action	Outcome
Illness & treatment beliefs	More realistic illness and treatment beliefs	↑ Quality of life ↓ Healthcare utilisation

5.11.10.1 Mediation analysis

It was hypothesised that changes in the psychosocial outcome and process variables over the trial period may mediate the relationship between trial arm (X) and healthcare utilisation (Y), and trial arm (X) and quality of life (Y). The variables that were hypothesised to be potential mediators of the relationships between trial arm and healthcare utilisation were changes in clinical variables (i.e. pain, fatigue, functional disability and disease activity), quality of life, mood, self-efficacy and illness and treatment beliefs, from baseline to final follow-up. The variables that were hypothesised to be potential mediators of the relationships between trial arm and quality of life were changes in clinical variables (i.e. pain, fatigue, functional disability and disease activity), mood, self-efficacy and illness and treatment beliefs, from baseline to final follow-up.

Figure 5.8 illustrates the total effect (c) which assumes that trial arm causes healthcare utilisation or quality of life. It is possible, however, that changes over time in the above variables may mediate the relationship between trial arm (X) and healthcare utilisation/quality of life (Y). This path (c') is known as the indirect effect and is a product of coefficients of path a and b.

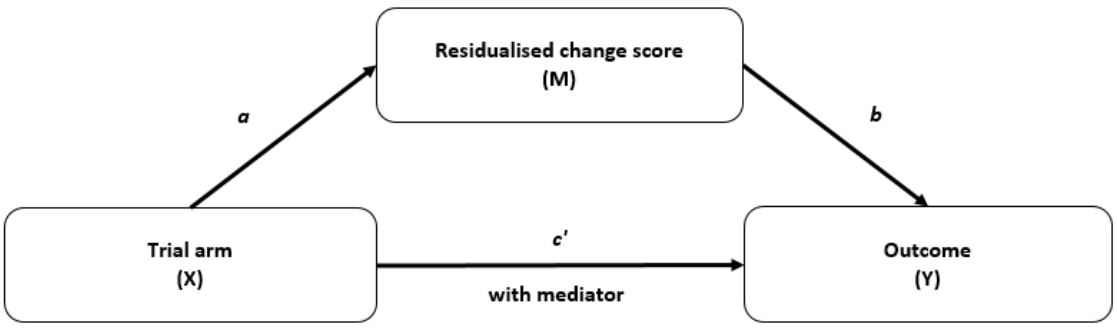


Figure 5.8. A simple mediation model depicted as a conceptual diagram

Healthcare utilisation was modelled as the total number of outpatient visits to the CNS, rheumatologist and GP individually, as well as overall healthcare utilisation (i.e. a

total of all visits). Residualised change scores (standardized) were calculated for each of the possible mediators by regressing scores at baseline (IV) onto scores at the final follow-up (DV). As all measurement contains some degree of error (i.e. not perfect reliability) a change score calculated by subtracting baseline scores from follow-up would contain error from both time points. Residualised change scores also remove the correlation between pre and post test scores, thereby reducing the problem of regression to the mean. A phenomenon in which an "abnormal" score returns to the mean or "norm" in a repeated measures design, this can affect the true magnitude of the change scores but is overcome by calculating residualised change scores.

Mediation was assessed using the simple mediation model within the PROCESS macro developed by Hayes (2013) and conducted in IBM SPSS version 21.0. This estimates the total and direct effect of trial arm on healthcare utilisation/quality of life, as well as the indirect effect of trial arm on healthcare utilisation/quality of life through any change in the clinical and psychosocial outcomes, and process variables. The macro generates bias-corrected 95% bootstrap CIs for the indirect effect using 10,000 bootstrap samples. An indirect effect is considered significant when the bias-corrected 95% CI do not contain zero.

5.11.10.2 Moderation analysis

In order to establish if there were subgroups of the population who benefited more from the intervention moderation analysis was performed. In order to assess whether a variable is a moderator it must have been measured prior to the start of the intervention, the moderator and trial arm must also be independent (Kenny, 2013). Therefore, all baseline variables were hypothesised as potential moderators, this included all demographic, clinical and psychosocial variables (Figure 5.9).

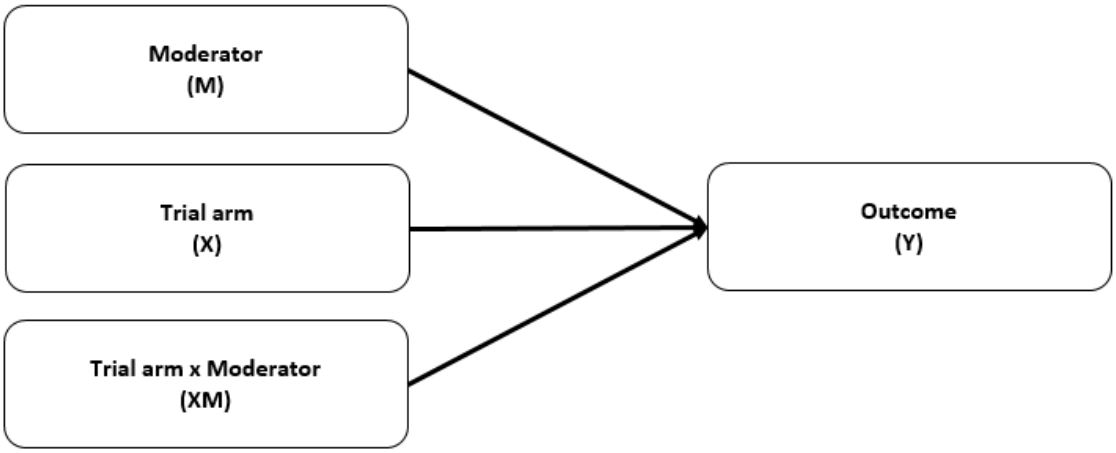


Figure 5.9. A simple moderation model depicted as a conceptual diagram

Moderation was assessed using the simple moderation model as part of the PROCESS macro developed by Hayes (2013) and implemented in IBM SPSS version 21.0. The macro mean centres x and the moderator prior to analysis so that the coefficients for the two variables that define the product will be interpretable within the range of the data (Hayes, 2012).

For a categorical IV, as in this trial, and a continuous moderator variable, moderation means, for example that the difference in the mean number of visits to the CNS between the intervention and control group differs according to the level of the moderator variable. For two categorical variables, moderation means that the difference in the mean number of visits to the CNS between the intervention and control group differs depending on group membership on the moderator variable.

Line graphs have been used to provide a visual representation of the significant interaction effects. The main effect is plotted on the X axis, the DV on the Y axis, and the moderating variable is represented by the lines that are plotted on the graphs.

In order to probe any significant interaction effects PROCESS is able to provide information on the conditional effects of X on Y at different values of the moderator. This allows an investigation of whether the effects of the intervention were significant for different levels of the moderator. Values for dichotomous moderators are for the two values of the moderator. Values for quantitative moderators are for the 10th, 25th, 50th, 75th, and 90th percentiles. The Johnson-Neyman technique was also

implemented which provides a “floodlight” analysis (Spiller, Fitzsimons, Lynch Jr, & McClelland, 2013) of where the significant interaction effect lies. Only applied when a moderator is a continuous variable the technique provides values along the continuum of the moderator where the conditional effect of X on Y transitions from being statistically significant to non-significant (p=0.05).

CHAPTER 6 - BASELINE CHARACTERISTICS OF THE SAMPLE

6.1 PROLOGUE

This chapter presents the baseline characteristics of the participants approached and recruited into the RCT. It begins by presenting the reliability and validity of the measurement tools, a description of missing data and an exploration of statistical assumptions. This is followed by a description of participation rates and attrition from the trial using a consort flow diagram and concludes with participant demographic, clinical and psychosocial characteristics at baseline, along with analysis to explore differences between trial arms at baseline. It concludes with a comparison between the study sample and other available literature with the aim of assessing sample representativeness.

6.2 PARTICIPATION RATES

6.2.1 Enrolment

Three hundred and one patients were assessed for eligibility within the recruitment period (Figure 6.1). Seventy-four (24.58%) of these were not eligible to take part in the trial as they did not meet the inclusion criteria; therefore, 227(75.42%) patients were approached to take part. A total of 128(63.05%) gave their consent and were randomised into the trial. One (0.49%) participant was already taking part in another study which meant they were unwilling to take part in this trial and of the 99(48.77%) patients who did not consent the most frequently reported reasons for refusal were too busy to participate (n=58, 59.09%), a preference to see their rheumatology face-to-face (n=31, 31.82%) and two participants felt they were already able to monitor their blood tests and did not see the advantage of taking part in the trial (9.09%).

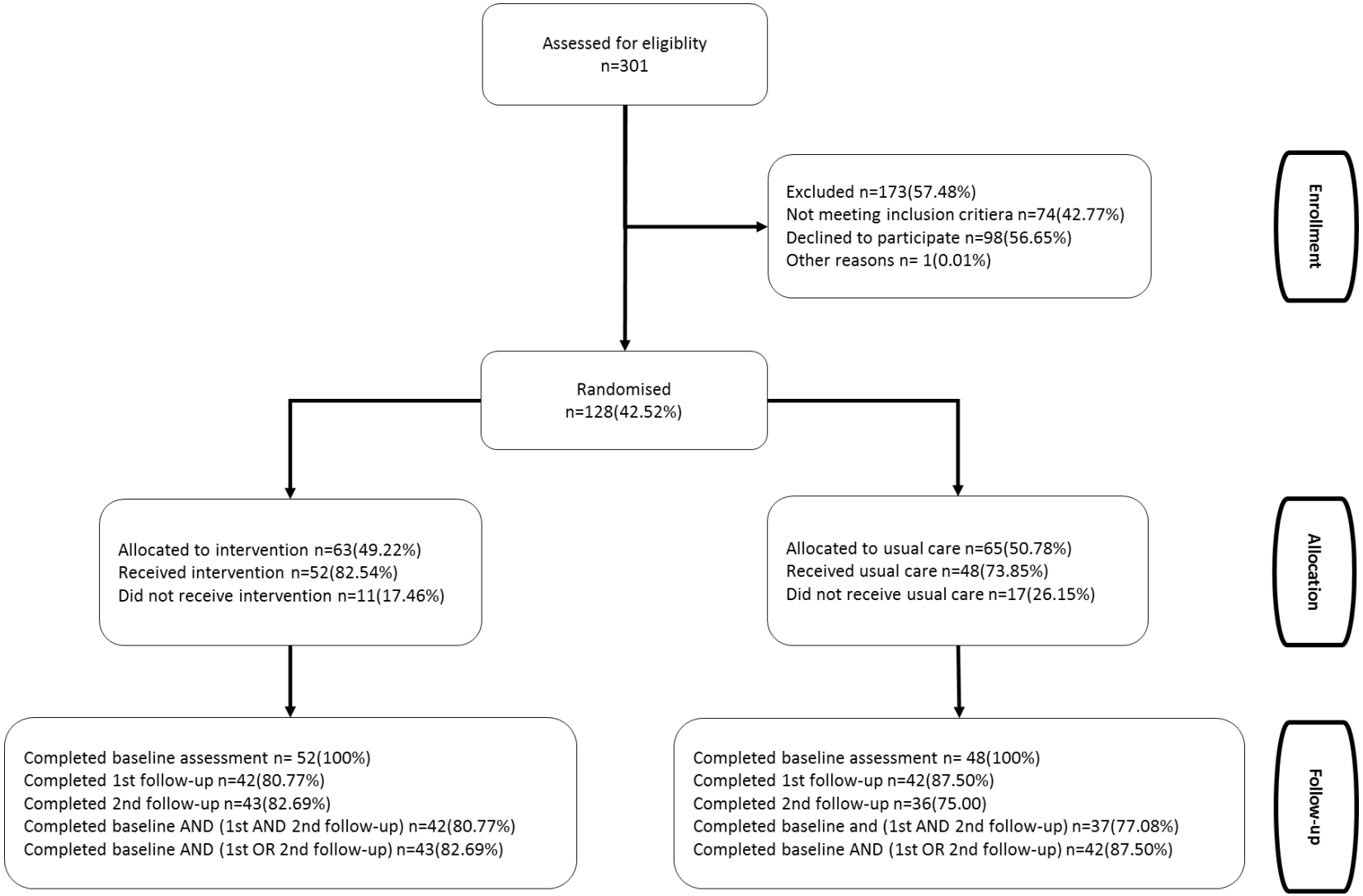


Figure 6.1. Consort flow diagram for RCT

6.2.2 Allocation

Of the 128 patients who were randomised, 16(12.50%) failed to complete a baseline questionnaire, 9(7.03%) failed to attend the intervention training session despite repeated reminders and 3(2.34%) participants were no longer eligible to take part in the trial, as they either changed their medication prior to attending the training session (n=2) or were found to be monitored by their GP (n=1). A total of 100 participants, therefore, received their allocated group, 52(85.54%) in the intervention arm and 48(73.85%) in the control arm and entered the trial.

In order to explore whether there were any differences in demographic and clinical data between those who did (n=100) and did not receive their allocated group (n=28) and the interaction with trial arm a series of factorial ANOVA and factorial logistic regressions were performed. As participants at this stage of the trial had not completed any of the self-report questionnaires or assessments of disease activity the only available data were those that could be accessed via the electronic patient records (i.e. age, gender, diagnosis, total number of co-morbidities, total number of prescribed medications and dose of methotrexate) along with the arm of the trial they were allocated to.

Table 6.1. Factorial ANOVAS - trial arm by receipt of allocation (*df*=1, 128)

	Trial arm		**Receipt of allocation**		**Trial arm*Receipt of allocation**	
Variable	**F**	***p***	**F**	***p***	**F**	***p***
Age	3.27	0.07	14.77	<0.001	0.12	0.73
No. of comorbidities	0.57	0.45	1.04	0.31	0.28	0.60
No. of medications†	0.19	0.66	0.01	0.92	0.01	0.91
Dose of methotrexate	0.21	0.65	0.12	0.73	1.22	0.27

ANOVA – analysis of covariance
†not including methotrexate

There were no significant differences in age, total number of co-morbidities or medications or dose of methotrexate between participants randomised to the

intervention and control group ($p \geq 0.07$) and no significant interaction effects between trial arm and receipt of allocated group ($p \geq 0.27$) (Table 6.1). Two factorial logistic regressions also indicated no significant association between trial arm, receipt of allocation and gender ($\chi^2=8.48$, $p=0.04$) or diagnosis ($\chi^2=5.49$, $p=0.14$). Those who did receive their allocated group were however, significantly older (M=56.71, S.D=11.82, n=100) than and those that did not (M=47.07, S.D=14.54, n=28; $F_{1,128}=14.77$, $p=0.0001$) (Figure 6.2). These results should however, be interpreted with caution as number of participants who did not receive their allocated intervention was small in comparison to those who did; therefore, breaking one of the assumptions of a factorial ANOVA, equal sample sizes in each cell.

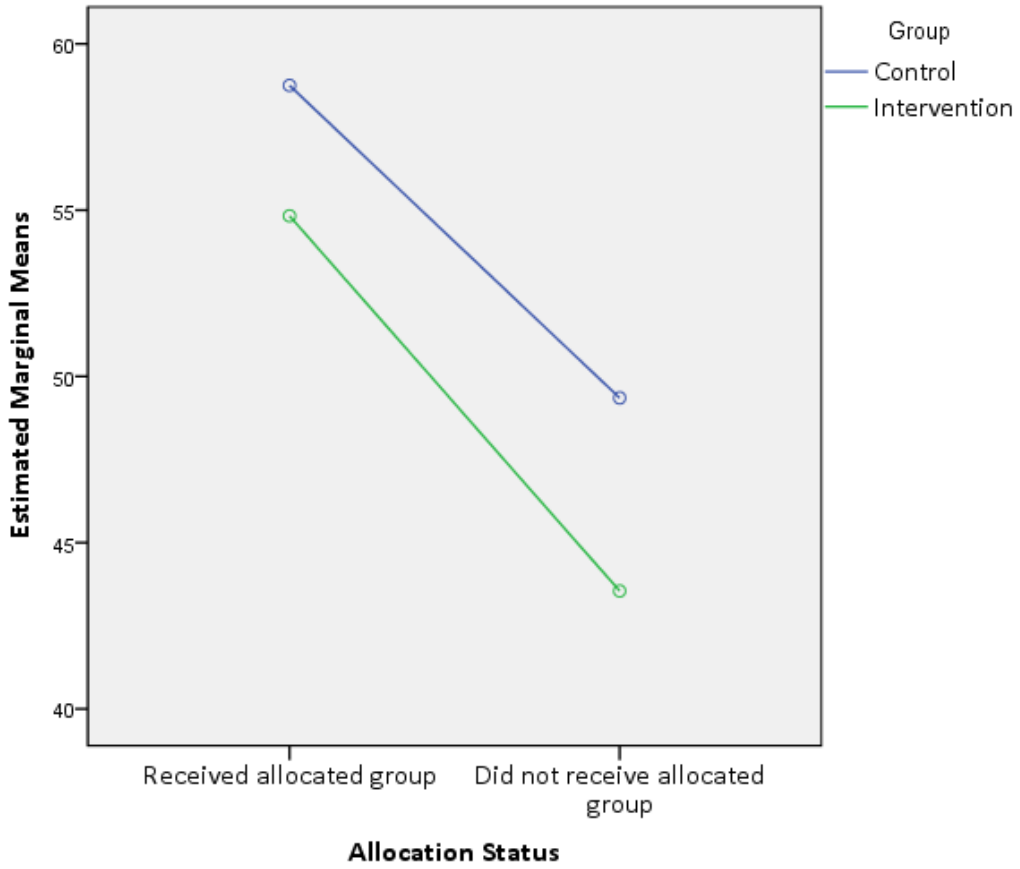


Figure 6.2. Plot of mean age by trial arm and receipt of allocation

6.2.3 Follow-up

Of the 100 participants who received their allocated group, and, therefore, completed a baseline questionnaire, a proportion failed to complete one or both of the follow-up questionnaires. Of the 52 participants who received the intervention 10(19.23%) failed

to complete either the first follow-up questionnaire (n=1) or both the first and final follow-up questionnaires (n=9). Of the 48 participants who were allocated to the usual care control group 12(25.00%) failed to complete either the final questionnaire (n=6) or both follow-up questionnaires (n=6). See consort diagram in Figure 6.1.

Analyses were performed on an ITT basis (n=100) and repeated in complete cases only (n=79). Healthcare utilisation and clinical variables continued to be collected for the 21 participants who did not complete a follow-up questionnaire, using electronic patient records. Therefore, all 100 participants are included in the analysis of these outcomes. As analysis of the questionnaire data used MLM which allows inclusion of participants with missing time points the analysis included all 100 participants.

Eight-five (85.00%) participants returned the baseline questionnaire and at least one follow-up questionnaire, 82.69% of the intervention group (n=43) and 87.50% of the control group (n=42). A chi squared test for independence indicated no significant difference between the intervention and control group on the number of participants who completed all three time points, $\chi^2(1, n=100)=0.20$, $p=0.65$, $\phi=0.05$.

This resulted in a total of 79(79.00%) participants who returned all administrations (known as complete cases), 80.77% (n=42) of the intervention group and 77.08% (n=37) of the control group. Analyses comparing complete cases (n=79) with non-complete cases (n=21) on all continuous demographic characteristics, pre-trial blood test results and baseline psychosocial variables also indicated no significant differences ($p \geq 0.01$) between the two groups on any variables (Appendix U).

6.3 DATA ASSUMPTIONS

6.3.1 Internal reliability and validity

Cronbach's alphas indicated good internal reliability for all scales at all three time points (Appendix V). Exceptions to this were the IPQ-R treatment control subscale and the BMQ specific concern subscale. Deletion of one item from each scale increased the Cronbach's alpha to greater than 0.62. Therefore, these scales were re-calculated removing the least reliable items at each of the three time points (Table 6.2).

Table 6.2. Measures with poor internal reliability

Variable	Total no. of items	Cronbach's alpha			Item removed	Cronbach's alpha		
		Baseline	First f/u	Final f/u		Baseline	First f/u	Final f/u
IPQ-R Treatment Control	5	0.48	0.57	0.54	My treatment will be effective in curing my RA (Item 14)	0.65	0.71	0.62
BMQ Specific Concern	5	0.63	0.68	0.70	My methotrexate is a mystery to me (Item 6)	0.67	0.75	0.71

IPQ-R – Illness Perceptions Questionnaire Revised; BMQ – Beliefs about Medicines Questionnaire; RA – Rheumatoid Arthritis; f/u – follow-up

A paired-sample t-test was performed comparing participant's scores on the IPQ-R symptoms experienced subscale and the IPQ-R identity subscale. This analysis indicated a significant difference between the symptoms patients experienced compared to those they associated with their arthritis with the exception of pain, fatigue, stiff joints and loss of strength providing support for the conceptual difference between somatisation and identity (Table 6.3). As instructed in the guidelines for the scale the identity items are used in subsequent analyses (Moss-Morris *et al.,* 2002).

All the symptoms were endorsed by a percentage of the patients, confirming the validity of the range of symptoms included in the subscale. Pain was the most frequently endorsed symptom, 97% of participants identified it as a symptom specific to their arthritis at baseline, 96.3% at the first follow-up and 97.4% at the final follow-up. Fatigue, stiff joints and loss of strength were also endorsed by at least 68(68%) participants at each time point. Wheeziness (17%) and weight loss (27%) were endorsed by the fewest number of participants at each of the three time points.

Table 6.3. Paired samples t-test for IPQ-R symptoms experienced and IPQ-R identity subscales

	Baseline		**First follow-up**		**Final follow-up**	
Symptom	**M(SD)**	**Statistical test**	**M(SD)**	**Statistical test**	**M(SD)**	**Statistical test**
Pain	0.02(0.20)	t(98)=1.00, *p*=0.32	0.05(0.22)	t(79)=2.04, *p*=0.05	0.04(0.19)	t(77)=2.04, *p*=0.08
Sore throat	0.38(0.49)	t(93)=7.60, *p*<0.001	0.26(0.49)	t(80)=4.72, *p*<0.001	0.33(0.47)	t(77)=2.04, *p*<0.001
Nausea	0.19(0.40)	t(92)=4.70, *p*<0.001	0.15(0.39)	t(79)=3.41, *p*=0.001	0.16(0.40)	t(76)=2.04, *p*=0.001
Breathlessness	0.19(0.39)	t(94)=4.69, *p*<0.001	0.16(0.40)	t(81)=3.59, *p*<0.001	0.14(0.35)	t(76)=2.04, *p*=0.001
Weight loss	0.13(0.42)	t(95)=2.94, *p*<0.001	0.12(0.33)	t(80)=3.36, *p*=0.001	0.12(0.33)	t(75)=2.04, *p*=0.002
Fatigue	0.09(0.33)	t(96)=2.81, *p*=0.01	0.14(0.35)	t(82)=3.72, *p*<0.001	0.10(0.31)	t(77)=2.04, *p*=0.004
Stiff joints	0.02(0.20)	t(97)=1.00, *p*=0.32	0.04(0.19)	t(81)=1.75, *p*=0.08	0.03(0.16)	t(78)=2.04, *p*=0.16
Sore eyes	0.20(0.40)	t(94)=4.85, *p*<0.001	0.15(0.39)	t(81)=3.41, *p*=0.001	0.15(0.36)	t(78)=2.04, *p*<0.001
Wheeziness	0.15(0.36)	t(92)=4.04, *p*<0.001	0.11(0.32)	t(80)=3.16, *p*=0.002	0.17(0.38)	t(76)=2.04, *p*<0.001
Headaches	0.29(0.46)	t(93)=6.12, *p*<0.001	0.28(0.45)	t(79)=5.47, *p*<0.001	0.41(0.50)	t(77)=2.04, *p*<0.001
Upset stomach	0.20(0.41)	t(92)=4.86, *p*<0.001	0.23(0.45)	t(79)=4.48, *p*<0.001	0.29(0.46)	t(74)=2.04, *p*<0.001
Sleep difficulties	0.21(0.46)	t(95)=4.47, *p*<0.001	0.27(0.45)	t(81)=5.45, *p*<0.001	0.19(0.40)	t(76)=2.04, *p*<0.001
Dizziness	0.14(0.35)	t(92)=3.87, *p*<0.001	0.14(0.35)	t(79)=3.55, *p*=0.001	0.19(0.40)	t(77)=2.04, *p*<0.001
Loss of strength	0.07(0.33)	t(97)=2.15, *p*=0.03	0.08(0.28)	t(82)=2.75, *p*=0.01	0.09(0.33)	t(78)=2.04, *p*=0.02

IPQ-R – Illness Perceptions Questionnaire Revised; M – Mean; SD – Standard Deviation

6.3.2 Normality, linearity and homodasticity

Inspection of the histograms and Q-Q plots, for the whole sample and within trial arms and time points, indicated a more normally distributed population than the Shapiro-Wilk statistic suggested (p<0.001). Appropriate transformation methods failed to alter the most significantly skewed variables; the Shapiro-Wilk test for normality remained significant (p<0.001). Transformed variables were not retained as it was reasonable to assume some level of non-normality in the population and because transformations introduce complexity and confusion in the interpretations of results. This does however, mean that statistical inferences become less robust as distributions depart more from normality. There are no non-parametric alternatives to multi-level modelling and hence these analyses were used despite data being non-normal.

6.4 PARTICIPANT CHARACTERISTICS

6.4.1 Demographic characteristics

The demographic characteristics of the sample can be found in Table 6.4. The intervention and control groups did not differ significantly on any of these variables and the effect sizes were all small (<0.02). The total sample consisted of 55 females and 45 males, with similar proportions in each trial arm. The age of participants ranged from 27 to 84 years. Most participants were married or living with their partner and identified themselves as being of white ethnicity.

Table 6.4. Demographic characteristics at baseline

Variable	**Total n=100**	**Intervention n=52**	**Control n=49**	**Statistical test**
Age, mean(SD)	56.71(11.82)	54.83(11.22)	58.75(12.22)	t(98.00)=-1.67, *p*=0.09, η^2=0.03
Female, n(%)	55(55.00)	24(46.15)	31(64.58)	χ^2(1, n =100)=2.72, *p*=0.10, ϕ=0.19
Living status, n(%)				
Married or living with partner	70(70.00)	37(71.15)	33(68.75)	
Living alone	18(18.00)	8(15.38)	10(20.83)	χ^2(1, n =100)=0.63, *p*=0.73, ϕ=0.08
Living with friends or family	12(12.00)	7(13.46)	5(10.42)	
Ethnicity,† n(%)				
White	89(89.00)	46(88.46)	43(89.58)	
Indian	4(4.00)	2(3.85)	2(4.17)	
Other	4(4.00)	3(5.77)	1(2.08)	
Black-African	1(1.00)	0(0.00)	1(2.08)	χ^2(1, n =100)=<0.001, *p*=1.00, ϕ=0.02
Black-Caribbean	1(1.00)	1(1.92)	0(0.00)	
Chinese	1(1.00)	0(0.00)	1(2.08)	

SD – Standard Deviation

†comparison between white and non-white due to small n

6.4.2 Clinical characteristics

Table 6.5 details the clinical characteristics of the sample by trial arm with the associated significance test. There were no significant group differences between the intervention and control group on any of these variables (p>0.01).

6.4.2.1 Disease and treatment history

A majority of the sample had RA and had been living with their diagnosis for between 1 and 54 years. Thirty-seven per cent of the sample was living with at least one co-morbidity. The most frequently reported co-morbid conditions were: hypertension (14%), hypercholesterolemia (13%), hyperthyroidism (6%) and osteoporosis (6%). The medications most frequently prescribed to participants in addition to methotrexate were: folic acid (73%), sulphasalazine (27%), diclofenac (22%), hydroxychloroquine (20%), adalimumab (17%) and etanercept (14%).

6.4.2.2 Current disease status

For those with RA, DAS28 scores indicated average to moderate disease activity at baseline. There was however, noticeable variation in this with 19(24.05%) participants in remission, 13(16.46%) with low disease activity, 33(41.77%) moderate and 6(7.59%) high disease activity. These percentages, however, did not differ between the intervention and control group (χ^2(1, n =79)=2.70, p=0.45, Cramer's V=0.19). Disease activity for patients with PsA was low, comparisons between the intervention and control group on swollen joints although not statistically significant did have a medium to large effect size but clinically the difference of one swollen joint between the trial arms was not considered meaningful.

6.4.2.3 Laboratory tests

The results of the baseline blood tests can be found in Table 6.6 (page 242). A series of independent sample t-tests and Mann-Whitney U tests indicated no significant differences between the intervention and control group at baseline (p>0.01) with all mean and median levels within the normal recommended ranges according to criteria outlined in Table 5.3 (page 201).

Table 6.5. Clinical characteristics at baseline

Variable	**Total n=100**	**Intervention n=52**	**Control n=48**	**Statistical test**
Disease type, n(%)				
Rheumatoid arthritis	71(71.00)	33(63.46)	38(79.17)	$\chi^2(1, n=100)=2.28$, $p=0.13$, $\phi=0.17$
Psoriatic arthritis	29(29.00)	19(36.54)	10(20.83)	
Disease duration in years, median(range)	8(1-54)	8(1-40)	6(1-54)	U=1222.75, z=-0.17, $p=0.86$, $r=0.02$
No. of years on methotrexate, median(range)	4(1-20)	4(1-20)	3.85(1-13)	U=1205.00, z=-0.30, $p=0.77$, $r=0.03$
Dose of methotrexate, median (range)	15(5-25)	15(5-22.5)	15(5-25)	U=11.29.50, z=-0.83, $p=0.40$, r=0.08
No. of medications, median(range)‡	4(1-11)	4(1-10)	5(2-11)	U=1170.00, z=-0.55, $p=0.59$, $r=0.06$
Co-morbidities, n(%)				
Hypertension	14(14.00)	9(17.31)	5(10.42)	$\chi^2(1, n=100)=0.98$, $p=0.39$, $\phi=0.10$
Hypercholesterolemia	13(13.00)	8(15.38)	5(10.42)	$\chi^2(1, n=100)=0.19$, $p=0.56$, $\phi=0.07$
Hyperthyroidism	6(6.00)	2(3.85)	4(8.33)	$p=0.42$†
Osteoporosis	6(6.00)	2(3.85)	4(8.33)	$p=0.42$†
Diabetes	4(4.00)	2(3.85)	2(4.17)	$p=1.00$†
Respiratory	3(3.00)	1(1.92)	2(4.17)	$p=0.61$†
No. of comorbidities, n(%)				
None	63(63.00)	35(67.31)	28(58.33)	$\chi^2(1,n=100)=0.52$, $p=0.47$, $\phi=0.09$
One or more	37(37.00)	17(32.69)	20(41.67)	

Variable	Total n=100	Intervention n=52	Control n=48	Statistical test
DAS28, mean(SD)	3.33(1.27)	3.54(1.36)	3.19(1.23)	t(69)=-1.15, *p*=0.27, η^2=0.01
PsARC				
Physician global assessment, median (range)	2(1-4)	2(1-3)	2(1-4)	U=75.1, z=-0.98, *p*=0.39, *r*=0.18
Patient global assessment, median (range)	2(1-3)	1(1-3)	2(1-3)	U=45.6, z=-0.38, *p*=0.04, *r*=0.07
Swollen joint count, median (range)	2(0-13)	1(0-13)	4(1-10)	U=39, z=-2.61, *p*=0.02, *r*=0.48
Tender joint count, mean(SD)	9.02(7.13)	7.79(6.75)	11.34(7.49)	t(27)=1.29, *p*=0.24, η^2_p=0.02
Fatigue, mean(SD)	4.27(2.66)	4.19(2.69)	4.35(2.65)	t(98)=-0.31, *p*=0.76, η^2_p=0.001
Pain, median(range)	3(0-9)	3(1-9)	3(0-9)	U=1226.60, z=-0.15, *p*=0.88, r=0.01
Functional Disability, median(range)	0.41(0-0.22)	0.40(0-0.22)	0.46(0-0.22)	U=1196.30, z=-0.36, *p*=0.72, r=0.04

SD – Standard Deviation; DAS28 – Disease Activity Scores -28; PsARC – Psoriatic Arthritis Response Criteria

† Fisher's Exact Probability test as the expected frequency assumption was violated; ǂ not including methotrexate

U = Mann-Whitney test; T=independent samples t-test

Table 6.6. Laboratory results for the whole sample (n=100) and by trial arm at baseline

Variable	Recommended range	Total n=100	Intervention n=52	Control n=48	Statistical test
Haemoglobin, mean(SD)	12.0 – 17.0	13.66(1.32)	13.91(1.25)	13.40(1.36)	t(98)=1.93, p=0.05, η^2=0.04
WBC, mean(SD)	3.0 - 10.0	6.74(1.69)	6.79(1.86)	6.69(1.50)	t(98)=0.28, p=0.78, η^2=0.001
Neutrophils, median(range)	2.0 – 7.5	3.73(1.35-8.7)	3.75(2.13-8.7)	3.74(1.35-6.20)	U=1160.95, z=-0.60, p=0.56, r=-0.06
Platelets, median(range)	150 - 400	248.90(130-510)	237(130-372)	260.55(183-510)	U=880.20, z=-2.54, p=0.01, r=-0.25
ALP, mean(SD)	35-104	72.09(20.03)	73.13(22.57)	70.96(17.03)	t(94.38)=0.55, p=0.59, η^2 =0.003
ALT, median(range)	10-35	24.55(9-90)	25.5(9-90)	22.80(14-71)	U=1131.75, z=-0.80, p=0.43, r=-0.08
ESR, median(range)	0 – 20	9(4-58)	8(4-58)	11.15(4-56)	U=1085.20, z=-1.13, p=0.26, r=-0.11
CRP, median(range)	0 - 5	2.78(0.6-33.30)	3.2(0.6-33.30)	2.66(0.6-20.4)	U=1223.35, z=-0.17, p=0.87, r=-0.02

SD – Standard Deviation; WBC – White Blood Count; ALP - Alkaline Phosphatase; ALT - Alanine Transaminase; ESR - Erythrocyte Sedimentation Rate; CRP - C-Reactive Protein

6.4.3 Psychosocial outcome variables

Mean scores on each of the psychosocial variables at baseline can be found in Table 6.9. A series of independent samples t-tests and Mann-Whitney U tests indicated no significant differences between the intervention and control group on any of these variables (p>0.01) and small effect sizes. Examination of the proportion of patients with normal, moderate and clinical anxiety and depression at baseline indicated that 86% of the sample was experiencing either normal or moderate levels of anxiety at the beginning of the trial and 14% were assessed to be clinically anxious (Table 6.7). The proportions did not differ significantly between the intervention and control group (χ^2(2, n=100)=2.14, p=0.35). Although the effect size did indicate a medium effect (ϕ=0.35).

Table 6.7. Proportion of sample with normal, moderate and clinical levels of anxiety at baseline

Group	Total n=100	Intervention n=52	Control n=48
Normal, n(%)	68(68.00)	36(69.23)	32(66.67)
Moderate, n(%)	18(18.00)	11(21.15)	7(14.58)
Caseness, n(%)	14(14.00)	5(9.62)	9(18.25)

Ninety-one percent of the sample was experiencing either normal or moderate levels of depression and 9% clinical depression (Table 6.8). The proportions did not differ significantly between trial arms (χ^2(2, n=100)=0.95, p=0.62). The effect size however, was large (ϕ=0.62). Two participants were experiencing clinical levels of both anxiety and depression (2.0%), one participant in each of the trial arms.

Table 6.8. Proportion of sample with normal, moderate and clinical levels of depression at baseline

Group	Total n=100	Intervention n=52	Control n=48
Normal, n(%)	82(82.00)	41(78.85)	41(85.42)
Moderate, n(%)	9(9.00)	5(9.62)	4(8.33)
Caseness, n(%)	9(9.00)	6(11.54)	3(6.25)

Table 6.9. Scores on the psychosocial outcome variables for the whole sample and by trial arm at baseline

Variable	Possible score	Total n=100	Intervention n=52	Control n=48	Statistical significance
SF-12v1® MCS, mean(SD)	0-100	30.72(5.52)	30.17(6.22)	31.32(4.62)	t(98)=-1.03, *p*=0.30, η^2=0.01
SF-12v1® PCS, mean(SD)	0-100	45.98(9.38)	46.51(9.71)	45.41(9.08)	t(98)=0.57, *p*=0.57, η^2=0.003
Anxiety, median(range)	0-21	5.25(0-17)	5.75(0-16)	5.00(1-17)	U=1167.30, z=-0.56, *p*=0.58, r=0.06
Depression, median(range)	0-21	3.75(0-12)	4(0-12)	3(0-11)	U=1168.55, z=-0.55, *p*=0.58, r=0.06

SD – Standard Deviation; MCS – Mental Component Scores; PCS – Physical Component Scores

6.4.4 Psychosocial process variables

Central tendency scores on each of the psychosocial process variables at baseline can be found in Table 6.10. A series of independent samples t-tests and Mann-Whitney U tests indicated no significant differences between the intervention and control group on any of these variables and small effect sizes.

Table 6.10. Central tendency scores on the psychosocial process variables at baseline for the whole sample and by trial arm

Variable	Possible score	Total n=100	Intervention n=52	Control n=48	Statistical significance
Generalised self-efficacy, mean(SD)	10-40	31.80(3.78)	31.79(3.79)	31.82(3.80)	t(98)=-0.04, *p*=0.97, η^2<0.001
HeiQ™ Self-monitoring & insight, mean(SD)	1-4	3.07(0.42)	3.00(0.41)	3.15(0.41)	t(98)=-1.81, *p*=0.07, η^2=0.03
MeiQ™ Active Communication, median(range)	1-6	5(1-6)	5(2.5-6)	5.25(1-6)	U=1204.00, z=-0.31, *p*=0.75, *r*=0.03
MeiQ™ Self-management ability, median(range)	1-6	4.83(2.5-6)	4.67(2.5-6)	4.92(3-6)	U=1061.50, z=-1.29, *p*=0.20, *r*=0.13
IPQ-R Identity, mean(SD)	0-12	5.19(2.31)	5.23(2.13)	5.15(2.51)	t(98)=0.18, *p*=0.85, η^2=0.0003
IPQ-R Consequences, mean(SD)	6-30	19.87(4.66)	19.69(4.78)	20.07(4.57)	t(98)=-0.40, *p*=0.69, η^2=0.002
IPQ-R Personal control, mean(SD)	6-30	20.86(4.22)	20.70(4.13)	21.03(4.34)	t(98)=-0.39, *p*=0.70, η^2=0.002
IPQ-R Treatment Control, mean(SD)	5-25	15.82(2.21)	15.66(2.17)	15.98(2.26)	t(98)=-0.71, *p*=0.48, η^2=0.01
IPQ-R Illness Coherence, mean(SD)	5-25	18.73(4.35)	18.54(4.35)	18.93(4.38)	t(98)=-0.45, *p*=0.66, η^2=0.002
BMQ Specific Concern, mean(SD)	5-25	12.33(2.90)	12.13(2.83)	12.54(2.99)	t(98)=-0.69, *p*=0.49, η^2=0.01
BMQ Specific Necessity, mean(SD)	5-25	16.65(2.94)	16.13(2.96)	17.20(2.86)	t(98)=1.83, *p*=0.07, η^2=0.03
Treatment burden, median(range)	1-5	2(1-5)	2(1-5)	1.75(1-4)	U=1043.60, z=-1.47, *p*=0.14, *r*=0.15
Knowledge about methotrexate, mean(SD)	8-57	18.16(4.74)	18.37(4.73)	17.94(4.78)	t(98)=0.45, *p*=0.65, η^2=0.002

SD – Standard Deviation; HeiQ™ – Health Education Impact Questionnaire; MeiQ™ – Medication Education Impact Questionnaire; IPQ-R – Illness Perceptions Questionnaire Revised; BMQ – Beliefs about Medicines Questionnaires

6.5 DISCUSSION

6.5.1 Acceptability of the intervention

The acceptability of an intervention can be assessed in a number of ways including the ability to consent patients into a trial, reasons for refusal, along with rates of attrition. In the current study all methods were utilized. Overall it would be expected that a "one size fits all" approach is not appropriate (Trappenburg *et al.,* 2013) and consideration must be made for those who would prefer the more traditional model of care.

Refusing to participate may be a rejection of research in general or a rejection of the intervention itself. This may not only be because the intervention is not acceptable to the participant but the threat of being randomized to a non-preferred group may not be acceptable and, therefore, the participant refuses to take part. In addition some participants may not wish to experience a perceived disruption to their care. In common with all studies that require consent the sample recruited may not be representative of the population under examination. This would compromise the external validity of the findings (Britton *et al.,* 1999). It can however, be difficult to disentangle the true reasons for rejection.

Over 40% of patients receiving rheumatology services feel they should be able to decide how frequently they need a check-up (Neame *et al.,* 2005) and take responsibility for organizing their own DMARD monitoring appointments (Kay & Lapworth, 2004). The 63% participation rate in this trial suggests that in practice more patients may be willing to take on these responsibilities. This rate is similar to the 68% reported in the trial of shared care by Hewlett *et al.,* (2000, 2003, 2005b) but greater than the 26% in the shared-care trial by Primdahl *et al.,* (2012; 2014). The participation rates found within this trial also reflect the findings of Garcia-Alamino *et al.,* (2010) who reviewed the literature on self-monitoring in thrombophilia and found that the average proportion of patients that could or would take part in the trials was 68% (range 31-88%). These figures are also comparable to van der Vaart, Drossaert, Taal and van de Laar (2011) who found that 68% of patients with arthritis would like access to their electronic patient records, 63% would be interested in performing online

symptom monitoring with their care provider and 51% would be interested in autonomous symptom monitoring.

Due to ethical constraints in accessing patient data, an analysis comparing the characteristics of those who did and did not consent was not possible. The patients approached did however, provide reasons for refusal. The primary reason was a perception of being "too busy" to participate. It is unclear if this was due to the perceived demands of being in a research study or because of the nature of the intervention. Trials of self-management interventions in rheumatology have also found that patients report being too busy as reason for non-participation (Yip *et al.,* 2007; Bair *et al.,* 2009; Wu, Kao, Wu, Tsai, & Chang, 2011). It may be reasonable to think that this model of care could be burdensome to time but as opposed to the disease management skills learnt in generalised self-management programmes this intervention specifically aimed to reduce the time burden of attending clinic visits. On reflection the potential for patients to save time in the long-term by taking part in the intervention could have been emphasised more in the recruitment process. The design and provision of future models of care in rheumatology, therefore, need to consider the intensity of patient involvement and the time required of patients in order to increase acceptability of services to the patient.

Thirty-two percent of the patients approached to take part in the trial declined to participate because they preferred to attend the outpatient clinic to see their rheumatology CNS face-to-face. This was also reported as a reason for refusal in the trial by Primdahl *et al.,* (2012; 2014), which evaluated a shared care approach between the patient and general practice but far exceeds the rate reported by Hennell *et al.,* (2005) who found that 8% of patients preferred to see their nurse in person although this was in comparison to a nurse-led rheumatology telephone clinic. The increased level of involvement and the additional responsibility for self-monitoring blood tests in this trial may explain this difference. Refusal to participate in trials that increase patient involvement in healthcare have been linked to a reluctance to disrupt services and relationships that are working well and are highly valued (Sanders *et al.,* 2012) which may go some way in explaining the rates found within the current trial.

Many of the patients who refused on this basis also spoke about their own ability to self-monitor and the concern they had about their numeracy skills. Although these are anecdotal data it is reasonable to assume that the perceived intellectual requirements of this model of care, and in particular numeracy skills, may have influenced an individual's likelihood of participating. There is a perception that patients with poorer literacy or numeracy skills may have difficulty interpreting and acting on abstract or complex health information related to their chronic illness (Ad Hoc Committee on Health Literacy for the Council on Scientific Affairs & American Medical Association, 1999). Recent evidence in diabetes suggests that despite low health literacy and numeracy being related to poor knowledge there is little sufficient or consistent evidence to suggest a link between literacy or numeracy skills and diabetes self-care, including self-monitoring and clinical outcomes (Al Sayah, Majumdar, Williams, Robertson, & Johnson, 2013). The inclusion criteria of this trial did not specify a particular level of literacy or education.

Attrition is another indication of intervention acceptability. Of the 128 participants who were consented into the study, 22% did not proceed onto the trial. In a majority of cases this was because, despite reminders, participants either failed to complete a baseline questionnaire or did not attend the intervention training session. Although participants had already consented into the trial, these drop outs also reflect participants declining to take part in the trial, as they were yet to receive their allocated intervention. The analysis suggested that those who did not receive their allocated intervention were significantly younger than those that did. This is in opposition to both Hogg *et al.,* (1997) and Primdahl *et al.,* (2012; 2014) who found that those who declined to participate in an evaluation of a shared cared approach to rheumatology services were significantly older than those who took part in the trial. In the trial by Hewlett *et al.,* (2000) attrition was linked to greater disease activity and disability. Although levels of functional disability were not available for those who did not receive their allocated intervention in the current trial, the overall level of functional disability was significantly lower than that found within the trial by Hewlett *et al.,* (2000) possibly indicating the population as a whole were less disabled.

The dropout of younger participants in the current trial also supports the notion that the perceived requirements of taking part in the research and/or intervention placed additional time demands on younger patients who may be more likely to be working than their older counterparts. In the design of the trial consideration was given to delivering the education training session at times outside of working hours, which aimed to provide an opportunity, for patients who would otherwise be unable to attend due to work commitments, to participate. As randomisation was undertaken prior to the collection of baseline data it was not possible to include these participants in any subsequent analysis. Although this means the integrity and validity of the ITT analysis is somewhat threatened, the drop-out rate was equal across the trial arms. The decision was taken during the design of the trial to randomise prior to baseline assessment in order for participants randomised to the intervention group to be allocated to a particular training session. It was felt that commitment to a particular session at the time of consenting would reduce drop-outs from the intervention group. This was not necessarily the case given that 9(7.03%) intervention participants did not attend the training session.

Of the 100 participants who received their allocated intervention, 15% did not complete one of the follow-up questionnaires. Other patient-initiated services in rheumatology and systematic reviews of self-monitoring interventions report similar dropout rates (Hewlett *et al.,* 2000; Jaana *et al.,* 2007; Turnock *et al.,* 2005; Clark *et al.,* 2007; Polisena *et al.,* 2010), whilst some have dropout rates as low as 5% (Primdahl *et al.,* 2014; Inglis *et al.,* 2010). It is reassuring however, that there were no significant difference in demographic characteristics, pre-trial blood test results or baseline psychosocial variables between those who did not complete both follow-up questionnaires and those who did, particularly as other trials of self-monitoring intervention have found that patients who withdraw during or after training tended to be older and female (Connock *et al.,* 2007). Due to these dropouts, however, the study did not achieve the planned numbers and was, therefore, not adequately powered to find an effect.

6.5.2 Representativeness of the study sample

Baseline differences between the intervention and control group on all measures suggest no significant differences; therefore, indicating that randomisation of participants was successful.

6.5.2.1 Demographic characteristics

In terms of the demographic composition of the study population, overall the sample was similar to that of the general arthritis population and to other evaluations of patient-initiated services in arthritis. Although the higher proportion of females found within this trial is typical of the population, the actual percentage is lower than that of the general UK arthritis population (Humphreys *et al.,* 2012) and those recruited to other intervention studies, which report approximately 65-74% of the population being female (Primdahl *et al.,* 2014; Hewlett *et al.,* 2000; Sands & Adams, 2009), as opposed to the 55% found within the current trial. Although some intervention studies have recruited older patients with arthritis (Primdahl *et al.,* 2014) the current study is comparable to other trials of patient-initiated services in regards to age (Hewlett *et al.,* 2000; Mitchell *et al.,* 2001; Hewlett *et al.,* 2005b; Sands & Adams, 2009). The ethnic composition of study samples is often not reported in intervention trials, this may reflect a bias towards white participants. The current study demonstrates a more ethnically diverse sample than the general intercity UK rheumatology population (MacGregor, Riste, Hazes, & Silman, 1994) but does more closely represent the London Borough of Camden in which the site of recruitment is located (Greater London Authority, 2012). The living status of participants was also found to be comparable to other trials (Primdahl *et al.,* 2014).

6.5.2.2 Clinical characteristics

Overall the clinical status of participants in this trial was as expected of the general arthritis population and reflected other arthritis intervention studies, with some minor variations. The longer disease duration of 8 years reflected that of other trials of patient-initiated follow-up services (Hewlett *et al.,* 2000; Kirwan *et al.,* 2003b; Hewlett *et al.,* 2005b; Primdahl *et al.,* 2014) but these were all significantly longer than the trial conducted by Sands and Adams (2009) in which the average disease duration was 23-26 months. A majority of the sample had no other co-morbidities which reflects the general arthritis population (Cumming, Stannett, & Hull, 2013) and those who take

part in trials of this nature (Primdahl *et al.,* 2014). For those who did have another co-morbidity the most frequently reported were hypertension and hypercholesterolemia. These proportions were significantly lower than prevalence rates reported for hypertension in the overall arthritis population (Panoulas *et al.,* 2007) and are in fact more similar to those found within the general population (Standing, Deakin, Norman, & Standing, 2005; Boyer, Gourraud, Cantagrel, Davignon, & Constantin, 2011; Tolonen, Keil, Ferrario, Evans, & for the WHO MONICA Project, 2005).

Levels of self-reported pain and fatigue vary in other trials of self-management and patient-initiated rheumatology services. When comparing the same visual numeric scale, self-reported pain and fatigue were slightly lower in the trials by Lorig *et al.,* (2008) and Lorig, Ritter, Laurent and Plant (2008) of the ASMP, whereas comparisons with similar interventions but different measurement tools indicate either similar levels of pain (Hewlett *et al.,* 2000; Kirwan *et al.,* 2003b; Hewlett *et al.,* 2005b) or greater levels of pain and fatigue (Primdahl *et al.,* 2014). Levels of functional disability were slightly lower than that of the general arthritis population (ten Klooster, Taal, & van de Laar, 2008; Wolfe *et al.,* 2004) and that reported in other patient-initiated trials (Hewlett *et al.,* 2000; Kirwan *et al.,* 2003b; Hewlett *et al.,* 2005b) but higher than other trials of this nature (Primdahl *et al.,* 2014). The sample were, therefore, fairly unremarkable on these measures.

6.5.2.3 Psychosocial well-being

Baseline scores for the study sample on the SF-12v1® can be compared to US 1998 normative data for healthy people (Ware *et al.,*2007), data from a psychometric evaluation of the measure in a population of patients with RA (Gandhi *et al.,* 2001) and other trials of patient-initiated services (Primdahl *et al.,* 2014). There are currently no UK normative data for this version of the SF-12v1®. With higher scores on the SF-12v1® indicating better quality of life, this suggests the physical quality of life of participants in this trial is almost the same of the healthy US population (Ware *et al.,*2007) and better than norms for patients with RA or PsA (Gandhi *et al.,* 2001; Fernández-Sueiro *et al.,* 2010). But despite being able to maintain their physical health quality of life participants in this trial were experiencing considerably impaired mental quality of life, significantly lower than US norms for both healthy participants (Ware *et al.,*2007) and

those with RA or PsA (Gandhi *et al.,* 2001; Fernández-Sueiro *et al.,* 2010). Scores were however, similar to other trials of shared care services in RA (Primdahl *et al.,* 2014).

The HADS is a widely used measure in patients with arthritis and, therefore, baseline scores in this trial can be compared to other trials of patient-initiated services and normative scores for the general arthritis population. Mean levels of anxiety were within one standard deviation of scores found within the trial of patient-initiated services by Hewlett *et al.,* (2000; 2003b; 2005b), as were levels of depression. Similar scores have also been reported for participants entering trials of arthritis self-management interventions (Buszewicz *et al.,* 2006; Barlow *et al.,* 2009). Mean levels and the proportion of participants with clinical levels of depression and anxiety also reflected the general RA and PsA populations (Covic *et al.,* 2012; Cauli *et al.,* 2011; Williamson *et al.,* 2004). Higher scores on the anxiety and depression subscales of the HADS represented greater anxiety and depression; therefore, suggesting that patients with RA or PsA experience greater levels of anxiety and depression compared to the general population.

CHAPTER 7 – PATIENTS' ABILITY TO INITIATE CARE

7.1 PROLOGUE

As reported in Chapter 2 patient-initiated follow-up services have so far involved patients successfully understanding what symptoms and side effects should trigger contact with the rheumatology team. By integrating the interpretation of laboratory tests as additional triggers it was important to establish whether patients could be taught how to interpret these blood tests and use this information along with their symptoms and side effects to safely initiate care from the CNS. The following analyses includes only those participants randomised to the intervention group (n=52)

7.2 DID INTERVENTION PARTICIPANTS INITIATE THEIR OWN CARE SAFELY?

Receipt of the laboratory results triggered a series of decisions for intervention participants about their need to seek help from their CNS and initiate a telephone consultation. These decisions were made in relation to (i) laboratory tests and (ii) any associated symptoms and side effects that the patient recorded at the time of receiving these results. As described in section 5.7.6 (page 196) safety of help-seeking was assessed according to:

a) Whether patients could safely decide if a telephone consultation was needed as a result of their laboratory results;
b) Whether patients could safely decide if a telephone consultation was needed as a result of their symptoms and side effects.

On each of the six occasions the decision was coded as:

a) Safe either because:
    - The participant did not initiate a telephone consultation when either a laboratory result had remained the same and was within the normal range, or there was no new or change in symptoms or side effects.

- The participant initiated a telephone consultation when either a laboratory result had significantly changed or was outside the normal range, or there was a new or worsening symptom or side effect.
- The participant initiated a telephone consultation when either a laboratory result had remained the same and was within the normal range, or there was no new or change in symptoms or side effects.

b) Unsafe because the participant did not initiate a telephone consultation when either a laboratory result had significantly changed or was outside the normal range, or there was a new or worsening symptom or side effect.

Across the entire trial period 77% of all decisions made in response to laboratory results were safe and 23% were unsafe (Figure 7.1). On average participants made unsafe decisions in response to laboratory results on 23.94% of occasions. Three (5.77%) participants were in phase one of the trial for an addition 2 or 3 blood tests as they were unable to correctly interpret two of their first three blood tests within the trial. They did however, manage to interpret two consecutive blood tests after this point and entered phase two of the trial. An additional 2(3.84%) participants were removed from the trial in phase one of the trial for safety reasons as they were deemed unable to self-monitor their laboratory results safely. These two participants were in the trial for four and five blood tests respectively and despite receiving the same training and feedback as other intervention participants they were unable to accurately initiate care on any of these occasions.

In response to symptoms and side effects 73% of decisions across the entire trial period were deemed safe and 27% unsafe (Figure 7.2). On average participants made unsafe decisions in response to their symptoms and side effects on 29.95% of occasions.

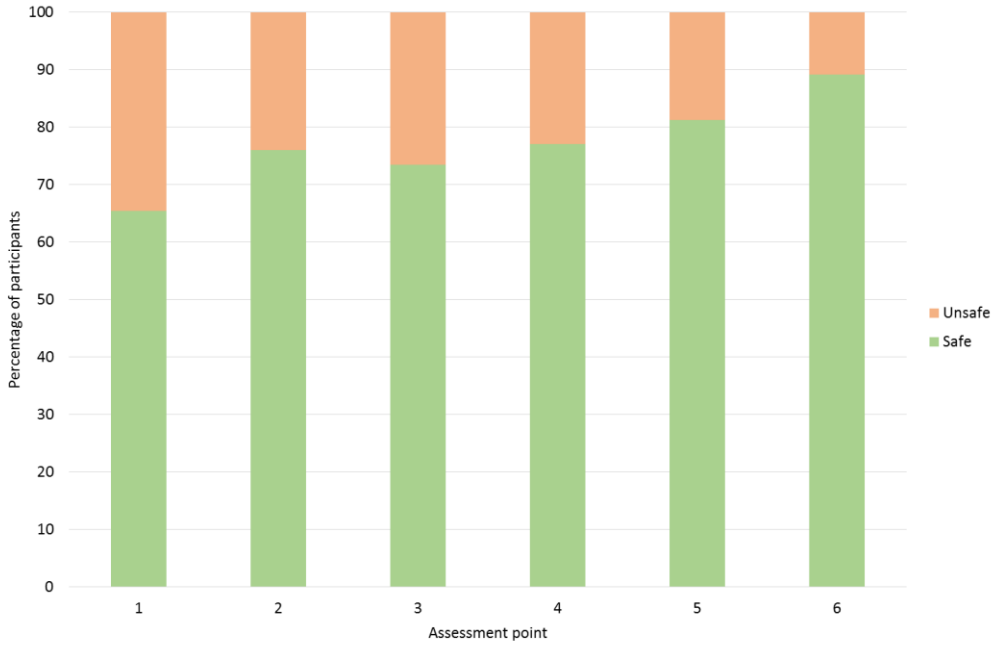


Figure 7.1. Safety of participant decision making in relation to laboratory results.

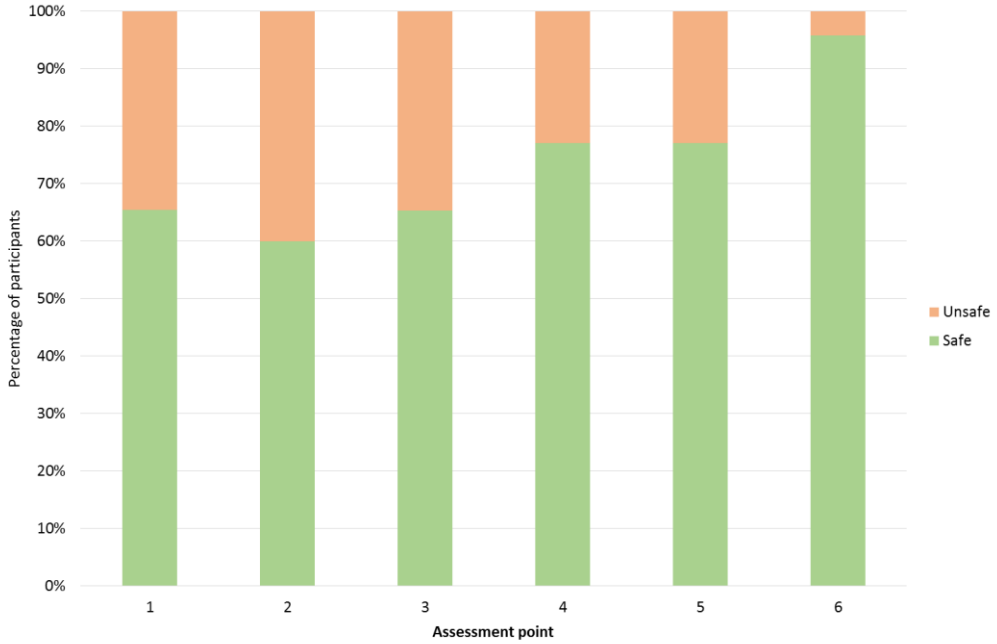


Figure 7.2. Safety of participant decision making in relation to symptoms and side effects.

7.3 DID SAFETY OF HELP-SEEKING IMPROVE OVERTIME?

Statistically significant effects for time were found in regards to laboratory results ($F_{1,278=}9.24$, p=0.003) and for symptoms and side effects ($F_{1,278}$=5.00, p=0.03) (Table 7.1), indicating that participants' ability to safely initiate care from their CNS improved significantly over time.

Table 7.1. Estimates of the fixed effects for safe decision making overtime in the intervention group

Model term	**β**	**SE**	**t**	***p***	**Exp(β)**	**95% CI for Exp(β)**
Laboratory results						
Intercept	0.44	0.28	1.57	0.12	1.56	0.90, 2.71
Time	0.24	0.08	3.04	0.003	0.27	1.09, 1.48
Symptoms and side-effects						
Intercept	0.27	0.29	0.92	0.36	1.30	0.74, 2.30
Time	0.20	0.09	2.24	0.03	1.22	1.02, 1.45

SE – Standard Error; CI – Confidence Interval

7.4 WHAT ARE THE BASELINE PREDICTORS OF SAFE HELP-SEEKING?

In order to explore whether any of the demographic, clinical or psychosocial variables were associated with the number of safe decisions made within the trial period Poisson regressions were performed using the forward selection algorithm (Famoye & Rothe, 2003) described in section 5.11.8.3 (page 218).

The final model in the Poisson regressions revealed a significant effect for age, co-morbidity and the MeiQ™ subscales of self-management ability and active communication (Table 7.2 and Table 7.3). The models were identical for decision making in relation to laboratory tests and decision making in relation to symptoms and side effects. The exponentiated β statistic indicated that those with a co-morbid medical condition made more safe decisions in relation to both their laboratory tests and symptoms, as did younger participants and those who felt they had a greater ability to self-manage their arthritis at baseline. In contrast to what might be expected those who felt less confident in their ability to communicate with their healthcare team at baseline made more safe decisions.

Table 7.2. Predictors of safe decision-making in response to laboratory tests

Step	Variable	β	SE	95% Wald CI		Hypothesis Test			Exp(β)	95% Wald CI for Exp(β)		AIC
				Lower	Upper	χ^2	df	*p*		Lower	Upper	
1	(Intercept)	-4.65	0.08	-4.81	-4.49	3501.35	1	<0.0001	0.01	0.01	0.01	251.96
	MeiQ™ self-management ability	0.38	0.11	0.16	0.60	11.55	1	0.0009	1.46	1.17	1.82	
2	(Intercept)	-4.59	0.07	-4.72	-4.45	4734.31	1	<0.0001	0.01	0.01	0.01	241.32
	MeiQ™ active communication	-0.38	0.10	-0.57	-0.18	15.25	1	0.0001	0.69	0.57	0.83	
	MeiQ™ self-management ability	0.50	0.11	0.29	0.72	21.95	1	<0.0001	1.66	1.34	2.05	
3	(Intercept)	-4.61	0.07	-4.74	-4.48	4921.50	1	<0.0001	0.01	0.01	0.01	237.07
	Age	-0.02	0.00	-0.03	-0.01	11.21	1	0.001	0.98	0.97	0.99	
	MeiQ™ self-management ability	0.46	0.10	0.26	0.65	21.72	1	<0.0001	1.58	1.30	1.91	
	MeiQ™ active communication	-0.29	0.09	-0.48	-0.11	10.15	1	0.002	0.75	0.62	0.89	
4	(Intercept)	-4.76	0.09	-4.94	-4.58	2772.74	1	<0.0001	0.01	0.01	0.01	231.80
	Has a co-morbid medical condition	0.42	0.13	0.16	0.69	9.96	1	0.002	1.52	1.17	1.98	
	MeiQ™ self-management ability	0.44	0.07	0.29	0.58	36.78	1	<0.0001	1.55	1.34	1.78	
	MeiQ™ active communication	-0.24	0.08	-0.40	-0.07	8.56	1	0.004	0.79	0.67	0.92	
	Age	-0.02	0.01	-0.03	-0.01	22.51	1	<0.0001	0.98	0.97	0.99	

MeiQ™ – Medication Education Impact Questionnaire; SE – Standard Error; CI – Confidence Interval; AIC - Akaike Information Criterion

Table 7.3. Predictors of safe decision-making in response to symptoms and side effects

				95% Wald CI		Hypothesis Test				95% Wald CI for Exp(β)		
Step	**Variable**	**β**	**SE**	**Lower**	**Upper**	**χ^2**	**df**	***p***	**Exp(β)**	Lower	Upper	**AIC**
1	(Intercept)	-4.64	0.08	-4.79	-4.48	3451.90	1	<0.0001	0.01	0.01	0.01	248.09
	MeiQ™ Self-management ability	0.38	0.11	0.15	0.60	11.29	1	0.001	1.46	1.17	1.82	
2	(Intercept)	-4.57	0.07	-4.70	-4.44	4697.08	1	<0.0001	0.01	0.01	0.01	233.19
	MeiQ™ Active Communication	-0.43	0.10	-0.63	-0.23	18.10	1	<0.0001	0.65	0.53	0.79	
	MeiQ™ Self-management ability	0.52	0.11	0.31	0.74	23.05	1	<0.0001	1.69	1.36	2.09	
3	(Intercept)	-4.59	0.07	-4.72	-4.46	4897.00	1	<0.0001	0.01	0.01	0.01	228.66
	Age	-0.02	0.00	-0.03	-0.01	11.41	1	0.0009	0.98	0.97	0.99	
	MeiQ™ Self-management ability	0.47	0.10	0.28	0.67	23.24	1	<0.0001	1.61	1.32	1.95	
	MeiQ™ Active Communication	-0.34	0.09	-0.53	-0.16	13.83	1	0.0003	0.71	0.59	0.85	
4	(Intercept)	-4.73	0.09	-4.91	-4.56	2789.80	1	<0.0001	0.01	0.01	0.01	224.19
	Has a co-morbid medical condition	0.40	0.14	0.13	0.66	8.54	1	0.004	1.49	1.14	1.94	
	MeiQ™ Self-management ability	0.45	0.08	0.31	0.60	37.28	1	<0.0001	1.57	1.36	1.82	
	MeiQ™ Active Communication	-0.29	0.09	-0.46	-0.13	12.51	1	0.0005	0.75	0.63	0.88	
	Age	-0.02	0.01	-0.03	-0.01	21.14	1	<0.0001	0.98	0.97	0.99	

MeiQ™ – Medication Education Impact Questionnaire; SE – Standard Error; CI – Confidence Interval; AIC - Akaike Information Criterion

7.5 DISCUSSION

These results suggest that overall patients with RA and PsA on methotrexate are able to learn the knowledge and skills required to understand and interpret their symptoms, side effects and blood test results and use this information to safely initiate care from their CNS. It is important to firstly distinguish between correct or incorrect decision making as opposed to safe/unsafe. The latter classification differs from the correct/incorrect groupings, as patients may have made a decision that was incorrect but was not unsafe i.e. contacting the CNS when blood tests were normal and there was no new or worsening symptoms or side effects. It was important to single out unsafe decisions as these could threaten the aim of tight control over the arthritis and lead to potentially serious consequences. Although a safe decision to initiate care does not represent more help-seeking, it does represent more appropriate help-seeking. In a systematic review of help-seeking in early RA Stack *et al.,* (2012) concluded that the key challenge facing the development of interventions in this area was that appropriate help-seeking must be encouraged, which the current intervention was able to foster.

7.5.1 Discrepancy between objective and subjective triggers

It is important to establish whether patients were able to safely self-monitor and use this information to seek appropriate help from their CNS via initiation of a telephone consultation. Across the entire trial period 77% of all decisions made in response to blood test results (deemed "objective triggers") were safe and 23% unsafe. In response to symptoms and side effects (deemed "subjective triggers") 73% of all decisions across the entire trial period were safe and 27% unsafe. On average participants made unsafe decisions in response to blood test results on 23.94% of occasions and on 29.95% of occasions when responding to symptoms and side effects, suggesting that participants were more able to accurately judge when contact with the CNS was required in response to objective rather than subjective triggers. This is particularly interesting considering patients would in usual care be encouraged to report symptoms and side effects to their healthcare team.

The discrepancy between patients ability to safely monitor their blood tests as opposed to symptoms could be attributed to a combination of reasons. Theoretical explanations could illuminate on the discrepancy between the objective and subjective triggers for contact with the services. According to social cognitive theory, outcome expectancies are the beliefs a person holds about the positive or negative consequences of performing the behaviour (Bandura, 1986). These expectations could be physical, social or personal outcomes. In the context of the current trial the physical outcome expectancies of not contacting the CNS in response to abnormal blood test results may have been perceived as being more serious than compared with abnormal symptoms, which could be a legitimate concern. Hence accuracy was higher for blood test results. There is little research to indicate when rapid access in response to symptoms and side effects is clinically necessary and what the appropriate tipping point is from self-managing symptoms to help-seeking. From the patient perspective research by Flurey (2014) indicates that the tipping points of help-seeking in established RA are increased pain, lack of control and longevity of the flare. This lack of specificity may have led to more "unsafe" decisions being made in response to symptoms.

It is also possible that social outcomes expectancies, such as the anticipated reaction of healthcare professionals, may have influenced a person's decision to contact their CNS, such as a fear that they were wasting the clinician's time, as suggested by Flurey (2014). It is also possible that patients felt that subjective indicators such as self-reported symptoms and side effects may not be taken as legitimate markers of disease status; which could have influenced participants' behaviour. The legitimisation of symptoms in arthritis has been found to be an important part of successful communication with healthcare professionals (Paskins, Sanders, & Hassell, 2014). Research in chronic disease indicates that when objective measures are absent or if subjective reports are incongruent to objective markers patients can perceive their communication with healthcare professionals as discrediting their symptoms. When biomarkers exist and these are in line with subjective experiences this adds credibility (Thorne, Harris, Mahoney, Con, & McGuinness, 2004). Assessment of both RA and PsA involves a combination of objective and subjective markers; therefore, healthcare professionals should be aware of the impact of this incongruence and how this could

hinder communication. While biomarkers and other objective indicators may play a useful role in disease monitoring and management it is also important for healthcare professionals to be responsive to subjective reports along with the interpretation patients make of these symptoms.

Another possible reason for this discrepancy could be related to a patient's perceived ability to self-manage symptoms and side effects without the need to seek help. In this trial participants were asked to contact the team when they had a new symptom or a continuing symptom had worsened since their last blood test; however, self-managing these symptoms is now part of living with arthritis. Therefore, by asking people to initiate care in circumstance which they felt they could manage themselves the criteria in this study may have been too rigid and in direct opposition to how participants were managing their arthritis prior to starting the study. This may have left them feeling either confused or that contact was unnecessary, hence leading them to make more unsafe decisions according to the study criteria. The decision was taken by the clinical team to use individual symptoms as triggers for patients initiating care. This was primarily taken as a precautionary decision as there was concern that contact wouldn't be made in the presence of serious symptoms or side effects. Increasing symptoms, which are unmanageable and persistent, are more commonly known as periods of disease flare (Hewlett *et al.,* 2012) and incorporate not just the symptoms reported in the current trial (e.g. pain, fatigue, nausea) but also use of medications, physical functioning and emotional well-being. Had measures such as The FLARE instrument (Berthelot *et al.,* 2012) - a tool to identify recent or present RA flare, been published prior to the start of this trial it may have been more appropriate for the criteria for patient action to be the experience of a disease flare rather than the experience of individual symptoms. There would still however, need to be an agreed cut-off point for contact with the clinical team.

7.5.2 Ability to safely seek help

The clinical care and safety of participants in the intervention group was of high priority; therefore, criteria for the return of participants back to usual care if they continually made unsafe decisions were decided *a priori*. Of the 52 participants randomised to the intervention group two participants returned to usual care due to

concerns about safety. Despite receiving the standardised training session and support from the research team, which included a CNS and rheumatologist, these patients were unable to accurately initiate care when their blood test results were either outside of the normal range or had changed significantly since their last blood test. Concerns for participant safety, specifically in relation to deterioration of disease status, was reported within the trial by Hewlett *et al.,* (2000; 2003b; 2005b). At the 2 year follow-up 12.5% of participants either withdrew or were withdrawn because of non-compliance with the safety monitoring procedures, which included 3-monthly questionnaires assessing clinical status (Hewlett *et al.,* 2000). Primdahl *et al.,* (2014) also reported incidences of missing out-of-range blood tests, but these situations were largely in the control of GP who took on the monitoring of patients in the evaluation of a shared-care service, as opposed to the patient undertaking these tasks within the current trial.

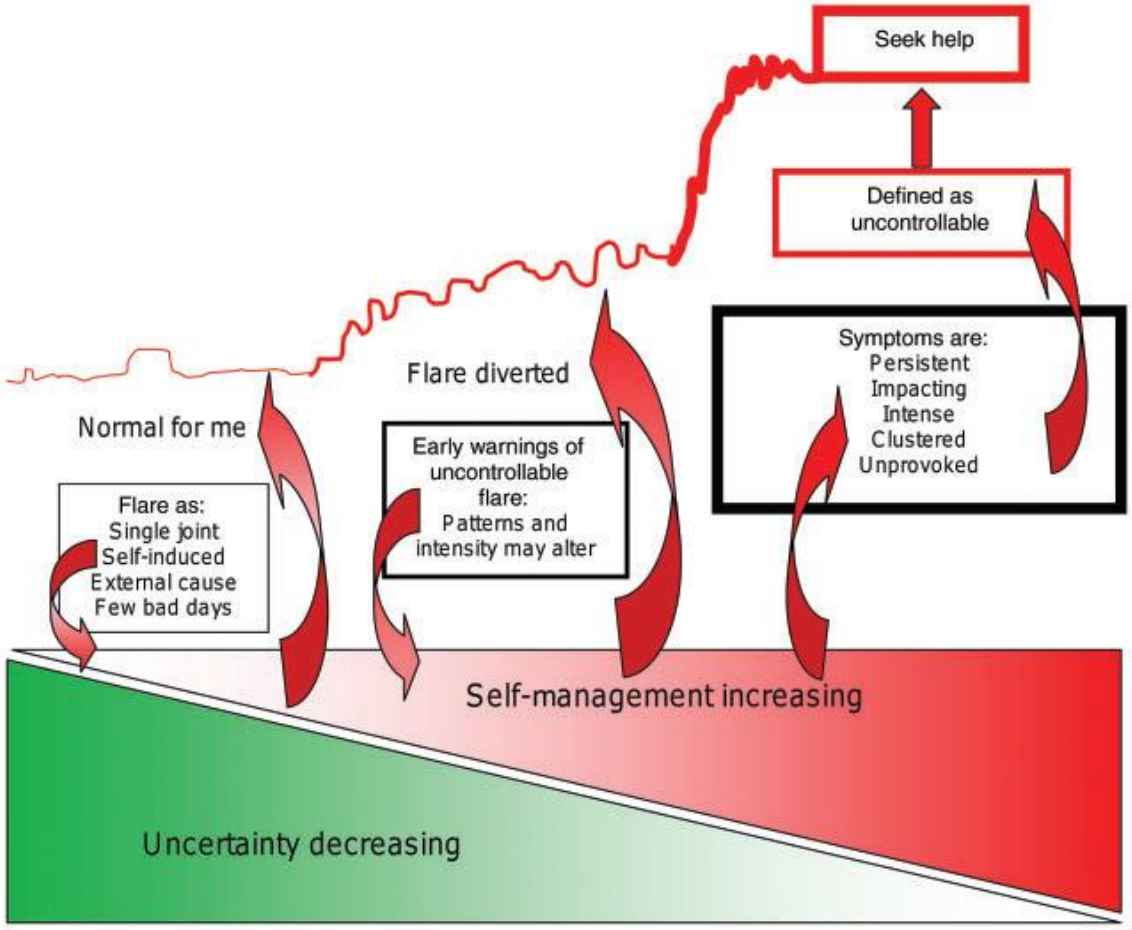
It was not possible to determine whether any of the baseline variables could distinguish these participants from the rest of the intervention group due to too small a sample size. Of particular concern to the clinical team were situations in which blood test results were out-of-range or had changed significantly since their last blood test. These situations were deemed potentially "unsafe" if the patient did not respond correctly, as signs of inflammation or liver damage can have serious consequences. At the first blood test 34.62% of the sample made an "unsafe" decision to not seek help from their CNS when their blood test results were either outside of their specified range or had changed significantly since their last blood test, this decreased to 10.87% of the sample at the final blood test. As part of the design of the trial the initial phase of self-monitoring was undertaken in collaboration with the researcher, with support from the CNS, this enabled ongoing training for the patient and feedback about incorrect help-seeking. The feedback given to participants, therefore, provided an opportunity for accuracy to improve over time which was demonstrated in the significant time effect found in the MLM analysis, lending support for the fact that a majority of patients knew when they needed to seek medical help. Only 9.81% of the sample, however, made safe decisions on every occasion. Therefore, in order to implement such a service and allow patients to independently self-monitor and initiate care clinicians would need to be sure that patients could undertake these tasks safely

and accurately. It appears that six blood tests were not a sufficient number of opportunities for all participants to grasp the knowledge and skills required, if the trial had been extended to encapsulate more blood tests accuracy may have improved further. This may mean that any service implemented would need to have a pilot phase for each patient to ensure a high level of accuracy is achieved prior to independent self-monitoring.

7.5.3 Drivers of safe help-seeking

Results from the current trial found that patients made more safe decisions to initiate care if they had additional co-morbidities, were younger and felt more confident in their ability to self-manage their arthritis, but less confident in their ability to communicate with their healthcare team at baseline. Interestingly no clinical variables, including pain, fatigue, physical functioning or disease activity, were found to be significant predictors in this model, indicating that rather than the symptoms or laboratory results driving help-seeking it was participants' confidence which was primarily important.

Results from the current trial found that patients who made more safe decisions to initiate care from their CNS were more confident in their ability to self-manage their arthritis at baseline. These findings could suggest that seeking help is seen as part of the self-management process rather than as a consequences of failed self-management strategies as suggested by Hewlett *et al.,* (2012). Hewlett *et al.,* (2012) propose that as the intensity of a flare increases efforts to self-manage also increase, but if symptoms remain uncontrollable this leads patients to seek help. Over this period a patient's uncertainty about the likelihood of the symptoms being a flare decreases, which together increases the likelihood of a patient seeking medical help, which is often seen as a last resort (Flurey, Morris, Richards, Hughes, & Hewlett, 2014).



Source: Hewlett *et al.,* (2012)

Figure 7.3. Cycles of self-managing flare symptoms on the patient journey to seeking help

As well as the fear of time wasting identified by Flurey (2014) in established RA, the systematic review by Stack *et al.,* (2012) found that help-seeking behaviours in early RA are influenced not only by a person's beliefs about their illness and treatment but also by the relationship they have with their healthcare team. Stack *et al.,* (2012) suggested that having a good relationship with your healthcare professionals was a driver for help-seeking, but when a patient anticipated negative communication or attitudes this contributed towards delayed help-seeking. In the current trial safer help-seeking was associated with lower scores on the active communication subscale of the MeiQ™ at baseline. Although this was a trial in which help-seeking behaviour was manipulated, this suggests that those who felt less confident in their ability to communicate with their rheumatology team about their beliefs, knowledge and capabilities made a greater number of safe help-seeking decisions. One explanation for this negative relationship could be that providing a structured approach to help-seeking and clear guidelines on the triggers for contacting the CNS could have provided

participants who were experiencing poor self-efficacy for communicating with their healthcare team, with the "permission" they needed to make contact, without the fear of time wasting. This could highlight a wider issue about healthcare professionals' communication styles and the possibility of previous encounters affecting patients' future help-seeking behaviour (Stack *et al.,* 2012).

These findings tentatively suggest a possible extension to the cycle of managing a flare (Figure 7.3) proposed by Hewlett *et al.,* (2012) by incorporating self-efficacy for self-management and self-efficacy for communicating with the rheumatology team in this process. The findings from this trial could indicate that in a similar pattern to uncertainty a person's confidence in their ability to self-manage their arthritis could decrease over time as an increasing number of failed self-management attempts are made, whilst self-efficacy for communicating with healthcare professionals could have a moderating effect on help-seeking. These relationships would, however, require further exploration.

In addition to self-efficacy for self-management ability and active communication, those with a co-morbid medical condition made more safe decisions, as did younger participants. Living with more than one chronic condition may lead someone to become acutely aware of the importance of clinical indicators and seeking appropriate medical assistance in order to prevent deterioration. In contrast to the current study help-seeking in chronic illness has typically been associated with older age, for instance in a review of help-seeking in chronic pain by Cornally and McCarthy (2011) 8 of the 17 quantitative studies found that increasing age was a significant predictor of help-seeking behaviour.

7.5.4 Alternative explanations for unsafe help-seeking

The first and most obvious reason why patients made decisions not to contact the CNS when either their blood test results were abnormal or when they experienced a new or worsening symptom could have been people's inability to understand and interpret the information they were given during the training session. The tasks required of participants in the intervention group required basic numeracy skills – calculating change scores from one blood test to another and using this information to

understand whether there had been a significant change since there last blood test or if the results remained abnormal.

Health numeracy skills have been found to impact upon clinical outcomes in the context of self-monitoring interventions (Estrada, Martin-Hryniewicz, Peek, Collins, & Byrd, 2004; Cavanaugh *et al.,* 2008) and was one of the potential reasons why patients refused to take part in the current trial (see section 6.5.1, page 247). A recent systematic review of health literacy in patients with a musculoskeletal disorder suggests that between 7 and 42% of the population experience low health literacy, dependant on the measure of literacy used (Loke *et al.,* 2012). With 1 in 6 people with RA in UK deemed functionally illiterate (Gordon, Hampson, Capell, & Madhok, 2002). These patients struggle to understand patient education materials or prescription labels and attend three times more often for hospital visits compared with disease, age and sex matched controls (Gordon, Hampson, Capell, & Madhok, 2002). Since this review multivariate analysis by Caplan, Wolfe, Michaud, Quinzanos and Hirsh (2014) found that limited health literacy in RA was a stronger predictor of functional disability than prednisolone use, smoking history and biologic agent use, independent of educational attainment; therefore, confirming that health literacy could have been a legitimate reason why participants made "unsafe" decisions to contact the CNS.

Another potential reason for the inaccuracies made by participants in relation to their blood test results could come from evidence that suggests that when patients self-monitor aspects of their clinical well-being, such as blood test results, an assumption is made that "someone is watching" over them, "in the background" monitoring their clinical readings. Qualitative studies in telehealth suggest that this gives people a sense of security and peace of mind as they feel that if their results are dangerously high or low a healthcare professional would contact them (Fairbrother *et al.,* 2014; Liddy *et al.,* 2008; Rogers, Kirk, Gately, May, & Finch, 2011). One of the objectives of this trial was to establish whether patients had the ability to accurately self-monitor and initiate care, but in order for these activities to be achieved safely and within the ethical constraints of the trial, measures were put in place which involved the researcher and CNS checking blood test results in order to ensure that potentially serious abnormalities were picked up and the patient contacted when necessary. This was

communicated to participants during the training session, providing credibility to the hypothesis that participants knew someone was "watching over them" and were, therefore, more complacent about seeking help in relation to abnormal blood test results. Although the procedure of cross checking results was deemed necessary by the clinical team and was a condition of the local ethics board, whether this level of healthcare professional monitoring would be expected or feasible if this model of care was rolled out across the service is unclear. These beliefs would need to be considered and addressed prior to any implementation in order to avoid dangerous clinical situations. Self-monitoring in for example diabetes and anti-coagulation therapy do not have this level of cross checking and may, therefore, not be necessary or feasible in arthritis either.

Recent research into the experience of flare in established RA may also provide clarity on the inaccuracies made by intervention participants. Reflecting on the telephone conversations had between the researcher and participants during phase one of the trial, despite acknowledging that a new symptom had developed or a blood test result was outside the advisable range, participants who made incorrect decisions tended to normalise their clinical status. In many cases they would report that a symptom had worsened but were able to provide a reason for this, for example increased pain was due to increased activity. This may have been a legitimate explanation but under the conditions of the trial, all worsening or new symptoms had to be discussed with the CNS to ensure that serious events were dealt with appropriately.

Being able to regain and maintain a normal lifestyle is regarded as an important outcome for people living with arthritis (Hewlett *et al.,* 2005a; Kristiansen *et al.,* 2012; Kristiansen *et al.,* 2012). Normalisation is a common coping mechanism for people living with a long-term condition and involves separating the impact of the illness so that its effects on the person's identity are minimised. Qualitative research by Hewlett *et al.,* (2012) found that patients with RA initially normalise their symptoms early in the cycle of managing a flare, when symptoms are less severe. Sanderson, Calnan, Morris, Richards and Hewlett (2011) also found that in an attempt to maintain a normal life symptoms can be ignored even when severe or fluctuating, which may have serious and devastating consequences. The training session delivered to intervention

participants in this trial looked to emphasise the importance of seeking clinical care when blood tests or symptoms were abnormal even if the patient felt they could provide an explanation, this clearly did not resonate with all participants. Although the training did not aim to explore participants understanding of "normal" the subsequent feedback sessions with the researcher did endeavour to address these attitudes; however, not in a systematic or explicit way. Eliciting these attitudes in the training session using a structured approach could have provided an opportunity to address issues around normalisation prior to the start of the intervention which may have improved the accuracy and safety of participant decision making.

CHAPTER 8 – INTERVENTION EFFECTIVENESS

8.1 PROLOGUE

As previously reported, patient-initiated follow-up services have been found to be an effective model of care for people with RA (section 2.5.6.1, page 82). This type of service has not been trialled in a nurse-led DMARD monitoring clinic; and has not been implemented in conjunction with patients self-monitoring their own laboratory results and using this information along with their symptoms and side effects to initiate their own rheumatology care. This RCT has, therefore, evaluated of this service as compared to usual care.

As the timing of the data collection points were dictated by the frequency with which participants had their scheduled blood tests participants spent varying times within the trial. An independent samples t-test was undertaken to explore whether there were any significant differences between the intervention and control group on the number of laboratory tests participants had within the trial and the length of time (in days) participants spent within the study. There was no significant difference in the number of laboratory tests participants spent within the trial (Intervention: M=5.75, SD=1.31; Control: M=5.58, SD=1.07; t(98)=-0.69, p=0.49, η^2=0.004) or the length of time in days participants were in the study for (Intervention: M=256.02, SD=86.48; Control: M=257.48, SD=113.33; t(98)=0.07, p=0.94, η^2<0.001). Therefore, the following analysis did not need to control for these factors.

A full description of analytical methodology can be found in section 5.11.9.3 (page 223). Analyses were conducted in the whole sample and again in only those participants who completed all three time points, as a means of sensitivity analysis. The results presented were for the whole sample (n=100) as there were no differences in the results of the significance test. The results of the complete case analysis can be found in Appendix W.

8.2 WHAT WERE THE EFFECTS OF THE INTERVENTION ON HEALTHCARE UTILISATION?

As frequency of healthcare utilisation was count data a series of univariate Poisson regressions were performed in order to explore whether trial arm (IV) was associated with healthcare utilisation (DV). The total number of appointments attended by intervention and control group participants varied (Table 8.1).

Table 8.1. Total number of face-to-face arthritis-related healthcare visits by trial arm for whole sample

Healthcare professional	Total n=100	Intervention n=52	Control n=48	Difference between groups (Control – Intervention)
CNS	96	30	66	36
Rheumatologist	199	96	103	7
GP	76	29	47	18
Overall	371	155	216	61

GP – General Practitioner

Overall the intervention group had 54.55% fewer appointments with their CNS compared to control participants (Figure 8.1). A majority of participants in the intervention group had no visits (Median=0; range 0-4, mean=0.58, SD=0.80) and a majority of control group participants had one (Median=1; range 0-4, mean=1.38, SD=1.00); very few participants in the intervention had more than one visit over the trial period compared with control group participants who had up to four visits. The Poisson regression indicated that group was a significant predictor of outpatient visits to CNS (Exp(β)=2.37, $\chi^2(1, n=100)=15.48$, $p<0.0001$). Control group participants attended the CNS 2.37 times more than those in the intervention group.

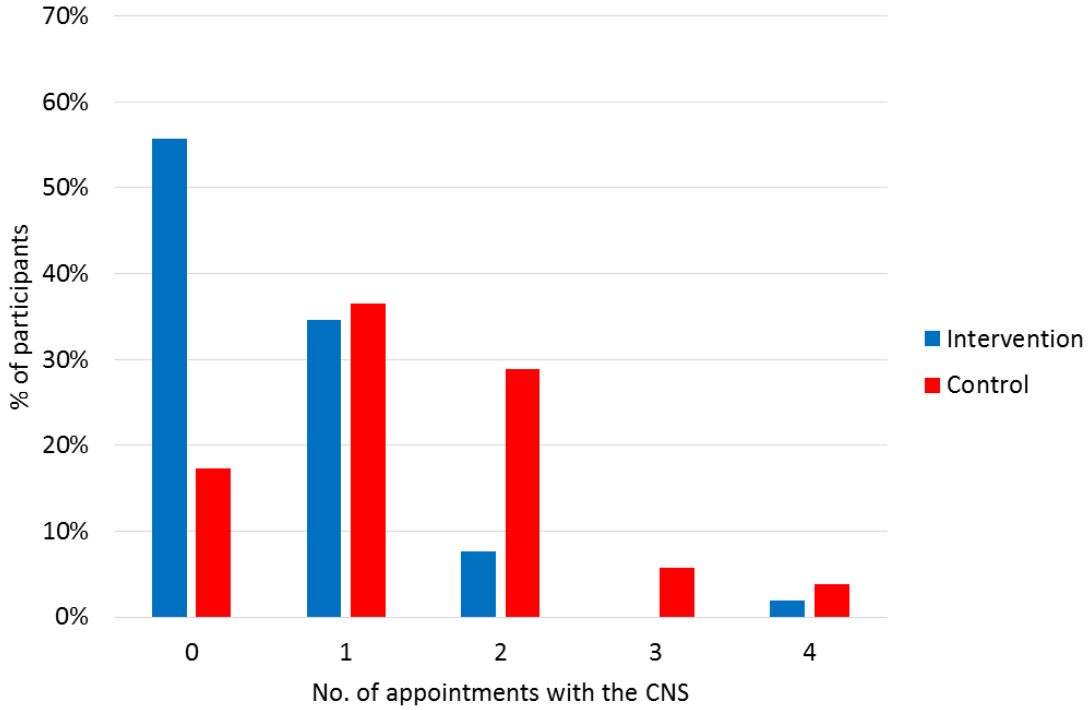


Figure 8.1. Frequency of visits to the CNS by trial arm

Overall the intervention group had 6.80% fewer reviews with their rheumatologist over the trial period compared to control group participants (Figure 8.2). A majority of participants in the intervention group had two visits (Median=2; range 0-4, mean=1.85, SD=1.00) and a majority of control group participants also attended twice. The distribution in the control group (Median=2; range 0-7, mean=2.15, SD=1.58) did indicate that a number of these participants did have more than four visits over the trial period. Poisson regression indicated that group was not a significant predictor of outpatient visits to the rheumatologist (Exp(β)=1.04, $\chi^2(1, n=100)=1.16$, $p=0.23$) indicating that participants in the intervention and control group did not differ in the number of visits they had to their rheumatologist.

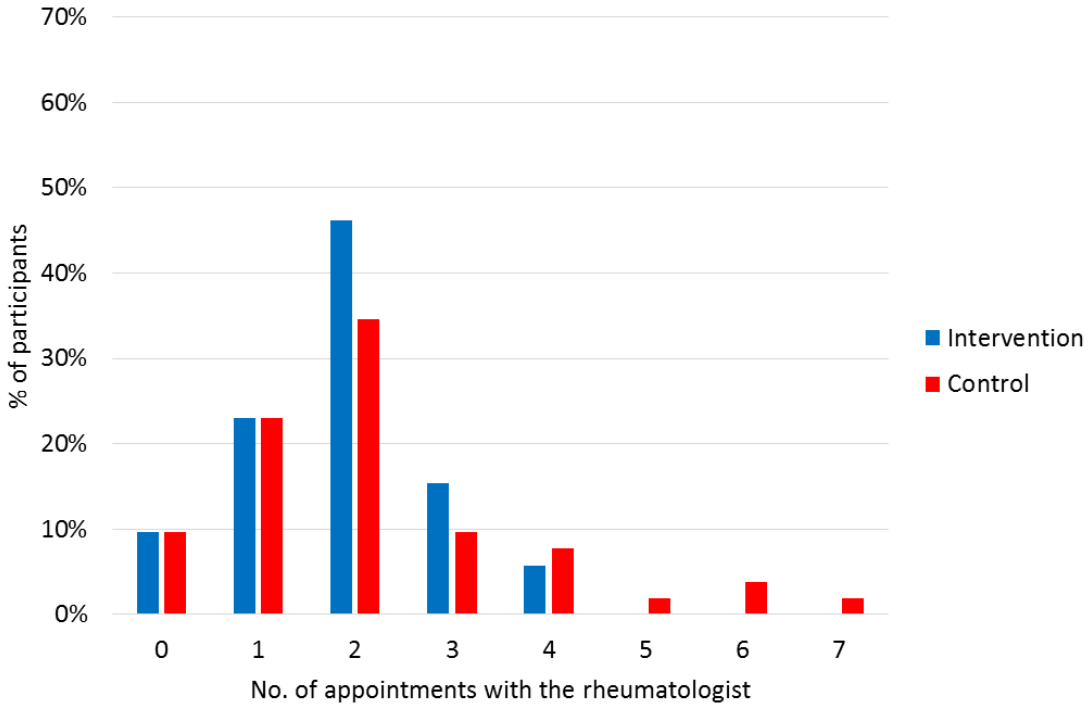


Figure 8.2. Frequency of visits to the rheumatologist by trial arm

Overall the intervention group had 38.80% fewer appointments with their GP in relation to their arthritis than control group participants (Figure 8.3). A majority of participants in both trial arms did not visit their GP about their arthritis at all (Intervention: Median=0; range 0-3, mean=0.56, SD=0.87; Control: Median=0.05; range 0-5, mean=0.94, SD=1.30). In the regression, participants in the control group had 1.78 times as many arthritis-related GP visits than those in the intervention group, although this difference was not statistically significant (Exp(β)=1.78, $\chi^2(1, n=100)=3.64$, $p=0.07$).

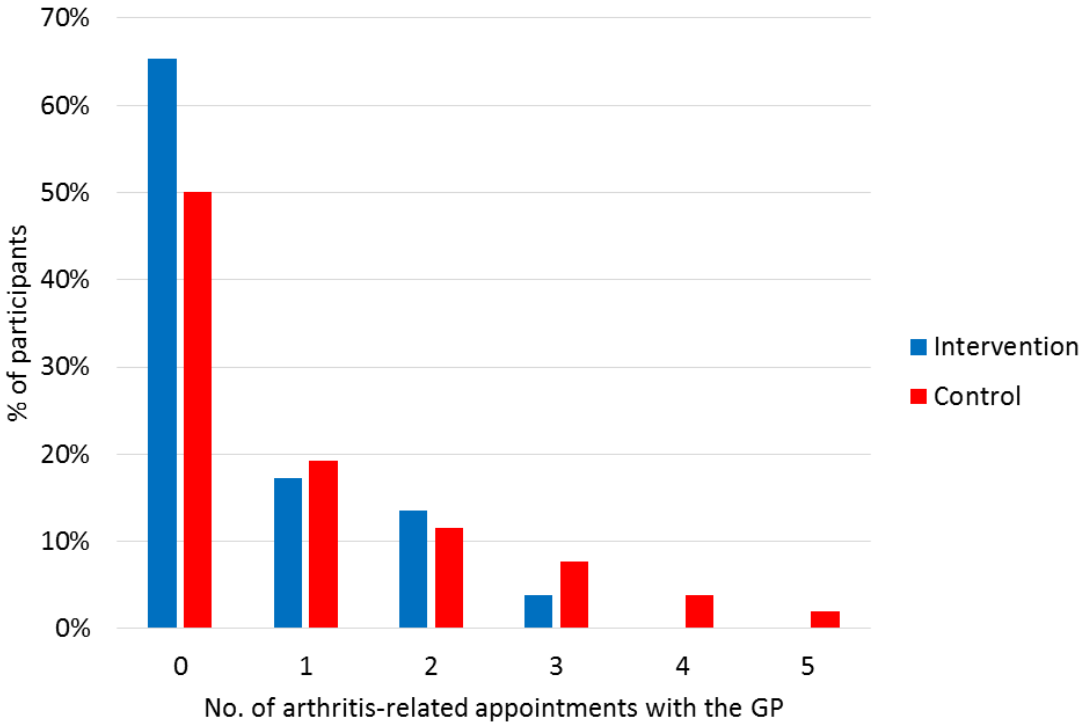


Figure 8.3. Frequency of visits to the GP by trial arm

When analysing the total number of visits to the GP, CNS and rheumatologist together, participants in the control group had 28.44% more appointments with their healthcare team compared to those in the intervention group. The Poisson regression indicated that group was a significant predictor of total healthcare utilisation (Exp(β)=1.49, χ^2(1, n=100)=12.54, p<0.001). Control group participants used for 1.49 times more health services than those in the intervention group.

Out-of-range blood tests in the intervention group triggered a total of 231 telephone consultations, with a mean per participant of 4.43(SD=1.43). All intervention participants required at least one telephone consultation during the trial period, 15(29.23%) participants required a telephone consultation at each of the six blood tests (Figure 8.4). These 231 telephone consultations led to 96(41.56%) face-to-face outpatient appointments with the CNS. Therefore, for approximately every five telephone consultations, two outpatient appointments were requested.

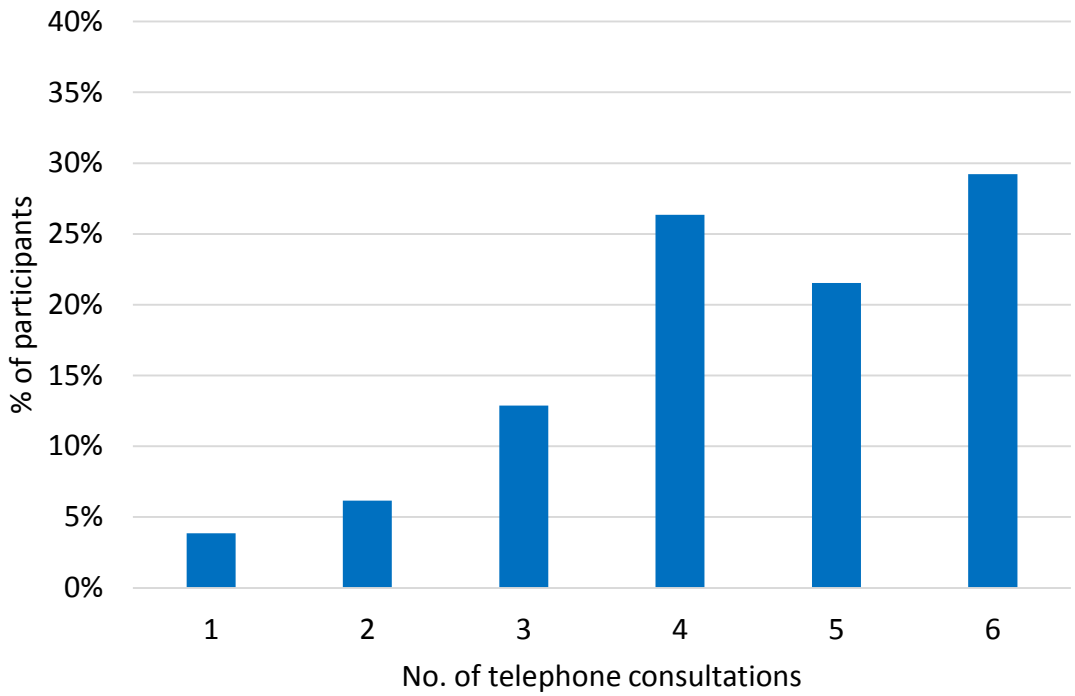


Figure 8.4. Frequency of telephone consultations in the intervention group

When these telephone consultations were added to the total number of face-to-face visits patients had with their healthcare team (including CNS, rheumatologist and GP) the intervention group had 55.84% more contact with healthcare professionals about their arthritis than participants in the control group. Poisson regression indicated that group was a significant predictor (Exp(β)=0.60, $\chi^2(1, n=100)=27.08$, $p<0.0001$) indicating that participants in the control group attended 40% fewer (0.60 times more) healthcare visits than those in the intervention group.

8.3 WHAT WERE THE EFFECTS OF THE INTERVENTION ON HEALTHCARE COSTS?

The analysis of healthcare utilisation indicated that there were significant reductions in relation to the number of outpatient visits participants had with their CNS and overall healthcare utilisation. However, when taking into account the number of telephone consultations as a result of new or worsening symptoms or out-of-range blood tests, the reverse was found (i.e. the intervention group had significantly more contact with their healthcare team). It was, therefore, important to assess whether there were any cost savings attached to a telephone consultation as opposed to face-to-face contact. Therefore, the following analyses looked at the economic impact of the intervention using the Department of Health Reference costs (Department of Health, 2011a; Department of Health, 2013a) and the Unit Costs of Health & Social Care 2012 (Curtis,

2012) as described in section 5.11.9.2 (page 219). As stated in Chapter 5 these analyses were post-hoc and, therefore, results should be interpreted with caution, p-values were adjusted to 0.001 to compensate for these additional tests.

Table 8.2 indicates that irrespective of the model or unit price the cost of providing face-to-face rheumatology nursing care for patients in the intervention group was significantly cheaper than that of the control group (U=652.50, z=-4.36, p<0.001, r=-0.44) but there were no significant differences between the intervention and control group on the cost of providing rheumatologist outpatient visits (U=1194.50, z=-0.39, p=0.70, r=-0.04), arthritis-related GP care (U=1070.45, z=-1.39, p=0.18, r=-0.14), travel (U=992.00, z=-1.78, p=0.08, r=-0.18) or laboratory tests (U=1112.00, z=-1.40, p=0.16, r=-0.14). No statistical comparisons can be made between the intervention and control on the cost of training or telephone consultations as these did not take place in the control group.

Table 8.2. Group comparisons between trial arms on healthcare costs for each model per participant (whole sample)‡

Healthcare professional	**Intervention n=52**	**Control n=48**	**Significance statistic**
CNS, median(range)			
Lower	£0(£0-208)	£52(£0-208)	
Average	£0(0-356)	£89(£0-356)	**U=652.50, z=-4.36, *p*<0.001, *r*=-0.44**
Upper	£0(£0-420)	£105(£0-420)	
Rheumatologist, median(range)			
Lower	£210(£0-420)	£210(£0-735)	
Average	£266(£0-532)	£266(£0-931)	U=1194.50, z=-0.39, *p*=0.70, *r*=-0.04
Upper	£300(£0-600)	£300(£0-1050)	
GP, median(range)			
Lower	£0(£0-108)	£1.80(£0-180)	
Average	£0(£0-118.50)	£1.98(£0-197.50)	U=1070.45, z=-1.39, *p*=0.18, *r*=-0.14
Upper	£0(£0-129)	£2.15(£0-215)	
Telephone consultations, median(range)			
Lower	£241.80(£52-312)	-	
Average	£372(£80-480)		n/a
Upper	£520.80(£112-672)		

Healthcare professional	Intervention n=52	Control n=48	Significance statistic
Travel, median(range)	£41(£5-113)	£54(£0-126)	U=992.00, z=-1.78, *p*=0.08, *r*=-0.18
Laboratory tests, median(range)	£192.66(£32.11-256.88)	£192.66(£64.22-192.66)	U=1112.00, z=-1.40, *p*=0.16, *r*=-0.14
Education, mean(SD)			
Lower	£35(£0)	-	
Average	£41.70(£0)		n/a
Upper	£48.40(£0)		
Total costs (Lower quartile unit cost)			
Model One, mean(SD)	£743.17(£209.58)	£574.72(£232.89)	**t(98)=-3.84, *p*<0.001, η^2=0.16**
Model Two, mean(SD)	£512.17(£178.85)	£574.72(£233.98)	t(85.99)=1.48, *p*=0.14, η^2=0.02
Total costs (National average unit cost)			
Model One, mean(SD)	£949.25(£271.51)	£689.10(£282.65)	**t(98)=-4.68, *p*<0.001, η^2=0.23**
Model Two, mean(SD)	£593.86(£222.53)	£689.10(£285.58)	t(86.78)=1.83, *p*=0.07, η^2=0.03
Total costs (Upper quartile unit cost)			
Model One, mean(SD)	£1140.67(£319.99)	£751.01(£304.28)	**t(98)=-6.10, *p*<0.001, η^2=0.41**
Model Two, mean(SD)	£650.15(£246.75)	£751.01(£315.90)	t(86.76)=1.87, *p*=0.06, η^2=0.04

GP – General Practitioner; SD – Standard Deviation

‡ The results of the significance tests remain the same irrespective of whether the task was costed at lower, national or upper rates

Model One – Total costs including nurse-led telephone consultations. Model Two – Total costs excluding all nurse-led telephone consultations

Model One: When including the cost of the telephone consultations the overall cost of a self-monitoring and patient-initiated follow-up service for patients with RA or PsA on DMARD therapy was between 29.31% and 51.88% more *expensive* per patient than usual care (Table 8.3) and this difference was statistically significant for each of the three unit costs (Lower quartile: $t(98)=-3.84$, $p<0.001$, $\eta^2=0.16$; National average: $t(98)=-4.68$, $p<0.001$, $\eta^2=0.23$; Upper quartile: $t(98)=-6.10$, $p<0.001$, $\eta^2=0.41$) (Table 8.2).

Model Two: Excluding the cost of telephone consultations meant that the intervention was between 10.88% and 13.88% *cheaper* to run than the control group (Table 8.4). This difference, however, remained statistically non-significant (Lower quartile: $t(85.99)=1.48$, $p=0.14$, $\eta^2=0.02$; National average: $t(86.78)=1.83$, $p=0.07$, $\eta^2=0.03$; Upper quartile: $t(86.76)=1.87$, $p=0.06$, $\eta^2=0.04$).

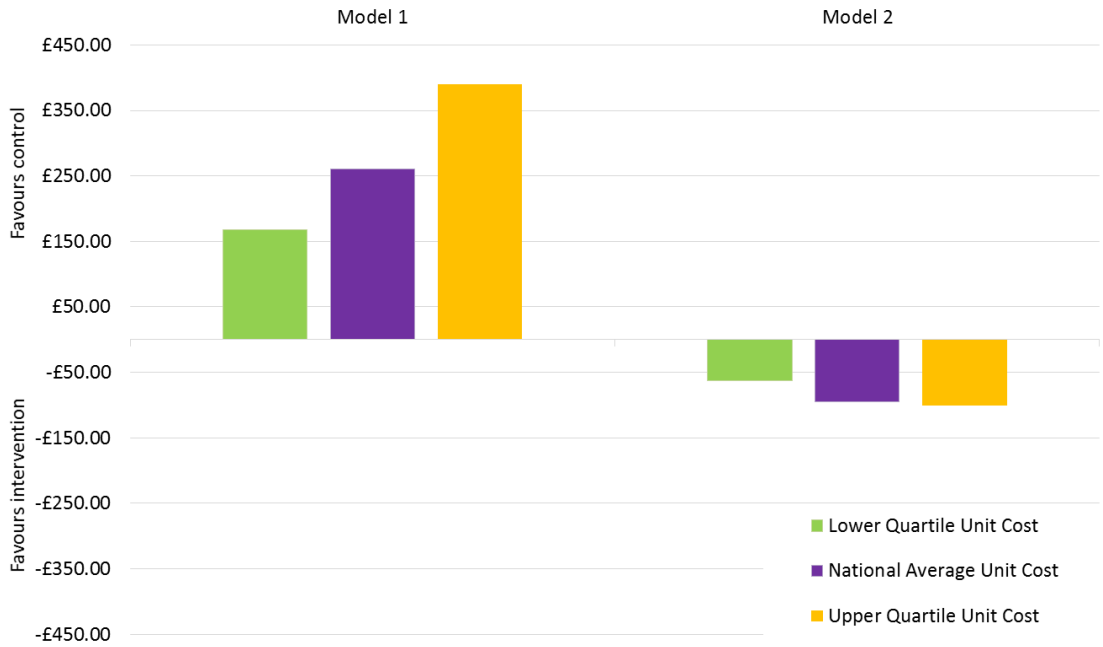


Figure 8.5. Overall cost difference between the intervention and control group (whole sample)

Table 8.3. Model One: Healthcare utilisation usage and costs across the trial period and the associated costs (whole sample)

Healthcare usage	Trial arm	No. of visits	Lower quartile		National average		Upper quartile	
			Unit cost	Total cost	Unit cost	Total cost	Unit cost	Total cost
CNS	Intervention	30	£52	£1,560	£89	£2,670	£105	£3,150
	Control	66		£3,432		£5,874		£6,930
Rheumatologist	Intervention	96	£105	£10,080	£133	£12,768	£150	£14,400
	Control	103		£10,815		£13,699		£15,450
GP	Intervention	29	£36	£1,044	£39.50	£1,146	£43	£1,247
	Control	47		£1,692		£1,857		£2,021
Training session	Intervention	52	£35	£1,820	£41.70	£2,168	£48.40	£2,517
	Control	0		£0		£0		£0
Transport to outpatients	Intervention	126	£18	£2,268	£18	£2,268	£18	£2,268
	Control	169		£3,042		£3,042		£3,042
Transport to training session	Intervention	52	£5	£260	£5	£260	£5	£260
	Control	0		£0		£0		£0
Telephone	Intervention	231	£52	£12,012	£80	£18,480	£112	£25,872
	Control	0		£0		£0		£0
Laboratory tests	Intervention	299	£32.11	£9,600.89	£32.11	£9,600.89	£32.11	£9,600.89
	Control	268		£8,605.48		£8,605.48		£8,605.48

Healthcare usage	Trial arm	No. of visits	Lower quartile		National average		Upper quartile	
			Unit cost	Total cost	Unit cost	Total cost	Unit cost	Total cost
Total cost per group	Intervention	-		£38,644.89		£49,360.79		£59,314.69
	Control			£27,586.48		£33,076.98		£36,048.48
Cost per patient	Intervention	-		£743.17		£949.25		£1,140.67
	Control			£574.72		£689.10		£751.01

GP – General Practitioner

Table 8.4. Model Two: Healthcare utilisation usage and costs across the trial period and the associated costs (whole sample)

Healthcare usage	Group	No. of visits	Lower quartile		National average		Upper quartile	
			Unit cost	Total cost	Unit cost	Total cost	Unit cost	Total cost
CNS	Intervention	30	£52	£1,560	£89	£2,670	£105	£3,150
	Control	66		£3,432		£5,874		£6,930
Rheumatologist	Intervention	96	£105	£10,080	£133	£12,768	£150	£14,400
	Control	103		£10,815		£13,699		£15,450
GP	Intervention	29	£36	£1,044	£39.50	£1,146	£43	£1,247
	Control	47		£1,692		£1,857		£2,021
Training session	Intervention	52	£35	£1,820	£41.70	£2,168	£48.40	£2,517
	Control	0		£0		£0		£0
Transport to outpatients	Intervention	126	£18	£2,268	£18	£2,268	£18	£2,268
	Control	169		£3,042		£3,042		£3,042
Transport to training session	Intervention	52	£5	£260	£5	£260	£5	£260
	Control	0		£0		£0		£0
Laboratory tests	Intervention	299	£32.11	£9,600.89	£32.11	£9,600.89	£32.11	£9,600.89
	Control	268		£8,605.48		£8,605.48		£8,605.48
Total cost per group	Intervention			£26,632.89		£30,880.79		£33,807.69
	Control	-		£27,586.48		£33,076.98		£36,048.48

Healthcare usage	Group	No. of visits	Lower quartile		National average		Upper quartile	
			Unit cost	Total cost	Unit cost	Total cost	Unit cost	Total cost
Cost per patient	Intervention	-		£512.17		£593.86		£650.15
	Control			£574.72		£689.10		£751.01

GP – General Practitioner

8.4 WHAT WERE THE EFFECTS OF THE INTERVENTION ON CLINICAL OUTCOMES?

8.4.1 Disease activity

In order to explore if there were any significant interaction effects between group and time on disease activity a mixed between-within participants ANOVA was undertaken to look at changes over time in the intervention and control on the DAS28 and the individual subscales of the PsARC (Table 8.5). This test was chosen instead of MLM as there were only two time points (baseline and final follow-up). There was an improvement in DAS28, PsARC patient global health scores and PsARC tender joint count in both the intervention and control group. Physical PsARC global health scores remained the same over time in both groups and there was an increase in the number of swollen joints in both the intervention and control groups. The mixed between-within participants ANOVAs revealed that none of these differences were statistically significant for the DAS28 (Wilks's lambda=0.99, $F_{1, 69}$=0.42, p=0.63, η^2_p=0.02), PsARC physician global score (Wilks's lambda=0.99, $F_{1, 69}$=0.43, p=0.70, η^2_p=0.04), PsARC patient global score (Wilks's lambda=0.97, $F_{1, 69}$=0.66, p=0.58, η^2_p=0.13), PsARC swollen joints (Wilks's lambda=0.93, $F_{1, 69}$=2.11, p=0.27, η^2_p=0.04) or PsARC tender joints (Wilks's lambda=0.97, $F_{1, 69}$=0.88, p=0.50, η^2_p=0.05).

Table 8.5. Disease activity scores by trial arm across the 2 time points, mean(SD)

	Intervention		**Control**	
Variable	**Baseline**	**Final f/u**	**Baseline**	**Final f/u**
DAS28[†]	3.54(1.36)	3.29(1.46)	3.19(1.23)	3.09(1.34)
PsARC[‡] physician global	2.05(0.71)	2.00(1.46)	2.40(0.74)	2.40(1.46)
PsARC[‡] patient global	1.43(0.61)	2.03(1.32)	2.15(0.67)	2.41(1.36)
PsARC[‡] swollen joints	1.84(3.00)	6.11(6.10)	4.64(3.20)	5.98(5.34)
PsARC[‡] tender joints	7.79(6.75)	6.41(7.12)	11.34(7.49)	7.38(6.90)

SD – Standard Deviation; DAS28 – 28-Item Disease Activity Score; PsARC – Psoriatic Arthritis Response Criteria; f/u – follow-up

[†] n=71 whole sample (33 intervention, 38 control); [‡] n=29 whole sample (19 intervention, 10 control)

A majority of participants did not respond according to the EULAR treatment response criteria for RA or on the PsARC (Table 8.6). When the frequency of responders was compared to none responders at the end of the trial period, there was no significant

association between trial arm and disease response, $\chi^2(1, n=100)=0.35$, $p=0.77$, $\phi=-0.03$.

Table 8.6. Disease response over the trial period by trial arm, n(%)

Variable	Whole n=100	Intervention n=52	Control n=48
DAS28 response			
None	52(73.24)	25(75.76)	27(71.05)
Moderate	7(9.86)	3(9.09)	4(10.53)
Good	12(16.90)	5(15.15)	7(18.42)
PsARC response			
No response	22(75.86)	14(73.68)	8(80.00)
Response	7(24.14)	5(26.32)	2(20.00)

DAS28 – 28-item Disease Activity Score; PsARC – Psoriatic Arthritis Response Criteria

8.4.2 Time between laboratory tests

An independent samples t-test was conducted in order to explore whether there was a significant difference between the intervention and control group on the time between laboratory tests. Analysis indicated that intervention participants attended for their laboratory tests more frequently (M=39.35 days, SD=9.12 days) than control group participants (M=47.88 days, SD=13.50 days; t(79.84)=3.63, $p=0.001$, $\eta^2=0.12$).

8.4.3 Laboratory tests

Data were entered for the pre-trial blood test and the six laboratory tests within the trial period (Table 8.8). There were no statistically significant interaction effects between group and time on any of the laboratory results (Table 8.7). See Appendix X for a graphical representation of the laboratory tests over time. A majority of the effect sizes were also small .

Table 8.7. MLM analysis for laboratory tests (n=100)

Test	Group	Time	Group*Time
Haemoglobin	$F_{1,92.59} = 4.74$, $p=0.03$	$F_{6,302.56} = 1.51$, $p=0.18$	$F_{6,302.56} = 0.75$, $p=0.61$
WBC	$F_{1,88.79} = 0.02$, $p=0.90$	$F_{6,290.87} = 0.86$, $p=0.53$	$F_{2,290.87} = 0.39$, $p=0.89$
Neutrophils	$F_{1,89.72} = 0.08$, $p=0.78$	$F_{6,288.13} = 0.71$, $p=0.64$	$F_{6,288.13} = 1.33$, $p=0.25$
Platelets	$F_{1,92.19} = 9.00$, $p=0.003$	$F_{6,299.34} = 1.09$, $p=0.37$	$F_{6,299.34} = 1.00$, $p=0.43$
ALP	$F_{1,92.65} = 0.02$, $p=0.90$	$F_{6,297.91} = 1.22$, $p=0.30$	$F_{6,297.91} = 1.19$, $p=0.31$
ALT	$F_{1,93.46} = 1.37$, $p=0.25$	$F_{6,307.46} = 1.08$, $p=0.37$	$F_{6,209.46} = 1.58$, $p=0.15$
ESR	$F_{1,94.06} = 0.28$, $p=0.60$	$F_{6,300.96} = 0.41$, $p=0.87$	$F_{6,300.96} = 0.35$, $p=0.91$
CRP	$F_{1,88.59} = 0.88$, $p=0.35$	$F_{6,279.19} = 1.13$, $p=0.34$	$F_{6,279.19} = 0.53$, $p=0.78$

MLM – Multi-Level Modelling; WBC – White Blood Count; ALP – Alkaline Phosphatase; ALT – Alanine Transaminase; ESR – Erythrocyte Sedimentation Rate; CRP – C-Reactive Protein

Table 8.8. Descriptive statistics adjusted mean(SD) for laboratory tests over time by trial arm (n=100)

Test	Trial arm	Pre-trial	1	2	3	4	5	6
Haemoglobin	Intervention	13.91(1.37)	14.01(1.37)	13.96(1.38)	13.88(1.33)	13.88(1.33)	13.95(1.34)	13.82(1.40)
	Control	13.35(1.53)	13.29(1.53)	13.25(1.47)	13.23(1.47)	13.39(1.49)	13.54(1.55)	13.29(1.56)
		Effect size (99% CI)	0.49(0.00,0.98)	0.49(0.00,0.99)	0.46(-0.03,0.95)	0.34(-0.15,0.84)	0.28(-0.22,0.78)	0.36(-0.15,0.86)
WBC	Intervention	6.79(1.77)	6.76(1.77)	6.93(1.78)	7.11(1.73)	6.73(1.74)	6.99(1.75)	6.80(1.85)
	Control	6.65(1.96)	6.88(1.98)	7.00(1.90)	6.97(1.92)	7.00(1.95)	7.01(2.04)	6.86(2.05)
		Effect size (99% CI)	0.06(-0.57,0.69)	0.04(-0.60,0.68)	0.08(-0.57,0.72)	0.14(-0.50,0.79)	0.01(-0.64,0.67)	0.03(-0.63,0.69)
Neutrophils	Intervention	4.28(1.53)	3.96(1.53)	4.04(1.55)	4.26(1.50)	3.96(1.50)	4.15(1.54)	3.93(1.62)
	Control	3.84(1.70)	4.23(1.71)	4.20(1.65)	4.30(1.66)	4.13(1.70)	4.22(1.77)	4.16(1.78)
		Effect size (99% CI)	0.16(-0.38,0.71)	0.10(-0.45,0.66)	0.02(-0.53,0.58)	0.11(-0.46,0.67)	0.04(-0.53,0.61)	0.13(-0.44,0.71)
Platelets	Intervention	241.27(57.39)	238.27(57.39)	239.51(57.66)	240.82(55.59)	242.74(55.76)	245.19(56.32)	239.34(58.87)
	Control	273.81(63.86)	277.70(64.06)	279.82(61.60)	278.44(61.79)	270.92(62.39)	273.21(62.05)	264.31(65.28)
		Effect size (99% CI)	0.64(-19.89,21.18)	0.67(-19.96,21.30)	0.64(-20.06,21.34)	0.47(-20.29,21.24)	0.46(-20.57,21.43)	0.40(-20.66,21.46)
ALP	Intervention	73.13(20.60)	75.10(20.60)	72.71(20.71)	72.80(19.93)	70.87(19.99)	73.14(20.08)	73.20(20.97)
	Control	70.81(22.92)	72.83(22.98)	73.20(22.10)	73.03(22.15)	74.46(22.44)	75.68(23.36)	74.56(23.38)
		Effect size (99% CI)	0.10(-7.27,7.47)	0.02(-7.39,7.43)	0.01(-7.41,7.43)	0.17(-7.27,7.61)	0.12(-7.36,7.59)	0.06(-7.44,7.56)
ALT	Intervention	28.88(16.51)	29.08(16.51)	31.75(16.70)	32.27(16.11)	30.10(16.28)	31.59(16.40)	31.59(17.21)
	Control	26.93(18.37)	26.02(18.70)	28.34(17.77)	25.05(17.96)	29.85(18.51)	26.93(19.37)	28.70(19.22)
		Effect size (99% CI)	0.17(-5.73,6.08)	0.20(-5.78,6.17)	0.42(-5.58,6.42)	0.01(-6.05,6.08)	0.26(-5.85,6.37)	0.16(-6.00,6.31)
ESR	Intervention	13.54(12.63)	13.15(12.69)	13.09(12.77)	12.21(12.60)	12.63(12.49)	13.04(12.63)	12.17(13.23)
	Control	13.55(14.06)	15.69(14.51)	13.88(13.69)	12.68(13.96)	14.17(14.19)	13.36(14.58)	14.36(14.80)
		Effect size (99% CI)	0.19(-4.35,4.72)	0.06(-4.51,4.63)	0.04(-4.66,4.73)	0.11(-4.53,4.76)	0.02(-4.68,4.73)	0.16(-4.58,4.89)

Test	Trial arm	Pre-trial	1	2	3	4	5	6
CRP	Intervention	5.07(8.34)	4.60(8.41)	4.87(8.62)	5.89(8.23)	4.73(8.46)	4.52(8.55)	5.23(8.91)
	Control	4.26(9.28)	5.89(9.47)	6.96(9.11)	7.50(9.21)	5.80(9.65)	4.23(9.96)	7.17(9.96)
		Effect size (99% CI)	0.14(-2.86,3.15)	0.23(-2.85,3.32)	0.18(-2.88,3.25)	0.12(-3.03,3.27)	0.03(-3.15,3.22)	0.21(-2.98,3.39

SD – Standard Deviation; WBC – White Blood Cell; ALP – Alkaline Phosphatase; ALT – Alanine Transaminase; ESR – Erythrocyte Sedimentation Rate; CRP – C-Reactive Protein; CI – Confidence Interval

8.4.4 Functional disability, pain and fatigue

Scores at the first and final follow-up indicated that participants in the intervention group experienced less pain, functional disability and either more or the same levels of fatigue as participants in the control group (Appendix Y). Over time, however, levels of fatigue, pain and functional disability remained stable and effect sizes were small at both time points (Table 8.9).

Table 8.9. Descriptive statistics adjusted mean(SD) and MLM analysis for pain, fatigue and functional disability (n=100)

Variable	Trial arm	Baseline	First f/u	Final f/u	Group	Time	Time*Group
Fatigue	Intervention	4.20(2.74)	4.53(2.87)	4.30(2.90)	$F_{1,97.20}$=0.11, *p*=0.74	$F_{2,115.21}$=0.68, *p*=0.51	$F_{2,115.21}$=0.45, *p*=0.64
	Control	4.35(2.70)	4.50(2.79)	4.69 (2.93)			
	Effect size(99% CI)		0.01(-0.97, 0.99)	0.13(-0.90, 1.16)			
Pain	Intervention	3.64(2.46)	3.56(2.70)	3.68(2.60)	$F_{1,95.62}$=0.24, *p*=0.63	$F_{2,159.60}$=0.65, *p*=0.53	$F_{2,159.60}$=0.84, *p*=0.43
	Control	3.50(2.43)	4.12(2.56)	3.86(2.70)			
	Effect size(99% CI)		0.21(-0.67, 1.09)	0.07(-0.90, 1.03)			
Functional Disability	Intervention	0.59(0.62)	0.55(0.64)	0.56(0.63)	$F_{1,95.18}$=1.12, *p*=0.29	$F_{2,110.04}$=0.51, *p*=0.60	$F_{2,110.04}$=2.01, *p*=0.14
	Control	0.64(0.62)	0.74(0.63)	0.70(0.64)			
	Effect size(99% CI)		0.29(0.07, 0.51)	0.22(0.00, 0.45)			

SD – Standard Deviation; MLM – Multi-Level Modelling; CI – Confidence Interval; f/u – follow-up

8.5 WHAT WERE THE EFFECTS OF THE INTERVENTION ON PSYCHOSOCIAL OUTCOMES?

Table 8.10 illustrates the descriptive statistics for the intervention and control group at each of the three time points for quality of life and mood, along with the associated F-tests for the MLM analyses. The associated graphs (Appendix Z) indicate very little change in any of these outcomes either in the intervention or control group. None of the interaction effects were significant, in either the whole sample or for complete cases only (Appendix W).

Table 8.10. Descriptive statistics mean(SD) and MLM analysis for quality of life and psychosocial well-being (n=100)

Variable	Trial arm	Baseline	First f/u	Final f/u	Group	Time	Time*Group
Anxiety	Intervention	5.73(4.22)	5.84(4.39)	5.06(4.38)	$F_{1,98.61}$=2.51, *p*=0.12	$F_{1,107.47}$=1.28, *p*=0.28	$F_{1,107.47}$=1.85, *p*=0.16
	Control	6.46(4.21)	7.01(4.34)	6.97(4.45)			
		Effect size(99% CI)	0.26(-1.25,1.78)	0.43(-1.14, 2.00)			
Depression	Intervention	4.63(3.33)	4.44(3.49)	4.11(3.46)	$F_{1,97.24}$=0.001, *p*=0.98	$F_{1,132.01}$=0.22, *p*=0.81	$F_{1,132.01}$=1.20, *p*=0.31
	Control	4.25(3.33)	4.50(3.42)	4.51(3.52)			
		Effect size(99% CI)	0.02(-1.18, 1.21)	0.11(-1.14, 1.36)			
SF-12v1® MCS	Intervention	30.15(7.48)	29.18(7.72)	30.99(7.80)	$F_{1,89.00}$=0.02, *p*=0.89	$F_{2,84.85}$=1.49, *p*=0.23	$F_{2,84.85}$=1.48, *p*=0.23
	Control	30.91(8.36)	29.60(7.62)	29.26(8.22)			
		Effect size(99% CI)	0.05(-2.62, 2.73)	0.21(-2.55, 2.97)			
SF-12v1® PCS	Intervention	46.82(11.41)	46.34(11.83)	45.26(11.71)	$F_{1,90.22}$=0.28, *p*=0.60	$F_{2,99.16}$=0.07, *p*=0.94	$F_{2,99.16}$=1.02, *p*=0.36
	Control	44.30(12.57)	45.22(11.73)	45.59(12.38)			
		Effect size(99% CI)	0.09(-3.99, 4.18)	0.03(-4.20, 4.26)			

SD – Standard Deviation; MLM – Multi-Level Modelling; CI – Confidence Interval; MCS – Mental Component Score; PCS – Physical Component Score; f/u – follow-up

8.5.1 Quality of life

There were no statistically significant interaction effects between group and time on either the mental ($F_{2,84.85}$=1.48, p=0.23) or physical health ($F_{2,99.16}$=1.02, p=0.36) SF-12v1® component scores. At first follow-up participants in the intervention group had slightly poorer mental health quality of life and marginally better physical quality of life than those in the control group, and the reverse was found at final follow-up; however, effect sizes were very small (Table 8.10).

8.5.2 Mood

There were no statistically significant interaction effects between group and time for depression ($F_{1,132.01}$=1.20, p=0.31) or anxiety ($F_{1,107.47}$=1.85, p=0.16). At both follow-ups participants in the intervention group had lower levels of anxiety and depression, the effect sizes were all small except for anxiety at final follow-up when the difference between the intervention and control group suggested a medium size effect (Table 8.10).

8.6 WHAT WERE THE EFFECTS OF THE INTERVENTION ON PSYCHOSOCIAL PROCESS VARIABLES?

Table 8.11 illustrates the descriptive statistics for the intervention and control group at each of the three time points on all psychosocial process variables, along with the associated F-tests for MLM analyses. There were no significant interaction effects for any of the psychosocial process variables, in either the whole sample or for complete cases only (Appendix W).

8.6.1 Self-effficacy

8.6.1.1 Generalised self-efficacy

There was no statistically significant interaction effects between group and time for generalised self-efficacy ($F_{1,130.49}$=1.50, p=0.23). At both follow-ups participants in the intervention group exhibited greater levels of self-efficacy than control group participants, although not significant and effect sizes indicated these differences were small (Table 8.11).

Table 8.11. Descriptive statistics adjusted mean(SD) and MLM analysis for self-efficacy (n=100)

Variable	Trial arm	Baseline	First f/u	Final f/u	Group	Time	Time*Group
Generalised self-efficacy	Intervention	31.78(4.57)	31.60(4.83)	32.33(4.76)	$F_{1,94.97}$=0.85, *p*=0.36	$F_{1,130.49}$=0.26, *p*=0.77	$F_{1,130.49}$=1.50, *p*=0.23
	Control	31.42(4.57)	31.13(4.67)	30.82(4.85)			
	Effect size(99% CI)		0.10(-1.54, 1.73)	0.31(-1.42, 2.04)			
HeiQ™ Self-monitoring & insight	Intervention	3.00(0.41)	3.07(0.44)	3.10(0.44)	$F_{1,99.05}$=1.57, *p*=0.21	$F_{2,121.44}$=0.87, *p*=0.42	$F_{2,121.44}$=1.36, *p*=0.26
	Control	3.15(0.41)	3.18(0.43)	3.11(0.45)			
	Effect size(99% CI)		0.26(0.11, 0.40)	0.03(-0.13, 0.18)			
MeiQ™ Active communication	Intervention	5.16(0.87)	5.08(0.92)	5.10(0.93)	$F_{1,95.43}$=0.35, *p*=0.56	$F_{2,121.77}$=0.14, *p*=0.87	$F_{2,121.77}$=0.99, *p*=0.37
	Control	5.16(0.87)	5.28(0.90)	5.18(0.95)			
	Effect size(99% CI)		0.22(-0.09, 0.53)	0.09(-0.24, 0.42)			
MeiQ™ Self-management ability	Intervention	4.69(0.74)	4.80(0.77)	4.80(0.77)	$F_{1,100.52}$=0.37, *p*=0.54	$F_{2,131.50}$=0.52, *p*=0.60	$F_{2,131.50}$=0.78, *p*=0.46
	Control	4.85(0.74)	4.82(0.76)	4.87(0.79)			
	Effect size(99% CI)		0.02(-0.24, 0.29)	0.09(-0.19, 0.36)			

SD – Standard Deviation; MLM – Multi-Level Modelling; CI Confidence Interval; HeiQ™ – Health Education Impact Questionnaire; MeiQ™ – Medication Education Impact Questionnaire; f/u – follow-up

8.6.1.2 Confidence in ability to self-monitor, communicate with healthcare professionals and self-manage

There were no statistically significant interaction effects between group and time on any of the HeiQ™ or MeiQ™ subscales in either the whole sample (Table 8.11) or for complete cases only. The effect sizes at both follow-ups were small.

8.6.2 Illness and treatment beliefs

8.6.2.1 Illness beliefs

There were no statistically significant interaction effects between group and time on any of the IPQ-R subscales (Table 8.12). All effect sizes were small at both follow-ups, except IPQ-R illness identity at final follow-up, which suggested that the difference between the intervention and control group was medium, with control group participants identifying more symptoms associated with their arthritis than those in the intervention group.

8.6.2.2 Treatment beliefs

There were no statistically significant interaction effects between group and time on BMQ specific necessity or concern subscale or perceptions of treatment burden (Table 8.12). All effect sizes were also small at both follow-ups.

8.6.2.3 Knowledge about methotrexate

There was no statistically significant interaction effect between group and time on knowledge about methotrexate ($F_{1,76.84}$=1.67, p=0.20) (Table 8.13) the effect size was also small at both follow-ups.

Table 8.12. Descriptive statistics adjusted mean(SD) and MLM analysis for illness beliefs (n=100)

Variable	Trial arm	Baseline	First f/u	Final f/u	Group	Time	Time*Group
IPQ-R Identity	Intervention	5.23(2.40)	4.60(2.58)	4.28(2.56)	$F_{1,92.81}$=1.21, p=0.28	$F_{2,140.83}$=1.77, p=0.17	$F_{2,140.83}$=2.75, p=0.07
	Control	5.15(2.40)	5.01(2.51)	5.32(2.63)			
	Effect size(99% CI)		0.16(-0.70, 1.02)	0.40(-0.53, 1.32)			
IPQ-R Consequences	Intervention	19.54(4.99)	18.63(5.17)	18.45(5.15)	$F_{1,98.58}$=1.32, p=0.25	$F_{2,113.04}$=4.06, p=0.02	$F_{2,113.04}$=0.25, p=0.78
	Control	20.40(5.04)	19.95(5.13)	19.56(5.28)			
	Effect size(99% CI)		0.25(-1.53, 2.04)	0.21(-1.64, 2.06)			
IPQ-R Personal Control	Intervention	20.78(4.34)	21.44(4.52)	21.45(4.53)	$F_{1,97.10}$=0.04, p=0.84	$F_{2,116.26}$=2.04, p=0.14	$F_{2,116.26}$=0.04, p=0.96
	Control	21.00(4.42)	21.51(4.57)	21.67(4.64)			
	Effect size(99% CI)		0.01(-1.54, 1.57)	0.05(-1.57, 1.67)			
IPQ-R Treatment Control	Intervention	15.61(2.28)	15.56(2.43)	16.05(2.43)	$F_{1,94.26}$=0.13, p=0.72	$F_{2,117.43}$=1.03, p=0.36	$F_{2,117.43}$=1.95, p=0.15
	Control	15.98(2.25)	15.43(2.40)	15.39(2.51)			
	Effect size(99% CI)		0.05(-0.76, 0.87)	0.26(-0.61, 1.13)			
IPQ-R Coherence	Intervention	18.40(4.22)	19.58(4.46)	19.42(4.46)	$F_{1,97.10}$=0.28, p=0.60	$F_{2,112.73}$=2.76, p=0.03	$F_{2,112.73}$=2.76, p=0.07
	Control	18.94(4.20)	19.27(4.34)	17.97(4.58)			
	Effect size(99% CI)		0.07(-1.44, 1.58)	0.32(-1.28, 1.92)			

SD – Standard Deviation; MLM – Multi-Level Modelling; CI Confidence Interval; IPQ-R – Illness Perceptions Questionnaire-Revised; f/u – follow-up

Table 8.13. Descriptive statistics mean(SD) and MLM analysis for treatment beliefs and knowledge (n=100)

Variable	Trial arm	Baseline	First f/u	Final f/u	Group	Time	Time*Group
BMQ Specific Necessity	Intervention	16.13(2.99)	16.56 (3.17)	16.68(3.21)	$F_{1,99.28}$=1.56, p=0.21	$F_{2,113.51}$=0.77, p=0.47	$F_{2,113.51}$=1.19, p=0.31
	Control	17.22(3.05)	17.37(3.14)	16.80(3.33)			
	Effect size(99% CI)		0.26(0.81, 1.32)	0.03(-1.10, 1.17)			
BMQ Specific Concern	Intervention	12.14(3.05)	12.01(3.22)	11.47(3.26)	$F_{1,99.08}$=0.92, p=0.34	$F_{2,109.62}$=1.56, p=0.22	$F_{2,109.62}$=0.14, p=0.87
	Control	12.56(3.08)	12.47(3.21)	12.18(3.37)			
	Effect size(99% CI)		0.14(-0.95, 1.23)	0.21(-0.94, 1.37)			
Treatment burden	Intervention	2.25(1.02)	1.97(1.11)	2.12(1.08)	$F_{1,95.53}$=0.46, p=0.50	$F_{2,144.13}$=0.71, p=0.50	$F_{2,144.13}$=1.91, p=0.15
	Control	1.98(1.03)	2.06(1.06)	1.92(1.11)			
	Effect size(99% CI)		0.09(-0.28, 0.45)	0.17(-0.22, 0.57)			
Knowledge about methotrexate	Intervention	18.49 (5.29)	19.86(5.47)	20.45(5.53)	$F_{1,96.35}$=2.10, p=0.15	$F_{2,95.06}$=5.13, p=0.01	$F_{2,95.06}$=1.28, p=0.28
	Control	17.78 (5.50)	17.98(5.63)	18.65(5.81)			
	Effect size(99% CI)		0.34(-1.56, 2.23)	0.32(-1.64, 2.27)			

SD – Standard Deviation; MLM – Multi-Level Modelling; CI Confidence Interval; BMQ – Beliefs about Medicines Questionnaire; f/u – follow-up

8.7 WHAT WERE THE MECHANISMS OF EFFECTIVENESS?

8.7.1 Mediators of intervention effectiveness

It was hypothesised that changes in the clinical and psychosocial variables would mediate the relationship between trial arm and healthcare utilisation, and trial arm and quality of life. The psychosocial outcomes variables which were identified as possible mediators were mood and quality of life (for healthcare utilisation only). The potential psychosocial processes which were identified as possible mediators were self-efficacy, illness and treatment beliefs and knowledge.

As described in section 5.11.10.1 (page 225) residualised change scores were computed for each process variable and mediation analysis was performed using these changes scores and the PROCESS macro designed by Hayes (2013). This macro tests the statistical significance of the indirect effect c', which is a product of coefficients of path a and b (Figure 8.6). The following analysis includes only those participants with complete cases (n=79). Multiply imputed datasets cannot be used with this macro and hence participants with missing data on either the outcome or mediator are not included in the analysis. Traditionally mediation analysis would only be recommended if the intervention was found to have an effect the study outcome. More recently, however, it has been argued this is no longer necessary for mediation to be possible (Hayes, 2009; Collins, Graham, & Flaherty, 1998). Therefore, mediation analysis was performed on healthcare utilisation and quality of life as DVs.

Changes in the clinical, psychosocial process and outcome variables from baseline to final follow-up did not mediate the relationship between trial arm and healthcare utilisation, for CNS, GP, rheumatologist or overall visits as the a bias-corrected bootstrap CI for the indirect effect based on 10,000 bootstrap samples contained zero.

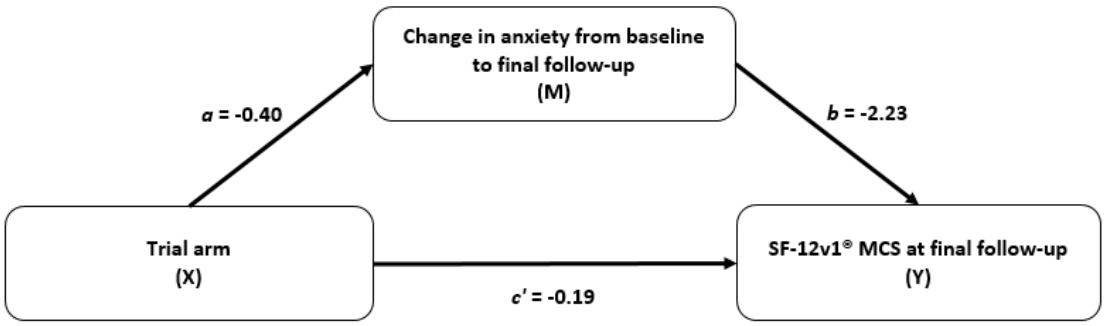


Figure 8.6. Simple mediation model for anxiety in the form of a statistical diagram

The only significant mediator of the relationship between trial arm and quality of life was change in anxiety. From a simple mediation analysis conducted using ordinary least squares path analysis, trial arm indirectly influenced mental health quality of life at final follow-up through its effect on changes in anxiety over the trial period. As can be seen in Figure 8.6 and Table 8.14, participants in the intervention arm experienced greater decline in anxiety than those in the control group (a=-0.40), and participants who experienced greater decline in anxiety over the trial period also experienced increased quality of life at final follow-up. A bias-correct bootstrap CI for the indirect effect (ab=0.89) based on 10,000 bootstrap samples was entirely above zero (0.12 to 2.52). There was no evidence that trial arm influenced mental health quality of life independent of its effects on anxiety (c'=-0.19, *p*=0.90).

Table 8.14. Model coefficients for anxiety

		Consequent						
		M (anxiety)				**Y (SF-12v1® MCS)**		
Antecedent		**Coeff.**	***SE***	***p***		**Coeff.**	***SE***	***p***
X (trial arm)	*a*	-0.40	0.22	0.07	*c'*	-0.19	1.44	0.90
M (anxiety)		-	-	-	*b*	-2.23	0.73	0.003
Constant	i_1	0.22	0.16	0.19	i_2	30.73	1.05	<0.001
		R^2=0.04				R^2=0.11		
		$F_{1,77}$=3.28, *p*=0.07				$F_{2,76}$=4.85, *p*=0.01		

MCS – Mental Component Score; SE – Standard Error

8.7.2 Moderators of the relationship between intervention and healthcare utilisation

Moderation analysis was performed in order to establish whether any baseline demographic, clinical or psychosocial variables moderated the effect of the intervention on healthcare utilisation or quality of life (Figure 8.7).

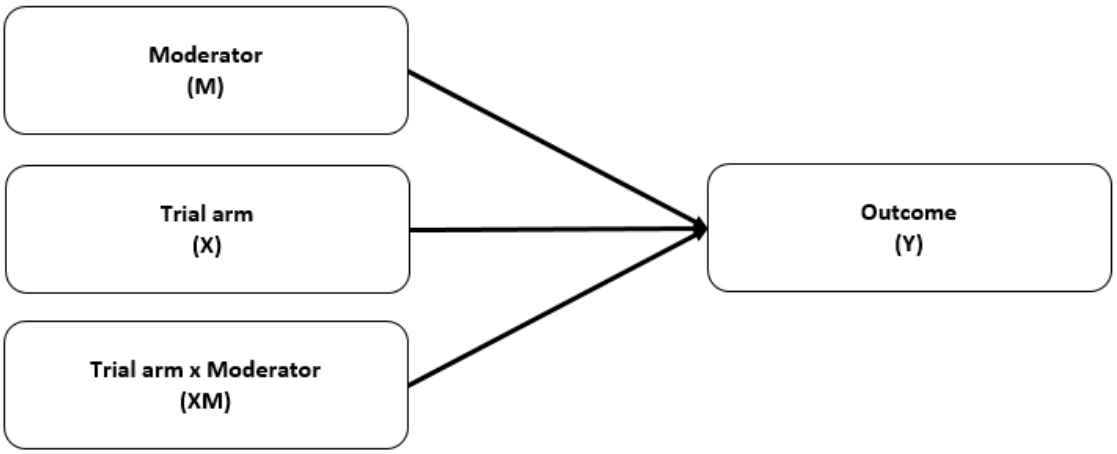


Figure 8.7. Moderation model

8.7.2.1 CNS visits

The SF-12v1.0® MCS (β= 0.10, t=3.03, *p*=0.003, R^2 change=0.07, $F_{1,96}$=9.15) was the only significant moderator of CNS outpatient visits. As SF-12v1.0® MCS increased by one unit, the difference in the number of appointments had with the CNS between the intervention and control group increased by 0.10 units. The Johnson-Neyman technique indicated that there was a conditional effect of trial arm on healthcare usage only when participants scored below 34.64 on the SF-12v1.0® MCS (β=-0.43, t=-1.99, *p*=0.05). Specifically, when mean SF-12v1.0® MCS scores were below 34.64 at baseline, the intervention decreased the number of visits to the CNS, as participants with a SF-12v1.0® MCS of less than 34.64 at the start of the trial assigned to the intervention group made fewer visits to their CNS over the trial period than those in the control group (Figure 8.8).

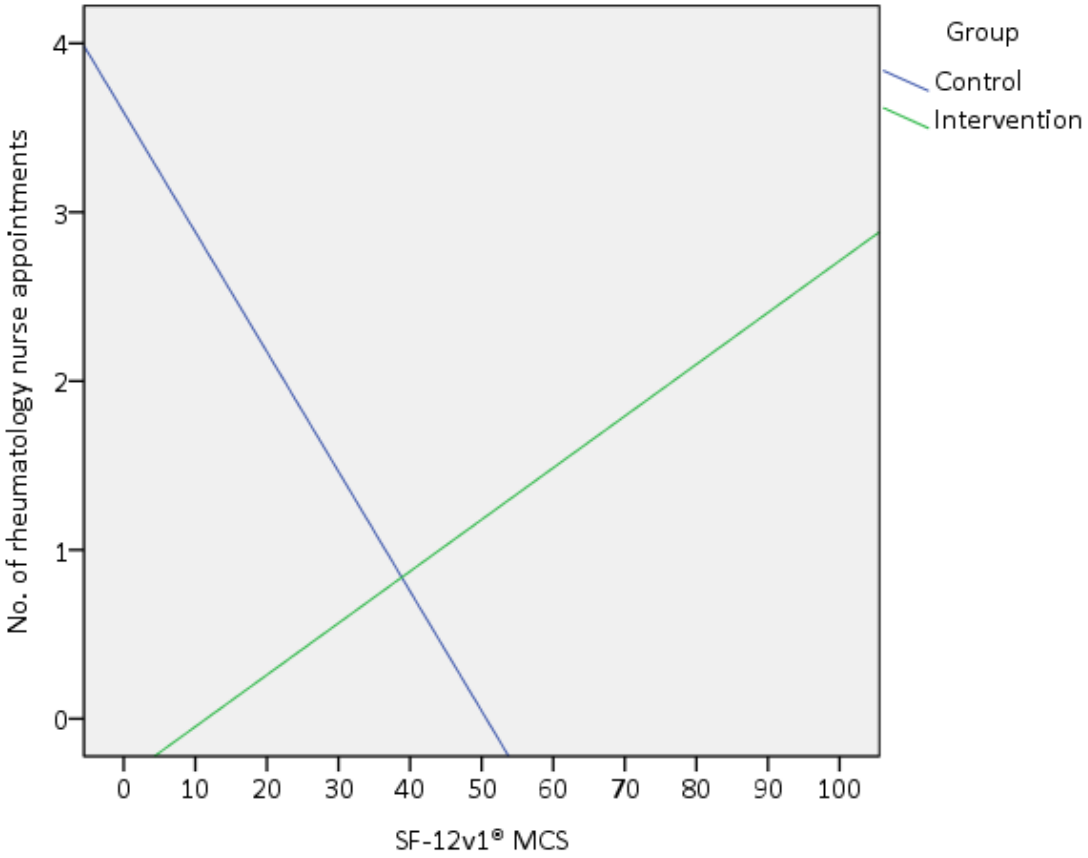


Figure 8.8. Moderating effect of mental health QoL on visits to the CNS

8.7.2.2 Rheumatologist visits

There were no significant moderators of the relationship between trial arm and the number of outpatient visits participants had with their rheumatologist.

8.7.2.3 GP visits

The only significant moderator of self-reported GP visits was gender (β=-1.28, t=-2.84, p=0.01, R^2 change=0.07, $F_{1,96}$=8.08). Probing of the significant moderating effect of gender (Figure 8.9) indicated that for female participants the relationship between intervention arm and arthritis-related GP appointments was negative and statistically significant (β=-0.97, t=-3.24, p=0.002) but was positive and non-significant for male participants (β=0.32, t=0.93, p=0.35), meaning that females randomised to the control group attended more visits than females randomised to the intervention group. There were no differences between trial arms for male participants.

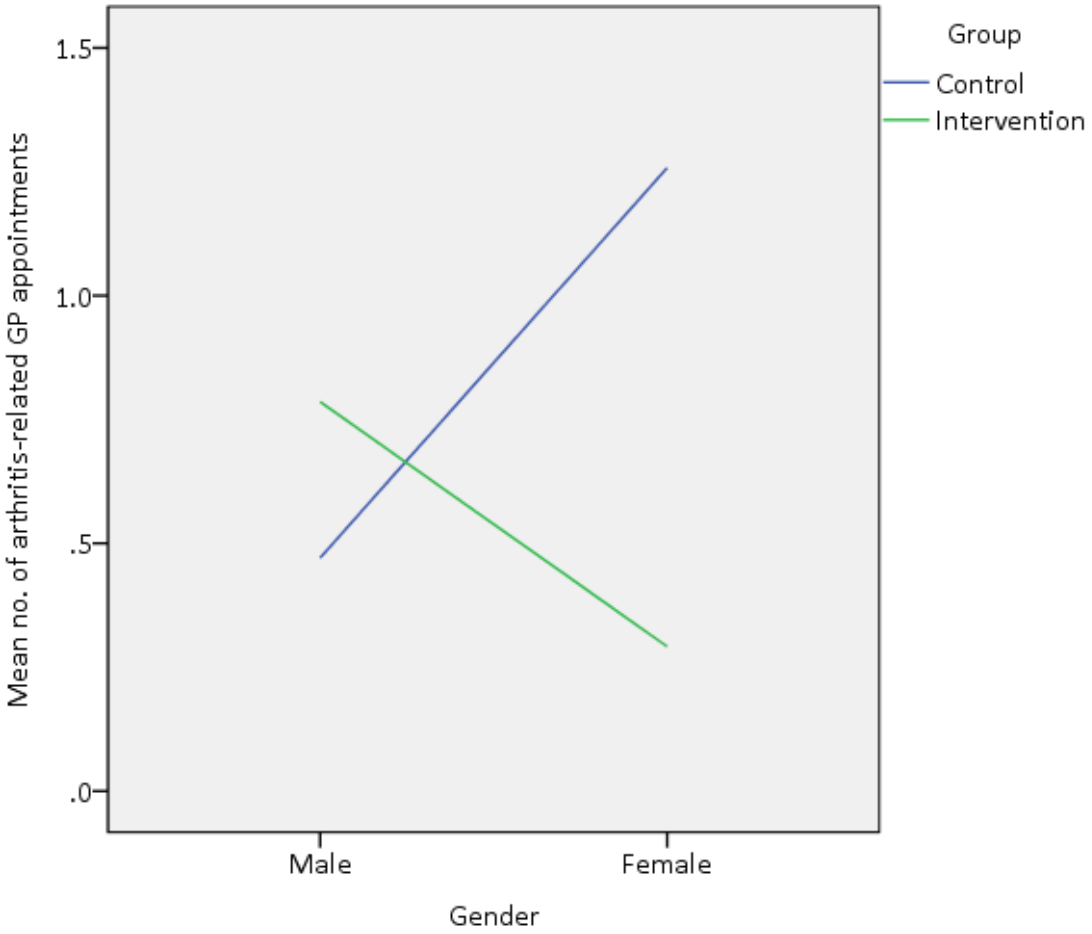


Figure 8.9. Moderating effect of gender on visits to the GP

8.7.2.4 Overall healthcare utilisation

The only significant moderator of overall healthcare utilisation was baseline haemoglobin levels (β=0.82, t=2.55, *p*=0.01, R^2 change=0.05, $F_{1,96}$=6.48). As haemoglobin levels increased by one unit, the difference in overall healthcare utilisation between the intervention and control group increased by 0.82 units. The Johnson-Neyman technique indicated that there was a conditional effect of trial arm on healthcare usage when participants haemoglobin levels were below 14.26 (β=-0.91, t=-1.99, *p*=0.05). Specifically, when mean haemoglobin levels at baseline were lower than 14.26 the intervention decreased the number of overall healthcare visits, as participants with haemoglobin of less than 14.26 at the start of the trial assigned to the intervention group made less visits to healthcare professionals over the trial period than those in the control group (Figure 8.10).

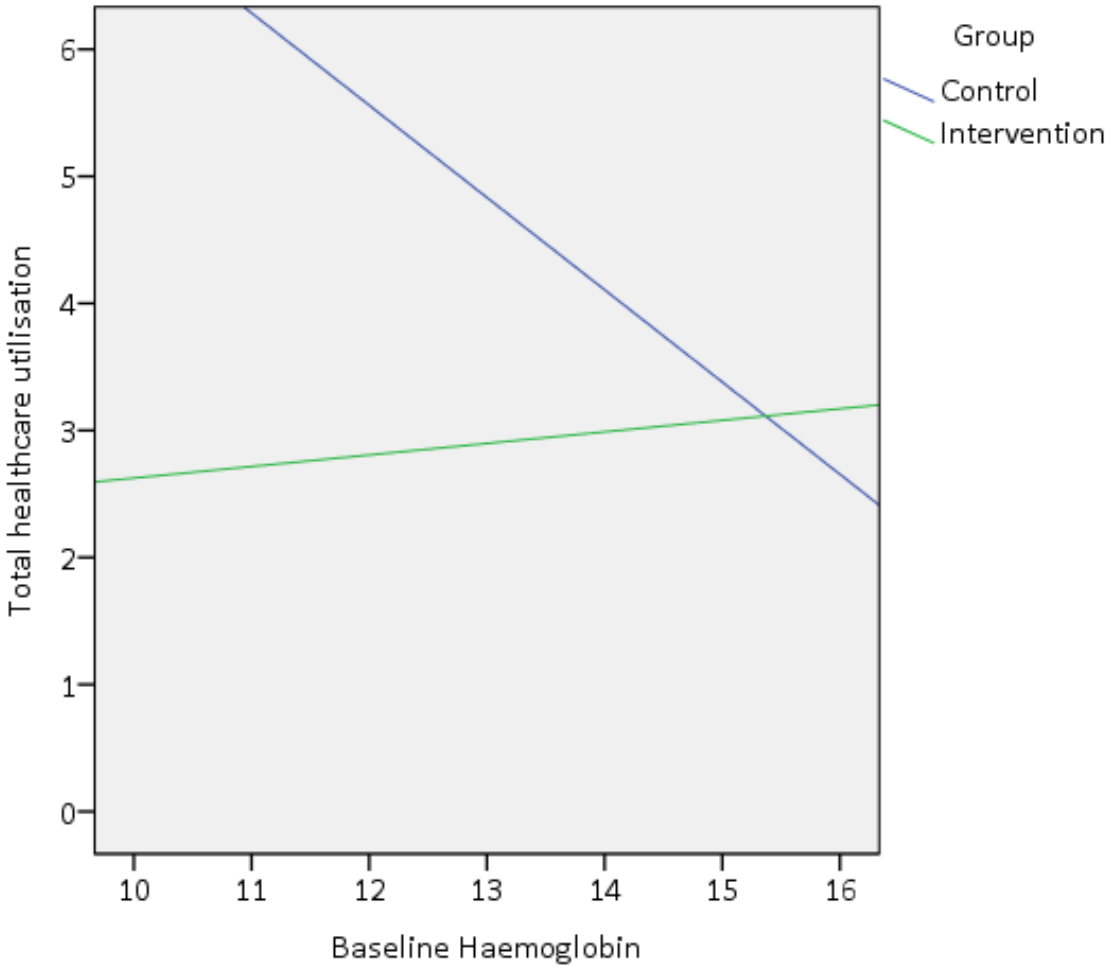


Figure 8.10. Moderating effect of haemoglobin on overall healthcare utilisation

8.7.2.5 Quality of life

The only significant moderator of the SF-12v1® MCS was knowledge about methotrexate (β=-0.64, t=-2.15, p=0.04, R^2 change=0.06, $F_{1,75}$=4.63). As knowledge about methotrexate increased by one unit, the difference in SF-12v1® MCS between the intervention and control group decreased by 0.64 units. The Johnson-Neyman technique indicated that there was a conditional effect of trial arm on SF-12v1® MCS when participants knowledge about methotrexate was <10.88 (β=5.22, t=2.65, p=0.05). Specifically, when the mean knowledge score was less than 10.88 at baseline the intervention increased SF-12v1® MCS. As participants with scores on less than 10.88 on knowledge of methotrexate assigned to the intervention group had higher SF-12v1® MCS at final follow-up than those in the control group. Figure 8.11 does not necessarily reflect this, which could be attributed to the fact that 91.14% of the sample scored over 10.88 on the scale. Therefore, this region of significance may be less

robust as there are not enough participants at this end of the scale to be confident of this claim (Hayes, 2013).

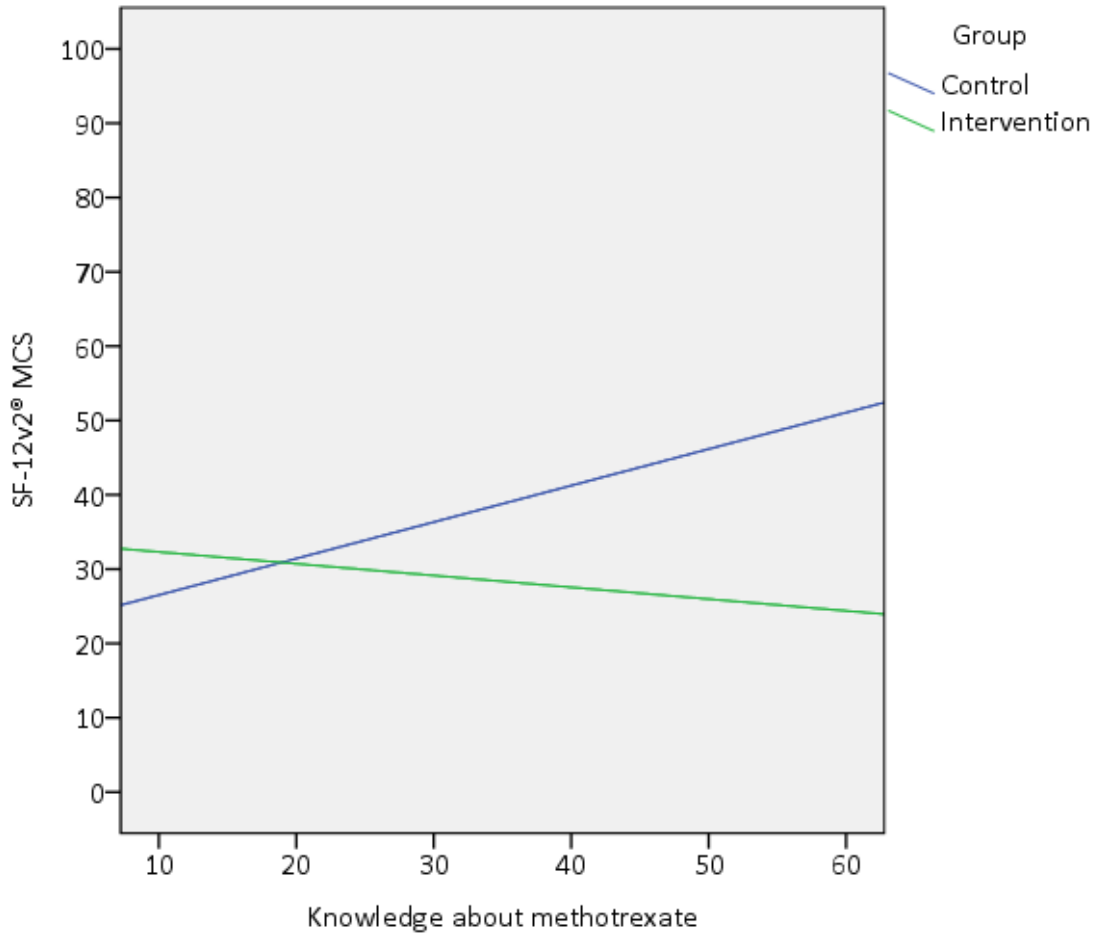


Figure 8.11. Moderating effect of knowledge on mental health-related QoL

The MeiQ™ active communication construct (β=5.21, t=2.06, *p*=0.04, R^2 change=0.05, $F_{1,96}$=4.23) and baseline ESR (β=0.38, t=2.23, *p*=0.03, R^2 change=0.06, $F_{1,75}$=4.96) were the only significant moderators of SF-12v1® PCS. As confidence in communicating with the rheumatology team increased by one unit at baseline, the difference in SF-12v1® PCS between the intervention and control group increased by 5.21 units at final follow-up. As ESR increased by one unit at baseline, the difference in SF-12v1® PCS between the intervention and control group increased by 0.38 units at final follow-up.

The Johnson-Neyman technique indicated that there was a conditional effect of trial arm on SF-12v1® PCS when scores on the MeiQ™ active communication construct were <4.14 (β=-6.88, t=-1.99, *p*=0.05). Specifically, when the mean scores on the

MeiQ™ active communication construct were less than 4.14 at baseline the intervention decreased SF-12v1® PCS, as participants with scores on less than 4.14 on the MeiQ™ active communication construct assigned to the intervention group had lower SF-12v1® PCS at final follow-up than those in the control group (Figure 8.12).

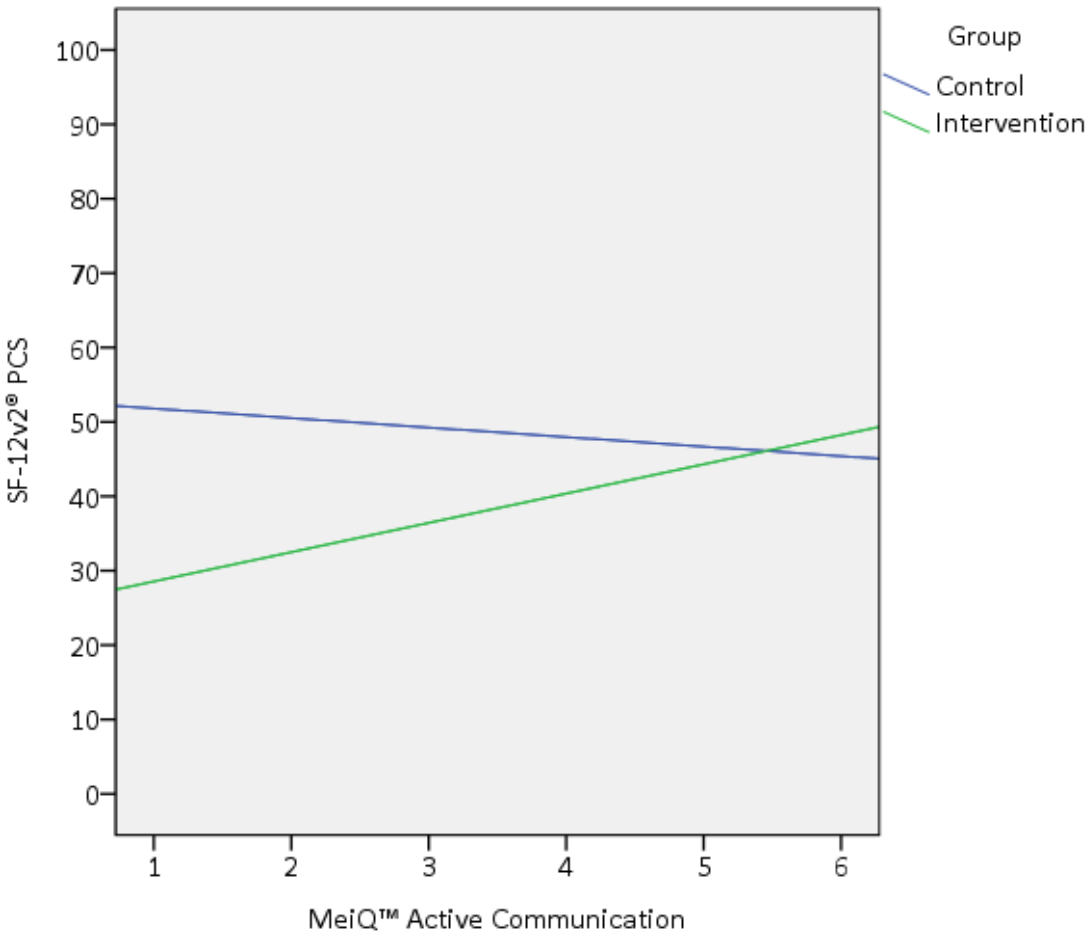


Figure 8.12. Moderating effect of MeiQ™ Active Communication on physical health-related QoL

Probing of the interaction effect for baseline ESR, however, revealed no statistically significant transition points within the observed range of ESR levels. Figure 8.13 does, however, suggest that for those participants with higher ESR levels at the start of the trial allocation to the intervention group is associated with increased SF-12v1® PCS scores at final follow-up than those in the control group.

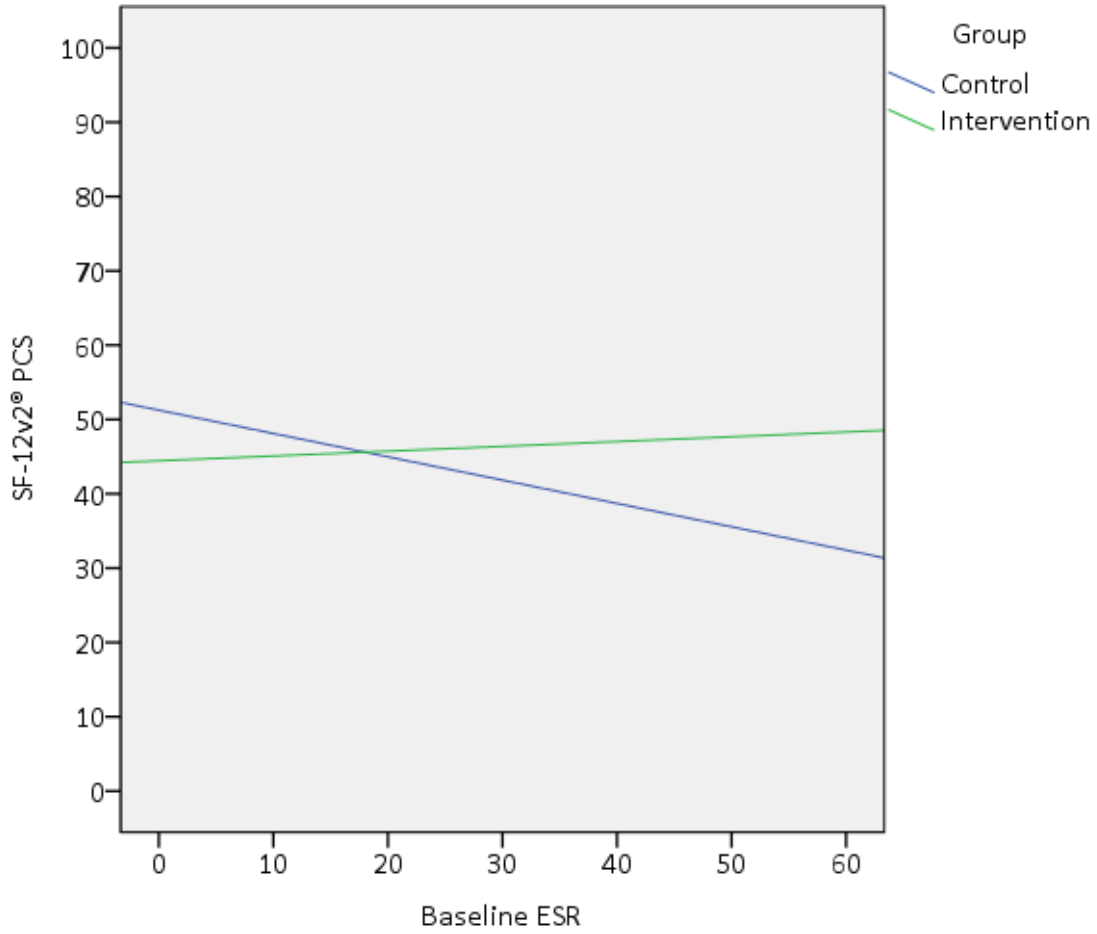


Figure 8.13. Moderating effect of knowledge on physical health-related QoL

CHAPTER 9 - INTERVENTION EFFECTIVENESS DISCUSSION

9.1 PROLOGUE

The aims of this RCT were to establish whether a patient-initiated and self-monitoring service for patients with RA or PsA on methotrexate had an impact on healthcare utilisation, psychosocial and clinical outcomes in comparison to usual care. An additional aim was to explore the mechanisms through which the intervention affected healthcare utilization and quality of life and the baseline variables which may have altered the strength of these relationships.

This chapter will discuss the results presented in Chapter 8 within the context of these aims, along with the strengths and weaknesses of the study. In considering the findings of this trial it is important to locate the intervention within the current literature. The current intervention included a number of behaviour change techniques, focusing primarily on patients self-monitoring clinical information and then using this as part of a patient-initiated service. This type of intervention can, therefore, be placed under the umbrella of self-management, in that it enabled patients to manage the consequences of living with a long-term condition (i.e. accessing care) and incorporated patients monitoring their condition (Barlow *et al.,* 2002). Therefore, comparisons of the effectiveness of this trial will be made in relation to chronic disease and arthritis self-management programmes, interventions in self-monitoring which were reviewed in Chapter 3 and other rheumatology based patient-initiated follow-up services, which were presented in section 2.5.6.1 (page 82). As the current study is the first to combine these approaches for patients with arthritis it is not strictly comparable with many previous disease management programmes but this approach provides an understanding of how this intervention performs in relation to other similar and related programmes.

9.2 INTERVENTION EFFECTIVENESS AND MECHANISMS OF CHANGE

9.2.1 Healthcare utilisation

The primary outcome within this trial was healthcare utilisation, assessed in relation to overall arthritis-related visits in both primary and secondary care, as well individual

appointments with the CNS, rheumatologist and GP. The intervention had a significant effect on outpatient visits to the CNS resulting in fewer visits made by the intervention group compared to usual care, but had no effect on visits to the rheumatologist or GP.

The intervention led to 55% fewer visits to the CNS compared to those in the control group and hence a 55% saving in regards to the cost of delivering rheumatology nursing care. This suggests that a large proportion of follow-up appointments in the CNS-led DMARD monitoring clinic were made habitually and may, therefore, not be entirely necessary, thus reflecting the findings of Hehir *et al.,* (2001), which found that 42% of all visits to rheumatologist were deemed unnecessary.

A majority of participants in the intervention group had either no appointments or just one appointment to see their CNS over the course of the trial period, whilst control group participants were more likely to have either one or two scheduled visits. Whilst the current trial focused on reducing the number of follow-up visits scheduled within the nurse-led DMARD monitoring clinic all other trials of patient-initiated services in arthritis have sought to reduce visits to the rheumatologist (Hewlett *et al.,* 2000; Hewlett *et al.,* 2005b; Sands & Adams, 2009). It is, therefore, logical to compare the primary outcome in this trial with the primary outcome in these other evaluations rather than a comparing like for like visits.

The 55% reduction in follow-up visits to the CNS found within this trial, is greater than the 43.8% difference in consultant reviews found by Hewlett *et al.,* (2000) 2 years after implementing their patient-initiated outpatient follow-up service and is considerably greater than the 38% difference found after 6 years of running the same service (Hewlett *et al.,* 2005b). This higher rate could be attributed to the shorter follow-up found within the current trial and hence a trial with a longer follow-up would be needed in order to compare results at the same time-point. The mean number of visits to the CNS in this trial per participant indicated that participants in the control group visited their CNS 2.37 times more than intervention participants. This reflects the mean number of visits to the consultant found within the trials by Hewlett *et al.,* (2000) and Sands and Adams (2009).

The intervention did not have any effect on the number of visits patients had with their rheumatologist and hence there were no significant cost savings in relation to these consultations. In the current trial these visits were measured to ensure that patients did not redirect their care to other members of the specialist team and also because rheumatologists were not blinded to treatment group it was important to ensure that the rheumatologists themselves did not increase the frequency with which they offered intervention participants appointments. All participants in the intervention group did, however, have between 0 and 4 visits to the rheumatologist whilst the control group had between 0 and 7 visits. So although the median number of appointments was the same, the spread and the mean number of visits per person indicated that more of the intervention group attended less frequently. These effects are akin to the changes in nurse visits in the other trials of patient-initiated services. The trial by Hewlett *et al.,* (2000; 2003b; 2005b) did not measure the effect of the intervention on visits to the rheumatology nurse. Sands and Adams (2009) did, however, find that the mean number of times patients attended the specialist nurse over a 12 month period was similar in the conventional and patient-initiated group. The current thesis, therefore, supports these findings and offers evidence for the potential for formal self-monitoring to reduce outpatient visits which was not demonstrated in the overview reported in Chapter 3.

Although there were no statistically significant effects on arthritis-related GP visits and hence no economic savings, the intervention did lead to 39% fewer appointments with the GP than usual care. Despite this large reduction in GP attendance, the study was not powered to find an effect on this variable. Again, the aim of the study was not to reduce visits to the GP, these were measured to ensure that patients who were not scheduled to visit their CNS did not seek additional care from community services. This does not appear to be the case and in fact participants in the control group saw their GP about their arthritis almost twice as often as those in the intervention group; suggesting that intervention participants felt better able to manage their arthritis themselves rather than seek help in primary care. The reduction in arthritis-related GP visits in the current trial could be associated with patients feeling more empowered to manage their problems for longer at home as they know rapid access to the CNS was available if necessary, as suggested in a similar service by Pope *et al.,* (2005). Similar

findings are reported in the trial by Hewlett and colleagues at both 2 (Hewlett *et al.,* 2000) and 6 years (Hewlett *et al.,* 2005b) post implementation, for GP visits to the surgery, GP home visits and practice and district nurse consultations. The systematic review presented in Chapter 3 identified three reviews of self-monitoring that had synthesised the evidence in relation to GP attendance. All three reviews also failed to find any statistically significant differences in scheduled or unscheduled GP visits between usual care and either action planning in COPD or home blood pressure monitoring in hypertension (Turnock *et al.,* 2005; Jaana *et al.,* 2007; AbuDagga *et al.,* 2010).

The lack of any significant indirect effect for changes in clinical or psychosocial variables between trial arm and healthcare utilisation in the mediation analysis indicated that the trial had a direct effect on healthcare utilisation, rather than via another mechanism. Hence simply by removing all scheduled appointments and delivering a needs based service, unnecessary appointments can be eliminated. There were, however, moderators of this relationship including gender, mental health quality of life and baseline haemoglobin levels.

Gender moderated the relationship between trial arm and the number of arthritis-related GP visits with females randomised to the intervention group attending for fewer visits than females in the control group. Men randomised to the intervention group, however, attended the GP as much as men in the control group. Evidence suggests that men are less likely to attend the GP than women generally (Jatrana & Crampton, 2010). An intervention of this nature was unable to alter the frequency with which men attend.

Baseline haemoglobin levels also moderated the relationship between trial arm and overall arthritis-related healthcare utilisation. Specifically, participants with a haemoglobin of less than 14.26 at the start of the trial and assigned to the intervention group made fewer visits over the trial period than those in the control group. This result is difficult to interpret as the advisable range for haemoglobin for a patient with arthritis was between 12 and 17, with a drop of more than one a trigger for contact. Mental health quality of life moderated the relationship between trial arm and CNS

visits. Specifically participants with a mental health quality of life score on the SF-12© of less than 34.64 at the start of the trial and assigned to the intervention group made fewer visits to their CNS over the trial period than those in the control group. Hence poorer quality of life at baseline was associated with fewer visits over the trial period in the intervention compared to control group.

These finding could raise possible concerns about patients experiencing anaemia or with poor mental health quality of life taking part in a self-monitoring and patient-initiated service and attending fewer visits to the CNS. Since nurse-led consultations not only treat the clinical aspects of arthritis but also provide a more holistic approach to patient care (Goh *et al.,* 2006) these appointments could provide an opportunity to address issues of physical as well as mental well-being. It is important to acknowledge, however, that mental health quality of life and haemoglobin did not change significantly over the trial period either within groups or between groups suggesting that not seeing the CNS as often did not have a detrimental impact on either of these variables.

It is also worth noting that for every five telephone consultations undertaken in the intervention group, two led to a face-to-face outpatient appointment with the CNS. This 40% conversion rate is substantially higher than in the activity analysis of a telephone helpline by McCabe *et al.,* (2000), in which 2.9% of calls resulted in a discussion with a rheumatologist. It is unclear, however, if this "discussion" was a face-to-face outpatient appointment or another telephone consultation, or if the helpline was in addition to usual care or an alternative to follow-up, as within the current trial.

9.2.2 Healthcare costs

In order to make equitable comparisons between the current trial and the trial run by Hewlett *et al.,* (2000), two models of healthcare costs were analysed. One which included the additional costs of running the telephone consultations, as per Department of Health recommendations (Health & Social Care Information Centre, 2014) and one which did not include these costs, akin to the model assessed by Hewlett *et al.,* (2000).

The comparative model to that of Hewlett *et al.,* (2000) indicated that a self-monitoring and patient-initiated follow-up service was between 10.88% and 13.88% *cheaper* to run than the control group, depending on whether the estimate was based on the lower, upper or average Department of Health figures (Department of Health, 2011a; Department of Health, 2013a). This was despite the additional costs of running the training session, the cost for the patient to travel to the hospital to attend, and the associated costs of running the telephone consultations for those patients in need. This financial gain, however, was not statistically significant. The overall cost of the service for 52 patients over a 256 day period (the length of the trial) was between £38,645 and £59,315, resulting in an average cost between £512.17 and £650.15 per patient. These figures are substantially higher than those reported by Hewlett *et al.,* (2000) which were £208 per patient for running the service over a 12 month period. Although Hewlett *et al.,* (2000) did not include outpatient visits to the CNS, they did include other allied health professionals appointments including the occupational therapist, physiotherapist, orthotist, podiatrists and orthopaedic surgeon. In addition a comparison of unit costs since this 2000 publication indicates that the average cost of a hospital doctor has almost doubled from £70 in 2000 to £133 in 2012-13. It is, however, unclear if the figure of £70 in the Hewlett *et al.,* (2000) trial was specific to a rheumatologist or general hospital consultant. The unit cost for a GP visit has also quadrupled from £10 in 2000 to £39.50 in 2012-13. The cost of hospital transport has, however, decreased from £33.59 to £18. It is, therefore, difficult to understand whether these costs are comparable considering the differing times periods.

The economic analysis conducted by Hewlett *et al.,* (2000) costed 0% of the CNS time for running the nurse helpline. The cost of running a nurse helpline can be substantial depending on the size of the population. The NHS Data Model and Dictionary (Health & Social Care Information Centre, 2014) which provides a reference point for assured information standards to support health care activities states that a telephone consultation which directly supports diagnosis and care planning and replaces either a face-to-face outpatient attendance with the rheumatologist or nurse should be costed as such. Details of the telephone consultation should also be retained in the patient's records. Telephone contact solely for informing patients of results is excluded from this definition. It is unclear in the other trials of patient-initiated follow-up services

whether the telephone contact between the nurse and patient resulted in any care planning and hence should be costed as such. In the current trial the telephone consultations provided the CNS with an opportunity to assess the needs of the patient. In many cases the consultation was triggered by an abnormal blood test result which, after discussion with the CNS, required a "watch and wait" approach to see if the test returned to normal at the next blood test. In this case the consultation did not lead to any change in care and, therefore, would not fulfil the above criteria. The outcome of these telephone consultations, therefore, ranged in their complexity from this "watch and wait" approach to the booking of an outpatient appointment. It was, however, important to consider how the expenditure on these telephone consultations would impact on the overall cost-effectiveness of the service. Inclusion of the telephone consultations meant that the self-monitoring and patient-initiated follow-up service was between 29.31% and 51.88% more ***expensive*** per patient than usual care and this difference was statistically significant at the lower, upper and average unit cost. Whereas without these costs the service was between 10.88% and 13.88% ***cheaper*** to run than the control group.

Over the 39 months the trial was running, 231 telephone consultations took place for 52 patients. That is 71 per year or 1-2 calls per week, just short of the 2.4 average calls per week in the Hewlett *et al.,* (2000) trial but is almost double that reported by Primdahl *et al.,* (2014). If this service was scaled up to all 450 DMARD patients at UCLH this would equate to approximately 12 telephone consultations per week. There are currently three CNSs running this clinic and, therefore, these 12 calls could be managed within the current roles of these existing CNSs (4 per CNS) and hence would not necessarily need to be costed in as an additional expenditure.

Analyses of the cost-effectiveness for self-monitoring across other long-term conditions have also found similar effects. In a cost-effectiveness review of different models of care for people on long-term anticoagulation therapy Connock *et al.,* (2007) found seven studies. Only one was in the UK and this study found that patient self-management was more expensive than current routine care (£417 versus £122 per patient-year). Similar self-monitoring of peak flow in asthma was found to have mixed economic effects with some interventions demonstrating cost savings and others that

self-monitoring was more expensive to run than usual care or a less intensive intervention (Willems, Joore, Hendriks, Wouters, & Severens, 2006).

These findings suggest that more work is required to establish the cost effectiveness of these types of interventions and a wider debate needs to take place about the cost of running nurse helplines in secondary care. Due to problems with data collection information was not available on the exact content of these telephone consultations but it is likely that many did not lead to any changes in care planning. There does, however, need to be capacity within system to take on these additional tasks. As highlighted in the survey by the Royal College of Nurse Rheumatology Forum (2009) many rheumatology nurses are being asked to change their usual work pattern or take on extra work which nurses themselves have described as "increased activity without increased resources". Therefore, consideration needs to be taken when implementing interventions of this nature on the work load of current staff and the real cost of resourcing such services.

It is important to acknowledge that the number of contacts patients in the control group had with the nurse helpline was not recorded due to problems with data collection. At the time of the trial usual care did not require notes to be made about telephone contact despite recommendations from the Royal College of Nursing (2006). It was likely that many of the control group participants also contacted the nurse via the helpline and, therefore, these should have also been included in the cost-effectiveness analysis. This may have reduced the financial loss of providing the new service. Primdahl *et al.,* (2014) did collect this data and found that there were no significant differences in the number of telephone consultations which were conducted in the shared care compared to rheumatologist-led group. This suggests that if the data were collected for the control group in the current trial the number of telephone consultations may have been the same and hence the service would more likely to have resulted in a cost saving.

9.2.3 Clinical outcomes

It was important to ensure that the intervention did not lead to any deterioration in clinical outcomes. Analyses of the standardized assessments indicated that a majority

of patients did not respond according to the disease-specific treatment response criteria and analyses of blood tests indicated no interaction effects between trial arm and time, hence confirming that the intervention did not have any detrimental effect on the clinical biomarkers of the diseases, or disease activity.

The longitudinal analysis also confirmed no significant differences in pain, fatigue or functional disability between the intervention and control group over time. For comparison at both the 1 and 2 year follow-up Primdahl *et al.,* (2012; 2014) found that there was no difference in DAS28-CRP, functional disability, pain, fatigue or the odds of having an out-of-range blood test, between a shared care service and rheumatologist-led follow-up for patients with RA. Similarly, Hewlett *et al.,* (2000) found no significant difference in change in disability, disease activity, CRP and haemoglobin from 0-24 months post implementation, but did find that the shared care patients experienced significantly less pain than those in the control group at 24 months and increase in pain was also significantly less in the shared care group (Hewlett *et al.,* 2000). At 4 years post implementation there were again no significant differences between the intervention and control group on any of these clinical outcomes except levels of pain which increased in the patient-initiated service and decreased in the control group from 24-48 months, this difference was significant but changes in pain from 0-48 months were not (Kirwan *et al.,* 2003b). At 6 years post intervention there were no significant differences between the two arms on any clinical variables including pain (Hewlett *et al.,* 2005b). Although these findings are similar, care must be taken in extrapolating results from a short intervention and monitoring procedure as found in this trial to the larger time scales of past research.

The evidence from Chapter 3 suggested that self-monitoring of blood tests leads to significant reductions in mortality and thromboembolic events for patients on anti-coagulation therapy and significant reductions in HbA1c in diabetes. Symptom monitoring in heart failure also led to a significant reduction in mortality and blood pressure for those with hypertension. The primary aim of a majority of the primary research studies in Chapter 3 were to improve clinical well-being whereas the primary aim of the current study was to maintain clinical status whilst at the same time reducing healthcare usage. The failure of the current study to improve clinical well-

being is, therefore, not unexpected particularly given the short follow-up and the distal relationship between observing an abnormal symptom, side effect or blood test results, a change in treatment and its impact upon clinical well-being (i.e. the effect for example of SMBG on HbA1c is likely to be more immediate).

In the current trial participants in the intervention group attended more frequently for their blood tests than control group participants. For those in the intervention group this was within the 4-6 week range (average = 5.62 weeks) advised for DMARD monitoring, but was on average every 6.8 weeks for control group participants. Adherence to DMARD monitoring has rarely been reported in the literature. A conference abstract published by Zakout, Pugh and Healey (2009) found that of 100 consecutive rheumatology outpatients 72% were 100% adherent with their DMARD blood monitoring over a 2 month period, 14% were between 80-100% compliant, 11% 50-80% and 3% less than 50% adherent using BSR guidelines for monitoring individual DMARDs. Zakout *et al.,* (2009) found no significant differences between men and women; however, only 50% of patients aged 30-40 achieved 100% adherent compared with 80% in those over 60. Worse adherence was also associated with a longer disease duration. Zakout *et al.,* found that the average level of adherence had improved since 2004 which the authors attributed to the implementation of DMARD education and the supply of pre-filled blood test forms sufficient to allow appropriate monitoring until the patients next visit. Primdahl *et al.,* (2014), however, found that significantly more participants in the shared care group were less than 90% adherent to their blood monitoring schedule than those monitored by a rheumatologist.
Education and the provision of pre-filled blood test forms were strategies which were also employed within the current intervention and could help to explain the more frequent attendance of intervention participants for blood monitoring and the difference in findings reported by Primdahl *et al.,* (2014). The close monitoring of participants in the current trial may also explain these differences. Rather than having a set time in which participants were within the trial, the protocol dictated that intervention and control group participants were in the trial for a minimum of six blood tests. There were two reasons for this; six blood tests were considered a sufficient number in which participants could be deemed as being able to safely self-monitor and if the trial period was time limited, i.e. 6 or 12 months, it could not be guaranteed that

all participants would have the same number of blood tests and hence be given the same opportunities to gain the relevant skills. As a result of this, attendance was monitored more closely which could have affected adherence behaviour. Alternatively taking on the additional responsibility of self-monitoring may have encouraged participants to attend more regularly. All of these hypotheses are speculative and would require further investigations.

9.2.4 Psychosocial outcomes

9.2.4.1 Quality of life

Patient-initiated services are designed to not only to relieve the burden of stable patients in clinic but also empower patients to know more about their condition and take control of their monitoring and treatment. It was, therefore, hypothesized that the intervention group would experience significantly better quality of life post intervention compared to control group participants. This hypothesis was not supported as the study found no significant interaction effects between group and time on either the physical or mental health component scores of the SF-12v1®. The results do, however, confirm that the intervention did not have any detrimental effects on quality of life and thus supports the findings of other evaluations of patient-initiated rheumatology services.

Primdahl *et al.,* (2014) is the only other trial of patient-initiated services in rheumatology to measure quality of life using the SF-12v1®. In comparison to a rheumatologist-led follow-up service Primdahl *et al.,* (2014) also found no significant differences in either mental or physical quality of life at either the one and two year follow-up. The SF-12v1® has been found to be responsive to changes over time and, therefore, a lack of an effect is likely to be due to lack of differences in intervention efficacy (Ware Jr, Kosinski, Turner-Bowker, & Gandeck, 2002). Use of generic measures of quality of life allow for comparisons across chronic conditions, but may fail to capture the specific impact of arthritis and its associated symptoms and may, therefore, not be as sensitive to small, but clinically significant, changes in quality of life over time. A disease specific measure may have, therefore, been more sensitive to any changes and may have been more likely to find an effect for the intervention. Despite this hypothesis however, Sands and Adams (2009) assessed quality of life in

their evaluation of a patient-initiated follow-up service using the disease specific Arthritis Impact Measurement Scales-2 Short Form (AIMS2-SF) (Guillemin *et al.,* 1997) and also found no significant differences between the patient-initiated and conventional follow-up group, although these differences were between the intervention and control group at a single time-point and not over time. Obtaining similar results on both these measures may reinforce the validity of the findings in the current study and could suggest that patient-initiated follow-up services are unlikely to change the quality of life of people with arthritis. It is also possible that quality of life may have failed to capture the granularity of the effects of the intervention and may have been too broad an outcome measure to be affected by the service. It is nevertheless encouraging that an intervention that required patients to pay closer attention to their illness and that led to significant reductions in healthcare utilisation did not have a detrimental effect on quality of life.

The findings are, however, somewhat in contrast to the literature on self-monitoring which tentatively suggested an improvement in quality of life (Chapter 3). Self-monitoring in COPD was associated with clinically significant improvements in quality of life, although again not statistically significant (McLean *et al.,* 2012) and self-management in thrombophilia, which included patients monitoring their INR values and adjusting their dose of anticoagulants have also been linked to enhanced quality of life (Siebenhofer *et al.,* 2004; Connock *et al.,* 2007). In contrast to the present study all three of these systematic reviews included trials in which participants were required to monitor and use this information to adjust their medication regimens. Participants in this trial and in other trials of patient-initiated services in rheumatology do not allow this level of involvement in medication titration and focus on patients using their symptoms and side effects, and in the case of this trial their blood test results to seek medical assistance. This enhanced level of self-monitoring which empowers patients to make decisions about adjusting their treatment may, therefore, be more likely to lead to improvements in quality of life, as opposed to those in which patients are required to seek help and decisions to adjust treatment and care remain with healthcare professionals. This provides support for the conclusions of the overview presented in Chapter 3 that suggested there may be additional benefits to patients using their

monitored data to adjust their own medication, lifestyle and help-seeking behaviours, but these relationships require further exploration.

9.2.4.2 Mood

It was hypothesised that intervention participants would report improved levels of anxiety and depression compared with those in the control group. This hypothesis was not supported in relation to levels of depression or anxiety, demonstrated by the non-significant differences between the intervention and control group participants over time. Both groups did decrease slightly from baseline to follow-up in contrast to the trial by Hewlett *et al.,* (2000; 2005b) which reported slight increases in depression across their 6 year trial period, although again these differences were not statistically significant. It is nevertheless encouraging that an intervention which required patients to pay closer attention to their illness and attend fewer visits to their healthcare team did not have a detrimental effect on levels of depression or anxiety, replicating the results of self-monitoring in diabetes (Simon *et al.,* 2008; O'Kane, Bunting, Copeland, & Coates, 2008).

The intervention in the current study did not directly target depression or anxiety and, therefore, it may have been unrealistic to expect significant improvements in symptoms over the trial. A review of psychological, self-management and educational interventions in diabetes (Steed, Cooke, & Newman, 2003) suggested that in order to improve depression interventions need to clearly aim to address negative mood. Therefore, in order to improve depression the intervention would have needed to incorporate techniques that directly address depression. This could have included relaxation, biofeedback, cognitive–behavioural therapy and stress management which have all been found to improve depression in arthritis (Astin *et al.,* 2002). Baseline levels of depression and anxiety were, however, not indicative of clinical caseness and in fact 85% of sample were within the normal range for depression and 66% anxiety, so it may not have been reasonable to expect a significant change in mood to have occurred.

The descriptive statistics and effect size at final follow-up however, do provide tentative evidence that participants who received the intervention experienced less

anxiety compared to participants in the control group. Whereas levels of anxiety in the control group increased very slightly over time, intervention participants experienced a decrease in anxiety over the trial period. These changes did, however, occur in the context of a mean level of anxiety which was within the normal range. A similarly pattern was found by Hewlett *et al.,* (2000; 2005b) in which anxiety levels remained stable in the patient-initiated service and increased in the control group, although these differences were not statistically significant. Sands and Adams (2009) also measured mood using the HADS but reported a sum score for overall negative mood rather than the individual subscales for anxiety and depression and found no significant difference between the patient-initiated and conventional follow-up service for patients with RA. The study was, however, a comparative pragmatic trial collecting data retrospectively from two groups of already established patients and hence changes over time were not explored.

The higher levels of anxiety found within the control group at final follow-up may be contra to expectation as one might assume that increasing patient knowledge, understanding and exposure to blood test results and decreasing healthcare utilisation could increase levels of anxiety. The impact of self-monitoring on anxiety discussed in Chapter 3 suggested inconclusive results. Qualitative work in diabetes does, however, indicate that patients feel anxious if blood glucose readings are high and they are unable to understand why (Peel *et al.,* 2004). Clinicians have also expressed concerns that patients predisposed to anxiety might not be suitable for self-monitoring in heart failure (Seto *et al.,* 2010). In rheumatology van der Vaart, Drossaert, Taal and van de Laar (2013) conducted a Delphi study with healthcare professionals and also found that healthcare providers felt that although online access to electronic medical records could improve patient participation and involvement in the treatment process they were concerned that access to information which patients did not understand could cause fear and distress due to misinterpretation. The training session within the current intervention presented information on the meaning of blood test results, why results could be outside of the normal range and a specific action plan should abnormal results be found. This appears to have given participants reassurance and led to reductions in anxiety despite patients seeing their CNS and GP less often.

These changes in anxiety from baseline to final follow-up also mediated the relationship between trial arm and mental health quality of life. Participants who experienced a greater decline in anxiety over the trial period experienced better quality of life at final follow-up. Since trial arm did not directly affect mental health quality of life independent of its effects on anxiety this analysis demonstrates an indirect effect for changes in anxiety. Although both in the original model of quality of life by Wilson and Cleary (1995) and the revised version by Ferrans, Zerwic, Wilbur and Larson (2005) the individual characteristics of the patient, which include levels of mood, are thought to influence quality of life in a unidirectional manner. The relationship between mood and quality of life is likely to be somewhat bidirectional in that increases in quality of life may improve levels of anxiety, and vice versa (Wilson & Cleary, 1995). This relationship, therefore, requires further exploration in this population.

9.2.5 Psychosocial process variables

9.2.5.1 Self-efficacy beliefs

It was hypothesised that participants in the intervention group would experience increased self-efficacy compared with those in the control group. In line with social cognitive theory it was further hypothesised that any changes in self-efficacy beliefs would mediate the relationship between trial arm and healthcare utilisation and trial arm and quality of life at final follow-up. Baseline self-efficacy was also hypothesized to moderate the effects of the intervention on these outcomes.

The results indicated that the first hypothesis was not supported as the interaction effects between group and time for generalised self-efficacy and participants' confidence in their ability to monitor and manage their arthritis as well as actively communicate with healthcare professionals, as measured by the MeiQ™ and HeiQ™ subscales, were not significant. There was a trend for all measures of self-efficacy to increase in the intervention group and either decrease or remain stable in the control group; however, these differences were very small.

Other trials of patient-initiated services in rheumatology have also measured self-efficacy and found differing results. Hewlett *et al.,* (2000) measured self-efficacy using

the ASES developed by Lorig *et al.,* (1989) which consists of three subscales: pain, function and other symptoms. Hewlett *et al.,* (2000) found that self-efficacy for function was significantly higher in the intervention compared to control group at 6, 15, 18 and 21 months post intervention, but not at 24 months. The results for the other subscales are not reported and are, therefore, assumed to be non-significant. Changes in all three self-efficacy subscales from 0-24, 24-48, 0-48 months (Kirwan *et al.,* 2003b) and 0 to 6 years were not significantly different between the patient-initiated service and usual care (Hewlett *et al.,* 2005b). Primdahl *et al.,* (2012; 2014) also used the ASES along with the RASE scale (Hewlett *et al.,* 2001) which measures self-efficacy for performing 28 self-management behaviours. The authors also found no significant difference between the patient-initiated service and rheumatologist-led follow-up on any of these measures at either 3 months (Primdahl *et al.,* 2012) or 1 and 2 years post intervention (Primdahl *et al.,* 2014).

The GSES (Schwarzer & Jerusalem, 1995) was selected for use in this trial as in a review of three generalised self-efficacy measures (Scherbaum *et al.,* 2006) only the GSES had been assessed for comprehensibility, reliability and validity in patients with arthritis (Barlow *et al.,* 2005). Generalised self-efficacy represents a person's global confidence in one's ability to cope across a range of demanding situations. It has, however, been conceptualised as a trait measure of "optimistic self-beliefs" and assumed to be relatively stable over time and domains of functioning. The lack of change in GSES in this study suggests that this concept may be more stable than was originally thought. In retrospect it seems unrealistic to have hypothesised that the intervention would have led to significant changes in this measure. An arthritis-specific measure of self-efficacy like the ASES or RASE was not selected for inclusion in this evaluation as the intervention was not designed to change behaviour in relation to the specific subscales or items within these measures, such as pain or function. This may, therefore, explain the lack of effect found within the other evaluations of patient-initiated follow-up services. As these interventions were also likely to lack specific content in order to bring about a change in for example pain and functional self-efficacy.

Bandura (2006) argued the importance of measuring self-efficacy beliefs tailored to specific activity domains. Hence self-efficacy beliefs in relation to participants' ability

to self-manage and specifically self-monitor their arthritis, along with self-efficacy for active communication with healthcare professionals were also measured within the current study using the MeiQ™ and HeiQ™. These constructs were selected as they mapped specifically on to self-monitoring element of the intervention (i.e. MeiQ™ self-management ability construct and HeiQ™ self-monitoring and insight construct) and initiation of a telephone consultations (i.e. HeiQ™ Active Communication construct) whilst still being applicable for participants within the control group. The current study found no significant interaction effect between time and group on any of these variables. In hindsight, a more specific measure could have been developed in order to assess people's confidence in their ability to interpret their symptoms and blood test results and use these data to initiate a telephone consultation. Although this could have only been measured within the intervention group, it would have given some indication of whether participants felt confident about performing the specific tasks required in the intervention.

The MeiQ™ has yet to be published by the developers, hence there are no reported data on how these constructs may change over time as a result of health education or self-management interventions and nor have the active communication or self-management ability constructs from the HeiQ™ been measured over time. Neither scales have been used to evaluate self-monitoring or patient-initiated follow-up interventions. The original version of the HeiQ™ has, however, been used to evaluate general self-management interventions which included the self-monitoring and insight construct. Nolte, Elsworth, Sinclair and Osborne (2007) performed secondary analysis using data from 142 self-management courses across a range of chronic conditions, with osteoarthritis and RA two of the most frequently reported diseases. The authors also found that a majority of participants experienced either minimal or no change in this construct over time, a large proportion experienced substantial improvement and some a substantial decline. The stability found within the intervention group in this trial supports the findings of Nolte *et al.,* (2007). Since this publication a number of other arthritis self-management interventions have also failed to find any change in this outcome over time. This included an evaluation of self-management and peer support for people with arthritis on a hospital joint replacement waiting list (Crotty *et al.,* 2009), a community-based osteoporosis education and self-management course

(Francis, Matthews, Van Mechelen, Bennell, & Osborne, 2009) and a generic self-management programme for a range of chronic conditions including RA (Packer *et al.,* 2012).

As reported in Chapter 6, at the beginning of the trial there were significant ceiling effects for all measures of self-efficacy. Indicating that participants in both the intervention and control group already felt able to cope across a range of demanding situations, were confident in their ability to communicate with healthcare professionals, perform self-management tasks and monitor their arthritis. Due to these ceiling effects, a lack of effect, therefore, does not necessarily mean that the intervention could not be effective in improving these outcomes but means it was unlikely to happen as this population were already confident in their own abilities. These ceiling effects mean any analysis including these variables should be interpreted with caution as although the intervention may appear to have no significant impact on the variables there was little room for improvement (Hessling, Traxel, & Schmidt, 2004).

The second hypotheses in relation to self-efficacy beliefs was also not supported as changes in self-efficacy beliefs over time failed to mediate the relationship between trial arm and healthcare utilisation, or between trial arm and quality of life at final follow-up. This is the first evaluation of a patient-initiated service to look at the mediating effects of self-efficacy on outcomes. Other trials have considered self-efficacy as a primary or secondary dependant variable rather than a mechanism through which the intervention is effective. In support of social cognitive theory (Bandura, 1986; Bandura, 1997) baseline scores on the MeiQ™ active communication construct did moderate the relationship between trial arm and physical health related quality of life and hence the third hypothesis in relation to self-efficacy beliefs was supported. The role of self-efficacy as a moderator rather than mediator for outcomes in RA supports the work of Schiaffmo and Revenson (1992) which suggested that perceived self-efficacy was a stronger moderational factor between causal attributions and depression and disability than mediator.

This study found that when participants who felt less confident in their ability to communicate with healthcare professionals at baseline were randomised to the intervention compared to control group their physical health related quality of life was poorer at final follow-up. This suggests that those who were less confident in communicating with their rheumatology team found the intervention less beneficial. One possible explanation for this finding is that if someone who is already finding it difficult to interact and communicate with their clinical team takes part in an intervention designed to encourage them to initiate contact with their CNS but the intervention fails to increase their confidence in their ability to communicate with healthcare professionals (as found in this trial), this may have a detrimental impact on their psychological well-being.

As described in section 5.8.1.1 (page 204) the intervention contained a number of behaviour change techniques targeting two key behaviours (i) self-monitoring – including interpretation of symptoms and blood test results and (ii) initiating a telephone consultation with the CNS. The intervention contained instruction on how to perform the behaviour i.e. contact the CNS; however, there were no techniques which aimed to target people's ability to communicate with healthcare professionals more generally and at no point were barriers to seeking medical assistance explored. General self-management interventions in rheumatology, such as the ASMP have been found to significantly improve people's ability to communicate with their physician at both short and long-term follow-up (Barlow, Turner, & Wright, 1998; Barlow *et al.,* 2000) but the ASMP includes topics and skills training on how to communicate effectively with healthcare professionals in order to facilitate this change in beliefs and behaviour. Self-management interventions which include elements of communication skills training have also been found to improve the quality of life of patients with arthritis (Maisiak, Austin, & Heck, 1996). The quality of the communication patients have with their doctor is seen as one of the most important issues for people with arthritis (Buckley, Vacek, & Cooper, 1990) and good communication is engrained in arthritis treatment guidelines (National Institute for Health and Care Excellence, 2013b). It, therefore, may have been beneficial to integrate these elements of generalised self-management programmes into this intervention in order improve

patients confidence and ability to interact and communicate with their healthcare team.

In a recent evidence based analysis of self-management support interventions for people with chronic disease Franek (2013) conducted a meta-analysis and found a small but statistically significant increase in self-efficacy in favour of chronic disease self-management programme (CDSMP). When attempting to syntheses the evidence in relation to who benefits from CDSMP, of the nine studies that conducted secondary analysis on this question, the evidence was difficult to interpret. Many of these studies attempted to identify moderators or predictors of response to the CDSMP; however, these analyses were not identified *a priori*, no adjustments were made for multiple comparisons, and results were inconsistent across studies and varied according to outcome. Whilst some studies found that baseline self-efficacy and change in self-efficacy were significant predictors of health-related quality of life post intervention (Reeves *et al.,* 2008) and healthcare utilisation (Lorig *et al.,* 2001), others failed to replicate these findings (Ritter, Lee, & Lorig, 2011; Harrison *et al.,* 2011).

In all of these studies however, the authors explored baseline predictors of intervention effectiveness. By conducting the analysis in this way it is unclear if these baseline variables are moderators or non-specific predictors (i.e. patient baseline characteristics that predict response in both treatment and control groups). Moderation analysis, as described by Kenny (2013), provides a complete picture of which participant characteristics at baseline interact with the treatment to affect the outcome and hence which patients might be most responsive to the treatment and for which patients, other, more appropriate treatments may be sought (Kraemer, Wilson, Fairburn, & Agras, 2002). Hence the analysis in this thesis provides more robust support for self-efficacy as a moderator.

As far back as 1989 researchers in chronic disease self-management have highlighted the need to examine the mechanisms by which health education affects health status (Lorig *et al.,* 1989). Despite more recent rhetoric highlighting the importance of the mediating role of self-efficacy on outcomes in self-management interventions (Taal, Rasker, & Wiegman, 1996; Jerant, Friederichs-Fitzwater, & Moore, 2005) there is still a

lack of studies which have explored this relationship. The mechanisms at work in patient-initiated interventions and self-management interventions are also rarely explored and, therefore, there is little evidence on the role of theoretically derived concepts such as self-efficacy. This trial is, therefore, one of the first to explore mechanisms of change and thus provide insight into who may benefit more from a self-monitoring and patient-initiated follow-up service or potential avenues that could enhance the effects of the intervention. Further studies of this kind are required to establish the mechanisms of action. Future trials that prospectively stratify patients based on hypothesized predictors of response should also be conducted to better confirm these findings (Franek, 2013).

9.2.5.2 Illness and medication beliefs

Other variables that were hypothesized to change as a result of the intervention as well as have an effect on the outcome of the intervention were the beliefs patients held about their arthritis and medication, along with their knowledge about methotrexate. It was hypothesised that participants who took part in the intervention would experience a significant increase in knowledge about methotrexate and personal and treatment control compared with the control group. Intervention participants were also predicted to attribute fewer symptoms and consequences to their arthritis, experience less treatment burden and have fewer concerns about their arthritis and methotrexate. In line with self-regulation theory it was also hypothesised that changes in illness and medication beliefs would mediate the relationship between trial arm and outcomes, and baseline scores would also moderate this relationship.

The first of these hypotheses was not supported as there were no significant interaction effects between trial arm and time in the MLM analyses. In order to understand why illness and treatment beliefs remained stable it is important to reflect on the content of the intervention and likelihood of change. It is surprising that the intervention did not affect treatment burden, concerns about taking methotrexate or its necessity, or the negative consequences of living with the condition since the content of the training session and the service aimed to teach people about their treatment and provide them with the skills that could reduce the burden of attending clinic.

This is the first evaluation of a self-monitoring or patient-initiated follow-up intervention which has explored the impact of the intervention on illness and treatment beliefs and whether these beliefs are the mechanisms through which these interventions work. Other health education and self-management interventions have been found to impact upon beliefs about illness, although the outcomes are not entirely consistent and no studies have been undertaken in arthritis. A disease-specific expert patient programme for people with bronchiectasis led to no significant differences between groups over time on any of the IPQ-R subscales (Lavery, O'Neill, Parker, Elborn, & Bradley, 2011) and in a review of illness perceptions in diabetes Mc Sharry, Moss-Morris and Kendrick (2011) identified four RCTs that had evaluated psychosocial interventions to improve HbA1c in type 1 and 2 diabetes. The four interventions consisted of structured education, SMBG or motivational interviewing and were found to have mixed effects on illness perceptions. One RCT found no significant between-group changes in any of the IPQ subscales, another found that the intervention led to a more negative view of diabetes and the two remaining studies found positive improvements in illness coherence, personal and treatment control, illness concern and identity. Only motivational interviewing, the only intervention to have a cognitive component, led to positive changes in both illness perceptions and HbA1c lending support to the self-regulatory model (Leventhal *et al.,* 1980). Suggesting that in order to change beliefs specific cognitive strategies need to be employed within an intervention.

According to self-regulation theory (Leventhal *et al.,* 1980) the beliefs a patient holds about their illness and treatment will influence how they respond and in turn this will impact upon outcomes. In this trial, however, beliefs about arthritis and methotrexate failed to mediate or moderate the relationship between trial arm and either quality of life or healthcare utilisation. There is a sizeable amount of literature which has explored the link between illness perceptions and quality of life in arthritis. The dimensions of the IPQ-R that have been found to predict physical and social quality of life include the identity, control and consequences subscales in RA (Scharloo *et al.,* 1998; Graves *et al.,* 2009; Kotsis *et al.,* 2012) and illness identity subscale in PsA (Kotsis *et al.,* 2012). These studies all indicate that more positive beliefs, i.e. attributing fewer symptoms to arthritis and perceiving greater control over the condition and fewer

negative consequences, are associated with increased quality of life. The link between illness and treatment beliefs and healthcare utilisation is less established. There is some evidence to suggest that perceiving your health problem as being highly symptomatic, believing it will last a long time and have serious consequences are key predictors of health care use in primary care (Frostholm *et al.,* 2005). The results from this trial, however, fail to support these findings and to the author's knowledge is the only study which looks at the impact of illness and treatment beliefs on healthcare utilisation in secondary and primary care.

Despite illness and treatment beliefs not being significant mediators or moderators of intervention outcomes, knowledge about methotrexate was a significant moderator of mental health quality of life; but this was not in the expected direction, considering knowledge remained stable over the intervention period. The intervention was found to be more effective, i.e. led to better mental health quality of life post intervention, for those participants with poorer knowledge and more specifically those scoring below 10.88 at the beginning of the trial. The lowest possible score on this scale is eight and hence 10 represents a very poor level of knowledge; however, it is important to consider these results in relation to the percentage of the sample who scored below 10.88 on this measure. Hayes (2013) suggests that some caution is required when interpreting interaction effects. Only 8.86% of the sample or five participants scored below 10.88 on the knowledge questionnaire in this study. Hayes (2013) suggests that this region of significance may, therefore, be less robust as there are not enough participants at this end of the scale to be confident in this claim. The relationship still remains but the cut-off of 10.88 should, therefore, not be taken too rigidly. Even when considering this caveat as knowledge did not significantly change over time or between groups it is important to consider why this relationship exists. Change in anxiety from baseline to final follow-up was the only significant mediator of the relationship between trial arm and mental health quality of life. Speculatively it could be that for participants with poor knowledge at baseline who were randomised to the intervention group, their anxiety levels decreased at a greater rate than those in the control group and this led to better quality of life at baseline. This is theory is purely speculatively and further analyses would be needed to explore this relationship further.

9.3 STRENGTHS AND WEAKNESSES OF THE TRIAL

A number of factors contributed to the strength and weaknesses of this study.

9.3.1 Study design

Whear *et al.,* (2013) argued that although UK policy was eager to implement patient-initiated services robust evaluations were still needed in order to provide a quality evidence base for this model of care. This was to ensure that the time of both patients and healthcare professionals was used efficiently and effectively without compromising clinical care or psychological well-being. The results of this study go some way to addressing this gap in the literature, and remains the only RCT to evaluate the use of self-monitoring of blood tests for patients with arthritis in a CNS-led DMARD monitoring clinic.

The RCT remains the "gold" standard in scientifically robust research methodologies, by eliminating bias and hence providing evidence for healthcare policy and practice. The random allocation of patients, reporting of pre and post-intervention data and intention-to-treat analysis all indicate the good methodological rigour of this trial (Michie & Abraham, 2004).

9.3.1.1 Random allocation

Random allocation is undertaken in order to reduce potential bias; however, in this trial it was undertaken prior to baseline assessment. This was to enable the researcher to assign participants randomised to the intervention group to a training date prior to leaving the clinic, with the aim of reducing the likelihood of drop out. Randomisation should take place after baseline assessment so that allocation of group does not impact on any self-report measures. Brooks *et al.,* (1998) found that patients who completed a quality of life questionnaire prior to knowing their randomization assignment had significantly better mental health quality of life and lower levels of depression compared with those who completed it after knowing their randomization assignment. This could indicate that participants in the current trial were significantly poorer in psychosocial well-being than if they had been randomised after baseline assessment.

Randomization was undertaken using a randomization plan generator (Dallall, 2010). Randomly permuted blocks of 10 participants were used; this ensured that for every 10 participants entering into the study, five were randomized to the control and five to the intervention group. This prevented serious imbalance should the study have been terminated prematurely. The process of random allocation however, consists of two steps, generating an unpredictable random sequence and implementing the sequence in a way that conceals the treatments until patients have been formally assigned to their groups (Dettori, 2010). In the case of this trial the first step was successfully achieved however, the researcher was not blinded to this list. This non-concealment could have influenced whether a patient was included or excluded and has been found to bias treatment effects as much as 37% (Moher *et al.,* 1998). This was unlikely to have happened as the researcher would not have known the individual patients and hence been able to form an impression about which group they thought they would do better in. This would have been of more concern if one of the clinical team had been randomizing patients. Central randomization or sequentially numbered sealed, opaque envelopes could have overcome this potential bias.

9.3.1.2 Blinding

The practice of keeping the trial participants, care providers, those collecting data, and those analysing data unaware of which intervention is being administered to which participant is known as blinding or masking. Blinding is intended to prevent bias on the part of study personnel; however, this is a complex issue when evaluating non-pharmacological interventions. CONSORT have amended their guidelines to recognize these difficulties and changed their checklist from assessing whether or not participants, those administering the interventions, and those assessing the outcomes were blinded to group assignment to whether or not those administering co-interventions were blinded to group assignment (Boutron *et al.,* 2008).

In the current study one of the conditions of recruiting patients into the trial was informing the respective rheumatologist when one of their patients was consented and which group they were randomised to. In addition, the patient's usual CNS remained in charge of their care, irrespective of which trial arm they were in. Therefore, those delivering standard care were not blinded. As the rheumatologists

were not blinded to the allocation of participants it was important to ensure that the rheumatologists themselves did not increase the frequency with which they offered intervention participants appointments in their clinic or the CNS-led clinic, this was confirmed in the analyses of healthcare utilisation which in fact indicated a significant reduction in CNS visits and no significant difference in rheumatologist visits. Differences, however, could have occurred in other aspects of the care delivered to intervention participants which were not measured such as performing additional tests or referrals to other allied healthcare professionals.

9.3.1.3 Intention-to-treat analysis

ITT analysis provides a realistic assessment of the effectiveness of the intervention in the real world. This means all participants analysed according to the group to which they were assigned, whether or not they completed the intervention. ITT analysis prevents bias caused by the loss of participants, which may disrupt the baseline equivalence established by random assignment and reflect non-adherence to the protocol. ITT is now widely recommended as the preferred analysis strategy for RCTs (Hollis & Campbell, 1999).

This trial performed an ITT analysis in relation to the primary outcome measures of healthcare utilization and secondary clinical outcomes, which did not rely on self-report. Assessment of baseline differences on all variables were performed according to ITT. It was, however, not possible to conduct a comprehensive ITT analysis when looking at changes over time in the psychosocial variables as data were missing for those participants who failed to complete a questionnaire at follow-up. Analysis as received was, however, maintained. In order to provide a suitable sensitivity analysis on all outcomes, analysis was conducted on all participants who were randomized and who provided data, and again for only those who completed all three self-report assessments. There were no significant differences between these analyses, suggesting that those who did not complete all assessments were no different to those who did.

9.3.2 Study outcomes

9.3.2.1 Breadth of outcomes

The study employed a wide range of study outcomes, including healthcare utilisation, clinical and psychosocial well-being and theoretically driven constructs such as illness

and treatment beliefs and self-efficacy. This enabled a comprehensive evaluation of the effects of the intervention from the service delivery and patient perspective. The primary outcomes of healthcare utilisation and quality of life allowed a direct comparison with other trials in the field and the measurement of psychosocial process variables shed light on the mechanisms through which the intervention was effective.

Michie and Abraham (2004) argue that the choice of outcome is critical to any trial but the selection of a health outcome as an index of success is limiting. This is because factors other than the targeted behaviour change may affect health status, therefore, measuring health as a primary outcome could underestimate the effects of the intervention. In this study healthcare utilisation was the primary outcome measure and the fact that clinical and many of the psychosocial variables remain unchanged in this trial adds credence to this argument. This was also evidenced in the study by Primdahl *et al.,* (2014) who failed to find any additional benefit to a patient-initiated service in comparison to a rheumatologist-led follow-up clinic; however, success was judged primarily in relation to clinical and psychosocial outcomes with very few behavioural measures of success relevant to the aims of the intervention measured in the trial. Clinical outcomes, however, remain an important outcome when evaluating alternative models of care. In order to change health policy and practice, if measures of behaviour are primary outcomes then at the very least the intervention should not have a detrimental impact on either clinical or psychosocial well-being in order to warrant any change in practice.

As highlighted previously it may have been useful to have included a behaviour specific measures of self-efficacy in order to reflect the recommendations of Bandura *et al.,* (1986; 1997; 2006) and provide a more detailed understanding of how confident patients felt in performing specific aspects of the intervention such as understanding and interpreting their blood results, calculating change scores and initiating their own reviews. Inclusion of an arthritis-specific rather than generalised measure of quality of life may have been more sensitive to change and provided a more detailed understanding of how the intervention impacted upon specific aspects of arthritis.

As with most studies there were a number of measures that were not included in the evaluation which could have provided a more detailed picture of the impact of the intervention and are, therefore, weaknesses of the study. Although not explored as a possible moderator of intervention effects Primdahl *et al.,* (2014) collected data on level of education at the start of the trial and as highlighted in section 7.5.4 (page 266) level of education and more specifically health numeracy and literacy could have been important factors in how effective the intervention was and whether patients took part in the trial (section 6.5.1, page 247).

As reported elsewhere clinical measures such as early morning stiffness, range of movement and grip strength (Hewlett *et al.,* 2005b; Kirwan *et al.,* 2003b), change in medications and arthritis-related complications (Hewlett *et al.,* 2000) may have also provided a greater understanding of the interventions impact on clinical well-being. In addition outpatient visits to allied health professionals (Hewlett *et al.,* 2000) as well as confidence and satisfaction in the system (Hewlett *et al.,* 2005b; Kirwan *et al.,* 2003b; Primdahl *et al.,* 2014; Sands & Adams, 2009) could have been explored. Due to participant burden, the potential of poorer retention rates as a result of more assessments and the capacity of the researcher a decision was taken not to measure these outcomes.

9.3.2.2 Self-report

The self-report nature of some of the measures also introduced bias. For instance the number GP visits were collected at each of the follow-up time points and could have either been deliberately altered or forgotten by patients. This is a distinct possibility given that Ritter *et al.,* (2001) found that participants who took part in a CDSMP programme were found to significantly under report the number visits they had with their GP over the previous 6 months, and of the sample 61% were patients with arthritis. An objective measure of GP visits taken from the GP electronic health records would have increased the accuracy and reliability of this data, unfortunately access to these data was not possible.

9.3.2.3 Cost-effectiveness analysis

Clinical trials are often viewed as a suitable method via which an economic analysis can be performed (Drummond & Davies, 1991) and MRC guidelines for complex

interventions states that part of the evaluation should include an assessment of cost-effectiveness (Craig *et al.,* 2008). Despite this, and as is typical for many trials designed to assess the effectiveness of an intervention, a cost-effectiveness analysis was not envisaged at the beginning of this trial and hence was performed post-hoc. All post-hoc tests should be treated with caution as they could be a chance finding, despite being statistical significance (Rothwell, 2005). The sample size required to detect statistically significant differences in costs was not determined at the beginning of the study and is likely to be larger than those needed for trials of efficacy (Kraemer & Thiemann, 1987). These post hoc analyses do not necessarily mean the results are invalid, as they do reflect the results of other similarly conducted cost-effectiveness analyse (Hewlett *et al.,* 2000) and the p-value was adjusted to 0.001 in order to compensate for the number of tests performed.

A full economic evaluation is, however, complex and should include all the potential costs of running an intervention including direct and indirect costs in order to capture the impact for the patient, employer and policy maker. This trial only looked at direct costs, including the costs of running the service from the perspective of the NHS. By only looking at these outcomes the most cost-effective treatment may not always be the most effective treatment. In order to establish whether an intervention is both effective from the patient and financial perspective a cost-utility analysis is recommended, particularly when quality of life is either *an* important outcome or *the* important outcome of a trial (Cunningham, 2001). This however, was beyond the scope of the current study, but is recommended for future research.

9.3.3 Generalizability

Pincus and Stein (1996) outlined the limitations of RCTs in depicting accurate long-term outcomes for patients with RA. The first limitation is the implementation of exclusion criteria. As reported in section 6.2.1 (page 229), 24.58% of patients assessed were not eligible to take part in the trial due to the limited inclusion criteria. The main reasons were: not on methotrexate, did not have RA or PsA, or were not stable. The inclusion criteria in this trial were selected so that the sample was a homogenous group of patients who were likely to be experiencing similar symptoms and side effects and also similar treatment plans. Although this does mean that these specific results are not generalizable to other rheumatic conditions or other DMARD therapies

hypothetically an intervention of this kind could be effective in reducing healthcare utilisation in any long-term conditions which require close monitoring, this has already been demonstrated in a range of long-term conditions as found in Chapter 3.

9.3.4 Implementation

In addition to the limitations discussed, a further drawback of the study is that the researcher rather than the CNS administered parts of the intervention. This included the education training session and telephone follow-ups in phase one of the trial. This would obviously not be possible in practice and, therefore, these elements of the intervention would need to be incorporated into the nurse role. This has implications on the generalizability of the results, as the intervention evaluated in this study would not be the same as implemented in practice. It is however, unlikely that the nurse delivering these aspects of the intervention would differ widely from that delivered by the researcher if a detailed protocol was used. Therefore, the influence of this factor is likely to be minimal.

A related concern is the acceptability of the intervention by healthcare professionals and the potential objection of more intensive patient involvement in monitoring laboratory results. Despite this being part of standard care in both diabetes and anti-coagulation therapy, this process is entirely new in rheumatology and could be perceived as being a step too far in patient empowerment. In a Delphi study conducted by van der Vaart *et al.,* (2013), healthcare professionals in rheumatology felt that online access to electronic medical records could improve patient participation and involvement in the treatment process. They were, however, concerned that access to information which patients did not understand could cause fear and distress due to misinterpretation. Interestingly opinions varied on what medical data could be released to patients. According to several healthcare professionals information on laboratory results should not be available to patients until after the consultation in order to provide more explanation and to put results into context. The subsequent quantitative questionnaire suggested that the most frequently agreed upon disadvantage regarded patients' skills to interpret their medical information. Despite this a majority of care providers felt that laboratory results should be available to patients but this should be done with a lag time so that

any consultations came prior to reviewing. Demonstrating effectiveness for an intervention is an important step in informing whether an intervention should be rolled out across the service, but clearly the views of healthcare professionals could be an important barrier to implementation and this requires further exploration.

CHAPTER 10 - A QUALITATIVE EXPLORATION OF INTERVENTION PARTICIPANTS' VIEWS ON SELF-MONITORING AND INITIATING THEIR OWN CARE.

10.1 PROLOGUE

This chapter outlines the methods and results from the qualitative study which directly followed the RCT. The aim of this study was to gain a greater understanding of the experiences of receiving training and taking part in the intervention by interviewing a consecutive sample of participants from the intervention group on their completion in the trial. This was to further explore perceptions of value and acceptability of this model of care from the patient perspective.

10.2 RATIONALE FOR A MIXED METHODS APPROACH

Mixed methods research has evolved as a result of the paradigm debate between quantitative and qualitative research methodologies. This "third methodological movement" argues that the two approaches are compatible and can be used in conjunction with one another to understand an issue or problem from varying perspectives (Teddlie & Tashakkori, 2011). Although consensus has now been achieved for the label "mixed methods research", over 19 different definitions have been proposed by leading mixed methods researchers (Johnson, Onwuegbuzie, & Turner, 2007). Based on an analysis of these 19 definitions Johnson *et al.,* (2007) have proposed the following general definition:

> *"Mixed methods research is the type of research in which a researcher or team of researchers combines elements of qualitative and quantitative research approaches (e.g., use of qualitative and quantitative viewpoints, data collection, analysis, inference techniques) for the broad purposes of breadth and depth of understanding and corroboration."*

This definition refers to mixed methods research as a type of research design, and involves "mixing" within a program of research or across a closely related set of studies.

The mixed method approach has been recommended for the evaluation of complex health interventions (Craig *et al.,* 2008). In the context of an RCT designed to evaluate a complex intervention, qualitative research may be used before, during or after a trial (Simon, Claire, & Andrew, 2009). The current qualitative study was undertaken during the trial phase and was used to examine whether the intervention was acceptable to patients and to explore participants' experiences. This method is known as the concurrent embedded strategy (Curry *et al.,* 2013) whereby quantitative and qualitative data collection occurs at the same time; however, one component is predominant. In the case of this thesis the quantitative element was the predominant method and the qualitative study was embedded within this.

O'Cathain, Thomas, Drabble, Rudolph and Hewison (2013) conducted a systematic mapping review which identified 296 RCTs that had been combined with qualitative research. A majority of the qualitative studies were undertaken at the pre-trial stage (28%). Only 1% were conducted to explore patient's views about the acceptability of the trial in practice. The potential value of conducting research at this stage is to aid implementation of the intervention and add relevance and interpretation to the findings of the RCT (O'Cathain *et al.,* 2013). By embedding a qualitative study into the RCT this thesis aimed to explore this model of care from the patient perspective in order to provide a better understanding of the findings of the RCT, whilst enhancing the benefits of these individual methods and overcoming their limitations.

10.3 AIMS AND OBJECTIVES OF THE STUDY

The attitudes, experiences and expectations of patients are essential to the implementation of any new model of care. The aims of this study were, therefore, to explore not only the experiences of participation from the patient perspective but specifically the value placed on the intervention and implementation of this new model of care.

10.4 ETHICS APPROVAL

The study received full ethics approval from Camden and Islington Community Local Research Ethics Committee (Ref. 09/H0722/91).

10.5 STUDY DESIGN

This qualitative study utilised semi-structured interviews. Individual interviews were selected over focus groups primarily because data collection could take place immediately following participation rather than waiting for a sufficient number of people to complete the trial before a focus group could commence. This allowed the experience to be fresh in the minds of the participants and reduced the likelihood of recall bias which can be problematic when collecting retrospective data (Hassan, 2006).

10.6 PROCEDURE

10.6.1 Identification of participants and consent

All intervention group participants who took part in the RCT were eligible for participation in the interview study. As part of obtaining consent for the RCT participants were asked if they would be willing to be approached to take part in a qualitative interview at the end of their participation in the trial. At which point participants were written to and asked if they would be willing to be interviewed. Additional written consent was obtained before the interview was undertaken (Appendix AA).

10.6.2 Location of the interview

All interviewees were offered a choice of location either at home, at the hospital or university, and at a time convenient for them.

10.6.3 Topic guide

The topic schedule was developed by the researcher in collaboration with the supervisory team and covered the decision to take part in the trial, questions about the training and information received in the education session, the tasks involved and their reflections on their experiences, views of standard care and the value they attached to the system introduced as part of this study (Figure 10.1). The semi-structured nature of the interviews meant that rather than using the guide as a strict interview schedule questions were used as prompts for discussion.

1. Can you tell me the reasons why you decided to take part in this trial?
2. Can you tell me what expectations you had at the start of the trial?
3. Was the information we provided to you [in the training session] clear in outlining what the study was about in relation to what actually happened?
4. How useful did you find the training session?
5. *Prompt*: information, skills, did you learn anything new
6. At the end of the training session were you clear about what you had to do?
7. Was there other information that would have been useful?
8. What was it like receiving your blood test results?
9. *Prompt:* were they on time, what did you do if they did not arrive?
10. How did you feel about interpreting your results?
11. How easy or difficult did you find interpreting the blood test results and your symptoms?
12. How did you find the telephone calls with the researcher?
13. How did your experience compare with your normal care?
14. Can you describe what it was like not visiting your nurse specialist face to face?
15. Has taking part in the study changed your relationship with the rheumatology team?
16. How did it feel when the programme ended?
17. Has the programme made you feel differently about your future care?
18. Are there any changes you would recommend?
19. Is there anything else you would like to tell us about your experience of the programme that we haven't covered?
20. Would you recommend this way of care to other patients with arthritis?

Figure 10.1. Interview guide for qualitative study

All interviews were conducted by the researcher, digitally recorded with the participant's permission and transcribed verbatim, with any identifiable data removed. The researcher made notes after each interview outlining their initial impressions of how the interview went, any factors which may have influenced the participants' responses and any potential themes or sub-themes which emerged.

10.7 SAMPLE SIZE

As opposed to quantitative research which aims to count opinions or beliefs, qualitative research is about the richness of the data and hence sample size calculations are not conducted in the same way (Kuzel, 1992). The study aimed to recruit an initial sample of 10 interviews with a stopping criterion of a further three interviews to confirm that data saturation had been achieved, as suggested by Francis *et al.,* (2010). Data saturation was defined as the emergence of no new themes in relation to the research question. In practice, this meant that the interviewer had a sense of when nothing new was emerging from the interviews in relation to the research question and then begin coding to explore the reality of this. If saturation is not reached this simply means that the phenomenon has not yet been fully explored rather than that the findings are invalid (Morse & Field, 1995).

10.8 ANALYSIS

The data generated from these semi-structured interviews were analysed using thematic analysis (Braun & Clarke, 2006) which is a method for identifying, analysing and reporting patterns within data. This method was selected as it is flexible, allows themes to be identified across a dataset, is suitable for larger samples and appropriate for use in studies with a focused research question, as in the case of this study.

Grounded theory (Glaser & Strauss, 2012) was not selected as this aims to develop a theory from the data which was not the overall aim of the study. Interpretative Phenomenological Analysis (IPA) was not chosen because thematic analysis focuses mainly on patterns of meaning across participants whereas IPA has a dual focus on the unique characteristics of individual participants and on patterns of meaning across participants (Smith, Flowers, & Larkin, 2009). The current study was not concerned with the experience of individuals per se but the experiences across the sample. In addition IPA requires a small homogenous sample of between three and six participants (Smith *et al.,* 2009) which in the context of this study was not deemed appropriate to explore a full range of participants' experiences. Framework analysis (Ritchie & Spencer, 1994; Ritchie, Spencer, & O'Connor, 2003) a type of thematic analysis was considered as a legitimate alternative to the methods outlined by Braun and Clarke (2006). As the researcher had experience of thematic analysis in a number

of other studies (Griva *et al.,* 2013; Walker, James, & Burns, 2012) this method of analysis was deemed most appropriate.

Thematic analysis involves searching across a data set to find repeated patterns of meaning. All coding was undertaken manually by the researcher following six steps:

Phase One: Familiarizing yourself with your data – In order to get to know the data, the transcripts were first checked for errors by listening to the digital recordings. They were then read and re-read and by actively searching for meaning within the text, the researcher made some initial notes about possible themes and patterns. The researcher did not complete transcription of the interviews and as transcription is seen as a key part of the analysis process (Bird, 2005) additional time and focus were placed on this phase of the analysis in an attempt to overcome this potential limitation.

Phase Two: Generating initial codes – Using the preliminary list of themes and patterns produced in phase one, the researcher then set about generating an initial set of codes from the data. A code is defined as a feature of the data that is interesting to the researcher, and is the most basic element of the raw data that can be assessed in a meaningful way (Boyatzis, 1998). Relevant parts of the transcripts were highlighted in the text and given a code in the margin that best described that excerpt. Text thought to be in the same code were highlighted in the same colour in order to indicate possible patterns within the data. When overlap occurred, or a piece of text was thought to relate to more than one code, this was highlighted in the margin. Additional notes were also taken in a separate notebook if any initial themes came to mind.

Phase Three: Searching for themes – When all the data had been coded, the codes were collated into one list and then the process of clustering codes into coherent groups began. This was achieved by writing the codes on post-it notes and then using a large surface to group codes together.

Phase Four: Reviewing themes – This phase involved letting go of themes that did not have sufficient data, collapsing themes together and breaking others down further. This was achieved by going back to the original extracts within each code and reading these within a theme to ensure they grouped together meaningfully (internal homogeneity), whilst checking that both the themes and codes were distinct from one another (external heterogeneity) (Patton, 1990). When there was inconsistency the

researcher "stepped back" to evaluate whether the theme was a problem or a particular extract within the theme was better represented elsewhere or dropped altogether. When a coherent pattern had formed within a theme these were refined using a thematic map which represented the data as a whole.

Phase Five: Defining and naming themes – Once the thematic map had been finalised the themes were renamed where necessary in order to reflect the true meaning of the theme and decide what aspect of the data it was aiming to capture.

Phase Six: Producing the report - The results of this analysis are presented in this chapter. The results aim to tell the story of the data in a manner that answers the primary research question and includes quotes in order to demonstrate and support each of the codes and themes; and is part of an overall analytic narrative which will be reviewed in the discussion.

In addition to this six phase process, four validity criteria were employed:

- Audit Trail: Detailed quotes from the participants' transcripts provided evidence for the interpretation of the data.
- Peer Panel: An auditor was asked to go through randomly selected sections of 25% (n=3) of transcripts to confirm the pattern of analysis.
- Researcher Reflexivity: This is the researchers' attempt to recognize their own values, interests and views and the role that they may play in their understanding of the transcripts. Doing this can help the reader to interpret the researcher's data and analysis. A reflective diary was kept by the researcher, where notes were taken about initial thoughts and feelings, the main points that arose in the interview and any factors that the researcher felt influenced the interviewee. These were taken into account throughout the analysis process.
- Independent Audit: An independent auditor familiar with thematic analysis was asked to check the validity of the "final report".

10.9 RESULTS

10.9.1 Sample characteristics

All 52 intervention participants were eligible to take part in the study and agreed to be approached to take part in a qualitative interview at the end of their participation in the trial. A total of 12 (27.91%) semi-structured interviews were conducted which is deemed adequate for mixed methods studies (Sandelowski, 1995; Francis *et al.,* 2010), at that point no new themes were emerging. To achieve this sample a total of 43 participants who completed the trial were approached to take part in an interview. All of the interviews took place either in a room at University College London (a location near to UCLH) or at the participants' place of work. The interviews lasted between 20 and 38 minutes. Participant characteristics can be found in Table 10.1.

Table 10.1. Participant characteristics for interviewees

ID	Gender	Age	Condition	Disease duration (years)	MTX duration (years)	MTX dose (mg)†	DAS28†	PsARC physician†	PsARC patient†	PsARC tender†	PsARC swollen†
5	Female	76	RA	26	1	12.5	6.13	-	-	-	-
7	Male	49	RA	8	5	10	3.46	-	-	-	-
23	Female	44	RA	7	5	7.5	4.20	-	-	-	-
31	Female	47	RA	22	17	22.5	3.76	-	-	-	-
53	Male	50	RA	10	5	15	3.42	-	-	-	-
56	Female	64	RA	22	5	15	5.67	-	-	-	-
71	Female	58	PsA	3	1	10	-	2	2	3	1
78	Male	60	PsA	11	10	20	-	2	1	17	2
80	Male	35	PsA	4	2	15	-	2	2	14	1
81	Male	27	PsA	6	4	17.5	-	2	1	0	0
82	Male	66	PsA	31	16	15	-	2	2	21	5
83	Male	76	RA	7	6	7.5	1.72	-	-	-	-

ID – Identification Number; MTX – Methotrexate; DAS28 – 28-item Disease Activity Score; PsARC – Psoriatic Arthritis Response Criteria; RA – Rheumatoid Arthritis; PsA – Psoriatic Arthritis

† - at baseline

10.9.2 Themes

The analysis revealed five themes talked about by a majority of participants in relation to their experience of and the value they placed on both usual care and the self-monitoring and patient-initiated service.

Theme One – Burden of usual care

- Sub-theme: Efficiency
- Sub-theme: Impact on work life
- Sub-theme: Normality

Theme Two – The self-management process

- Sub-theme: Knowledge
- Sub-theme: Control
- Sub-theme: Behavioural adjustment

Theme Three – Conflict

- Sub-theme: Between laboratory tests and symptoms
- Sub-theme: Between study guidelines and practice

Theme Four – Anxiety

Theme Five – A tailored service

- Sub-theme: Right time
- Sub-theme: Right method

Figure 10.2. Qualitative themes

10.9.2.1 Theme one – burden of usual care

With few exceptions participants described attendance for rheumatology outpatient visits prior to the commencement of the trial as *"burdensome", "useless"* and an "*absolute waste of time"*. Patients felt quite strongly that usual care was inconvenient and did not meet there desire to lead a *"normal"* life. Whilst self-monitoring and initiating their own care was *"much more convenient"* and *"took away a burden"*.

10.9.2.1.1 Sub-theme – Efficiency

All participants spoke about their rheumatology outpatient appointments being *"a waste of time"* (EK) for both them and the clinical team *"sometimes, you know they are a waste of time for everyone I think" (AS).* Many participants described situations in

which they had made the journey to hospital, waited in some cases for hours and were then seen by the CNS for a matter of minutes. These appointments often consisted of discussions around what patients felt were very minor symptoms or were used to obtain blood tests forms; activities which could have been dealt with in other ways. These appointments often led to no changes to treatment, which patients found extremely frustrating, unnecessary and an inefficient use of everyone's time.

> *"it just seems to be more efficient use of everybody's time, mine, [the nurse's] and why should the hospital need to bother with an appointment for something that is really straight forward" – NP*

> *"….today I mean [the nurse] was running half an hour late, my appointment was at 11.15 and it was in fact at 11.45 but I was out of [the nurse's] office by 11.50 for a 15 minute appointment, basically we don't have anything to say, there aren't any issues and really the whole purpose was for me to get some more blood test forms." – PN*

> *"No, I think that was one of the reasons why I found it quite irritating was that when I came to see the rheumatologist you know I waited for like two hours sometimes and got seen for two minutes, seeing the nurse was better it was pretty quick, but still generally things were ok so I just got sent away again it seemed a bit tedious to wait all that time to be told everything was fine come back in a couple of month." – JD*

This was not due to the capabilities of the CNS *"…no criticism of [the nurse] because it's absolutely not" (EK)* but was due to the perceived lack of value or usefulness of appointment.

> *"Well, I try to make them coincide with doing a blood test so to that extent it was not a huge imposition and it's always nice to see [the nurse] and she is always friendly, a cheerful kind of person so it's not onerous at all but equally I wouldn't say it was very valuable." – VH*

10.9.2.1.2 Sub-theme – Impact on work life

For those participants who were in employment, the impact of attending outpatients appointments along with juggling the other demands of monitoring their condition such as attending for the blood test, obtaining blood test forms and the difficulties involved in obtaining prescriptions was a challenge. This led to frustration and was hence a driver for taking part in the trial.

> *"I think for me the most burdensome aspects of having to be on this medication is the fact that there was a period where I was having to go into hospital pretty much every month, probably more than every month the combined total of coming to see the nurse, having blood tests done, getting your prescription and seeing the rheumatologist quite regularly and it was quite inconvenient for me, because I was having to do it during work hours most of the time and so the idea of me being able to do some part of that at home and, therefore, removing the need to be in hospital quite so often I thought was really attractive so it was fairly selfish reasons I would have to admit, but, yeah that was kind of attracted me to [the study] I guess" – JD*

Those in current employment or who had been employed at some point since their diagnosis spoke about the frustration of trying to fit in regular appointments around their work commitments. Regular reviews with the CNS were described as *"coming at a cost"*, both in terms of time as described above but also financially as a result of missed work time particularly for those on an hourly wage. Again participants spoke about this in the context of unnecessary appointments which led to little or no changes to treatment which further compounded the frustration.

> *"You know, and I've spend 45 minutes in the waiting room and you know, it comes at a time cost, particularly when you're paid by the hour it can come at a much larger cost" AS*
> *"Yeah, I mean I was working in those days and I'd have to take time off to fit in and go to the hospital and then see either [the nurse] or [the consultant] and invariably everything was okay it was just follow ups to*

> *make sure that everything was okay. Well now I don't have to do that because if I can monitor my own results, I only go to see them if it's absolutely necessary, saves them time and saves me as well, saves them bothering." – AP*

> *"And the other thing was that [the new service] meant one less visit to the hospital and because I work full-time I thought that is definitely going to benefit me and especially as the nurse starts at 9.30 and because I work full-time it was an issue because I wasn't getting in to work until after the 10 o'clock deadline" – EK*

10.9.2.1.3 Normality

Although in all cases employees were understanding, one participant spoke about how she did not want to draw attention to her illness by taking time off to attend appointments. This participant worried that as a result of being late and taking time off colleagues would think that she was not committed to her job. Self-monitoring and initiating her own care allowed her to spend less time at the hospital and hence feel more *"normal".* This sense of normality was spoken about by another patient, who also felt that attending clinic regularly did not allow him to lead a *"normal"* life.

> *"The number one thing I do is keep my appointments to outside of work time so that no one knows I'm at the hospital" – EK*

> *"well if you're well you don't want to be involved in these types of things [attending clinic], you want to be getting on with life like normal" DW*

10.9.2.2 Theme two – the self-management process

The knowledge gained in the training session paired with the ability to initiate their own care allowed patients to obtain greater control over their illness and its treatment. It also made the link between taking their medication, lifestyle and the impact these were having on the results of their laboratory tests and their symptoms more salient, suggesting behavioural adjustment was taking place.

10.9.2.2.1 Sub-theme - Knowledge

All participants felt that the training session increased their knowledge of their arthritis, the available treatment options - which in some cases had never been explained to them the reasons why they were having regular blood tests and their meaning, along with the important symptoms and side effects that needed to be monitored.

> *"I probably learnt, you know, some of the information that was provided with the training in terms of the disease and the medication. I mean it was actually, quite good to have." AS*

> *"I did enjoy because it gave me an insight into what the hieroglyphs were that I was getting for my blood tests and now I know what to look for. You know and the ranges, if my bloods are in certain limits" – AP*

> *"I wanted to know more about the condition and I thought I'd probably know more from this pilot thing and I actually did." – EK*

One patient appreciated that we had *"just put it all in a package and reminded me of things" (EK),* as information was often delivered primarily at diagnosis but then sporadically throughout the disease course.

This knowledge allowed people to feel more involved in the consultation process, which provided them with the ability to ask more relevant questions of their clinical team and also to be an active participant in the treatment process.

> "*But yes I was probably more knowledgeable and I was able to ask him more relevant questions." EK.*

> *"And so, you know, if I could be involved with this and also that it was a little bit with more, you know, taking kind of control and understanding, you know, more involved what was actually going on rather than going off and getting tests done and not knowing what it means, and waiting for someone to tell you that everything is OK." AS*

10.9.2.2.2 Sub-theme - Control

A sense of control was identified as important by all participants. Patients felt that their increased knowledge, along with the additional responsibility of initiating their own care allowed them to feel more control over their health in general.

> *"I guess it's quite nice to have more responsibility for my own health it's nice" – JD*

> *"And yes that was a bonus as well it was having the responsibility for your own health as well I think that helps definitely" – EK*

As well a general sense of control, many participants spoke about feeling in control of their arthritis and specific aspects of living with their condition such as accessing care when they wanted to rather than it being dictated by the clinical team and hence the ability to manage their own time effectively. This allowed them to take *"ownership"* of their illness and treatment.

> *"…anything I can do to gain more information, more insight and have more control over my illness the better" – JH.*

> *"Because at the end of the day, if I go to [the nurse] and say to her my hands are sore, whether I say it to her over the phone, the end result is same and the one over the phone is me doing it and organizing it myself without having to go into a hospital and do it". DW*

> *"…it's just more control of my own time…..it allows me to control the monitoring to suit my requirements rather than the hospital schedule" – NP*

> *"I thought it was important to own your illness, you know what I mean to take responsibility for it by looking at the data" – PN*

10.9.2.2.3 Sub-theme – Behavioural adjustment

A number of participants felt that self-monitoring allowed them to make a connection between their behaviour and laboratory results and provided them with the opportunity to understand how their condition was changing over time in a more systematic manner. It enabled them to see how taking new medications or increasing their dose of current medications had an effect on their laboratory results and hence see the link between medication and blood results as well as see tangible improvements or deteriorations in their arthritis.

> *"No problem, it's always quite interesting actually in some ways it's better than going to see [the nurse] because she says this was up and that was up and you think what does it mean but when I read what the initials stand for, what I'm monitoring and it's interesting to see how they change from blood test to blood test" – ME*

> *"…seeing my results has enabled me to understand my body and its reactions to the disease and to methotrexate." – RG*

Having access to their laboratory data was described as being better than pharmacological treatments, as having understanding of why they were feeling unwell or why their laboratory tests were abnormal enabled them to take control of how they managed they arthritis and allowed them to change their behaviour accordingly.

> *"information tends to be better than pills sometimes, yeah because if you know why you are feeling that way or what's happening, you're in control of it then you're also in control of what you do" – DW*

One participant spoke about how his alcohol intake, diet and smoking had an effect on his symptoms and laboratory results. As a result he had already made steps to change his behaviour including stopping smoking which he felt had led to better control of his arthritis. He also pondered on whether changes in his alcohol consumption, either by drinking less or by drinking more water after consuming alcohol, would alter his liver function tests.

> *"Yeah I mean if I had a glass or 2 over the 10 [units of alcohol] limit [my liver function test] was fractionally higher, or if I had put on a bit of weight it got a bit higher and maybe the fat content of the food. I would have thought that there would be a relationship between something, because if you went on a drinking binge then it's going to go up. So there are obviously some, some kind of causal relationship but is there anything else I don't know. You know finished your drink and then 2 litres of water over the next 2 days does it come back down again I don't know" – PN*

10.9.2.3 Theme three - conflict

10.9.2.3.1 Sub-theme – Between laboratory tests and symptoms

Patients expressed confusion about the disparity between their laboratory tests and the symptoms and side effects they were experiencing. In many interviews participants reported excruciating pain and swelling but their inflammation markers failed to reflect these symptoms, which they found confusing. One participant attributed this lack of concordance to the fact that he had arthritis in many of his joints and he felt that his CRP would only go up when his flare was extremely severe and not in the case of short periods of *"feeling rough"*. He, therefore, regarded the test as *"useless*".

> *"Yeah, I don't know why [CRP is low] I don't know if it's because, because I have the arthritis in so many joints. So actually in many ways it's not a big flare. Therefore, CRP doesn't pick it up but it's affecting me in so many places that its making me feel rough. I simply don't, I don't know what that it…..but in my case actually, when my arthritis flares, [CRP] doesn't change very much so it's not much use to me" – AS*
>
> *"I get confused because sometimes the results would tell me the opposite of what I'm feeling and sometimes, like you are low, you go for a test and you got low inflammatory factors but your hands are puffed up and you're in pain" – DW*

This lack of concordance led one participant to question his diagnosis as even though he was experiencing what he described as a flare, his blood test results were normal.

> *"but I still think sometimes I haven't got the disease they are talking about because when I was really flared up the medical professionals who saw me said I was fine according to blood test. It's bizarre." DW*

For others when congruence did happen this was reassuring and helped provide an explanation for their symptoms and validate their experiences.

> *"To be able to read my own blood results and then at least when I am feeling particularly ill I could see, oh this is why because this factor has gone up or this has gone down" – JH*

> *"I noticed that if your ESR goes up it relates directly to your inflammation which is good. I think I've noticed that my white blood cell count has gone up when I've had an infection you know stuff like that" – PN*

10.9.2.3.2 Sub-theme - Between study guidelines and practice

The intervention contained clear criteria on the triggers patients should use for contact with their CNS. A number of participants however, spoke about the confusion which arose when less stringent criteria were implemented by the CNSs during their telephone consultations. Participants felt that it was important that these criteria were aligned and this was identified as an area for future improvement if the service was to be implemented. If addressed participants felt that this could lead to further reductions in the number of telephone consultations undertaken.

> *"Just one thing I'm just remembering what we had to look for and what variances we had to look when I rang [the nurse] a couple of times on changes she would say, you were using too low a benchmark for when someone needed to ring her because every time I phoned her she was like no no that's fine you don't need to worry. So I think they would need to be some kind of liaising with the nurses about changing those benchmarks. A couple of times that happened. And she was like no no*

> *that's fine. That's not a worry. So if that changed that would prevent as many calls to the nurse."- EK*

> *"I think if you were doing it long term I think you would find that quite difficult, when you knew that a tiny change wasn't worth fussing about going through the motions when you knew how busy people like [the nurse] are, I think that would be dilemma" – VH*

Although a majority of participants did seek help despite there being only small deviations in their blood test results, the following quotes suggest that participants were experiencing an internal struggle between needing to contact their CNS according to the study criteria and either feeling like they knew the outcome of that consultation or not valuing these abnormalities. This raises concerns regarding the safety of the intervention due to the risk of not appropriately seeking help when required.

> *"You know you follow them accordingly and I guess sometimes, you would see that your figure was just outside the range or just moved by a certain amount and you think that's probably no big deal but I knew what to do" AS*

> *"I mean having to phone if it's slightly out of range each time but as she said some of them out of range is normal for me anyway they've always been that way" – ME*

One participant who had been living with RA for 22 years described predicting this inconsistency when she had received the training. She felt over the course of her arthritis and hence she had come to know not only her own condition but the views of her CNS.

> *"I knew there would be some ambiguity and there was because every time I have a blood test done almost invariable there is something that's out of range and I am kind of familiar after all these years of how [the*

> *nurse] would view it and so minor changes or the minor breaches of the limit, I know they are not something to get terribly het up about. There were one of the two times when I thought do I need to bother her about because I knew she would view it as something important." – VH*

10.9.2.4 Theme four – anxiety

Some participants spoke of feeling anxious about taking on the responsibility of monitoring, this made them extra diligent in checking their laboratory results against the criteria given to them during the training session. These participants were concerned about the *"risk"* of allowing patients to take full responsibility of their monitoring, which could lead to mistakes being made and hence serious side effects being missed with possible devastating consequences. These participants suggested that additional safety nets should be in place to ensure that any serious abnormalities were also flagged to the clinical team to ensure that nothing was missed.

> *"I think there was clearly a possibility for careless mistakes and in the back of my mind it would worry me if the patient had full responsibility for identifying if there was a real problem – such as a side effect of methotrexate. I did feel quite nervous I'd always get the forms out and try not to do it from memory but I think it is quite demanding quite risky that aspect of it" – VH*
>
> *"what I would like to be able to do, is feel certain at the back of my mind that if the things aren't going well it isn't entirely left me to decide find that's all. That I do have someone to consult with as I would worry about that" - RG*

Others implied that the intervention may not be appropriate for people who were already anxious and worried about their health as they may find it difficult to deal with abnormal blood test results.

> *"Yes and I think some people would find it difficult to cope with if they had a rather nervous disposition or [if they were] a worrying sort anyway" – RG*

But whilst some expressed concern others acknowledged the seriousness of interpreting their blood tests but weren't worried about the additional responsibilities. One participant attributed this lack of anxiety to being more comfortable with his treatment regimen. This particular patient had recently started on Enbrel which had controlled his debilitating nausea and hence was happier with his treatment regimen and current disease status.

> *"I don't think I was ever blasé about them I was reading them and taking them seriously but they didn't worry me at all" – EK*

> *"I didn't feel any anxiety about the process at all that's more because I feel comfortable with the treatment and what's happening" – NP*

10.9.2.5 Theme five – a tailored service

There was an underlying narrative across all of the interviews that the services offered in rheumatology outpatients should be tailored to the needs of the individual and delivered at an appropriate time and via the most convenient method. Many participants spoke about usual care being a mismatch between delivery of care and disease status. The fluctuating nature of the disease often meant patients were seen at times when they were well, which led patients to describe the service as *"inefficient",* as described above. Patients described the desire for a tailored service, with care and education delivered at the right time and via the right method.

10.9.2.5.1 Sub-theme - Right time

Participants described usual care as being a *"snap shot"* in the disease course and that between their outpatient appointments significant changes in their disease status often occurred but were not known to the clinical team. This was frustrating for patients as in many cases by the time their appointment had arrived their symptoms had subsided.

> *"things can change so much over a 6 month period by the time I come to the hospital to see them things might have changed dramatically and so something that was really bad 3 months ago is no longer bad" – JD*

> *"Because the things were so snap shotty, it's impossible for people, for three months you could be really ill but the whole care is based on how you were there and then. That's frustrating." – DW*

One participant went to on to describe how this approach made him feel that his experiences weren't believed and that someone *"seeing him ill"* was an important part of validating his experiences. In his case this was friends.

> *"It was like they won't believe I'm ill, I've got one or two friends who have seen me really ill and that kind of helped because they know you're ill. When you're doing that 3 month thing and you're in the middle and you're then being told that you're alright that's quite distressing when you've just have your life turned up side and down. So just realizing that doesn't mean that am not ill but it's good that someone else has seen it." DW*

As a result of this lack of alignment between ill health and delivery of care all participants described an *"ideal"* service which is tailored to the needs of the patient and their current disease state. The tailored service offered in the trial allowed patients to access care when they needed it rather than the prescriptive model of care driven by healthcare professionals currently delivered and this was highly valued by participants. Self-monitoring and initiating their own reviews was recognised as particularly important when they were well and their disease was stable. A majority of participants recognised that if their condition deteriorated, they were experiencing a flare or a laboratory test was considered abnormal, they needed to make contact with their clinical team as a matter of urgency and at that point wanted to have more regular face to face contact with their CNS.

> *"Yeah I mean as long as my results were within the ranges specified, I was quite happy not to see anybody". – AP*

> *"if I had a series of results that showed deterioration that might change things, that's a different thing it's separate from the monitoring, the*

monitoring is one thing the outcome is another so as long as the monitoring and the results are fine then I would imagine things would just continue as they are." – NP

"…saying that my psoriatic arthritis is relatively under control, now if mine wasn't under control I think I might not be saying that. I think I would like, if things weren't under control and I was in pain all the time, related to the arthritis I think I would feel more comfortable seeing someone on a more regular basis….I'm going to be in pain more in that scenario from my arthritis, then I think in fact that's fine, that's what I would expect and that's what they would expect, to see me. But when everything's ok and I get the occasional niggle they don't really need to see people". – PN

Participants also spoke about this need for more appropriate access to the rheumatology team from not only their perspective but also other patients. Participants acknowledge that self-monitoring and initiating their own care could also benefit newly diagnosed patients and established patients who were unwell which they felt was hugely beneficial and important.

"that was pretty much what it was like this morning, which is also a waste of [the nurse's] time. I don't mind but it's a waste of my time as well. [The nurse's] time could be better off seeing people who really need it and there were one or two people in [the clinic] who looked as if they needed to be seen." – PN

"I mean I think this idea for freeing up specialist nurse's time to see people who really need to be seen just seems to be to be incredible important and I think you should press ahead with that" – VH

"I just feel it was really good thing to take part in because it's really worthwhile and if it cuts down unnecessary appointments and frees up appointments so that newly diagnosed patients do not have to wait as

long as I did it to the point where I could not make it and ended up for six weeks in hospital then that can only be a good thing."- JH

Participants also spoke more generally about receiving education and information at the right time. In usual care information and education seemed to come at times when it was not relevant to their needs and they were unable to apply the knowledge to their specific situation. Those with longer disease duration had, however, learnt how to select information that was relevant to them and filter other information out.

"….it's just you can get all the information you want. But until it's applied, it's a little hard to grasp" – AS

"to be honest when I first got the arthritis I just wanted to be pain free and thinking of long term wasn't something that was in my mind I just needed to get better, so now that I am better it's what are the long term issues for me" – EK
"So you seek it out when you get further in to it you know the forest opens up you and know when the information is not going to be of any use to you."- DW

"*The more information you get, at first I read everything I could get my hands on and didn't understand any of it but now I can see what's useful to me and what isn't." – DW*

10.9.2.5.2 Sub-theme - Right method

All participants spoke about the benefits of having direct access to the CNS via telephone, as this provided the "*opportunity to apply for help"* when *"anything was worrying"* them. Despite not seeing the CNS face-to-face, telephone contact was considered equal in regards to the amount of access participants had to their rheumatology team and was, therefore, an acceptability method of both accessing urgent care and undertaking follow-up consultations.

"I did access [the nurse] a couple of times through this period I just phoned her up if there was something on the reading that I needed clarification on. So I've had access, I feel as if I've had as much access to her during that period as I did before and just it's by another method, it's absolutely not necessary for go for special appointments." – EK

"I knew that if I had a problem that if I felt unwell, really unwell then I would phone [the nurse] anyways and I knew I could always speak to her. So I did not feel I was just put in the study and shipped out and left on my own to deal with it I felt there was support there in place for me if I needed it." – JH

10.10 DISCUSSION

The aim of this study was to understand the experiences of the participants who were randomised to the intervention arm of the trial and to explore the value they placed on this new model of care. The overall narrative indicated that participants were positive about the new service, valuing its efficiency and tailored approach. The service enabled knowledge and a sense of control to grow; however, some participants expressed worry and concern about aspects of the intervention. Each of these themes will now be discussed in relation to previous research, the implications of these findings will then discussed in more detail in Chapter 11 in combination with the findings from the overview in Chapter 3 and the quantitative results of the RCT.

10.10.1 Burden of usual care

Participants weighed the advantages of self-monitoring and initiating their own care against usual care. A majority of participants spoke about usual care within the context of being "*a complete waste of time*" with the new service thought to be a more efficient use of their time as well as that of the CNS. This, the patients felt, would enable the CNSs to see more urgent cases such as patients with newly diagnosed arthritis and established patients who were unwell. Many participants described occasions on which they travelled to the hospital for their appointment, often having to take time away from work, waiting in clinic and then to be seen by the CNS for a matter of minutes to be told everything was ok. This patients found frustrating and

reflects the findings of both Mitchell (2000) and Hehir *et al.,* (2001) who found that follow-up appointments for patients with arthritis who are feeling well often result in little or no intervention and are often deemed inappropriate by rheumatologists. The current findings also support qualitative work by Primdahl *et al.,* (2011b) in their trial of shared care. Three months after the implementation of the service for patients with RA, Primdahl *et al.,* (2011b) conducted focus groups with patients who took part in each of the three trial arms. Participants in the shared care setting appreciated the time saved by not having to attend planned consultations and felt relieved they no longer had to negotiate the practical problems experienced when they did have to attend.

Data from the current trial suggests this was particularly salient for people in employment, which may explain why people with arthritis who are employed are more likely to prefer an evening or weekend appointment than those not in employment (Douglas *et al.,* 2005). The difficulties participants reported in terms of managing their arthritis-related appointments and monitoring schedule alongside their work commitments reflects findings from a survey conducted by Gignac *et al.,* (2008). Gignac *et al.,* (2008) found that a significant proportion of patients with arthritis experienced work transitions such as occasional loss of work hours. This was either in the form of interruptions of greater than 20 minutes experienced by 38.2% of patients, taking more than three days absence from work due to their arthritis - experienced by 26.8% of patients and use of holiday for arthritis-related reasons experienced by 9.6% of patients. Although Gignac *et al.,* (2008) did not specify the reasons for these work transitions, it is reasonable to assume given the intensive monitoring of the condition that a proportion of this was due to attendance in outpatients. Gignac *et al.,* (2008) also found that more arthritis-related work transitions were associated with being younger, increased levels of depression, greater workplace limitations such as the ability to get to work and perform work-related activities, and an increased perception of the impact of arthritis on their capacity and goals. Work disability not only constitutes a financial burden for patients and their families and an economic burden for society but has a negative impact on self-esteem (MacKinnon & Miller, 2003) and is associated with poorer quality of life (Chorus, Miedema, Boonen, & van der Linden, 2003). The findings from the qualitative study in this thesis and the survey by Gignac *et*

al., (2008) suggest that it is not just a complete inability to work that may be associated with poor psychological well-being but also frequent interruptions to work life.

10.10.2 The self-management process

One of the only other qualitative studies to explore patients' views of their follow-up care in a trial of a patient-initiated service was that of Sands and Adams (2009). The authors interviewed 12 participants who took part in their comparative pragmatic study. They sampled six participants from the intervention and six from the group who received conventional care. This qualitative study generated four themes, one of which was "provision of information and managing their condition" in which patients described the importance of information provision which enabled them to take control of their symptoms and access their own hospital reviews in times of needs. This theme directly reflects "the self-management process" theme found within the current study which indicated that patients not only valued the information provided in the intervention training sessions but felt that the training increased their knowledge. This they described as enabling them to be a more active participant in the consultation process and gain more control over their health in general and specific aspects of their arthritis including accessing care when they needed to.

This process allowed patients to gain "*ownership*" over their arthritis, an under researched concept in the context of chronic illness (Karnilowicz, 2011). These findings support the work of Winkelman, Leonard and Rossos (2005), a qualitative exploration of how patients with chronic IBD valued internet-based access to their electronic patient records. Winkelman *et al.,* (2005) found that illness ownership was an important part of gaining control over the condition. Having access to their own test results, and explanatory information about relevant laboratory and disease markers promoted illness ownership by allowing patients with IBD to take an active role in managing disease exacerbations and complications, arranging appointments and performing some autonomous decision making.

The findings in the current study also tentatively suggested that behavioural regulation was taking place as a result of patients self-monitoring laboratory results. Participants

were able to see how their behaviour was affecting their blood test results. This included the link between taking their methotrexate and improvements in their inflammatory markers. As well as making a connection between their lifestyle behaviours including alcohol intake, diet and weight and their clinical well-being. This connection provided a basis on which to change behaviour and make healthier lifestyle choices. This self-regulatory process is central to both social cognitive theory (Bandura, 1986; Bandura, 1997) and self-regulation theory (Leventhal *et al.,* 1980); therefore, providing support for the use of these two theories in grounding of this thesis.

10.10.3 Conflict

This study found that frustration and confusion arose when there was conflict between laboratory tests and the participant's experience of symptoms, for example the presence of intense pain and swelling in the absence of elevated inflammatory markers. Research has demonstrated discordance between objective and subjective measures of functional disability (van den Ende, Hazes, Le Cessie, Breedveld, & Dijkmans, 1995) and hand function (O'Connor *et al.,* 1999) in RA and it is now well established that the association between subjective reports of pain with radiographic damage are modest at best (Sarzi-Puttini *et al.,* 2002). This discordance has been linked to both psychological and social determinants of the illness experience, reflected in development of the bio-psychosocial model of chronic illness. Nevertheless, this lack of relationship confused and frustrated patients suggesting that these relationships have not been adequately communicated. This corresponds to the findings of Winkelman *et al.,* (2005) that suggested when the reality of living with IBD was not captured in laboratory tests or consultant reports patients found it difficult to recognize their illness experience represented in the records and hence the record became meaningless to the patient and as a result, less useful. In the context of the current trial this may mean that patients placed less value on the meaning of their blood test results when they did not correspond to how they felt, which is supported by the views of one patient who felt that his CRP test was *"useless"* as it did not reflect his symptoms.

The legitimization and validation of the fluctuating nature of arthritis was viewed as an important factor. Patients felt their symptoms were validated when there was

consistency between symptoms and laboratory tests. Validation focuses on expressing acceptance of the patient's experience as being real and "valid" without judgment (Epstein *et al.,* 2005; Epstein *et al.,* 2006). Legitimization of symptoms is acknowledged as important part of the diagnosis of arthritis (Undeland & Malterud, 2007; Brand, Claydon-Platt, McColl, & Bucknall, 2010) but has not been explored to the same extent in the experience of patients with established arthritis beyond diagnosis. Being *"seen"* during a flare was important to the validation process, which wasn't occurring when hospital reviews were taking place at inappropriate times. Main, Buchbinder, Porcheret and Foster (2010) recognized that in primary care one of the main reason for patients seeking helping is legitimization of symptoms and in order to maximise the effectiveness of the consultation this should be acknowledged from the outset. Validation of pain in particular appears to be important to psychological well-being (Linton, Boersma, Vangronsveld, & Fruzzetti, 2012) and is, therefore, key to our understanding of arthritis since this is the most frequently reported symptom (Carr *et al.,* 2003). Employing more validating responses has been associated with greater positive affect and less worry in patients (Linton *et al.,* 2012) and hence could have been used during any communication between the CNS and patient to address the frustration and confusion people felt in relation to the conflict between laboratory tests and symptoms. By providing a service which allows patients to access care at the time they need it could also overcome some of these frustrations as control is placed back in the hands of the patient who can then contact services during a flare and hence receive the validation they require.

10.10.4 Anxiety

The current study found that a number of participants experienced worry and anxiety about being given full responsibility for monitoring their blood test results. Slight increases in anxiety have been found in quantitative evaluations of patient-initiated services (Hewlett *et al.,* 2000), although not statistically significant. It is, therefore, important to recognise that access to laboratory results could negatively impact upon mood. Whilst this has been attributed to a lack of understanding about abnormal readings (van der Vaart *et al.,* 2013; Peel *et al.,* 2004) it could also reflect a clear understanding and genuine concern about the underlying advancement of the condition.

10.10.5 A tailored service

All interviews contained an underlying narrative that reflected the patients need to be able to access a rheumatology service which was tailored to their current needs. There was an incongruence between usual care which was directed and dictated by the healthcare professional and the *"ideal service"* in which they could access services in times of need and not need to be reviewed when they were feeling well. This desire for personalised care was also expressed in relation to information provision and being given information at relevant times rather than just at diagnosis which was an already complex time or sporadically throughout the disease course. As a result of the untimely nature of information provision, patients felt that they had become apt in filtering out irrelevant information. It was also important to participants that they were able to access the CNS via the most convenient method and a majority of patients felt that the nurse helpline and telephone consultations were an acceptable model of care. This service enabled them to seek help at appropriate times and quickly. Hence supporting for the findings of Pal (1998) and Hennell *et al.,* (2005), who both found high levels of patient satisfaction with rheumatology telephone follow-up clinics held by CNSs, and that the advantages of saving time and money, less stress and greater convenience outweighed the disadvantages.

10.11 STRENGTHS AND WEAKNESS OF THE STUDY

In all research settings there are issues of power between the researcher and participant and this can be particularly problematic in qualitative research which has the potential to magnify these issues due to the close intense nature of the data collection process. In the context of this study there is potential for bias as the interviewer also delivered the intervention which raises concerns about social desirability and researcher bias. Social desirability occurs when respondents give the answers that they believe the researcher wants to hear (Stevenson, Britten, Barry, Barber, & Bradley, 2000). In the context of the current study this may have led participants to be wary of reporting anything that might appear critical of the intervention, as it may have been perceived as a criticism of the researcher. Although some qualitative researchers consider their interviewees as collaborators (Collins, Shattell, & Thomas, 2005) the direction of the interview is most certainly steered by the interviewer who decides what particular part of the participant's answers to

pursue (Rapley, 2001). Hence it is possible that the researcher was able to bias the results of the study by actively pursuing and encouraging dialogue which suggested a more positive response to the intervention. This would have been overcome to a certain extent by the interview guide, along with making a conscious effort to explore all avenues not just those which were positive. The fact that the analysis reports both positive and negative aspects of the service supports this latter hypothesis.

A sample of 12 participants were interviewed as part of this study which could be criticised as being too small to be generalizable. The sample were, however, diverse in their age, disease duration and length of time on methotrexate, as well as being a mix of genders and disease types. Qualitative research, however, aims for conceptual rather than statistical generalizability (Stevenson *et al.,* 2000). Therefore, the focus is to draw inferences from one setting to another rather than on the statistical representativeness of the sample.

The clearly outlined phases in thematic analysis provided rigour to the study and the four validity checks undertaken, including providing detailed quotes from the participant's transcripts to support the interpretation offered, a proportion of the transcripts being analysed by an independent auditor to confirm the pattern of analysis and the overall results and discussion being reviewed by the supervisory team increased the validity of the study. In addition the researcher kept a reflective diary in an attempt to understand the role they played in directing the interviews and understanding the transcripts which was used during the analysis.

10.12 SUMMARY

The aim of this study was to understand the experiences of the participants who were randomised to the intervention arm of the RCT and to explore the value they placed on the rheumatology outpatient service they experienced. The overall narrative indicated that participants were positive about the new service, valuing its efficiency and tailored approach. The service allowed patients to gain new knowledge and use this information along with the skills they obtained to take control of their health and arthritis. For some participants, however, there were feelings of conflict and anxiety, which concerned participants and would need to be addressed prior to any

widespread implementation of the service. The following chapter will now bring together these findings, along with the results of the overview in Chapter 3 and RCT in order to discuss the areas of new knowledge and the implications for research, theory and practice.

CHAPTER 11 - OVERALL DISCUSSION

11.1 PROLOGUE

This final chapter considers the results of the literature review and overview of reviews reported in Chapters 2 and 3, and the quantitative and qualitative findings of the RCT and qualitative study reported in Chapters 6 to 10, in order in provide an understanding of the findings of this thesis. The overall aims of the thesis will be discussed in relation to how the studies make a novel contribution to the literature. The chapter will conclude with a discussion on the recommendations for future research and practice along with the overall strengths and weaknesses of this thesis.

11.2 THESIS AIMS

This thesis sought to establish whether a self-monitoring and patient-initiated service for patients with RA or PsA on methotrexate could be effective in reducing healthcare utilisation, improve psychosocial well-being as well as being acceptable to patients. The specific aims of this thesis were:

- To establish the current evidence for patient-initiated services in rheumatology in comparison to other models of care.
- To understand the benefits, to healthcare utilisation and psychosocial well-being, of formal self-monitoring across a range of long-term conditions.
- To design a self-monitoring and patient-initiated service that could be delivered in rheumatology outpatients.
- To evaluate the effectiveness and safety of the intervention in relation to usual care.
- To identify the mediators and moderators of intervention effectiveness.
- To establish patient acceptability and the value placed on this model of care.

11.3 NOVEL CONTRIBUTIONS TO THE LITERATURE

This thesis has led to a number of novel contributions to the literature, specific findings in relation to previous research have been discussed in greater detail within Chapters

7, 9 and 10. This section aims to bring the contributions made by the research in this thesis together and highlights the distinctness of the findings.

11.3.1 Novel intervention

This intervention drew on the evidence base derived from evaluations of patient-initiated services in rheumatology and the broader self-monitoring literature in other long-term conditions. As a result, this thesis presents the first attempt either in research or service redesign to involve patients with arthritis in the monitoring of their own blood test results. In addition, although many of the interventions presented in section 2.5.6.1 (page 82) are described as "patient-initiated" services, the majority included an element of shared care with the GP. This intervention is, therefore, one of very few studies which has not integrated primary care services into this model of care and is, therefore, truly patient driven. Consequently, both the quantitative and qualitative findings from this thesis represent the first evaluation of effectiveness and acceptability of this model of care. In addition, use of a concurrent embedded experimental mixed methods design and within that, novel statistical techniques in health psychology (Marques & Hamilton, 2014), underlies the unique approach adopted in this thesis.

This model of care led to clear reductions in healthcare utilisation in relation to CNS outpatient visits and arthritis-related GP appointments. These, in combination, led to statistically significant reductions in overall healthcare utilisation, despite no changes in visits to the rheumatologist. The results in relation to economic benefits were, however, less persuasive. This could in part be due to the post-hoc nature of the analysis, which meant the study was not powered to find an effect on this outcome, but also because of the lack clarity in how elements of service delivery should be accounted for. This issue has been fully discussed in section 9.2.2 (page 311). Importantly there was no negative impact on clinical or psychosocial well-being as a result of taking part in the intervention. The results of this study in relation to previous research have been discussed at length in Chapter 9. In summary, these findings reflect those of other evaluations of patient-initiated services in rheumatology, particularly in relation to reductions in healthcare utilisation (Hewlett *et al.,* 2000; Hewlett *et al.,* 2005b; Kirwan *et al.,* 2003b; Adams & Sands, 2009; Chattopadhyay & Hickey, 2008)

and no significant detrimental effect on clinical or psychosocial well-being (Kirwan *et al.,* 2003b; Hewlett *et al.,* 2005b; Primdahl *et al.,* 2012; Primdahl *et al.,* 2014; Adams & Sands, 2009; Sands & Adams, 2009).

11.3.2 Mechanisms of effectiveness

This is the first trial of patient-initiated services which has explored, using appropriate analytical techniques, the mechanisms of effectiveness. Under more traditional methods of testing mediation the lack of effect of the intervention on consultant visits, arthritis-related GP visits and quality of life would have precluded an investigation of mediation. More contemporary methods of mediations analysis, however, such as those used within this thesis, state that the existence of an effect of the intervention on the study outcomes is no longer necessary for mediation to be possible (Collins *et al.,* 1998; Hayes, 2009).

The analysis, however, identified no significant mediating variables indicating that the intervention was having no effect on quality of life, consultant visits or arthritis-related GP visits either direct or indirectly. The significant impact on CNS outpatient visits was, therefore, a direct effect of not having any pre-scheduled appointments. A number of moderators were identified suggesting that female participants, those with poorer mental health-related quality of life, poorer knowledge about methotrexate, lower haemoglobin levels and higher ESR at baseline would benefit more from the intervention (i.e. used less health services and had better quality of life post intervention) than control group. Those with poorer self-efficacy for active communication at baseline, however, experienced better quality of life if they were allocated to the control group.

By identifying moderators of the intervention this provides useful information on the type of patient who may benefit more from a self-monitoring and patient-initiated service and those who would benefit more from remaining within standard care. This information has two potential uses, the first and most obvious is identifying which patients are likely to be more responsive to this new model of care and could, therefore, be used to guide referrals into the service. The second is to help guide researchers in the best choice of inclusion and exclusion criteria for future evaluations

(Kraemer *et al.,* 2002). As the study was not powered for mediation or moderation analysis however, these findings should be considered as hypothesis generating.

11.3.3 Predictors of help-seeking

An important element of establishing whether patients could safely monitor their own blood tests results was to establish the accuracy with which they made decisions about contacting the CNS. The results from this thesis indicated that, with training, participants were able to make safe help-seeking decisions, and this improved over the trial period. There were, however, a small proportion of patients who were unable to self-monitor safely and these participants returned to standard care according to criteria defined in the study protocol. The findings of this thesis provides unique insight into the drivers of appropriate help-seeking, under experimental conditions, and identified that rather than symptoms or clinical status being associated with help-seeking, self-efficacy played an important role, as did age and the presence of co-morbidities.

Little is known about help-seeking in patients with established arthritis. Much of the literature has to date focused on help-seeking during the initial phases of the disease, and the delay found in reporting symptoms to a healthcare professional prior to diagnosis (Stack *et al.,* 2012). Outside of experimental conditions patients with arthritis seek help when they become more certain that they are experiencing a disease flare often after a number of failed self-management attempts (Hewlett *et al.,* 2012). It appears that patients during this process either decide to access services early in a flare in order to stop symptoms having a more serious and widespread impact on their life or they wait in the belief that they may be wasting the medical team's time (Flurey, 2014). This thesis extends this model by suggesting a possible role of self-efficacy, specifically in relation to patients' confidence in communicating with their rheumatology team and their ability to self-manage.

The findings presented in Chapter 7 suggest that the more confident participants were about self-managing their arthritis and the less confident they were about communicating with healthcare professionals the more safe help-seeking decisions they made. As these findings are within the context of an experimental study which

aimed to manipulate help-seeking behaviour it is difficult to compare them to the work of Hewlett *et al.,* (2012) and Flurey (2014), particularly as the intervention failed to increase self-efficacy over time. These results could, however, suggest that seeking help is considered an element of self-management rather than as a consequence of failed self-management attempts as suggested in the model by Hewlett *et al.,* (2012). Hence when someone is more confident about their ability to manage their arthritis they are able to seek help more appropriately. It could also indicate that the intervention gave patients who were less confident about communicating with their rheumatology team with a structured approach to seeking help and clear guidelines on the triggers for contacting the CNS. In this interpretation although the intervention did not improve self-efficacy for communication it gave the participants the "permission" they needed to make contact, without fear of time wasting. These explanations are, however, purely speculative and do require further exploration.

11.3.4 Conceptualisation of self-monitoring

By synthesising the evidence in relation to self-monitoring, across a range of long-term conditions, the overview of reviews presented in Chapter 3 has provided the basis for a schematic representation how self-monitoring is implemented within these interventions. This conceptualisation recognises that self-monitoring interventions run on a continuum from less patient involvement to those in which patients are full and active participants in the monitoring and interpretation of their data and making of autonomous decisions to adjust their lifestyle and treatment plans. This latter intervention can be defined as purely patient self-management, according to Barlow *et al.,* (2002) and the former clinical monitoring. The common thread between them is their aim to change behaviour, and both target similar outcomes i.e. clinical or psychosocial well-being, and/or healthcare utilisation.

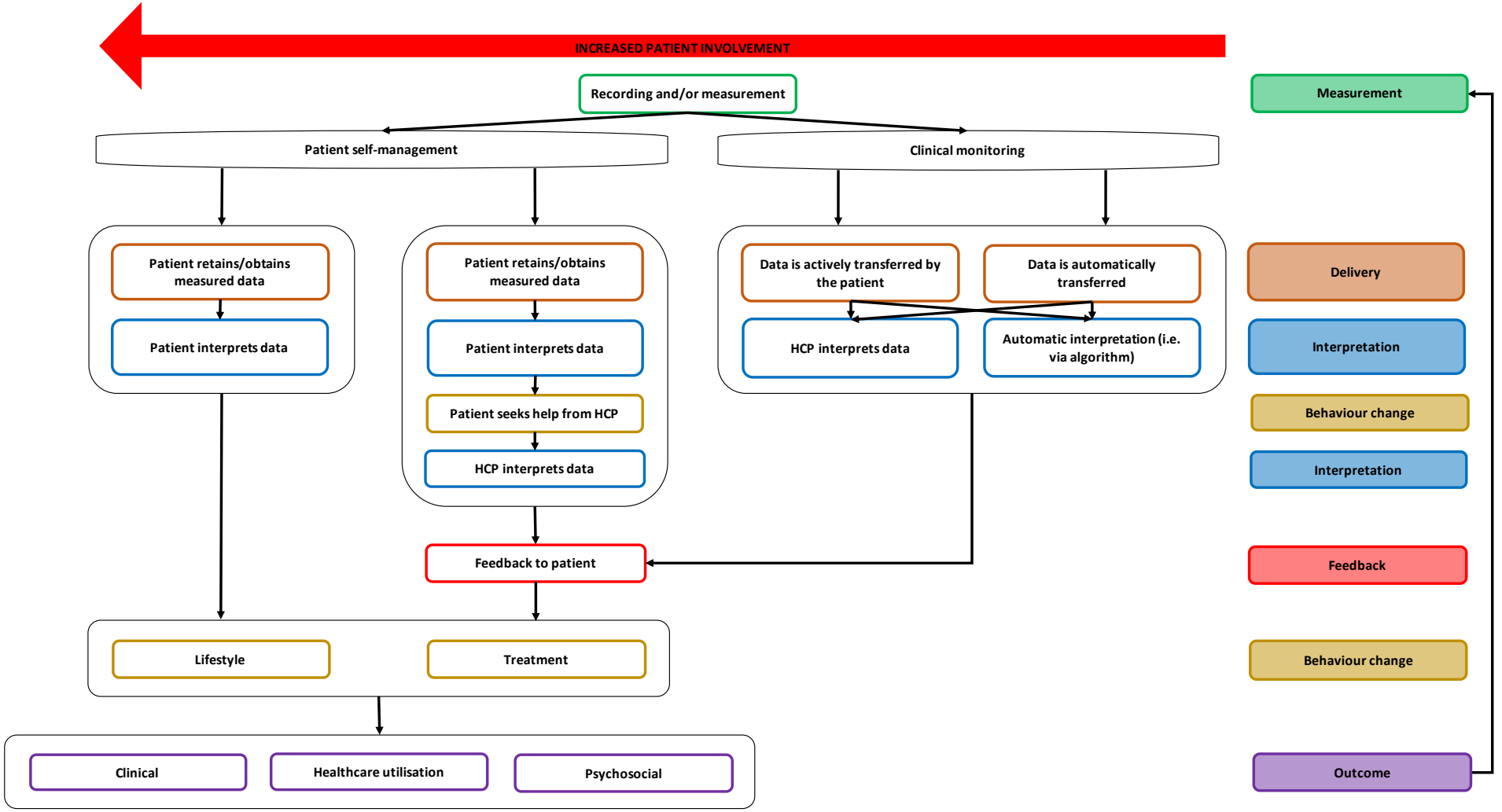


Figure 11.1. A schematic representation of self-monitoring interventions in long-term conditions

However, those that are patient-self-management directly target the behaviour of patients whilst the latter initially aim to change the behaviour of healthcare professionals by enabling tighter disease control but make either an explicit or implicit assumption that patient behaviour will need to change in order for outcomes to improve. Other self-monitoring interventions, including the one evaluated within this thesis, lie somewhere in the middle of these two approaches, whereby patients use their monitored data to make decisions about help-seeking in accordance with pre-defined clinical criteria. Healthcare professionals then make the decisions to change either a treatment plan or lifestyle behaviour, but again this assumes that patients then make these recommended changes.

This conceptualisation provides a structure in which interventions that include patient self-monitoring can be classified, evaluated and synthesised, and also provides a clearer understanding of the mechanisms through which these intervention may affect outcomes. The results from the overview of reviews and this schematic representation could provide an alternative explanation for why the current intervention failed to change psychosocial outcomes. Participants randomised to the intervention arm in this thesis were required to seek help from their CNS who then made all decisions in regards to any necessary lifestyle or treatment changes. The inability of participants to make autonomous decisions about lifestyle and treatment changes may have hindered the effects of the intervention on psychosocial outcomes as patients still heavily relied on the rheumatology team to manage their condition.

The distinction between these three types of self-monitoring interventions is not well represented in the literature. These interventions have often been grouped together in systematic reviews making a synthesis of their effectiveness difficult, as evidenced in Chapter 3. The conclusions of the overview of reviews in this thesis, however, proposes that there may be additional clinical and psychological benefits to self-monitoring untaken in the context of patient self-management as opposed to clinical monitoring. Allowing patients with a long-term condition to make autonomous decisions about necessary treatment and lifestyle adjustments may empower patients to implement and adhere to these behaviours. In contrast adjustment decisions made by a healthcare professional may allow for a more passive patient and lead to

comparatively poorer outcomes due to a lack of awareness between behaviour and outcome. Anti-coagulation therapy appears to be the only chronic condition to have made this clear distinction, and have hence designed and evaluated interventions in order to compare these two distinct conceptualisations of self-monitoring, but with somewhat mixed results (for a full discussion see section 3.7.4, page 155). Only more recently has this distinction been recognised in diabetes (Ng *et al.,* 2013), which is particularly surprising given that SMBG is part of standard care in diabetes management (National Collaborating Centre for Chronic Conditions, 2008). It was not possible in the overview in Chapter 3 to distinguish between these types of intervention; hence further work would need to be conducted to test this hypothesis.

11.3.5 Behaviour change theory

This is one of the first studies under the umbrella of chronic disease self-management to utilise the recently published behaviour change taxonomy (BCTv1) (Michie *et al.,* 2013) to describe the content of the active intervention and is certainly the first within patient-initiated services to do so. The intervention contained a total of 13 behaviour change techniques that can be directly linked to social cognitive theory (Bandura, 1997) and self-regulation theory (Leventhal *et al.,* 1980). By defining the current intervention in terms of behaviour change techniques this has identified the active ingredients within the intervention, which will allow for easier replication of the study (Michie & Johnston, 2013). It is, however, important to recognise that the behaviour change techniques contained within the current intervention could be techniques that are delivered within standard care, along with other behavioural strategies. The effects of the intervention, therefore, cannot be attributed to these techniques until the content of usual care is assessed in accordance with the BCTTv1; however, this was outside of the scope of this thesis.

11.4 SYNTHESIS OF THE QUANTITATIVE AND QUALITATIVE FINDINGS

The following section will present the primary similarities and differences between the results of the RCT and qualitative study in order to establish the degree to which triangulation of study findings were achieved. Triangulation is one of the primary benefits of a mixed methods approach and is discussed in more detail in section 11.7

(page 389). As well as providing an opportunity to cross-check data from multiple sources, mixed methods research brings to light inconsistencies in the study data. Embedding a piece qualitative research nuanced the findings of the RCT and provided valuable insights into participants' perceptions of the benefits of this model of care.

11.4.1 Acceptability

As monitoring of laboratory results is a novel activity for patients with arthritis there was some uncertainty about whether patients would find this model of care acceptable. Acceptability was assessed in a number of ways in this thesis including uptake and drop-out rates, reasons for refusing participation and the findings from the qualitative study. These sources indicated a mixed picture in terms of the acceptability of this model of care for patients with RA or PsA on methotrexate. This supports the rhetoric of Trappenburg *et al.,* (2013) who highlighted that a "one size fits all" approach to helping patients manage their chronic illness is not appropriate and, therefore, consideration must be made to those who would prefer the more traditional model of care.

This thesis found uptake rates of approximately 60%, reflecting the findings of Hewlett *et al.,* (2000; 2003b; 2005b) and van der Vaart *et al.,* (2011); significantly higher than Primdahl *et al.,* (2012; 2014) who had a 26% response rate. The current trial found that around 30% of those approached to take part preferred the more traditional system of having regular scheduled visits to the CNS. Of the 63% who consented into the study, 22% failed to enter the trial despite consenting to take part. There was, however, no difference between the intervention and control group on drop-out rates at this point, indicating that it was not necessarily the intervention itself but possibly the research in general which was unappealing. Despite 30% preferring face-to-face contact with their CNS, once in the trial, participants were committed to this model of care. This was evidenced by the responses of those who took part in the qualitative interviews and the fact that no intervention participants requested to return to usual care and in fact were disappointed at the end of their participation in the trial. The qualitative narratives indicated that overall participants were positive about the new service, valuing its efficiency and tailored approach. In comparison to usual care it was deemed "*much more convenient"* and *"less burdensome"* and allowed them to develop self-

management strategies, which patients valued, such as increased knowledge and a sense of control. Overall this suggests that a majority of patients with RA or PsA on methotrexate may deem this model of care acceptable and could, therefore, be a suitable way in which patients could be followed-up.

11.4.2 Treatment burden

Disparate findings were evidenced in relation to treatment burden. Whilst the RCT failed to find any statistically significant differences between the intervention and control group on treatment burden, participants in the qualitative study emphasised the burden of usual care and described this new model as a more efficient use of their time. The self-report measure of burden used within the RCT was, however, a one-item general measure of treatment burden, which participants could have conceptualised as meaning medication rather than the care they received in outpatients. Greater specificity in the quantitative measurement may have led to more consistent findings between the qualitative and quantitative findings. Another possible explanation is that participants saw this concept as being on a continuum from burdensome to convenient, but the quantitative measure failed to capture this full spectrum.

11.4.3 Time and cost saving

The results of the RCT suggested that a significant proportion of outpatient visits made to the CNS-led DMARD monitoring clinic may not be necessary. Fifty-five percent fewer appointments with the CNS in the intervention compared to control group suggests that even when abnormal blood tests or symptoms do occur they can be sufficiently addressed in a telephone consultation rather than face-to-face visit. The time saved by healthcare professionals and patients evidenced in these quantitative findings, were corroborated by patients in the qualitative study some of whom described usual care as a "*complete waste of time*".

> *"it just seems to be more efficient use of everybody's time, mine, [the nurse's] and why should the hospital need to bother with an appointment for something that is really straight forward" – NP*

Telephone contact was considered equal in regards to the access participants had to their rheumatology team and was, therefore, an acceptable method of both accessing urgent care and undertaking follow-up consultations.

> *"I knew that if I had a problem that if I felt unwell, really unwell then I would phone [the nurse] anyways and I knew I could always speak to her. So I did not feel I was just put in the study and shipped out and left on my own to deal with it I felt there was support there in place for me if I needed it." – JH*

The results of the RCT with regards to cost-effectiveness were mixed dependant on the model evaluated and the level at which the cost was estimated (i.e. lower, mean, upper limit). There was, however, potential for this service to be cost saving for the health service and this was also reflected by patients in the qualitative interviews. Regular reviews with the CNS were described as *"coming at a cost"*, both in terms of being a waste time or not a valuable use of time due to little changes to treatment, but also financially as a result of missed work. The findings of the RCT do, however, indicate that agreement needs to be reached on how telephone contact with patients is costed and integrated into the CNS role. In addition a full cost analysis with indirect as well as direct costs may have provided a more complete picture of the benefits described by patients in the qualitative interviews.

11.4.4 Knowledge

The qualitative data suggested that patients felt that the intervention increased their knowledge and gave them greater control over their arthritis and its treatment. This enabled them to feel more involved in the consultation process and change their lifestyle behaviours accordingly.

> *"And so, you know, if I could be involved with this and also that it was a little bit with more, you know, taking kind of control and understanding, you know, more involved what was actually going on rather than going off and getting tests done and not knowing what it means, and waiting for someone to tell you that everything is OK." AS*

Despite this qualitative evidence, the quantitative findings found only a very small non-significant increase in participants' knowledge about methotrexate. The following quote could shed light on these conflicting results.

> *"I did enjoy because it gave me an insight into what the hieroglyphs were that I was getting for my blood tests and now I know what to look for. You know and the ranges, if my bloods are in certain limits" – AP*

The knowledge scale utilised within the trial evaluated knowledge specific to methotrexate and although the training session presented information about methotrexate and its side effects it appears possible from this quote that the knowledge improvements spoke about by people in the qualitative study were associated with the specifics of laboratory results rather than a broader understanding of methotrexate.

11.4.5 Conflict between study and CNS criteria

The results from the RCT revealed that all participants made some errors when monitoring their own blood test results and symptoms, often choosing not to contact their CNS when their results were either outside of the specified range or had changed significantly since their last blood test. The qualitative data illuminated this issue and provided a possible explanation for these findings.

A number of the participants who took part in a semi-structured interview reported an internal conflict between the criteria outlined in the study protocol and the less stringent criteria implemented by the CNS during their telephone consultations.

> *"I knew there would be some ambiguity and there was because every time I have a blood test done almost invariable there is something that's out of range and I am kind of familiar after all these years of how [the nurse] would view it and so minor changes or the minor breaches of the limit, I know they are not something to get terribly het up about. There were one of the two times when I thought do I need to bother her about because I knew she would view it as something important." – VH*

Participants felt that it was important that these criteria were aligned and this was identified as an important area for improvement if the service was to be implemented. If this issue was addressed some participants felt that this could lead to further reductions in the number of telephone consultations required.

> *"Just one thing I'm just remembering what we had to look for and what variances we had to look when I rang [the nurse] a couple of times on changes she would say, you were using too low a benchmark for when someone needed to ring her because every time I phoned her she was like no no that's fine you don't need to worry. So I think they would need to be some kind of liaising with the nurses about changing those benchmarks. A couple of times that happened. And she was like no no that's fine. That's not a worry. So if that changed that would prevent as many calls to the nurse."- EK*

11.4.6 Communication between patient and rheumatology team

Patients' confidence in their ability to communicate with their rheumatology team was both a predictor of appropriate help-seeking and was a significant moderator of the effect between trial arm and patients' post intervention quality of life. The qualitative data elaborated on these findings and suggested that patients valued legitimization of their symptoms and that this was primarily found when laboratory results were congruent with the symptoms they experienced but was also achieved when patients were "*seen"* during a flare or when the fluctuating nature of their arthritis was validated during the consultation process. The importance of good communication between the rheumatology team and patient has be found to be important part of the consultation process (Thorne *et al.,* 2004) and legitimization of symptoms is not only central to that process but a significant driver of help-seeking (Main *et al.,* 2010).

11.4.7 Anxiety

Whilst the RCT found no statistically significant differences in levels of anxiety between the intervention and control group overtime, the qualitative interviews revealed that some participants experienced anxiety and worry about self-monitoring whilst others were not concerned. In fact the estimated marginal means indicated that participants

in the intervention group experienced a small decrease in anxiety overtime and the control group an increase. These contradictory findings support the conclusions of the systematic review presented in Chapter 3 which found that many articles were unable to make definite conclusions about the impact of self-monitoring on anxiety as some primary research studies found significant improvements whilst others failed to find any effects.

There could be a number of explanations for the contrasting findings found within this thesis. The most obvious is that the study was not powered to find an effect for anxiety, although the use of MLM allowed for trajectories of change to be estimated within a participant rather than pooled at a group level, therefore, individuals were represented more accurately within the statistical model. Nevertheless it is likely that there was a combination of people within the intervention group who experienced a decline in anxiety, stability or an improvement across the trial period, as demonstrated by the mixed responses of those within the qualitative study.

Another possible explanation relates to the RCT measuring generalised anxiety whilst those in the qualitative study were reflecting on anxiety specific to self-monitoring. So whilst generalised anxiety may have improved over time, this does not necessarily mean that anxiety specific to self-monitoring would follow the same pattern. It is, however, important to acknowledge that the anxiety and concern expressed by participants in the qualitative could be a legitimate concern about a deteriorating disease state.

Although anxiety was thought to be a possible moderator of the effects of the intervention in the qualitative study:

> *"Yes and I think some people would find it difficult to cope with if they had a rather nervous disposition or [if they were] a worrying sort anyway" – RG*

The results of the RCT did not demonstrate that anxiety moderated the relationship between trial arm and either healthcare utilisation or quality of life. Anxiety did,

however, mediate the relationship between trial arm and quality of life, suggesting that participants who experienced a greater decline in anxiety over the trial period reported higher levels of quality of life at final follow-up.

11.5 RECOMMENDATIONS FOR FUTURE RESEARCH

There are a number of clear avenues for research which have been identified from the results of the RCT and qualitative study, as well as the literature review and overview of reviews found within Chapters 2 and 3 of this thesis. Each of these will now be discussed in order of their appearance within the thesis, and not in order of importance.

11.5.1 Community-based rheumatology services

Given the current Government's desire to shift hospital-based care of long-term conditions into the community, there is a need to establish the best way in which this can be delivered and a sufficient evidence base to suggest that it is at least equitable to current standard care, if cost savings are demonstrated. The literature review presented in section 2.5.4 (page 74) suggests that there is a lack of methodological robust evaluations of GP-led and community based rheumatology services within the UK. The evidence that is presented suggests neither an equitable or beneficial effect for the patient or health service. The publication of a systematic review would be beneficial in order to establish more thoroughly the evidence base, including a formal evaluation of study quality. The literature review in section 2.5.4 (page 74) does, however, suggest that more robust RCTs need to be conducted in order to establish the effectiveness of community led rheumatology services in comparison to specialist-led care.

11.5.2 Self-monitoring in long-term conditions

As the articles included in the overview of reviews in Chapter 3 suffered from poor reporting it was not possible to establish whether self-monitoring was taking place in the context of self-management or purely as a tool for clinical monitoring. As acknowledged by Ng *et al.,* (2013) and Clar *et al.,* (2010) it is important to establish whether self-monitoring which takes place within patient self-management has

differing effects on clinical, psychosocial and healthcare utilisation in comparison to interventions which use self-monitoring as a clinical tool. This could be achieved by classifying the 321 primary research studies identified within the overview of reviews according to the three types of intervention conceptualised in Figure 11.1 and assessing whether these different interventions lead to differing effects.

11.5.3 Predictors of help-seeking in established arthritis

Given that self-efficacy for self-management and communicating with healthcare professionals appeared to play an important role in the ability of patients to appropriately seek help from their specialist nurse, future research would benefit from exploring how these factors impact on help-seeking outside of experimental conditions. There is generally a lack of research exploring help-seeking in established arthritis. Building on the findings of this thesis and the work of Hewlett *et al.,* (2012) and Flurey (2014), a longitudinal study to explore predictors of help-seeking in RA would be a valuable contribution to the literature.

11.5.4 Acceptability from the healthcare professional perspective

Although the intervention was successful in reducing healthcare utilisation and had the potential for economic benefits to the health service more generally, the thesis failed to explore this model of care from the perspective of healthcare professionals in rheumatology. This service could have implications on the role of the CNS, in terms of their identity within the rheumatology team and a possible change in work load and the manner in which they work i.e. a transfer from face-to-face to telephone consultations. It would be important to explore the experiences of the CNSs who were part of the research team to understand their views and acceptability of the service and that of the rheumatologists within the wider team. This could provide important information on the value placed on this model of care and the likelihood and manner in which it may be integrated into standard care. A general understanding of the views of healthcare professionals in rheumatology and those commissioning services within rheumatology on this model of care would also shed further light on the potential for implementation.

11.5.5 Overall lack of literature on PsA

This thesis was focused on patients receiving methotrexate and, therefore, those with RA were assumed to experience similar symptoms and side effects to those with PsA, and were not expected to have different outcomes in relation to the intervention. This was confirmed in both the quantitative and qualitative findings. A general finding from this thesis, however, was a distinct lack of literature relating to patients with PsA, from a lack of prevalence estimates in the UK, through to the design of interventions to enable patients with PsA to self-manage their condition. Although the incidence rate of PsA is significantly lower than that of RA the combination of both arthritis and psoriasis brings with it the complexities of managing both conditions, from both a clinical and psychological perspective. Hence future research would benefit from exploring the impact of this condition and how formal self-management programmes could help patients adjust to the psychosocial effects of both the skin condition and arthritis.

11.6 RECOMMENDATIONS FOR PRACTICE

There are a number of important issues when considering whether a new model of care should or could be implemented in practice, this includes its impact on the clinical and psychological well-being of patients and staff, the implications to the health service including healthcare utilisation and economic impact, and the acceptability of the intervention from a patient and healthcare professional perspective. Individually these issues have been discussed in relation to the strengths and weakness of each study in section 9.3 (page 330) and section 10.11 (page 368).

An intervention of this nature would contribute towards Domain 4 of the NHS Outcomes Framework (Department of Health, 2013f) which looks to ensure that patients have a positive experience of the care that they receive in outpatients. Implementation of the service in UCLH, however, would require careful consideration as a consequence of changes in usual care at UCLH since the start of this thesis. As highlighted in section 2.6 (page 93) in 2013 NHS Camden CCG, the local CCG for UCLH, published their key interests. One of these was to ensure that patients were seen in the appropriate setting of their choice in a timely manner whilst ensuring that best value for money is achieved (Camden Clinical Commissioning Group, 2013). Since the completion of the RCT more concerted steps have been taken to move the monitoring

of DMARDS from the CNS-led rheumatology clinics held at the hospital to individual GPs.

Although at the start of this thesis UCLH had shared-care guidelines which included GPs (Appendix A) an overwhelming majority of GPs refused to take on these additional responsibilities. Despite this resistance, the CNSs running the hospital based clinics are now being asked to refer patients with arthritis on a stable dose of methotrexate back to their GPs for ongoing monitoring. Anecdotal evidence suggests this has not been welcomed by patients, although more formal evaluation needs to be conducted. This does not necessarily mean that the model of care evaluated within this thesis could not be implemented, but the views of GPs would also need to be considered carefully as their commitment to any change would be critical. There would also need to be greater clarity on how future services are likely to run in order to understand how a self-monitoring and patient-initiated service could be integrated within the planned framework. This would make the service evaluated by Hewlett *et al.,* (2000; 2003; 2005) and Primdahl *et al.,* (2012; 2014), which was a shared-care approach between the patient, GP and rheumatology team, a more applicable option; with the additional element of patients monitoring their blood test results as well as their symptoms and side effects. Any implementation would need to consider the triggers for patients contacting the service, so that discrepancies did not occur between the service protocol and the views of the healthcare professionals administering the telephone consultations. This discrepancy identified within the current trial caused some confusion and potentially led to mistakes being made by the patient about when to make contact.

Although the RCT identified potential mediators and moderators, and hence the mechanisms of action and type of patient who may benefit more from the intervention. These results are at present considered to be hypothesis generating as the study was not powered adequately to identify all possible moderators and mediators. Therefore, offering the service to only those patients in which it appeared to be more beneficial would at this stage be inappropriate as this question requires further research.

The findings from the RCT and qualitative study suggest that the ability and confidence patients have in communicating with their rheumatology team plays an important role in their help-seeking behaviour and quality of life. This highlights a wider issue about healthcare professionals' communication styles and the possibility of previous encounters affecting patients' future help-seeking behaviour (Stack *et al.,* 2012). Therefore, healthcare professionals in rheumatology should be aware of how they interact and communicate with their patients, particularly in regards to the legitimization and validation of the fluctuating nature of arthritis which is important to patients and could have a potential impact on their reluctance to contact health services in times of need.

11.7 STRENGTHS AND WEAKNESS

The strengths and weakness of each study have been discussed in their respective chapters. The primary weaknesses being the lack of power, the number of statistical tests performed, ecological validity, social desirability and lack of a full health economic evaluation. The primary strengths of the trial include the robust study designs and analytical techniques; however, the overall strength of this thesis lies in its mixed methods approach. The concurrent embedded experimental strategy, whereby the quantitative and qualitative data collection were collected at the same time but with the RCT as the predominant study (Curry *et al.,* 2013) addressed a number of the benefits of mixed methods research as outlined by Doyle *et al.,* (2009). These benefits will now be discussed within the context of this thesis.

- Triangulation – Methodological triangulation indicates that two research methods have been used in order to check the overall conclusions of a study (Denzin, 2006). The idea is that one can be more confident with a result if different methods lead to the same conclusions. By seeking corroboration between quantitative and qualitative data this thesis has increased the validity of the findings. The embedding of the qualitative study within the RCT has highlighted both similarities and differences between the effectiveness of this intervention each of which have been discussed in section 11.4 (page 378). Synthesis of the results from the two methodologies has highlighted a number

of consistent findings particularly in relation to the acceptability of the intervention and the time and cost-saving benefits to both patients and the health system. There were, however, inconsistencies in the conclusions of the two studies specifically in relation to a number of the psychosocial outcomes and this is likely due to the lack of specificity of the quantitative measures. Although the RCT failed to find any effects on psychosocial outcomes, the information collected on patients' experiences nuanced these findings and provided valuable insights into participants' perceptions of the value of this model of care.

- Completeness - By using an RCT and embedded qualitative approach this thesis provides a more complete picture of the impact and experience of a self-monitoring and patient-initiated service for patients with RA or PsA on methotrexate. This could have been further enhanced by undertaking additional qualitative interviews with healthcare professionals delivering and those commissioning services in order to explore their views and acceptability of this model of care which could have provided useful insight into the potential for wider implementation.
- Offsetting weaknesses and providing stronger inferences – Both quantitative and qualitative methods have their strengths and weaknesses. Therefore, by combining these approaches the limitations of each method are diminished whilst the strengths preserved. In this thesis, the RCT was able to explore the overall effectiveness of the intervention and the qualitative study an insight into the personal experiences of individual participants which could not have been captured or represented within an RCT.
- Answering different research questions - Creswell and Clark (2007) argue that mixed methods research helps answer the research questions that cannot be answered by quantitative or qualitative methods alone particularly in complex interventions, such as the one evaluation within this thesis. As stated above the RCT evaluated the effects of the intervention at a group level, whilst the qualitative study explored the acceptability of the intervention in order to understand how the target population experienced this new model of care. Questions of this nature are best suited to qualitative research designs as they are able to explore experiences in greater depth (Ayala & Elder, 2011).

- Illustration of data – By using the findings of the qualitative research to illustrate the findings of the RCT it has helped paint a better picture of how patients experience this new model of care and the potential benefits to both them and the health service.

11.8 OVERALL CONCLUSIONS

The current study has made a number of novel contributions to the literature particularly in regards to the unique nature of the intervention. The RCT demonstrated that a self-monitoring and patient-initiated service can lead to significant reductions in healthcare utilisation, whilst maintaining clinical and psychosocial well-being. The economic benefits, however, require further investigation. Patients were able to safely self-monitor and use this information to seek appropriate help from their CNS. More in-depth investigation of patient acceptability using qualitative interviews indicated that patients found usual care inconvenient and burdensome, which the new service was able to overcome. It also enabled patients to gain knowledge about their laboratory results and provided a link between their medications and disease status. Participants also reported increased control over the impact of their condition on their lives. The implementation of this intervention now needs to be considered in light of the move in parts of the UK towards GP-led DMARD monitoring.

REFERENCES

AbuDagga, A., Resnick, H., & Alwan, M. (2010). Impact of blood pressure telemonitoring on hypertension outcomes: a literature review. *Telemedicine and e-Health, 16*(7), 830-838.

Ad Hoc Committee on Health Literacy for the Council on Scientific Affairs, & American Medical Association. (1999). Health literacy: Report of the council on scientific affairs. *JAMA : the journal of the American Medical Association, 281*(6), 552-557.

Adams, N., & Sands, A. (2009). Patient versus practitioner-initiated follow-up for rheumatoid arthritis. *European Journal of Pain, 13*(S1), S132.

Al Sayah, F., Majumdar, S. R., Williams, B., Robertson, S., & Johnson, J. A. (2013). Health literacy and health outcomes in diabetes: a systematic review. *Journal of general internal medicine, 28*(3), 444-452.

Alamanos, Y., Voulgari, P., & Drosos, A. (2006). Incidence and Prevalence of Rheumatoid Arthritis, Based on the 1987 American College of Rheumatology Criteria: A Systematic Review. *Seminars in Arthritis & Rheumatism, 36*(3), 182-188.

Alamanos, Y., Voulgari, P. V., & Drosos, A. A. (2008). Incidence and Prevalence of Psoriatic Arthritis: A Systematic Review. *Journal of Rheumatology, 35*(7), 1354-1358.

Aletaha, D., Neogi, T., Silman, A. J., Funovits, J., Felson, D. T., Bingham, C. O. *et al.,* (2010). 2010 Rheumatoid arthritis classification criteria: An American College of Rheumatology/European League Against Rheumatism collaborative initiative. *Arthritis & Rheumatism, 62*(9), 2569-2581.

Allemann, S., Houriet, C., Diem, P., & Stettler, C. (2009). Self-monitoring of blood glucose in non-insulin treated patients with type 2 diabetes: A systematic review and meta-analysis. *Current Medical Research and Opinion, 25*(12), 2903-2913.

American Geriatrics Society Expert Panel on the Care of Older Adults with Multimorbidity. (2012). Guiding Principles for the Care of Older Adults with

Multimorbidity: An Approach for Clinicians. *Journal of the American Geriatrics Society, 60*(10), E1-E25.

Arnett, FC., Edworthy, SM., Bloch, D., McShane, D., Fries, J., Cooper, N. *et al.,* (1988). The American Rheumatism Association 1987 revised criteria for the classification of rheumatoid arthritis. *Arthritis & Rheumatism, 31*(3), 315-324.

Arthritis and Musculoskeletal Alliance. (2009). *Joint Working? An audit of the implementation of the Department of Health's musculoskeletal services framework.* London: Arthritis and Musculoskeletal Alliance.

Arthritis and Musculoskeletal Alliance. (2012). *Joint Delivery? An updated audit to assess progress in the implementation of the Musculoskeletal Services Framework in England* London: Arthritis and Musculoskeletal Alliance.

Arthritis UK. (2012). *New National Clinical Directors to be appointed for musculoskeletal conditions.* Retrieved from http://www.arthritisresearchuk.org/news/press-releases/2012/december/new-national-clinical-directors-to-be-appointed-for-musculoskeletal-conditions.aspx

Arthur, V., & Clifford, C. (2004a). Rheumatology: a study of patient satisfaction with follow-up monitoring care. *Journal of Clinical Nursing, 13*(3), 325-331.

Arthur, V., & Clifford, C. (2004b). Rheumatology: the expectations and preferences of patients for their follow-up monitoring care: a qualitative study to determine the dimensions of patient satisfaction. *Journal of Clinical Nursing, 13*(2), 234-242.

Arvidsson, S. B., Petersson, A., Nilsson, I., Andersson, B., Arvidsson, B. I., Petersson, I. F. *et al.,* (2006). A nurse–led rheumatology clinic's impact on empowering patients with rheumatoid arthritis: A qualitative study. *Nursing & health sciences, 8*(3), 133-139.

Astin, J. A., Beckner, W., Soeken, K., Hochberg, M. C., & Berman, B. (2002). Psychological interventions for rheumatoid arthritis: A meta–analysis of randomized controlled trials. *Arthritis Care & Research, 47*(3), 291-302.

Ayala, G. X., & Elder, J. P. (2011). Qualitative methods to ensure acceptability of behavioral and social interventions to the target population. *Journal of public health dentistry, 71*(s1), S69-S79.

Badley, E. M., & Tennant, A. (1993). Impact of disablement due to rheumatic disorders in a British population: estimates of severity and prevalence from the Calderdale Rheumatic Disablement Survey. *Annals of the Rheumatic Diseases, 52*(1), 6-13.

Badley, E. M., & Davis, A. M. (2012). Meeting the challenge of the ageing of the population: Issues in access to specialist care for arthritis. *Best Practice & Research Clinical Rheumatology, 26*(5), 599-609.

Bair, M. J., Matthias, M. S., Nyland, K. A., Huffman, M. A., Stubbs, D. L., Kroenke, K. *et al.,* (2009). Barriers and Facilitators to Chronic Pain Self–Management: A Qualitative Study of Primary Care Patients with Comorbid Musculoskeletal Pain and Depression. *Pain Medicine, 10*(7), 1280-1290.

Bala, S.-V., Samuelson, K., Hagell, P., Svensson, B., Fridlund, B., & Hesselgard, K. (2012). The Experience of Care at Nurse-Led Rheumatology Clinics. *Musculoskeletal Care, 10*(4), 202-211.

Bandura, A. (1986). *Social foundations of thought and action: Social cognitive theory*. Engkewood Cliff, NJ: Prentice-Hall.

Bandura, A. (1997). *Self-efficacy; the exercise of control.* New York: Freeman.

Bandura, A. (2006). Guide for constructing self-efficacy scales. In F. Pajares & T. C. Urdan (Eds.), *Self-efficacy beliefs of adolescents* (pp. 307-337) Information Age Publishing.

Barlow, J., Turner, A., Swaby, L., Gilchrist, M., Wright, C., & Doherty, M. (2009). An 8-yr follow-up of arthritis self-management programme participants. *Rheumatology, 48*(2), 128-133.

Barlow, J. H., Williams, B., & Wright, C. (2005). The generalized self-efficacy scale in people with arthritis. *Arthritis & Rheumatism, 9*(3), 189-195.

Barlow, J. H., Turner, A. P., & Wright, C. C. (1998). Long-term outcomes of an arthritis self-management programme. *Rheumatology, 37*(12), 1315-1319.

Barlow, J., Wright, C., Sheasby, J., Turner, A., & Hainsworth, J. (2002). Self-management approaches for people with chronic conditions: a review. *Patient Education & Counseling, 48*(2), 177-187.

Barlow, J. H., Turner, A. P., & Wright, C. C. (2000). A randomized controlled study of the Arthritis Self-Management Programme in the UK. *Health Education Research, 15*(6), 665-680.

Bathon, J. M., Martin, R. W., Fleischmann, R. M., Tesser, J. R., Schiff, M. H., Keystone, E. C. *et al.,* (2000). A comparison of etanercept and methotrexate in patients with early rheumatoid arthritis. *New England Journal of Medicine, 343*(22), 1586-1593.

Belza, B. L. (1995). Comparison of self-reported fatigue in rheumatoid arthritis and controls. *Journal of Rheumatology, 22*(4), 639-643.

Belza, B. L., Henke, C. J., Yelin, E. H., Epstein, W. V., & Gilliss, C. L. (1993). Correlates of fatigue in older adults with rheumatoid arthritis. *Nursing research, 42*(2), 93-99.

Bergsten, U. (2014). *GotNet Study, The Gothenburg Nurse-led Tight Control Study*. Retrieved from http://clinicaltrials.gov/ct2/show/NCT02019901

Berthelot, J. M., De Bandt, M., Morel, J., Benatig, F., Constantin, A., Gaudin, P. *et al.,* (2012). A tool to identify recent or present rheumatoid arthritis flare from both patient and physician perspectives: The 'FLARE' instrument. *Annals of the Rheumatic Diseases, 71*(7), 1110-1116.

Bhalerao, J., & Bowcock, AM. (1998). The Genetics of Psoriasis: A Complex Disorder of the Skin and Immune System. *Human Molecular Genetics, 7*(10), 1537-1545.

Bird, C. M. (2005). How I stopped dreading and learned to love transcription. *Qualitative Inquiry, 11*(2), 226-248.

Blamey, R., Jolly, K., Greenfield, S., & Jobanputra, P. (2009). Patterns of analgesic use, pain and self-efficacy: a cross-sectional study of patients attending a hospital rheumatology clinic. *BMC Musculoskeletal Disorders, 10*(137).

Bloomfield, H. E., Krause, A., Greer, N., Taylor, B. C., MacDonald, R., Rutks, I. *et al.,* (2011). Meta-analysis: effect of patient self-testing and self-management of long-term anticoagulation on major clinical outcomes. *Annals of internal medicine, 154*(7), 472-482.

Blumberg, B. S., Bunim, J. J., Calmns, E., Pirani, C. L., & Zvaifler, N. J. (1964). ARA nomenclature and classification of arthritis and rheumatism (tentative). *Arthritis & Rheumatism, 7*(1), 93-97.

Bodner, T. E. (2008). What improves with increased missing data imputations? *Structural Equation Modeling, 15*(4), 651-675.

Boers, M., Kostense, P. J., Verhoeven, A. C., & Van Der Linden, S. (2001). Inflammation and damage in an individual joint predict further damage in that joint in patients with early rheumatoid arthritis. *Arthritis & Rheumatism, 44*(10), 2242-2246.

Boutron, I., Moher, D., Altman, D. G., Schulz, K. F., Ravaud, P. & CONSORT Group. (2008). Extending the CONSORT statement to randomized trials of nonpharmacologic treatment: explanation and elaboration. *Annals of internal medicine, 148*(4), 295-309.

Bower, P., Cartwright, M., Hirani, S. P., Barlow, J., Hendy, J., Knapp, M. *et al.,* (2011). A comprehensive evaluation of the impact of telemonitoring in patients with long-term conditions and social care needs: protocol for the whole systems demonstrator cluster randomised trial. *BMC health services research, 11*(1), 184.

Boyatzis, R. E. (1998). *Transforming qualitative information: Thematic analysis and code development* Sage.

Boyer, J. F., Gourraud, P. A., Cantagrel, A., Davignon, J. L., & Constantin, A. (2011). Traditional cardiovascular risk factors in rheumatoid arthritis: A meta-analysis. *Joint Bone Spine, 78*(2), 179-183.

Brand, C., Claydon-Platt, K., McColl, G., & Bucknall, T. (2010). Meeting the needs of people diagnosed with rheumatoid arthritis: an analysis of patient-reported experience. *Journal of Nursing and Healthcare of Chronic Illness, 2*(1), 75-83.

Braun, V., & Clarke, V. (2006). Using thematic analysis in psychology. *Qualitative Research in Psychology, 3*(2), 77-101.

Bray, E. P. H., Holder, R., Mant, J., & McManus, R. J. (2010). Does self-monitoring reduce blood pressure? Meta-analysis with meta-regression of randomized controlled trials. *Annals of Medicine, 42*(5), 371-386.

Breedveld, F. C., Weisman, M. H., Kavanaugh, A. F., Cohen, S. B., Pavelka, K., Vollenhoven, R. v. *et al.,* (2006). The PREMIER study: A multicenter, randomized, double-blind clinical trial of combination therapy with adalimumab plus methotrexate versus methotrexate alone or adalimumab alone in patients with early, aggressive rheumatoid arthritis who had not had previous methotrexate treatment. *Arthritis & Rheumatism, 54*(1), 26-37.

Breivik, H., Collett, B., Ventafridda, V., Cohen, R., & Gallacher, D. (2006). Survey of chronic pain in Europe: Prevalence, impact on daily life, and treatment. *European Journal of Pain, 10*(4), 287.

Brekke, M., Hjortdahl, P., & Kvien, T. K. (2001). Involvement and satisfaction: A norwegian study of health care among 1,024 patients with rheumatoid arthritis and 1,509 patients with chronic non-inflammatory musculoskeletal pain. *Arthritis Care & Research, 45*(1), 2001.

Britton, A., McKee, M., Black, N., McPherson, K., Sanderson, C., & Bain, C. (1999). Threats to applicability of randomised trials: exclusions and selective participation. *Journal of Health Services Research & Policy, 4*(2), 112.

Brooks, M., Jenkins, L., Schron EB, Steinberg, J., Cross, J., Paeth, D. *et al.,* (1998). Quality of Life at Baseline: Is Assessment After Randomization Valid? *Medical care, 36*(10), 1515-1519.

Bryk, A. S., & Raudenbush, S. W. (1992). *Hierarchical linear models: Applications and data analysis methods*. Newbury Park, CA: Sage.

Buckley, C., Cavil, C., Taylor, G., Kay, H., Waldron, N., Korendowych, E. *et al.,* (2010). Mortality in Psoriatic Arthritis - Single-center Study from the UK. *Journal of Rheumatology, 37*(10), 2141-2144.

Buckley, L. M., Vacek, P., & Cooper, S. M. (1990). Educational and psychosocial needs of patients with chronic disease: A survey of preferences of patients with rheumatoid arthritis. *Arthritis & Rheumatism, 3*(1), 5-10.

Bukhari, M., Bamji, A. N., & Deighton, C. (2007). Is it ever appropriate to discharge patients with rheumatoid arthritis? *Rheumatology, 46*(11), 1631-1633.

Bukhari, M., Dixey, J., & Deighton, C. (2011). A survey of new to follow-up ratios in rheumatology outpatients departments. *Clinical Medicine, 11*(1), 99-100.

Buszewicz, M., Rait, G., Griffin, M., Nazareth, I., Patel, A., Atkinson, A. *et al.,* (2006). Self management of arthritis in primary care: randomised controlled trial. *British Medical Journal, 333*(7574), 879.

Camden Clinical Commissioning Group. (2013). *Working for people in Camden to achieve the best possible health for all*. Retrieved from Camden Clinical Commissioning Group http://www.camdenccg.nhs.uk/Downloads/ccg-public/about-us/camden-ccg-plan-page-2013_14-full.pdf

Cantini, F., Nicoli, L., Nannini, C., Kaloudi, O., Bertoni, M., & Cassarà, E. (2010). Psoriatic arthritis: a systematic review. *International Journal of Rheumatic Diseases, 13*(4), 300-317.

Caplan, L., Wolfe, F., Michaud, K., Quinzanos, I., & Hirsh, J. M. (2014). Strong Association of Health Literacy With Functional Status Among Rheumatoid Arthritis Patients: A Cross-Sectional Study. *Arthritis Care & Research, 66*(4), 508-514.

Cappuccio, F. P., Kerry, S. M., Forbes, L., & Donald, A. (2004). Blood pressure control by home monitoring - meta-analysis of randomised trials. *British Medical Journal, 329*(7458), 145.

Care Quality Commission. (2012). *Outpatient Department Survey 2011: University College London Hospitals NHS Foundation Trust* London: Care Quality Commission. Retrieved from: http://www.nhssurveys.org/Filestore/documents/OP11_RRV.pdf

Carlisle, A., John, A. M., Fife-Schaw, C., & Lloyd, M. (2005). The self-regulatory model in women with rheumatoid arthritis: Relationships between illness representations, coping strategies, and illness outcome. *British Journal of Health Psychology.12(3), 323-345.*

Carr, A., Hewlett, S., Hughes, R., Mitchell, H., Ryan, S., Carr, M. *et al.,* (2003). Rheumatology outcomes: the patient's perspective. *Journal of Rheumatology, 30*(4), 880-883.

Cartwright, M., Hirani, S. P., Rixon, L., Beynon, M., Doll, H., Bower, P. *et al.,* (2012). Effect of telehealth on quality of life and psychological outcomes over 12 months (Whole Systems Demonstrator telehealth questionnaire study): nested study of patient reported outcomes in a pragmatic, cluster randomised controlled trial. *British Medical Journal, 346*, f653.

Cauli, A., Gladman, D. D., Mathieu, A., Olivieri, I., Porru, G., Tak, P. P. *et al.,* (2011). Patient global assessment in psoriatic arthritis: A multicenter GRAPPA and OMERACT study. *Journal of Rheumatology, 38*(5), 898-903.

Cavanaugh, K., Huizinga, M. M., Wallston, K. A., Gebretsadik, T., Shintani, A., Davis, D. *et al.,* (2008). Association of numeracy and diabetes control. *Annals of internal medicine, 148*(10), 737-746.

Centre for Reviews and Dissemination. (2009). *Systematic Review: The CRD's guidance for undertaking reviews in health care* York: CRD, University of York.

Chakravarty, K., McDonald, H., Pullar, T., Taggart, A., Chalmers, R., Oliver, S. *et al.,* (2008). BSR/BHPR guideline for disease-modifying anti-rheumatic drug (DMARD) therapy in consultation with the British Association of Dermatologists. *Rheumatology, 47*(6), 924-925.

Chattopadhyay, C., & Hickey, P. (2008). Are Routine Appointments Cost-Effective in Modern Rheumatology Practice? A Comparative Outcome Audit of Routine Follow-ups and Patient Initiated Consultations. *American College of Rheumatology 2008 Annual Scientific Meeting*.

Chaudhry, S.I.P., Phillips, C.O., Stewart, S.S., Riegal, B.J., Mattera, J.A., Jerrant, A.F. & Krumholz, H.M. (2007). Telemonitoring for Patients with Chronic Heart Failure: A Systematic Review. *Journal of Cardiac Failure, 13*(1), 56-62.

Cherry, L., Crossland, V., Field, R., Ainsworth, P., & Edwards, C. (2014). Is There Evidence to Support Multidisciplinary Healthcare Working in Rheumatology? A Systematic Review of the Literature. *Rheumatology, 53*(suppl 1), i123.

Chew, L. C., & Yee, S. L. (2013). The Rheumatology Monitoring Clinic in Singapore – A Novel Advanced Practice Nurse-/Pharmacist-Led Clinic. *Proceedings of Singapore Healthcare, 22*(1), 48-55.

Chew, L.-C., Lim, T. G., Loy, K. L., Kong, M. C., Chang, W. T., Tan, S. B. *et al.,* (2012). A questionnaire survey of patient experience with the Rheumatology Monitoring Clinic in Singapore. *International Journal of Rheumatic Diseases, 15*(4), 390-398.

Chorus, A. M. J., Miedema, H. S., Boonen, A., & van der Linden, S. (2003). Quality of life and work in patients with rheumatoid arthritis and ankylosing spondylitis of working age. *Annals of the Rheumatic Diseases, 62*(12), 1178-1184.

Christensen, T. D., Johnsen, S. P., Hjortdal, V. E., & Hasenkam, J. M. (2007). Self-management of oral anticoagulant therapy: A systematic review and meta-analysis. *International Journal of Cardiology, 118*(1), 54-61.

Ciciriello, S., Buchbinder, R., Wicks, I., & Osborne, R. H. (2010). Measuring the Impact of Patient Educational Materials about Medications in Meeting Patient Needs: Development and Validation of the Medication Education Impact Questionnaire (MeiQ). *Arthritis & Rheumatism, 62* (Suppl 10), 1001.

Ciciriello, S., Wicks, I., Osborne, R., & Buchbinder, R. (2010). Testing Patient Knowledge about Methotrexate: Development and Validation of the Methotrexate in Rheumatoid Arthritis Knowledge Test (MiRAK). *Arthritis & Rheumatism, 62* (Suppl 10), 1009.

Ciere, Y., Cartwright, M., & Newman, S. P. (2012). A systematic review of the mediating role of knowledge, self-efficacy and self-care behaviour in telehealth patients with heart failure. *Journal of Telemedicine and Telecare, 18*(7), 384-391.

Clar, C., Barnard, K., Cummins, E., Royle, P., & Waugh, N. (2010). Self-monitoring of blood glucose in type 2 diabetes: Systematic review. *Health Technology Assessment, 14*(12).

Clark, R. A., Inglis, S. C., McAlister, F. A., Cleland, J. G. F., & Stewart, S. (2007). Telemonitoring or structured telephone support programmes for patients with chronic heart failure: systematic review and meta-analysis. *British Medical Journal, 334*(7600), 942-950.

Clarke, M., Shah, A., & Sharma, U. (2011). Systematic review of studies on telemonitoring of patients with congestive heart failure: a meta-analysis. *Journal of Telemedicine and Telecare, 17*(1), 7-14.

Clegg, D. O., Reda, D. J., Mejias, E., Cannon, G. W., Weisman, M. H., Taylor, T. *et al.,* (1996). Comparison of sulfasalazine and placebo in the treatment of psoriatic arthritis. A department of veterans affairs cooperative study. *Arthritis & Rheumatism, 39*(12), 2013-2020.

Coates L, Tillett W, Chandler, D., Helliwell, P., orendowych, E., yle, S. *et al.,* (2012). *Guidelines for the treatment of psoriatic arthritis with biologics*. Retrieved from http://www.rheumatology.org.uk/includes/documents/cm_docs/2012/b/bsr_guidelines_2012_treatment_of_psoriatic_arthritis_with_biologics.pdf

Coates, L. C., Tillett, W., Chandler, D., Helliwell, P. S., Korendowych, E., Kyle, S. *et al.,* (2013). The 2012 BSR and BHPR guideline for the treatment of psoriatic arthritis with biologics. *Rheumatology, 52*(10), 1754-1757.

Cohen, J. (1988). *Statistical power analysis for the behavioral sciences.* (2nd ed.). Hillsdale, New Jersey: Lawrence Erlbaum Associates.

Collins, L. M., Graham, J. J., & Flaherty, B. P. (1998). An alternative framework for defining mediation. *Multivariate behavioral research, 33*(2), 295-312.

Collins, M., Shattell, M., & Thomas, S. (2005). Problematic interviewee behaviors in qualitative research. *Western Journal of Nursing Research, 27*(2), 188-199.

Connock, M., Stevens, C., Fry-Smith, A., Jowett, S., Fitzmaurice, D., Moore, D. *et al.,* (2007). Clinical effectiveness and cost-effectiveness of different models of managing long-term oral anticoagulation therapy: a systematic review and economic modelling. *Health Technology Assessment, 11*(38).

Cornally, N., & McCarthy, G. (2011). Help-seeking behaviour for the treatment of chronic pain. *British journal of community nursing, 16*(2), 90-98.

Cottrell, J. E. D., Jonas, M., Bergsten, U., Blaas, E., de la Torre Aboki, J., Howse, C. *et al.,* (2012). The Nurse's Role in Addressing Unmet Treatment and Management Needs of Patients With Rheumatoid Arthritis: Delphi-Based Recommendations. *International Journal of Nursing Knowledge, 24*(2), 66-76.

Courvoisier, D. S., Agoritsas, T., Glauser, J., Michaud, K., Wolfe, F., Cantoni, E. *et al.,* (2012). Pain as an important predictor of psychosocial health in patients with rheumatoid arthritis. *Arthritis Care & Research, 64*(2), 190-196.

Covic, T., Cumming, S. R., Pallant, J. F., Manolios, N., Emery, P., Conaghan, P. G. *et al.,* (2012). Depression and anxiety in patients with rheumatoid arthritis: prevalence rates based on a comparison of the Depression, Anxiety and Stress Scale (DASS) and the hospital, Anxiety and Depression Scale (HADS). *BMC psychiatry, 12*(1), 6.

Craig, P., Dieppe, P., Macintyre, S., Michie, S., Nazareth, I., & Petticrew, M. (2008). Developing and evaluating complex interventions: the new Medical Research Council guidance. *British Medical Journal, 337*, a1655.

Creswell, J. W., & Clark, V. L. P. (2007). *Designing and conducting mixed methods research*. Thousand Oaks, CA, US: Sage Publications, Inc.

Criswell, L. A., Such, C. L., & Yelin, E. H. (1997). Differences in the use of second-line agents and prednisone for treatment of rheumatoid arthritis by rheumatologists and non-rheumatologists. *Journal of Rheumatology, 24*(12), 2283-2290.

Cronbach, L. J. (1951). Coefficient alpha and the internal structure of tests. *Psychometrika, 16*(3), 297-334.

Crotty, M., Prendergast, J., Battersby, M. W., Rowett, D., Graves, S. E., Leach, G. *et al.,* (2009). Self-management and peer support among people with arthritis on a hospital joint replacement waiting list: a randomised controlled trial. *Osteoarthritis and Cartilage, 17*(11), 1428-1433.

Cumming, J., Stannett, P., & Hull, R. (2013). Analysis of comorbidities reported by people living with arthritis contacting a national helpline service. *Rheumatology, 52*(suppl 1), i75-i76.

Cunha-Miranda, L., Costa, L., & Ribeiro, J. S. (2010). Near study: Needs and expectations in rheumatoid arthritis - Do we know our patients needs? *Acta Reumatologica Portuguesa, 35*(3), 314-323.

Cunningham, S. J. (2001). An introduction to economic evaluation of health care. *Journal of Orthodontics, 28*(3), 246-250.

Curry, L. A., Krumholz, H. M., O'Cathain, A., Clark, V. L. P., Cherlin, E., & Bradley, E. H. (2013). Mixed Methods in Biomedical and Health Services Research. *Circulation, 6*(1), 119-123.

Curtis, L. (2012). *Unit costs of Health and Social Care 2012*. Canterbury: Personal Social Services Research Unit.

Dadoun, S., Zeboulon-Ktorza, N., Combescure, C., Elhai, M., Rozenberg, S., Gossec, L. *et al.,* (2013). Mortality in rheumatoid arthritis over the last fifty years: Systematic review and meta-analysis. *Joint Bone Spine, 80*(1), 29-33.

Dallall, G. (2010). *Randomization Plans*. In *Randomization.com* Retrieved from http://www.randomization.com/

Dang, S., Dimmick, S., & Kelkar, G. (2009). Evaluating the evidence base for the use of home telehealth remote monitoring in elderly with heart failure. *Telemedicine and e-Health, 15*(8), 783-796.

Davies, L. M., Fargher, E. A., Tricker, K., Dawes, P., Scott, D. L., & Symmons, D. (2007). Is shared care with annual hospital review better value for money than predominantly hospital-based care in patients with established stable rheumatoid arthritis? *Annals of the Rheumatic Diseases, 66*(5), 658-663.

Dávila-Fajardo, C. L. a., Swen, J. J., Barrera, J. C., & Guchelaar, H. J. (2013). Genetic risk factors for drug-induced liver injury in rheumatoid arthritis patients using low-dose methotrexate. *Pharmacogenomics, 14*(1), 63-73.

Deeming, G. M. J., Collingwood, J., & Pemberton, M. N. (2005, print). Methotrexate and oral ulceration. *British Dental Journal, 198*(2), 83-85.

Denzin, N. K. (2006). *Sociological methods: A sourcebook: Aldine Transaction*. New York: Aldine Transaction.

Department of Health. (2005a). *Supporting people with long-term conditions: improving care, improving lives.* London: Department of Health.

Department of Health. (2005b). *The National Service Framework for long-term conditions* London: Department of Health.

Department of Health. (2006). *The Musculoskeletal Services Framework* London: Department of Health.

Department of Health. (2010a). *Equity and excellence: Liberating the NHS* London: Department of Health.

Department of Health. (2010b). *Long term condition*. Retrieved from Department of Health http://webarchive.nationalarchives.gov.uk/+/www.dh.gov.uk/en/Healthcare/Longtermconditions/DH_064569

Department of Health. (2010c). *The NHS Outcomes Framework 2011 to 2012* London: Department of Health.

Department of Health. (2011a). *2010-11 reference costs publication*. Retrieved from Department of Health https://www.gov.uk/government/publications/2010-11-reference-costs-publication

Department of Health. (2011b). *The NHS Outcomes Framework 2012 to 2013* London: Department of Health.

Department of Health. (2012a). *2003-04 to 2010-11 programme budgeting data*. Retrieved from Department of Health https://www.gov.uk/government/publications/2003-04-to-2010-11-programme-budgeting-data

Department of Health. (2012b). *The NHS Outcomes Framework 2013 to 2014* London: Department of Health.

Department of Health. (2013a). *Department of Health Reference costs for 2012-13*. Retrieved from https://www.gov.uk/government/publications/nhs-reference-costs-2012-to-2013

Department of Health. (2013b). *Indicator reference no. 2.1: Proportion of people feeling supported to manage their condition*. Retrieved from Department of Health http://www.nice.org.uk/media/D49/D0/2-1ProportionOfPeopleFeelingSupportedToManageTheirCondition.pdf

Department of Health. (2013c). *Payment by Results in the NHS: tariff for 2013 to 2014* London: Department of Health.

Department of Health. (2013d). *Payment by Results tariff information spreadsheet for 2013 to 2014*. Retrieved from Department of Health https://www.gov.uk/government/publications/payment-by-results-pbr-operational-guidance-and-tariffs

Department of Health. (2013e). *The Mandate: A mandate from the Government to the NHS Commissioning Board: April 2013 to March 2015* London: Department of Health.

Department of Health. (2013f). *The NHS Outcomes Framework 2014 to 2015* London: Department of Health.

Dettori, J. (2010). The random allocation process: two things you need to know. *Evidence-Based Spine-Care Journal, 1*(3), 7-9.

Dickens, C., McGowan, L., Clark-Carter, D., & Creed, F. (2002). Depression in rheumatoid arthritis: A systematic review of the literature with meta-analysis. *Psychosomatic Medicine, 64*(1), 52-60.

Dombrowski, S. U., Sniehotta, F. F., Avenell, A., Johnston, M., MacLennan, G., & Araújo-Soares, V. (2010). Identifying active ingredients in complex behavioural interventions for obese adults with obesity-related co-morbidities or additional risk factors for co-morbidities: a systematic review. *Health Psychology Review, 6*(1), 7-32.

Doran, M., Crowson, C., O'Fallon, W., & Gabriel, S. (2004). The effect of oral contraceptives and oestrogen replacement therapy on the risk of rheumatoid arthritis: a population based study. *Journal of Rheumatology, 31*(2), 207-213.

Douglas, B., Giles, S., Keating, H., Sheeran, T., Price, T., & Chalam, V. (2009). Community rheumatology? Is this the way forward? *Rheumatology, 48*(Suppl 1), i147.

Douglas, K. M., Potter, T., Treharne, G. J., Obrenovic, K., Hale, E. D., Pace, A. *et al.,* (2005). Rheumatology patient preferences for timing and location of out-patient clinics. *Rheumatology, 44*(1), 80-82.

Drummond, M. F., & Davies, L. (1991). Economic analysis alongside clinical trials: revisiting the methodological issues. *International journal of technology assessment in health care, 7*(04), 561-573.

Elkayam, O., Ophir, J., Yaron, M., & Caspi, D. (2000). Psoriatic arthritis: interrelationships between skin and joint manifestations related to onset, course and distribution. *Clinical Rheumatology, 19*(4), 301-305.

Emery, P., Sebba, A., & Huizinga, T. W. J. (2013). Biologic and oral disease-modifying antirheumatic drug monotherapy in rheumatoid arthritis. *Annals of the Rheumatic Diseases, 72*(12), 1897-1904.

Epstein, R. M., Franks, P., Shields, C. G., Meldrum, S. C., Miller, K. N., Campbell, T. L. *et al.,* (2005). Patient-centered communication and diagnostic testing. *The Annals of Family Medicine, 3*(5), 415-421.

Epstein, R. M., Shields, C. G., Meldrum, S. C., Fiscella, K., Carroll, J., Carney, P. A. *et al.,* (2006). Physicians' responses to patients' medically unexplained symptoms. *Psychosomatic Medicine, 68*(2), 269-276.

Espinoza, L. R., Zakraoui, L., Espinoza, C. G., Gutiérrez, F., Jara, L. J., Silveira, L. H. *et al.,* (1992). Psoriatic arthritis: clinical response and side effects to methotrexate therapy. *Journal of Rheumatology, 19*(6), 872-877.

Estrada, C. A., Martin-Hryniewicz, M., Peek, B. T., Collins, C., & Byrd, J. C. (2004). Literacy and numeracy skills and anticoagulation control. *The American journal of the medical sciences, 328*(2), 88-93.

Fairbrother, P., Ure, J., Hanley, J., McCloughan, L., Denvir, M., Sheikh, A. *et al.,* (2014). Telemonitoring for chronic heart failure: the views of patients and healthcare professionals - a qualitative study. *Journal of Clinical Nursing, 23*(1-2), 132-144.

Famoye, F., & Rothe, D. E. (2003). Variable selection for Poisson regression model. *Journal of Modern Applied Statistical Methods, 2*(2), 380-388.

Faul, F., Erdfelder, E., Lang, A. G., & Buchner, A. (2007). G*Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behavior Research Methods, 39*(2), 175-191.

Felson, D. T., Anderson, J. J., Boers, M., Bombardier, C., Furst, D., Goldsmith, C. *et al.,* (1995). American College of Rheumatology. Preliminary definition of improvement in rheumatoid arthritis. *Arthritis & Rheumatism, 38*(6), 727-735.

Fernández-Sueiro, J., Willisch, A., Pértega-Díaz, S., Tasende, J., Fernández-López, J., Villar, N. *et al.,* (2010). Validity of the bath ankylosing spondylitis disease activity index for the evaluation of disease activity in axial psoriatic arthritis. *Arthritis Care & Research, 62*(1), 78-85.

Ferrans, C. E., Zerwic, J. J., Wilbur, J. E., & Larson, J. L. (2005). Conceptual Model of Health-Related Quality of Life. *Journal of Nursing Scholarship, 37*(4), 336-342.

Finckh, A., Liang, M. H., van Herckenrode, C. M., & de Pablo, P. (2006). Long-term impact of early treatment on radiographic progression in rheumatoid arthritis: A meta-analysis. *Arthritis Care & Research, 55*(6), 864-872.

Fitzpatrick, M. (2005). A patient-led NHS? *British Journal of General Practice, 55*(521), 973.

Flurey, C. (2014). Life as Fluctuating Balance: Flare Tipping Points, Inflammatory and Avalanche Flares. *Rheumatology, 53*(suppl 1), i5.

Flurey, C. A., Morris, M., Richards, P., Hughes, R., & Hewlett, S. (2014). It's like a juggling act: rheumatoid arthritis patient perspectives on daily life and flare while on current treatment regimes. *Rheumatology, 53*(4), 696-703.

Francis, J. J., Johnston, M., Robertson, C., Glidewell, L., Entwistle, V., Eccles, M. P. *et al.,* (2010). What is an adequate sample size? Operationalising data saturation for theory-based interview studies. *Psychology & Health, 25*(10), 1229-1245.

Francis, K. L., Matthews, B. L., Van Mechelen, W., Bennell, K. L., & Osborne, R. H. (2009). Effectiveness of a community-based osteoporosis education and self-management course: a wait list controlled trial. *Osteoporosis international, 20*(9), 1563-1570.

Franek, J. (2013). Self-Management Support Interventions for Persons With Chronic Disease: An Evidence-Based Analysis. *Ontario health technology assessment series, 13*(9), 1-60.

Franke, L. C., Ament, A. J. H. A., Laar, M. A. F. J., Boonen, A., & Severens, J. L. (2009). Cost-of-illness of rheumatoid arthritis and ankylosing spondylitis. *Clinical and experimental rheumatology, 27*(Suppl. 55), 118-123.

Fransen, J., & van Riel, P. L. (2005). The Disease Activity Score and the EULAR response criteria. *Clinical and experimental rheumatology, 23*(Suppl 39), S93-S99.

Fries, J. F., Spitz, P., Kraines, R. G., & Holman, H. R. (1980). Measurement of patient outcome in arthritis. *Arthritis & Rheumatism, 23*(2), 137-145.

Frostholm, L., Fink, P., Christensen, K. S., Toft, T., Oernboel, E., Olesen, F. *et al.,* (2005). The patients' illness perceptions and the use of primary health care. *Psychosomatic Medicine, 67*(6), 997-1005.

Galloway, J. B., Hyrich, K. L., Mercer, L. K., Dixon, W. G., Fu, B., Ustianowski, A. P. *et al.,* (2011). Anti-TNF therapy is associated with an increased risk of serious infections in patients with rheumatoid arthritis especially in the first 6 months of treatment: updated results from the British Society for Rheumatology Biologics Register with special emphasis on risks in the elderly. *Rheumatology, 50*(1), 124-131.

Gandhi, S. K., Warren Salmon, J., Zhao, S. Z., Lambert, B. L., Gore, P. R., & Conrad, K. (2001). Psychometric evaluation of the 12-item short-form health survey (SF-12) in osteoarthritis and rheumatoid arthritis clinical trials. *Clinical Therapeutics, 23*(7), 1080-1098.

Garcia-Alamino, J. M., Ward, A. M., Alonso-Coelle, P., Bankhead, C., Fitzmaurice, D., & Heneghan, C. (2010). Self-monitoring and self-management of oral anticoagulation. *Cochrane Database of Systematic Reviews*.

Garfield, S., Smith, F., Francis, S. A., & Chalmers, C. (2007). Can patients' preferences for involvement in decision-making regarding the use of medicines be predicted? *Patient Education & Counseling, 66*(3), 361-367.

Gasparyan, A. Y., Stavropoulos-Kalinoglou, A., Mikhailidis, D. P., Douglas, K. M., & Kitas, G. D. (2011). Platelet function in rheumatoid arthritis: arthritic and cardiovascular implications. *Rheumatology international, 31*(2), 153-164.

Giamouzis, G., Mastrogiannis, D., Koutrakis, K., Karayannis, G., Parisis, C., Rountas, C. *et al.,* (2012). Telemonitoring in chronic heart failure: A systematic review. *Cardiology Research and Practice*.

Gignac, M. A. M., Cao, X., Lacaille, D., Anis, A. H., & Badley, E. M. (2008). Arthritis-related work transitions: A prospective analysis of reported productivity losses, work changes, and leaving the labor force. *Arthritis Care & Research, 59*(12), 1805-1813.

Gladman, D. D., Hing, E. N., Schentag, C. T., & Cook, R. J. (2001). Remission in psoriatic arthritis. *Journal of Rheumatology, 28*(5), 1045-1048.

Gladman, D., Farewell, V., Wong, K., & Husted, J. (1998). Mortality studies in psoriatic arthritis: Results from a single outpatient center. II. Prognostic indicators for death. *Arthritis & Rheumatism, 41*(6), 1103-1110.

Gladman, DD., Farewell, V., Pellett, F., Schentag, C., & Rahman, P. (2003). HLA is a candidate region for psoriatic arthritis: evidence for excessive HLA sharing in sibling pairs. *Human Immunology, 64*(9), 887-889.

Glaser, B. G., & Strauss, A. L. (2012). *The discovery of grounded theory: Strategies for qualitative research*. New Jersey, US: AldineTransaction.

Glasziou, P., Irwig, L., & Mant, D. (2005). Monitoring in chronic disease: a rational approach. *British Medical Journal, 330*(7492), 644-648.

Glazier, R. (1996). The Future of Rheumatology: Paradigm Shift or Turf War? *Journal of Rheumatology, 23*(9), 1494-1496.

Goh, L., Samanta, J., & Samanta, A. (2006). Rheumatology nurse practitioners' perceptions of their role. *Musculoskeletal Care, 4*(2), 88-100.

Graves, H., Scott, D. L., Lempp, H., & Weinman, J. (2009). Illness beliefs predict disability in rheumatoid arthritis. *Journal of Psychosomatic Research, 67*(5), 417-423.

Greater London Authority. (2012). *GLA ethnic group projections 2011 round, SHLAA, borough - high fertility*. Retrieved from http://data.london.gov.uk/datastore/package/gla-ethnic-group-projections-2011-round-shlaa-borough-high-fertility

Grigor, C., Capell, H., Stirling, A., McMahon, A. D., Lock, P., Vallance, R. *et al.,* (2004). Effect of a treatment strategy of tight control for rheumatoid arthritis (the TICORA study): a single-blind randomised controlled trial. *The Lancet, 364*(9430), 263-269.

Griva, K., Ng, H. J., Loei, J., Mooppil, N., McBain, H., & Newman, S. P. (2013). Managing treatment for end-stage renal disease – A qualitative study exploring cultural perspectives on facilitators and barriers to treatment adherence. *Psychology & Health, 28*(1), 13-29.

Groarke, A., Curtis, R., Coughlan, R., & Gsel, A. (2005). The impact of illness representations and disease activity on adjustment in women with rheumatoid arthritis: A longitudinal study. *Psychology & Health, 20*(5), 597-613.

Grønning, K., Skomsvoll, J. F., Rannestad, T., & Steinsbekk, A. (2012). The effect of an educational programme consisting of group and individual arthritis education for patients with polyarthritis – A randomised controlled trial. *Patient Education & Counseling, 88*(1), 113-120.

Guillemin, F., Coste, J., Pouchot, J., Ghézail, M., Bregeon, C., & Sany, J. (1997). The AIMS2–SF. A short form of the arthritis impact measurement scales 2. *Arthritis & Rheumatism, 40*(7), 1267-1274.

Hagger, M. S., & Orbell, S. (2003). A Meta-Analytic Review of the Common-Sense Model of Illness Representations. *Psychology & Health, 18*(2), 141-184.

Han, C., Robinson, D., Hackett, M., Paramore, L., Fraeman, K., & Bala, M. (2006). Cardiovascular disease and risk factors in patients with rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis. *Journal of Rheumatology, 33*(11), 2167-2172.

Harrison, B. J., Silman, A., Barrett, E., Scott, D. G., & Symmons, D. P. (1997). Presence of psoriasis does not influence the presentation or short-term outcome of patients with early inflammatory polyarthritis. *Journal of Rheumatology, 24*(9), 1744-1749.

Harrison, M., Fullwood, C., Bower, P., Kennedy, A., Rogers, A., & Reeves, D. (2011). Exploring the mechanisms of change in the chronic disease self-management

programme: Secondary analysis of data from a randomised controlled trial. *Patient Education & Counseling, 85*(2), e39-e47.

Harrison, M. J., Lee, S., Deighton, C., & Symmons, D. P. (2011). UK rheumatology consultant workforce provision 2007–9: results from the BSR/Arthritis Research UK Consultant Workforce Register. *Clinical Medicine, 11*(2), 119-124.

Harty, L. C., Ng, C. T., Fearon, C., Murray, C. A., FitzGerald, O., & Veale, D. J. (2012). Joint tenderness and swelling in biologic-treated inflammatory arthritis patients - A tricky trade off? *International Journal of Clinical Practice, 66*(2), 128-131.

Hassan, E. (2006). Recall Bias can be a Threat to Retrospective and Prospective Research Designs. *Internet Journal of Epidemiology, 3*(2), 4.

Hawley, L. M., & Quilty, B. M. (2009). Telephone review for patients with rheumatoid arthritis: A viable option? *Rheumatology, 48*, i152.

Hay, E. M., & Adebajo, A. (2005). Musculoskeletal general practitioners with special interests: where are we up to? *Rheumatology, 44*(10), 1210-1211.

Hay, E. M., Campbell, A., Linney, S., & Wise, E. (2007). Development of a competency framework for general practitioners with a special interest in musculoskeletal/rheumatology practice. *Rheumatology, 46*(2), 360-362. Retrieved from Br Soc Rheumatology.

Hayes, A. F. (2009). Beyond Baron and Kenny: Statistical mediation analysis in the new millennium. *Communication Monographs, 76*(4), 408-420.

Hayes, A. F. (2012). *PROCESS: A versatile computational tool for observed variable mediation, moderation, and conditional process modeling*. Retrieved from http://www.afhayes.com/public/process2012.pdf

Hayes, A. F. (2013). *Introduction to mediation, moderation, and conditional process analysis: A regression-based approach* Guilford Press.

Health & Social Care Information Centre. (2014). *Consultation medium used*. Retrieved from

http://www.datadictionary.nhs.uk/data_dictionary/attributes/c/cons/consultation_medium_used_de.asp?query=telemedicine&rank=1&shownav=1

Heck, R., Thomas, S., & Tabata, L. (2013). *Multilevel Modeling of Categorical Outcomes Using IBM SPSS*. New York: Routledge.

Hehir, M., Mitchell, K., Hewlett, S., Kirwan, J., Memel, D., & Pollack, J. (2001). What happens in rheumatoid arthritis out-patient clinics? *Rheumatology, 40*(Suppl 1), 146.

Helliwell, P. S. (1996). Comparison of a community clinic with a hospital out-patient clinic in rheumatology. *Rheumatology, 35*(4), 385-388.

Helliwell, P. S., & Hetthen, J. (1999). Primary care rheumatology - leading the way? *Rheumatology, 38*(12), 1174-1176.

Heneghan, C., Ward, A., Perera, R., Self-monitoring Trialist Collaboration, Bankhead, C., Fuller, A. *et al.,* (2011). Self-monitoring of oral anticoagulation: systematic review and meta-analysis of individual patient data. *The Lancet, 379*(9813), 322-334.

Heneghan, C., Alonso-Coello, P., Garcia-Alamino, J. M., Perera, R., Meats, E., & Glasziou, P. (2006). Self-monitoring of oral anticoagulation: a systematic review and meta-analysis. *The Lancet, 367*(9508), 404-411.

Hennell, S., Spark, E., Wood, B., & George, E. (2005). An evaluation of nurse–led rheumatology telephone clinics. *Musculoskeletal Care, 3*(4), 233-240.

Hessling, R., Traxel, N., & Schmidt, T. (2004). Ceiling Effect. In M. Lewis-Beck, A. Bryman, & T. Liao (Eds.), *Encyclopedia of Social Science Research Methods.* Thousand Oaks, California: Sage Publications, Inc.

Hetthen, J., & Helliwell, P. S. (1999). A comparison between primary care-led rheumatology services and secondary care provision. *Rheumatology, 38*(12), 1294-1295.

Hewlett, S., Cockshott, Z., Barrett, K. J., Stamp, J., & Haslock, I. (2001). Development and validation of a self-efficacy scale for use in British patients with rheumatoid arthirtis (RASE). *Rheumatology, 40*(11), 1221-1230.

Hewlett, S., Mitchell, K., & Kirwan, J. (1999). Patients who access or don't access open review: Reasonable decisions? *Arthritis & Rheumatism, 42*, S221.

Hewlett, S. (2005). Implementation of patient-initiated review in rheumatoid arthritis. *Foundation of Nursing Studies: Developing Practice Improving Care Dissemination Series, 3*(3), 1-4.

Hewlett, S., Mitchell, K., Haynes, J., Paine, T., Korendowych, E., & Kirwan, J. R. (2000). Patient-initiated hospital follow-up for rheumatoid arthritis. *Rheumatology, 39*(9), 990-997.

Hewlett, S., Carr, M., Ryan, S., Kirwan, J., Richards, P., Carr, A. *et al.,* (2005a). Outcomes generated by patients with rheumatoid arthritis: how important are they? *Musculoskeletal Care, 3*(3), 131-142.

Hewlett, S., Kirwan, J., Pollock, J., Mitchell, K., Hehir, M., Blair, P. S. *et al.,* (2005b). Patient initiated outpatient follow up in rheumatoid arthritis: six year randomised controlled trial. *British Medical Journal, 330*(7484), 171.

Hewlett, S., Sanderson, T., May, J., Alten, R., Bingham, C. O., Cross, M. *et al.,* (2012). 'I'm hurting, I want to kill myself': rheumatoid arthritis flare is more than a high joint count - an international patient perspective on flare where medical help is sought. *Rheumatology, 51*(1), 69-76.

Hill, J., Bird, H. A., Harmer, R., Wright, V., & Lawton, C. (1994). An evaluation of the effectiveness, safety and acceptability of a nurse practitioner in a rheumatology outpatient clinic. *Rheumatology, 33*(3), 283-288.

Hill, J., Thorpe, R., & Bird, H. (2003). Outcomes for patients with RA: a rheumatology nurse practitioner clinic compared to standard outpatient care. *Musculoskeletal Care, 1*(1), 5-20.

Hill, J. (1997). Patient satisfaction in a nurse–led rheumatology clinic. *Journal of advanced nursing, 25*(2), 347-354.

Hoffman, L. (2010). *An Introduction to Growth Curves via Multilevel Models*. Retrieved from http://www.coe.uga.edu/research/conference-workshops/files/2010/07/ws_UGA_MLM_2010_Handout.pdf

Hoffmann, T. C., Glasziou, P. P., Boutron, I., Milne, R., Perera, R., Moher, D. *et al.,* (2014). Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. *British Medical Journal, 348*, g1687.

Hogg, J. A., Hewlett, S., & Kirwan, J. R. (1997). Do patients, given direct access to specialist care, make appropriate self-referral? *Arthritis & Rheumatism, 40*(9), 1144.

Hollis, S., & Campbell, F. (1999). What is meant by intention to treat analysis? Survey of published randomised controlled trials. *British Medical Journal, 319*(7211), 670-674.

Hopewell, S., McDonald, S., Clarke, M., & Egger, M. (2007). Grey literature in meta-analyses of randomized trials of health care interventions. *Cochrane Database of Systematic Reviews*.

Horne, R. (2003). Treatment perceptions and self regulation. In L.D. Cameron & H. Leventhal (Eds.), *The self-regulation of health and illness behaviour* (pp. 139-152). New York: Routledge.

Horne, R., Weinman, J., & Hankins, M. (1999). The beliefs about medicines questionnaire: the development and evaluation of a new method for assessing the cognitive representation of medication. *Psychology & Health, 14*(1), 1-24.

Horreau, C., Pouplard, C., Brenaut, E., Barnetche, T., Misery, L., Cribier, B. *et al.,* (2013). Cardiovascular morbidity and mortality in psoriasis and psoriatic arthritis: a systematic literature review. *Journal of the European Academy of Dermatology and Venereology, 27*(s3), 12-29.

House of Commons Library Research. (2010). *Key issues for the new parliment in 2010* House of Commons Library Research.

Hozo, S. P., Djulbegovic, B., & Hozo, I. (2005). Estimating the mean and variance from the median, range, and the size of a sample. *BMC Medical Research Methodology, 5*(1), 13.

Humphreys, J. H., Verstappen, S. M. M., Hyrich, K. L., Chipping, J. R., Marshall, T., & Symmons, D. P. M. (2012). The incidence of rheumatoid arthritis in the UK: comparisons using the 2010 ACR/EULAR classification criteria and the 1987 ACR classification criteria. Results from the Norfolk Arthritis Register. *Annals of the Rheumatic Diseases, 72*(8), 1315-1320.

Hurst, N. P., Ruta, D. A., & Kind, P. (1998). Comparison of the MOS short form-12 (SF12) health status questionnaire with the SF36 in patients with rheumatoid arthritis. *Rheumatology, 37*(8), 862-869.

Husted, J. A., Tom, B. D., Schentag, C. T., Farewell, V. T., & Gladman, D. D. (2009). Occurrence and correlates of fatigue in psoriatic arthritis. *Annals of the Rheumatic Diseases, 68*(10), 1553-1558.

Husted, J. A., Gladman, D. D., Farewell, V. T., & Cook, R. J. (2001). Health-related quality of life of patients with psoriatic arthritis: A comparison with patients with rheumatoid arthritis. *Arthritis Care & Research, 45*(2), 151-158.

Husted, J. A., Tom, B. D., Farewell, V. T., & Gladman, D. D. (2012). Longitudinal study of the bidirectional association between pain and depressive symptoms in patients with psoriatic arthritis. *Arthritis Care & Research, 64*(5), 758-765.

Huyser, B. A., Parker, J. C., Thoreson, R., Smarr, K. L., Johnson, J. C., & Hoffman, R. (1998). Predictors of subjective fatigue among individuals with rheumatoid arthritis. *Arthritis & Rheumatism, 41*(12), 2230-2237.

Inglis, S. C., Clark, R. A., McAlister, F. A., Ball, J., Lewinter, C., Cullington, D. *et al.,* (2010). Structured telephone support or telemonitoring programmes for patients with chronic heart failure. *Cochrane Database of Systematic Reviews*.

Ishikawa, H., Hashimoto, H., & Yano, E. (2006). Patients' preferences for decision making and the feeling of being understood in the medical encounter among patients with rheumatoid arthritis. *Arthritis Care & Research, 55*(6), 15.

Iversen, M. D., Hammond, A., & Betteridge, N. (2010). Self-management of rheumatic diseases: state of the art and future perspectives. *Annals of the Rheumatic Diseases, 69*(6), 955-963.

Jaana, M., Pare, G., & Sicotte, C. (2007). Hypertension home telemonitoring: current evidence and recommendations for future studies. *Disease Management & Health Outcomes, 15*(1), 19-31.

Jacobi, C. E., Boshuizen, H. C., Rupp, I., Dinant, H. J., & Van Den Bos, G. A. (2004). Quality of rheumatoid arthritis care: the patient's perspective. *International Journal for Quality in health care, 16*(1), 73-81.

Jansen, J. P. (2006). Self-monitoring of glucose in type 2 diabetes mellitus: A Bayesian meta-analysis of direct and indirect comparisons. *Current Medical Research and Opinion, 22*(4), 671-681.

Jatrana, S., & Crampton, P. (2010). Gender differences in general practice utilisation in New Zealand. *Journal of primary health care, 1*(4), 261-269.

Jerant, A. F., Friederichs-Fitzwater, M. M., & Moore, M. (2005). Patients' perceived barriers to active self-management of chronic conditions. *Patient Education & Counseling, 57*(3), 300-307.

Johnson, R. B., Onwuegbuzie, A. J., & Turner, L. A. (2007). Toward a definition of mixed methods research. *Journal of mixed methods research, 1*(2), 112-133.

Jones, P. W., Quirk, F. H., & Baveystock, C. M. (1991). The St George's respiratory questionnaire. *Respiratory medicine, 85*(Suppl B), 25-31.

Jovicic, A., Jolroyd-Leduc, J. M., & Straus, S. E. (2006). Effects of self-management intervention on health outcomes of patients with heart failure: A systematic review of randomized controlled trials. *BMC Cardiovascular Disorders, 6*(43).

Karnilowicz, W. (2011). Identity and psychological ownership in chronic illness and disease state. *European Journal of Cancer Care, 20*(2), 276-282.

Kay, L. J., & Lapworth, K. (2004). Safety monitoring for disease-modifying anti-rheumatic drugs in primary and secondary care: Adherence to local and national guidelines and patient's views. *Rheumatology, 43*(1), 105.

Kaye, BR., Kaye, RL., & Bobrove, A. (1984). Rheumatoid nodules: Review of the spectrum of associated conditions and proposal of a new classification, with a report of four seronegative cases. *The American journal of medicine, 76*(2), 279-292.

Kenny, D. A. (2013). *Moderator Variables: Introduction*. Retrieved from http://davidakenny.net/cm/moderation.htm

Khan, N. A., Yazici, Y., Calvo-Alen, J., Dadoniene, J., Gossec, L., Hansen, T. M. *et al.,* (2009). Reevaluation of the role of duration of morning stiffness in the assessment of rheumatoid arthritis activity. *Journal of Rheumatology, 36*(11), 2435-2442.

Kirwan, J. R., Averns, H., Creamer, P., Davies, M., Hickling, P., Hutton, C. *et al.,* (2003a). Changes in rheumatology out–patient workload over 12–years in the South West of England. *Rheumatology, 42*(1), 175-179.

Kirwan, J. R., Minnock, P., Adebajo, A., Bresnihan, B., Choy, E., De Wit, M. *et al.,* (2007). Patient perspective: Fatigue as a recommended patient centered outcome measure in rheumatoid arthritis. *Journal of Rheumatology, 34*(5), 1174-1177.

Kirwan, J. R., Mitchell, K., Hewlett, S., Hehir, M., Pollock, J., Memel, D. *et al.,* (2003b). Clinical and psychological outcome from a randomized controlled trial of patient-initiated direct-access hospital follow-up for rheumatoid arthritis extended to 4 years. *Rheumatology, 42*(3), 422-426.

Kirwan, J. R., & Snow, S. M. (1991). Which patients see a rheumatologist? *British Journal of Rheumatology, 30*(4), 285-287.

Kirwan, J. R., De Saintonge, D. C., Joyce, C. R., & Currey, H. L. (1984). Clinical judgment in rheumatoid arthritis. III. British rheumatologists' judgments of'change in response to therapy'. *Annals of the Rheumatic Diseases, 43*(5), 686-694.

Kjeken, I., Dagfinrud, H., Mowinckel, P., Uhlig, T., Kvien, T. K., & Finset, A. (2006). Rheumatology care: Involvement in medical decisions, received information,

satisfaction with care, and unmet health care needs in patients with rheumatoid arthritis and ankylosing spondylitis. *Arthritis Care & Research, 55*(3), 394-401.

Klarenbeek, N. B., Güler-Yüksel, M., van der Heijde, D. M. F. M., Hulsmans, H. M. J., Kerstens, P. J. S. M., Molenaar, T. H. E. *et al.,* (2010). Clinical synovitis in a particular joint is associated with progression of erosions and joint space narrowing in that same joint, but not in patients initially treated with infliximab. *Annals of the Rheumatic Diseases, 69*(12), 2107-2113.

Klareskog, L., van der Heijde, D., de Jager, J. P., Gough, A., Kalden, J., Malaise, M. *et al.,* (2004). Therapeutic effect of the combination of etanercept and methotrexate compared with each treatment alone in patients with rheumatoid arthritis: double-blind randomised controlled trial. *The Lancet, 363*(9410), 675-681.

Kleefstra, N., Hortensius, J., van Hateren, K. J. J., Logtenberg, S. J. J., Houweling, S. T., Gans, R. O. B. *et al.,* (2009). Self-monitoring of blood glucose in noninsulin-treated type 2 diabetes: an overview. *Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy, 2*, 155-163.

Klersy, C., De Silvestri, A., Gabutti, G., Regoli, F., & Auricchio, A. (2009). A Meta-Analysis of Remote Monitoring of Heart Failure Patients. *Journal of the American College of Cardiology, 54*(18), 1683-1694.

Knittle, K., Maes, S., & de Gucht, V. (2010). Psychological interventions for rheumatoid arthritis: Examining the role of self-regulation with a systematic review and meta-analysis of randomized controlled trials. *Arthritis Care & Research, 62*(10), 1460-1472.

Koksvik, H. S., Hagen, K. B., Rødevand, E., Mowinckel, P., Kvien, T. K., & Zangi, H. A. (2013). Patient satisfaction with nursing consultations in a rheumatology outpatient clinic: a 21-month randomised controlled trial in patients with inflammatory arthritides. *Annals of the Rheumatic Diseases, 72*(6), 836-843.

Kotsis, K., Voulgari, P. V., Tsifetaki, N., Machado, M. O., Carvalho, A. F., Creed, F. *et al.,* (2012). Anxiety and depressive symptoms and illness perceptions in psoriatic arthritis and associations with physical health-related quality of life. *Arthritis Care & Research, 64*(10), 1593-1601.

Kraemer, H. C., & Thiemann, S. (1987). *How many subjects?: Statistical power analysis in research*. London: Sage.

Kraemer, H. C., Wilson, G. T., Fairburn, C. G., & Agras, W. S. (2002). Mediators and moderators of treatment effects in randomized clinical trials. *Archives of General Psychiatry, 59*(10), 877-883.

Kristiansen, T. M., Primdahl, J., Antoft, R., & HØrslev-Petersen, K. (2012). It Means Everything: Continuing Normality of Everyday Life for People with Rheumatoid Arthritis in Early Remission. *Musculoskeletal Care, 10*(3), 162-170.

Kristiansen, T. M., Primdahl, J., Antoft, R., & Hørslev-Petersen, K. (2012). Everyday Life with Rheumatoid Arthritis and Implications for Patient Education and Clinical Practice: A Focus Group Study. *Musculoskeletal Care, 10*(1), 29-38.

Kruger, J., Helmick, C. G., Callahan, L. F., & Haddix, A. C. (1998). Cost-effectiveness of the arthritis self-help course. *Archives of Internal Medicine, 158*(11), 1245.

Kuzel, A. J. (1992). Sampling in qualitative inquiry. In B. Crab & M. Miller (Eds.), *Doing qualitative research. Research methods for primary care.* (pp. 31-44). Thousand Oaks, CA, US: SAGE Publications, Inc.

Lacaille, D., Anis, A. H., Guh, D. P., & Esdaile, J. M. (2005). Gaps in care for rheumatoid arthritis: A population study. *Arthritis Care & Research, 53*(2), 241-248.

Laine, L., Bombardier, C., Hawkey, C. J., Davis, B., Shapiro, D., Brett, C. *et al.,* (2002). Stratifying the risk of NSAID-related upper gastrointestinal clinical events: results of a double-blind outcomes study in patients with rheumatoid arthritis. *Gastroenterology, 123*(4), 1006-1012.

Larsson, I., Bergman, S., Fridlund, B., & Arvidsson, B. (2012). Patients' experiences of a nurse–led rheumatology clinic in Sweden: A qualitative study. *Nursing & health sciences, 14*(4), 501-507.

Larsson, I., Fridlund, B., Arvidsson, B., Teleman, A., & Bergman, S. (2013). Randomized controlled trial of a nurse-led rheumatology clinic for monitoring biological therapy. *Journal of advanced nursing, Epub ahead of print*.

Lavery, K. A., O'Neill, B., Parker, M., Elborn, J. S., & Bradley, J. M. (2011). Expert patient self-management program versus usual care in bronchiectasis: a randomized controlled trial. *Archives of physical medicine and rehabilitation, 92*(8), 1194-1201.

Lawrence, J. S. (1961). Prevalence of Rheumatoid Arthritis. *Annals of the Rheumatic Diseases, 20*(1), 11-17.

Leung, Y.-Y., Tam, L. S., Lee, K. W., Leung, M. H., Kun, E. W., & Li, E. K. (2009). Involvement, satisfaction and unmet health care needs in patients with psoriatic arthritis. *Rheumatology, 48*(1), 53-56.

Leventhal, H., Meyer, D., & Nerenz, D. (1980). The common sense representation of illness danger. In S. Rachman (Ed.), *Medical Psychology* (2 ed., pp. 7-30). New York: Pergamon.

Li, L. C., Badley, E. M., MacKay, C., Mosher, D., Jamal, S., Jones, A. *et al.,* (2008). An evidence-informed, integrated framework for rheumatoid arthritis care. *Arthritis Care & Research, 59*(8), 1171-1183.

Liddy, C., Dusseault, J. J., Dahrouge, S., Hogg, W., Lemelin, J., & Humber, J. (2008). Telehomecare for patients with multiple chronic illnesses. *Canadian Family Physician, 54*(1), 58-65.

Lim, A. Y., Ellis, C., Brooksby, A., & Gaffney, K. (2007). Patient satisfaction with rheumatology practitioner clinics: can we achieve concordance by meeting patients' information needs and encouraging participatory decision making? *Annals of the Academy of Medicine, 36*(2), 110-114.

Linton, S. J., Boersma, K., Vangronsveld, K., & Fruzzetti, A. (2012). Painfully reassuring? The effects of validation on emotions and adherence in a pain test. *European Journal of Pain, 16*(4), 592-599.

Loke, Y. K., Hinz, I., Wang, X., Rowlands, G., Scott, D., & Salter, C. (2012). Impact of health literacy in patients with chronic musculoskeletal disease - systematic review. *PloS one, 7*(7), e40210.

Lorig, K., Chastain, R. L., Ung, E., Shorr, S., & Holman, H. R. (1989). Development and evaluation of a scale to measure perceived self-efficacy in people with arthritis. *Arthritis & Rheumatism, 32*(1), 37-44.

Lorig, K., & Holman, H. (1993). Arthritis self-management studies: a twelve-year review. *Health Education Quarterly, 20*(1), 17-28.

Lorig, K., Lubeck, D., Kraines, R. G., Seleznick, M., & Holman, H. R. (1985). Outcomes of self-help education for patients with arthritis. *Arthritis & Rheumatism, 28*(6), 680-685.

Lorig, K., Seleznick, M., Lubeck, D., Ung, E., Chastain, R. L., & Holman, H. R. (1989). The beneficial outcomes of the arthritis self–management course are not adequately explained by behavior change. *Arthritis & Rheumatism, 32*(1), 91-95.

Lorig, K. R., Ritter, P., Stewart, A. L., Sobel, D. S., Brown Jr, B. W., Bandura, A. *et al.,* (2001). Chronic disease self-management program: 2-year health status and health care utilization outcomes. *Medical care, 39*(11), 1217-1223.

Lorig, K. R., Ritter, P. L., Dost, A., Plant, K., Laurent, D. D., & Mcneil, I. (2008). The expert patients programme online, a 1-year study of an Internet-based self-management programme for people with long-term conditions. *Chronic Illness, 4*(4), 247-256.

Lorig, K. R., Ritter, P. L., Laurent, D. D., & Plant, K. (2008). The internet-based arthritis self-management program: A one-year randomized trial for patients with arthritis or fibromyalgia. *Arthritis Care & Research, 59*(7), 1009-1017.

Louis, A. A. T., Turner, T., Gretton, M., Baksh, A., & Cleland, J. G. F. (2003). A systematic review of telemonitoring for the management of heart failure. *European Journal of Heart Failure, 5*(5), 583-590.

Lowe, R., Cockshott, Z., Greenwood, R., Kirwan, J. R., Almeida, C., Richards, P. *et al.,* (2008). Self-efficacy as an appraisal that moderates the coping-emotion relationship: Associations among people with rheumatoid arthritis. *Psychology & Health, 23*(2), 155-174.

Lowe, W., Ballinger, C., Protheroe, J., Lueddeke, J., Nutbeam, D., Armstrong, R. *et al.,* (2013). Effectiveness of Musculoskeletal Education Interventions in People With Low Literacy Levels: A Systematic Review. *Arthritis Care & Research, 65*(12), 1976-1985.

Lowry, R. (2014). *Estimation of a Sample's Mean and Variance from Its Median and Range*. Retrieved from http://vassarstats.net/median_range.html

Lundkvist, J., Kastang, F., & Kobelt, G. (2008). The burden of rheumatoid arthritis and access to treatment: health burden and costs. *The European journal of health economics, 8*(Suppl 2), 49-60.

Maas, C. J., & Hox, J. J. (2005). Sufficient sample sizes for multilevel modeling. *Methodology: European Journal of Research Methods for the Behavioral and Social Sciences, 1*(3), 86-92.

Maas, M., Van Der Linden, S., & Boonen, A. (2009). A review of instruments to assess illness representations in patients with rheumatic diseases. *Annals of the Rheumatic Diseases, 68*(3), 305-309.

MacAlister, A., Perry, C., & Parcel G. (2008). How individuals, environments and health behaviours interact: Social cognitive theory. In K.Glanz, B.K.Rimer, & K.Viswanath (Eds.), *Health behaviour and health education: Theory, research and practice* (4th ed.,). San Francisco, C.A: Jossey-Bass.

MacGregor, A. J., Riste, L. K., Hazes, J. M., & Silman, A. J. (1994). Low prevalence of rheumatoid arthritis in black-Caribbeans compared with whites in inner city Manchester. *Annals of the Rheumatic Diseases, 53*(5), 293-297.

MacGregor, A., Sneider, H., Rigby, A. S., Koskenvuo, M., Kaprio, J., Aho, K. *et al.,* (2000). Characterizing the quantitative genetic contribution to rheumatoid arthritis using data from twins. *Arthritis & Rheumatism, 43*(1), 30-37.

MacKinnon, J. R., & Miller, W. C. (2003). Rheumatoid arthritis and self esteem: the impact of quality occupation. *Journal of Occupational Science, 10*(2), 90-98.

Main, C. J., Buchbinder, R., Porcheret, M., & Foster, N. (2010). Addressing patient beliefs and expectations in the consultation. *Best Practice & Research Clinical Rheumatology, 24*(2), 219-225.

Maisiak, R., Austin, J., & Heck, L. (1996). Health outcomes of two telephone interventions for patients with rheumatoid arthritis or osteoarthritis. *Arthritis & Rheumatism, 39*(8), 1391-1399.

Malanda, U. L., Welschen, L. M., Riphagen, I. I., Dekker, J. M., Nijpels, G., & Bot, S. D. (2012). Self-monitoring of blood glucose in patients with type 2 diabetes mellitus who are not using insulin. *Cochrane Database of Systematic Reviews*.

Mancuso, C. A., Rincon, M., Sayles, W., & Paget, S. A. (2006). Psychosocial variables and fatigue: A longitudinal study comparing individuals with rheumatoid arthritis and healthy controls. *Journal of Rheumatology, 33*(8), 1496-1502.

Mann, C. (2006). Is the drive to manage long–term conditions in the community compatible with improving standards of care for those with inflammatory arthritis? *Musculoskeletal Care, 4*(2), 67-77.

Maric, B., Kaan, A., Ignaszewski, A., & Lear, S. A. (2009). A systematic review of telemonitoring technologies in heart failure. *European Journal of Heart Failure, 11*(5), 506-517.

Marques, M., & Hamilton, K. (2014). Health psychology and statistical methods: out with the old and in with the new. *The European Health Psychologist, 16*(2), 36-39.

Martin, C., & Johnson, K. (2011). Doctor-patient involvement in biologic treatment choice: The benefits of a collaborative approach. *Arthritis & Rheumatism, 63* (S10), 1891.

Martinez, A., Everss, E., Rojo-Alvarez, J. L., Pascual, F. D., & Garcia-Alberola, A. (2006). A systematic review of the literature on home monitoring for patients with heart failure. *Journal of Telemedicine and Telecare, 12*(5), 234-241.

Maska, L., Anderson, J., & Michaud, K. (2011). Measures of functional status and quality of life in rheumatoid arthritis: Health Assessment Questionnaire Disability Index

(HAQ), Modified Health Assessment Questionnaire (MHAQ), Multidimensional Health Assessment Questionnaire (MDHAQ), Health Assessment Questionnaire II (HAQ-II), Improved Health Assessment Questionnaire (Improved HAQ), and Rheumatoid Arthritis Quality of Life (RAQoL). *Arthritis Care & Research, 63*(S11), S4-S13.

Matsuo, T., Kono, R., Matsuo, N., Ezawa, K., Natsumeda, M., Soda, K. *et al.,* (1997). Incidence of ocular complications in rheumatoid arthritis and the relation of keratoconjunctivitis sicca with its systemic activity. *Scandinavian Journal of Rheumatology, 26*(2), 113-116.

May, C., Montori, V. M., & Mair, F. S. (2009). We need minimally disruptive medicine. *British Medical Journal, 339*, b2803.

Mc Sharry, J., Moss-Morris, R., & Kendrick, T. (2011). Illness perceptions and glycaemic control in diabetes: a systematic review with meta-analysis. *Diabetic Medicine, 28*(11), 1300-1310.

McAuley, L., Pham, B., Tugwell, P., & Moher, D. (2000). Does the inclusion of grey literature influence estimates of intervention effectiveness reported in meta-analyses? *The Lancet, 356*(9237), 1228-1231.

McCabe, C., McDowell, J., Cushnaghan, J., Butts, S., Hewlett, S., Stafford, S. *et al.,* (2000). Rheumatology telephone helplines: An activity analysis. *Rheumatology, 39*(12), 1390-1395.

McGeoch, G., Derry, S., & Moore, R. A. (2007). Self-monitoring of blood glucose in type-2 diabetes: what is the evidence? *Diabetes Metabolic Research and Reviews, 23*(6), 423-440.

McHorney, C. A., Ware Jr, J. E., & Raczek, A. E. (1993). The MOS 36-Item Short-Form Health Survey (SF-36): II. Psychometric and clinical tests of validity in measuring physical and mental health constructs. *Medical care, 31*(3), 247-263.

McIntosh, E. (1996). The cost of rheumatoid arthritis. *British Journal of Rheumatology, 35*(8), 781-790.

McLean, S., Nurmatov, U., Liu, J. L. Y., Pagliari, C., Car, J., & Sheikh, A. (2012). Telehealthcare for chronic obstructive pulmonary disease: Cochrane Review and meta-analysis. *British Journal of General Practice, 62*(604), e739-e749.

McLean, S., Nurmatov, U., Liu, J. L., Pagliari, C., Car, J., & Sheikh, A. (2011). Telehealthcare for chronic obstructive pulmonary disease. *Cochrane Database of Systematic Reviews*.

Medical Research Council. (2000). *A framework for the development and evaluation of RCTs for complex interventions to improve health* London: Medical Research Council.

Michie, S., Abraham, C., Whittington, C., McAteer, J., & Gupta, S. (2009). Effective techniques in healthy eating and physical activity interventions: a meta-regression. *Health psychology, 28*(6), 690-701.

Michie, S., Fixsen, D., Grimshaw, J. M., & Eccles, M. P. (2009). Specifying and reporting complex behaviour change interventions: the need for a scientific method. *Implementation Science, 4*(40).

Michie, S., Johnston, M., Abraham, C., Francis, J. J., & Eccles, M. P. (2013). The behavior change technique taxonomy (v1) of 93 hierarchically clustered techniques: Building an international consensus for the reporting of behavior change interventions. *Annals of Behavioral Medicine, 46*(1), 81-95.

Michie, S., & Abraham, C. (2004). Interventions to change health behaviours: evidence-based or evidence-inspired? *Psychology & Health, 19*(1), 29-49.

Michie, S., & Johnston, M. (2013). Behavior change techniques. In M. Gellman & J. Rick Turner (Eds.), *Encyclopedia of Behavioral Medicine* (pp. 182-187) Springer.

Mitchell, K. (2000). Shared care–the way forward for patient–orientated follow–up care in rheumatoid arthritis. *Rheumatology, 39*(5), 457-458.

Mitchell, K., Hewlett, S., Hehir, M., Kirwan, J., Pollack, J., Memel, D. *et al.,* (2001). Is it safe for patients with rheumatoid arthritis to have no regular follow up for 4 years? *Rheumatology, 40*(Suppl 1), 145-146.

Mitchell, K., Hewlett, S., & Kirwan, J. R. (1999). Will patients disease status deteriorate if they do not receive regular out-patient follow up care? *Annals of the Rheumatic Diseases, EULAR abstract supplement* (58), Suppl. 1-81.

Moher, D., Liberati, A., Tetzlaff, J., & Altman, D. G. (2009). Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Annals of internal medicine, 151*(4), 264-269.

Moher, D., Pham, B., Jones, A., Cook, D., Jadad, A., Moher, M. *et al.,* (1998). Does quality of reports of randomised trials affect estimates of intervention efficacy reported in meta-analyses? *The Lancet, 352*(9128), 609-613.

Morse, J. M., & Field, P. A. (1995). *Qualitative research methods for health professionals* (2nd ed.). Thousand Oaks, CA, US: Sage Publications.

Moser, D. K., McKinley, S., Riegel, B., Doering, L. V., Meischke, H., Pelter, M. *et al.,* (2011). Relationship of persistent symptoms of anxiety to morbidity and mortality outcomes in patients with coronary heart disease. *Psychosomatic Medicine, 73*(9), 803-809.

Moss-Morris, R., Weinman, J., Petrie, K. J., Horne, R., Cameron, L. D., & Buick, D. (2002). The revised illness perception questionnaire (IPQ-R). *Psychology & Health, 17*(1), 1-16.

Murphy, H., Dickens, C., Creed, F., & Bernstein, R. (1999). Depression, illness perception and coping in rheumatoid arthritis. *Journal of Psychosomatic Research, 46*(2), 155-164.

Myers, A., Kay, L. J., Lynch, S. A., & Walker, D. J. (2005). Recurrence risk for psoriasis and psoriatic arthritis within sibships. *Rheumatology, 44*(6), 773-776.

National Audit Office. (2009a). *Services for people with rheumatoid arthirtis: census findings* London: The Stationart Office.

National Audit Office. (2009b). *Services for people with rheumatoid arthritis.* (HC 823 Session 2008-2009). London: The Stationart Office.

National Collaborating Centre for Chronic Conditions. (2008). *Type 2 diabetes: National clinical guideline for management in primary and secondary care (update)* London: National Institute for Clinical Excellence.

National Collaborating Centre for Chronic Conditions. (2009). *Rheumatoid arthritis: national clinical guideline for management and treatment in adults* London: Royal College of Physicians.

National Health Service Institute for Innovation and Improvement. (2006). *Delivering quality and value: focus on: productivity and efficiency*. London: Department of Health.

National Institute for Clinical Excellence. (2010). *Type 1 diabetes: diagnosis and management of type 1 diabetes in children, young people and adults.* London: National Institute for Health and Care Excellence.

National Institute for Health and Care Excellence. (2013a). *Quality standards for rheumatoid arthritis* London: National Institute for Health and Care Excellence.

National Institute for Health and Care Excellence. (2013b). *Rheumatoid arthritis: the management of rheumatoid arthritis in adults* (NICE clinical guideline 79). London: National Institute for Health and Care Excellence.

National Institute for Health and Care Excellence. (2013c). *The NHS Outcomes Framework and Clinical Commissioning Group Outcomes Indicator Set to NICE Quality Standards* National Institute for Health and Care Excellence.

National Institute for Health and Clinical Excellence. (2010). *Etanercept, Infliximab, and Adalimumab for the treatment of psoriatic arthritis* (NICE Technology Appraisal Guideance 199). London: National Institute for Health and Clinical Excellence.

Ndosi, M., Lewis, M., Hale, C., Quinn, H., Ryan, S., Emery, P. *et al.,* (2013). The outcome and cost-effectiveness of nurse-led care in people with rheumatoid arthritis: a multicentre randomised controlled trial. *Annals of the Rheumatic Diseases, Epub ahead of print*.

Ndosi, M., Vinall, K., Hale, C., Bird, H., & Hill, J. (2011). The effectiveness of nurse-led care in people with rheumatoid arthritis: A systematic review. *International journal of nursing studies, 48*(5), 642-654.

Neame, R., & Hammond, A. (2005). Beliefs about medications: a questionnaire survey of people with rheumatoid arthritis . *Rheumatology, 44*(6), 762-767.

Neame, R., Hammond, A., & Deighton, C. (2005). Need for information and for involvement in decision making among patients with rheumatoid arthritis: a questionnaire survey. *Arthritis & Rheumatism, 53*(2), 249-255.

Nell, V. P. K., Machold, K. P., Eberl, G., Stamm, T. A., Uffmann, M., & Smolen, J. S. (2004). Benefit of very early referral and very early therapy with disease-modifying anti-rheumatic drugs in patients with early rheumatoid arthritis. *Rheumatology, 43*(7), 906-914.

Nestoriuc, Y., Orav, E. J., Liang, M. H., Horne, R., & Barsky, A. J. (2010). Prediction of nonspecific side effects in rheumatoid arthritis patients by beliefs about medicines. *Arthritis Care & Research, 62*(6), 791-799.

Newman, E. D., & Harrington, J. T. (2007). Redesigning the care of rheumatic diseases at the practice and system levels. Part 2: system level process improvement (Redesign 201). *Clinical & Experimental Rheumatology, 25*(6), S64. Retrieved from CLINICAL AND EXPERIMENTAL RHEUMATOLOGY SAS.

Ng, C. N., Liew, S. M., Vethakkan, S. R., Abdullah, A., & Teng, C. L. (2013). Patient-adjusted versus health professional-adjusted insulin dosing for type 2 diabetes mellitus: Intervention Protocol. *Cochrane Database of Systematic Reviews, 6*.

Niedermann, K., Fransen, J., Knols, R., & Uebelhart, D. (2004). Gap between short- and long–term effects of patient education in rheumatoid arthritis patients: A systematic review. *Arthritis Care & Research, 51*(3), 388-398.

Nolte, S., Elsworth, G. R., Sinclair, A. J., & Osborne, R. H. (2007). The extent and breadth of benefits from participating in chronic disease self-management courses: a

national patient-reported outcomes survey. *Patient Education & Counseling, 65*(3), 351-360.

Norton, S., Hughes, L. D., Chilcot, J., Sacker, A., van Os, S., Young, A. *et al.,* (2013). Negative and positive illness representations of rheumatoid arthritis: a latent profile analysis, *37*(3), 524-532.

O'Cathain, A., Thomas, K. J., Drabble, S. J., Rudolph, A., & Hewison, J. (2013). What can qualitative research do for randomised controlled trials? A systematic mapping review. *BMJ Open, 3*(6), e002889.

O'Connor, D., Kortman, B., Smith, A., Ahern, M., Smith, M., & Krishnan, J. (1999). Correlation between objective and subjective measures of hand function in patients with rheumatoid arthritis. *Journal of Hand Therapy, 12*(4), 323-329.

O'Kane, M. J., Bunting, B., Copeland, M., & Coates, V. E. (2008). Efficacy of self monitoring of blood glucose in patients with newly diagnosed type 2 diabetes (ESMON study): randomised controlled trial. *British Medical Journal, 336*(7654), 1174-1177.

Ødegård, S., Landewé, R., van der Heijde, D., Kvien, T. K., Mowinckel, P., & Uhlig, T. (2006). Association of early radiographic damage with impaired physical function in rheumatoid arthritis: A ten-year, longitudinal observational study in 238 patients. *Arthritis & Rheumatism, 54*(1), 68-75.

Office for National Statistics. (2012). *2012-based National Population Projections* Office for National Statistics.

Orr, J. M., Sackett, P. R., & Dubois, C. (1991). Outlier detection and treatment in I/O psychology: A survey of researcher beliefs and an empirical illustration. *Personnel Psychology, 44*(3), 473-486.

Osborne, J. (2002). Notes on the use of data transformations. *Practical Assessment, Research & Evaluation, 8*(6), 1-8.

Osborne, R. H., Elsworth, G. R., & Whitfield, K. (2007). The Health Education Impact Questionnaire (heiQ): an outcomes and evaluation measure for patient education and

self-management interventions for people with chronic conditions. *Patient Education & Counseling, 66*(2), 192-201.

Oxford Economics. (2010). *The economic costs of arthritis for the UK economy* Oxford: Oxford Economics.

Packer, T. L., Boldy, D., Ghahari, S., Melling, L., Parsons, R., & Osborne, R. H. (2012). Self-management programs conducted within a practice setting: Who participates, who benefits and what can be learned? *Patient Education & Counseling, 87*(1), 93-100.

Pal, B. (1997). Telemedicine. Pilot study of telephone follow up in rheumatology has just been completed. *British Medical Journal, 314*(7079), 520-521.

Pal, B. (1998). Following up outpatients by telephone: pilot study. *British Medical Journal, 316*(7145), 1647.

Pallant, J. F. (2007). *SPPS Survival Manual* (3rd ed.). Maidenhead: Open University Press.

Pandor, A., Gomersall, T., Stevens, J. W., Wang, J., Al-Mohammad, A., Bakhai, A. *et al.,* (2013). Remote monitoring after recent hospital discharge in patients with heart failure: A systematic review and network meta-analysis. *Heart, 99*(23), 1717-1726.

Pang, J., & Malhotra, B. (2009). *Shared Care Guideline: Methotrexate - Treatment of moderate to severe active rheumatoid arthritis or treatment of severe psoriasis* University College Hospitals London.

Panoulas, V. F., Douglas, K. M. J., Milionis, H. J., Stavropoulos-Kalinglou, A., Nightingale, P., Kita, M. D. *et al.,* (2007). Prevalence and associations of hypertension and its control in patients with rheumatoid arthritis. *Rheumatology, 46*(9), 1477-1482.

Paskins, Z., Sanders, T., & Hassell, A. B. (2014). Comparison of patient experiences of the osteoarthritis consultation with GP attitudes and beliefs to OA: a narrative review. *BMC family practice, 15*(1), 46.

Pattison, D., Harrison, A., & Symmons, D. (2004). The role of diet in susceptibility to rheumatoid arthritis: A a systematic review. *Journal of Rheumatology, 31*(7), 1310-1319.

Patton, M. (1990). *Qualitative evaluation and research methods, second edition.* California: Sage Publications Inc.

Paudyal, P., Perry, M., Child, S., & Gericke, C. A. (2012). Evaluation of a patient-initiated review system in rheumatoid arthritis: An implementation trial protocol. *BMC Musculoskeletal Disorders, 13*(120).

Peel, E., Parry, O., Douglas, M., & Lawton, J. (2004). Blood glucose self-monitoring in non-insulin-treated type 2 diabetes: a qualitative study of patients' perspectives. *British Journal of General Practice, 54*(500), 183-188.

PenCLAHRC. (2010a). *PenCLAHRC Priority Briefing: Round 2 (Oct 09 - Feb 10)*. Retrieved from http://clahrc-peninsula.nihr.ac.uk/priority-briefings/round-2-oct-09-feb-10.php

PenCLAHRC. (2010b). *Q6 Patient initiated care: Priority Briefing*. Retrieved from http://clahrc-peninsula.nihr.ac.uk/includes/site/files/files/priority-briefing/oct-09-feb-10/Q6%20PIC%20PB.pdf

Pieper, D., Antoine, S. L., Mathes, T., Neugebauer, E. A., & Eikermann, M. (2014). Systematic review finds overlapping reviews were not mentioned in every other overview. *Journal of Clinical Epidemiology, 67*(4), 368-375.

Pincus, T., & Stein, C. M. (1996). Why randomized controlled clinical trials do not depict accurately long-term outcomes in rheumatoid arthritis: some explanations and suggestions for future studies. *Clinical & Experimental Rheumatology, 15*(Suppl 17), S27-S38.

Polisena, J., Tran, K., Cimon, K., Hutton, B., McGill, S., Palmer, K. *et al.,* (2010). Home telemonitoring for congestive heart failure: a systematic review and meta-analysis. *Journal of Telemedicine and Telecare, 16*(2), 68-76.

Pollard, L., Choy, E. H., & Scott, D. L. (2005). The consequences of rheumatoid arthritis: quality of life measures in the individual patient. *Clinical & Experimental Rheumatology, 23*(Suppl 39), S43-S52.

Poole, C. D., Lebmeier, M., Ara, R., Rafia, R., & Currie, C. J. (2010). Estimation of health care costs as a function of disease severity in people with psoriatic arthritis in the UK. *Rheumatology, 49*(10), 1949-1956.

Poolsup, N., Suksomboon, N., & Jiamsathit, W. (2008). Systematic Review of the Benefits of Self-Monitoring of Blood Glucose on Glycemic Control in Type 2 Diabetes Patients. *Diabetes technology & therapeutics, 10*(s1), S51-S66.

Poolsup, N., Suksomboon, N., & Rattanasookchit, S. (2009). Meta-analysis of the benefits of self-monitoring of blood glucose on glycemic control in type 2 diabetes patients: an update. *Diabetes technology & therapeutics, 11*(12), 775-784.

Pope, D., Tipler, S., Kirwan, J., & Hewlett, S. (2005). Implementing a patient-led service for chronic conditions. *Nursing times, 101*(49), 28-31.

Prevoo, M. L. L., Van't Hof, M. A., Kuper, H. H., Van Leeuwen, M. A., Van De Putte, L. B. A., & Van Riel, P. L. C. M. (1995). Modified disease activity scores that include twenty-eight-joint counts development and validation in a prospective longitudinal study of patients with rheumatoid arthritis. *Arthritis Care & Research, 38*(1), 44-48.

Primdahl, J., Wagner, L., & Hørslev-Petersen, K. (2011a). Self-Efficacy as an Outcome Measure and its Association with Physical Disease-Related Variables in Persons with Rheumatoid Arthritis: A Literature Review. *Musculoskeletal Care, 9*(3), 125-140. Retrieved from John Wiley & Sons, Ltd.

Primdahl, J., Sørensen, J., Horn, H. C., Petersen, R., & Hørslev-Petersen, K. (2014). Shared care or nursing consultations as an alternative to rheumatologist follow-up for rheumatoid arthritis outpatients with low disease activity – patient outcomes from a 2-year, randomised controlled trial. *Annals of the Rheumatic Diseases, 73*(2), 357-364.

Primdahl, J., Wagner, L., Holst, R., & Hørslev-Petersen, K. (2012). The impact on self-efficacy of different types of follow-up care and disease status in patients with

rheumatoid arthritis - A randomized trial. *Patient education and counseling, 88*(1), 121-128.

Primdahl, J., Wagner, L., & Hørslev-Petersen, K. (2011b). Being an outpatient with rheumatoid arthritis - a focus group study on patients' self-efficacy and experiences from participation in a short course and one of three different outpatient settings. *Scandinavian Journal of Caring Sciences, 25*(2), 394-403.

Radboud University Nijmegen. (2014). *How to calculate the DAS28*. Retrieved from Radboud University Nijmegen http://www.das-score.nl/das28/en/difference-between-the-das-and-das28/how-to-measure-the-das28/how-to-calculate-the-das28.html

Radhakrishnan, K., Jacelon, C., & Roche, J. (2012). Perceptions on the Use of Telehealth by Homecare Nurses and Patients With Heart Failure: A Mixed Method Study. *Home Health Care Management & Practice, 24*(4), 175-181.

Rahman, P., & Elder, J. T. (2005). Genetic epidemiology of psoriasis and psoriatic arthritis. *Annals of the Rheumatic Diseases, 64*(Suppl 2), ii37-ii39.

Rakkhit, T., Wong, B., Nelson, T. S., Hansen, C., Papenfuss, J., Panko, J. *et al.,* (2007). Time to development of psoriatic arthritis decreases with smoking prior to psoriasis onset and increases with smoking after psoriasis onset. *Journal of Investigative Dermatology, 127*(Suppl 1), S52.

Ramos-Casals, M., Brito-Zerón, P., & Font, J. (2007). The Overlap of Sjögren's Syndrome with Other Systemic Autoimmune Diseases. *Seminars in Arthritis & Rheumatism, 36*(4), 246-255.

Rapley, T. J. (2001). The art(fulness) of open-ended interviewing: some considerations on analysing interviews. *Qualitative Research, 1*(3), 303-323.

Raychaudhuri, S. P., & Farber, E. M. (2001). The prevalence of psoriasis in the world. *Journal of the European Academy of Dermatology and Venereology, 15*(1), 16-17.

Raychaudhuri, S. P., & Gross, J. (2000). Psoriasis risk factors: role of lifestyle practices. *Cutis, 66*(5), 348-352.

Rector, T. S., Kubo, S. H., & Cohn, J. N. (1987). Patients' self-assessment of their congestive heart failure. Part 2: content, reliability and validity of a new measure, the Minnesota Living with Heart Failure Questionnaire. *Heart failure, 3*(5), 198-209.

Reeves, D., Kennedy, A., Fullwood, C., Bower, P., Gardner, C., Gately, C. *et al.,* (2008). Predicting who will benefit from an Expert Patients Programme self-management course. *British Journal of General Practice, 58*(548), 198-203.

Renzi, C., Di, P. C., & Tabolli, S. (2011). Participation, satisfaction and knowledge level of patients with cutaneous psoriasis or psoriatic arthritis. *Clinical & Experimental Rheumatology, 36*(8), 885-888.

Repping-Wuts, H., Fransen, J., van Achterberg, T., Bleijenberg, G., & van Riel, P. (2007). Persistent severe fatigue in patients with rheumatoid arthritis. *Journal of Clinical Nursing, 16*(11C), 377-383.

Riemsma, R. P., Taal, E., Kirwan, J. R., & Rasker, J. J. (2004). Systematic review of rheumatoid arthritis patient education. *Arthritis Care & Research, 51*(6), 1045-1059.

Ritchie, J., & Spencer, L. (1994). Qualitative data analysis for applied policy research. In A. Bryman & R. Burgess (Eds.), *Analysing qualitative data* (pp. 172-194). London: Routledge.

Ritchie, J., Spencer, L., & O'Connor, W. (2003). Carrying out qualitative analysis. In J. Ritchie & J. Lewis (Eds.), (pp. 219-262). London: Sage Publications.

Ritter, P. L., Gonzalez, V. M., Laurent, D. D., & Lorig, K. R. (2006). Measurement of Pain Using the Visual Numeric Scale. *Journal of Rheumatology, 33*(3), 574-580.

Ritter, P. L., Lee, J., & Lorig, K. (2011). Moderators of chronic disease self-management programs: who benefits? *Chronic Illness, 7*(2), 162-172.

Ritter, P. L., Stewart, A. L., Kaymaz, H., Sobel, D. S., Block, D. A., & Lorig, K. R. (2001). Self-reports of health care utilization compared to provider records. *Journal of Clinical Epidemiology, 54*(2), 136-141.

Roberts, C., Adebajo, A. O., & Long, S. (2002). Improving the quality of care of musculoskeletal conditions in primary care. *Rheumatology, 41*(5), 503-508.

Roberts, C., Dolman, E. A., Adebajo, A. O., & Underwood, M. (2003). A national qualitative survey of community–based musculoskeletal services in the UK. *Rheumatology, 42*(9), 1074-1078.

Rogers, A., Kirk, S., Gately, C., May, C. R., & Finch, T. (2011). Established users and the making of telecare work in long term condition management: implications for health policy. *Social Science & Medicine, 72*(7), 1077-1084.

Rothwell, P. M. (2005). Subgroup analysis in randomised controlled trials: importance, indications, and interpretation. *The Lancet, 365*(9454), 176-186.

Royal College of General Practitioners. (2014). *GP with a Special Interest (GPwSI) accreditation*. Retrieved from Royal College of General Practitioners http://www.rcgp.org.uk/clinical-and-research/clinical-resources/gp-with-a-special-interest-gpwsi-accreditation.aspx

Royal College of Nurse Rheumatology Forum. (2009). *Rheumatology Nursing: Results of a survey exploring the performance and activity of rheumatology nurses.* London: Royal College of Nursing.

Royal College of Nursing. (2006). *Telephone advice lines for people with long term conditions: Guidance for nursing practitioners* London: Royal College of Nursing.

Royal College of Physicians. (2011). *Consultant physicians working with patients: The duties, responsibilities and practice of physicians in medicine.* London: Royal College of Physicians.

Royal College of Physicians. (2013). *Census of consultant physicians in the UK 2011. Speciality report: rheumatology.* London: Royal College of Physicians.

Rubin, D. B. (2009). *Multiple imputation for nonresponse in surveys.* USA: John Wiley & Sons, Inc.

Ryan, S., Hassell, A. B., Lewis, M., & Farrell, A. (2006). Impact of a rheumatology expert nurse on the wellbeing of patients attending a drug monitoring clinic. *Journal of advanced nursing, 53*(3), 277-286.

Sakkas, L. I., Alexiou, I., Simopoulou, T., & Vlychou, M. (2013). Enthesitis in psoriatic arthritis. *Seminars in Arthritis & Rheumatism, 43*(3), 325-334.

Sandelowski, M. (1995). Sample size in qualitative research. *Research in Nursing & Health, 18*(2), 179-183.

Sanders, C., Rogers, A., Bowen, R., Bower, P., Hirani, S., Cartwright, M. *et al.,* (2012). Exploring barriers to participation and adoption of telehealth and telecare within the Whole System Demonstrator trial: a qualitative study. *BMC health services research, 12*(1), 220.

Sanderson, T., Calnan, M., Morris, M., Richards, P., & Hewlett, S. (2011). Shifting normalities: interactions of changing conceptions of a normal life and the normalisation of symptoms in rheumatoid arthritis. *Sociology of Health & Illness, 33*(4), 618-633.

Sands, A., & Adams, N. (2009). A comparison of patient-initiated versus conventional follow-up for rheumatoid arthritis. *Rheumatology, 48*, i157-i158.

Sarol Jr, J. R., Nicodemus Jr, N. A., Tan, K. M., & Grava, M. B. (2005). Self-monitoring of blood glucose as part of a multi-component therapy among non-insulin requiring type 2 diabetes patients: A meta-analysis (1966-2004). *Current Medical Research and Opinion, 21*(2), 173-183.

Sarzi-Puttini, P., Fiorini, T., Panni, B., Turiel, M., Cazzola, M., & Atzeni, F. (2002). Correlation of the score for subjective pain with physical disability, clinical and radiographic scores in recent onset rheumatoid arthritis. *BMC Musculoskeletal Disorders, 3*(1), 18.

Sayah, A., & English, J. (2005). Rheumatoid arthritis: A review of the cutaneous manifestations. *Journal of the American Academy of Dermatology, 53*(2), 191-209.

Scharloo, M., Kaptein, A. A., Weinman, J., Hazes, J. M., Willems, L. N. A., Bergman, W. *et al.,* (1998). Illness perceptions, coping and functioning in patients with rheumatoid arthritis, chronic obstructive pulmonary disease and psoriasis. *Journal of Psychosomatic Research, 44*(5), 573-585.

Scherbaum, C. A., Cohen-Charash, Y., & Kern, M. J. (2006). Measuring General Self-Efficacy: A Comparison of Three Measures Using Item Response Theory. *Educational and Psychological Measurement, 66*(6), 1047-1063.

Schiaffmo, K. M., & Revenson, T. A. (1992). The Role of Perceived Self-Efficacy, Perceived Control, and Causal Attributions in Adaptation to Rheumnatoid Arthritis: Distinguishing Mediator from Moderator Effects. *Personality and Social Psychology Bulletin, 18*(6), 709-718.

Scholz, U., Doña, B., Sud, S., & Schwarzer, R. (2002). Is general self-efficacy a universal construct? Psychometric findings from 25 countries. *European journal of psychological assessment, 18*(3), 242.

Schuler, M., Musekamp, G., Faller, H., Ehlebracht-König, I., Gutenbrunner, C., Kirchhof, R. *et al.,* (2012). Assessment of proximal outcomes of self-management programs: translation and psychometric evaluation of a German version of the Health Education Impact Questionnaire (heiQ™). *Quality of life research, 22*(6), 1391-1403.

Schulpen, G. J. C., Vierhout, W. P. M., van der Heijde, D. M., Landewé, R. B., Winkens, R. A. G., Wesselingh-Megens, A. M. K. *et al.,* (2003). Patients at the outpatient rheumatology clinic: do they really need to be there? *European Journal of Internal Medicine, 14*(3), 158-161.

Schwarzer, R., & Jerusalem, M. (1995). Generalized Self-Efficacy scale. In J. Weinman, S. Wright, & M. Johnston (Eds.), *Measures in health psychology: A user's portfolio. Causal and control beliefs.* (pp. 35-37). Windsor, UK: NFER-NELSON.

Serarslan, G., Güler, H., & Karazincir, S. (2007). The relationship between nail-and distal phalangeal bone involvement severity in patients with psoriasis. *Clinical Rheumatology, 26*(8), 1245-1247.

Serlachius, A., & Sutton, S. (2009). Self-management and behaviour change: theorectical models. In S. Newman, L. Steed, & K. Mulligna (Eds.), *Chronic Physical Illness: Self-management and Behavioural Interventions* (pp. 47-63). Berkshire, England: Open University Press.

Seto, E., Leonard, K. J., Masino, C., Cafazzo, J. A., Barnsley, J., & Ross, H. J. (2010). Attitudes of heart failure patients and health care providers towards mobile phone-based remote monitoring. *Journal of medical Internet research, 12*(4), e55.

Setty, AR., Curhan, G., & Choi, H. (2007). Smoking and the Risk of Psoriasis in Women: Nurses' Health Study II. *The American journal of medicine, 120*(11), 953-959.

Sharpe, L., Sensky, T., & Allard, S. (2001). The course of depression in recent onset rheumatoid arthritis: the predictive role of disability, illness perceptions, pain and coping. *Journal of Psychosomatic Research, 51*(6), 713-719.

Shbeeb, M., Uramoto, K. M., Gibson, L. E., O'Fallon, W. M., & Gabriel, S. E. (2000). The epidemiology of psoriatic arthritis in Olmsted County, Minnesota, USA, 1982-1991. *Journal of Rheumatology, 27*(5), 1247-1250.

Shea, B., Grimshaw, J., Wells, G., Boers, M., Andersson, N., Hamel, C. *et al.,* (2007). Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. *BMC Medical Research Methodology, 7*(1), 1-7.

Shea, B. J., Hamel, C., Wells, G. A., Bouter, L. M., Kristjansson, E., Grimshaw, J. *et al.,* (2009). AMSTAR is a reliable and valid measurement tool to assess the methodological quality of systematic reviews. *Journal of Clinical Epidemiology, 62*(10), 1013-1020.

Shipton, D., Glazier, R. H., Guan, J., & Badley, E. M. (2004). Effects of Use of Specialty Services on Disease-Modifying Antirheumatic Drug Use in the Treatment of Rheumatoid Arthritis in an Insured Elderly Population. *Medical care, 42*(9), 907-913.

Siebenhofer, A., Berghold, A., & Sawicki, P. T. (2004). Systematic review of studies of self-management of oral anticoagulation. *Thrombosis and Haemostasis, 91*(2), 225-232.

Sierakowski, S., & Cutolo, M. (2011). Morning symptoms in rheumatoid arthritis: a defining characteristic and marker of active disease. *Scandinavian Journal of Rheumatology, 40*(S125), 1-5.

Silman, A. J., Kay, A., & Brennan, P. (1992). Timing of Pregnancy in Relation to the Onset of Rheumatoid Arthritis. *Arthritis & Rheumatism, 35*(2), 152-155.

Silman, A. J., & Pearson, J. E. (2002). Epidemiology and genetics of rheumatoid arthritis. *Arthritis & Rheumatism, 4*(Suppl 3), S265-S272.

Simon, J., Gray, A., Clarke, P., Wade, A., Neil, A., Farmer, A. *et al.,* (2008). Cost effectiveness of self monitoring of blood glucose in patients with non-insulin treated type 2 diabetes: economic evaluation of data from the DiGEM trial. *British Medical Journal, 336*(7654), 1177-1180.

Simon, L., Claire, G., & Andrew, D. O. (2009). Use of qualitative methods alongside randomised controlled trials of complex healthcare interventions: methodological study. *British Medical Journal, 339*, b3496.

Smith, J. A., Flowers, P., & Larkin, M. (2009). *Interpretative Phenomenological Analysis: Theory, Method and Research* Sage Publications Ltd.

Smith, V., Devane, D., Begley, C. M., & Clarke, M. (2011). Methodology in conducting a systematic review of systematic reviews of healthcare interventions. *BMC Medical Research Methodology, 11*(1), 15.

Smolen, J. S., Landewé, R., Breedveld, F. C., Buch, M., Burmester, G., Dougados, M. *et al.,* (2013). EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2013 update. *Annals of the Rheumatic Diseases, 69*(6), 964-975.

Snijders, T., & Bosker, R. (2012). *Multilevel Analysis: An Introduction to Basic & Advanced Multilevel Modeling* (2nd ed.). London: Sage Publications.

Song, M., & Lipman, T. H. (2008). Concept analysis: self-monitoring in type 2 diabetes mellitus. *International journal of nursing studies, 45*(11), 1700-1710.

Soubrier, M., Zerkak, D., Gossec, L., Ayral, X., Roux, C., & Dougados, M. (2006). Which variables best predict change in rheumatoid arthritis therapy in daily clinical practice? *Journal of Rheumatology, 33*(7), 1243-1246.

Spence, D. (2013). Bad medicine: monitoring patients' drugs. *British Medical Journal, 347*, f5779.

Spiller, S. A., Fitzsimons, G. J., Lynch Jr, J. G., & McClelland, G. H. (2013). Spotlights, floodlights, and the magic number zero: Simple effects tests in moderated regression. *Journal of Marketing Research, 50*(2), 277-288.

Stack, R. J., Shaw, K., Mallen, C., Herron-Marx, S., Horne, R., & Raza, K. (2012). Delays in help seeking at the onset of the symptoms of rheumatoid arthritis: a systematic synthesis of qualitative literature. *Annals of the Rheumatic Diseases, 71*(4), 493-497.

Standing, P., Deakin, H., Norman, P., & Standing, R. (2005). Hypertension – Its detection prevalence, control and treatment in a quality driven British general practice. *British Journal of Cardiology, 12*(6), 471-476.

Steed, L., Cooke, D., & Newman, S. (2003). A systematic review of psychosocial outcomes following education, self-management and psychological interventions in diabetes mellitus. *Patient Education & Counseling, 51*(1), 5-15.

Sterba, K. R., DeVellis, R. F., Lewis, M. A., DeVellis, B. M., Jordan, J. M., & Baucom, D. H. (2008). Effect of couple illness perception congruence on psychological adjustment in women with rheumatoid arthritis. *Health psychology, 27*(2), 221-229.

Stevenson, F. A., Britten, N., Barry, C. A., Barber, N., & Bradley, C. P. (2000). Qualitative methods and prescribing research. *Journal of Clinical Pharmacy and Therapeutics, 25*(5), 317-324.

Steventon, A., Bardsley, M., Billings, J., Dixon, J., Doll, H., Hirani, S. *et al.,* (2012). Effect of telehealth on use of secondary care and mortality: findings from the Whole System Demonstrator cluster randomised trial. *British Medical Journal, 344*, e3874.

Stewart, M. W., & Knight, R. G. (1991). Coping strategies and affect in rheumatoid and psoriatic arthritis relationship to pain and disability. *Arthritis & Rheumatism, 4*(3), 116-122.

Strand, V., & Singh, J. A. (2007). Improved health-related quality of life with effective disease-modifying antirheumatic drugs: evidence from randomized controlled trials. *The American journal of managed care, 13*(9), S237-S251.

Sugiyama, D., Nishimura, K., Tamaki, K., Tsuji, G., Nakazawa, T., Morinobu, A. *et al.,* (2010). Impact of smoking as a risk factor for developing rheumatoid arthritis: A meta-analysis of observational studies. *Annals of the Rheumatic Diseases, 69*(1), 70-81.

Svendsen, A., Holm, N., Kyvik, K., Petersen, P., Junker, P., & Silman, A. J. (2002). Relative importance of genetic effects in rheumatoid arthritis: historical cohort study of Danish nationwide twin population Commentary: Do genes or environment influence development of rheumatoid arthritis? *British Medical Journal, 324*(7332), 264-266.

Svensson, B., Andersson, M. L. E., Bala, S. V., Forslind, K., Hafström, I., & on behalf of the BARFOT study group. (2013). Long-term sustained remission in a cohort study of patients with rheumatoid arthritis: choice of remission criteria. *BMJ Open, 3*(9), e003554.

Symmons, D., Tricker, K., Harrison, M., Roberts, C., Davis, M., Dawes, P. *et al.,* (2006). Patients with stable long-standing rheumatoid arthritis continue to deteriorate despite intensified treatment with traditional disease modifying anti-rheumatic drugs – results of the British Rheumatoid Outcome Study Group randomized controlled clinical trial. *Rheumatology, 45*(5), 558-565.

Symmons, D., Tricker, K., Roberts, C., Davies, L., Dawes, P., & Scott, D. L. (2005). The British Rheumatoid Outcome Study Group (BROSG) randomised controlled trial to compare the effectiveness and cost-effectiveness of aggressive versus symptomatic therapy in established rheumatoid arthritis. *Health Technology Assessment, 9*(34), iii-iiv.

Symmons, D. P., Turner, G., Webb, R., Asten, P., Barrett, E., Lunt, M. *et al.,* (2002). The prevalence of rheumatoid arthritis in the United Kingdom new estimates for a new century. *Rheumatology, 41*(7), 793-800.

Symmons, D. P. M. (2002). Epidemiology of rheumatoid arthritis: determinants of onset, persistence and outcome. *Best Practice & Research Clinical Rheumatology, 16*(5), 707-722.

Symmons, D. P. M. (2003). Environmental factors and the outcome of rheumatoid arthritis. *Best Practice & Research Clinical Rheumatology, 17*(5), 717-727.

Symmons, D. P. M., Bankhead, C. R., Harrison, B. J., Brennan, P., Silman, A. J., Barrett, E. M. *et al.,* (1997). Blood transfusion, smoking, and obesity as risk factors for the development of rheumatoid arthritis. Results from a primary care-based incident case-control study in Norfolk, England. *Arthritis & Rheumatism, 40*(11), 1955-1961.

Taal, E., Rasker, J. J., & Wiegman, O. (1996). Patient education and self-management in the rheumatic diseases: a self-efficacy approach. *Arthritis & Rheumatism, 9*(3), 229-238.

Tabachnick, B. G., & Fidell, L. S. (2013). *Using Multivariate Statistics* (Sixth Edition ed.). Boston: Pearson Education Inc.

Tanaka, E., Mannalithara, A., Inoue, E., Hara, M., Tomatsu, T., Kamatani, N. *et al.,* (2008). Efficient management of rheumatoid arthritis significantly reduces long-term functional disability. *Annals of the Rheumatic Diseases, 67*(8), 1153-1158.

Taylor, P., Manger, B., Alvaro-Gracia, J., Johnstone, R., Gomez-Reino, J., Eberhardt, E. *et al.,* (2010). Patient Perceptions concerning Pain Management in the Treatment of Rheumatoid Arthritis. *Journal of International Medical Research, 38*(4), 1213-1224.

Taylor, W., Gladman, D., Helliwell, P., Marchesoni, A., Mease, P., & Mielants, H. (2006). Classification criteria for psoriatic arthritis: Development of new criteria from a large international study. *Arthritis & Rheumatism, 54*(8), 2665-2673.

Teddlie, C., & Tashakkori, A. (2011). Mixed Methods Research: Comtemporary Issues in an Emerging Field. In N.K. Denzin & Y. Lincoln (Eds.), *The SAGE Handbook of Qualitative Research* (pp. 285-300).

ten Klooster, P. M., Taal, E., & van de Laar, M. A. F. J. (2008). Rasch analysis of the Dutch health assessment questionnaire disability index and the health assessment questionnaire II in patients with rheumatoid arthritis. *Arthritis Care & Research, 59*(12), 1721-1728.

The King's Fund. (2009). *Perceptions of patients and professionals on rheumatoid arthritis care: a consulatncy report by the King's Fund for the Rheumatology Futures Group* London: King's Fund.

Thorne, S. E., Harris, S. R., Mahoney, K., Con, A., & McGuinness, L. (2004). The context of health care communication in chronic illness. *Patient Education & Counseling, 54*(3), 299-306.

Thumboo, J., Uramoto, K., Shbeeb, M., O'Fallon, W., Crowson, C., Gibson, L. *et al.,* (2002). Risk factors for the development of psoriatic arthritis: a population based nested case control study. *Journal of Rheumatology, 29*(4), 757-762.

Tijhuis, G. J., Kooiman, K. G., Zwinderman, A. H., Hazes, J. M. W., Breedveld, F. C., & Vliet Vlieland, T. P. M. (2003). Validation of a novel satisfaction questionnaire for patients with rheumatoid arthritis receiving outpatient clinical nurse specialist care, inpatient care, or day patient team care. *Arthritis Care & Research, 49*(2), 193-199.

Tijhuis, G. J., Zwinderman, A. H., Hazes, J. M., Breedveld, F. C., & Vlieland, P. M. (2003). Two–year follow–up of a randomized controlled trial of a clinical nurse specialist intervention, inpatient, and day patient team care in rheumatoid arthritis. *Journal of advanced nursing, 41*(1), 34-43.

Tijhuis, G. J., Zwinderman, A. H., Hazes, J. M., Van Den Hout, W. B., Breedveld, F. C., & Vliet Vlieland, T. P. (2002). A randomized comparison of care provided by a clinical nurse specialist, an inpatient team, and a day patient team in rheumatoid arthritis. *Arthritis Care & Research, 47*(5), 525-531.

Tolonen, H., Keil, U., Ferrario, M., Evans, A., & for the WHO MONICA Project. (2005). Prevalence, awareness and treatment of hypercholesterolaemia in 32 populations: results from the WHO MONICA Project. *International Journal of Epidemiology, 34*(1), 181-192.

Towfigh, A., Romanova, M., Weinreb, J. E., Munjas, B., Suttorp, M. J., Zhou, A. *et al.,* (2008). Self-monitoring of blood glucose levels in patients with type 2 diabetes mellitus not taking insulin: A meta-analysis. *American Journal of Managed Care, 14*(7), 468-475.

Trappenburg, J., Jonkman, N., Jaarsma, T., van Os-Medendorp, H., Kort, H., de Wit, N. *et al.,* (2013). Self-management: One size does not fit all. *Patient Education & Counseling, 92*(1), 134-137.

Treharne, G. J., Lyons, A. C., & Kitas, G. D. (2004). Medication adherence in rheumatoid arthritis: Effects of psychosocial factors. *Psychology, health & medicine, 9*(3), 337.

Treharne, G. J., Lyons, A. C., Hale, E. D., Douglas, K. M. J., Kitas, G. D., Neame, R. L. *et al.,* (2005). Predictors of medication adherence in people with rheumatoid arthritis: Studies are necessary but non-validated measures of medication adherence are of concern (multiple letters). *Rheumatology, 44*(10), 1330-1331.

Turner, H. M., & Bernard, R. M. (2006). Calculating and synthesizing effect sizes. *Contemporary Issues in Communication Science and Disorders, 33*, 42-55.

Turnock, A. C., Walters, E. H., Walters, J. A., & Wood-Baker, R. (2005). Action plans for chronic obstructive pulmonary disease. *Cochrane Database of Systematic Reviews*.

Undeland, M., & Malterud, K. (2007). The fibromyalgia diagnosis-hardly helpful for the patients? A qualitative focus group study. *Scandinavian journal of primary health care, 25*(4), 250-255.

Ure, J., Pinnock, H., Hanley, J., Kidd, G., McCall Smith, E., Tarling, A. *et al.,* (2012). Piloting tele-monitoring in COPD: a mixed methods exploration of issues in design and implementation. *Primary Care Respiratory Journal, 21*(1), 57-64.

Van De Bemt, B. J. F., Van Den Hoogen, F. H. J., Benraad, B., Hekster, Y. A., Van Riel, P. L. C. M., & Van Lankveld, W. (2009). Adherence Rates and Associations with

Nonadherence in Patients with Rheumatoid Arthritis Using Disease Modifying Antirheumatic Drugs. *Journal of Rheumatology, 36*(10), 2164-2170.

van den Broek, M., Dirven, L., Kroon, H. M., Kloppenburg, M., Ronday, H. K., Peeters, A. J. *et al.,* (2013). Early Local Swelling and Tenderness Are Associated with Large-joint Damage After 8 Years of Treatment to Target in Patients with Recent-onset Rheumatoid Arthritis. *Journal of Rheumatology, 40*(5), 624-629.

van den Ende, C. H. M., Hazes, J., Le Cessie, S., Breedveld, F. C., & Dijkmans, B. A. C. (1995). Discordance between objective and subjective assessment of functional ablity of patients with rheumatoid arthritis. *Rheumatology, 34*(10), 951-955.

Van den Hout, W. B., Tijhuis, G. J., Hazes, J. M. W., Breedveld, F. C., & Vlieland, T. V. (2003). Cost effectiveness and cost utility analysis of multidisciplinary care in patients with rheumatoid arthritis: a randomised comparison of clinical nurse specialist care, inpatient team care, and day patient team care. *Annals of the Rheumatic Diseases, 62*(4), 308-315.

van der Vaart, R., Drossaert, C., Taal, E., & van de Laar, M. (2013). Giving rheumatology patients online home access to their electronic medical record (EMR): advantages, drawbacks and preconditions according to care providers. *Rheumatology international, 33*(9), 2405-2410.

van der Vaart, R., Drossaert, C. H. C., Taal, E., & van de Laar, M. A. F. J. (2011). Patient preferences for a hospital-based rheumatology Interactive Health Communication Application and factors associated with these preferences. *Rheumatology, 50*(9), 1618-1626.

van Eijk-Hustings, Y., Ammerlaan, J., Voorneveld-Nieuwenhuis, H., Maat, B., Veldhuizen, C., & Repping-Wuts, H. (2013). Patients' needs and expectations with regard to rheumatology nursing care: results of multicentre focus group interviews. *Annals of the Rheumatic Diseases, 72*(6), 831-835.

van Eijk-Hustings, Y., van Tubergen, A., Boström, C., Braychenko, E., Buss, B., Felix, J. *et al.,* (2012). EULAR recommendations for the role of the nurse in the management of chronic inflammatory arthritis. *Annals of the Rheumatic Diseases, 71*(1), 13-19.

van Gestel, A. M., Prevoo, M. L. L., Van't Hof, M. A., Van Rijswijk, M. H., Van De Putte, L. B. A., & Van Riel, P. L. C. M. (1996). Development and validation of the European League Against Rheumatism response criteria for rheumatoid arthritis: Comparison with the preliminary American College of Rheumatology and the World Health Organization/international league against rheumatism criteria. *Arthritis & Rheumatism, 39*(1), 34-40.

van Os, S., Norton, S., Hughes, L. D., & Chilcot, J. (2012). Illness perceptions account for variation in positive outlook as well as psychological distress in Rheumatoid Arthritis. *Psychology, health & medicine, 17*(4), 427-439.

Verberk, W. J., Kessels, A. G. H., & Thien, T. (2011). Telecare is a valuable tool for hypertension management, a systematic review and meta-analysis. *Blood Pressure Monitoring, 16*(3), 149-155.

Vliet Vlieland, T. P. M. (2004). Multidisciplinary team care and outcomes in rheumatoid arthritis. *Current Opinion in Rheumatology, 16*(2), 153-156.

Vliet Vlieland, T. P., & Hazes, J. M. (1997). Efficacy of multidisciplinary team care programs in rheumatoid arthritis. *Seminars in Arthritis & Rheumatism, 27*(2), 110-122.

Walker, R., James, H., & Burns, A. (2012). Adhering to behaviour change in older pre-dialysis population - what do patients think? A qualitative study. *Journal of renal care, 38*(1), 34-42.

Wallenius, M., Skomsvoll, J. F., Koldingsnes, W., Rødevand, E., Mikkelsen, K., Kaufmann, C. *et al.,* (2009). Work disability and health-related quality of life in males and females with psoriatic arthritis. *Annals of the Rheumatic Diseases, 68*(5), 685-689.

Waltz, M. (2000). The disease process and utilization of health services in rheumatoid arthritis: The relative contributions of various markers of disease severity in explaining consumption patterns. *Arthritis Care & Research, 13*(2), 74-88.

Ware Jr, J. E., Kosinski, M., Turner-Bowker, D. M., & Gandeck, B. (2002). *User's Manual for the SF-12v2™ Health Survey With a Supplement Documenting SF-12® Health Survey*. Lincoln, RI: QualityMetric Incorporated.

Ware Jr, J. E., Kosinski, M., & Keller, S. D. (1996). A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. *Medical care, 34*(3), 220-233.

Ware Jr, J. E., & Sherbourne, C. D. (1992). The MOS 36-item short-form health survey (SF-36): I. Conceptual framework and item selection. *Medical care, 30*(6), 473-483.

Warsi, A., LaValley, M. P., Wang, P. S., Avorn, J., & Solomon, D. H. (2003). Arthritis self-management education programs: a meta-analysis of the effect on pain and disability. *Arthritis & Rheumatism, 48*(8), 2207-2213.

Weinman, J., Petrie, K. J., Moss-Morris, R., & Horne, R. (1996). The illness perception questionnaire: a new method for assessing the cognitive representation of illness. *Psychology & Health, 11*(3), 431-445.

Welschen, L. M., Bloemendal, E., Nijpels, G., Dekker, J. M., Heine, R. J., Stalman, W. A. *et al.,* (2005a). Self-monitoring of blood glucose in patients with type 2 diabetes mellitus who are not using insulin. *Cochrane Database of Systematic Reviews*.

Welschen, L. M., Bloemendal, E., Nijpels, G., Dekker, J. M., Heine, R. J., Stalman, W. A. *et al.,* (2005b). Self-monitoring of blood glucose in patients with type 2 diabetes who are not using insulin: a systematic review. *Diabetes Care, 28*(6), 1510-1517.

Westlake, S., Colebatch, A., Baird, J., Kiely, P., Quinn, M., Choy, E. *et al.,* (2010). The effect of methotrexate on cardiovascular disease in patients with rheumatoid arthritis: a systematic literature review. *Rheumatology, 49*(2), 295-307.

Whear, R., Abdul-Rahman, A. K., Boddy, K., Thompson-Coon, J., Perry, M., & Stein, K. (2013). The Clinical Effectiveness of Patient Initiated Clinics for Patients with Chronic or Recurrent Conditions Managed in Secondary Care: A Systematic Review. *PloS one, 8*(10), e74774.

Whiting-O'Keefe, Q. E., Fye, K. H., & Sack, K. D. (1991). Methotrexate and histologic hepatic abnormalities: a meta-analysis. *The American journal of medicine, 90*(1), 711-716.

Whittle, S. L., Richards, B. L., & Buchbinder, R. (2013). Opioid Analgesics for Rheumatoid Arthritis Pain. *JAMA : the journal of the American Medical Association, 309*(5), 485-486.

Wilde, M. H., & Garvin, S. (2007). A concept analysis of self-monitoring. *Journal of advanced nursing, 57*(3), 339-350.

Willems, D., Joore, M. A., Hendriks, J. J., Wouters, E. F., & Severens, J. L. (2006). Cost-effectiveness of self-management in asthma: a systematic review of peak flow monitoring interventions. *International journal of technology assessment in health care, 22*(4), 436-442.

Williamson, L., Dalbeth, N., Dockerty, J. L., Gee, B. C., Weatherall, R., & Wordsworth, B. P. (2004). Extended report: nail disease in psoriatic arthritis – clinically important, potentially treatable and often overlooked. *Rheumatology, 43*(6), 790-794.

Wilson, F., Icen, M., Crowson, C. S., McEvoy, MT., Gabriel, S. E., & Kremers, H. (2009). Time Trends in Epidemiology and Characteristics of Psoriatic Arthritis Over 3 Decades: A Population-based Study. *Journal of Rheumatology, 36*(2), 361-367.

Wilson, I. B., & Cleary, P. D. (1995). Linking clinical variables with health-related quality of life: a conceptual model of patient outcomes. *JAMA : the journal of the American Medical Association, 273*(1), 59-65.

Winkelman, W. J., Leonard, K. J., & Rossos, P. G. (2005). Patient-perceived usefulness of online electronic medical records: employing grounded theory in the development of information and communication technologies for use by patients living with chronic illness. *Journal of the American Medical Informatics Association, 12*(3), 306-314.

Wise, E. M., & Isaacs, J. D. (2005). Management of rheumatoid arthritis in primary care: an educational need? *Rheumatology, 44*(11), 1337-1338.

Wolfe, F., Hawley, D. J., & Wilson, K. (1996). The prevalence and meaning of fatigue in rheumatic disease. *Journal of Rheumatology, 23*(8), 1407-1417.

Wolfe, F., & Hawley, D. J. (1998). The longterm outcomes of rheumatoid arthritis: Work disability: a prospective 18 year study of 823 patients. *Journal of Rheumatology, 25*(11), 2108-2117.

Wolfe, F., Michaud, K., & Pincus, T. (2004). Development and validation of the health assessment questionnaire II: a revised version of the health assessment questionnaire. *Arthritis & Rheumatism, 50*(10), 3296-3305.

Wollina, U., Ständer, K., & Barta, U. (2001). Toxicity of methotrexate treatment in psoriasis and psoriatic arthritis – short - and long-term toxicity in 104 patients. *Clinical Rheumatology, 20*(6), 406-410.

Wong, K., Gladman, D., Husted, J., Long, J., Farewell, V., & Long, J. (1997). Mortality studies in psoriatic arthritis. Results from a single outpatient clinic. I. Causes and risk of death. *Arthritis & Rheumatism, 40*(10), 1868-1872.

Wright, G. E., Parker, J. C., Smarr, K. L., Schoenfeld-Smith, K., Buckelew, S. P., Slaughter, J. R. *et al.,* (1996). Risk factors for depression in rheumatoid arthritis. *Arthritis & Rheumatism, 9*(4), 264-272.

Wu, S., Kao, M., Wu, M., Tsai, M., & Chang, W. (2011). Effects of an osteoarthritis self–management programme. *Journal of advanced nursing, 67*(7), 1491-1501.

Yazici, Y., Pincus, T., Kautiainen, H., & Sokka, T. (2004). Morning stiffness in patients with early rheumatoid arthritis is associated more strongly with functional disability than with joint swelling and erythrocyte sedimentation rate. *Journal of Rheumatology, 31*(9), 1723-1726.

Yelin, E. H., Such, C. L., Criswell, L. A., & Epstein, W. V. (1998). Outcomes for persons with rheumatoid arthritis with a rheumatologist versus a non-rheumatologist as the main physician for this condition. *Medical care, 36*(4), 513-522.

Yip, Y. B., Sit, J. W., Fung, K. K., Wong, D., Chong, S. Y., Chung, L. H. *et al.,* (2007). Impact of an Arthritis Self-Management Programme with an added exercise component for osteoarthritic knee sufferers on improving pain, functional outcomes,

and use of health care services: An experimental study. *Patient Education & Counseling, 65*(1), 113-121.

Zakout, S., Pugh, M., & Healey, E. (2009). Compliance of Patients on DMARDS to Blood Monitoring. *BSR/BHPR Annual Meeting 2009 Glasgow* (pp. i146).

APPENDIX A. UCLH SHARED CARE GUIDELINES

Shared Care Guideline
METHOTREXATE
Treatment of moderate to severe active rheumatoid arthritis or Treatment of severe psoriasis

Dear GP,

Progressing to a stable, optimal dose usually takes about three months. Once achieved, a Shared Care arrangement with you will be requested. It will clarify responsibilities between the specialist and general practitioner (GP) for managing the prescribing of methotrexate such as:

- Who will prescribe;
- Who will monitor;
- How often blood tests will be conducted and in which location;
- Which clinician will be responsible for receipt and review of the results;
- Who will communicate any necessary changes in dose to the patient and the GP;
- Who will record test results in the Patient-Held Monitoring and Dosage Record booklet.

GPs are **invited** to participate. If the GP is not confident to undertake these roles, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist.

Sharing of care assumes communication between the specialist, GP and patient. The intention to share care should be explained to the patient by the Consultant / specialist nurse when treatment is initiated. It is important that patients are consulted about treatment and are in agreement with it.

Shared Care Criteria

Patients who are stabilised on methotrexate and have been monitored appropriately at baseline and after initiation of treatment with no problems identified during this period.

RESPONSIBILITIES and ROLES

Consultant and Specialist Nurse
1. Perform baseline tests (FBC, LFTs, U&Es, creatinine, chest X-ray). 2. Initiate and stabilise treatment with methotrexate and continue to prescribe until the GP formally agrees to shared care. 3. Discuss the benefits and side effects of treatment with the patient. Provide the patient with a Patient Information Leaflet, explain it and ensure that the patient understands that dosing is at weekly intervals. Issue a Methotrexate Monitoring Booklet to the patient and explain monitoring schedule. 4. Write to the GP with a standard letter asking whether he or she is willing to participate in shared care. 5. Discuss the shared care arrangement with the patient. 6. Provide results of baseline tests and recommend frequency of monitoring to GP. Record results in the patient's Methotrexate Monitoring Booklet and continue to do so until GP agrees to shared care. Recommend dose and timing of concomitant folic acid. 7. Periodically review the patient's condition and communicate promptly with the GP when treatment is changed. Counsel the patient on any dose changes that are made during clinic appointments. 8. Inform GP of blood test results, actions to take in case of abnormal results, and advise the GP on when to adjust the dose, stop treatment, or consult with specialist. 9. Evaluate adverse effects reported by GP or patient. 10. Report adverse events to the MHRA and GP. 11. Ensure that clear backup arrangements exist for GPs to obtain advice and support.

Written by Jay Pang – Royal Free Hospital and Balram Malhotra – University College London Hospitals, Rheumatology and Dermatology Pharmacists.

Agreed with lead commissioning PCT, NHS Camden: May 2009.

Date of next review: April 2011.

General Practitioner
1. Reply to the request for shared care as soon as practicable by completing standard letters to the Consultant and Primary Care Trust accepting or declining shared care. 2. Monitor patient's overall health and wellbeing. 3. Prescribe methotrexate at the dose recommended and ensure patient understands the number of tablets and strength of tablets to take. Only 2.5 mg tablets should be prescribed. 10 mg tablets **SHOULD NOT** be prescribed. Prescriptions should specify "once a week" and the day of administration. The term "as directed" **SHOULD NOT** be used. 4. Ensure that the patient understands that dosing is at weekly intervals. 5. Ensure that the patient knows that he/she must report the warning symptoms as listed under "Adverse Effects". 6. Ensure compatibility with other concomitant medication. 7. Monitor blood counts, hepatic and renal function at recommended frequencies as described (see "Monitoring"), and inform consultant if abnormal. All test results to be recorded in patient's Methotrexate Monitoring Booklet. 8. Record the date of the next blood test in the "Patient-Held Monitoring and Dosage Record", and arrange it. 9. Adjust the dose as advised by the specialist and counsel patient on any dose changes. Record dose changes in the "Patient-Held Monitoring and Dosage Record". 10. Stop treatment on the advice of the specialist or immediately if an urgent need to stop treatment arises. 11. Report adverse events to the specialist and MHRA. 12. All requests for repeat prescriptions should be reviewed individually prior to issuing. 13. Offer annual influenza vaccination to the patient.

Patient
1. Report to the specialist or GP if he or she does not have a clear understanding of the treatment. 2. Share any concerns in relation to treatment with methotrexate. 3. Inform specialist or GP of any other medication being taken, including over-the-counter products. 4. Report any adverse effects or warning symptoms (sore throat, bruising, mouth ulcers, nausea, vomiting, abdominal discomfort, dark urine, shortness of breath) to the specialist or GP whilst taking methotrexate. 5. Bring the Methotrexate Monitoring Booklet to all appointments and when collecting supply of tablets.

Primary Care Trust
1. To support GPs to decide whether or not to accept clinical responsibility for prescribing. 2. To support Trusts in resolving issues that may arise as a result of shared care.

SUPPORTING INFORMATION

1. Licensed indications

- Methotrexate is licensed for the treatment of adults with severe, active, classical or definite rheumatoid arthritis who are unresponsive to or intolerant of conventional therapy.
- Methotrexate is licensed for the treatment of severe, uncontrolled psoriasis, which is not responsive to other therapy.

2. Dosage and Administration

Rheumatoid Arthritis

Methotrexate is started at a dose of 7.5mg orally once weekly. The schedule may be adjusted gradually to achieve an optimal response (licensed maximum weekly dose is 25mg although some patients may require higher doses on advice of the specialist).

Psoriasis

Patients are given a small test dose of methotrexate (usually 5mg) orally once weekly. If after 7 days the full blood count (FBC) is stable methotrexate is continued. The schedule may be adjusted gradually (usually in 2.5-5mg steps) to achieve an optimal response. The licensed maximum weekly dose is 25mg, although few patients require more than 20mg, and some patients may require higher doses (up to 30mg) on advice of the specialist.

The lowest possible effective dose should be used. Methotrexate should be used with extreme caution in elderly patients and a lower dose should be considered.

Regular folic acid supplements should be given to reduce the risk of toxicity.

Please follow the regime detailed in the handover summary. Folic acid should not be taken on the same day as methotrexate

Methotrexate will be issued as 2.5mg tablets. Patients should consistently receive the same strength of tablets to avoid confusion with the 10mg strength and, therefore, the risk of overdose. All patients should be fully counselled regarding the strength and number of tablets to take as a single weekly dose.

Patients will be issued with a Methotrexate Monitoring Booklet from the hospital. All blood results and dose or change in dose should be recorded in this booklet.

Patients should be offered annual influenza vaccination.

3. Cautions and Contraindications

- Profound impairment of renal or hepatic function or haematological impairment
- Liver disease including fibrosis, cirrhosis, recent or active hepatitis; active infectious disease; and overt or laboratory evidence of immunodeficiency syndrome(s)
- Serious cases of anaemia, leucopenia, or thrombocytopenia
- Pregnancy or breast-feeding
- Patients with a known allergic hypersensitivity to methotrexate
- Exposure to chicken pox – patients who have had significant exposure to chicken pox but do not know if they have had chicken pox in the past, will need to have their varicella zoster antibody titre checked. If it is low, the patient will need varicella zoster immunoglobulin within 10 days of the initial exposure. If this is necessary, please contact the appropriate specialist nurse or specialist registrar or consultant
- Localised or systemic infection – including hepatitis B or C

Immunisations - live vaccines should be avoided. Influenza vaccine is safe. For a full list of cautions and contraindications, refer to the Summary of Product Characteristics.

The National Patient Safety Agency has published actions to reduce the risks associated with oral methotrexate (www.npsa.nhs.uk).

4. Monitoring

Regular monitoring according to the BSR/BHPR guideline for disease-modifying anti-rheumatic drug (DMARD) therapy in consultation with the British Association of Dermatologists[1] during treatment is essential to detect adverse reactions at an early stage and patients should be counselled about the risk factors and to report all signs and symptoms of toxicity.

- FBC, U&Es, creatinine, LFTs and chest X-ray should be measured before starting treatment.
- FBC, U&Es and LFTs should then be monitored fortnightly until dose of methotrexate and monitoring is stable for 6 weeks, then monthly thereafter

until the dose and disease is stable for 1 year. Thereafter, the monitoring may be reduced in frequency to every two to three months, based on clinical judgement with due consideration for risk factors including age, comorbidity, renal impairment, etc.

(NB. The frequency of monitoring advised by the specialist to the GP may vary from the above recommendations depending on patient factors.)

The following threshold laboratory values and symptoms require action as detailed in the table below.

Monitoring parameter	**Action to be taken if changed**
WBC <3.5x10^9/l	Withhold methotrexate until discussed with rheumatologist / dermatologist
Neutrophils<2.0x10^9	Withhold methotrexate until discussed with rheumatologist / dermatologist
Platelets<150x10^9 /l	Withhold methotrexate until discussed with rheumatologist / dermatologist
>2-fold rise in AST, ALT (from upper limit of reference range)	Withhold methotrexate until discussed with rheumatologist / dermatologist
Unexplained fall in albumin (in absence of active disease)	Withhold methotrexate until discussed with rheumatologist / dermatologist
Rash or oral ulceration, nausea and vomiting, diarrhoea	Withhold methotrexate until discussed with rheumatologist / dermatologist
New or increasing dyspnoea or dry cough	Withhold methotrexate until discussed with rheumatologist / dermatologist
MCV>105fl	Withhold and check serum B12, folate and TFT and discuss with specialist team if necessary
Significant deterioration in renal function	Withhold methotrexate until discussed with rheumatologist / dermatologist
Abnormal bruising or severe sore throat	Immediate FBC and withhold methotrexate until FBC result available

The specialist may conduct additional investigations as required e.g. CRP, ESR, (and PIIINP and liver biopsy for psoriatic patients). The results will be sent to the GP.

5. Adverse Effects

Possible adverse effects and what to do if they occur:

1. **Nausea and diarrhoea** – these will be minimised by the folic acid therapy. Some patients benefit by taking their NSAID (if they are on one) a few hours before or after, rather than at the same time as their methotrexate dose. If severe despite these measures, the methotrexate must be stopped, and the specialist nurse or specialist registrar or Consultant, contacted.
2. **Mouth ulcers, hair loss, and skin rash** – these usually respond to omitting a dose and resuming at a dose reduced by 2.5mg. Topical hydrocortisone may be used for skin rash. If any are severe (particularly stomatitis), the methotrexate must be stopped, and the specialist nurse or specialist registrar or Consultant, contacted.
3. **Recurrent sore throat, infections and fevers** – these may indicate neutropenia, so the methotrexate must be stopped, the FBC checked, and the specialist nurse or specialist registrar or Consultant, contacted.
4. **Unexplained bruising or bleeding** – if severe, the APTT and FBC should be checked. If they are normal (see "Monitoring"), methotrexate may be continued and the specialist nurse or specialist registrar or Consultant, contacted. If they are abnormal, the methotrexate should be stopped, and the specialist nurse or specialist registrar or Consultant, contacted.
5. **Unexplained cough or shortness of breath** – these may indicate pneumonitis or pulmonary fibrosis, so the methotrexate should be stopped and the specialist nurse or specialist registrar or Consultant, contacted.
6. **Jaundice, abdominal discomfort, or dark urine** – these may indicate liver damage, so the methotrexate should be stopped and the specialist nurse or specialist registrar or Consultant, contacted.

Methotrexate was launched in 1989 and no longer has black triangle status. Serious suspected reactions (even if well recognised or causal link uncertain) should be reported to the CHM.

6. Drug Interactions

Methotrexate is extensively protein-bound and may be displaced by other protein-bound drugs (e.g. diuretics, salicylates, hypoglycaemics), with a potential for increased toxicity.

NSAIDs can be continued whilst on methotrexate. The NSAID or its dose should not be changed without discussion with the Consultant. All patients should be regularly advised to avoid over-the-counter medications including aspirin and ibuprofen without the knowledge of the specialist team.

Concomitant use of other drugs with nephrotoxic or hepatotoxic potential should be avoided. Folate antagonists such as trimethoprim and co-trimoxazole should not be given concomitantly.

For a full list of drug interactions, refer to the Summary of Product Characteristics.

7. Pregnancy and Lactation

- All patients, male and female, should be advised to avoid conception and pregnancy during treatment with methotrexate as it is an abortificient as well as a teratogenic drug.
- Patients and their partners should be advised to continue contraception for at least 3 months after cessation of methotrexate therapy.
- Patients should not breastfeed whilst taking methotrexate.

References

1. BSR/BHPR guideline for disease-modifying anti-rheumatic drug (DMARD) therapy in consultation with the British Association of Dermatologists. K Chakravarty *et al.,* Rheumatology, 2008. accessed via http://rheumatology.oxfordjournals.org/cgi/data/kel216a/DC1/1
2. MTRAC guidance VS97/15 http://www.keele.ac.uk/schools/pharm/MTRAC/
3. National Patient Safety Agency www.npsa.nhs.uk
4. Summary of Product Characteristics Maxtrex tablets 2.5 mg. Pharmacia 2004 accessed via www.medicines.org.uk

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Centre for Rheumatology, University College London Hospitals, 3rd Floor Central, 250 Euston Road, London, NW1 2PG. Switchboard telephone number: 0845 155 5000

Further information and support: **Monday to Friday, 8 a.m. to 5 p.m., rheumatology helpline (Rheumatology Clinical Nurse Specialist) on tel. [redacted] At all other times, a rheumatology specialist registrar can be paged by the hospital switchboard, on 0845 155 5000.**

University College London Hospitals - Dermatology

Department of Dermatology, University College London Hospitals, 3rd Floor Central, 250 Euston Road, London, NW1 2PG. Switchboard telephone number: 0845 155 5000

Further information and support: **Monday to Friday, 8 a.m. to 5 p.m., dermatology helpline (Dermatology Clinical Nurse Specialist) on tel. [redacted]. At all other times, a dermatology specialist registrar can be paged by the hospital switchboard, on 0845 155 5000.**

APPENDIX B. PRISMA 2009 CHECKLIST

Section/topic	#	Checklist item	Reported on page #	Notes
TITLE				
Title	1	Identify the report as a systematic review, meta-analysis, or both.	99	
ABSTRACT				
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	No	Not a published review (but will be undertaken for publication)
INTRODUCTION				
Rationale	3	Describe the rationale for the review in the context of what is already known.	99-101	
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	101	
METHODS				
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	No	
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	104	

Section/topic	#	Checklist item	Reported on page #	Notes
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	103	
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Appendix C	
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	106	
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	106, Appendix F	
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	106	
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	No	Quality was assessed not risk of bias.
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	102	NB: data were not meta-analysed
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	102	
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	No	Quality was assessed not risk of bias.

Section/topic	#	Checklist item	Reported on page #	Notes
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	n/a	
RESULTS				
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	107, Figure 3.2	
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	108-140, Table 3.1	
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	No	Quality was assessed not risk of bias.
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Appendix H, I, J	
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	n/a	
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	No	Quality was assessed not risk of bias.
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	n/a	

Section/topic	#	Checklist item	Reported on page #	Notes
DISCUSSION				
Summary of evidence	24	Summarise the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	140	
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	163	
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	152	
FUNDING				
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	No	Will be provided for publication

APPENDIX C. SYSTEMATIC REVIEW SEARCH STRATEGY

1. Cochrane Library (Title, abstract or keywords)

self care
self monitor*
self administer*
self examin*
self medicat*
self inject*
self evaluat*
self test*
self manage*
self adjust*
self measure*
patient participation
patient monitor*
patient manage*
patient adjust*
patient administer*
patient control*
patient cent?d
telemedicine
telehealth
telecare
telemonitor*
telemetry
home monitor*

2. DARE & HTA

self care
self monitor*
self administer*
self examin*
self medicat*
self inject*
self evaluat*
self test*
self manage*
self adjust*
self measure*
patient participation
Monitoring, Physiologic[Mesh]
patient manage*
patient adjust*
patient administ*
patient control*
patient centered
patient centred
telemedicine

telehealth
telecare
telemonitor*
home monitor*

3. Pub med

self care[Mesh]
self monitor*
self administration[Mesh]
self examination[Mesh]
self medication[Mesh]
self inject*
self test*
self management[Mesh]
self adjust*
self evaluat*
self measure*
patient-centered care[Mesh]
patient participation[Mesh]
Monitoring, Physiologic[Mesh]
patient manage*
patient adjust*
patient administ*
patient control*
telemedicine[Mesh]
telecare
telehealth
telemonitor*
home monitor*

AND

Meta-Analysis[Publication Type][Mesh]
Review[Publication Type][Mesh]
overview
narrative review

5, 6, 7 & 8. AMED, HMIC, EMBASE & PsycINFO

Self Care/
self monitor$.mp.
self administer$.mp.
self examin$.mp.
self medicat$.mp.
self inject$.af
self evaluat$.mp.
self test$.af.
self management.mp.
self adjust$.mp.

self measure$.mp
Patient participation/
Patient monitor$.mp.
Patient manage$.mp.
Patient adjust$.mp.
Patient administer$.mp.
Patient control$.mp.
Patient centred.mp.
Telemedicine/
Telehealth.mp.
Telecare.mp.
telemonitoring.ab. or telemonitoring.ti.
telemetry.mp.
home monitor*

4. CINAHL plus
MH Self Care+
self monitor*
MH Self Administration+
self examine*
MH Self Medication
self inject*
self evaluat*
self test*
self manage*
self adjust*
self measure*
MH Health Services+
MH Monitoring, Physiologic+
patient manage*
patient adjust*
patient administer*
patient control*
MH Telehealth+
telecare
telemonitor*
home monitor*

APPENDIX D. DATA EXTRACTION FORM

Reference.	**Title**
	Aim
	Objective
Type of review	
Literature search	
Level of self-monitoring	
Inclusion/exclusion criteria **Design** **Participants** **Interventions** **Outcomes** **Other** **Study selection procedure**	
Methods **Statistical analysis** **Quality assessment tool**	

Quality assessment procedure **Data extracted from primary studies** **Data extraction procedure** **How were studies combined in the review** **How was bias assessed** **How was heterogeneity assessed** **Was a sensitivity analysis conducted?**
Results **Number of studies included in the review** **Number of participants** **Results of quality assessment** **Main outcome** **Secondary outcome** **Publication bias** **Heterogeneity & sensitivity**
Conclusions and Interpretations

Authors interpretation **Conclusion** **Implications for research** **Implication for practice**
Reviewers comments

APPENDIX E. AMSTAR CRITERIA FOR REVIEW QUALITY

1. Was an *a priori* design provided?

The research question and inclusion criteria should be established before the conduct of the review.

2. Was there duplicate study selection and data extraction?

There should be at least two independent data extractors and a consensus procedure for disagreements should be in place.

3. Was a comprehensive literature search performed?

At least two electronic sources should be searched. The report must include years and databases used (e.g. Central, EMBASE, and MEDLINE). Key words and/or MESH terms must be stated and where feasible the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found.

4. Was the status of publication (i.e. grey literature) used as an inclusion criterion?

The authors should state that they searched for reports regardless of their publication type. The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status, language etc.

5. Was a list of studies (included and excluded) provided?

A list of included and excluded studies should be provided.

6. Were the characteristics of the included studies provided?

In an aggregated form such as a table, data from the original studies should be provided on the participants, interventions and outcomes. The ranges of characteristics in all the studies analysed e.g. age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported.

7. Was the scientific quality of the included studies assessed and documented?

A priori methods of assessment should be provided (e.g., for effectiveness studies if the author(s) chose to include only randomized, double-blind, placebo controlled studies, or allocation concealment as inclusion criteria); for other types of studies alternative items will be relevant.

8. Was the scientific quality of the included studies used appropriately in formulating conclusions?

The results of the methodological rigor and scientific quality should be considered in

the analysis and the conclusions of the review, and explicitly stated in formulating recommendations.

9. Were the methods used to combine the findings of studies appropriate?

For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e. Chi-squared test for homogeneity, I2). If heterogeneity exists a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e. is it sensible to combine?).

10. Was the likelihood of publication bias assessed?

An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test).

11. Was the conflict of interest stated?

Potential sources of support should be clearly acknowledged in both the systematic review and the included studies.

APPENDIX F. SYSTEMATIC REVIEW - EXCLUDED STUDIES

Excluded at stage 2 – included children

Centre for Reviews and Dissemination. The effect of nurse-led diabetes self-management education on glycosylated hemoglobin and cardiovascular risk factors: a meta-analysis (Structured abstract). Database of Abstracts of Reviews of Effects 4. 2013.
Ref Type: Abstract

Centre for Reviews and Dissemination. The value of self-monitoring of blood glucose: a review of recent evidence (Structured abstract). Database of Abstracts of Reviews of Effects 4. 2013.
Ref Type: Abstract

Centre for Reviews and Dissemination. The impact of telemedicine interventions involving routine transmission of blood glucose data with clinician feedback on metabolic control in youth with type 1 diabetes: a systematic review and meta-analysis (Provisional abstract). Database of Abstracts of Reviews of Effects 4. 2013.
Ref Type: Abstract

Centre for Reviews and Dissemination. Electronic media-based health interventions promoting behavior change in youth: a systematic review (Structured abstract). Database of Abstracts of Reviews of Effects 4. 2013.
Ref Type: Abstract

Centre for Reviews and Dissemination. A systematic review of internet-based self-management interventions for youth with health conditions (Structured abstract). Database of Abstracts of Reviews of Effects 4. 2013.
Ref Type: Abstract

Centre for Reviews and Dissemination. Health technologies for monitoring and managing diabetes: a systematic review (Structured abstract). Database of Abstracts of Reviews of Effects 4. 2013.
Ref Type: Abstract

Centre for Reviews and Dissemination. Do school-based asthma education programs improve self-management and health outcomes? (Structured abstract). Database of Abstracts of Reviews of Effects 4. 2013.
Ref Type: Abstract

Centre for Reviews and Dissemination. The socio-economic impact of telehealth: a systematic review (Provisional abstract). Database of Abstracts of Reviews of Effects 4. 2013.
Ref Type: Abstract

Centre for Reviews and Dissemination. Beneficial effect of real-time continuous glucose monitoring system on glycemic control in type 1 diabetic patients: systematic review and meta-analysis of randomized trials (Structured abstract). Database of Abstracts of Reviews of Effects 4. 2013.
Ref Type: Abstract

Centre for Reviews and Dissemination. Efficacy of continuous glucose monitoring in improving glycemic control and reducing hypoglycemia: a systematic review and meta-analysis of randomized trials (Provisional abstract). Database of Abstracts of Reviews of Effects 4. 2013.
Ref Type: Abstract

Coster S., Gulliford, M.C., Seed, P.T., Royle, P., & Swaminathan, R. 2000. Monitoring blood glucose control in diabetes mellitus:a systematic review. *Health Technology Assessment*, 4, (12)

Cox, N.S., Alison, J.A., Rasekaba, T., & Holland, A.E. Telehealth in cystic fibrosis: A systematic review. *Journal Of Telemedicine And Telecare*, 18, (2) March

Farmer, A., Gibson, O.J., Tarassenko, L., & Neil, A. 2005. A systematic review of telemedicine interventions to support blood glucose self-monitoring in diabetes. *Diabetic Medicine*, 22, (10) 1372-1378

George, M. & Topaz, M. 2013. A systematic review of complementary and alternative medicine for asthma self-management. *The Nursing Clinics Of North America*, 48, (1) 53-149 available from: http://search.ebscohost.com/login.aspx?direct=true&db=mnh&AN=23465447&site=ehost-live

Hailey, D., Ohinmaa, A., & Roine, R. 2014. Evidence for the benefits of telecardiology applications: a systematic review (Structured abstract). *Health Technology Assessment Database* (1)

Jaana, M. & Pare, G. 2007. Home telemonitoring of patients with diabetes: A systematic assessment of observed effects. *Journal of Evaluation in Clinical Practice*, 13, (2) 242-253

Jaana, M., Pare, G., & Sicotte, C. 2009. Home telemonitoring for respiratory conditions: A systematic review. *American Journal of Managed Care*, 15, (5) 313-320

Labre, M.P., Herman, E.J., Dumitru, G.G., Valenzuela, K.A., & Cechman, C.L. Public health interventions for asthma: An umbrella review, 1990-2010. *American Journal of Preventive Medicine*, 42, (4) April

Lefevre, F., Piper, M., Weiss, K., Mark, D., Clark, N., & Aronson, N. 2002. Do written action plans improve patient outcomes in asthma? An evidence-based analysis. *The Journal of Family Practice*, 51, (10) 842-848 available from: http://search.ebscohost.com/login.aspx?direct=true&db=psyh&AN=2002-04648-004&site=ehost-live;f-lefevre@northwestern.edu

Marcano Belisario, J.S., Huckvale, K., Greenfield, G., Car, J., & Gunn, L.H. 2013. Smartphone and tablet self management apps for asthma. *Cochrane Database of Systematic Reviews*, 11, available from: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD010013.pub2/pdf

McIntosh, B., Yu, C., Lal, A., Chelak, K., Cameron, C., Singh, S., & Dahl, M. 2010. Efficacy of self-monitoring of blood glucose in patients with type 2 diabetes mellitus managed without insulin: a systematic review and meta-analysis. *Open Medicine*, 4, (2) e102-e113 available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3116681/pdf/OpenMed-04-e102.pdf

McLean, S., Chandler, D., Nurmatov, U., Liu, J., Pagliari, C., Car, J., & Sheikh, A. 2011. Telehealthcare for asthma: A Cochrane review. *CMAJ*, 183, (11) 09-E742

Montori, V.M., Helgemoe, P.K., Guyatt, G.H., Dean, D.S., Leung, T.W., Smith, S.A., & Kudva, Y.C. 2004. Telecare for patients with type 1 diabetes and inadequate glycemic control: a randomized controlled trial and meta-analysis. *Diabetes Care*, 27, 1088-1094

Pare, G., Jaana, M., & Sicotte, C. 2007. Systematic review of home telemonitoring for chronic diseases: the evidence base. *Journal of the American Medical Informatics Association*, 14, (3) 269-277 available from: http://search.ebscohost.com/login.aspx?direct=true&db=cin20&AN=2009592387&site=ehost-live;Publisher URL: www.cinahl.com/cgi-bin/refsvc?jid=2362&accno=2009592387

Pare, G., Moqadem, K., Pineau, G., & St-Hilaire, C. 2010. Clinical effects of home telemonitoring in the context of diabetes, asthma, heart failure and hypertension: a systematic review. *Journal of medical Internet research*, 12, (2) e21

St John, A., Davis, W.A., Price, C.P., & Davis, T.M.E. 2010. The value of self-monitoring of blood glucose: a review of recent evidence. *Journal of Diabetes and its Complications*, 24, (2) 129-141

Sutcliffe, P., Martin, S., Sturt, J., Powell, J., Griffiths, F., Adams, A., & Dale, J. 2011. Systematic review of communication technologies to promote access and engagement of young people with diabetes into healthcare. *BMC Endocrine Disorders*, 11,

Yeh, H.-C., Brown, T.T., Maruthur, N., Ranasinghe, P., Berger, Z., Suh, Y.D., Wilson, L.M., Haberl, E.B., Brick, J., Bass, E.B., & Golden, S.H. Comparative effectiveness and safety of methods of insulin delivery and glucose monitoring for diabetes mellitus: A systematic review and meta-analysis. *Annals of Internal Medicine*, 157, (5) 16

Excluded at stage 2 – not a systematic review

Agarwal, R., Bills, J.E., Hecht, T.J.W., & Light, R.P. 2011. Role of home blood pressure monitoring in overcoming therapeutic inertia and improving hypertension control: A systematic review and meta-analysis. *Hypertension*, 57, (1) January-38

Aldcroft, S.A., Taylor, N.F., Blackstock, F.C., & O'Halloran, P.D. 2011. Psychoeducational rehabilitation for ealth behavior change in coronary artery dsease: A systematic review of controlled trials. *Journal of Cardiopulmonary Rehabilitation and Prevention*, 31, (5) September-October

Alonso-Coello, P., Zhou, Q., & Guyatt, G. Home-monitoring of oral anticoagulation vs. dabigatran: An indirect comparison. *Thrombosis and Haemostasis*, 108, (4) September

Anderson, E. & Esper, G. 2012. A systematic review of teleneurology. *Neurology.Conference: 64th American Academy of Neurology Annual Meeting New Orleans, LA United States.Conference Start: 20120421 Conference End: 20120428.Conference Publication: (var.pagings)*, 78, (1 Meeting Abstract) 22

Ann, M.K., Lokker, C., Handler, S.M., Dolovich, L.R., Holbrook, A.M., O'Reilly, D., Tamblyn, R., Hemens, B.J., Basu, R., Troyan, S., & Roshanov, P.S. 2012. The effectiveness of integrated health information technologies across the phases of medication management: A systematic review of randomized controlled trials. *Journal of the American Medical Informatics Association*, 19, (1) January/February-30

Arad, Y., Fonseca, V., Peters, A., & Vinik, A. 2011. Beyond the monofilament for the insensate diabetic foot: A systematic review of randomized trials to prevent the occurrence of plantar foot ulcers in patients with diabetes. *Diabetes Care*, 34, (4) April-1046

Aspry, K.E., Furman, R., Karalis, D.G., Jacobson, T.A., Zhang, A.M., Liptak, G.S., & Cohen, J.D. Effect of health information technology interventions on lipid management in clinical practice: A systematic review of randomized controlled trials. *Journal of Clinical Lipidology*, 7, (6) November-December

Avery, L., Flynn, D., Van, W.A., Sniehotta, F.F., & Trenell, M.I. Changing physical activity behavior in type 2 diabetes: A systematic review and meta-analysis of behavioral interventions. *Diabetes Care*, 35, (12) December

Aziz, K.M.A. Management of type-1 and type-2 diabetes by insulin injections in diabetology clinics - a scientific research review. *Recent Patents on Endocrine, Metabolic and Immune Drug Discovery*, 6, (2) May

Baradaran, H.R.S. 2010. Effectiveness of diabetes educational interventions in Iran: A systematic review. *Diabetes Technology and Therapeutics*, 12, (4) 317-331

Beatty, L. & Lambert, S. 2013. A systematic review of internet-based self-help therapeutic interventions to improve distress and disease-control among adults with chronic health conditions. *Clinical Psychology Review*, 33, (4) 609-622 available from: http://search.ebscohost.com/login.aspx?direct=true&db=mnh&AN=23603521&site=ehost-live

Bentsen, S.B., Langeland, E., & Holm, A.L. Evaluation of self-management interventions for chronic obstructive pulmonary disease. *Journal of Nursing Management*, 20, (6) September

Birns, J., Roots, A., & Bhalla, A. Role of telemedicine in the management of acute ischemic stroke. *Clinical Practice*, 10, (2) 2013

Bliziotis, I.A., Destounis, A., & Stergiou, G.S. 2012. Home versus ambulatory and office blood pressure in predicting target organ damage in hypertension: A systematic review and meta-analysis. *Journal of Hypertension*, 30, (7) July-1299

Boland, M.R.S., Tsiachristas, A., Kruis, A.L., Chavannes, N.H., & Rutten-Van Molken, M.P.M.H. The health economic impact of disease management programs for COPD: A systematic literature review and meta-analysis. *BMC Pulmonary Medicine*, 13, (1) 40

Bonner, K., Mezochow, A., Roberts, T., Ford, N., & Cohn, J. Viral load monitoring as a tool to reinforce adherence: A systematic review. *Journal of Acquired Immune Deficiency Syndromes*, 64, (1) 01

Boren, S.A., Wakefield, B.J., Gunlock, T.L., & Wakefield, D.S. 2009. Heart failure self-management education: A systematic review of the evidence. *International Journal of Evidence-Based Healthcare*, 7, (3) 159-168 available from: http://search.ebscohost.com/login.aspx?direct=true&db=psyh&AN=2009-12861-002&site=ehost-live;borens@health.missouri.edu

Bourbeau, J. 2003. Disease-specific self-management programs in patients with advanced chronic obstructive pulmonary disease: a comprehensive and critical evaluation (Structured abstract). *Disease Management and Health Outcomes*, 11, 311-319

Boyde, M., Turner, C., Thompson, D.R., & Stewart, S. 2011. Educational interventions for patients with heart failure: a systematic review of randomized controlled trials. *The Journal of cardiovascular nursing*, 26, (4) 2011-2Aug

Boyers, D., McNamee, P., Clarke, A., Jones, D., Martin, D., Schofield, P., & Smith, B.H. 2013. Cost-effectiveness of self-management methods for the treatment of chronic pain in an aging adult population: a systematic review of the literature. *The Clinical Journal Of Pain*, 29, (4) 366-375 available from: http://search.ebscohost.com/login.aspx?direct=true&db=mnh&AN=23042472&site=ehost-live

Breland, H.L. & Kamen, D.L. Lupus patient education: An examination of approaches. *International Journal of Clinical Rheumatology*, 7, (5) October

Brewster, L.B. 2010. Systematic Review of the Use of Spot and Overnight Urine for Assessment of Sodium Excretion: 5D.05. *Journal of Hypertension*, Conference, (var.pagings) June

Brouwer, W., Kroeze, W., Crutzen, R., de, N.J., de Vries, N.K., Brug, J., & Oenema, A. 2011. Which intervention characteristics are related to more exposure to internet-delivered healthy lifestyle promotion interventions? A systematic review. *Journal of medical Internet research*, 13, (1) 2011

Bryant, J., McDonald, V.M., Boyes, A., Sanson-Fisher, R., Paul, C., & Melville, J. Improving medication adherence in chronic obstructive pulmonary disease: A systematic review. *Respiratory Research*, 14, (1) 109

Bussey-Smith, K.L. & Rossen, R.D. 2007. A systematic review of randomized control trials evaluating the effectiveness of interactive computerized asthma patient education programs (Structured abstract). *Annals of Allergy, Asthma and Immunology*, 98, 507-516

Carlier, I.V.E., Meuldijk, D., Van Vliet, I.M., Van, F.E., Van Der Wee, N.J.A., & Zitman, F.G. Routine outcome monitoring and feedback on physical or mental health status: Evidence and theory. *Journal of Evaluation in Clinical Practice*, 18, (1) February

Carnes, D., Homer, K.E., Miles, C.L., Pincus, T., Underwood, M., Rahman, A., & Taylor, S.J.C. Effective delivery styles and content for self-management interventions for chronic musculoskeletal pain: A systematic literature review. *Clinical Journal of Pain*, 28, (4) May

Castrejon, I., Silva-Fernandez, L., Bombardier, C., & Carmona, L. 2011. Clinical composite measures of disease activity for diagnosis and followup of undifferentiated peripheral inflammatory arthritis: A systematic review. *Journal of Rheumatology*, 38, (SUPPL.#87) March-53

Catalani, C., Philbrick, W., Fraser, H., Mechael, P., & Israelski, D.M. mHealth for HIV treatment & prevention: A systematic review of the literature. *Open AIDS Journal*, 7, (1) 2013

Centre for Reviews and Dissemination. Communication-related behavior change techniques used in face-to-face lifestyle interventions in primary care: a systematic review of the literature (Structured abstract). Database of Abstracts of Reviews of Effects 4. 2013.

Ref Type: Abstract

Centre for Reviews and Dissemination. Computer-based education for patients with hypertension: a systematic review (Structured abstract). Database of Abstracts of Reviews of Effects 4. 2013.

Ref Type: Abstract

Centre for Reviews and Dissemination. Telehealth interventions for the secondary prevention of coronary heart disease: a systematic review (Structured abstract). Database of Abstracts of Reviews of Effects 4. 2013.

Ref Type: Abstract

Centre for Reviews and Dissemination. Pharmacist interventions to enhance blood pressure control and adherence to antihypertensive therapy: review and meta-analysis (Structured abstract). Database of Abstracts of Reviews of Effects 4. 2013.

Ref Type: Abstract

Centre for Reviews and Dissemination. A systematic review of randomized trials of disease management programs in heart failure (Structured abstract). Database of Abstracts of Reviews of Effects 4. 2013.

Ref Type: Abstract

Centre for Reviews and Dissemination. Nurse-led telephone interventions for people with cardiac disease: a review of the research literature (Structured abstract). Database of Abstracts of Reviews of Effects 4. 2013.

Ref Type: Abstract

Centre for Reviews and Dissemination. A systematic review of psychosocial outcomes following education, self-management and psychological interventions in diabetes mellitus (Structured abstract). Database of Abstracts of Reviews of Effects 4. 2013.

Ref Type: Abstract

Centre for Reviews and Dissemination. A systematic review of community-based health interventions on depression for older adults with heart disease (Structured abstract). Database of Abstracts of Reviews of Effects 4. 2013.

Ref Type: Abstract

Centre for Reviews and Dissemination. Systematic review of the chronic care model in chronic obstructive pulmonary disease prevention and management (Structured abstract). Database of Abstracts of Reviews of Effects 4. 2013.

Ref Type: Abstract

Centre for Reviews and Dissemination. Systematic review: self-management support interventions for irritable bowel syndrome (Structured abstract). Database of Abstracts of Reviews of Effects 4. 2013.

Ref Type: Abstract

Centre for Reviews and Dissemination. Self-monitoring and other non-pharmacological interventions to improve the management of hypertension in primary care: a systematic review (Structured abstract). Database of Abstracts of Reviews of Effects 4. 2013.

Ref Type: Abstract

Centre for Reviews and Dissemination. Effectiveness of chronic obstructive pulmonary disease-management programs: systematic review and meta-analysis (Structured abstract). Database of Abstracts of Reviews of Effects 4. 2013.

Ref Type: Abstract

Centre for Reviews and Dissemination. Effectiveness of chronic care model-oriented interventions to improve quality of diabetes care: a systematic review (Structured abstract). Database of Abstracts of Reviews of Effects 4. 2013.

Ref Type: Abstract

Centre for Reviews and Dissemination. Educational interventions for migrant South Asians with type 2 diabetes: a systematic review (Structured abstract). Database of Abstracts of Reviews of Effects 4. 2013.

Ref Type: Abstract

Centre for Reviews and Dissemination. Effectiveness of web-based interventions on patient empowerment: a systematic review and meta-analysis (Provisional abstract). Database of Abstracts of Reviews of Effects 4. 2013.
Ref Type: Abstract
Centre for Reviews and Dissemination. Self-care and quality of life outcomes in heart failure patients (Structured abstract). Database of Abstracts of Reviews of Effects 4. 2013.
Ref Type: Abstract
Centre for Reviews and Dissemination. Problem solving in diabetes self-management and control: a systematic review of the literature (Structured abstract). Database of Abstracts of Reviews of Effects 4. 2013.
Ref Type: Abstract
Centre for Reviews and Dissemination. Evaluation of self-management interventions for chronic obstructive pulmonary disease (Structured abstract). Database of Abstracts of Reviews of Effects 4. 2013.
Ref Type: Abstract
Centre for Reviews and Dissemination. Psychological intervention following implantation of an implantable defibrillator: a review and future recommendations (Structured abstract). Database of Abstracts of Reviews of Effects 4. 2013.
Ref Type: Abstract
Centre for Reviews and Dissemination. Heart failure self-management education: a systematic review of the evidence (Structured abstract). Database of Abstracts of Reviews of Effects 4. 2013.
Ref Type: Abstract
Centre for Reviews and Dissemination. Patient self-administration of medication: a review of the literature (Structured abstract). Database of Abstracts of Reviews of Effects 4. 2013.
Ref Type: Abstract
Centre for Reviews and Dissemination. Interventions to improve outcomes for minority adults with asthma: a systematic review (Structured abstract). Database of Abstracts of Reviews of Effects 4. 2013.
Ref Type: Abstract
Centre for Reviews and Dissemination. Interventions to enhance adherence to medications in patients with heart failure: a systematic review (Structured abstract). Database of Abstracts of Reviews of Effects 4. 2013.
Ref Type: Abstract
Centre for Reviews and Dissemination. Self-management education interventions for persons with schizophrenia: a meta-analysis (Provisional abstract). Database of Abstracts of Reviews of Effects 4. 2013.
Ref Type: Abstract
Centre for Reviews and Dissemination. Self-management education programs for age-related macular degeneration: a systematic review (Structured abstract). Database of Abstracts of Reviews of Effects 4. 2013.
Ref Type: Abstract
Centre for Reviews and Dissemination. Self-management education programs for people living with HIV/AIDS: a systematic review (Provisional abstract). Database of Abstracts of Reviews of Effects 4. 2013.
Ref Type: Abstract
Centre for Reviews and Dissemination. Internet-based physical activity interventions: a systematic review of the literature (Structured abstract). Database of Abstracts of Reviews of Effects 4. 2013.
Ref Type: Abstract
Centre for Reviews and Dissemination. Self-management interventions for type 2 diabetes: a systematic review (Structured abstract). Database of Abstracts of Reviews of Effects 4. 2013.
Ref Type: Abstract
Centre for Reviews and Dissemination. Effectiveness of innovations in nurse led chronic disease management for patients with chronic obstructive pulmonary disease: systematic review of evidence (Structured abstract). Database of Abstracts of Reviews of Effects 4. 2013.
Ref Type: Abstract
Centre for Reviews and Dissemination. Self-management programmes for people post stroke: a systematic review (Provisional abstract). Database of Abstracts of Reviews of Effects 4. 2013.
Ref Type: Abstract

Centre for Reviews and Dissemination. Effectiveness of diabetes educational interventions in Iran: a systematic review (Structured abstract). Database of Abstracts of Reviews of Effects 4. 2013.
Ref Type: Abstract
Centre for Reviews and Dissemination. Integrated exercise and self-management programmes in osteoarthritis of the hip and knee: a systematic review of effectiveness (Structured abstract). Database of Abstracts of Reviews of Effects 4. 2013.
Ref Type: Abstract
Centre for Reviews and Dissemination. Impact of telemedicine intensive care unit coverage on patient outcomes: a systematic review and meta-analysis (Structured abstract). Database of Abstracts of Reviews of Effects 4. 2013.
Ref Type: Abstract
Centre for Reviews and Dissemination. Nonpharmacological strategies for improving heart failure outcomes in the community: a systematic review (Structured abstract). Database of Abstracts of Reviews of Effects 4. 2013.
Ref Type: Abstract
Centre for Reviews and Dissemination. A systematic review of variability and reliability of manual and automated blood pressure readings (Structured abstract). Database of Abstracts of Reviews of Effects 4. 2013.
Ref Type: Abstract
Centre for Reviews and Dissemination. Relative effectiveness of clinic and home blood pressure monitoring compared with ambulatory blood pressure monitoring in diagnosis of hypertension: systematic review (Structured abstract). Database of Abstracts of Reviews of Effects 4. 2013.
Ref Type: Abstract
Centre for Reviews and Dissemination. Home versus hospital-based cardiac rehabilitation: a systematic review (Structured abstract). Database of Abstracts of Reviews of Effects 4. 2013.
Ref Type: Abstract
Centre for Reviews and Dissemination. Home-based pulmonary rehabilitation in chronic obstructive pulmonary disease patients (Structured abstract). Database of Abstracts of Reviews of Effects 4. 2013.
Ref Type: Abstract
Centre for Reviews and Dissemination. Efficacy of multicomponent treatment in fibromyalgia syndrome: a meta-analysis of randomized controlled clinical trials (Structured abstract). Database of Abstracts of Reviews of Effects 4. 2013.
Ref Type: Abstract
Centre for Reviews and Dissemination. Can we identify how programmes aimed at promoting self-management in musculoskeletal pain work and who benefits? A systematic review of sub-group analysis within RCTs (Provisional abstract). Database of Abstracts of Reviews of Effects 4. 2013.
Ref Type: Abstract
Centre for Reviews and Dissemination. Biomedical informatics applications for asthma care: a systematic review (Structured abstract). Database of Abstracts of Reviews of Effects 4. 2013.
Ref Type: Abstract
Centre for Reviews and Dissemination. Behavioral treatments of chronic tension-type headache in adults: are they beneficial? (Structured abstract). Database of Abstracts of Reviews of Effects 4. 2013.
Ref Type: Abstract
Centre for Reviews and Dissemination. Anticoagulation intensity and outcomes among patients prescribed oral anticoagulant therapy: a systematic review and meta-analysis (Structured abstract). Database of Abstracts of Reviews of Effects 4. 2013.
Ref Type: Abstract
Centre for Reviews and Dissemination. Accuracy of blood-glucose measurements using glucose meters and arterial blood gas analyzers in critically ill adult patients: a systematic review (Provisional abstract). Database of Abstracts of Reviews of Effects 4. 2013.
Ref Type: Abstract
Chetty, V.T., Almulla, A., Odueyungbo, A., & Thabane, L. 2008. The effect of continuous subcutaneous glucose monitoring (CGMS) versus intermittent whole blood finger-stick glucose monitoring (SBGM) on hemoglobin A1c (HBA1c) levels in type 1 diabetic patients: a systematic review. *Diabetes Research and Clinical Practice*, 81, 79-87

Chodosh, J., Morton, S.C., Mojica, W., Maglione, M., Suttorp, M.J., Hilton, L., Rhodes, S., & Shekelle, P. 2005. Meta-analysis: chronic disease self-management programs for older adults. *Annals of Internal Medicine*, 143, (6) 427 available from: http://search.ebscohost.com/login.aspx?direct=true&db=cin20&AN=2009069631&site=ehost-live;Publisher URL: www.cinahl.com/cgi-bin/refsvc?jid=686&accno=2009069631

Clark, R.A., Inglis, S.C., McAlister, F.A., Cleland, J.G., & Stewart, S. 2007. Telemonitoring or structured telephone support programmes for patients with chronic heart failure: systematic review and meta-analysis (Structured abstract). *BMJ*, 334, 942

Clarkesmith, D.E., Pattison, H.M., & Lane, D.A. 2013. Educational and behavioural interventions for anticoagulant therapy in patients with atrial fibrillation. *The Cochrane Database Of Systematic Reviews*, 6, CD008600 available from: http://search.ebscohost.com/login.aspx?direct=true&db=mnh&AN=23736948&site=ehost-live

Cramp, F., Hewlett, S., Almeida, C., Kirwan, J.R., Choy, H.E., Chalder, T., Pollock, J., & Christensen, R. 2013. Non-pharmacological interventions for fatigue in rheumatoid arthritis [Systematic Review]. *Cochrane Database of Systematic Reviews*, 8,

Dantic, D.E. A critical review of the effectiveness of 'teach-back' technique in teaching COPD patients self-management using respiratory inhalers. *Health Education Journal*, 73, (1) January

de, B.J., Legierse, C.M., Prinsen, C.A., & de, K.J. 2011. Patient education in chronic skin diseases: a systematic review. [Review]. *Acta Dermato-Venereologica*, 91, (1) 12-17

DelliFraine, J.L. & Dansky, K.H. 2008. Home-based telehealth : a review and meta-analysis. *Journal of Telemedicine and Telecare* (2) 62-66

Ditewig, J.B., Blok, H., Havers, J., & van Veenendaal, H. 2010. Effectiveness of self-management interventions on mortality, hospital readmissions, chronic heart failure hospitalization rate and quality of life in patients with chronic heart failure: A systematic review. *Patient Education and Counseling*, 78, (3) 297-315 available from: http://search.ebscohost.com/login.aspx?direct=true&db=psyh&AN=2010-05266-006&site=ehost-live;jb.ditewig@gmail.com

Dolan, G., Smith, L.A., Collins, S., & Plumb, J.M. 2008. Effect of setting, monitoring intensity and patient experience on anticoagulation control: a systematic review and meta-analysis of the literature (Structured abstract). *Current Medical Research and Opinion*, 24, 1459-1472

Dorstyn, D.S., Mathias, J.L., & Denson, L.A. 2011. Psychosocial Outcomes of Telephone-Based Counseling for Adults With an Acquired Physical Disability: A Meta-Analysis. *Rehabilitation Psychology*, 56, (1) February-14

Egginton, J.S., Ridgeway, J.L., Shah, N.D., Balasubramaniam, S., Emmanuel, J.R., Prokop, L.J., Montori, V.M., & Murad, M.H. 2012. Care management for Type 2 diabetes in the United States: a systematic review and meta-analysis. *BMC Health Services Research*, 12, (pp 72) 2012

El-Gayar, O., Timsina, P., Nawar, N., & Eid, W. Mobile applications for diabetes self-management: status and potential. *Journal of diabetes science and technology*, 7, (1) 2013

El-Gayar, O., Timsina, P., Nawar, N., & Eid, W. A systematic review of IT for diabetes self-management: Are we there yet? *International Journal Of Medical Informatics*, 82, (8) August available from: http://www.sciencedirect.com/science/article/pii/S1386505613001135#

Ferrier, S., Blanchard, C.M., Vallis, M., & Giacomantonio, N. 2011. Behavioural interventions to increase the physical activity of cardiac patients: A review. *European Journal of Cardiovascular Prevention and Rehabilitation*, 18, (1) February-32

Franek, J. Self-management support interventions for persons with chronic disease: An evidence-based analysis. *Ontario Health Technology Assessment Series*, 13, (9) 2013

Fuchs, S.C., De Mello, R.G.B., & Fuchs, F.C. Home blood pressure monitoring is better predictor of cardiovascular disease and target organ damage than office blood pressure: A systematic review and meta-analysis. *Current Cardiology Reports*, 15, (11) 413

Gaikwad, R.W. 2009. The role of home-based information and communications technology interventions in chronic disease management: A systematic literature review. *Health Informatics Journal*, 15, (2) 122-146

Greaves, C.J., Sheppard, K.E., Abraham, C., Hardeman, W., Roden, M., Evans, P.H., Schwarz, P., & IMAGE Study Group 2011. Systematic review of reviews of intervention components associated with increased effectiveness in dietary and physical activity interventions. *BMC public health*, 11, (pp 119) 2011

Gucciardi, E., Chan, V.W.S., Manuel, L., & Sidani, S. A systematic literature review of diabetes self-management education features to improve diabetes education in women of Black African/Caribbean and Hispanic/Latin American ethnicity. *Patient Education and Counseling*, 92, (2) August

Gupta, V.K., Shobha, P., Maria, A.K., Narang, V.K., Arora, S., Gupta, V., Gupta, M., & Nohria, S. To study the prescription pattern of inhaler devices and medication in management of chronic obstructive pulmonary disease in primary care practice. *Respirology.Conference: Airway Vista 2013 Seoul South Korea.Conference Start: 20130329 Conference End: 20130331.Conference Publication: (var.pagings)*, 18, (pp 22-23) April

Gwadry-Sridhar, F.H., Manias, E., Lal, L., Salas, M., Hughes, D.A., Ratzki-Leewing, A., & Grubisic, M. Impact of interventions on medication adherence and blood pressure control in patients with essential hypertension: A systematic review by the ISPOR medication adherence and persistence special interest group. *Value in Health*, 16, (5) July-August

Haag, G., Diener, H.-C., May, A., Meyer, C., Morck, H., Straube, A., Wessely, P., & Evers, S. 2011. Self-medication of migraine and tension-type headache: Summary of the evidence-based recommendations of the Deutsche Migrane und Kopfschmerzgesellschaft (DMKG), the Deutsche Gesellschaft fur Neurologie (DGN), the Osterreichische Kopfschmerzgesellschaft (OKSG) and the Schweizerische Kopfwehgesellschaft (SKG). *Journal of Headache and Pain*, 12, (2) April-217

Hackam, D.G., Quinn, R.R., Ravani, P., Rabi, D.M., Dasgupta, K., Daskalopoulou, S.S., Khan, N.A., Herman, R.J., Bacon, S.L., Cloutier, L., Dawes, M., Rabkin, S.W., Gilbert, R.E., Ruzicka, M., McKay, D.W., Campbell, T.S., Grover, S., Honos, G., Schiffrin, E.L., Bolli, P., Wilson, T.W., Feldman, R.D., Lindsay, P., Hill, M.D., Gelfer, M., Burns, K.D., Vallee, M., Prasad, G.V.R., Lebel, M., McLean, D., Arnold, J.M.O., Moe, G.W., Howlett, J.G., Boulanger, J.-M., Larochelle, P., Leiter, L.A., Jones, C., Ogilvie, R.I., Woo, V., Kaczorowski, J., Trudeau, L., Petrella, R.J., Milot, A., Stone, J.A., Drouin, D., Lavoie, K.L., Lamarre-Cliche, M., Godwin, M., Tremblay, G., Hamet, P., Fodor, G., Carruthers, S.G., Pylypchuk, G.B., Burgess, E., Lewanczuk, R., Dresser, G.K., Penner, S.B., Hegele, R.A., McFarlane, P.A., Sharma, M., Reid, D.J., Tobe, S.W., Poirier, L., & Padwal, R.S. The 2013 Canadian hypertension education program recommendations for blood pressure measurement, diagnosis, assessment of risk, prevention, and treatment of hypertension. *Canadian Journal of Cardiology*, 29, (5) May

Han, H.-R., Song, H., Nguyen, T., & Kim, M. Measuring self-care in hypertensive patients: A systematic review of literature. *Journal of Clinical Hypertension.Conference: American Society of Hypertension, Inc*, 27th, (var.pagings) April

Hesselbjerg, L.J., Pedersen, H.S., Asmussen, M.B., & Petersen, K.D. Is dabigatran considered a cost-effective alternative to warfarin treatment: A review of current economic evaluations worldwide. *Journal of Medical Economics*, 16, (7) July

Hoeks, L., Greven, W., & de Valk, H. Real-time continuous glucose monitoring system for treatment of diabetes: a systematic review (Structured abstract). Diabetic Medicine 28[4], 386-394. 2011.
Ref Type: Abstract

Huckvale, K., Car, M., Morrison, C., & Car, J. 2012. Apps for asthma self-management: A systematic assessment of content and tools. *BMC Medicine*, 10,

Huibers, L., Smits, M., Renaud, V., Giesen, P., & Wensing, M. 2011. Safety of telephone triage in out-of-hours care: A systematic review. [References]. *Scandinavian Journal of Primary Health Care* (4) 198-209

Iversen, M.D. 2012. Rehabilitation interventions for pain and disability in osteoarthritis: A review of interventions including exercise, manual techniques, and assistive devices. *American Journal of Nursing*, 112, (3 SUPPL.#1) March-S37

Jang, Y. & Yoo, H. Self-management programs based on the social cognitive theory for Koreans with chronic diseases: A systematic review. *Contemporary Nurse*, 40, (2) February

Janssen, V., De, G., V, Dusseldorp, E., & Maes, S. Lifestyle modification programmes for patients with coronary heart disease: A systematic review and meta-analysis of randomized controlled trials. *European Journal of Preventive Cardiology*, 20, (4) August

Jaramillo, A., Welch, V.A., Ueffing, E., Gruen, R.L., Bragge, P., Lyddiatt, A., & Tugwell, P. 2013. Prevention and self-management interventions are top priorities for osteoarthritis systematic reviews. *Journal Of Clinical Epidemiology*, 66, (5) 503-510 available from: http://search.ebscohost.com/login.aspx?direct=true&db=mnh&AN=22995854&site=ehost-live

Jia, C.E., Zhang, H.P., Lv, Y., Liang, R., Jiang, Y.Q., Powell, H., Fu, J.J., Wang, L., Gibson, P.G., & Wang, G. The asthma control test and asthma control questionnaire for assessing asthma control: Systematic review and meta-analysis. *Journal of Allergy and Clinical Immunology*, 131, (3) March

Johansson, T. & Wild, C. 2014. Telemedicine in Stroke Management. Systematic Review (Structured abstract). *Health Technology Assessment Database* (1)

Jonsdottir, H. Self-management programmes for people living with chronic obstructive pulmonary disease: A call for a reconceptualisation. *Journal of Clinical Nursing*, 22, (5-6) March

Kruis, A.L., Smidt, N., Assendelft, J.W., Gussekloo, J., Boland, R.M., Ruttenvan Molken, M., & Chavannes, N.H. 2013. Integrated disease management interventions for patients with chronic obstructive pulmonary disease [Systematic Review]. *Cochrane Database of Systematic Reviews*, 10,

Kuethe, M.C., VaessenVerberne, A.A., Elbers, R.G., & Van Aalderen, M.W. 2013. Nurse versus physician-led care for the management of asthma [Systematic Review]. *Cochrane Database of Systematic Reviews*, 2,

Lami, M.J., Martinez, M.P., & Sanchez, A.I. Systematic review of psychological treatment in fibromyalgia. *Current Pain and Headache Reports*, 17, (7) 345

Lawrence, M., Booth, J., Mercer, S., & Crawford, E. A systematic review of the benefits of mindfulness-based interventions following transient ischemic attack and stroke. *International Journal of Stroke*, 8, (6) August

Lee, T.W., Lee, S.H., Kim, H.H., & Kang, S.J. Effective intervention strategies to improve health outcomes for cardiovascular disease patients with low health literacy skills: A systematic review. *Asian Nursing Research*, 6, (4) December

Lehman, A., Yohannes, S., & MacDonald, C. 2011. Moving from patient-centred to family-centred care? A systematic review of psycho-educational programs for people and partners affected by arthritis. *Journal of Rheumatology.Conference: 2nd Mexican-Canadian Congress of Rheumatology Cancun Mexico.Conference Start: 20110210 Conference End: 20110215.Conference Publication: (var.pagings)*, 38, (6) June

Lemmens, K.M.M., Lemmens, L.C., Boom, J.H.C., Drewes, H.W., Meeuwissen, J.A.C., Steuten, L.M.G., Vrijhoef, H.J.M., & Baan, C.A. 2011. Chronic care management for patients with COPD: A critical review of available evidence. *Journal of Evaluation in Clinical Practice*, 19, (5) October available from: http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2753.2011.01805.x/pdf

Linn, A.J., Vervloet, M., van, D.L., Smit, E.G., & Van Weert, J.C. 2011. Effects of eHealth interventions on medication adherence: a systematic review of the literature. [Review]. *Journal of medical Internet research*, 13, (4) e103

Liu, H., Li, S., & Feldman, M.W. 2012. Forced bachelors, migration and HIV transmission risk in the context of China's gender imbalance: A meta-analysis. *AIDS Care*, 24, (12) 1487-1495 available from: http://search.ebscohost.com/login.aspx?direct=true&db=rzh&AN=2011723962&site=ehost-live

Loveman, E., Frampton, G., & Clegg, A.J. 2008. The clinical effectiveness of diabetes education models for type 2 diabetes: a systematic review. *Health Technology Assessment*, 12, (9) 1-136 available from: http://www.journalslibrary.nihr.ac.uk/__data/assets/pdf_file/0017/65213/FullReport-hta12090.pdf

Lu, Z., Cao, S., Chai, Y., Liang, Y., Bachmann, M., Suhrcke, M., & Song, F. 2012. Effectiveness of interventions for hypertension care in the community - a meta-analysis of controlled studies in China. *BMC Health Services Research*, 12, 216

Ludwig, W., Wolf, K.-H., Duwenkamp, C., Gusew, N., Hellrung, N., Marschollek, M., Wagner, M., & Haux, R. Health-enabling technologies for the elderly - An overview of services based on a literature review. *Computer Methods and Programs in Biomedicine*, 106, (2) May

Mahtani, K.R., Heneghan, C.J., Nunan, D., Bankhead, C., Keeling, D., Ward, A.M., Harrison, S.E., Roberts, N.W., Hobbs, R.F., & Perera, R. 2012. Optimal loading dose of warfarin for the initiation of oral anticoagulation [Systematic Review]. *Cochrane Database of Systematic Reviews*, 12,

Mazze, R., Akkerman, B., & Mettner, J. 2011. An overview of continuous glucose monitoring and the ambulatory glucose profile. *Minnesota medicine*, 94, (8) Aug-44

McDermott, M.n.S. & While, A.E. 2013. Maximizing the healthcare environment: a systematic review exploring the potential of computer technology to promote self-management of chronic illness in healthcare settings. *Patient Education and Counseling*, 92, (1) 13-22 available from: http://search.ebscohost.com/login.aspx?direct=true&db=mnh&AN=23566427&site=ehost-live

McLean, S., Chandler, D., Nurmatov, U., Liu, J., Pagliari, C., Car, J., & Sheikh, A. 2011. Telehealthcare for asthma: A Cochrane review. *CMAJ*, 183, (11) 09-E742

McLean, S., Chandler, D., Nurmatov, U., Liu, J., Pagliari, C., Car, J., & Sheikh, A. 2010. Telehealthcare for asthma. *McLean.Susannah., Chandler.David., Nurmatov.Ulugbek., Liu Joseph., Pagliari.Claudia., Car.Josip., Sheikh.Aziz.Telehealthcare.for asthma.Cochrane Database of Systematic Reviews: Reviews 2010 Issue 10 John.Wiley.& Sons., Ltd.Chichester, UK DOI.: 10.1002./*

Merolli, M., Gray, K., & Martin-Sanchez, F. Health outcomes and related effects of using social media in chronic disease management: A literature review and analysis of affordances. *Journal of Biomedical Informatics*, 46, (6) December

Millard, T., Elliott, J., & Girdler, S. Self-management education programs for people living with HIV/AIDS: A Systematic Review. *AIDS Patient Care and STDs*, 27, (2) 01

Minet, L.M. 2010. Mediating the effect of self-care management intervention in type 2 diabetes: A meta-analysis of 47 randomised controlled trials. *Patient Education and Counseling*, 80, (1) 29-41

Molloy, G.J., O'Carroll, R.E., Witham, M.D., & McMurdo, M.E.T. 2012. Interventions to enhance adherence to medications in patients with heart failure a systematic review. *Circulation: Heart Failure*, 5, (1) January-133

Monninkhof E.Van Der Valk 2003. Self-management education for patients with chronic obstructive pulmonary disease: A systematic review. *Thorax*, 58, (5) 394-398

Mosa, A.S., Yoo, I., & Sheets, L. A systematic review of healthcare applications for smartphones. *BMC medical informatics and decision making*, 12, (pp 67) 2012

Muller-Barna, P., Schwamm, L.H., & Haberl, R.L. 2012. Telestroke increases use of acute stroke therapy. *Current Opinion in Neurology*, 25, (1) February-10

Nakao, M.Y. 2003. Blood pressure-lowering effects of biofeedback treatment in hypertension: A meta-analysis of randomized controlled trials. *Hypertension Research*, 26, (1) 37-46

Neubeck, L.R. 2009. Telehealth interventions for the secondary prevention of coronary heart disease: A systematic review. *European Journal of Cardiovascular Prevention and Rehabilitation*, 16, (3) 281-289

Niiranen, T.J., Thijs, L., Asayama, K., Johansson, J.K., Ohkubo, T., Kikuya, M., Boggia, J., Hozawa, A., Sandoya, E., Stergiou, G.S., Tsuji, I., Jula, A.M., Imai, Y., & Staessen, J.A. 2012. The International Database of HOme blood pressure in relation to Cardiovascular Outcome (IDHOCO): moving from baseline characteristics to research perspectives. *Hypertension Research: Official Journal Of The Japanese Society Of Hypertension*, 35, (11) 1072-1079 available from: http://search.ebscohost.com/login.aspx?direct=true&db=mnh&AN=22763485&site=ehost-live

Oliveira, C., Simoes, M., Carvalho, J., & Ribeiro, J. Combined exercise for people with type 2 diabetes mellitus: A systematic review. *Diabetes Research and Clinical Practice*, 98, (2) November

Oliveira, V.C., Ferreira, P.H., Maher, C.G., Pinto, R.Z., Refshauge, K.M., & Ferreira, M.L. Effectiveness of self-management of low back pain: Systematic review with meta-analysis. *Arthritis Care and Research*, 64, (11) November

Olsson, L.E. Efficacy of person-centred care as an intervention in controlled trials a systematic review.

Omboni, S., Gazzola, T., Carabelli, G., & Parati, G. Clinical usefulness and cost effectiveness of home blood pressure telemonitoring:Meta-analysis of randomized controlled studies. *Journal of Hypertension*, 31, (3) 2013

Oosterom-Calo, R., Van Ballegooijen, A.J., Terwee, C.B., Te Velde, S.J., Brouwer, I.A., Jaarsma, T., & Brug, J. Determinants of heart failure self-care: A systematic literature review. *Heart Failure Reviews*, 17, (3) May

Peeters, J.M., Wiegers, T.A., & Friele, R.D. How technology in care at home affects patient self-care and self-management: A scoping review. *International Journal of Environmental Research and Public Health*, 10, (11) 29

Polisena, J., Tran, K., Cimon, K., Hutton, B., McGill, S., & Palmer, K. 2009. Home telehealth for diabetes management: A systematic review and meta-analysis. *Diabetes, Obesity and Metabolism*, 11, (10) 913-930

Polisena, J.T. 2010. Home telehealth for chronic obstructive pulmonary disease: A systematic review and meta-analysis. *Journal of Telemedicine and Telecare*, 16, (3) 120-127

Press, V.G., Pappalardo, A.A., Conwell, W.D., Pincavage, A.T., Prochaska, M.H., & Arora, V.M. 2012. Interventions to improve outcomes for minority adults with asthma: A systematic review. *Journal of General Internal Medicine*, 27, (8) August-1015

Primack, B.A., Carroll, M.V., McNamara, M., Klem, M.L., King, B., Rich, M., Chan, C.W., & Nayak, S. Role of video games in improving health-related outcomes: A systematic review. *American Journal of Preventive Medicine*, 42, (6) June

Purc-Stephenson, R.J. & Thrasher, C. Patient compliance with telephone triage recommendations: A meta-analytic review. *Patient Education and Counseling*, 87, (2) May

Radhakrishnan, K. The efficacy of tailored interventions for self-management outcomes of type 2 diabetes, hypertension or heart disease: A systematic review. *Journal of Advanced Nursing*, 68, (3) March

Rao, G., Burke, L.E., Spring, B.J., Ewing, L.J., Turk, M., Lichtenstein, A.H., Cornier, M.-A., Spence, J.D., & Coons, M. 2011. New and emerging weight management strategies for busy ambulatory settings: A scientific statement from the american heart association: Endorsed by the society of behavioral medicine. *Circulation*, 124, (10) 06-1203

Ridner, S.H., Fu, M.R., Wanchai, A., Stewart, B.R., Armer, J.M., & Cormier, J.N. 2012. Self-management of lymphedema: A systematic review of the literature from 2004 to 2011. *Nursing Research*, 61, (4) July-August

Rosse, B.A., Vowle, K.E., Keogh, E., Eccleston, C., & Mountain, G.A. 2009. Technologically-assisted behaviour change: A systematic review of studies of novel technologies for the management of chronic illness. *Journal of Telemedicine and Telecare*, 15, (7) 327-

338 available from: http://search.ebscohost.com/login.aspx?direct=true&db=psyh&AN=2009-21928-001&site=ehost-live;c.eccle5ton@bath.ac.uk

Rubin, M.N., Wellik, K.E., Channer, D.D., & Demaerschalk, B.M. 2013. A systematic review of telestroke. *Postgraduate Medicine*, 125, (1) 45-50 available from: http://search.ebscohost.com/login.aspx?direct=true&db=mnh&AN=23391670&site=ehost-live

Russell-Minda E.Jutai 2009. Health technologies for monitoring and managing diabetes: a systematic review. *Journal of diabetes science and technology*, 3, (6) 1460-1471

Schmidt-Hansen, M., Baldwin, D.R., & Hasler, E. 2012. What is the most effective follow-up model for lung cancer patients? A systematic review. *Journal of Thoracic Oncology*, 7, (5) 2012-2824

Smith, J.R., Mugford, M., Holland, R., Noble, M.J., & Harrison, B.D.W. 2007. Psycho-educational interventions for adults with severe or difficult asthma: A systematic review. *Journal of Asthma*, 44, (3) 219-241 available from: http://search.ebscohost.com/login.aspx?direct=true&db=psyh&AN=2007-07001-005&site=ehost-live;j.r.smith@uea.ac.uk

Solomon, M.R. 2008. Information technology to support self-management in chronic care: A systematic review. *Disease Management & Health Outcomes*, 16, (6) 391-401 available from: http://search.ebscohost.com/login.aspx?direct=true&db=psyh&AN=2009-00076-003&site=ehost-live;michaels@pocp.com

Steinsbekk, A., Rygg, L., Lisulo, M., Rise, M.B., & Fretheim, A. 2012. Group based diabetes self-management education compared to routine treatment for people with type 2 diabetes mellitus. A systematic review with meta-analysis. *BMC Health Services Research*, 12, 213

Stellefson, M., Dipnarine, K., & Stopka, C. The chronic care model and diabetes management in US primary care settings: a systematic review. *Preventing chronic disease*, 10, (pp E26) Feb

Stellefson, M., Chaney, B., Barry, A.E., Chavarria, E., Tennant, B., Walsh-Childers, K., Sriram, P.S., & Zagora, J. 2013. Web 2.0 chronic disease self-management for older adults: a systematic review. *Journal of medical Internet research*, 15, (2) e35 available from: http://search.ebscohost.com/login.aspx?direct=true&db=mnh&AN=23410671&site=ehost-live

Stoilkova, A., Janssen, D.J.A., & Wouters, E.F.M. Educational programmes in COPD management interventions: A systematic review. *Respiratory Medicine*, 107, (11) November

Sutcliffe, P., Martin, S., Sturt, J., Powell, J., Griffiths, F., Adams, A., & Dale, J. 2011. Systematic review of communication technologies to promote access and engagement of young people with diabetes into healthcare. *BMC Endocrine Disorders*, 11,

Thongsai, S. & Youjaiyen, M. 2013. The long-term impact of education on diabetes for older people: a systematic review. *Global Journal Of Health Science*, 5, (6) 30-39 available from: http://search.ebscohost.com/login.aspx?direct=true&db=mnh&AN=24171871&site=ehost-live

Thorpe, C.T., Fahey, L.E., Johnson, H., Deshpande, M., Thorpe, J.M., & Fisher, E.B. Facilitating Healthy Coping in Patients With Diabetes: A Systematic Review. *Diabetes Educator*, 39, (1) January-February

Vieira, D.S.R. 2010. Home-based pulmonary rehabilitation in chronic obstructive pulmonary disease patients. *Current Opinion in Pulmonary Medicine*, 16, (2) 134-143

Viswanathan, M., Golin, C.E., Jones, C.D., Ashok, M., Blalock, S.J., Wines, R.C.M., Coker-Schwimmer, E.J.L., Rosen, D.L., Sista, P., & Lohr, K.N. Interventions to improve adherence to self-administered medications for chronic diseases in the United States: A systematic review. *Annals of Internal Medicine*, 157, (11) 2012

Wagner, F., Basran, J., & Dal Bello-Haas, V. 2012. A review of monitoring technology for use with older adults. *Journal of Geriatric Physical Therapy*, 35, (1) January-March

Ward, A.M., Takahashi, O., Stevens, R., & Heneghan, C. 2012. Home measurement of blood pressure and cardiovascular disease: systematic review and meta-analysis of prospective studies. [Review]. *Journal of Hypertension*, 30, (3) 449-456

Wilcox, M.E. & Adhikari, N.K.J. The effect of telemedicine in critically ill patients: systematic review and meta-analysis. *Critical Care*, 16, (4) R127

Williams, J.L.S., Walker, R.J., Smalls, B.L., Campbell, J.A., & Egede, L.E. Effective interventions to improve medication adherence in Type 2 diabetes: A systematic review. *Diabetes Management*, 4, (1) January

Wilson, C., Alam, R., Latif, S., Knighting, K., Williamson, S., & Beaver, K. Patient access to healthcare services and optimisation of self-management for ethnic minority populations living with diabetes: A systematic review. *Health and Social Care in the Community*, 20, (1) January

Wofford, J.L.W. 2008. Best strategies for patient education about anticoagulation with warfarin: a systematic review. *BMC Health Services Research*, 8, (pp 40) 2008

Yehle, K.S. & Plake, K.S. 2010. Self-efficacy and educational interventions in heart failure: A review of the literature. *Journal of Cardiovascular Nursing*, 25, (3) 175-188 available from: http://search.ebscohost.com/login.aspx?direct=true&db=psyh&AN=2010-07730-001&site=ehost-live;kyehle@purdue.edu

Excluded at stage 2 – no relevant outcomes

Allemann, S., Houriet, C., Diem, P., & Stettler, C. 2009. Self-monitoring of blood glucose in non-insulin treated patients with type 2 diabetes: A systematic review and meta-analysis. *Current Medical Research and Opinion*, 25, (12) 2903-2913 available from: http://search.ebscohost.com/login.aspx?direct=true&db=psyh&AN=2009-22042-010&site=ehost-live;allemann@ispm.unibe.ch

Andalusian Agency for Health Technology Assessment 2014. Telemedicine application in Andalusia - systematic review (Structured abstract). *Health Technology Assessment Database* (1)

Andalusian Agency for Health Technology Assessment 2014. Telemedicine. Applications in emergencies - systematic review (Structured abstract). *Health Technology Assessment Database* (1)

Baron, J., McBain, H., & Newman, S. 2012. The impact of mobile monitoring technologies on glycosylated hemoglobin in diabetes: a systematic review. *Journal of diabetes science and technology*, 6, (5) 1185-1196 available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3570854/

Bartoli, L.Z. 2009. Systematic review of telemedicine services for patients affected by chronic obstructive pulmonary disease (COPD). *Telemedicine and e-Health*, 15, (9) 877-883

Belanger, E., Bartlett, G., Dawes, M., Rodriguez, C., & Hasson-Gidoni, I. Examining the evidence of the impact of health information technology in primary care: An argument for participatory research with health professionals and patients. *International Journal Of Medical Informatics*, 81, (10) October

Bensink, M., Hailey, D., & Wootton, R. 2006. A systematic review of successes and failures in home telehealth: Preliminary results. *Journal of Telemedicine and Telecare*, 12, (Suppl 3) 8-16 available from: http://search.ebscohost.com/login.aspx?direct=true&db=psyh&AN=2007-01443-001&site=ehost-live;m.bensink@coh.uq.edu.au

Bensink, M., Hailey, D., & Wootton, R. 2007. A systematic review of successes and failures in home telehealth. Part 2: Final quality rating results. *Journal of Telemedicine and Telecare*, 13, (Suppl 3) 10-14 available from: http://search.ebscohost.com/login.aspx?direct=true&db=psyh&AN=2008-01247-002&site=ehost-live;m.bensink@coh.uq.edu.au

Bray, E.P.H., Holder, R., Mant, J., & McManus, R.J. 2010. Does self-monitoring reduce blood pressure? Meta-analysis with meta-regression of randomized controlled trials. *Annals of Medicine*, 42, (5) 371-386

Cappuccio, F.P., Kerry, S.M., Forbes, L., & Donald, A. 2004. Blood pressure control by home monitoring - Meta-analysis of randomised trials. *British Medical Journal*, 329, (7464) 499

Carral, S.F., Sanchez, P., & Lizan, L. Costs analysis of a mobile phone telemonitoring system for glycaemic control in patients with diabetes mellitus (DM) in spain: Preliminary results. *Value in Health.Conference: ISPOR 15th Annual European Congress Berlin Germany.Conference Start: 20121103 Conference End: 20121107.Conference Publication: (var.pagings)*, 15, (7) November

Centre for Reviews and Dissemination. The clinical and cost-effectiveness of patient education models for diabetes: a systematic review and economic evaluation (Structured abstract). Database of Abstracts of Reviews of Effects 4. 2013.
Ref Type: Abstract

Centre for Reviews and Dissemination. Promoting the use of personal asthma action plans: a systematic review (Structured abstract). Database of Abstracts of Reviews of Effects 4. 2013.
Ref Type: Abstract

Centre for Reviews and Dissemination. Home blood pressure measurement: a systematic review (Structured abstract). Database of Abstracts of Reviews of Effects 4. 2013.
Ref Type: Abstract

Centre for Reviews and Dissemination. Using the common sense model of self-regulation to review the effects of self-monitoring of blood glucose on glycemic control for non-insulin-treated adults with type 2 diabetes (Provisional abstract). Database of Abstracts of Reviews of Effects 4. 2013.
Ref Type: Abstract

Centre for Reviews and Dissemination. Telecare for patients with type 1 diabetes and inadequate glycemic control: a randomized controlled trial and meta-analysis (Provisional abstract). Database of Abstracts of Reviews of Effects 4. 2013.
Ref Type: Abstract

Centre for Reviews and Dissemination. Home telemonitoring for type 2 diabetes: an evidence-based analysis (Provisional abstract). Database of Abstracts of Reviews of Effects 4. 2013.
Ref Type: Abstract
Centre for Reviews and Dissemination. Comparative analysis of the efficacy of continuous glucose monitoring and self-monitoring of blood glucose in type 1 diabetes mellitus (Provisional abstract). Database of Abstracts of Reviews of Effects 4. 2013.
Ref Type: Abstract
Centre for Reviews and Dissemination. Effects of self-management health information technology on glycaemic control for patients with diabetes: a meta-analysis of randomized controlled trials (Provisional abstract). Database of Abstracts of Reviews of Effects 4. 2013.
Ref Type: Abstract
Centre for Reviews and Dissemination. Effect of mobile phone intervention for diabetes on glycaemic control: a meta-analysis (Structured abstract). Database of Abstracts of Reviews of Effects 4. 2013.
Ref Type: Abstract
Centre for Reviews and Dissemination. Mediating the effect of self-care management intervention in type 2 diabetes: a meta-analysis of 47 randomised controlled trials (Structured abstract). Database of Abstracts of Reviews of Effects 4. 2013.
Ref Type: Abstract
Centre for Reviews and Dissemination. Glycaemic control in type 1 diabetes during real time continuous glucose monitoring compared with self monitoring of blood glucose: meta-analysis of randomised controlled trials using individual patient data (Structured abstract). Database of Abstracts of Reviews of Effects 4. 2013.
Ref Type: Abstract
Centre for Reviews and Dissemination. Effect of study setting on anticoagulation control: a systematic review and metaregression (Structured abstract). Database of Abstracts of Reviews of Effects 4. 2013.
Ref Type: Abstract
Centre for Reviews and Dissemination. Changes in home versus clinic blood pressure with antihypertensive treatments: a meta-analysis (Structured abstract). Database of Abstracts of Reviews of Effects 4. 2013.
Ref Type: Abstract
Chambers S.Chadda 2010. How much does international normalized ratio monitoring cost during oral anticoagulation with a vitamin K antagonist? A systematic review. *International Journal of Laboratory Hematology*, 32, (4) 427-442
Christensen, T.D. & Larsen, T.B. Precision and accuracy of point-of-care testing coagulometers used for self-testing and self-management of oral anticoagulation therapy. *Journal of Thrombosis and Haemostasis*, 10, (2) February
Christensen, T.D., Johnsen, S.P., Hjortdal, V.E., & Hasenkam, J.M. 2007. Self-management of oral anticoagulant therapy: A systematic review and meta-analysis. *International Journal of Cardiology*, 118, (1) 54-61 available from: http://www.sciencedirect.com/science/article/pii/S0167527306006140
Coster S., Gulliford, M.C., Seed, P.T., Powrie, J.K., & Swaminathan, R. 2000. Self-monitoring in type 2 diabetes mellitus: A meta-analysis. *Diabetic Medicine*, 17, (11) 755-761
Faas, A., Schellevis, F.G., & Van-Eijk, J.T. 1997. The efficacy of self-monitoring of blood glucose in NIDDM subjects: a criteria-based literature review. *Diabetes Care*, 20, 1482-1486
Farmer, A.J., Perera, R., Ward, A., Heneghan, C., Oke, J., Barnett, A.H., Davidson, M.B., Guerci, B., Coates, V., Schwedes, U., & O'Malley, S. Meta-analysis of individual patient data in randomised trials of self monitoring of blood glucose in people with non-insulin treated type 2 diabetes. *BMJ (Online)*, 344, (7847) e486
Heneghan, C., Alonso-Coello, P., Garcia-Alamino, J.M., Perera, R., Meats, E., & Glasziou, P. 2006. Self-monitoring of oral anticoagulation: a systematic review and meta-analysis. *Lancet*, 367, (9508) 404-411 available from: http://europepmc.org/abstract/MED/16458764
Heneghan, C.P. 2007. Assessing differential attrition in clinical trials: self-monitoring of oral anticoagulation and type II diabetes. *BMC Medical Research Methodology*, 7, (pp 18) 2007
Holmes, V. & Griffiths, P. 2002. Self-monitoring of glucose levels for people with type 2 diabetes. *British journal of community nursing*, 7, (1) 41-46
Jansen, J.P. 2006. Self-monitoring of glucose in type 2 diabetes mellitus: A Bayesian meta-analysis of direct and indirect comparisons. *Current Medical Research and Opinion*, 22, (4) 671-681

McAndrew, L., Schneider, S.H., Burns, E., & Leventhal, H. 2007. Does patient blood glucose monitoring improve diabetes control?: A systematic review of the literature. *Diabetes Educator*, 33, (6) 991-1011

Mistry, H. Systematic review of studies of the cost-effectiveness of telemedicine and telecare. Changes in the economic evidence over twenty years. *Journal of Telemedicine and Telecare*, 18, (1) January

Ogedegbe, G. & Schoenthaler, A. 2006. A systematic review of the effects of home blood pressure monitoring on medication adherence. *Journal of Clinical Hypertension*, 8, (3) 174-180

Pare, G., Poba-Nzaou, P., & Sicotte, C. Home telemonitoring for chronic disease management: An economic assessment. *International Journal of Technology Assessment in Health Care*, 29, (2) April

Polisena, J.C. 2009. Home telehealth for chronic disease management: A systematic review and an analysis of economic evaluations. *International Journal of Technology Assessment in Health Care*, 25, (3) 339-349

Poolsup, N., Suksomboon, N., & Jiamsathit, W. 2008. Systematic Review of the Benefits of Self-Monitoring of Blood Glucose on Glycemic Control in Type 2 Diabetes Patients. *Diabetes technology & therapeutics*, 10, (s1) S51-S66

Poolsup, N., Suksomboon, N., & Rattanasookchit, S. 2009. Meta-analysis of the benefits of self-monitoring of blood glucose on glycemic control in type 2 diabetes patients: an update. *Diabetes technology & therapeutics*, 11, (12) 775-784 available from: http://search.ebscohost.com/login.aspx?direct=true&db=cin20&AN=2010511583&site=ehost-live;Publisher URL: www.cinahl.com/cgi-bin/refsvc?jid=1924&accno=2010511583

Powell, H. & Gibson, P.G. 2002. Options for self-management education for adults with asthma. *Cochrane Database of Systematic Reviews* (3)

Renda, S.M. 2006. A practical look at self-monitoring of blood glucose. *Insulin*, 1, (4) 141-147

Sarol Jr, J.R., Nicodemus Jr, N.A., Tan, K.M., & Grava, M.B. 2005. Self-monitoring of blood glucose as part of a multi-component therapy among non-insulin requiring type 2 diabetes patients: A meta-analysis (1966-2004). *Current Medical Research and Opinion*, 21, (2) 173-183

Saudek, C.D., Derr, R.L., & Kalyani, R.R. 2006. Assessing glycemia in diabetes using self-monitoring blood glucose and hemoglobin A1c. *JAMA : the journal of the American Medical Association*, 295, (14) 1688-1697 available from: http://europepmc.org/abstract/MED/16609091

Song, M. & Lipman, T.H. 2008. Concept analysis: Self-monitoring in type 2 diabetes mellitus. *International journal of nursing studies*, 45, (11) 1700-1710 available from: http://search.ebscohost.com/login.aspx?direct=true&db=psyh&AN=2008-15170-013&site=ehost-live;minsong@nursing.upenn.edu

Towfigh, A., Romanova, M., Weinreb, J.E., Munjas, B., Suttorp, M.J., Zhou, A., & Shekelle, P.G. 2008. Self-monitoring of blood glucose levels in patients with type 2 diabetes mellitus not taking insulin: A meta-analysis. *American Journal of Managed Care*, 14, (7) 468-475

Uhlig, K., Patel, K., Ip, S., Kitsios, G.D., & Balk, E.M. 2013. Self-measured blood pressure monitoring in the management of hypertension: a systematic review and meta-analysis. *Annals Of Internal Medicine*, 159, (3) 185-194 available from: http://search.ebscohost.com/login.aspx?direct=true&db=mnh&AN=23922064&site=ehost-live

Verberk, W.J., Kessels, A.G.H., & Thien, T. 2011. Telecare is a valuable tool for hypertension management, a systematic review and meta-analysis. *Blood Pressure Monitoring*, 16, (3) June-155

Verberk, W.J., Kessels, A.G.H., & Thien, T. 2011. Telecare is a valuable tool for hypertension management, a systematic review and meta-analysis. *Blood Pressure Monitoring*, 16, (3) June-155

Verberk, W.J.K. 2005. Home blood pressure measurement: A systematic review. *Journal of the American College of Cardiology* , 46, (5) 743-751

Ward, A.M., Takahashi, O., Stevens, R., & Heneghan, C. 2012. Home measurement of blood pressure and cardiovascular disease: systematic review and meta-analysis of prospective studies. [Review]. *Journal of Hypertension*, 30, (3) 449-456

Willems, D.C.M. 2006. Cost-effectiveness of self-management in asthma: A systematic review of peak flow monitoring interventions. *International Journal of Technology Assessment in Health Care*, 22, (4) 436-442

Xu, Z., Wang, Z., Ou, J., Xu, Y., Yang, S., & Zhang, X. Two monitoring methods of oral anticoagulant therapy in patients with mechanical heart valve prothesis: A meta-analysis. *Journal of Thrombosis and Thrombolysis*, 33, (1) January

APPENDIX G. AMSTAR CHECKLIST

Item	Jaana, 2007	TurNck, 2005	Louis, 2003	Jovicic, 2006	Martinez, 2006	Chaudhry, 2007	Clark, 2007	Dang, 2009	Klersy, 2009	Maric, 2009	Polisena, 2009	Inglis, 2010	Siebenhofer, 2004	ConNck, 2007	Garcia-AlamiN, 2010	Bloomfield, 2011	Welschen, 2005	McGeoch, 2007	Kleefstra, 2009	Clar, 2010	Malanda, 2012
Was an *a priori* design provided?	Y	Y	Y	Y	Y	Y	Y	N	Y	N	Y	Y	Y	N	Y	Y	Y	N	Y	N	Y
Was there duplicate study selection and data extraction?	N	Y	N	Y	N	N	Y	N	Y	N	Y	Y	N	Y	Y	Y	Y	N	Y	N	Y
Was a comprehensive literature search performed?	Y	N	Y	Y	Y	Y	Y	Y	N	N	N	Y	Y	N	Y	Y	Y	Y	N	Y	Y
Was the status of publication (i.e. grey literature) used as an inclusion criterion?	N	N	N	Y	N	N	Y	N	N	N	N	Y	N	N	Y	N	Y	N	N	Y	Y
Was a list of studies (included and excluded) provided?	N	Y	N	N	N	N	N	Y	Y	N	N	Y	Y	N	Y	N	N	Y	N	N	Y
Were the characteristics of the included studies provided?	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	N	Y	Y	Y	Y	Y	N

Item	Jaana, 2007	TurNck, 2005	Louis, 2003	Jovicic, 2006	Martinez, 2006	Chaudhry, 2007	Clark, 2007	Dang, 2009	Klersy, 2009	Maric, 2009	Polisena, 2009	Inglis, 2010	Siebenhofer, 2004	ConNck, 2007	Garcia-AlamiN, 2010	Bloomfield, 2011	Welschen, 2005	McGeoch, 2007	Kleefstra, 2009	Clar, 2010	Malanda, 2012
Was the scientific quality of the included studies assessed and documented?	N	N	N	N	Y	N	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Was the scientific quality of the included studies used appropriately in formulating conclusions?	n/a	Y	n/a	N	Y	N	N	Y	N	n/a	N	N	N	N	Y	Y	N	N	Y	N	N
Were the methods used to combine the findings of studies appropriate?	Y	N	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Was the likelihood of publication bias assessed?	n/a	N	n/a	Y	n/a	n/a	Y	n/a	N	n/a	N	Y	n/a	Y	Y	N	Y	N	N	N	N
Was the conflict of interest stated?	N	N	N	N	N	N	N	N	N	N	N	Y	N	Y	Y	Y	N	N	N	N	N
TOTAL SCORE PER ARTICLE	4	4	4	7	6	4	8	5	6	2	5	9	6	6	10	8	8	5	6	5	7

APPENDIX H. HEALTHCARE UTILISATION OUTCOMES - OVERVIEW

First author, year	Type of intervention	Type of review	N primary research studies(n participants)	Results
Hypertension				
Jaana, 2007	BP TM	SR	14(1119)	Office visits – 1 RCT found no significant difference between groups
AbuDagga, 2010	TM	SR	15(3192)	Office visits – 5 RCTs found no significant differences between groups
COPD				
Turnock, 2005	Action planning	MA	3(367)	No. hospital admissions in past 12 months - No significant difference between groups in 2 RCTs (WMD=0.16, 95% CI -0.09 to 0.42). Visits to GP or practice nurse in 6 months – No significant difference between groups in 2 RCTs (WMD=1.00, 95% CI -0.57 to 2.57) No. of scheduled visits to GP in 12 months - No significant difference between groups in 1 RCT (MD=-0.50, 95% CI -4.06 to 3.06) No. of emergency visits to GP for COPD in 12 months - No significant difference between groups in 1 RCT (MD=-0.20, 95% CI -1.55 to 1.15) No. of ED visits in 12 months - No significant difference between groups in 2 RCTs (WMD=-0.01, 95% CI -0.12 to 0.10).

First author, year	Type of intervention	Type of review	N primary research studies(n participants)	Results
McLean 2011	Telehealthcare	MA	10(1307)	ED visits - A meta-analysis of 3 RCTs patients with telehealthcare were much less likely to attend the emergency department than patients in the control group: OR 0.27 (95% CI 0.11 to 0.66). 1 additional RCT had too few cases of hospitalisation to conduct an analysis. Another RCT recorded the average number of visits per patient over a three month period as greater in the control group, OR 0.17 (95% CI 0.04 to 0.67). Another RCT reported that the average number of ED visits per patient was greater in the intervention compared to control group but no statistical tests were performed. Hospitalisation - A meta-analysis of 4 RCTs suggested that the number of patients with one or more hospital admissions during the 12 month period was significantly greater in the control compared to telehealthcare (OR=0.46, 95% CI 0.33 to 0.65, p<0.00001). 1 additional RCT found no significant difference between the telephone and the control group in hospitalisation rates at three months: p=0.182. Discharge to higher levels of care - 1 RCT found that telehealthcare patients have a lower odds of being discharged to a higher level of care than usual care patients (OR=0.29, 95% CI 0.08 to 1.05).

First author, year	Type of intervention	Type of review	N primary research studies(n participants)	Results
Heart failure				
Louis, 2003	TM	SR	24(3643)	Hospitalisation - 7 non-randomised studies report reduced hospitalisation rates as a result of the intervention however, only 1 of these studies reports that the difference was significant. Readmissions - 2 RCTs found lower readmission rates as a result of the intervention; however, only 1 of these reports this as a significant difference. Another RCT found no significant difference in readmission rates. 5 non-randomised studies also found reduced readmission rates as a result of the intervention however, only 2 of these trials report significant differences. Length of stay - 1 RCT reported significantly reduced length of stay in the intervention compared to a nurse visit group. 4 non-randomised studies found reductions in the length of stay and hospital days however, only 1 of these studies reports that the difference is significant. ER visits - 4 non-randomised studies report reductions in the number of visits as a result of the intervention; however, 1 of these is not significant and the others do not report significance.
Jovicic 2006	Self-management	MA	6(857)	All-cause readmission - Results indicate a significant decrease in all-cause readmission (OR=0.59; 95% CI 0.44 to 0.80) in favour of self-management. HF-related readmission - Results indicate a significant decrease in HF-related readmission (OR=0.44; 95% CI 0.27 to 0.71) in favour of self-management.

First author, year	Type of intervention	Type of review	N primary research studies(n participants)	Results
Martinez, 2006	Home-monitoring	SR	42(2303)	Readmission - 11 studies found significantly fewer admissions as a result of the intervention. The other 11 studies found no significant difference between the 2 groups. Length of stay - 12 of 15 studies found a significantly shorter length of stay in the intervention compared to control group. 3 studies failed to find a significant difference.
Chaudhry, 2007	TM	SR	9(3582)	HF-related hospitalization - 4 studies found a significant decrease in HF-related hospitalisation in favour of the intervention group. 2 studies failed to find a difference and 1 reports a reduction but does not state if it is significant. All-cause hospitalization - 2 studies found a significant decrease in all-cause hospitalisation in favour of the intervention, 4 found no significant differences.
Clark, 2007	TM or STS	MA	14(4264)	All-cause hospital admission - No statistically significant differences between the intervention and control group for STS (RR=0.94, 95% CI 0.87 to 1.02, *p*=0.15) or TM (RR=0.98, 95% CI 0.84 to 1.15, *p*=0.83). HF-related hospitalization – There was statistically significant differences between the intervention and control group in favour of STS (RR=0.78, 95% CI 0.68 to 0.89, *p*=0.0003). 1 study of TM failed to find a significant effect on HF-related hospitalisation.

First author, year	Type of intervention	Type of review	N primary research studies(n participants)	Results
Dang, 2009	Home telehealth remote monitoring	SR	9(2017)	All-cause admissions - 4 studies found no significant difference between the groups. 4 studies found a significant reduction in favour of the intervention group at varying time points and another study reported a trend towards an increase as a result of the intervention however, significance is not reported. CHF-related admissions - 2 studies found no significant difference between groups. 2 studies report significantly fewer admissions in the intervention compared to control group and another 2 report a trend but no significance test. ED visits - 2 studies found a significant reduction in the intervention compared to control group. 4 other studies failed to find a difference between groups. Length of stay - 2 studies found a significant reduction as a result of the intervention compared to controls. The other 4 studies found no significant difference.
Klersy, 2009	Remote patient monitoring	MA	32(8612)	All-cause hospitalisation - RPM was associated with significantly fewer hospitalisations (RCTs: RR=0.93; 95% CI 0.73 to 0.95; p=0.030, Cohort: RR=0.52; 95% CI 0.28 to 0.96; p<0.001) when compared with usual care CHF-related hospitalisations - RPM was associated with significantly fewer CHF-related hospitalisations (RR=0.71; 95% CI 0.64 to 0.80; p<0.001) when compared with usual care.

First author, year	Type of intervention	Type of review	N primary research studies(n participants)	Results
Maric, 2009	TM	SR	56(NR)	Length of stay - 7 studies found reductions in the length of hospital stay; however, 3 of these studies failed to report if the differences were significant ER visits - 6 studies found reductions in the number of ER visits; however, 1 of these studies failed to report if the differences were significant. Readmissions - 4 studies found reductions in the number of readmissions; however, 1 of these studies failed to report if the difference was significant. Home visits - 1 study found a reduction when compared to data prior to intervention implementation; however, it is unclear if this is significant. Hospitalisation - 15 studies found reductions or low numbers of hospitalisation as a result of TM; however, 7 studies failed to report if these differences were significant. 2 studies found a significant increase in the hospitalisation as a result of the intervention.

First author, year	Type of intervention	Type of review	N primary research studies(n participants)	Results
Polisena, 2010	TM	MA & SR	22(3028)	No. of patients hospitalised all-cause - TM had significantly fewer patients hospitalised than usual care (RR=0.77; 95%CI 0.65 to 0.90). No. of patients hospitalised CHF-related - Significantly lower rates in TM compared with usual care in 1 study. All-cause hospitalisations - 6 studies reported a lower number of hospitalisations per patient in TM than in usual care. 2 pre/post studies report reductions at the end of the intervention compared to baseline. However, it is unclear if these reductions were significant. CHF-related hospitalisations - 2 studies found higher rates of the CHF-related hospitalisation in the TM compared to usual care and 1 RCT and 1 OB study found the reverse. However, it is unclear if these changes were significant. All-cause ED visits - 7 studies found a lower mean no. of ED visits per patient in TM compared with usual care. 1 pre-post study found a reduced mean no. of ED visits compared with the baseline period. 1 RCT found a higher no. of ED visits in the TM group and 1 study found no difference between groups. However, it is unclear if these differences were significant. CHF-related ED visits - Lower mean in the TM group compared with usual care in 1 study. However, it is unclear if these differences were significant. All-cause BDOC - 2 OB studies reported a lower mean BDOC per patient in the TM group. 2 pre-post studies reported a reduction in the mean BDOC at the end of the study compared with baseline. 1 RCT reported a slightly higher mean BDOC in the TM group compared with usual care. However, it is unclear if these reductions were significant. .

First author, year	Type of intervention	Type of review	N primary research studies(n participants)	Results
Polisena, 2010 (cont.)	TM	MA & SR	22(3028)	CHF-related BDOC - 2 RCTs reported a lower mean BDOC in TM compared to usual care. 1 pre-port study reported a reduced mean per patients at the end of the study period compared with the baseline. However, it is unclear if these reductions were significant. No. of outpatient visits - 2 RCTs reported a greater no. of outpatients visits for TM compared with usual care. 2 OB studies found a lower mean no. in TM compared with usual care. However, it is unclear if these reductions were significant. Home care visits - 2 RCTs reported a greater no. of home care visits for TM compared with usual care. However, it is unclear if these reductions were significant
Inglis, 2010	Telephone support or TM	MA & SR	30(10490)	All-cause hospitalisation - Significant reductions in the intervention compared to control group for telephone support (RR=0.91; 95% CI 0.85 to 0.99; *p*=0.02) and TM (RR=0.92; 95% CI 0.84 to 0.99; *p*=0.02) CHF-related hospitalisation – Significant reductions in the intervention compared to control group for telephone support (RR=0.77; 95% CI 0.68 to 0.87; *p*<0.0001) and TM (RR=0.79; 95% CI 0.67 to 0.94; *p*=0.008) Length of stay - 1 of 6 studies looking at telephone support reported significant reduction in length of stay in the intervention compared to control group, the 5 other studies found no significant differences.1 study in TM found a large difference in the total no. of days in hospital per patients (no details on if this was significant) and another study reported no significant differences.

First author, year	Type of intervention	Type of review	N primary research studies(n participants)	Results
Clarke, 2011	TM	MA & SR	13(NR)	All-cause hospital admission - MA of 6 studies found no significant reduction as a result of TM (RR=0.99, 95% CI 0.88 to 1.11, *p*=0.84). CHF-related hospital admission - MA of 6 studies found a significant reduction as a result of TM (RR=0.73, 95% CI 0.62 to 0.87, *p*=0.0004). All-cause emergency visits - A meta-analysis of 4 of 7 studies showed no significant reduction (RR=1.04, 95% CI 0.86 to 1.26, *p*=0.67). Length of hospital stay - 7 of 9 studies reported no difference between the groups on CHF-related to all-cause length of stay. 2 studies found a reduction in CHF-related length of stay for patients in the TM group.
Giamouzis, 2012	TM	SR	12(3877)	Hospitalization rates - 4 RCTs reported significantly reduced hospitalization rates in TM group compared to controls. 8 RCTs failed to find a significant difference between groups in hospitalization rates.

First author, year	Type of intervention	Type of review	N primary research studies(n participants)	Results
Pandor, 2013	TM or STS (human to human/machine)	MA & SR	21(6317)	All-cause hospitalisation - TM interventions with medical support during office hours or 24/7 were associated with a 25% (HR: 0.75, 95% CrI: 0.49 to 1.10) and 19% (HR: 0.81, 95% CrI: 0.33 to 2.00) reduction in all-cause hospitalisation respectively. STS HM or HH did not have a major effect on all-cause hospitalisation (HR: 1.06, 95% CrI: 0.44 to 2.53; HR: 0.97, 95% CrI: 0.70, 1.31 respectively). CHF-related hospitalisation - There were no major effects on HF-related hospitalisation for TM with medical support during office hours (HR: 0.95, 95% CrI: 0.70, 1.34). STS HM did not have a major effect on HF-related hospitalisation (HR: 1.03, 95% CrI: 0.66, 1.54). STS HH was associated with a 23% reduction in HF-related hospitalisations (HR: 0.77, 95% CrI: 0.62, 0.96). Length of hospital stay - Three studies found no significant between-group differences at 180 days or in the 1st year post-discharge on length of stay for TM interventions. Only 1 of 7 studies reported a statistically significant reduction in the length of hospital stay among the STS group.

BP – blood pressure; BDOC – Bed Days Of Care; COPD – chronic obstructive pulmonary disease; CHF – Chronic Heart Failure; CI – Confidence Interval; ED – Emergency Department; ER – Emergency Room; GP - general practitioner; HF – Heart Failure; HR – hazard ratio; MA – meta-analysis; OB – Observational; OR – Odds Ratio; TM – Telemonitoring; RCT – Randomized Controlled Trial; RR – Relative Risk; SR – Systematic Review; STS – structured telephone support; WMD – weighted mean difference

APPENDIX I. PATIENT-REPORTED OUTCOME MEASURES - OVERVIEW

First author, year	Intervention	Type of review	N primary research studies(n participants)	Results
Hypertension				
Jaana, 2007	TM	SR	14(1119)	Disease knowledge - 1 study found significant improvements as a result of the intervention. Satisfaction - 2 studies reported high satisfaction with the technology. Ease of use - 2 studies report measuring ease of use of device but fail to report results. Awareness of health benefits - 1 study found 54% of participants acknowledged the benefits of TM. QoL - 1 study reported no significant change in QoL.
AbuDagga, 2010	TM	SR	15(3192)	QoL - 3 RCTs & 1 single group study found no significant effects. Satisfaction - 3 studies reported high satisfaction. Acceptability - 1 study reported anecdotal information on high rates of technology acceptance among participants.
COPD				
Turnock, 2005	Action planning	MA & SR	3(367)	Mood - 1 RCT found no significant difference between groups. Self-management knowledge - 1 RCT found a significant difference in participant knowledge in favour of intervention. QoL - A MA of 3 RCTs found no statistically significant differences in QoL at 6 (MD=2.37, 95% CI -1.96 to 6.70, p=0.28) or 12 months (MD=-0.39, 95% CI -3.48 to 2.70, p=0.80) post intervention between the intervention & control group.

First author, year	Intervention	Type of review	N primary research studies(n participants)	Results
McLean, 2012	Telehealthcare	MA & SR	10(1307)	QoL - A meta-analysis of 2 RCTs found a MD of -6.57 (95% CI -13.62 to 0.48, *p*=0.15) in favour of telehealthcare, which is more than the minimally clinical significant difference. Patient satisfaction - 3 RCTs report high levels of satisfaction with telehealthcare.
Heart failure				
Louis, 2003	TM	SR	24(3643)	Acceptability - 2 OB studies report good acceptability ranging from 86-95%. QoL - 1 RCT & 1 OB study found improved QoL as a result of TM; however, it is unclear if this change was significant. Patient satisfaction - 1 RCT & 1 OB report high satisfaction with TM.
Jovicic, 2006	Self-management	SR	6(857)	QoL - No significant effect in 3 RCTs
Martinez, 2006	Home monitoring	SR	42(2303)	Acceptability - All 17 studies reported a high level of acceptance with home monitoring & no evidence of rejection by the patients of this kind of system. QoL - 11 studies (study design unclear) found a significant impact on QoL as a result of home monitoring when compared to a control group & pre-intervention period at 3 months post intervention. 5 RCTs & 2 non-controlled studies found no significant impact. Anxiety - 1 study (design unclear) found a significant reduction in anxiety in the intervention compared to control group.

First author, year	Intervention	Type of review	N primary research studies(n participants)	Results
Clark, 2007	TM or STS	SR	14(4264)	QoL - 3 RCTs report a significant improvement between the groups in favour of the intervention. 3 RCTs found no significant effect. Acceptability - 1 RCT found acceptability to be higher & another did not consider the intervention useful. Depression - 1 RCT found no significant effect. Health distress - 1 RCT found no significant effect. Satisfaction - 1 RCT reports significantly higher satisfaction in the intervention compared to control group. 2 other RCTs report high levels of satisfaction in the intervention group. Ease of use - 1 RCT found that 97% of patients found TM easy to use.
Maric, 2009	TM	SR	56(NR)	QoL - 3 RCTs report significant changes over time as a result of device-based TM but it was unclear if there were between group differences. 2 studies found significant improvements in QoL as a result of device-based TM compared to pre-intervention period. 1 pre-post study of website-based TM found significant differences on 3 QoL subscales when comparing participants to a pre intervention period. It is unclear if these differences were positive or significant. 1 non-RCT examined a number of TM modalities found no significant effect on QoL & another study found improvements but no significance test. Self-care skills - 1 RCT found no significant differences between device-based monitoring & usual care. Self-efficacy - 1 RCT found significant improvements in self-efficacy as a result of device-based monitoring compared with usual care. 1 RCT examining several TM modalities found that a telephone group reported a

First author, year	Intervention	Type of review	N primary research studies(n participants)	Results
Maric, 2009 (cont.)	TM	SR	56(NR)	significant decrease in self-efficacy whilst the other groups reported a significant increase. It is unclear if there were any between group differences. Mood - 1 RCT of device-based TM found no significant effect on anxiety or depression. 1 study of teleconsultation based TM found that mood ratings (sleeplessness, fatigue, depression & appetite) significantly improved in some instances & deteriorated in others, when comparing the intervention to a pre-intervention period. Stress - 1 study found significantly lower stress in device-based monitoring compared with usual care
Polisena, 2010	TM	SR	22(3028)	QoL, satisfaction, drug adherence - 7 studies reported no significant differences between groups in QoL or patient satisfaction. 6 studies reported a better QoL, higher satisfaction or drug adherence in the intervention compared with usual care (not possible to separate the outcomes).

First author, year	Intervention	Type of review	N primary research studies(n participants)	Results
Inglis, 2010	STS/TM	SR	30(10490)	QoL - 8 RCTs evaluating STS/TM reported statistically significant improvements in QoL in the intervention compared to control group. However, 7 failed to find a significant difference between groups. Health perceptions - 1 RCT found that TM significantly increased health perceptions; however, it unclear if between group differences were significant. Satisfaction - 4 RCTs of STS/TM found high levels of satisfaction. 1 RCT of STS found no significant differences between video & telephone self-monitoring. 1 RCT of STS found significant differences in favour of the intervention group compared to usual care. A video over telephone line was not considered to be useful in 1 RCT. 1 RCT reported consistently high levels of treatment satisfaction in the TM group. Knowledge - 2 RCT of TM/STS found that knowledge significantly increased; however, it is unclear if this was within or between groups. Depression - 1 RCT of STS found no significant effect. Acceptability/ease of use - 4 RCTs of both STS & TM found good to very high levels of acceptance & ease of use. Self-efficacy - 1 RCT of STS found significant improvements however, it is unclear if this is between or within groups. Self-care behaviour - 1 RCT of STS found significant improvements however, it is unclear if this is between or within groups.

First author, year	Intervention	Type of review	N primary research studies(n participants)	Results
Ciere, 2012	Telehealth	SR	12(943)	Knowledge - 1 RCT found that telehealth was associated with significantly higher HF knowledge at 3-months compared to a control group in 2 hospitals but there were no group differences in a third hospital. Another RCT found no significant differences in knowledge about medications at 90- & 180-days. Self-efficacy - 1 RCT found that telehealth improved self-efficacy compared to the control group. 4 RCTs found no significant benefits for telehealth compared to the control group. 1 case control study found no change in self-efficacy overtime. Self-care - 5 RCT & 1 CCT suggesting that telehealth improves self-care behaviour over timeframes from 4 weeks to 12 months; however, significance levels are not provided. 3 further RCTs failed to find any significant improvements in self-care behaviour for telehealth relative to alternative treatment or control groups.
Pandor, 2013	TM or STS	SR	21(6317)	QoL - 5 studies found significant improvements in QoL as a result of TM/STS. 3 other studies failed to find any significant differences between groups in QoL. Satisfaction - 2 studies report very high levels of patient satisfaction with TM, which was significantly higher than controls in 1 study. 3 studies report high levels of satisfaction with STS. Acceptability – 1 RCT reported high levels of patient acceptance for STS.
Thrombophilia				
Siebenhofer, 2004	PSM	SR	4(1547)	QoL - 2 studies reported significant differences in QoL in favour of self-management.

First author, year	Intervention	Type of review	N primary research studies(n participants)	Results
Connock, 2007	PST/PSM	SR	24(5567)	QoL - 2 RCTs found significant improvements in QoL in favour of the intervention group. Improvements were reported in another RCT; however, it is unclear if these were significant. 3 further RCTs found no significant differences between groups.
Garcia-Alamino, 2010	PST/PSM	SR	18(4723)	Satisfaction – 4 RCTs found significant differences in treatment satisfaction over time; however, it is unclear if there were significant between group differences.
Bloomfield, 2011	PST/PSM	SR	29(8413)	Satisfaction – 5 RCTs found significantly greater satisfaction in the intervention compared to usual care. 3 RCTs found no significant effects on patient satisfaction. Self-efficacy - 4 RCTs found significantly greater self-efficacy in the intervention compared to usual care. Distress & hassles - 4 RCTs found significantly less distress & hassles in the intervention compared to usual care. Preference for care - 3 RCTs found that participants in the intervention group had a preference for self-testing & wanted to continue the program. QoL - 1 RCT found that QoL was significantly higher in the intervention compared to usual care. 1 RCT found significant improvements over time in the intervention group & no improvement in usual care but no between group comparisons were conducted. 3 RCTs found no significant effects.
Diabetes				
Welschen, 2005b	SMBG	SR	6(1285)	QoL, well-being, satisfaction - No significant effect in 2 RCTs on any variables.

First author, year	Intervention	Type of review	N primary research studies(n participants)	Results
McGeoch, 2007	SMBG	SR	17(81901)	Treatment satisfaction - 1 RCT found equal increases in both intervention & control groups; however, it is unclear if these were significant changes. Well-being - Improved markedly in 1 RCT for the intervention group, but no details on analysis or significance.
Kleefstra, 2009	SMBG	SR	9(2532)	QoL/well-being - 6 RCTs found no significant differences in overall QoL/well-being between groups. 3 of these RCTs found significant reductions in depression & lack of well-being in favour of the intervention. 3 RCTs found significant reductions in QoL as a result of intensive SMBG when compared to controls. 1 RCT found that well-being (depression) was significantly reduced as a result of SMBG when compared to controls. Treatment satisfaction - 6 RCTs found no significant difference between the 2 groups. Attitudes to diabetes - 1 RCT found no significant differences in the diabetes attitude scale.
Clar, 201	SMBG	SR	66(146148)	QoL - 1 RCT found significantly lower QoL for SMBG compared to controls. 1 RCT found no significant differences between groups. Well-being - 2 RCTs found no significant effect. Mood/Affect - 1 RCT found no significant effect on anxiety but patients in SMBG were significantly more depressed than controls. 2 RCTs found that participants in the intervention were significantly less depression/negative affect than controls.

First author, year	Intervention	Type of review	N primary research studies(n participants)	Results
Malanda, 2012	SMBG	SR	12(3170)	QoL - 2 studies found no significant differences between groups on overall QoL. 1 of these studies did find a significant between group differences in health change (SF-36™ subscale) in favour of the control group. 1 further study found a significant improvement in QoL in the intervention compared to controls group. Treatment Satisfaction - No significant between group differences were found in 4 RCTs. Well-being - 4 RCTs found no significant differences between groups. Depression - 1 study found a significant increase & another significant decrease in depression as a result of SMBG.

CCT – case controlled trial; CI – confidence interval; COPD – chronic obstructive pulmonary disease; MA – Meta-Analysis; MD – mean difference; QoL – Quality of Life; SMBG – Self-Monitoring of Blood Glucose; SR – Systematic Review; OB – Observational; RCT – Randomised Controlled Trial; PSM – patient self-management; PST – patient self-testing; SMBG – self-monitoring of blood glucose; STS – structured telephone support; TM – telemonitoring

APPENDIX J. CLINICAL OUTCOMES - OVERVIEW

First author, year	Type of intervention	Method of summarising the effect	Participant characteristics	Results
Hypertension				
Jaana, 2007	BP TM	SR	Gender: NR Age: Mean range 43.6-76 Condition: Chronic hypertension Treatment: NR	SBP - 2 of 6 RCTs found a significant reduction in SBP compared to controls. 1 RCT and 1 pre- post-test study found no significant effect and 1 post-test study found a higher number of participants experiencing a weekly decrease in SBP as a result of HBPM but it was unclear if this was significant. DBP - 3 RCTs found a significant reduction as a result of TM when compared to controls, 1 pre-post found significant reductions overtime as a result of TM. Ambulatory BP - 1 RCT found a significant reduction as a result of TM. BP outliers - 1 post-test study found a significant decrease in the rate of occurrence at the end of the study period (1 month). Medication adherence - 1 RCT found a significantly greater increase in the intervention compared to controls. 2 studies suspected improvements but there was no clear evidence or statistical analysis. 1 study found no difference. Weight - 1 pre-post study found a significant improvement in weight for those in the intervention group.

First author, year	Type of intervention	Method of summarising the effect	Participant characteristics	Results
AbuDagga, 2010	TM	SR	Gender: NR Age: Mean range 51-76yrs Condition: Uncontrolled hypertension Treatment: Range of anti-hypertensive medications	Ambulatory BP - 2 RCTs & 1 single group study found significant reductions ranging from 2.8 to 11.9mm Hg for SBP. DBP reductions ranged from 2.0 to 6.6mm Hg. 1 RCT found no significant difference between intervention and control group. SBP - 2 RCTs found a significant reduction in SBP compared to controls. 2 single group studies and 1 quasi-experimental found significant reductions from pre to post intervention ranging from 3.9 to 13.0mm Hg. DBP - 2 RCTs found a significant reduction in DBP compared to controls. 2 single group and 1 quasi-experimental study found significant reductions from pre to post intervention ranging from 2.0 to 8.0mm Hg. % of participants with normal BP - 1 RCT and 1 single group studies found a favourable impact of TM. Adjusted BP improvement - 1 RCT found greater percentage of participants who improved in the intervention compared to control groups. % uncontrolled BP - 1 RCT found no significant difference between the intervention and control group. No. of medications or medication compliance - reported in 2 studies but no results documented. Medications altered - reported in 3 studies but no results documented.

First author, year	Type of intervention	Method of summarising the effect	Participant characteristics	Results
AbuDagga, 2010 (cont.)	TM	SR	Gender: NR Age: Mean range 51-76yrs Condition: Uncontrolled hypertension Treatment: Range of anti-hypertensive medications	Medication class - reported in 2 studies but no results documented.
COPD				
Turnock, 2005	Action planning	MA & SR	Gender: % female range 16-67 Age: Mean range 68-72.1 Condition: COPD Treatment: NR	Medication usage: 1 RCT found a significant increase in the use of antibiotics by the intervention group but no difference in the use of corticosteroids. 2 other RCT also found no significant difference in either antibiotics or oral corticosteroids. Mortality: No significant difference (OR=1.01; 95% CI 0.32 to 3.24). FEV1: At 6 months MD=50ml, 95% CI -29.86 to 129.86 in 1 RCT. At 12 months MD=43ml, 95% CI -63.30 to 149.30 in 1 study. % predicted FEV1: At 6 months WMD=1.83%; 95% CI -1.05 to 4.71 (2 studies). At 12 months MD=2%, 95% CI -1.89 to 5.89 (1 study). Symptoms - No significant change in symptoms in 1 RCT. No. of days with respiratory symptoms – In 1 RCT MD=-16.00 days, 95% CI -45.65 to 13.65..

First author, year	Type of intervention	Method of summarising the effect	Participant characteristics	Results
Turnock, 2005 (cont.)	Action planning	MA & SR	Gender: % female range 16-67 Age: Mean range 68-72.1 Condition: COPD Treatment: NR	Subjective breathing status - No significant differences in the percentage of days recorded as mild, moderate or severe in 1 RCT. Exacerbations: 1 study found a significantly greater number of participants treated for exacerbation of COPD in the intervention group. Functional capacity: No significant difference in 1 RCT
McLean, 2011	Telehealthcare	MA & SR	Gender: NR Age: NR Condition: Clinician diagnosed COPD Treatment: NR	Mortality - A MA of 4 studies found no significant effect on mortality (OR=1.05, 95% CI 0.63-1.75, *p*=0.86). 1 multi-group RCT (in which patients with COPD could not be separated from CHF patients) found no significant difference in mortality rate. There were no further deaths in any other study. Total exacerbations - 1 RCT found no significant difference between the intervention and control group. Mean no. of exacerbations/month - 1 RCT found that the mean no. of exacerbations/month was significantly greater in the control compared to intervention group. Time free from exacerbations - 1 RCT found that more intervention participants were free of an exacerbation in a 1 year period than in the control group. FEV1 - 1 RCT reported no significant change overtime within the intervention or control group. 1 RCT found no significant difference in FEV1 between the intervention and control group.

First author, year	Type of intervention	Method of summarising the effect	Participant characteristics	Results
McLean, 2011 (cont.)	Telehealthcare	MA & SR	Gender: NR Age: NR Condition: Clinician diagnosed COPD Treatment: NR	FVC - 1 RCT found no significant change overtime within the intervention or control group.
Heart failure				
Louis, 2003	TM	SR	Gender: NR Age: Mean range 53-82 Condition: HF Treatment: NR	Mortality - 1 study found a significant reduction (study design NR).
Jovicic, 2006	Self-management	MA & SR	Gender: % female range 24-47 Age: Mean range 56-76 Condition: HF Treatment: NR	Mortality - MA found no significant effect (OR 0.93; 95% CI 0.57 to 1.51, *p*=0.76). Adherence - Patients in the intervention group were significantly more likely to adhere to sodium and fluid restriction, exercise and not smoke in 1 study. 1 study found a significant improvement in adherence to general medical advice, but no significant improvement in medication adherence.

First author, year	Type of intervention	Method of summarising the effect	Participant characteristics	Results
Martinez, 2006	Home monitoring	SR	Gender: NR Age: Mean range 48-83 Condition: HF Treatment: NR	Mortality - 3 large RCTs found significant reductions in the intervention group compared to controls. 1 study (design NR) found no incidence of death in the intervention group. 2 studies found no significant differences between the groups (design NR).
Chaudhry, 2007	TM	SR	Gender: % men range 37-78 Age: Mean range 59-72 Condition: HF Treatment: Patients at baseline on; beta-blockers ranged 17-62%, ACE/ARB inhibitors ranged 54-93%	Mortality - In 5 RCTs comparing telephone-based symptom monitoring with controls the RR ranged from 0.59 (95% CI 0.20-1.71) to 1.17 (95% CI 0.36-3.84). 1 RCT comparing automated monitoring of signs and symptoms versus controls found a RR of 0.44 (95% CI 0.22-0.85). 1 RCT found RR of 0.66 (95% CI 0.40-1.11) when comparing nurse telephone support with usual care, 0.71 (95% CI 0.42-1.18) when comparing home TM with usual care and 1.07 (95% CI 0.66-1.73) when comparing home TM with nurse telephone support. The final RCT comparing video conferencing with nursing and usual care was unable to calculate RR due to small numbers.
Clark, 2007	TM or STS	MA	Gender: NR Age: Mean range 57-75 Condition: HF Treatment: NR	All-cause mortality - Significant 20% reduction (95% CI 8% to 31%) in the intervention group compared to controls. The benefits were greater with TM (RR=0.62, 95% CI 0.45 to 0.85, *p*=0.003), than with STS (RR=0.85, 95% CI 0.72 to 1.01, *p*=0.06), although the difference was not significant (p=0.18).

First author, year	Type of intervention	Method of summarising the effect	Participant characteristics	Results
Dang, 2009	Home telehealth remote monitoring	SR	Gender: NR Age: Mean range 53.2-79 Condition: HF Treatment: NR	Mortality - 1 study found significant within group reductions in mortality for the intervention group, but no between group comparisons. Another study also failed to report analysis for group comparisons. 2 studies found a significant reduction in mortality in the intervention compared to control group at 1 year. 1 study found no significant differences.
Klersy, 2009	Remote patient monitoring	MA	Gender: Mean % female 36-40 Age: Median 70 (RCTs), 66 (cohort) Condition: HF Treatment: NR	Mortality - RPM was associated with significantly fewer deaths compared to controls in the RCTs (RR=0.83; 95% CI 0.73 to 0.95) and in cohort studies (RR=0.53; 95% CI 0.29 to 0.96).

First author, year	Type of intervention	Method of summarising the effect	Participant characteristics	Results
Maric, 2009	Device based/telephone touch-pad/combination of TM modalities	SR	Gender: NR Age: NR Condition: HF Treatment: NR	Mortality - 1 RCT comparing device-based TM with controls reports significantly fewer deaths in the intervention compared to control group. 1 RCT comparing telephone touch-pad TM with controls found combined hospitalisation and mortality events to be significantly lower in the intervention group compared with controls. 1 RCT reported in 3 articles comparing usual care with monthly telephone calls and home TM including nurse calls reported decreased mortality in the intervention groups compared to controls, but no differences between interventions. Exercise adherence - 1 RCT comparing device-based TM with controls found significantly higher levels of exercise adherence in the intervention group compared to routine care. Functioning (definition unclear) - 1 RCT comparing device-based TM with controls found significant improvements in levels of functioning in the intervention compared to control. BP, weight, shortness of breath - 1 pre-post study found significant improvements in BP, weight and shortness of breath over time. Time to target dose - 1 RCT reported in 2 articles reported a significantly shorter time to achieve the target dose of carvedilol in the intervention group compared to controls.

First author, year	Type of intervention	Method of summarising the effect	Participant characteristics	Results
Maric, 2009	Device based/telephone touch-pad/combination of TM modalities	SR	Gender: NR Age: NR Condition: HF Treatment: NR	LVEF, NYHA class - A pre-post study found increased left injection fraction and improved NYHA class compared with baseline although does not report significance.
Polinsena, 2010	TM	MA & SR	Gender: NR Age: Mean 55 Condition: HF Treatment: NR	All-cause Mortality - TM decreased the risk of death significantly more than usual care in a MA of 5 RCTs (RR=0.64; 95% CI 0.48 to 0.85) CHF-related Mortality: 2 RCTs found significantly fewer deaths in the intervention group compared to usual care.
Inglis, 2010	Telephone support/ TM	MA & SR	Gender: Mean % men 64 (range 35-99) Age: Mean range 44.5-78 Condition: HF Treatment: NR	Mortality - Significant reduction in risk of all-cause mortality (RR=0.66, 95% CI 0.54 to 0.81; p<0.0001) when comparing telephone support with usual care. The MA comparing TM with usual care found no significant difference in all-cause mortality. NYHA class - 3 RCTs comparing telephone support with usual care and 1 RCT comparing TM with usual care found significant improvements in NYHA classification in favour of the intervention. Function - 2 RCTs comparing telephone support with usual care found significant improvements in the 6 minute walk test.

First author, year	Type of intervention	Method of summarising the effect	Participant characteristics	Results
Inglis, 2010 (cont.)	Telephone support/ TM	MA & SR	Gender: Mean % men 64 (range 35-99) Age: Mean range 44.5-78 Condition: HF Treatment: NR	Adherence - Improvements or high levels of adherence to diet, treatment and medications for the intervention group were reported in 4 RCTs comparing STS/TM with usual care However, it is unclear if these analyse were within or between group comparisons and for some the significance levels were not reported. Renal function - 1 RCT found significant improvements overtime in the intervention group. Unclear if there were any between group differences. Weight - 1 RCT found significant improvements over time in the intervention group. Unclear if there were any between group differences.
Clarke, 2011	TM	MA	Gender: Mean % men 64% (range 35-99%) Age: Mean ranged from 44.5 to 78 Condition: HF Treatment: NR	Mortality - A MA of 10 studies found an overall reduction in all-cause mortality (RR=0.77, 95% CI 0.61 to 0.97, *p*=0.02).

First author, year	Type of intervention	Method of summarising the effect	Participant characteristics	Results
Giamouzis, 2012	TM	SR	Gender: NR Age: Mean ranged from 57 to 78.1 Condition: CHF Treatment: NR	All-cause mortality - 3 RCTs reported significantly fewer deaths in the intervention compared to control group. 4 RCTs no significant differences and 1 a lower % in the intervention group but no significance test.
Pandor, 2013	Remote monitoring	MA	Gender: NR Age: Mean ranged from 57 to 78.1 Condition: CHF Treatment: NR	All-cause mortality - TM interventions with medical support during office hours or 24/7 were associated with mortality reductions of 24% (HR=0.76, 95% CrI 0.49 to 1.18) and 51% (HR=0.49, 95% CrI 0.20 to 1.18), respectively. STS HH was associated with a 23% reduction (HR=0.77, 95% CrI 0.55 to 1.08). No beneficial effect on mortality was observed with STS HM. The interventions exhibiting the greatest effects were TM 24/7 (HR=0.49, 95% CrI 0.26 to 0.88), TM during office hours (HR=0.62; 95% CrI: 0.42 to 0.89,) and STS HH (HR=0.75, 95% CrI 0.59 to 0.96).

First author, year	Type of intervention	Method of summarising the effect	Participant characteristics	Results
Thrombophilia				
Siebenhofer, 2004	PSM	SR	Gender: NR Age: Mean range 42-63 Condition: Mixed indication Treatment: Phenprocoumen or acenocoumarol	% INR in range - 1 study found no significant difference between groups. 3 found that the intervention group had more INR values within range than the control group; this was significantly different in 2 studies but unclear in the other. % mean time in range - 2 studies found that the deviation of the INR value from the mean of the INR target range was shown to be significantly lower in the intervention compared to control group. Major haemorrhage - 1 study found no significant differences between groups. The other 3 studies report too few events in both groups for analysis. Thromboembolism - 1 study found a significant reduction in major thromboembolism in the intervention group; however, it is unclear if this was significantly different to the control group. The other 3 studies report too few events in both groups for analysis.
Connock, 2007	PST/PSM	MA	Gender: % male range 43-76 Age: Mean ranged 42-75 Condition: Mixed indication Treatment: NR	% time in range - The pooled estimate for the RCTs was 67.4% in the intervention group and 63.4% in the control group. The pooled estimate for the non-RCTs was 69.5% in the control group and 82.9% in the PSM group. No statistical analysis was performed.

First author, year	Type of intervention	Method of summarising the effect	Participant characteristics	Results
Connock, 2007	PST/PSM	MA	Gender: % male range 43-76 Age: Mean ranged 42-75 Condition: Mixed indication Treatment: NR	No. of patients below, within & above range - For the RCTs more patients in the intervention group were within range than those in the control group. Conversely, more patients in the control groups were outside of range compared to the intervention group. For the non-RCTs the pooled values below range were 18.4% and 10.1% in the control and intervention group respectively and above the range 10.0 and 7.1% respectively. No statistical analysis was performed. Major haemorrhagic - No significant effect in either an MA of RCTs or non-RCTs (RD=–0.0039, 95% CI –0.0154 to 0.0077) Thromboembolic events - Significantly fewer events in favour of the intervention group for RCTs (RD=-0.0224; 95%CI -0.03 to -0.01) and non-RCTs (RD=-0.0199; 95% CI -0.03 to -0.01). Mortality - Significantly reduced risk of death in favour of the intervention group for RCTs (RD=-0.0170; 95% CI -0.03 to -0.01) and non-RCTs (RD=-0.01; 95% CI -0.03 to -0.004).

First author, year	Type of intervention	Method of summarising the effect	Participant characteristics	Results
Garcia-Alamino, 2010	PST/PSM	SR & MA	Gender: NR Age: Mean range 42-75 Condition: Mixed indication Treatment: Various anticoagulants	Thromboembolic event - The intervention halved thromboembolic events (RR=0.50; 95% CI 0.36 to 0.69, *p*<0.0001). Mortality - The intervention was associated with an overall significant reduction in all-cause mortality (RR 0.64; 95% CI 0.46 to 0.89, *p*=0.007) Major haemorrhage - No significant effect (RR=0.87, 95% CI 0.66 to 1.16, *p*=0.34). Minor haemorrhage - The intervention resulted in significant reduction in minor haemorrhage (RR=0.64; 95% CI 0.54 to 0.77, *p*<0.00001). % mean INR within range - 6 studies reported significant improvements in favour of the intervention group. 7 studies found no significant differences. % time within range - 3 studies reported a significant improvement in the intervention group. 8 studies found no significant differences.

First author, year	Type of intervention	Method of summarising the effect	Participant characteristics	Results
Bloomfield, 2011	PST/PSM	MA	Gender: Mean % men 75 (range 43-98) Age: Mean 65 (range 42-75) Condition: Mixed indication Treatment: Various anticoagulants	Thromboembolic events - Significantly fewer events in the intervention compared with control group (OR=0.58; 95% CI 0.45 to 0.75, *p*<0.001). Major haemorrhage - No significant effect (OR=0.89, 95% CI 0.75-1.05, *p*=0.169) Mortality - Significantly lower risk of death in the intervention group compared to control (OR=0.74; 95% CI 0.63 to 0.87, *p*<0.001) % mean time within range - No significant difference between PSR or PSM and usual care in a MA of RCTs (WMD=1.50%, 95% CI -0.63% to 3.63%, *p*=0.17). % INR results in range - No significant difference between PSR or PSM and usual care in a MA of RCTs (WMD=5.9%, 95% CI -0.18% to 12%, *p*=0.06).
Diabetes				
Welschen, 2005b	SMBG	MA & SR	Gender: NR Age: Mean range 49.8-60.9 Condition: T2DM Treatment: Not using insulin	HbA1c - 0.39% (95% CI -0.56 to -0.21, *p*<0.0001) decrease in HbA1c in favour of SMBG. FBG - No significant effects in 2 RCTs. Hypoglycaemia - 1 RCT found a significant difference in the number of patients who reported at least one episode of asymptomatic hypoglycaemia during the study. However, it was not possible for the control group to experience this type of hypoglycaemia.

First author, year	Type of intervention	Method of summarising the effect	Participant characteristics	Results
McGeoch, 2007	SMBG	SR	Gender: % male range 26-100 Age: Mean range 50.3-68 Condition: T2DM Treatment: Any	HbA1c - 2 RCTs reported a statistically significant lower HbA1c with SMBG. The other RCT found no significant effect. Mean reduction in HbA1c for SMBG was 1%, with a decrease of 0.5% more in patients who used SMBG than those who did not. 4 OB studies found an association between SMBG and lowering of HbA1c. 4 other OB studies found no association. Morbidity & Mortality - 1 OB study found that those undertaking SMBG compared to no SMBG had a significant reduction in both outcomes. Adherence - 1 RCT found no difference in the proportion exercising but more were following dietary advice in the intervention group, no details on significance.
Kleefstra, 2009	SMBG	SR	Gender: % male range 26-100 Age: Mean range 50-65.7 Condition:T2DM Treatment: Any	HbA1c: 3 RCTs found a beneficial effect on HbA1c for the intervention when compared to controls. No significant effect for the remaining 6 RCTs.

First author, year	Type of intervention	Method of summarising the effect	Participant characteristics	Results
Clar, 2010	SMBG	MA & SR	Gender: NR Age: Mean range 50-68.4 (RCTs only) Condition: T2DM Treatment: Any	HbA1c: A MA of 10 RCTs found a significant reduction of 0.21% in HbA1c (95% CI -0.31 to -0.10; *p*<0.001) in favour of the intervention group. 18 OB and non-randomised experimental studies found no favourable changes in HbA1c with SMBG, while 18 did. Hypoglycaemia: 2 RCTs found significant reductions as a result of the intervention. 2 found no significant difference and the results of the other 2 studies are not reported. Weight: 13 RCTs found no significant difference between groups in weight/BMI. Lipid parameters: 6 RCTs reported inconsistent results in terms of lipid parameters, with most finding no significant differences between groups. BP - There was no significant effect on BP in 4 RCTs. Morbidity/Mortality: 1 OB study found SMBG to be related to lower morbidity and mortality and another did not.

First author, year	Type of intervention	Method of summarising the effect	Participant characteristics	Results
Malanda, 2012	SMBG	MA	Gender: NR Age: Mean range 48.7-65.6 Condition: T2DM Treatment: NIDDM	HbA1c: In a meta-analysis of SMBG versus control the overall effect for short-term f/u (up to 6 months) in those with a diabetes duration of greater than 1 year, was a statistically significant decrease of 0.26% in HbA1c (95% CI -0.39 to -0.13, p<0.0001) in favour of SMBG. For medium term f/u (between 6 & 12 months) analysis revealed no significant decrease in HbA1c of 0.13% (95% CI -0.31 to 0.04, p=0.13). The pooled analysis for short term f/up in newly diagnosed patients could not be undertaken due to high heterogeneity. For medium-term f/u in the newly diagnosed there was a statistically significant decrease in HbA1c of 0.52% (95% CI -0.89 to -0.14, p=0.007).

ACE - angiotensin-converting-enzyme; ARB - angiotensin receptor blockers; BMI – body mass index; BP – Blood Pressure; CI – Confidence Interval; COPD - Chronic Obstructive Pulmonary Disease; CHF – Chronic Heart Failure; DBP – Diastolic Blood Pressure; FBG – Fasting Blood Glucose; FEV - Forced Vital Capacity; HbA1c - Glycated haemoglobin; HBPM – Home Blood Pressure Monitoring; HF – heart failure; HR – hazards ratio; INR – International Normalised Ratios; LVEF – Left Ventricle Injection Fraction; MA – meta-analysis; MD – mean difference; NIDDM – Non Insulin Dependent Diabetes Mellitus; NR – not reported; NYHA – New York Heart Association; PSM – Patient Self-Management; PST – Patient Self-Testing; RCT – Randomised Controlled Trial; RD – Risk Difference; RR – Relative Risk; SBP – Systolic Blood Pressure; SMBG – Self-Monitoring of Blood Glucose; SR – Systematic Review; T2DM – Type 2 Diabetes Mellitus; TM – Telemonitoring; STS – Structured Telephone Support; WMD – Weighted Mean Difference

APPENDIX K. RCT INFORMATION SHEET

UCLH Project ID number 09/H0722/91

CONFIDENTIAL

PATIENT INFORMATION SHEET

Title of Project: Self-monitoring of treatment with methotrexate alone or in combination with a self-injecting anti-tumour necrosis factor agent by patients with arthritis

Investigators: Hayley James Tel. [redacted]
Dr Michael Shipley Tel. [redacted]
Abigail Olaleye Tel. [redacted]

You are being invited to take part in a research study. Before you decide we think it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Please take your own time to decide whether or not you wish to take part.

Part 1

1. What is the purpose of the study?

We are a research team looking at alternatives to the traditional outpatient appointment procedure for patients with arthritis on the medication Methotrexate taken with and without an anti-TNF agent.

We know from previous research that attending outpatient appointments for your blood results to be checked can be inconvenient and often results in no changes to

your treatment or care. We are, therefore, investigating an alternative way of managing your treatment.

The aim of the study is to assess whether individuals on Methotrexate alone or with an anti-TNF agent can self-monitor part of their treatment and initiate their own outpatient appointments. This involves an intervention which teaches you how to read and interpret your own blood test results and symptoms and as a result book your own outpatient appointments. We are particularly interested in the factors which may predict success when it comes to deciding about whether to arrange an out-patient appointment or not.

Your participation in the study will help us understand more about how patient's understand and manage their medication. We hope that this information will enable us to develop a better and more efficient Rheumatology Service at University College Hospital London (UCLH). The research will be conducted over 3 years and is taking place at UCLH in conjunction with University College London (UCL).

2. Why have I been invited?

You are being invited to participate because you are a patient attending the Centre for Rheumatology at UCLH, you have arthritis and you have been receiving Methotrexate treatment for at least 6 months or Methotrexate with an anti-TNF agent for at least 3 months. We are seeking a total of 140 people over the age of 18 to take part in this study.

3. Do I have to take part?

No, taking part is voluntary. It is up to you to decide to join the study. If you agree to take part you will be given this information sheet to keep and be asked to sign a consent form.

If you decide to take part you are free to withdraw at any time and without giving a reason. Nobody will be upset if you do decide not to take part. Please be reassured that deciding to withdraw at any time, or choosing not to take part at all, will not affect the standard of care you receive at any time, either now or in the future.

4. What will happen to me if I take part?

If you decide to take part, you will be asked to complete a questionnaire booklet that asks questions about how you feel about having arthritis and taking Methotrexate or Methotrexate with anti-TNF treatment. We do not anticipate that this will take you more than 40 minutes to complete.

To test whether the self-monitoring approach works we need to compare people who are managed in this new way with people are managed normally. We can do this by putting people into two different groups by chance (randomly). Therefore, if you agree to take part you have a 50% chance of being allocated to group 1 (usual management) and a 50% of being allocated to group 2 (self-monitoring).

Group 1. You will continue to receive the same care that you normally receive, according to a strict plan agreed with your Rheumatologist.

Group 2. You will receive a 2 hour self-monitoring training session in which you will be told what self-monitoring is and how it works, how to interpret your blood tests and how to monitor any physical side effects related to the treatment and illness. You will practice interpreting blood test results and physical side effects and on the basis of all of this, how to decide whether you require an outpatient appointment.

Being part of group 2 will involve attending the hospital for your blood tests on a regular basis, but instead of attending a clinic appointment to have these blood tests interpreted we will train you to be able to do this at home and ask for an appointment if necessary. You will continue to see your Consultant Rheumatologist and GP when you see fit. You will of course be able to contact the nurse helpline if you are concerned at any time.

At the end of your participation in the study which maybe after the 6th blood test or earlier if you no longer wish to take part in the study, we will ask if you would be prepared to be interviewed at a place and time convenient for you. During the interview you will asked about how it was to take part in the study and what if there was anything you would change. If you do agree, we would like to tape record the

interview which will then be transcribed. At the end of the study, all the tape recordings will be destroyed.

If you tick the box on the consent form about further participation and provide your contact details we will contact you to discuss this in more detail. We assure you that ticking the box at this stage does not mean you have to take part in an interview – you are free to change your mind at any time in the future, without influencing the care you receive. You do not have to give a reason for changing your mind or for choosing not to take part in the research at all.

5. What will I have to do?

For those participants who are randomly allocated to Group 1 you will continue to receive the same care that you normally receive and will be asked to complete a questionnaire booklet at the beginning of the study, after your 3rd and 6th blood test. You will be given a freepost envelope to send these back to the research team.

For those participants who are randomly allocated to Group 2 after taking part in the training you will need to inform the Rheumatology Nurse Specialist once you have had your blood test. Your results will then be sent to you by your preferred method - this could be by post or email.

The training will give you the knowledge to understand these results and for the first 3 blood tests the Researcher will call you once you have had a chance to look at them to ask whether you blood results fall within the normal range, if you feel you need an outpatient appointment based on these results and how confident you feel about your decision. If you accurately interpret 2 consecutive blood tests you will then be able to independently interpret the results of your next 3 blood tests with no telephone call from the Researcher. If you feel you require an appointment based on the results of these blood tests you will be given a telephone number to speak to the Rheumatology Nurse Specialist. As in Group 1 you will be asked to complete a questionnaire at the beginning of the study and after the 3rd and 6th blood test.

The research team will also ask if you would be willing to take part in an interview after your participation in the study, this is entirely voluntary and taking part in the main study does not mean you have to take part in the interview.

6. What are the possible disadvantages and risks of taking part?

We are always required to tell you about any risks to you should you agree to take part in research; however, in this instance we are not aware of there being any such risks to you. For those people who are randomly put into group 2 and receive the training you will be given the contact details of the Rheumatology Nurse Specialist involved in the study whom you can contact at any time. Your safety is of utmost concern to the research and clinical team and, therefore, throughout the intervention period you will be closely monitored and contacted if deemed essential.

7. What are the possible benefits of taking part?

Not only will the intervention be more convenient for patients being monitored in this way, but it will also reduce wasted clinic visits and waiting times. Findings from the pilot study we conducted suggest that participants may experience increases in patient satisfaction and confidence.

Those who took part in the pilot study also expressed the wish to continue being monitored in this way, describing it as a positive experience, allowing them to take control of their condition. In taking part we expect that the information we get from this study will help us to provide more appropriate support to people with arthritis receiving Methotrexate treatment.

8. What happens when the research stops?

On completion of the study those within group 2 will return to usual care that they received before taking part in the research.

9. What if there is a problem?

Any complaint about the way you have been dealt with during the study or any possible harm you might suffer will be addressed. The detailed information on this is given in Part 2.

10. Will my taking part in the study be kept confidential?

Yes. We will follow ethical and legal practice and all information about you will be handled in confidence. The details are included in Part 2.

This completes part 1.

If the information in Part 1 has interested you and you are considering taking part, please read the additional information in Part 2 before making any decision.

Part 2

1. What will happen if I don't want to carry on with the study?

If you decide at any point in your participation in the study that you wish to withdraw from the study you can contact the research or clinical team to discuss this. It would be useful for us to use the information you have given us up until that point in the study; however, if you wish us to destroy this data this can also be arranged.

2. What if there is a problem?

If you have a concern about any aspect of this study you should speak to the researchers who will do their best to answer your questions either at your next appointment or on [redacted] or via email [redacted]. If you remain unhappy and wish to complain formally you can do this through the Complaints Manager, UCLH, 2nd Floor West, 250, Euston Road, London NW1 2PQ. Please quote the UCLH project number at the top of this information sheet.

3. Will my taking part in this study be kept confidential?

We need permission to access your medical records which relate directly to this study. All the information collected during the study will be held securely and in the strictest confidence and will only be used for research purposes.

If you agree, we would like to inform your GP that you are taking part. This is as a matter of courtesy, but rest assured that they will not know what information you have given to us.

The data that we collect will be kept anonymously on password protected computers and in locked filing cabinets. Only members of the research team will see this anonymous information, the researcher Ms Hayley James will be the only person who will have access to identifiable data.

If you take part in an interview we will ask your permission to audio-tape it, this will then be transcribed with any identifying information removed from the transcript. The audio-tape will then be destroyed.

4. What will happen to the results of the research study?

The findings of this research will be reported in professional publications or at meetings but you will not be identified in any report or publication. For those participants who take part in an interview any information which would allow someone to identify you will be removed from the transcribed interviews. The transcripts may also be used for teaching purposes with your permission.

If at any point during the study you lose capacity to take part the data you have provided up until that point will remain within the study, but only with the permission of your next of kin.

5. Who is organising and funding the research?

This research is being paid for by The Shipley-Rudge Fund for Rheumatology and the Otto Beit Fund both of which are held by the UCLH Charity and are specifically dedicated to rheumatology research. It is being organized by researchers at University College London and staff in the Centre for Rheumatology at UCLH.

6. Who has reviewed the study?

This study has been reviewed and approved by the Camden and Islington Community Research Ethics Committee and by the funders before they agreed to provide the funding.

7. Further Information and contact details

If you want some general information about taking part in research please contact the Patient Advice Liaison Service (PALS) at UCLH who are found in the Ground Floor Atrium of University College Hospital between 9 and 4pm or on [redacted].

If you have any questions about this study and what you are being asked to consider, please contact one of the research team.

If you would like any further information about this research or if you have any queries at any time in the future, please contact Hayley James in the Department of Health Services Research at City University on [redacted] or via email [redacted].

Thank you for reading this information sheet.

APPENDIX L. RCT CONSENT FORM

UCLH Project ID number 09/H0722/91

Patient Identification Number for this study:

CONFIDENTIAL

CONSENT FORM (RCT)

Title of Project: Self-monitoring of treatment with Methotrexate alone or in combination with a self-injecting anti-tumour necrosis factor agent by patients with arthritis

Name of Principal Investigator: Professor Stanton Newman

Please initial box

1. I confirm that I have read and understand the information sheet dated 08.10.10 (version 3) for the above study and have had the opportunity to ask questions ☐

2. I confirm that I have had sufficient time to consider whether or not want to be included in the study ☐

3. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. ☐

4. I understand that sections of any of my medical notes may be looked at by responsible individuals of the research team where it is relevant to my taking part in research. I give permission for these individuals to have access to my records. ☐

5. I understand that relevant sections of my medical notes and data collected during the study, may be looked at by individuals from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records". ☐

6. I agree to take part in the above study. ☐

7. I give my permission for my GP to be informed that I am taking part in this research. ☐

8. I understand that taking part in this research project will involve completing a questionnaire on one or more occasions and that I might also be asked to take part in an interview. At this stage I am giving my consent to complete the questionnaire study and I understand that the researchers will only contact me about the interview study if I give them permission to do so. ☐

9. I would like to received feedback about the findings of the study ☐

CONSENT FORM

Title of Project: Self-monitoring of treatment with methotrexate alone or in combination with a self-injecting anti-tumour necrosis factor agent by patients with arthritis

Name of Principal Investigator: Professor Stanton Newman

_____	_____	_____
Name of patient	Date	Signature

_____	_____	_____
Name of Person taking consent (If different from researcher)	Date	Signature

_____	_____	_____
Researcher (to be contacted if there are any problems)	Date	Signature

Comments or concerns during the study

If you have any comments or concerns you may discuss these with the investigator. If you wish to go further and complain about any aspect of the way you have been approached or treated during the course of the study, you should write or get in touch with the Complaints Manager, UCL hospitals. Please quote the UCLH project number at the top this consent form

APPENDIX M. RCT STUDY QUESTIONNAIRES

University College London Hospitals NHS
NHS Foundation Trust

UCLH Project ID number: 09/H0722/91

Patient Identification Number for this study:

Date:

Self-monitoring of treatment with methotrexate alone or in combination with a self-injecting anti-tumour necrosis factor agent by patients with arthritis

Thank you for agreeing to take part in this project. This booklet contains questions which will help us find out more about your thoughts and feelings about Rheumatoid Arthritis (RA) and Methotrexate. Please read each question carefully and answer them as honestly as you can. If you have any queries please contact a member of the research team.

This questionnaire asks your views about RA. It is not a 'test' of knowing the 'correct' answer, but about what you personally think and feel about your RA. Please ask if anything is unclear.

UCL HOSPITALS

UCL Hospitals is an NHS Foundation Trust comprising: The Eastman Dental Hospital, The Heart Hospital, Hospital for Tropical Diseases, National Hospital for Neurology and Neurosurgery, The Royal London Homoeopathic Hospital and University College Hospital (incorporating the former Middlesex and Elizabeth Garrett Anderson Hospitals).

SEX (please circle

Male Female

AGE: _____

YOUR LIVING STATUS (please circle the option closest to your situation)

Married/Living with partner

Living alone

Living with relatives/friends

YOUR ETHNIC BACKGROUND (please circle)

Bangladeshi Black – African Black - Caribbean Chinese

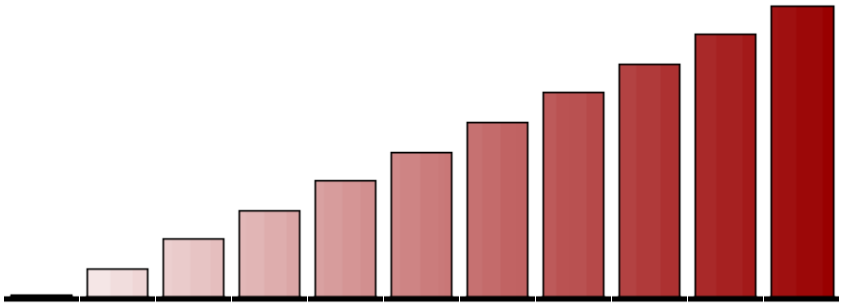
Indian Pakistani White

Other (please specify) _____

When were you **first** diagnosed with RA?

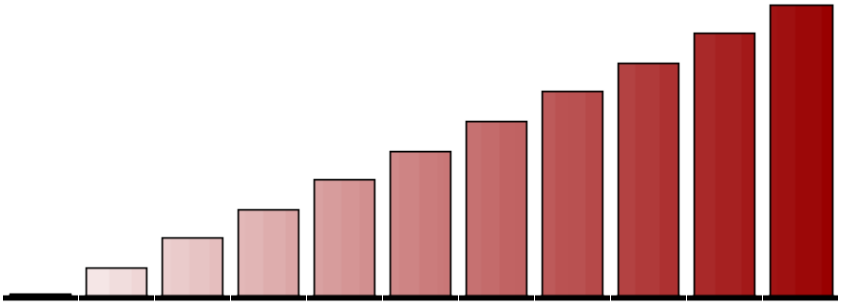
When did you **begin** taking methotrexate?

We are interested in learning whether or not you are affected by FATIGUE. Please **circle** the number below that describes your fatigue in the past 2 weeks:



No fatigue 0 1 2 3 4 5 6 7 8 9 10 Severe fatigue

We are interested in learning whether or not you are affected by PAIN. Please **circle** the number below that describes your pain in the past 2 weeks:



No pain 0 1 2 3 4 5 6 7 8 9 10 Severe pain

Listed below are a number of symptoms that you may or may not have experienced since having treatment for RA. Please circle **YES** or **NO** if you have experienced them and **YES** or **NO** if you think the symptom is related to RA.

	I have experienced this symptom *since my RA*		**This symptom is *related to my RA***	
Pain	YES	NO	YES	NO
Sore Throat	YES	NO	YES	NO
Nausea	YES	NO	YES	NO
Breathlessness	YES	NO	YES	NO
Weight loss	YES	NO	YES	NO
Fatigue	YES	NO	YES	NO
Stiff Joints	YES	NO	YES	NO
Sore Eyes	YES	NO	YES	NO
Wheeziness	YES	NO	YES	NO
Headaches	YES	NO	YES	NO
Upset stomach	YES	NO	YES	NO
Sleep difficulties	YES	NO	YES	NO
Dizziness	YES	NO	YES	NO
Loss of strength	YES	NO	YES	NO

We are interested in your own personal views of how you see your RA. Please indicate how much you agree or disagree with the following statements about RA by **circling** the appropriate number.

Your views about Rheumatoid Arthritis:	**Strongly Disagree**	**Disagree**	**Neither Agree or Disagree**	**Agree**	**Strongly Agree**
My RA is a serious condition.	1	2	3	4	5
My RA has major consequences on my life	1	2	3	4	5
My RA does not have much effect on my life	1	2	3	4	5
My RA strongly affects the way others see me	1	2	3	4	5
My RA has serious financial consequences	1	2	3	4	5
My RA causes difficulties for those who are close to me	1	2	3	4	5
There is a lot which I can do to control my symptoms	1	2	3	4	5

Your views about Rheumatoid Arthritis:	**Strongly Disagree**	**Disagree**	**Neither Agree or Disagree**	**Agree**	**Strongly Agree**
What I do can determine whether my RA gets better or worse	1	2	3	4	5
The course of my RA depends on me	1	2	3	4	5
Nothing I do will affect my RA	1	2	3	4	5
I have the power to influence my RA	1	2	3	4	5
My actions will have no effect on the outcome of my RA	1	2	3	4	5
There is very little that can be done to improve my RA	1	2	3	4	5
My treatment will be effective in curing my RA	1	2	3	4	5
The negative effects of my RA can be prevented (avoided) by my treatment	1	2	3	4	5

Your views about Rheumatoid Arthritis:	**Strongly Disagree**	**Disagree**	**Neither Agree or Disagree**	**Agree**	**Strongly Agree**
My treatment can control my RA	1	2	3	4	5
There is nothing which can help my condition	1	2	3	4	5
The symptoms of my condition are puzzling to me	1	2	3	4	5
My RA is a mystery to me	1	2	3	4	5
I don't understand my RA	1	2	3	4	5
My RA doesn't make any sense to me	1	2	3	4	5
I have a clear picture or understanding of my condition	1	2	3	4	5

We would like to ask you about your personal views of Methotrexate. These are statements other people have made about their medicines. Please indicate the extent to which you agree or disagree by circling the appropriate number. There are no right or wrong answers. We are interested in your personal views.

Your views about Methotrexate:	**Strongly Agree**	**Agree**	**Uncertain**	**Disagree**	**Strongly Disagree**
My health at present, depends on my Methotrexate	1	2	3	4	5
Having to take my Methotrexate worries me	1	2	3	4	5
My life would be impossible without my Methotrexate	1	2	3	4	5
Without my Methotrexate I would be very ill	1	2	3	4	5
I sometimes worry about the long-term effects of Methotrexate	1	2	3	4	5
My Methotrexate is a mystery to me	1	2	3	4	5
My health in the future will depend on my Methotrexate	1	2	3	4	5

Your views about Methotrexate:	**Strongly Agree**	**Agree**	**Uncertain**	**Disagree**	**Strongly Disagree**
Methotrexate disrupts my life	1	2	3	4	5
I sometimes worry about becoming too dependent on my Methotrexate	1	2	3	4	5
My Methotrexate protects me from becoming worse	1	2	3	4	5

This part of the questionnaire asks you about how you generally approach problems or challenges in life. Please read each statement carefully and **circle** the number which you feel is most true for you.

	Not at all true	**Hardly True**	**Moderately True**	**Exactly True**
I can always manage to solve difficult problems if I try hard enough	1	2	3	4
If someone opposes me, I can find ways and means to get what I want	1	2	3	4
It is easy for me to stick to my aims and accomplish my goals	1	2	3	4
I am confident that I could deal with unexpected events	1	2	3	4
Thanks to my resourcefulness, I know how to handle unforeseen situations	1	2	3	4
I can solve most problems if I invest the necessary effort	1	2	3	4

	Not at all true	**Hardly True**	**Moderately True**	**Exactly True**
I can remain calm when facing difficulties because I can rely on my coping abilities	1	2	3	4
When I am confronted with a problem, I can usually find several solutions	1	2	3	4
If I am in trouble, I can usually think of something to do	1	2	3	4
No matter what comes my way, I'm usually able to handle it.	1	2	3	4

Please read each item below and then place a tick in the box next to the reply which comes closest to how you have been feeling in the **past week**. Try to give your first reaction. This will probably be more accurate than spending a long time thinking about an answer.

1) *I feel tense or wound up*		**2)** *I feel as if I am slowed down*	
Most of the time	[ ]	Nearly all the time	[ ]
A lot of the time	[ ]	Very often	[ ]
Time to time, occasionally	[ ]	Sometimes	[ ]
Not at all	[ ]	Not at all	[ ]

3) *I still enjoy the things I used to enjoy*		**4)** *I get a sort of frightened feeling like "butterflies" in my stomach*	
Definitely as much	[ ]	Not at all	[ ]
Not quite so much	[ ]	Occasionally	[ ]
Only a little	[ ]	Quite often	[ ]
Hardly at all	[ ]	Very often	[ ]

5) *I get a sort of frightened feeling as if something awful is about to happen*		**6)** *I have lost interest in my appearance*	
Very definitely and quite badly	[ ]	Definitely	[ ]
Yes, but not too badly	[ ]	I don't take as much care as I should	[ ]
A little, but it doesn't worry me	[ ]	I may not take quite as much care	[ ]
Not at all	[ ]	I take just as much care as ever	[ ]

7) *I can laugh and see the funny side of things of things*		**8)** *I feel restless as if I have to be on the move*	
As much as I always could	[ ]	Very much indeed	[ ]
Not quite so much now	[ ]	Quite a lot	[ ]
Definitely not so much	[ ]	Not very much	[ ]
Not at all	[ ]	Not at all	[ ]

9) *Worrying thoughts go through my mind*		**10)** *I look forward with enjoyment to things*	
A great deal of the time	[ ]	As much as I ever did	[ ]
A lot of the time	[ ]	Rather less than I used to	[ ]
From time to time but not often [	[ ]	Definitely less than I used to	[ ]
Only occasionally	[ ]	Hardly at all	[ ]

11) *I feel cheerful*

Not at all	[ ]
Not often	[ ]
Sometimes	[ ]
Most of the time	[ ]

12) *I get sudden feelings of panic*

Very often indeed	
Quite often	[ ]
Not very often	[ ]
Not at all	[ ]

[ ]

13) *I can sit at ease and feel relaxed*

Definitely	[ ]
Usually	[ ]
Not often	[ ]
Not at all	[ ]

14) *I can enjoy a good book or TV programme*

Often	
Sometimes	[ ]
Not often	[ ]
Very seldom	[ ]

The following statements are about methotrexate and RA. Please **mark** whether you think these statements are true or false. These questions are testing the quality of the information you have been given. We, therefore, ask that if you do not know the answer to a question you mark "don't know" rather than trying to guess the answer or looking it up. Please answer all of the questions.

At present there is no cure for rheumatoid arthritis	**TRUE**	☐	**FALSE**	☐	**DON'T KNOW**	☐	
Methotrexate is effective at relieving joint stiffness	**TRUE**	☐	**FALSE**	☐	**DON'T KNOW**	☐	
Taking regular folate tablets (also known as folic acid or megafol) lessens the chance of getting side effects from methotrexate	**TRUE**	☐	**FALSE**	☐	**DON'T KNOW**	☐	
Rheumatoid arthritis affects people of all ages	**TRUE**	☐	**FALSE**	☐	**DON'T KNOW**	☐	
Methotrexate can cause mouth ulcers	**TRUE**	☐	**FALSE**	☐	**DON'T KNOW**	☐	
It takes many years for rheumatoid arthritis to cause joint damage	**TRUE**	☐	**FALSE**	☐	**DON'T KNOW**	☐	
The low dose of methotrexate used to treat rheumatoid arthritis has the same risks and side effects as the higher doses used to treat other conditions	**TRUE**	☐	**FALSE**	☐	**DON'T KNOW**	☐	
Rheumatoid arthritis often goes away by itself	**TRUE**	☐	**FALSE**	☐	**DON'T KNOW**	☐	

Alcohol use increases the chance of getting liver damage from methotrexate	**TRUE**	☐	**FALSE**	☐	**DON'T KNOW**	☐
If you forget a dose of methotrexate, you can still take it the next day	**TRUE**	☐	**FALSE**	☐	**DON'T KNOW**	☐
Methotrexate tablets are white	**TRUE**	☐	**FALSE**	☐	**DON'T KNOW**	☐
Methotrexate is also used to treat cancer	**TRUE**	☐	**FALSE**	☐	**DON'T KNOW**	☐
Trimethoprim (which is an antibiotic also known as Alprim and Triprim) can be safely taken while on methotrexate	**TRUE**	☐	**FALSE**	☐	**DON'T KNOW**	☐
Most people can safely continue taking methotrexate long-term	**TRUE**	☐	**FALSE**	☐	**DON'T KNOW**	☐
Methotrexate can cause a rare type of lymphoma (tumour of the lymph glands)	**TRUE**	☐	**FALSE**	☐	**DON'T KNOW**	☐
Rheumatoid arthritis causes joint inflammation	**TRUE**	☐	**FALSE**	☐	**DON'T KNOW**	☐
Regular folate tablets (also known as folic acid or megafol) should be taken by everyone who is taking methotrexate	**TRUE**	☐	**FALSE**	☐	**DON'T KNOW**	☐
The benefits of methotrexate should be noticeable within a few days of starting it	**TRUE**	☐	**FALSE**	☐	**DON'T KNOW**	☐

Methotrexate does not slow the joint damage caused by rheumatoid arthritis	**TRUE**	☐	**FALSE**	☐	**DON'T KNOW**	☐
Methotrexate can cause serious problems with your breathing	**TRUE**	☐	**FALSE**	☐	**DON'T KNOW**	☐
Nausea is a common side effect of methotrexate	**TRUE**	☐	**FALSE**	☐	**DON'T KNOW**	☐
Daily low dose aspirin (one tablet or less a day) should not be taken while on methotrexate	**TRUE**	☐	**FALSE**	☐	**DON'T KNOW**	☐
Treatment of rheumatoid arthritis with medications can prevent joint damage	**TRUE**	☐	**FALSE**	☐	**DON'T KNOW**	☐
You should seek medical attention if you have a cough that does not go away while taking methotrexate	**TRUE**	☐	**FALSE**	☐	**DON'T KNOW**	☐
Methotrexate can cause women to have irregular periods	**TRUE**	☐	**FALSE**	☐	**DON'T KNOW**	☐
Taking regular folate tablets (also known as folic acid or megafol) improves joint pain and swelling	**TRUE**	☐	**FALSE**	☐	**DON'T KNOW**	☐
Methotrexate is a commonly used treatment for rheumatoid arthritis	**TRUE**	☐	**FALSE**	☐	**DON'T KNOW**	☐
Treatment for rheumatoid arthritis is more effective it if is started early	**TRUE**	☐	**FALSE**	☐	**DON'T KNOW**	☐
Having untreated rheumatoid arthritis increases your chance of having a heart attack	**TRUE**	☐	**FALSE**	☐	**DON'T KNOW**	☐

You need to continue having regular blood tests as long as you keep taking methotrexate	**TRUE**	☐	**FALSE**	☐	**DON'T KNOW**	☐
Anti-inflammatory medications (for example Voltaren or Celebrex) should not be used while taking methotrexate	**TRUE**	☐	**FALSE**	☐	**DON'T KNOW**	☐
At present, joint damage caused by rheumatoid arthritis cannot be reversed	**TRUE**	☐	**FALSE**	☐	**DON'T KNOW**	☐
Methotrexate can cause stomach ulcers	**TRUE**	☐	**FALSE**	☐	**DON'T KNOW**	☐
Methoblastin is another name for methotrexate	**TRUE**	☐	**FALSE**	☐	**DON'T KNOW**	☐
If you forget a dose of methotrexate, you should double the dose next time to make up for it	**TRUE**	☐	**FALSE**	☐	**DON'T KNOW**	☐
Methotrexate is often combined with other medications that treat rheumatoid arthritis	**TRUE**	☐	**FALSE**	☐	**DON'T KNOW**	☐
You should not have the flu vaccine while on methotrexate	**TRUE**	☐	**FALSE**	☐	**DON'T KNOW**	☐
Methotrexate is safe to take if you are breastfeeding	**TRUE**	☐	**FALSE**	☐	**DON'T KNOW**	☐
Both men and women taking methotrexate should use reliable birth control (contraception)	**TRUE**	☐	**FALSE**	☐	**DON'T KNOW**	☐

Anti-inflammatory medications (for example Voltaren or Celebrex) can slow joint damage caused by rheumatoid arthritis	**TRUE**	☐	**FALSE**	☐	**DON'T KNOW**	☐
Methotrexate should be stopped if your rheumatoid arthritis flares up (becomes worse)	**TRUE**	☐	**FALSE**	☐	**DON'T KNOW**	☐
Methotrexate can cause thinning of the hair	**TRUE**	☐	**FALSE**	☐	**DON'T KNOW**	☐
All medications used to treat rheumatoid arthritis can cause side effects	**TRUE**	☐	**FALSE**	☐	**DON'T KNOW**	☐
It is safe to become pregnant 3 weeks after methotrexate has been stopped	**TRUE**	☐	**FALSE**	☐	**DON'T KNOW**	☐
You should restrict your alcohol intake while taking methotrexate	**TRUE**	☐	**FALSE**	☐	**DON'T KNOW**	☐
You should take Methotrexate daily (tablets or injections)	**TRUE**	☐	**FALSE**	☐	**DON'T KNOW**	☐
Scarring of the liver is a common side effect of methotrexate	**TRUE**	☐	**FALSE**	☐	**DON'T KNOW**	☐
Methotrexate can reverse joint damage caused by rheumatoid arthritis	**TRUE**	☐	**FALSE**	☐	**DON'T KNOW**	☐
You should keep taking methotrexate even when your joints are not painful	**TRUE**	☐	**FALSE**	☐	**DON'T KNOW**	☐

People who already have joint damage from rheumatoid arthritis will not get any better with methotrexate	**TRUE**	☐	**FALSE**	☐	**DON'T KNOW**	☐
Methotrexate is effective at relieving joint swelling	**TRUE**	☐	**FALSE**	☐	**DON'T KNOW**	☐
Treatment for newly diagnosed rheumatoid arthritis often includes methotrexate	**TRUE**	☐	**FALSE**	☐	**DON'T KNOW**	☐
Taking methotrexate more often than what was prescribed increases the chance of side effects	**TRUE**	☐	**FALSE**	☐	**DON'T KNOW**	☐
You should not have any vaccinations while on methotrexate	**TRUE**	☐	**FALSE**	☐	**DON'T KNOW**	☐
If you are unable to eat or drink you should still try to take your methotrexate	**TRUE**	☐	**FALSE**	☐	**DON'T KNOW**	☐
Methotrexate should not be taken during pregnancy	**TRUE**	☐	**FALSE**	☐	**DON'T KNOW**	☐
Blood tests are done to pick up side effects caused by methotrexate	**TRUE**	☐	**FALSE**	☐	**DON'T KNOW**	☐
Methotrexate treatment will be stopped once your arthritis is under control	**TRUE**	☐	**FALSE**	☐	**DON'T KNOW**	☐
Methotrexate should be stopped if you develop a cold	**TRUE**	☐	**FALSE**	☐	**DON'T KNOW**	☐

Methotrexate tablets come in two different strengths **TRUE** ☐ **FALSE** ☐ **DON'T KNOW** ☐

My treatment so far has been...

Not burdensome				**Extremely burdensome**
1	2	3	4	5

Please check the response which best describes your usual abilities **over the past week.**

Are you able to:	**Without ANY difficulty**	**With SOME difficulty**	**With MUCH difficulty**	**UNABLE to do**
Go up two or more flights of stairs	1	2	3	4
Walk outdoors on flat ground	1	2	3	4
Stand up from a straight chair	1	2	3	4
Lift heavy objects	1	2	3	4
Move heavy objects	1	2	3	4
Wait in line for 15 minutes	1	2	3	4
Do outside work (such as garden work)	1	2	3	4
Get on and off the toilet	1	2	3	4
Reach and get down a 5lb object from above your head	1	2	3	4
Open car doors	1	2	3	4

Please indicate how strongly you disagree or agree with the following statements by **circling** the number which best describes you **now**.

	Strongly disagree	**Disagree**	**Agree**	**Strongly Agree**
As well as seeing my doctor, I regularly monitor changes in my health	1	2	3	4
I know what things can trigger my health problems and make them worse	1	2	3	4
I have a very good understanding of when and why I am supposed to take my medication	1	2	3	4
When I have health problems, I have a clear understanding of what I need to do to control them	1	2	3	4
I carefully watch my health and do what is necessary to keep as healthy as possible	1	2	3	4
With my health in mind, I have realistic expectations of what I can and cannot do	1	2	3	4

The following statements relate to your experiences while starting methotrexate treatment for your arthritis. They are about the care and information you received as well as your feelings and attitude to your diagnosis and treatment. Please indicate how strongly you disagree or agree with the following statements by **circling** the response which best describes you. Answer each of these questions based on your feelings about Methotrexate, your arthritis and the care and information you received when starting methotrexate treatment.

	Disagree strongly	**Disagree**	**Disagree Slightly**	**Agree Slightly**	**Agree**	**Agree Strongly**
I am confident in my ability to communicate with my doctors	1	2	3	4	5	6
I am able to have good discussions with my doctors about my treatment	1	2	3	4	5	6
Overall I feel that I am able to ask my doctors questions	1	2	3	4	5	6
I feel comfortable about asking my doctors for more information	1	2	3	4	5	6

	Disagree strongly	**Disagree**	**Disagree Slightly**	**Agree Slightly**	**Agree**	**Agree Strongly**
I feel that I am able to make an educated decision about taking this medication	1	2	3	4	5	6
I feel I have enough knowledge to choose between treatment options	1	2	3	4	5	6
I understand the risks of taking this medication	1	2	3	4	5	6
I am able to assess how well I am responding to treatment	1	2	3	4	5	6
I am confident that I can recognise side effects caused by my medication	1	2	3	4	5	6

	Disagree strongly	**Disagree**	**Disagree Slightly**	**Agree Slightly**	**Agree**	**Agree Strongly**
I know what I need to do to improve my condition	1	2	3	4	5	6

INSTRUCTIONS: This questionnaire asks for your views about your health. Please answer every question by **circling** the relevant answer. If you are unsure how to answer please give the best answer you can.

1. In general, would you say your health is:

1	2	3	4	5
Excellent	Very good	Good	Fair	Poor

The following items are about activities you might do during a typical day. Does your health now limit you in these activities? If so how much?

2a. Moderate activities such as moving a table, pushing a vacuum cleaner, bowling or playing golf.	Yes, limited a lot	Yes, limited a little	No, not limited at all
2b. Climbing several flights of stairs	Yes, limited a lot	Yes, limited a little	No, not limited at all

During the **<u>past 4 weeks</u>** have you had any of the following problems with your work or other regular daily activities **<u>as a result of your physical health</u>**?

3a. Accomplished less than you would like?	Yes	No
3b. Were limited in the kind of work or activities?	Yes	No

During the past 4 weeks have you had any of the following problems with your work or other regular daily activities **as a result of any emotional problems** (such as feeling depressed or anxious)?

4a. Accomplished less than you would like	Yes	No
4b. Didn't do work or other activities as carefully as usual	Yes	No

5. During the past 4 weeks how much did pain interfere with your normal work (including work both outside the home and housework)?

1	2	3	4	5
Not at all	A little bit	Moderately	Quite a bit	Extremely

These questions are about how you feel and how things have been with you **during the past 4 weeks**. For each question, please indicate the one answer that comes closest to the way you have been feeling.

6a. Have you felt calm and peaceful?

1	2	3	4	5	6
All the time	Most of the time	A good bit of the time	Some of the time	A little of the time	None of the time

6b. Did you have a lot of energy?

1	2	3	4	5	6
All the time	Most of the time	A good bit of the time	Some of the time	A little of the time	None of the time

6c. Have you felt downhearted and blue?

1	2	3	4	5	6
All the time	Most of the time	A good bit of the time	Some of the time	A little of the time	None of the time

7. During the **past 4 weeks**, how much of the time has your **physical health or emotional problems** interfered with your social activities (like visiting with friends, relatives, etc.)?

1	2	3	4	5
All the time	Most of the time	Some of the time	A little of the time	None of the time

Thank you very much for completing this questionnaire. Please return the questionnaire to the researcher.

By taking part in this research you have contributed to a study that we anticipate will benefit many people.

If, at any point you wish to talk to someone regarding this project please do not hesitate to call **Hayley James** the Researcher in Health Services Research at City University, Tel **(0207) 040 0870** or e-mail **hayley.james.1@city.ac.uk**

APPENDIX N. INTERVENTION MATERIALS - TRAINING SLIDES

Self Monitoring Training for Patients with Inflammatory Arthritis

Welcome

Research Team

- Dr Mike Shipley, Consultant Rheumatologist
- Professor Stanton Newman, Health Services Research, City University London
- Hayley James, Research Associate, Health Services Research, City University London
- Abigail Olaleye, Clinical Nurse Specialist, Rheumatology
- Sam Moore, Clinical Nurse Specialist, Rheumatology
- Nicola Daly, Clinical Nurse Specialist, Rheumatology

Study pack includes…

- Contact sheet
- Contact details
- Copy of the slides
- Criteria for patient action
- Practice material
- A sheet for you to record all of your results, with your 2 previous blood test results
- Plastic wallets to store your blood test results
- Leaflets on Arthritis and Medications

What are we doing today?

- Explaining the purpose of the study and why you have been asked to help
- What are Rheumatoid & Psoriatic Arthritis?
- Methotrexate and its use alone and in combination with anti-TNF agents
- Symptoms and Side Effects
- Blood Tests – why they are done and what they mean?
- What will happen in the study and what will you have to do?
- Practice

Purpose of the study

- We know that many people are keen to be more involved in managing their arthritis
- There is evidence that this can be done successfully and that it helps people feel more in control of things, and generally better
- It also improves the regularity with which people have their blood tests!
- This research is to see whether such a plan is feasible and helpful

Aim of the study

- To find out whether people are able to decide if they need an outpatients appointment based upon
  - Symptoms
  - Side effects
  - Blood test results
- Who benefits from this type of intervention?

Why do we want to do this?

- We know that it can be difficult to;
  - get to a routine clinic appointment
  - get an outpatient appointment even if you are worried or are getting worse
- Some patients are asked to attend appointments when they don't really feel they need one

Why have you been chosen?

- You have Rheumatoid (RA) or Psoriatic Arthritis (PsA)
- You are receiving a stable dose of either
  - Methotrexate

  or
  - Methotrexate plus an anti-TNF agent

INFLAMMATORY ARTHRITIS AND DRUG TREATMENT

Dr Mike Shipley

Inflammatory Arthritis

- RA & PsA are diseases of unknown cause which can damage the joints and other tissues
- Psoriasis is a relatively common (2-3%) inflammatory condition of the skin & nails which is also of unknown cause. It is associated with arthritis in about 5-8% of affected people.
- Both are inherited. Psoriasis more clearly so than RA
- Both are auto-immune diseases in which the body's defence system attacks itself

Inflammatory Arthritis

- The symptoms of RA & PsA include;
  - joint pain
  - stiffness
  - joint swelling
  - Fatigue
- RA tends to be fairly constant and progressive, PsA may fluctuate in severity & improve even without treatment
- The skin and nails are almost always affected in psoritic arthritis
- Rarely RA also causes a skin rash, skin nodules or lung problems

Treatment of RA & PsA

- Aims of treatment
  - Control pain and stiffness
  - Reduce inflammation and swelling and the risk of longer term joint damage
- **Anti-inflammatory and pain relieving drugs** help to some extent with the pain and stiffness
  - they do **not** stop the inflammation in RA or PsA
  - they occasionally make psoriasis worse

Treatment of RA & PsA

- It is the joint inflammation (synovitis) which causes the swelling and can in the longer term lead to joint damage
- Drugs which reduce the inflammation in RA & PsA are often called 'second line' drugs or 'disease modifying drug' (DMARDs)
  - now used early on in the disease
  - earlier in RA than in PsA

Drugs to reduce the risk of damage in RA & PsA

- Sulfasalazine
- Hydroxychloroquine
- Methotrexate
- Anti-TNF agents such as etanercept, adalimumab and infliximab
- Steroids are very effective anti-inflammatory agents and also reduce the damage but are best used as short term treatments

Drugs that reduce the risk of damage in RA & PsA

- There is a trend to use several of these in combination – effectively hitting the arthritis hard and early
- Many people are well on Methotrexate which is regarded as the 'gold standard' treatment
- Anti-TNF agents are very expensive and therefore are controlled by the regulating body (NICE)
- They can only be used after two other DMARDs have been tried and if the arthritis is assessed to be active

Drugs to reduce the risk of damage

- Anti-TNF agents are usually taken in combination with Methotrexate to;
  - increase their effect
  - reduce the risk of side effects
  - reduce the risk of losing control of the arthritis
- this combination is more common in RA

Drug Side Effects

- As is the case with many drugs, there are some potential side effects
- The risk is small and has to be weighed against the risk of not treating inflammatory arthritis adequately – pain, stiffness & longer term damage
- Some side effects can be detected early before they become serious using blood tests
  - this is the reason for regular monitoring

Side effects with Methotrexate and anti-TNF agents

- Uncommon and usually mild
- MTX – side effects are prevented or reduced by taking folic acid
- Side effects can include…
  1. Nausea (MTX)
  2. Diarrhoea (MTX)
  3. Hair loss (MTX and anti-TNF)
  4. Skin rashes (MTX and anti-TNF)
  5. Mouth ulcers (MTX and anti-TNF)

Blood tests

- Are used a lot in medicine
- Initially they help decide the type of arthritis
- In inflammatory arthritis they test for;
  - **Disease activity** (joint pain, swelling, stiffness and fatigue)
  - **Rare side effects** in the bone marrow, liver and kidneys from drug treatment
- The aim is to pick up problems before they become serious – hence the importance of regular testing and checking the results

The Blood Tests

1. Warn us about the possible side effects of methotrexate and anti-TNF agents
2. Gives us information about how active your arthritis is

The blood tests include…

- Haemoglobin (anaemia)
- White Blood & Neutrophil Count (infection risk)
- Platelets (bruising risk)
- Liver Function
- Tests for inflammation

Haemoglobin (Hb)

- Haemoglobin is a substance present in the blood red cells. It carries oxygen around your body.
- When it is low, you are **anaemic**
- This can make you feel tired and run down, and sometimes breathless or dizzy
- Hb can be low for many reasons!
  - e.g. low iron, bleeding and active arthritis

White Blood Count & Neutrophils

- White cells help to fight infection
- A neutrophil is a type of white blood cell that helps fight bacterial infections
- Their numbers can fall when taking methotrexate and anti-TNF agents, causing an increased risk of infection
- They need to go up to fight a bacterial infection
- They can go up when you are taking steroids (which is not worrying)

ALP & ALT

- Liver function tests
- These are enzymes whose levels can go up when the liver is irritated by the methotrexate or anti-TNF agents
  – however there may also be other causes
- By watching trends and checking them regularly we can reduce the dose or stop the treatment **before** any damage is done

ESR & CRP

- Tests for inflammation
- Both of these markers can go up when your arthritis flares and down when it improves
- They usually change with your symptoms
  – Pain, stiffness, fatigue & swelling
  – They help us to decide to increase your treatment, or sometimes to reduce it
- They also go up with other illnesses

The Study

- You have been randomly allocated to the 'intervention' group – the group that is being trained
- You will be compared to another group who will continue with the usual pattern of care
- You may withdraw at any time but we hope that you will not!

What do you have to do?

- We will ask you to observe and record changes in;
  - Symptoms
  - Side-effects
  - Blood test results
- The blood test results can be sent to you by e-mail or post

IMPORTANT

Taking part in this study means:

1. your clinical care will continue and will **not** be compromised in any way
2. changes in your disease or reactions to your medication will still be monitored by us as usual but **you will be involved**

What do you have to do? Blood tests 1 - 3

1. You attend for your blood test and let the Researcher know by email or telephone
2. Within 48 hours of having your blood test, your results will be sent to you via your preferred method, along with a short questionnaire about your side effects and symptoms
3. You will compare your results with what is considered normal for you and along with your side effects and symptoms decide whether you need an outpatients appointment.
4. One of the research team will call you within 5 days of sending your results to discuss them and your decisions with you

What do you have to do? Blood tests 1 - 3

- After the 3rd blood test you will be sent a questionnaire booklet to complete and send back in a freepost envelope
- If you are doing well and you feel confident you will move onto the second part of the study

What do you have to do? Blood test 4 - 6

1. You attend for your blood test and let the Researcher know by email or telephone
2. Within 48 hours of having your blood test, your results will be sent to you via your preferred method, along with a short questionnaire about your side effects and symptoms
3. You will compare your results with what is considered normal for you and along with your side effects and symptoms decide whether you need an outpatients appointment.

IMPORTANT
Blood Tests 4 - 6

- During this part of the study you will not receive a telephone call from a nurse except in an emergency
- A member of the clinical team will always check your blood test results to ensure safety
- **BUT** If you are experiencing any problems or are concerned about the results please contact one of the research team immediately
- After the 6th blood test you will be sent a questionnaire booklet to complete and send back along with all of your other questionnaires in a freepost envelope

Blood Results – What is normal?

	Acceptable range	Significant change defined as..
Haemoglobin	12.0 (10 in some RA patients) - 17.0	Fall of more than 1.0
White Blood Cell Count	3.0 - 10.0 If on steroids 4 - 20	A fall of more than 2
Neutrophils	2.0 - 7.5	Two readings in a row each with a fall of more than 1.0
Platelets	150 - 400	Two readings in a row with falls of more than 50
ALP	35 - 104	A result which doubles from the previous blood test or rises above 208
ALT	10 - 35	A results which doubles from the previous blood test or rises above 70
ESR	0 - 20	A rise of more than 20 from the previous blood test results
CRP	0 - 5	A rise of more than 20 from the previous blood test results

Symptoms & side effects

since your last blood test

Symptom/side effect	Yes	No	New	Worse	Better	Same
Morning stiffness						
Pain						
Nausea						
Vomiting						
Fatigue						
Diarrhoea						
Mouth Ulcers						
Skin problems						
Bruising						
Joint swelling						
Bleeding						
Sore throat						
Fever						
Breathlessness						
Dry cough						
Hair loss						
Chicken pox/shingles						

Symptoms & side effects

- When completing the questionnaire if either of the following occur, this would require further attention from your Clinical Nurse Specialist.

1. The appearance of a new symptom or side effect since your last blood test
2. A symptom or side effect you have been experiencing has significantly worsened since your last blood test

When to seek help in between blood tests

Nausea	No contact necessary
Vomiting	Contact Nurse – if persists over 24 hours
Diarrhoea	Contact Nurse – if persists over 48 hours
Mouth Ulcers	Contact Nurse – if symptoms, causing discomfort and interference with normal eating
Skin problems	Contact –Nurse – if unexplained rash or itching occurs
Bruising	Contact Nurse – if unexplained bruising occurs
Bleeding	Contact Nurse – if frequent nose bleeds or excessive blooding following minor injury

Sore Throat	Contact Nurse – if episodes requiring treatment occur within a 4 week period
Fever	Contact Nurse – if fever persist for over 24 hours
Breathlessness	Contact Nurse – if breathlessness occurs in the absence of physical exertion
Dry Cough	Contact Nurse
Chicken pox/shingles	Contact Nurse – if been exposed to the chicken pox or shingles virus
Pregnancy	Contact Nurse – if pregnancy is suspected

PRACTICE MATERIAL

Practice 1 - Haemoglobin

	Last months blood test results	This months blood test results	Difference between the two results
Haemoglobin	11.3	10.0	- 1.3

Is the result out of the normal range of 12.0 to 17.0?

Has there been a fall of greater than 1.0?

Do you need to contact the Rheumatology Nurse Specialist? Yes

Practice 1 – White Blood Cell

	Last months blood test results	This months blood test results	Difference between the two results
White Blood Cells	6.4	4.8	- 1.6

Is the result out of the normal range of 3.0 to 10.0?

Has there been a fall of greater than 2?

Do you need to contact the Rheumatology Nurse Specialist? No

Practice 1 – Neutrophils

	Last months blood test results	This months blood test results	Difference between the two results
Neutrophils	4.6	4.3	- 0.3

Is the result out of the normal range of 2.0 to 7.5?

Has there been a two readings in a row each with a fall of >1.0?

Do you need to contact the Rheumatology Nurse Specialist? No

Practice 1 – Platelets

	Last months blood test results	This months blood test results	Difference between the two results
Platelets	220	305	+ 85

Is the result out of the normal range of 150 to 400?

Has there been two readings in a row with falls of greater than 50?

Do you need to contact the Rheumatology Nurse Specialist? No

Practice 1 – ALP

	Last months blood test results	This months blood test results	Difference between the two results
ALP	88	95	+ 7

Is the result out of the normal range of 35 to 104?

Has the result doubled since the previous blood test or risen above twice upper limit of normal (>208)?

Do you need to contact the Rheumatology Nurse Specialist? No

Practice 1 – ALT

	Last months blood test results	This months blood test results	Difference between the two results
ALT	30	35	+ 5

Is the result out of the normal range of 10 to 35?

Has the result doubled since the previous blood test or risen above twice upper limit of normal (>70)?

Do you need to contact the Rheumatology Nurse Specialist? No

Practice 1 – ESR

	Last months blood test results	This months blood test results	Difference between the two results
ESR	25	53	+28

Is the result out of the normal range of 0 to 20?

Has there been an increase of more than 20 since the previous blood test results?

Do you need to contact the Rheumatology Nurse Specialist? Yes – possible flare

Practice 1 – CRP

	Last months blood test results	This months blood test results	Difference between the two results
CRP	12	12	0

Is the result out of the normal range of 0 to 5?

Has there been an increase of more than 20 since the previous blood test results?

Do you need to contact the Rheumatology Nurse Specialist? Yes

Practice 1 – summary

	Last months blood test results	**This months blood test results**	Difference between the two results	Are these results out of the normal range?	Has there been a significant change?	Need for further advice
Haemoglobin	11.3	**10.0**	- 1.3	X	√	√
White Blood Cell Count	6.4	**4.8**	-1.6	X	X	X
Neutrophils	4.6	**4.3**	-0.3	X	X	X
Platelets	220	**305**	+ 85	X	X	X
ALP	88	**95**	+ 7	X	X	X
ALT	30	**35**	+ 5	X	X	X
ESR	25	**53**	+28	√	√	√
CRP	12	**12**	0	√	X	√

Do these results required further discussion with your rheumatology nurse specialist? **Yes**

Practice 2

	Last months blood test results	**This months blood test results**	Difference between the two results	Are these results out of the normal range?	Has there been a significant change?	Need for further advice
Haemoglobin	10.4	**10.8**	+ 0.4	√	X	√
White Blood Cell Count	7.3	**8.2**	+ 0.9	X	X	X
Neutrophils	4.2	**4.2**	0	X	X	X
Platelets	235	**260**	+ 25	X	X	X
ALP	65	**220**	+ 155	√	√	√
ALT	39	**126**	+87	√	√	√
ESR	19	**22**	+ 3	√	X	√
CRP	4.0	**5.0**	+ 1	X	X	X

Do these results required further discussion with your rheumatology nurse specialist? **Yes**

Practice 3

	Last months blood test results	**This months blood test results**	Difference between the two results	Are these results out of the normal range?	Has there been a significant change?	Need for further advic
Haemoglobin	12.0	**12.5**	+ 0.5	X	X	X
White Blood Cell Count	7.6	**8.0**	+ 0.4	X	X	X
Neutrophils	5.9	**6.1**	+ 0.2	X	X	X
Platelets	355	**320**	- 35	X	X	X
ALP	50	**43**	- 7	X	X	X
ALT	40	**32**	- 8	X	X	X
ESR	12	**15**	+ 3	X	X	X
CRP	2.0	**2.3**	+ 0.3	X	X	X

Do these results required further discussion with your rheumatology nurse specialist? **No**

Practice 4

	Last months blood test results	**This months blood test results**	Difference between the two results	Are these results out of the normal range?	Has there been a significant change?	Need for further advic
Haemoglobin	11.0	**10.2**	- 0.8	√	X	√
White Blood Cell Count	7.0	**8.1**	+ 1.1	X	X	X
Neutrophils	4.2	**4.5**	+ 0.3	X	X	X
Platelets	235	**460**	+ 225	√	X	√
ALP	65	**70**	+ 5	X	X	X
ALT	39	**52**	+ 13	√	X	√
ESR	19	**55**	+ 36	√	√	√
CRP	4	**25**	+ 21	√	√	√

Do these results required further discussion with your rheumatology nurse specialist? **Yes**

What happens next?

- You are now part of the study – thank you!
- We will note when you are going for your next blood test and the process will start
- You will not need to attend any appointments you have booked with your Rheumatology Nurse, these will be cancelled
- If at any time during your participation you have any questions please contact any member of the research team

Useful web sites

- Arthritis Care
  http://*www.**arthritiscare**.org.uk*
- Arthritis Research UK
  http://www.arthritisresearchuk.org
- Psoriasis Association

http://www.psoriasis-association.org.uk/arthritis.html

Any Questions….?

APPENDIX O. CRITERIA FOR PATIENT ACTION

CRITERIA FOR PATIENT ACTION

The following criteria will help you decide if your blood test results or symptoms and side effects you are experiencing require further attention from your Clinical Nurse Specialist.

Blood Results

When completing the questionnaire if either of the following occurs, this would require further attention from your Clinical Nurse Specialist.

1. A blood test result is out of the normal range

or

2. A blood test result changes significantly from the previous test

Test	**Normal range**	**Significant Change Defined As.**
Haemoglobin	12.0 – 17.0	Fall of more than 1.0
White Blood Cell Count	3.0 - 10.0	A fall of more than 2
Neutrophils	2.0 – 7.5	Two readings in a row each with a fall of more than 1.0
Platelets	150 - 400	Two readings in a row with falls of more than 50
ALP	35 - 104	A result which doubles from the previous blood test or rises 208
ALT	10 - 35	A results which doubles from the previous blood test or rises above 70
ESR	0 – 20	A rise of more than 20 from the previous blood test results
CRP	0 - 5	A rise of more than 20 from the previous blood test results

Symptoms & Side Effects

When completing the questionnaire if either of the following occurs, this would require further attention from your Clinical Nurse Specialist.

1. The appearance of any new symptom or side effect since your last blood test

or

2. A symptom or side effect you have been experiencing has **significantly** worsened since your last blood test

In between blood tests:

Symptom or Side Effect	**What action to take**
Nausea	No contact necessary
Vomiting	Contact Nurse – if persists over 24 hours
Diarrhoea	Contact Nurse – if persists over 48 hours
Mouth Ulcers	Contact Nurse – if symptoms, causing discomfort and interference with normal eating
Skin problems	Contact –Nurse – if unexplained rash or itching occurs
Bruising	Contact Nurse – if unexplained bruising occurs
Bleeding	Contact Nurse – if frequent nose bleeds or excessive bleeding following minor injury
Sore Throat	Contact Nurse – if episodes requiring treatment occur within a 4 week period
Fever	Contact Nurse – if fever persist for over 24 hours
Breathlessness	Contact Nurse – if breathlessness occurs in the absence of physical exertion
Dry Cough	Contact Nurse

Chicken pox/shingles	Contact Nurse – if been exposed to the chicken pox or shingles virus
Pregnancy	Contact Nurse – if pregnancy is suspected

APPENDIX P. CONTACT DETAILS FOR THE RESEARCH TEAM

Contact details

Ms. Hayley James	Telephone number: [redacted]
Researcher	Email: [redacted]
Ms. Abigail Olaleye	Telephone number: [redacted]
Rheumatology Nurse Specialist	Email: [redacted]
Ms. Sam Moore	Telephone number: [redacted]
Rheumatology Nurse Specialist	Email: [redacted]
Ms. Nicola Daly	Telephone number: [redacted]
Rheumatology Nurse Specialist	Email: [redacted]
Dr. Mike Shipley	Telephone number: [redacted]
Consultant Rheumatologist	Email: [redacted]

IF YOU CONTACT ANY OF THE ABOVE PEOPLE VIA EMAIL PLEASE PUT **'SELF-MONITORING INTERVENTION – URGENT'** IN THE SUBJECT HEADING

APPENDIX Q. BLOOD RECORD SHEET FORM

PERSONAL BLOOD RESULTS SHEET

When you receive your blood test letter enter your blood results in the table below. Please compare these with YOUR acceptable baseline range. This will help you decide whether your results fall within your normal range and will then help you make a decision about whether you require an out-patient appointment.

	Date:	Date:	Blood Test 1 Date:	Blood Test 2 Date:	Blood Test 3 Date:	Blood Test 4 Date:	Blood Test 5 Date:	Blood Test 6 Date:
Haemoglobin								
White Blood Cell Count								
Neutrophils								
Platelets								
ALP								
ALT								
ESR								
CRP								

APPENDIX R. PRACTICE DOCUMENTS

PRACTICE NUMBER 1

	Last month's blood test results	This month's blood test results	Difference between the two results	Are these results outside of the normal range?	Has there been a significant change?	Do I need further advice?
Haemoglobin	*11.3*	10.0				
White Blood Cell Count	*6.4*	4.8				
Neutrophils	*4.6*	4.3				
Platelets	*220*	305				
ALP	*88*	95				
ALT	*30*	35				
ESR	*25*	53				
CRP	*12*	12				

Instructions:

1. Calculate the change in blood test results between this month and last month

2. Using the Criteria for Patient Action sheet are the results within the normal range, has there been a significant change in the results

On the basis of these blood results do you need to speak with the Rheumatology Nurse Specialist?

Yes No

PRACTICE NUMBER 2

	Last month's blood test results	This month's blood test results	Difference between the two results	Are these results outside of the normal range?	Has there been a significant change?	Do I need further advice?
Haemoglobin	*10.4*	10.8				
White Blood Cell Count	*7.3*	8.2				
Neutrophils	*4.2*	4.2				
Platelets	*235*	260				
ALP	*65*	220				
ALT	*39*	126				
ESR	*19*	22				
CRP	*4.0*	5.0				

Instructions:

1. Calculate the change in blood test results between this month and last month

2. Using the Criteria for Patient Action sheet are the results within the normal range, has there been a significant change in the results

PRACTICE NUMBER 3

	Last month's blood test results	This month's blood test results	Difference between the two results	Are these results outside of the normal range?	Has there been a significant change?	Do I need further advice?
Haemoglobin	*12.0*	12.5				
White Blood Cell Count	*7.6*	8.0				
Neutrophils	*5.9*	6.1				
Platelets	*355*	320				
ALP	*50*	43				
ALT	*40*	32				
ESR	*12*	15				
CRP	*2.0*	2.3				

Instructions:

1. Calculate the change in blood test results between this month and last month

2. Using the Criteria for Patient Action sheet are the results within the normal range, has there been a significant change in the results

PRACTICE NUMBER 4

	Last month's blood test results	This month's blood test results	Difference between the two results	Are these results outside of the normal range?	Has there been a significant change?	Do I need further advice?
Haemoglobin	*11.0*	10.2				
White Blood Cell Count	*7.0*	8.1				
Neutrophils	*4.2*	4.5				
Platelets	*235*	460				
ALP	*65*	70				
ALT	*39*	52				
ESR	*19*	55				
CRP	*4.0*	25				

Instructions:

1. Calculate the change in blood test results between this month and last month

2. Using the Criteria for Patient Action sheet are the results within the normal range, has there been a significant change in the results

APPENDIX S. SAMPLE BLOOD TEST RESULTS

	31st January	2nd April	Difference between the two results	Are these results outside of the normal range?	Has there been a significant change?	Do I need further advice?
Haemoglobin	15.7	**14.2**				
White Blood Cell Count	6.34	**6.20**				
Neutrophil	2.90	**3.19**				
Platelets	275	**265**				
ALP	62	**54**				
ALT	31	**48**				
ESR	31	**4**				
CRP	5.7	**6.3**				

Instructions:

1. Calculate the change in blood test results between this month and last month

2. Using the **Criteria for Patient Action** sheet are the results within the normal range and has there been a significant change in the results

3. Complete the questionnaire overleaf

On the basis of these blood results do you need to speak with the Rheumatology Nurse Specialist?

Yes No

Please tick whether you have experienced any of these symptoms or side effects since you last blood test.

If you have please indicate whether this is a new symptom or side effect. If it is something you have experienced before please indicate whether it has got worse, better or remained the same.

Symptom (side effect)	Yes	No	New	Worse	Better	Same
Morning stiffness						
Pain						
Fatigue						

Symptom (side effect)	Yes	No	New	Worse	Better	Same
Nausea						
Vomiting						
Diarrhoea						
Mouth Ulcers						
Skin problems						
Bruising						
Joint swelling						
Bleeding						
Sore throat						
Fever						

Symptom (side effect)	Yes	No	New	Worse	Better	Same
Breathlessness						
Dry cough						
Hair loss						
Chicken pox/shingles						

On the basis of these symptoms do you need to speak with the Rheumatology Nurse Specialist?

Yes No

Are there any other reasons why you think you may need to speak with the Rheumatology Nurse Specialist?

Yes **No**

If yes, please give brief details:

Have you seen your GP regarding your arthritis or its treatment since your last blood test?

Yes No

If yes, how many times and please give reasons why:

Please contact the Researcher or your Clinical Nurse Specialist if any of the following has happened;

- Any of your blood test results are **out of range**
- Any of your blood test results have **significantly changed** since your last blood test
- You have experienced a **new symptom or side effect** since your last blood test
- A symptom or side effect you have experience before has **become worse** since your last blood test

If none of the above has happened there is no need to contact us, unless there is something else that you need to discuss.

APPENDIX T. MISSING DATA

Variable	% of missing data	Variable	% of missing data
T3 DAS28	48.44	BT4 ALT	10.00
T3 PsARC physician	43.48	BT4 CRP	10.00
T3 PsARC patient	43.48	BT6 Hb	9.20
T3 PsARC tender	39.13	BT6 Neutrophils	9.20
T3 PsARC swollen	39.13	BT6 Platelets	9.20
T1 MCS final	30.00	BT6 ESR	9.20
T1 PCS final	30.00	BT5 Hb	8.99
BT7 Hb	20.00	BT5 Neutrophils	8.99
BT7 Neutrophils	20.00	BT5 Platelets	8.99
BT7 Platelets	20.00	BT5 CRP	8.99
T1 PsARC patient	17.24	BT4 ESR	8.89
T1 DAS28	16.90	T3 Knowledge Total	8.86
BT3 ESR	14.58	BT3 ALT	8.33
T3 MCS final	13.92	BT3 CRP	8.33
T3 PCS final	13.92	BT2 ALP	8.16
T1 PsARC physician	13.79	BT2 ALT	8.16
T1 PsARC swollen	13.79	BT2 ESR	8.16
T1 PsARC tender	13.79	BT6 WCC	8.05
T1 Knowledge Total	12.00	BT5 ALP	7.87
BT1 ESR	12.00	BT5 ESR	7.87
T2 Knowledge Total	11.90	BT4 ALP	7.78
T2 MCS final	10.71	BT3 Hb	7.29
T2 PCS final	10.71	BT3 WCC	7.29
BT2 CRP	10.20	BT3 Neutrophils	7.29
BT5 ALT	10.11	BT3 Platelets	7.29
BT1 ALT	10.00	BT3 ALP	7.29
T2 IPQ PC	7.14	BT4 Platelets	5.56
BT1 CRP	7.14	T3 HAQ Total	5.06

Variable	% of missing data	Variable	% of missing data
BT2 Hb	7.14	Years on MTX	5.00
BT2 WCC	7.14	T1 IPQ C	5.00
BT2 Neutrophils	7.14	T2 IPQ TC v2	4.76
BT2 Platelets	7.14	T2 IPQ IC	4.76
BT1 Hb	7.00	T2 HADS anxiety	4.76
BT1 WCC	7.00	T2 HAQ Total	4.76
BT1 Neutrophils	7.00	T3 Fatigue	3.80
BT1 Platelets	7.00	T3 Pain	3.80
BT1 ALP	7.00	T2 Burden	3.57
BT6 ALP	6.90	T2 IPQ C	3.57
BT6 ALT	6.90	Disease duration	3.00
BT6 CRP	6.90	T1 IPQ IC	3.00
BT5 WCC	6.74	T1 SE Total	3.00
T1 IPQ PC	6.00	T3 Burden	2.53
T1 HAQ Total	6.00	T3 IPQ C	2.53
PreBT Hb	6.00	T2 Fatigue	2.38
PreBT WCC	6.00	T2 Pain	2.38
PreBT Neutrophils	6.00	T2 BMQ Concern v2	2.38
PreBT Platelets	6.00	T2 SE Total	2.38
PreBT ALP	6.00	T1 Fatigue	2.00
PreBT ALT	6.00	T1 Pain	2.00
PreBT ESR	6.00	T1 IPQ TC V2	2.00
PreBT CRP	6.00	T1 BMQ Necessity	2.00
BT4 Hb	5.56	T1 HADS depression	2.00
BT4 WCC	5.56	T3 IPQ IC	1.27
BT4 Neutrophils	5.56	T3 BMQ Concern v2	1.27
T3 BMQ Necessity	1.27	Cimzia	0.00
T3 SE Total	1.27	Topical preparations	0.00
T2 BMQ Necessity	1.19	Amitriptyline	0.00

Variable	% of missing data	Variable	% of missing data
T2 HADS depression	1.19	Chondroitin	0.00
T2 SM	1.19	Steroids	0.00
T2 SMA	1.19	Raloxifene	0.00
T1 Burden	1.00	Codeine phosphate	0.00
T1 BMQ Concern v2	1.00	Maxepa	0.00
T1 HADS anxiety	1.00	Ranitidine	0.00
T1 SM	1.00	Fosamax	0.00
No. of comorbidities	0.00	Homeopathic remedy	0.00
Total no. of drugs	0.00	Salazopyrin	0.00
MTX dose	0.00	Chondroitin	0.00
Age	0.00	Piroxicam	0.00
T1 IPQ I	0.00	Meloxicam	0.00
T1 AC	0.00	Tramadol	0.00
T1 SMA	0.00	Strontium ranelate	0.00
Retinitis pigmentosa	0.00	Aspirin	0.00
Ulcerative colitis	0.00	Etanercept	0.00
Epilepsy	0.00	Hydroxychloroquine	0.00
Respiratory	0.00	Vitamin supplements	0.00
Hypertension	0.00	Finasteride	0.00
Hyperthyroidism	0.00	Humira	0.00
Hypercholesterolemia	0.00	Ferrous sulphate	0.00
Diabetes	0.00	Cocodamol	0.00
Osteoporosis	0.00	Adcal	0.00
Mental health	0.00	Bendroflumethiazide	0.00
Bisphosphonate	0.00	Levothyroxine	0.00
Fish oils	0.00	Simivastin	0.00
Omeprazole	0.00	Gliclazide	0.00
Enbrel	0.00	Glyceryl trinitrate	0.00
Diclofenac	0.00	Diprobase cream	0.00

Variable	% of missing data	Variable	% of missing data
Folic acid	0.00	Perindopril	0.00
Paracetamol	0.00	Atorvastatin	0.00
Gabapentin	0.00	Acrivastine	0.00
Adalimumab	0.00	Bisoprolol	0.00
Sulphasalazine	0.00	Montelukast	0.00
Prednisolone	0.00	Desloratadine	0.00
Naproxen	0.00	Leveitiarcetam	0.00
Ibuprofen	0.00	Chlorphenamine	0.00
Calcium	0.00	Nebrivlol	0.00
Pamidronate	0.00	Risperidone	0.00
Arthrotec	0.00	Aripiprazole	0.00
Glucosamine	0.00	Carbimazole	0.00
Alendronic acid	0.00	Citalopram	0.00
Lansoprazole	0.00	Felodipine	0.00
Codydramol	0.00	Inhalers	0.00
Amlodipine	0.00	Diagnosis	0.00
Ramipril	0.00	Gender	0.00
Metformin	0.00	Living status	0.00
Atenolol	0.00	Ethnicity	0.00
Fosinopril	0.00	T2 IPQ I	0.00
Warfarin	0.00	T2 AC	0.00
HRT	0.00	T3 IPQ I	0.00
T3 IPQ PC	0.00	T3 HADS anxiety	0.00
T3 IPQ TC v2	0.00	T3 HADS depression	0.00
T3 SM	0.00	BT8 Hb	0.00
T3 AC	0.00	BT8 WCC	0.00
T3 SMA	0.00	BT8 Neutrophils	0.00
BT7 WCC	0.00	BT8 Platelets	0.00
BT7 ALP	0.00	BT8 ALP	0.00

Variable	% of missing data	Variable	% of missing data
BT7 ALT	0.00	BT8 ALT	0.00
BT7 ESR	0.00	BT8 ESR	0.00
BT7 CRP	0.00	BT8 CRP	0.00
Total % of missing data	**3.65%**		

APPENDIX U. DIFFERENCES BETWEEN COMPLETE CASES AND NON-COMPLETE CASES

Variable	Completed n=79	Non-completed n=21	Statistic
No. of years on MTX, median(range)	4(1-20)	3.70(1-20)	U=753.50, z=-0.65, *p*=0.52, *r*=-0.06
Total no. of medications, median(range)	4(1-11)	5(2-8)	U=811.50, z=-0.15, *p*=0.88, *r*=-0.02
Dose of MTX, median(range)	15(5-25)	15(7.5-20)	U=747.00, z=-0.71, *p*=0.48, *r*=-0.07
DAS28, mean(SD)	3.41(1.36)	3.13(1.01)	t(69)=0.75, *p*=0.53, □□=0.01
PsARC physician global assessment, median(range)	2(0.82-3.20)	2.16(1-3.51)	U=59.50, z=-0.55, *p*=0.62, *r*=-0.05
PsARC patient global assessment, median(range)	1.41(0.92-3)	1.95(1.01-3.06)	U=43.70, z=-1.43, *p*=0.23, *r*=-0.14
PsARC swollen joint count, median(range)	1.48(0-9.25)	3.89(0-13)	U=44.00, z=-1.36, *p*=0.21, *r*=-0.14
PsARC tender joint count, mean(SD)	8.52(7.33)	10.90(6.11)	t(27)= -0.71, *p*=0.54, □□=0.01
Age, mean(SD)	58.30(12.11)	50.71(8.46)	t(27)= 2.70, *p*=0.01, □□=0.07
Disease duration in years, median(range)	8.50(1-54)	4(1-35)	U=621.40, z=-1.77, *p*=0.08, *r*=-0.18
Fatigue, mean(SD)	4.11(2.63)	4.86(2.77)	t(98)=-1.14, *p*=0.26, □□□□=0.01
Pain, median(range)	3(0-9)	3.50(0-8)	U=759.10, z=-0.60, *p*=0.55, *r*=-0.06
Treatment burden, median(range)	2(1-5)	2(1-4)	U=764.40, z=-0.58, *p*=0.57, *r*=-0.06
IPQ Illness identity, mean(SD)	5.11(2.10)	5.48(3.01)	t(98)=25.40, *p*=060, □□<0.001
IPQ Consequences, mean(SD)	20.04(4.73)	19.24(4.44)	t(98)=0.70, *p*=0.48, □□<0.001
IPQ Personal control, mean(SD)	20.96(4.36)	20.46(3.68)	t(98)=0.49, *p*=0.63, □□<0.001

Variable	Completed n=79	Non-completed n=21	Statistic
IPQ Treatment control, mean(SD)	16.01(2.11)	15.10(2.49)	t(98)=11.69, *p*=0.09, η^2=0.03
IPQ Illness Coherence, mean(SD)	18.64(4.28)	19.05(4.70)	t(98)=-0.38, *p*=0.71, η^2<0.001
BMQ Specific concern, mean(SD)	11.92(2.78)	13.85(2.90)	t(98)=-2.80, *p*=0.01, η^2=0.07
BMQ Specific necessity, mean(SD)	16.71(3.08)	16.41(2.41)	t(98)=0.41, *p*=0.68, η^2<0.001
Generalised self-efficacy, mean(SD)	31.41(3.66)	33.28(3.94)	t(98)=-2.05, *p*=0.04, η^2=0.04
Anxiety, median(range)	5(0-17)	6(2-15)	U=783.20, z=-0.39, *p*=0.69, *r*=-0.04
Depression, median(range)	3(0-12)	4.50(0-11)	U=751.85, z=-0.66, *p*=0.51, *r*=-0.07
Knowledge, mean(SD)	18.01(4.83)	18.74(4.46)	t(98)=-0.63, *p*=0.53, η^2<0.001
Functional disability, median(range)	0.49(0-2.20)	0.23(0-1.91)	U=698.35, z=-1.12, *p*=0.29, *r*=-0.11
HeiQ Self-monitoring & insight, mean(SD)	3.09(0.42)	3.00(0.41)	t(98)=0.89, *p*=0.39, η^2=0.01
MeiQ Active Communication, median(range)	5(1-6)	5.5(2.75-6)	U=784.00, z=-0.40, *p*=0.69, *r*=-0.04
MeiQ Self-management ability, median(range)	4.83(2.50-6)	4.83(3.33-6)	U=744.50, z=-0.72, *p*=0.47, *r*=-0.07
SF-12v1® MCS, mean(SD)	30.78(5.68)	30.49(4.97)	t(98)=0.21, *p*=0.83, η^2<0.001
SF-12v1® PCS, mean(SD)	45.95(9.64)	46.10(8.52)	t(98)=-0.07, *p*=0.95, η^2<0.001

APPENDIX V. CRONBACH'S ALPHAS

Variable	Number of items	Baseline	First f/u	Final f/u
Functional disability	10	0.92	0.92	0.92
Anxiety	7	0.85	0.83	0.86
Depression	7	0.80	0.80	0.77
Generalised self-efficacy	10	0.87	0.94	0.93
HeiQ™ Self-monitoring & insight	6	0.78	0.79	0.80
MeiQ™ Active Communication	4	0.93	0.89	0.95
MeiQ™ Self-management ability	6	0.87	0.85	0.85
IPQ Consequences	6	0.84	0.85	0.86
IPQ Illness Coherence	5	0.92	0.90	0.92
IPQ Personal control	6	0.86	0.82	0.86
IPQ Treatment Control	5	0.48	0.57	0.54
BMQ Specific Necessity	5	0.76	0.85	0.75
BMQ Specific Concern	5	0.63	0.68	0.7
Knowledge	60	0.72	0.80	0.76

f/u – follow-up

APPENDIX W. CHANGES OVER TIME ON CLINICAL, PSYCHOSOCIAL OUTCOME AND PROCESS VARIABLES IN COMPLETE CASES ONLY

Variable	Trial arm	Baseline Mean(SD)	First f/u Mean(SD)	Final f/u Mean(SD)	Group	Time	Time*Group
Fatigue	Intervention	4.20(2.98)	4.56(2.99)	4.37(3.00)	$F_{1,76.28} = 0.19$, $p=0.67$	$F_{2,102.22} = 0.87$, $p=0.42$	$F_{2,102.22} = 0.52$, $p=0.60$
	Control	3.94(3.08)	4.11(3.08)	4.37(3.10)			
Pain	Intervention	3.65(2.68)	3.57(2.71)	3.69(2.68)	$F_{1,77.34} < 0.001$, $p=0.98$	$F_{2,147.62} = 0.44$, $p=0.64$	$F_{2,147.62} = 0.54$, $p=0.59$
	Control	3.36(2.76)	3.86(2.76)	3.72(2.81)			
Functional disability	Intervention	0.64(0.68)	0.60(0.68)	0.60(0.68)	$F_{1,75.06} = 0.21$, $p=0.65$	$F_{2,98.23} = 0.08$, $p=0.92$	$F_{2,98.23} = 1.32$, $p=0.27$
	Control	0.64(0.69)	0.70(0.69)	0.68(0.69)			

Variable	Trial arm	Baseline Mean(SD)	First f/u Mean(SD)	Final f/u Mean(SD)	Group	Time	Time*Group
SF-12v1® MCS	Intervention	30.51(8.30)	29.35(8.14)	31.03(8.19)	$F_{1,73.40} = 0.08$, $p=0.78$	$F_{2,74.65} = 0.77$, $p=0.47$	$F_{2,74.65} = 1.33$, $p=0.27$
	Control	30.37(9.42)	29.92(8.25)	29.39(8.60)			
SF-12v1® PCS	Intervention	46.26(12.69)	45.92(12.56)	44.75(12.57)	$F_{1,74.89} = 0.09$, $p=0.76$	$F_{2,87.40} = 0.07$, $p=0.93$	$F_{2,87.40} = 0.78$, $p=0.46$
	Control	44.68(14.10)	44.69(12.78)	45.45(13.21)			
Anxiety	Intervention	5.50(4.71)	5.64(4.72)	4.86(4.70)	$F_{1,76.06} = 1.97$, $p=0.17$	$F_{2,100.11}= 0.87$, $p=0.42$	$F_{2,100.11} = 1.74$, $p=0.18$
	Control	6.42(4.87)	6.64(4.87)	6.75(4.87)			

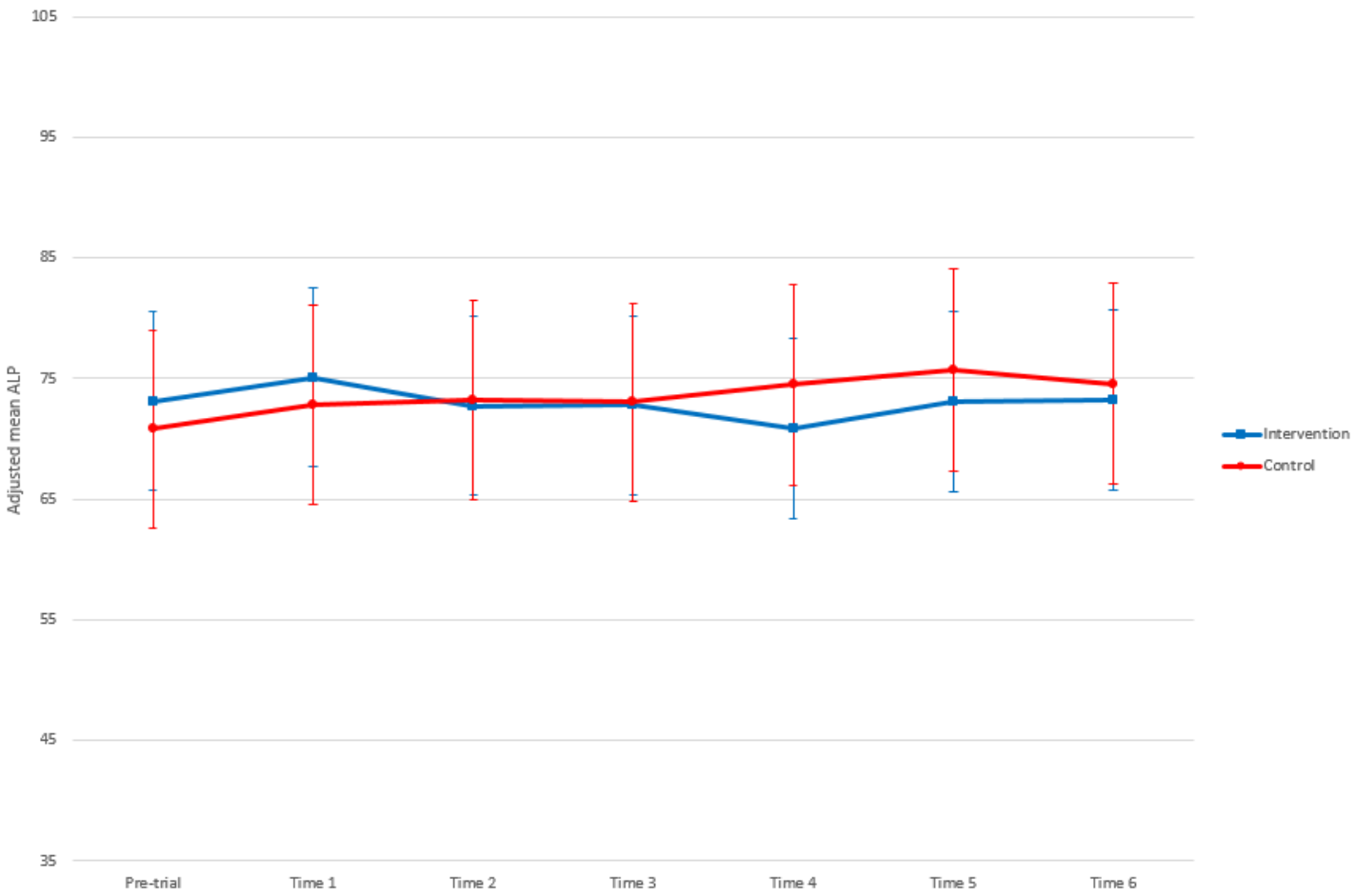
Variable	Trial arm	Baseline Mean(SD)	First f/u Mean(SD)	Final f/u Mean(SD)	Group	Time	Time*Group
Depression	Intervention	4.76(3.64)	4.56(3.64)	4.26(3.63)	$F_{1,76.03} = 0.64$, p=0.43	$F_{2,120.33} = 0.11$, p=0.90	$F_{2,120.33} = 1.23$, p=0.30
	Control	3.81(3.76)	4.03(3.76)	4.11(3.76)			
Generalised self-efficacy	Intervention	31.50(5.12)	31.45(5.17)	32.26(5.12)	$F_{1,73.77} = 1.13$, p=0.29	$F_{2,125.68}$= 0.22, p=0.81	$F_{2,125.68} = 1.76$, p=0.18
	Control	30.89(5.34)	30.81(5.32)	30.46(5.34)			
HeiQ™ self-monitoring & insight	Intervention	3.00(0.46)	3.07(0.46)	3.10(0.46)	$F_{176.54} = 2.70$, p=0.11	$F_{2,104.48} = 0.65$, p=0.52	$F_{2,104.48} = 1.98$, p=0.14
	Control	3.21(0.47)	3.22(0.47)	3.14(0.47)			

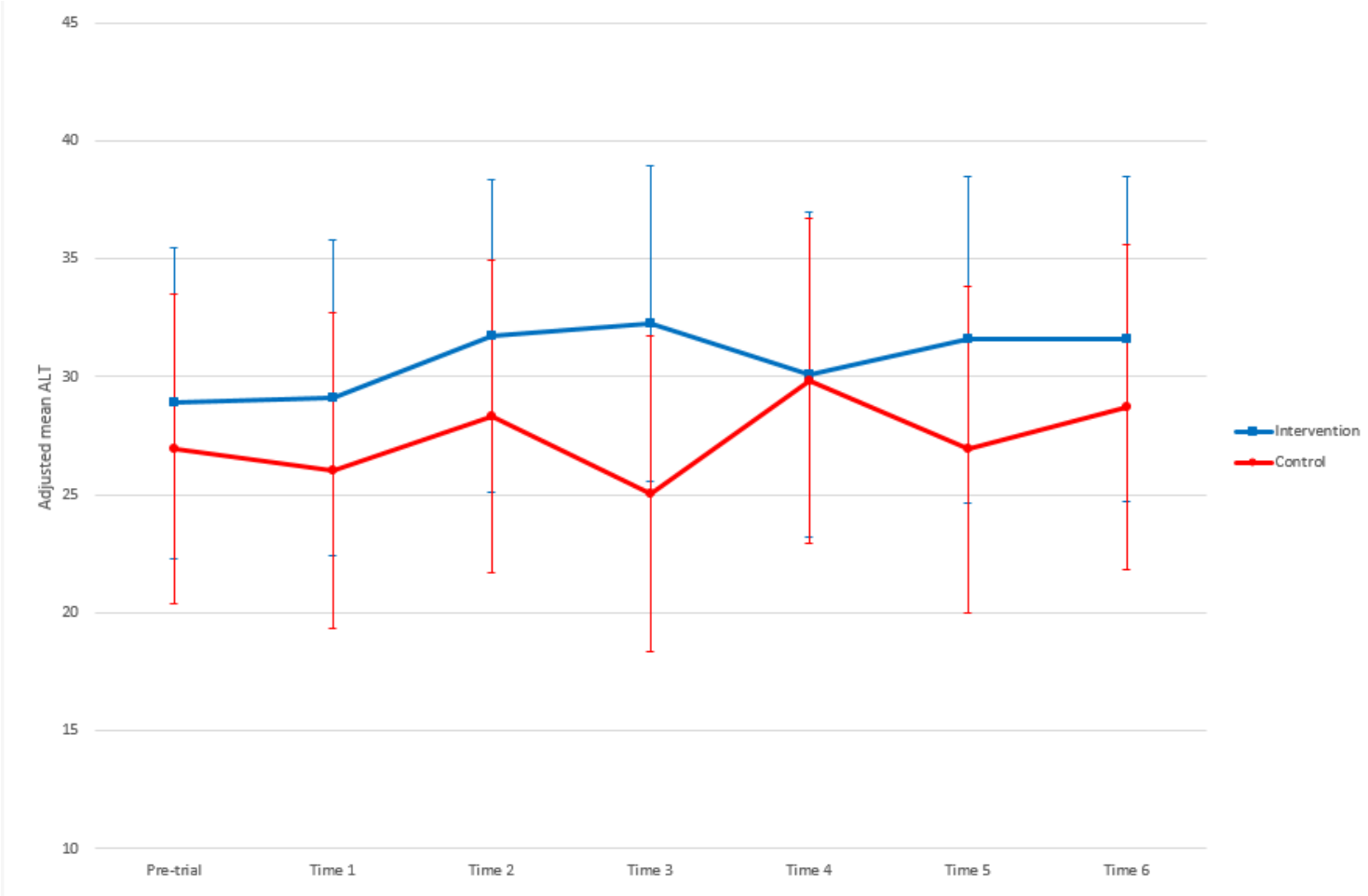
Variable	Trial arm	Baseline Mean(SD)	First f/u Mean(SD)	Final f/u Mean(SD)	Group	Time	Time*Group
MeiQ™ active communication	Intervention	5.26(0.75)	5.21(0.71)	5.14(0.91)	$F_{1,75.03} = 0.14$, $p=0.72$	$F_{2,105.36} = 0.20$, $p=0.82$	$F_{2,105.36} = 1.84$, $p=0.16$
	Control	5.02(1.03)	5.14(0.79)	5.13(0.91)			
MeiQ™ self-management ability	Intervention	4.68(0.85)	4.80(0.85)	4.81(0.85)	$F_{1,76.00} = 0.09$, $p=0.77$	$F_{2,117.97} = 0.76$, $p=0.47$	$F_{2,117.97} = 0.69$, $p=0.51$
	Control	4.81(0.89)	4.79(0.89)	4.84(0.89)			
IPQ-R Identity	Intervention	5.02(2.55)	4.48(2.55)	4.14(2.55)	$F_{1,75.91} = 2.87$, $p=0.09$	$F_{2,129.01}= 1.22$, $p=0.30$	$F_{2,129.01} = 2.24$, $p=0.11$
	Control	5.25(2.65)	5.17(2.65)	5.42(2.65)			
IPQ-R Consequences	Intervention	19.76(5.70)	18.90(5.70)	18.81(5.69)	$F_{1,75.91} = 0.86$, $p=0.36$	**$F_{2,105.86} = 4.04$, $p=0.02$**	$F_{2,105.86}= 0.08$, $p=0.92$
	Control	20.72(5.99)	20.07(5.99)	19.74(5.95)			

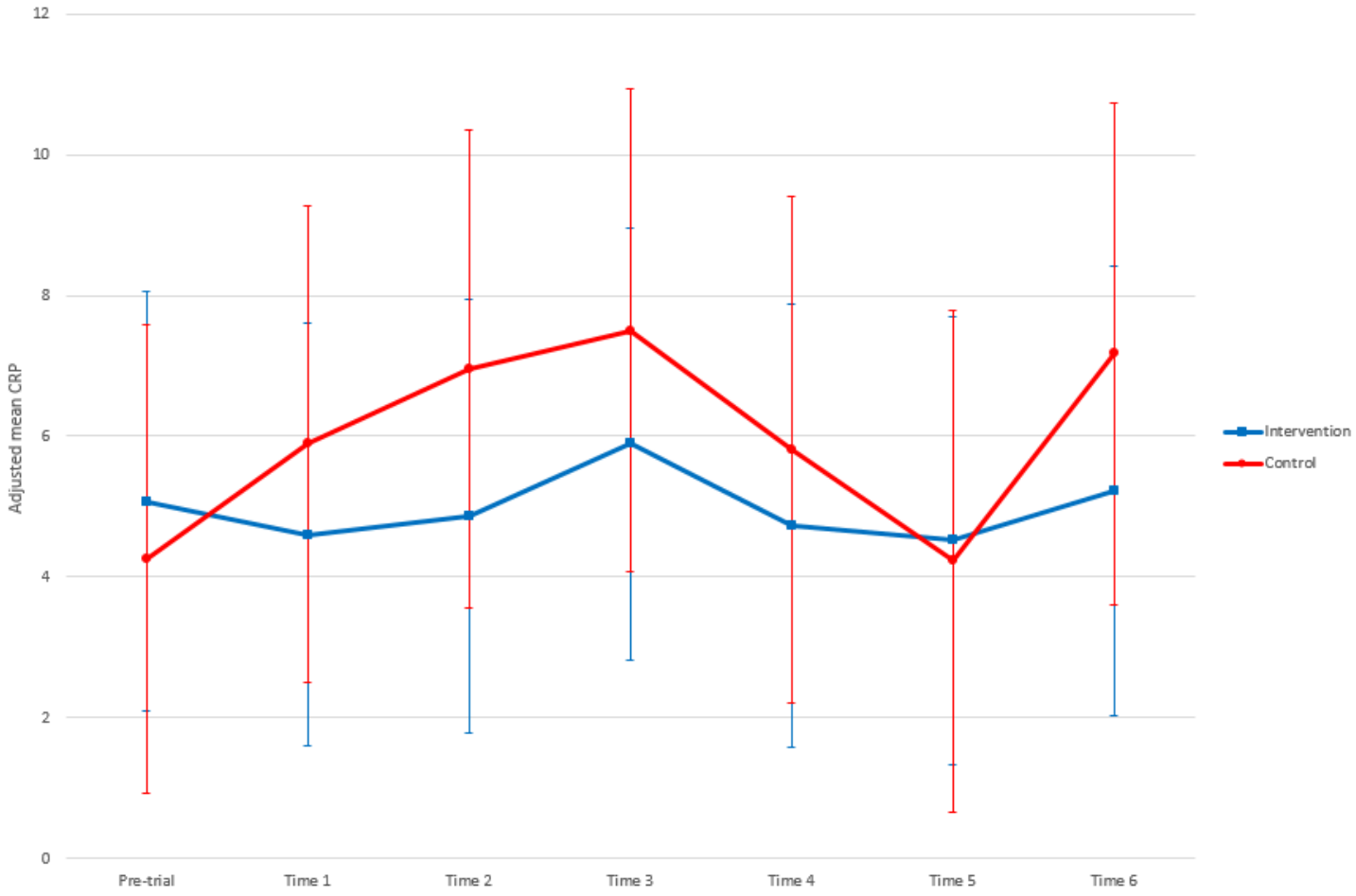
Variable	Trial arm	Baseline Mean(SD)	First f/u Mean(SD)	Final f/u Mean(SD)	Group	Time	Time*Group
IPQ-R Personal Control	Intervention	20.54(4.86)	21.23(4.85)	21.21(4.84)	$F_{1,76.38} = 1.00$, $p=0.32$	$F_{2,101.92} = 1.89$, $p=0.16$	$F_{2,101.92} = 0.01$, $p=0.99$
	Control	21.50(5.08)	22.08(5.12)	22.11(5.02)			
IPQ-R Treatment Control	Intervention	15.67 (2.46)	15.57(2.43)	16.02(2.04)	$F_{1,77.02} = 0.22$, $p=0.64$	$F2_{,102.24} = 0.90$, $p=0.41$	$F_{2,102.24} = 2.01$, $p=0.14$
	Control	16.36(2.51)	15.82(2.55)	15.64(2.51)			
IPQ-R Illness Coherence	Intervention	18.42(4.62)	19.60(4.63)	19.45(4.57)	$F_{1,76.20} = 0.58$, $p=0.45$	**$F_{2,98.68} = 3.42$, $p=0.04$**	$F_{2,98.68} = 2.33$, $p=0.10$
	Control	18.69(4.77)	19.09(4.76)	17.83(4.77)			
BMQ Concern	Intervention	11.67(3.32)	11.64(3.32)	11.12(3.32)	$F_{1,77.74} = 1.35$, $p=0.25$	$F_{2,95.47} = 1.12$, $p=0.33$	$F_{2,95.47} = 0.17$, $p=0.84$
	Control	12.31(3.44)	12.20(3.48)	11.99(3.47)			

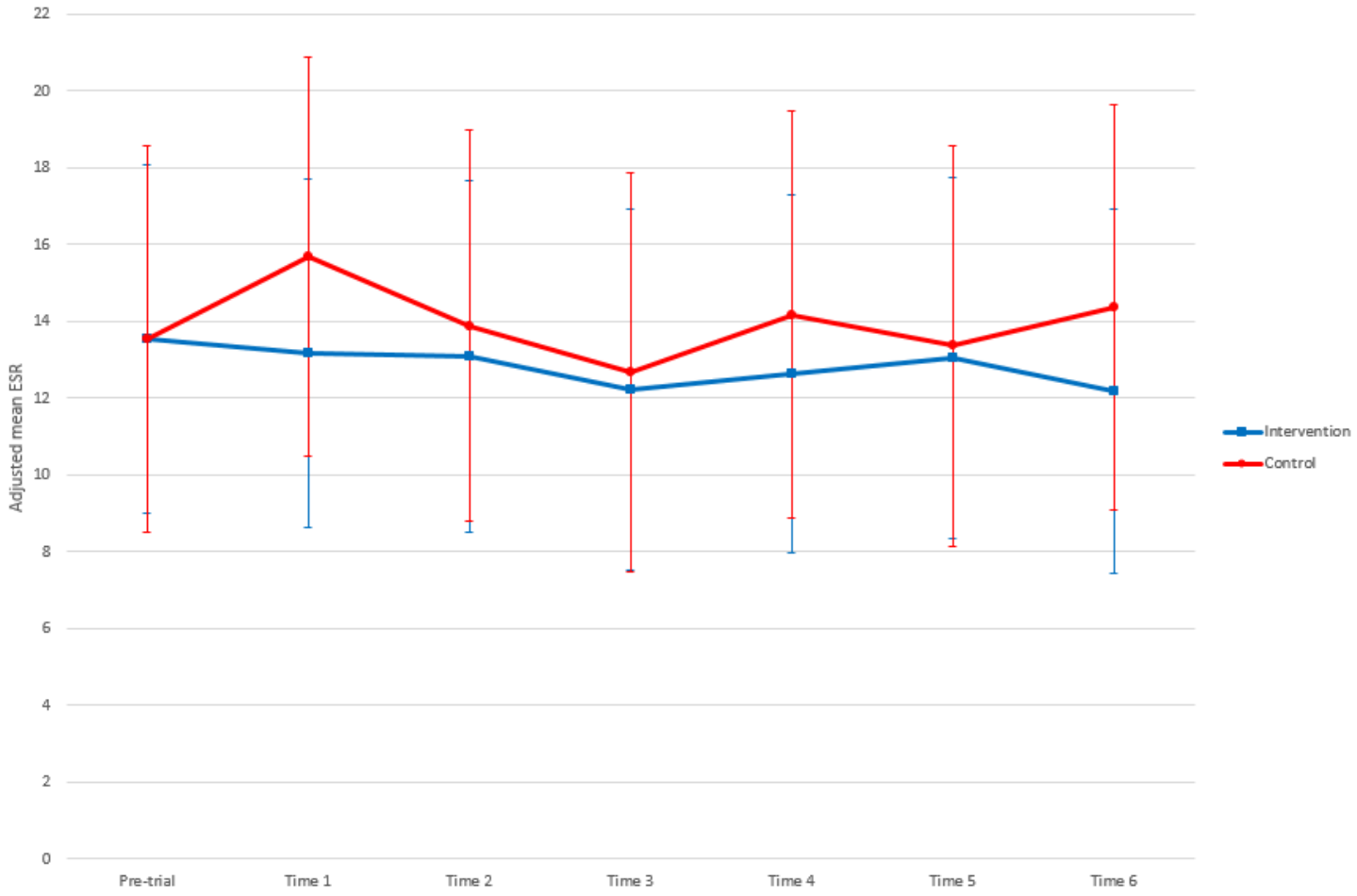
Variable	Trial arm	Baseline Mean(SD)	First f/u Mean(SD)	Final f/u Mean(SD)	Group	Time	Time*Group
BMQ Necessity	Intervention	16.21(3.39)	16.60(3.39)	16.69(3.39)	$F_{1,77.27} = 0.95$, p=0.33	$F_{2,96.71} = 0.48$, p=0.62	$F_{2,96.71} = 1.10$, p=0.34
	Control	17.25(3.52)	17.27(3.54)	16.74(3.54)			
Treatment burden	Intervention	2.19(1.12)	1.92(1.14)	2.05(1.12)	$F_{1,74.93} = 0.30$, p=0.59	$F_{2,128.85} = 1.58$, p=0.21	$F_{2,128.85} = 0.68$, p=0.51
	Control	2.00(1.16)	1.94(1.16)	1.89(1.17)			
Knowledge about methotrexate	Intervention	18.58(5.90)	19.89(5.87)	20.43(5.88)	$F_{1,7510} = 2.54$, p=0.12	**$F_{2,84.55} = 4.63$, p=0.01**	$F_{2,84.55} = 0.90$, p=0.41
	Control	17.45(6.33)	17.70(6.30)	18.39(6.29)			

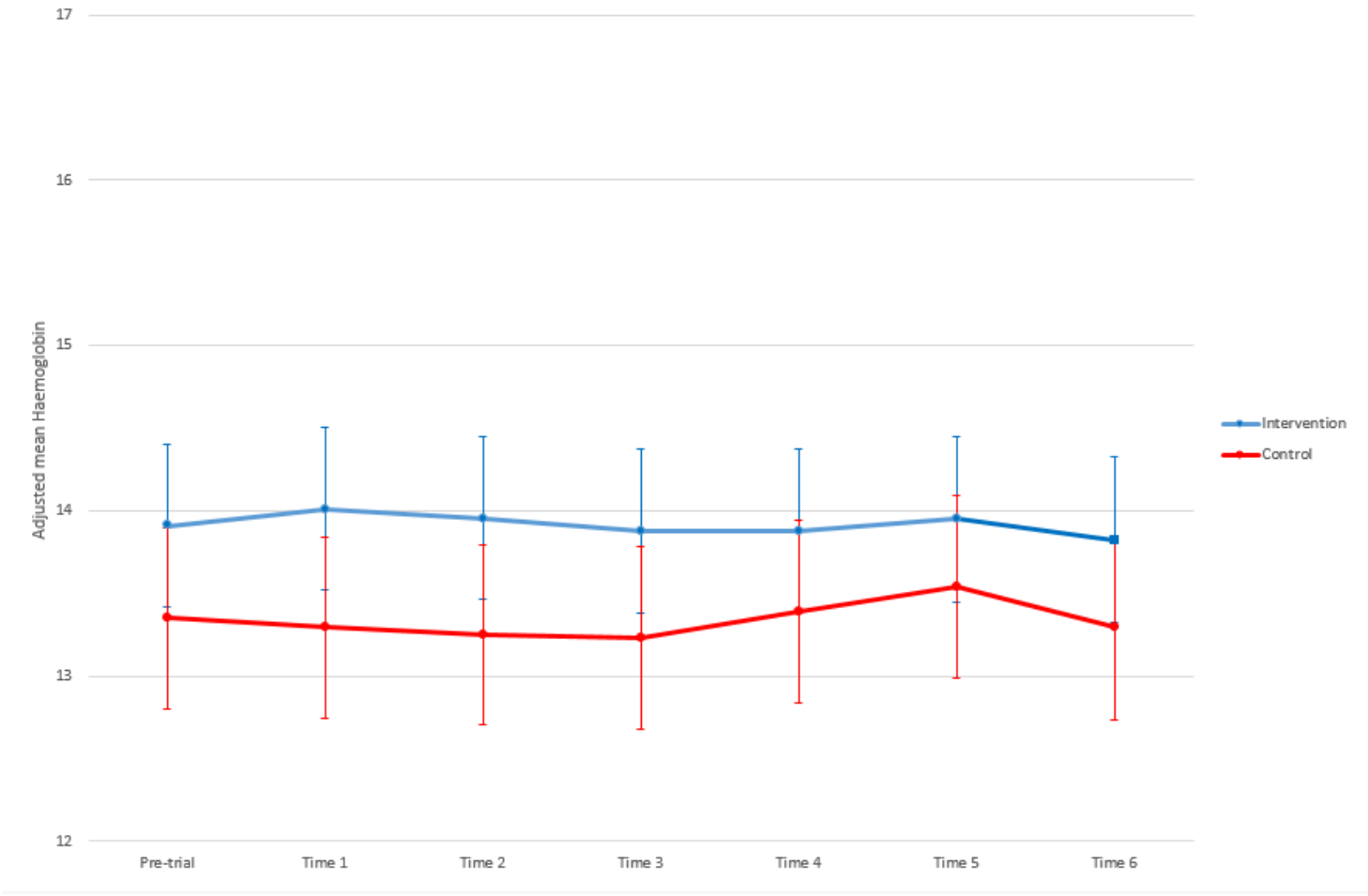
APPENDIX X. GRAPHICAL REPRESENTATION OF CHANGES OVER TIME (WITH 99% CI) ON CLINICAL VARIABLES (N=100)

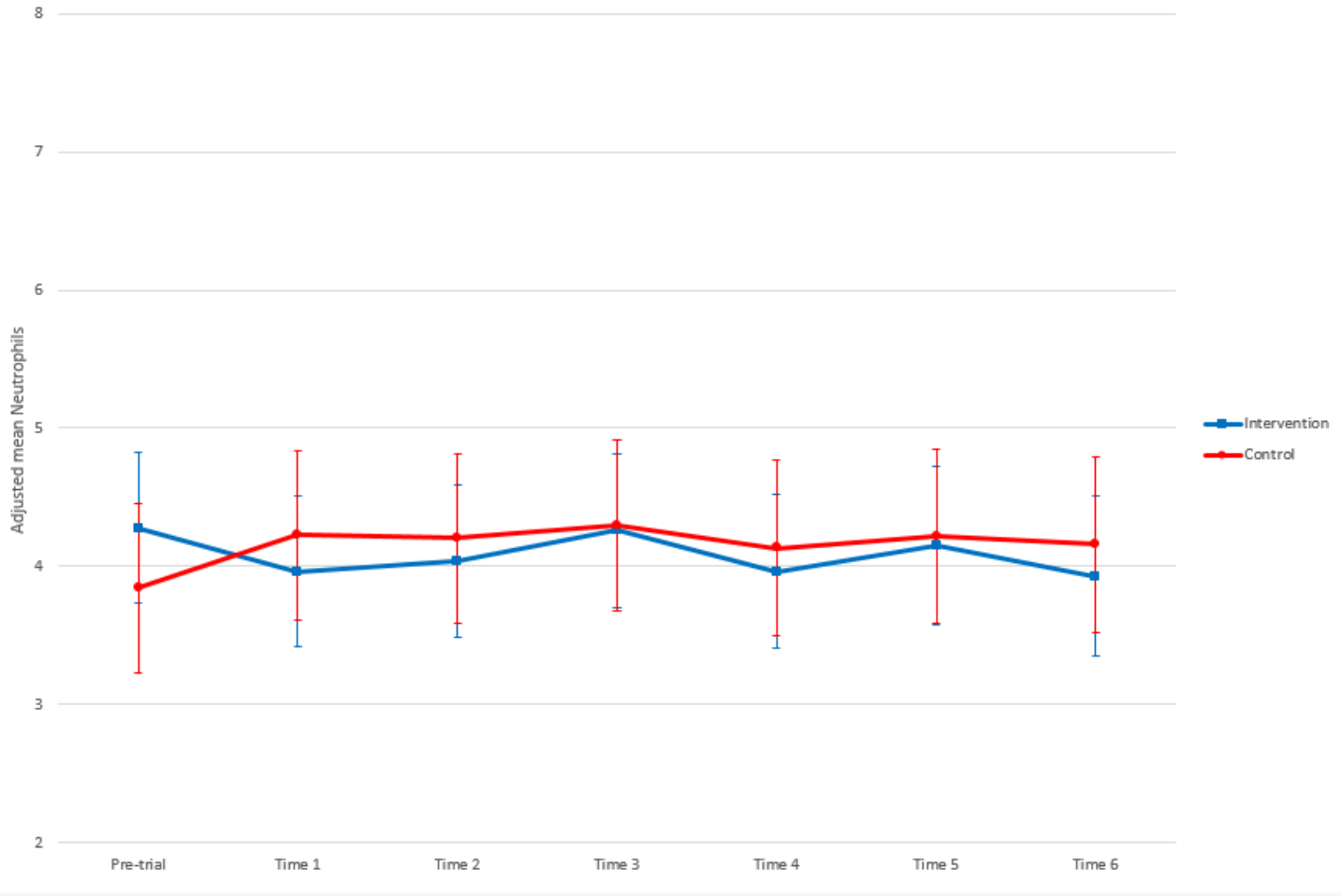


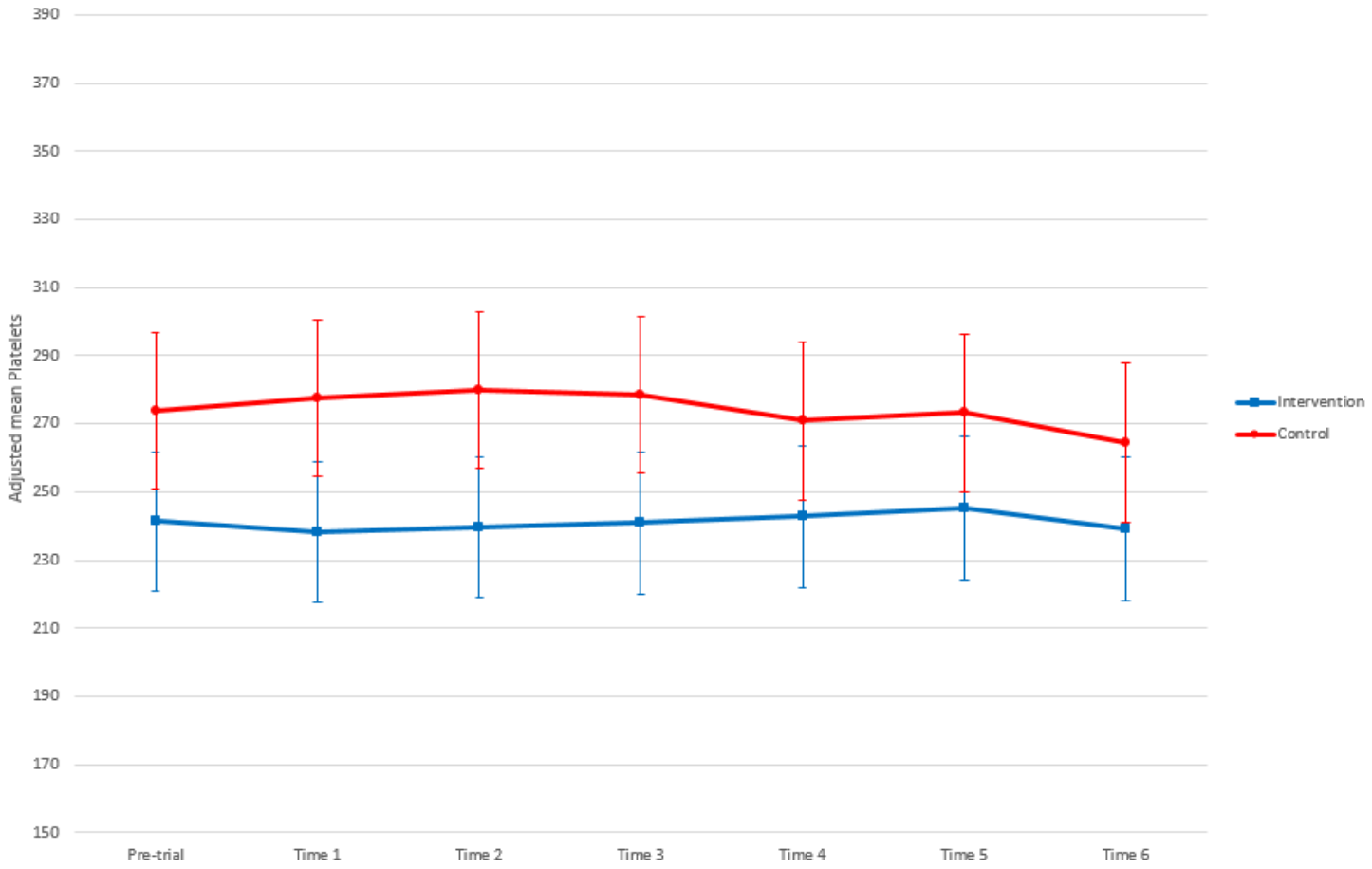

45
40
35
30
25
20
15
10
Adjusted mean ALT
Pre-trial
Time 1
Time 2
Time 3
Time 4
Time 5
Time 6
Intervention
Control

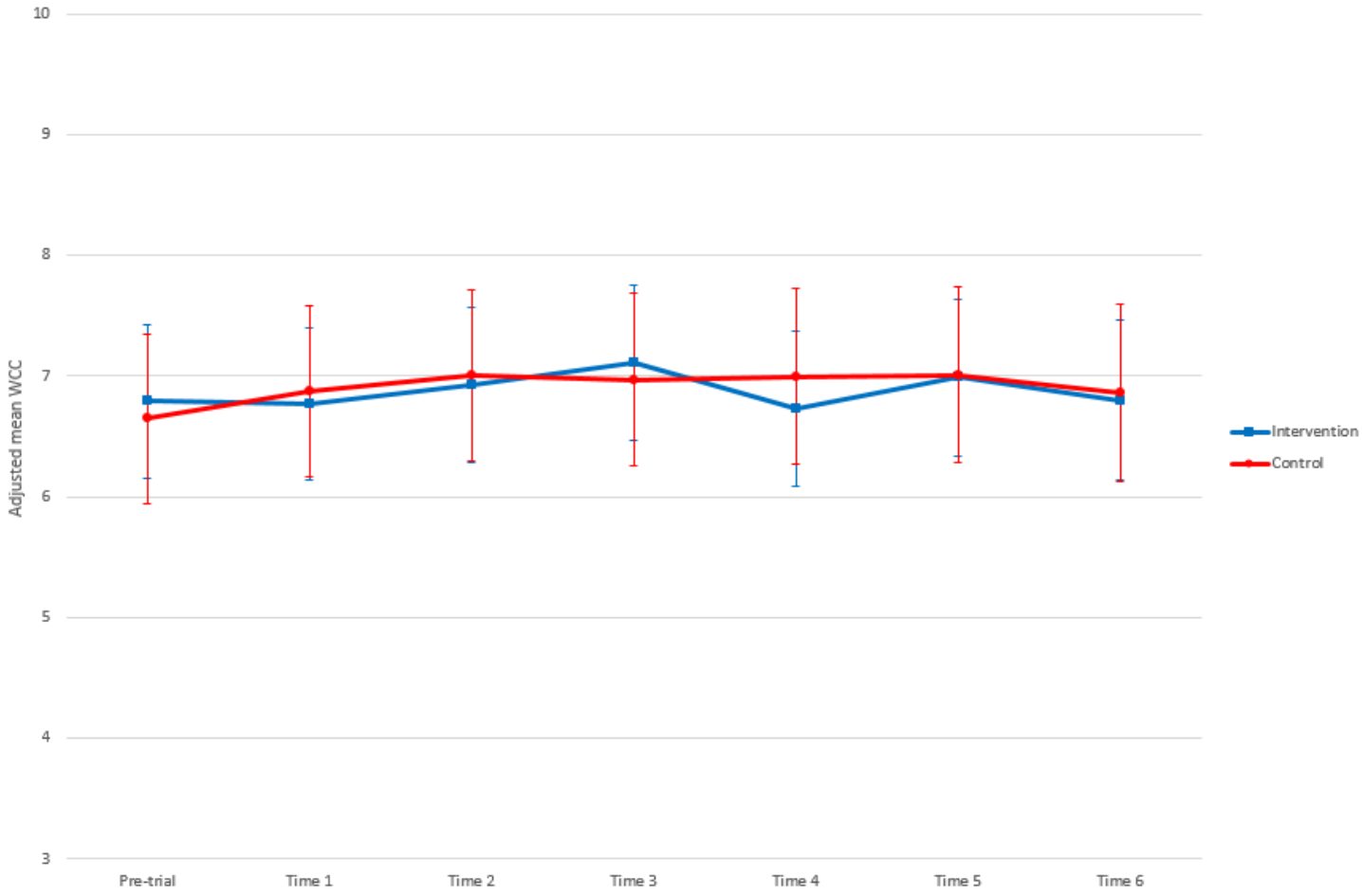

12
10
8
6
4
2
0
Adjusted mean CRP
Pre-trial
Time 1
Time 2
Time 3
Time 4
Time 5
Time 6
Intervention
Control

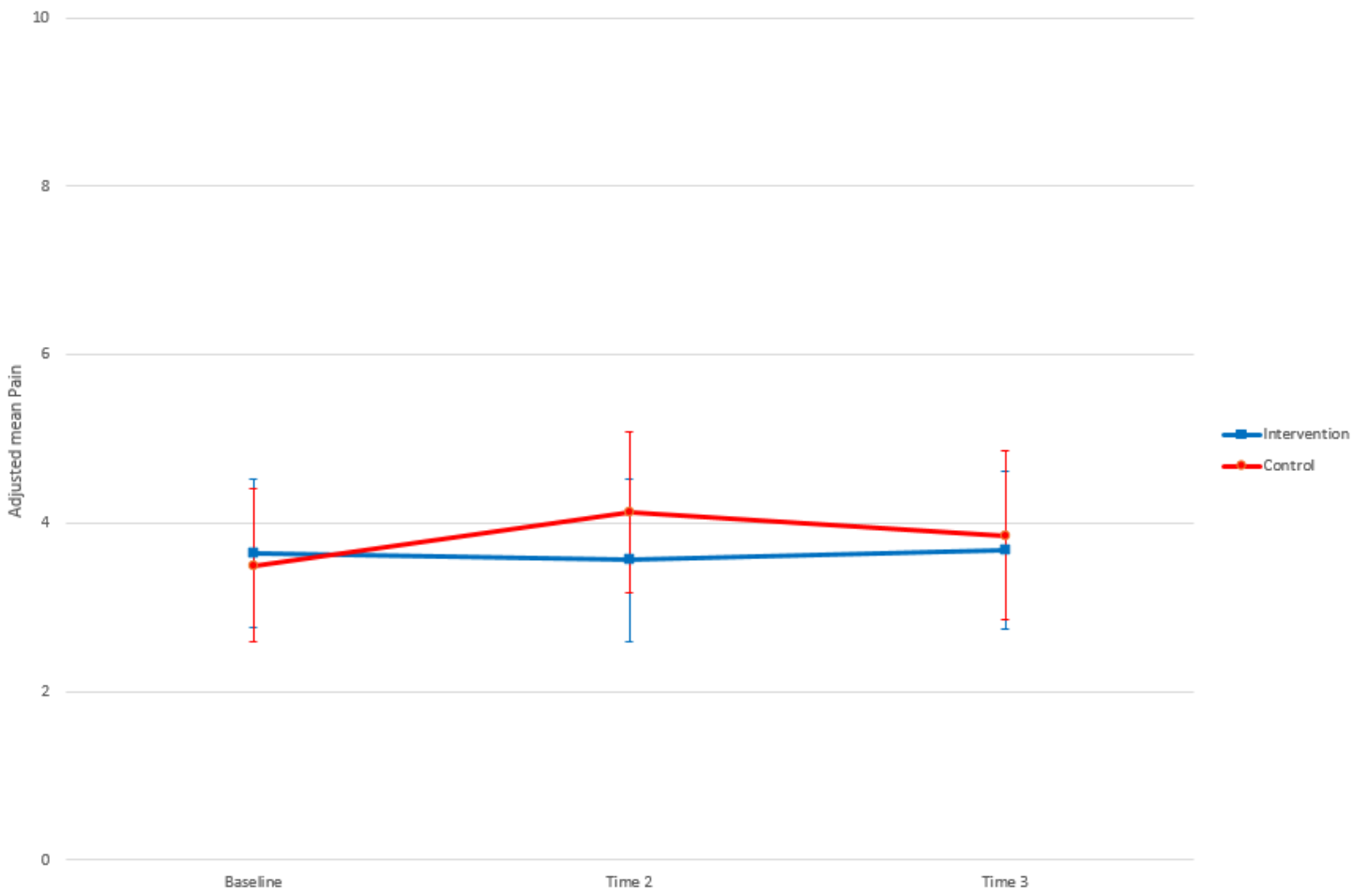

22
20
18
16
14
12
10
8
6
4
2
0
Adjusted mean ESR
Pre-trial
Time 1
Time 2
Time 3
Time 4
Time 5
Time 6
Intervention
Control

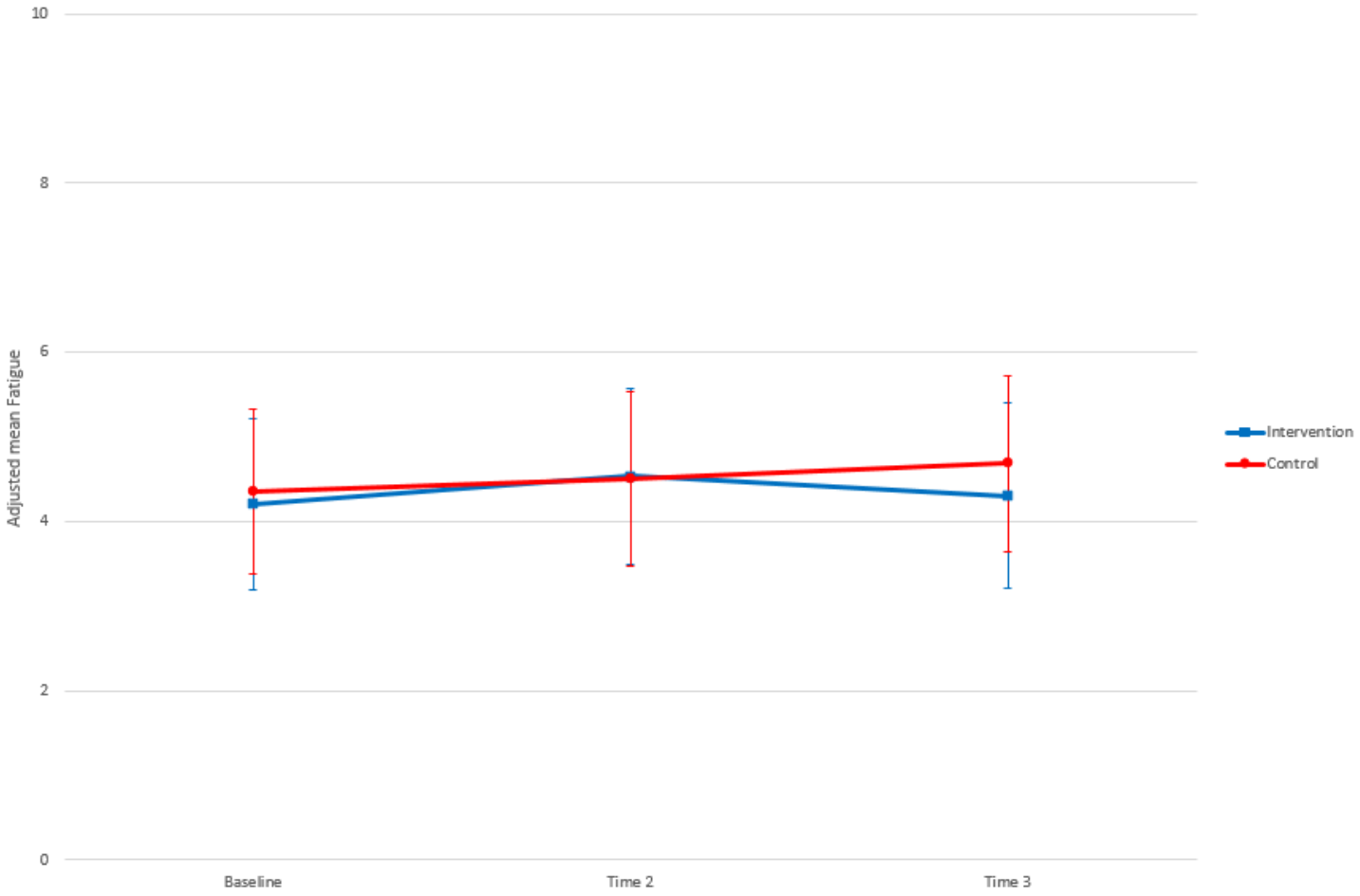

17
16
15
14
13
12
Adjusted mean Haemoglobin
Pre-trial
Time 1
Time 2
Time 3
Time 4
Time 5
Time 6
Intervention
Control

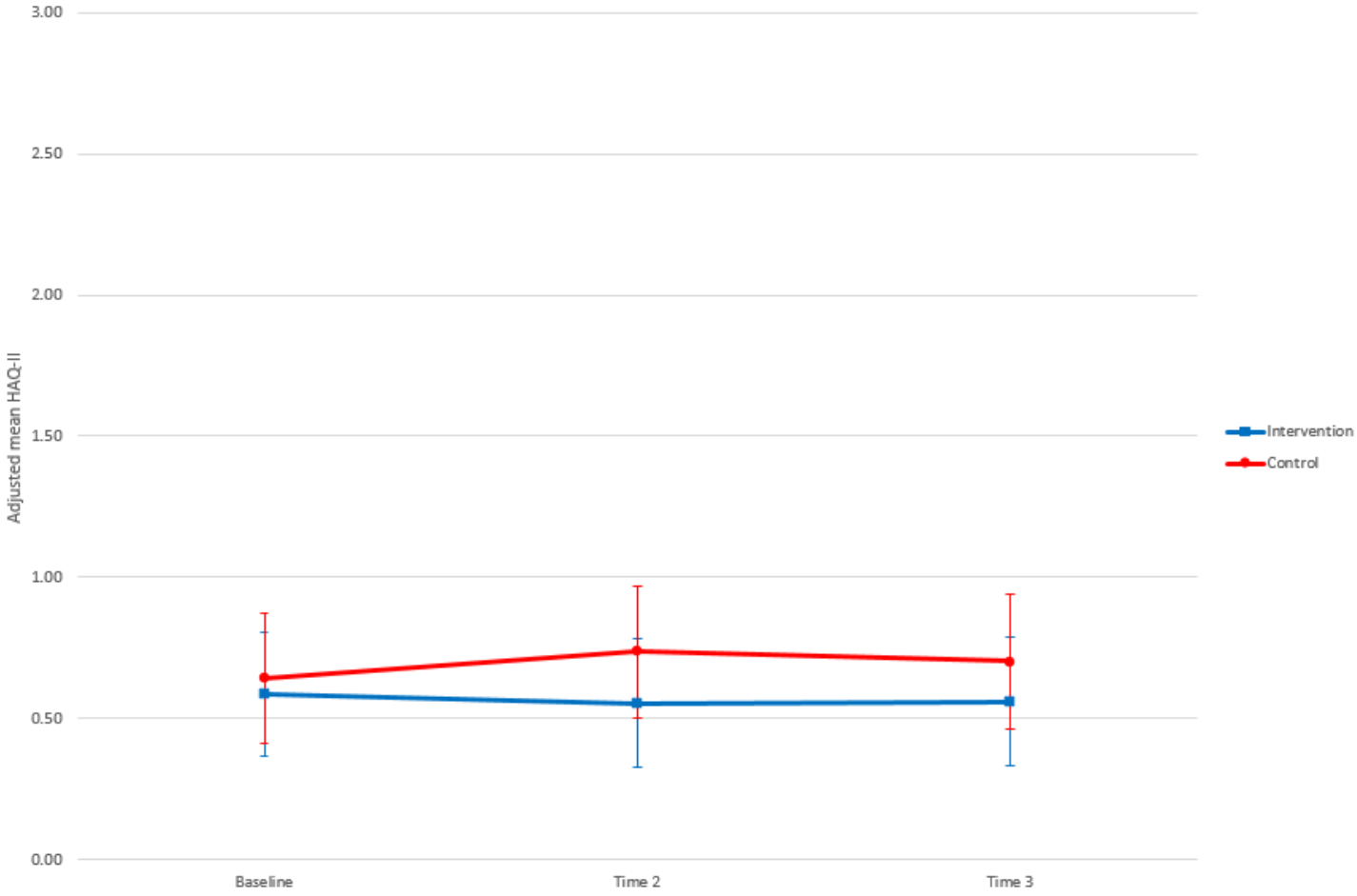

8
7
6
5
4
3
2
Adjusted mean Neutrophils
Pre-trial
Time 1
Time 2
Time 3
Time 4
Time 5
Time 6
Intervention
Control


390
370
350
330
310
290
270
250
230
210
190
170
150
Adjusted mean Platelets
Pre-trial
Time 1
Time 2
Time 3
Time 4
Time 5
Time 6
Intervention
Control

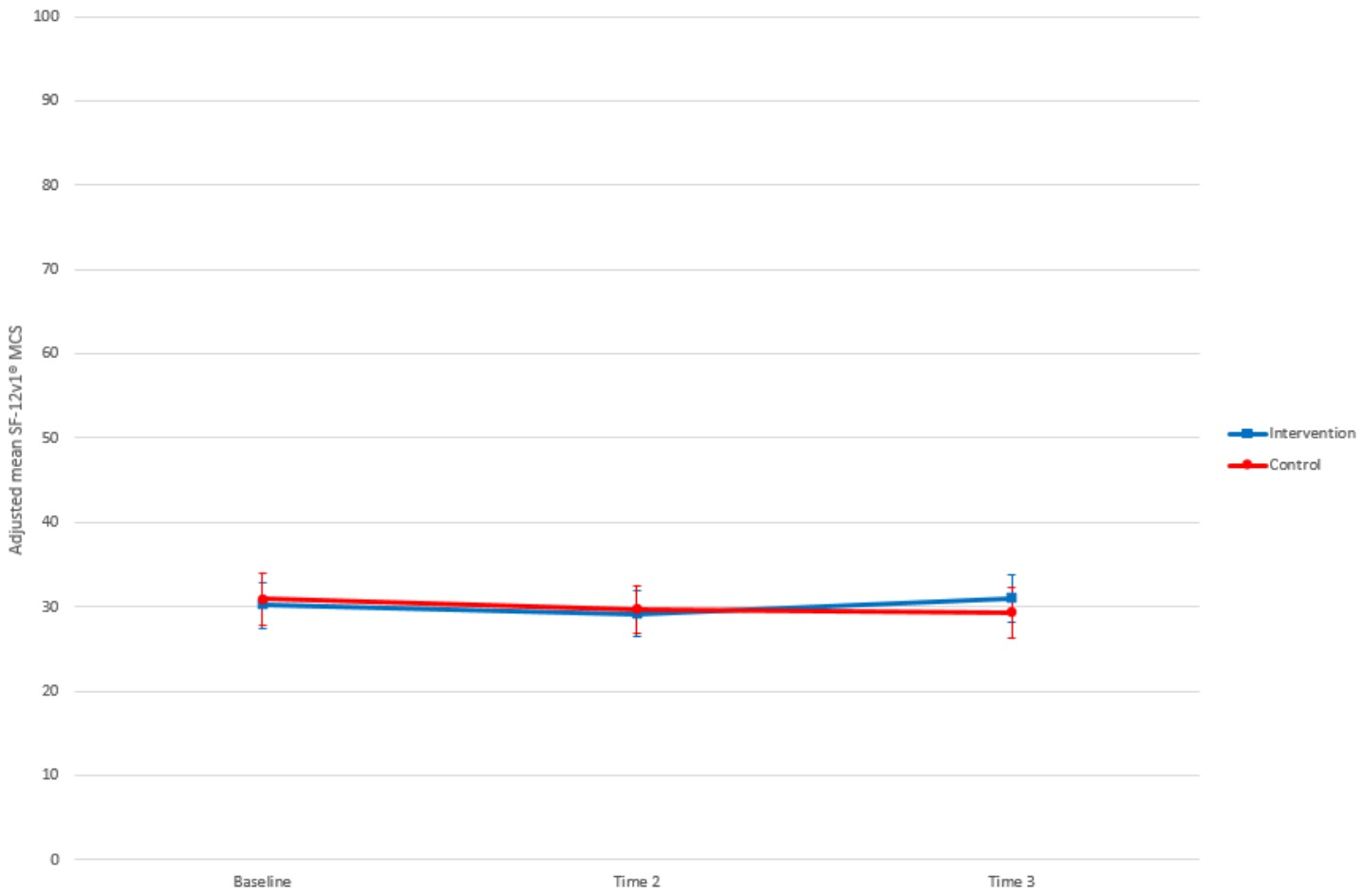

10
9
8
7
6
5
4
3
Adjusted mean WCC
Pre-trial
Time 1
Time 2
Time 3
Time 4
Time 5
Time 6
Intervention
Control

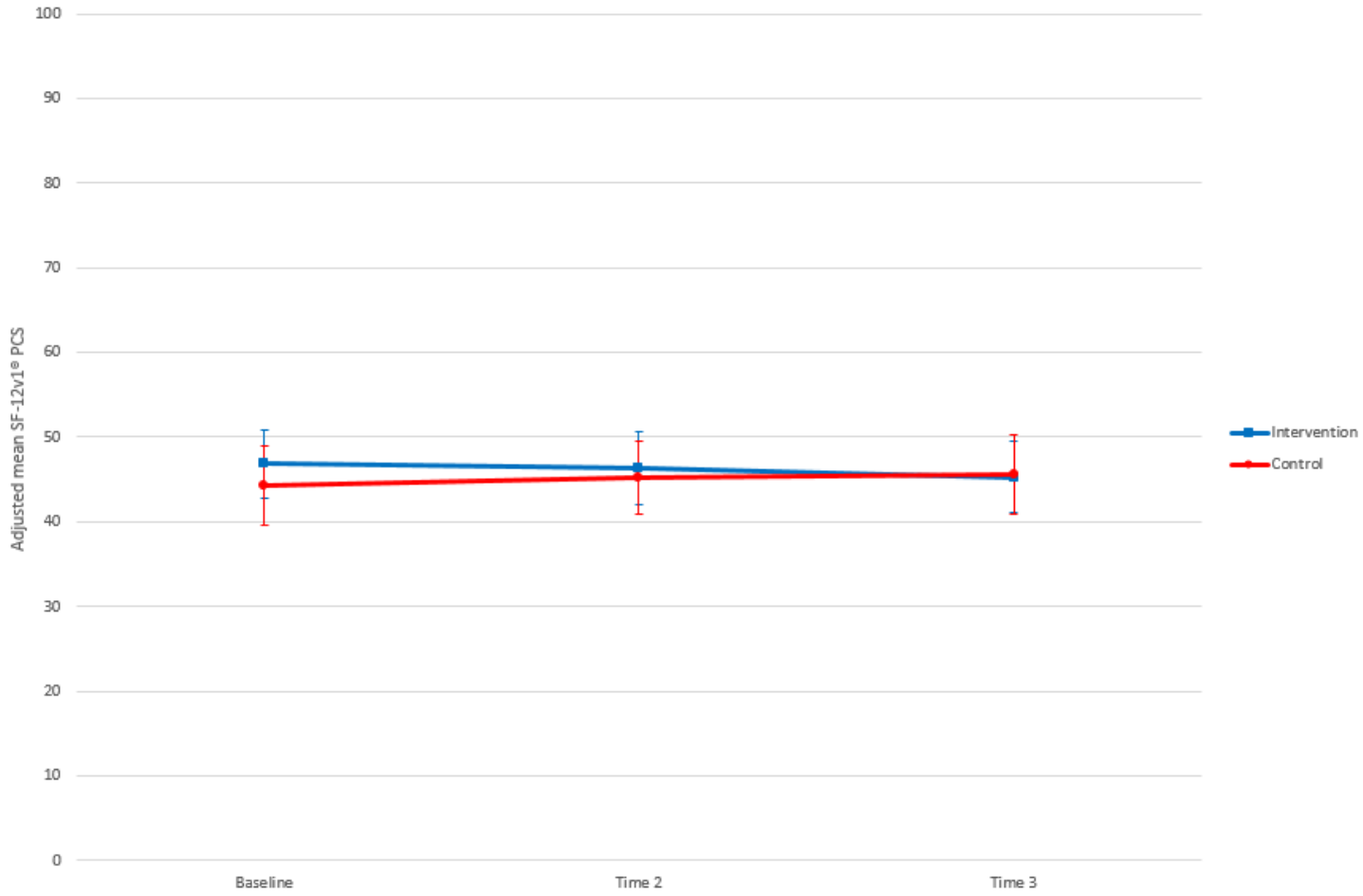

10
8
6
4
2
0
Adjusted mean Pain
Baseline
Time 2
Time 3
Intervention
Control

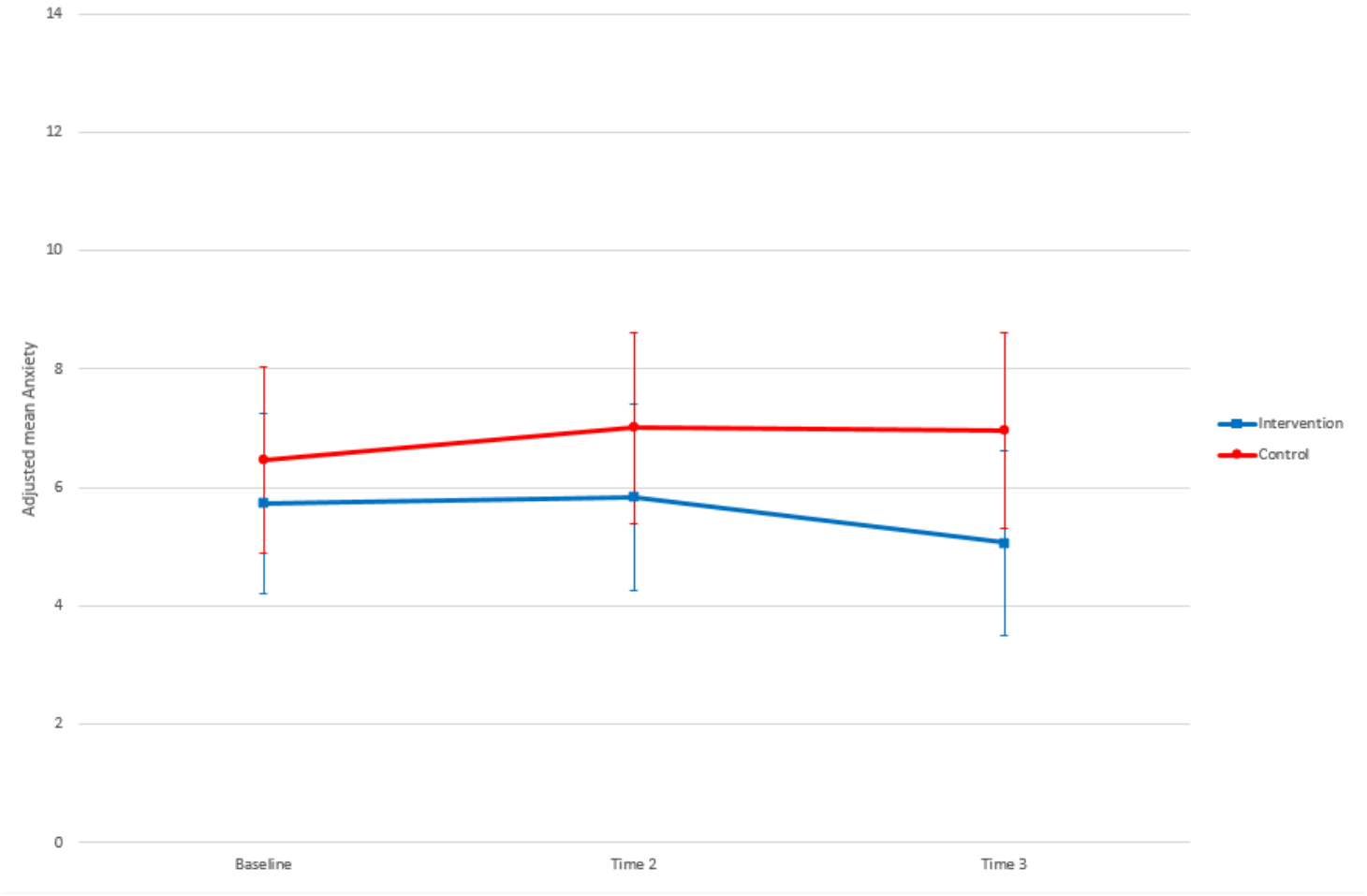

10
8
6
4
2
0
Adjusted mean Fatigue
Baseline
Time 2
Time 3
Intervention
Control

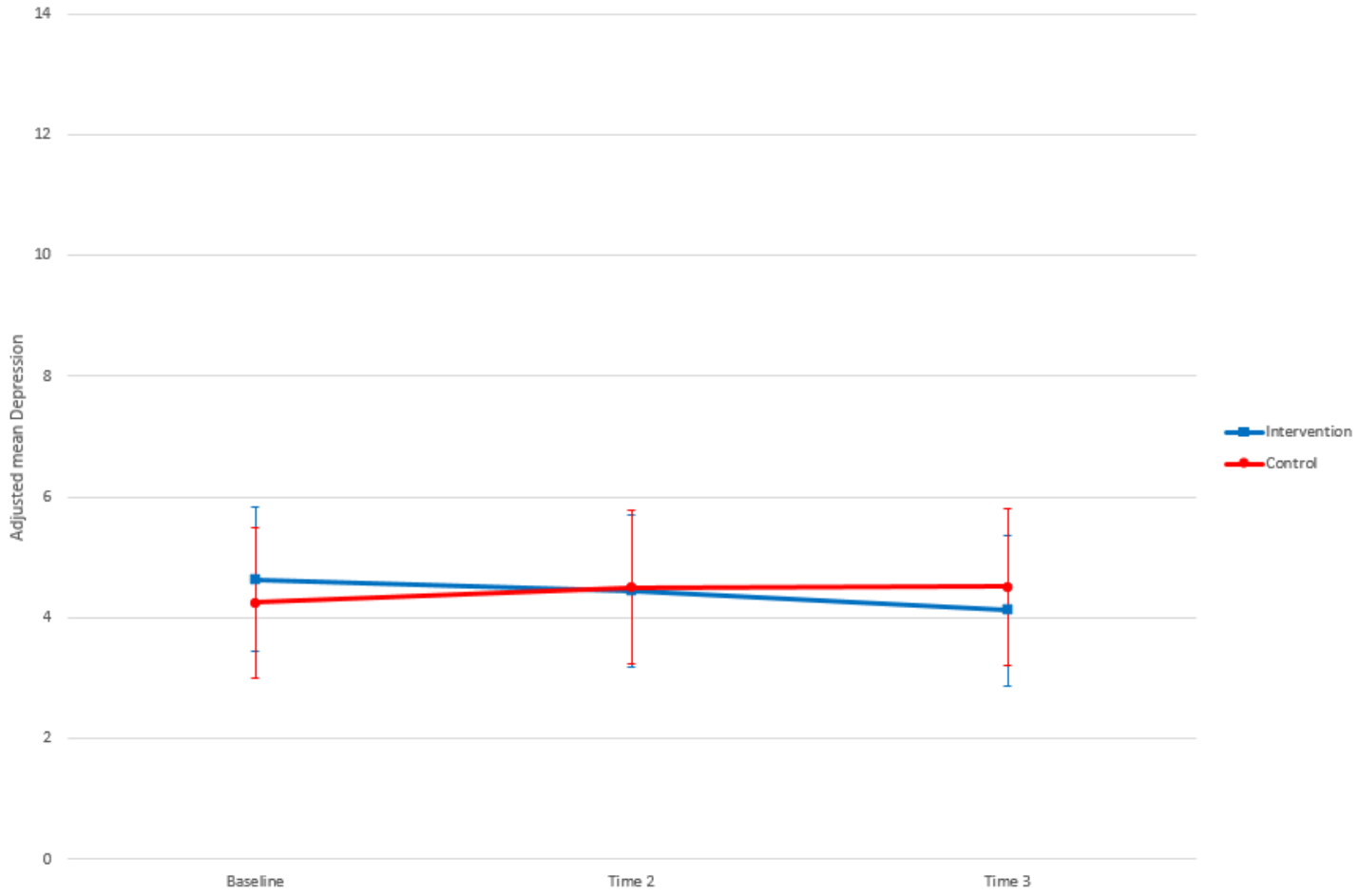

3.00
2.50
2.00
1.50
1.00
0.50
0.00
Adjusted mean HAQ-II
Baseline
Time 2
Time 3
Intervention
Control

APPENDIX Y. GRAPHICAL REPRESENTATION OF CHANGES OVER TIME (WITH 99% CI) ON THE PSYCHOSOCIAL OUTCOME VARIABLES (N=100)

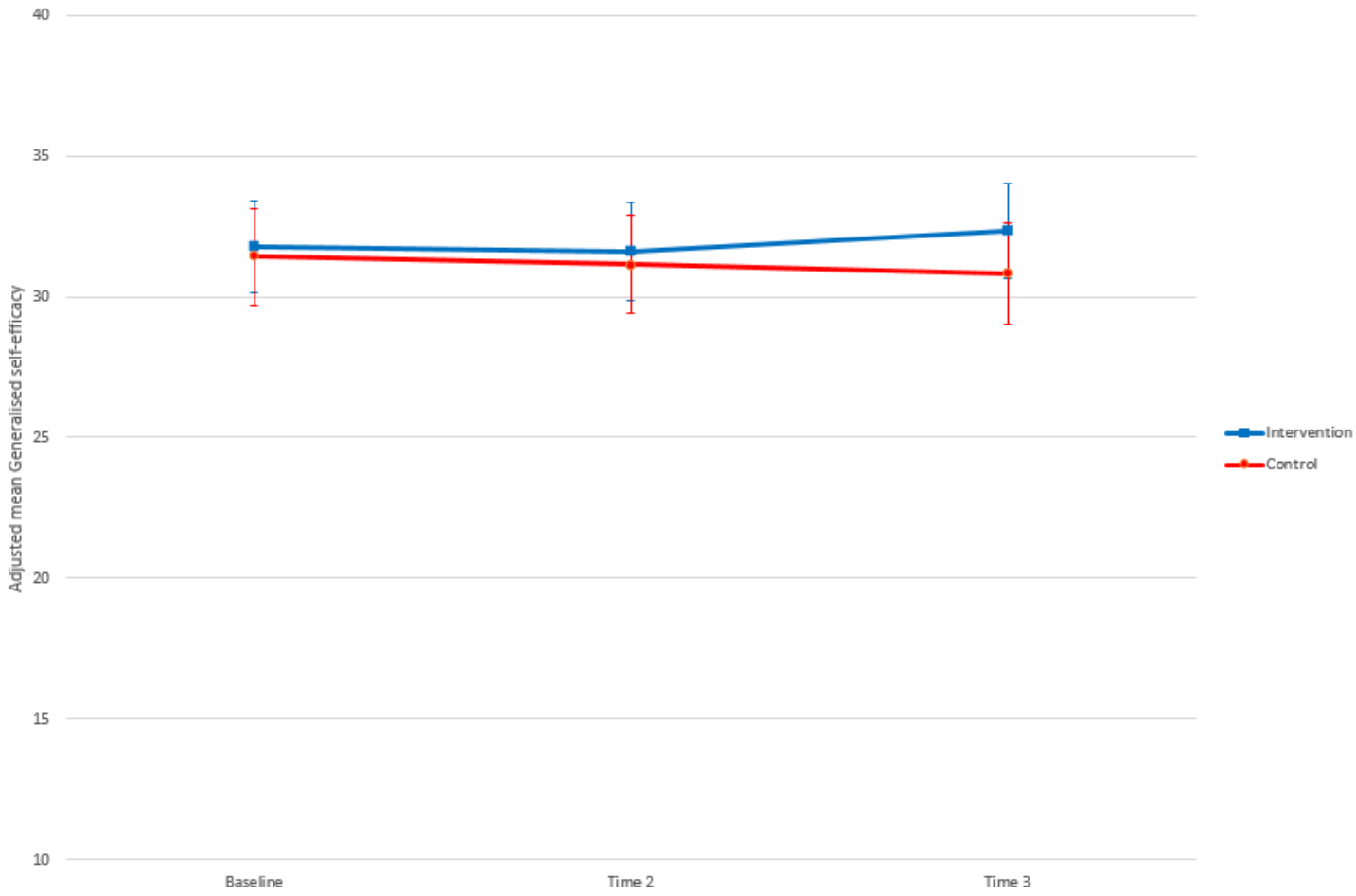


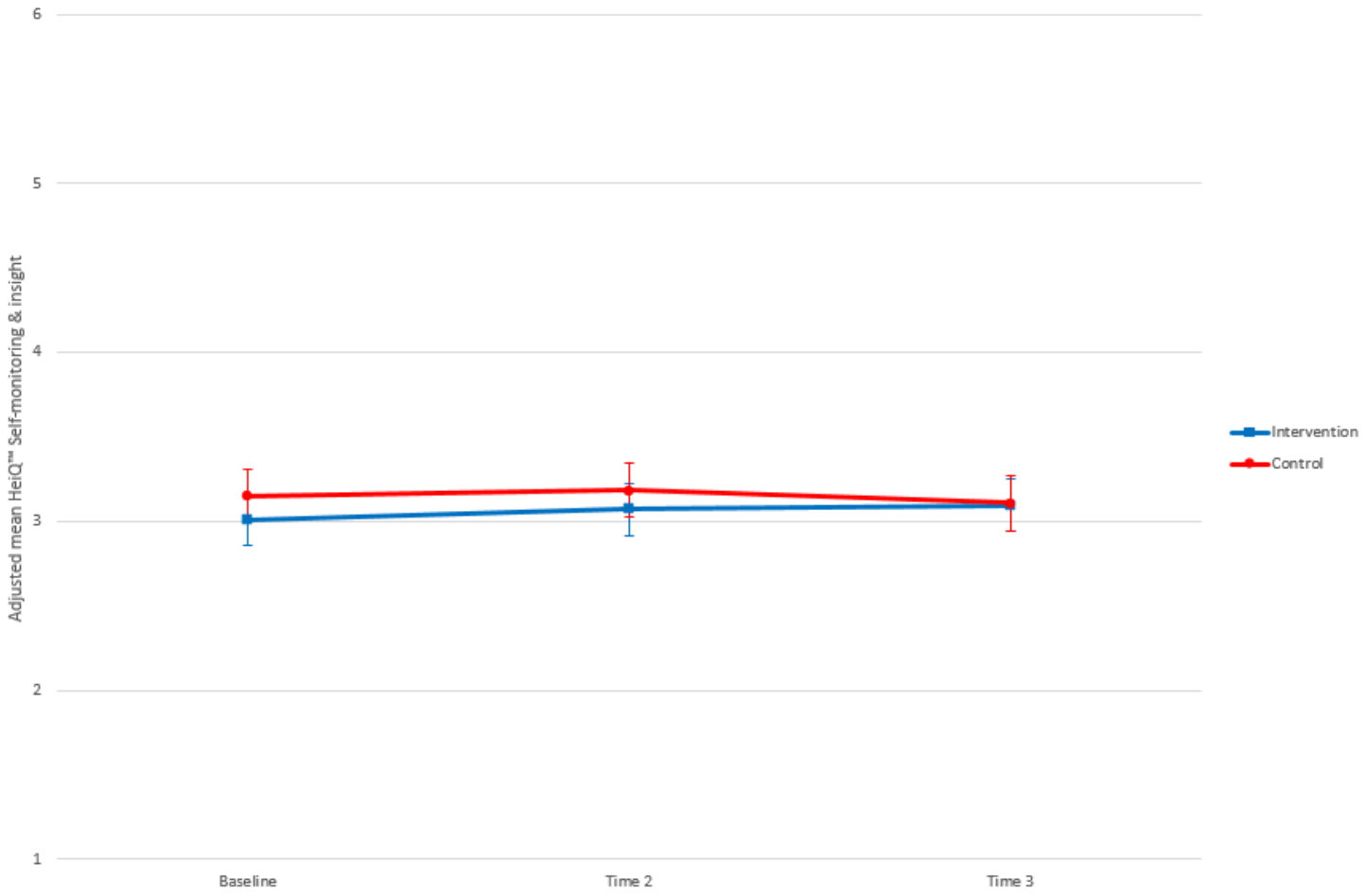

100
90
80
70
60
50
40
30
20
10
0
Adjusted mean SF-12v1® PCS
Baseline
Time 2
Time 3
Intervention
Control

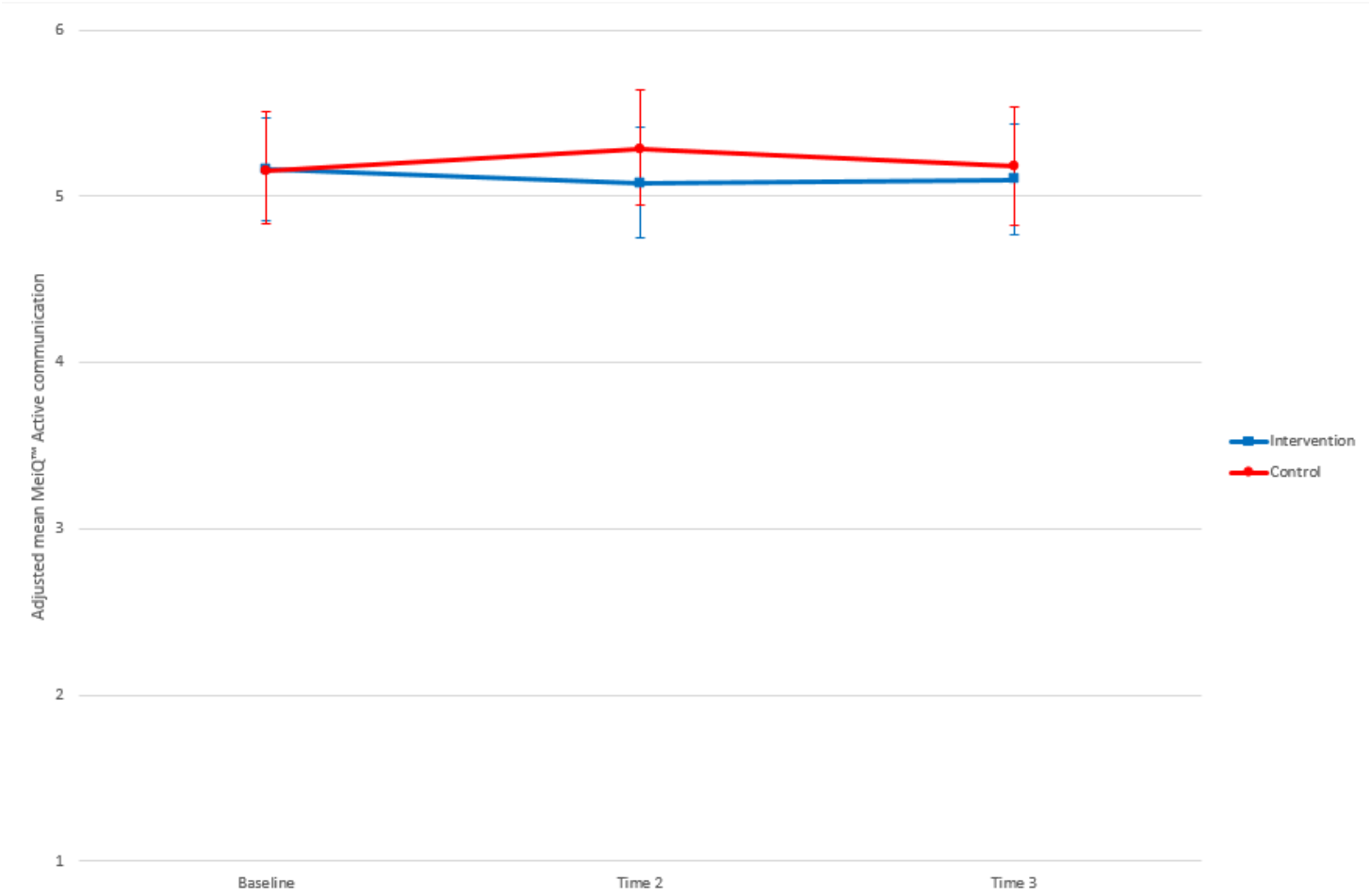

14
12
10
8
6
4
2
0
Adjusted mean Anxiety
Baseline
Time 2
Time 3
Intervention
Control

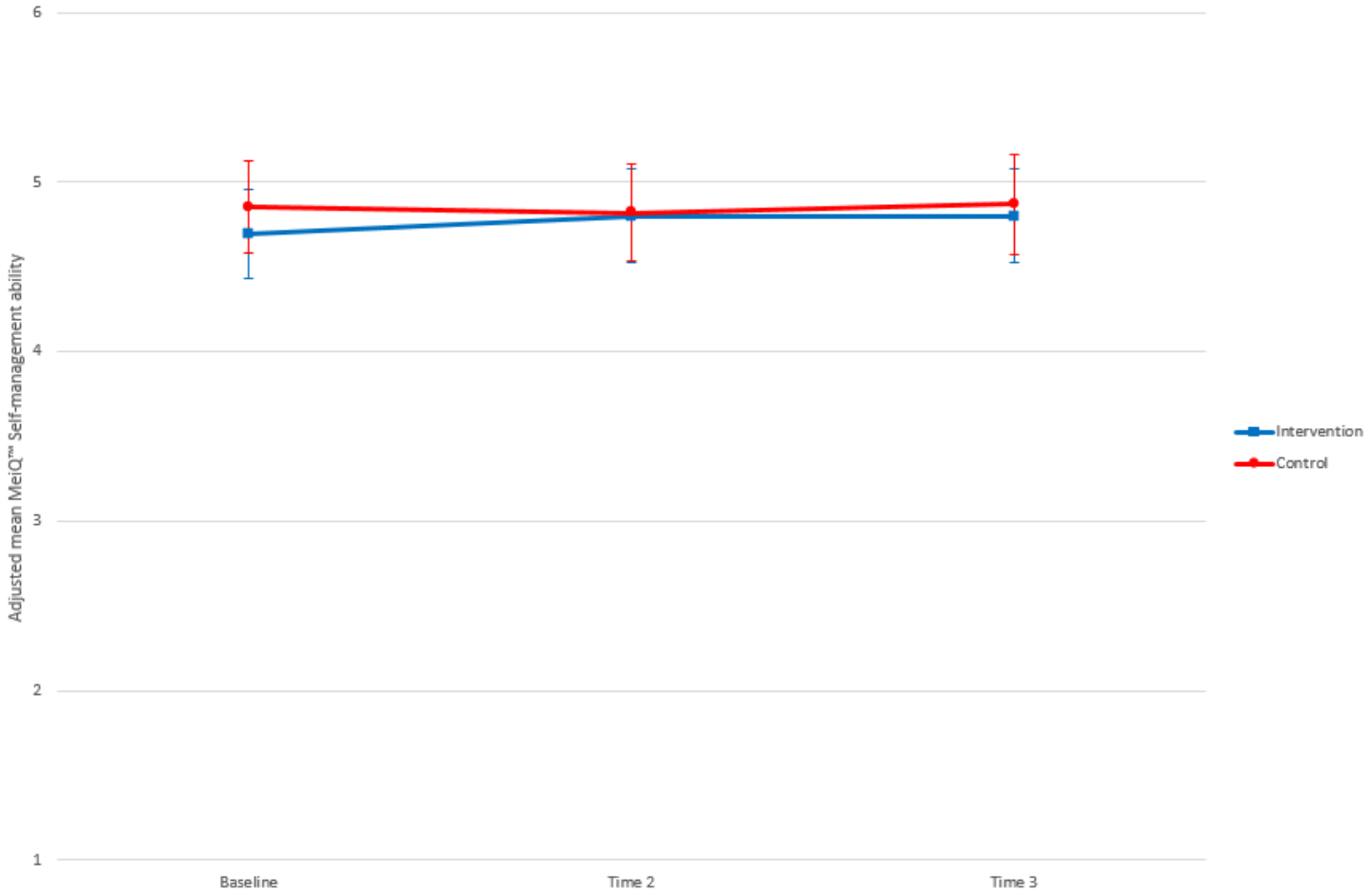

14
12
10
8
6
4
2
0
Adjusted mean Depression
Baseline
Time 2
Time 3
Intervention
Control

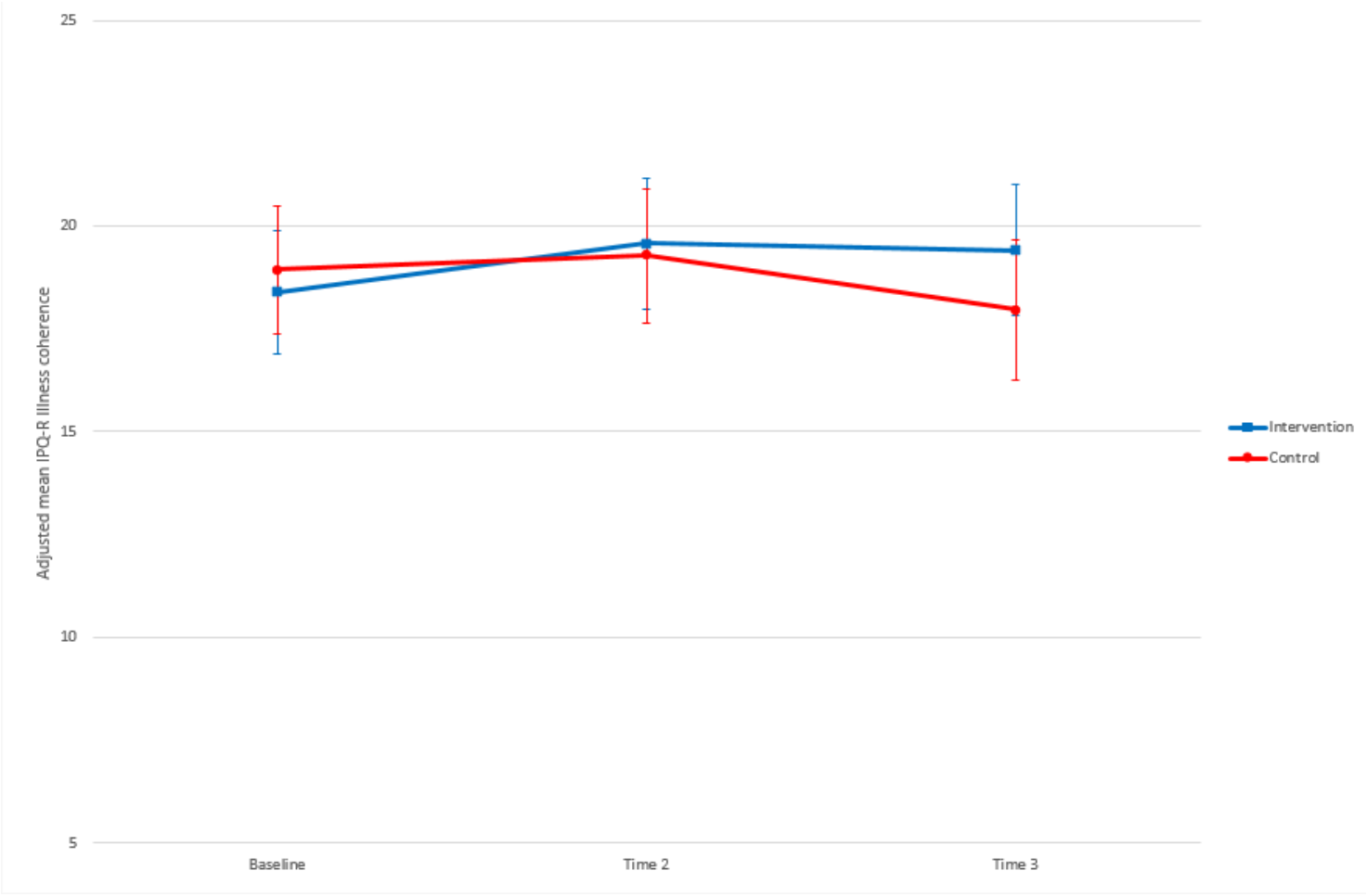
APPENDIX Z. GRAPHICAL REPRESENTATION OF CHANGES OVER TIME (WITH 99% CI) ON THE PSYCHOSOCIAL PROCESS VARIABLES (N=100)

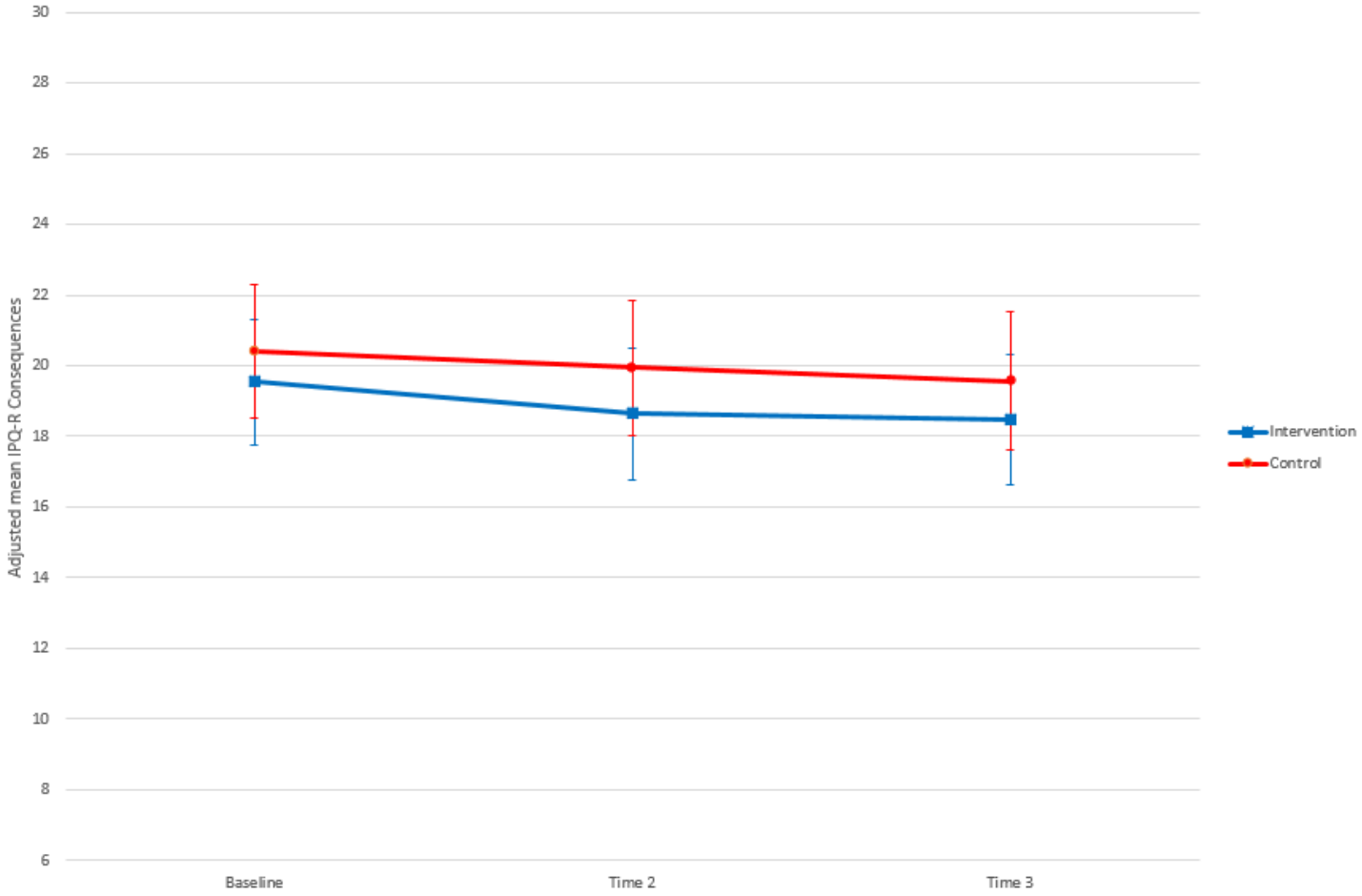


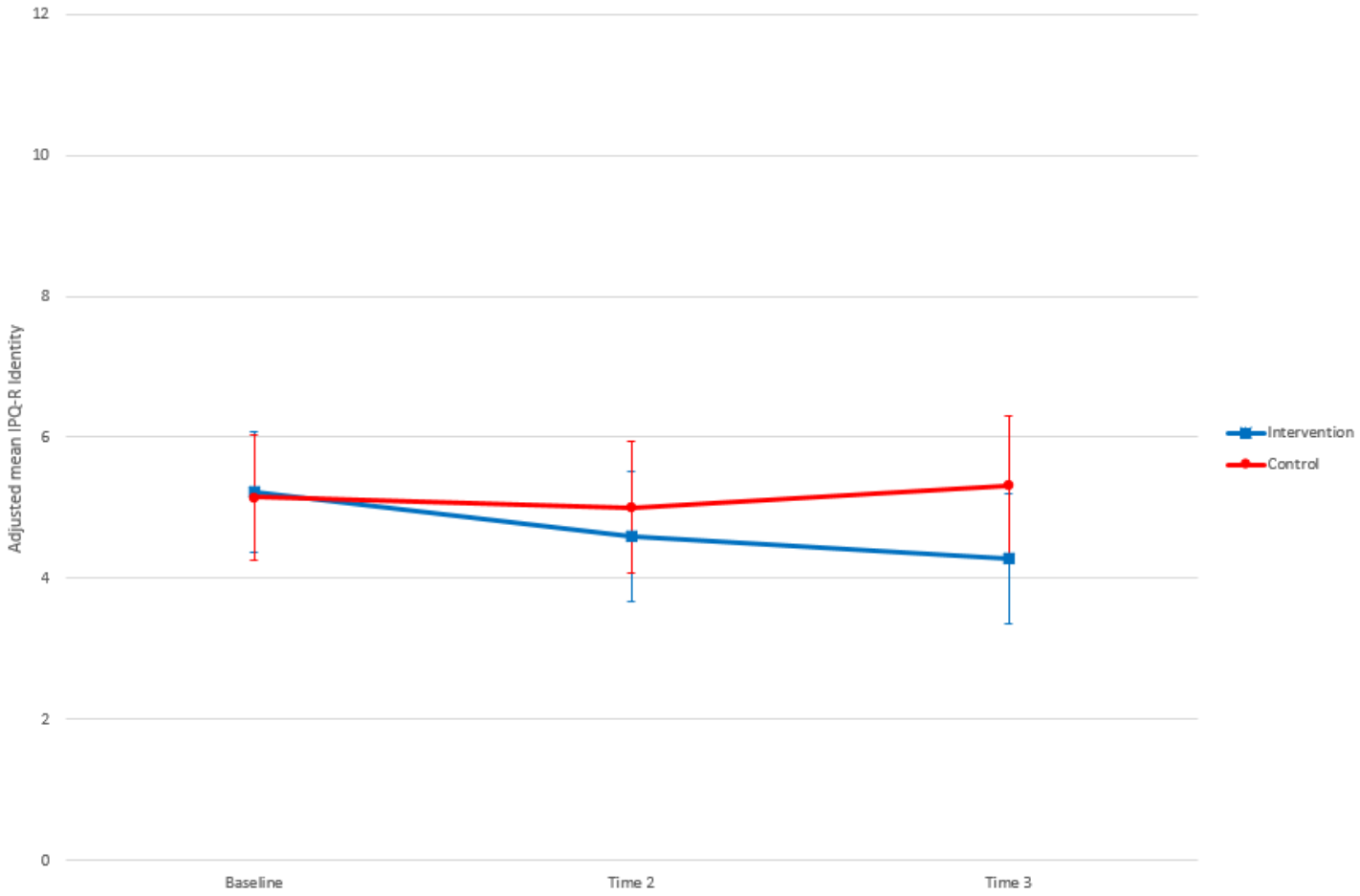

6
5
4
3
2
1
Adjusted mean HeiQ™ Self-monitoring & insight
Baseline
Time 2
Time 3
Intervention
Control

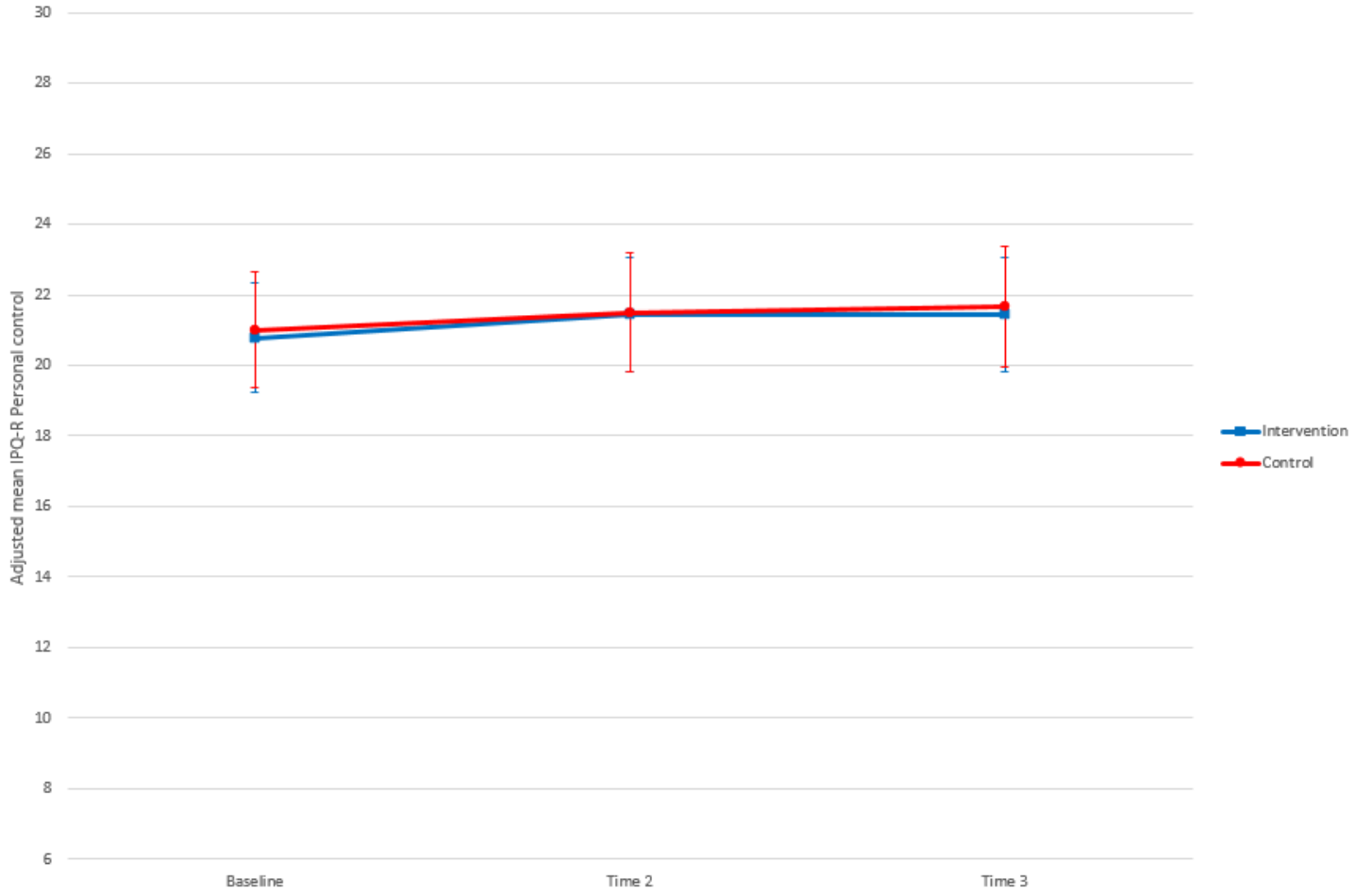

6
5
4
3
2
1
Adjusted mean MeiQ™ Active communication
Baseline
Time 2
Time 3
Intervention
Control

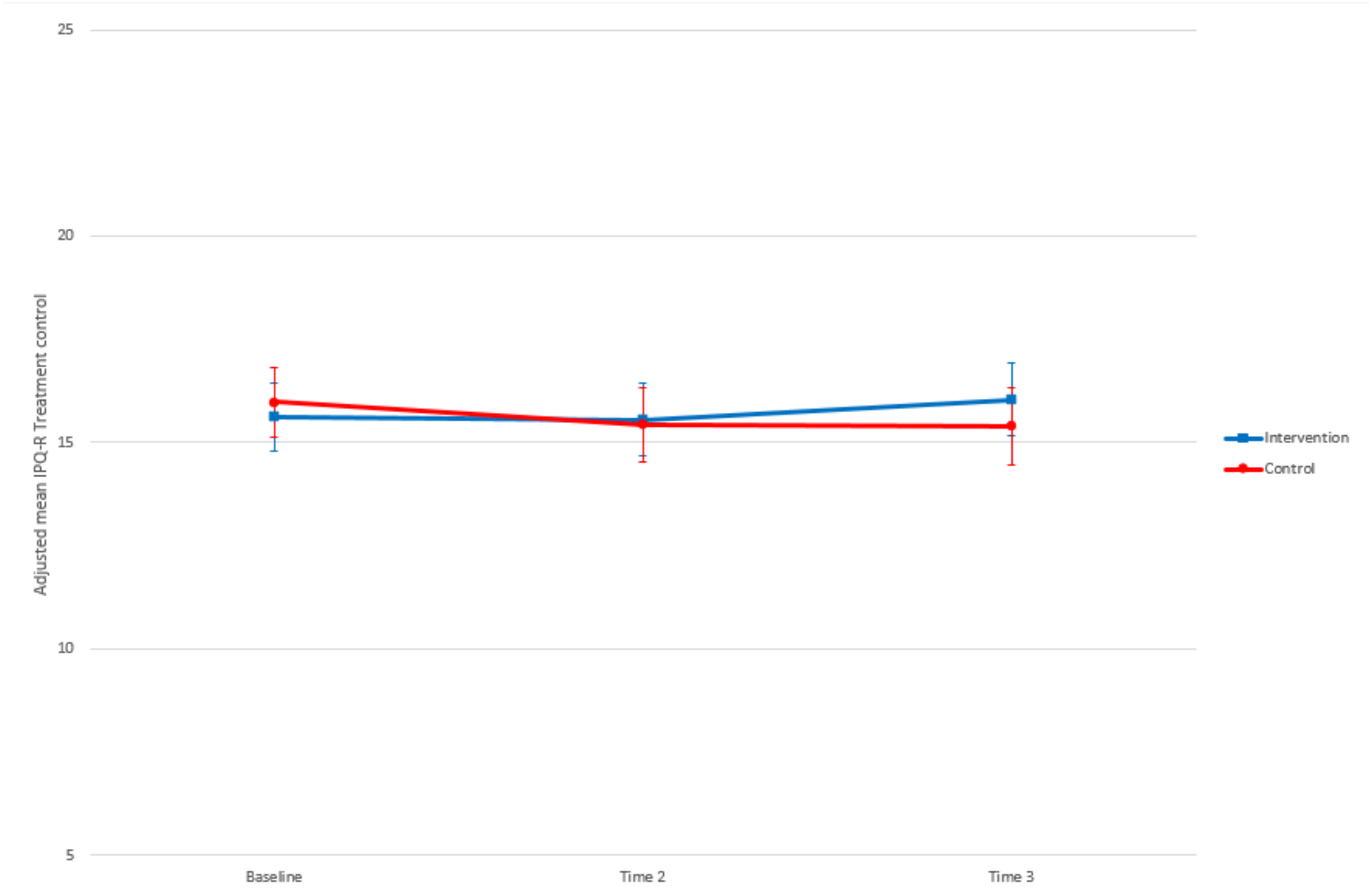

6
5
4
3
2
1
Adjusted mean MeiQ™ Self-management ability
Baseline
Time 2
Time 3
Intervention
Control

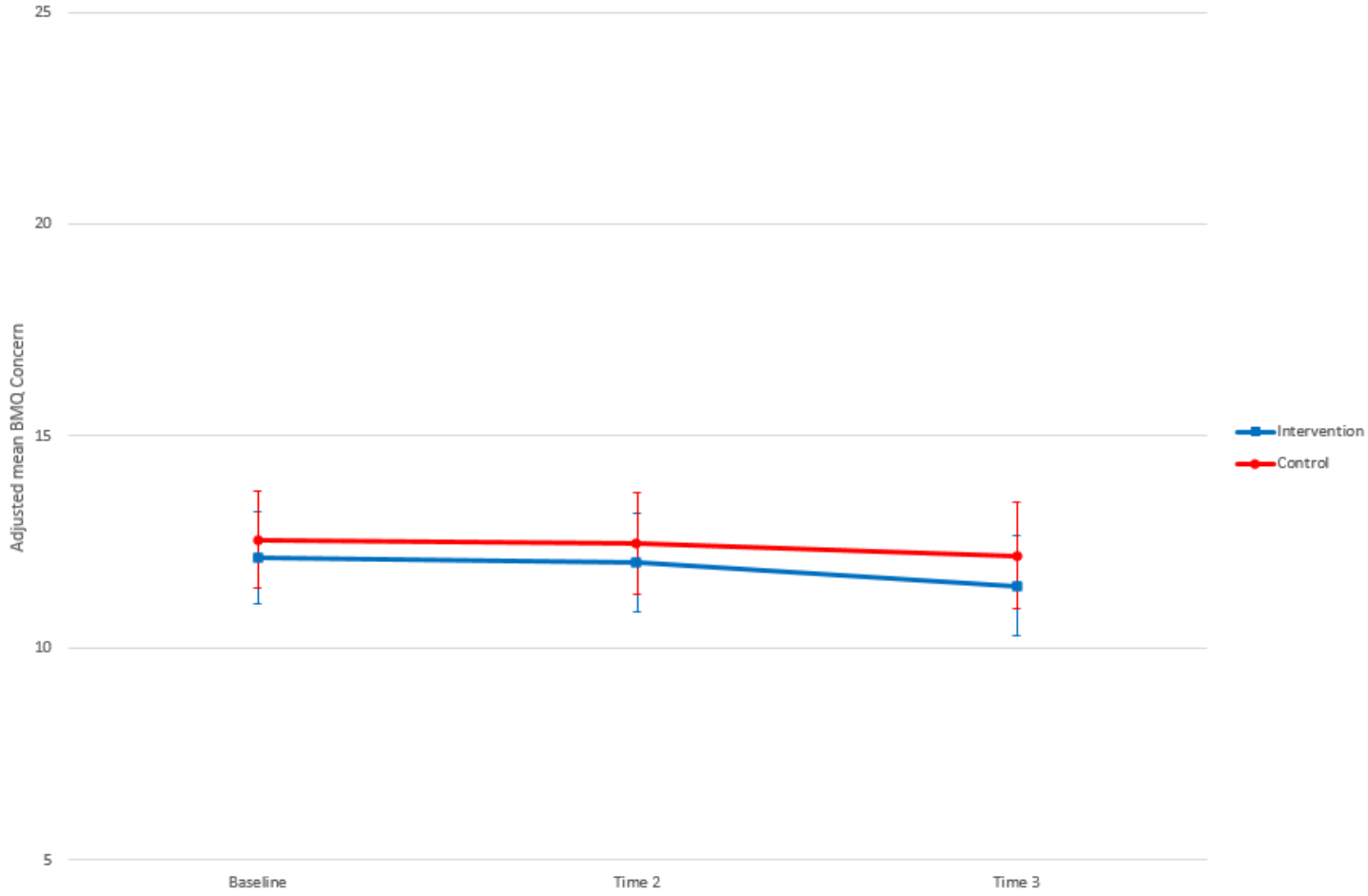

25
20
15
10
5
Adjusted mean IPQ-R Illness coherence
Baseline
Time 2
Time 3
Intervention
Control

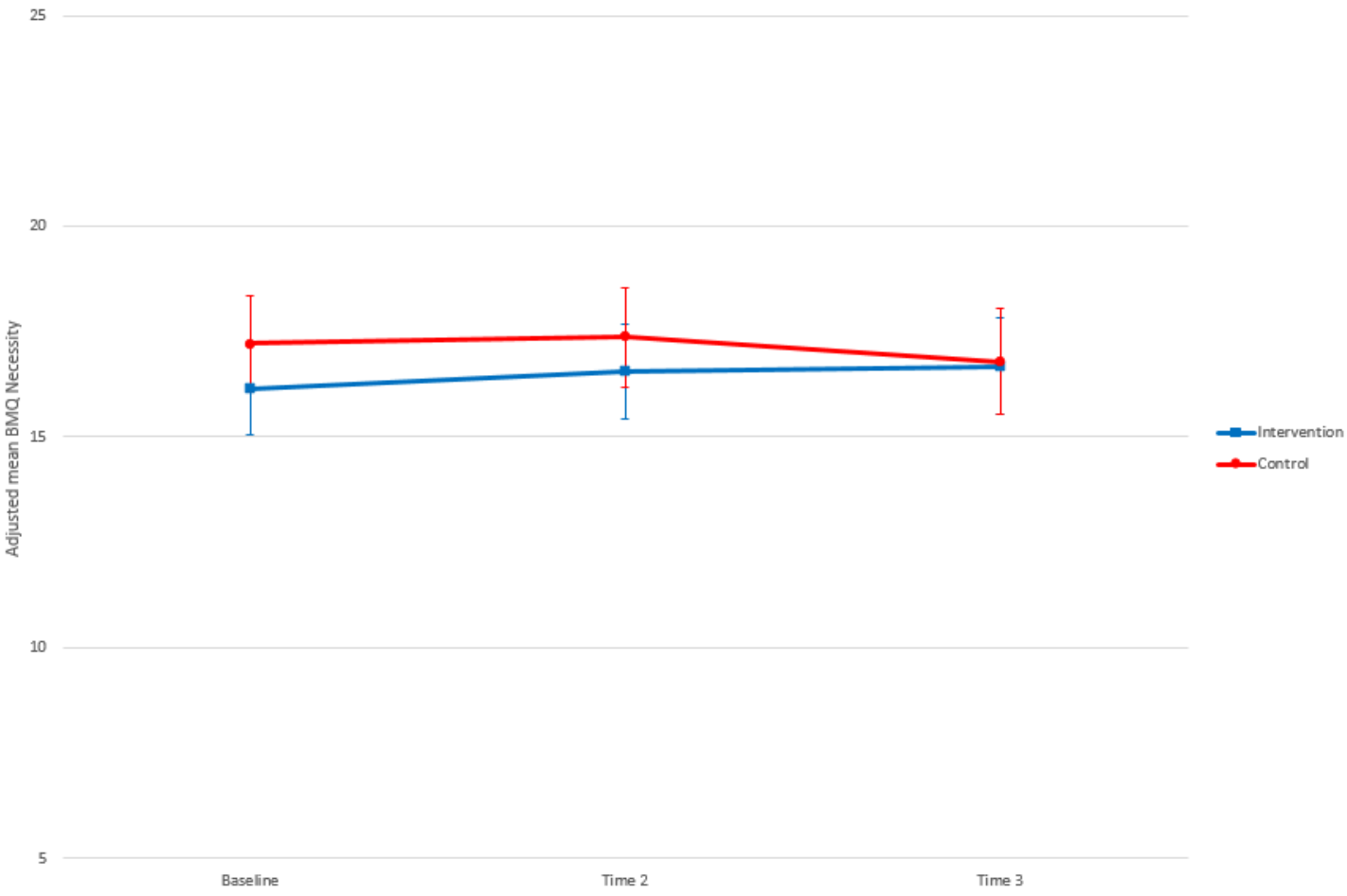

30
28
26
24
22
20
18
16
14
12
10
8
6
Adjusted mean IPQ-R Consequences
Baseline
Time 2
Time 3
Intervention
Control

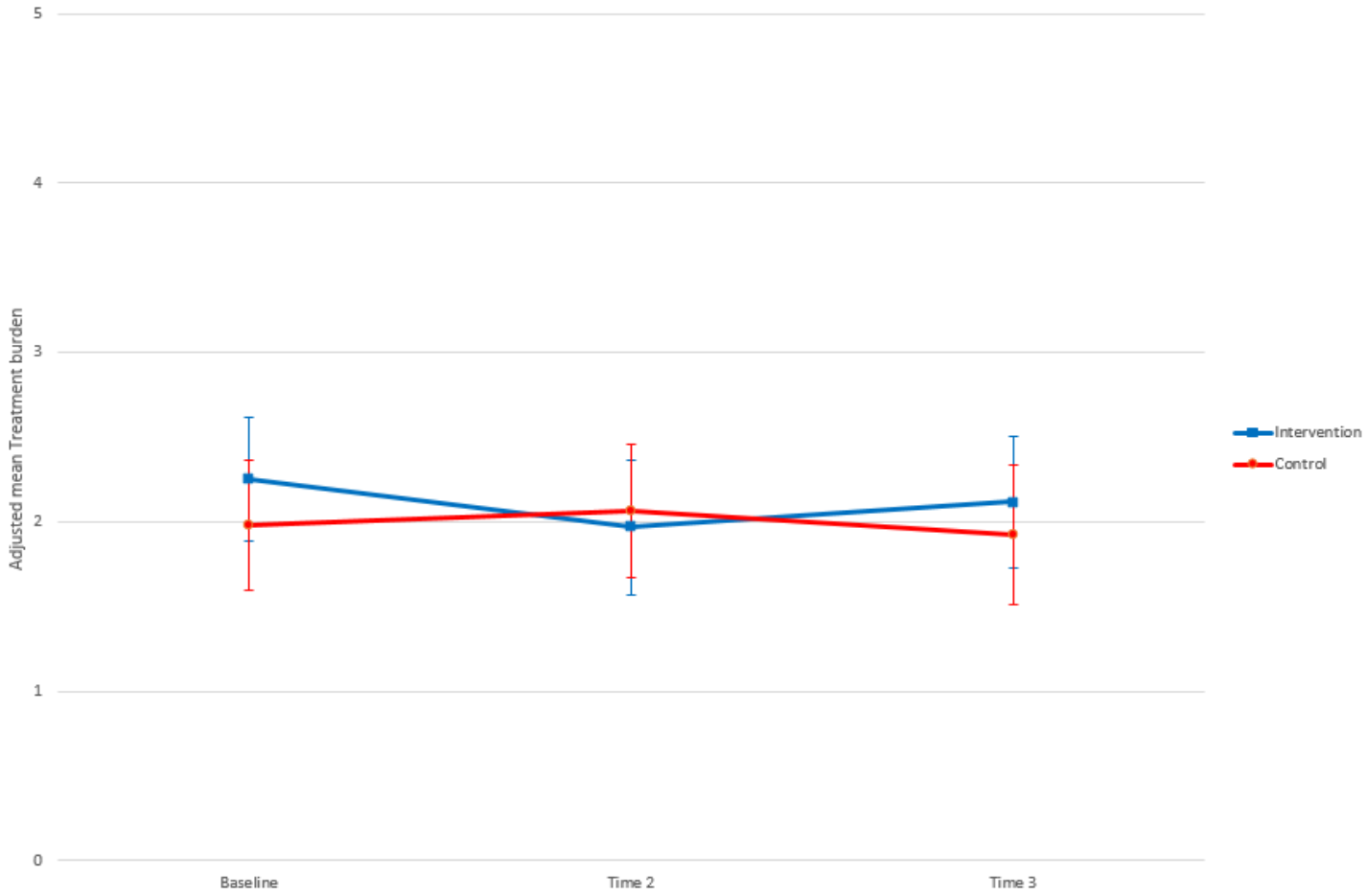

12
10
8
6
4
2
0
Adjusted mean IPQ-R Identity
Baseline
Time 2
Time 3
Intervention
Control

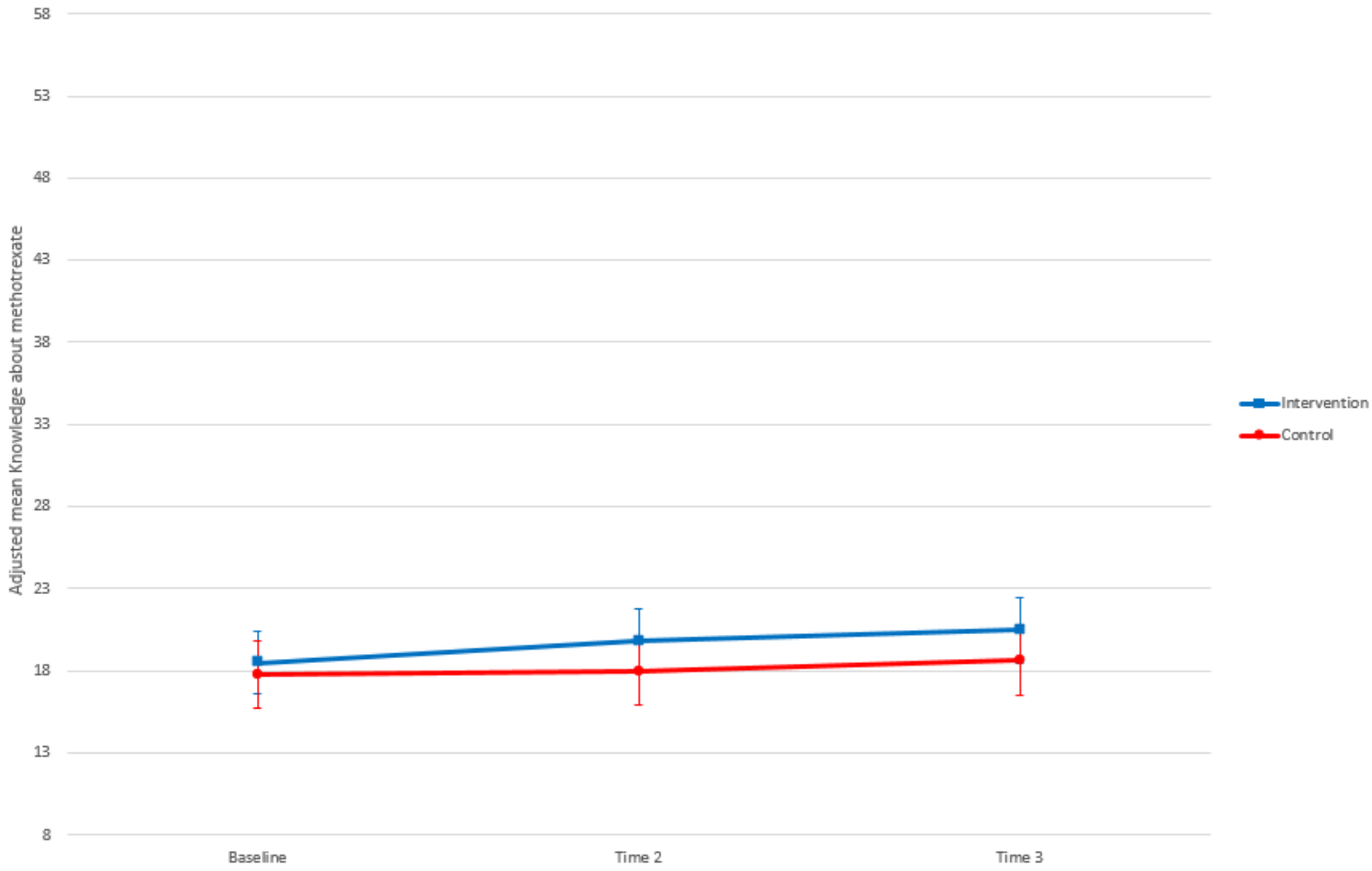

30
28
26
24
22
20
18
16
14
12
10
8
6
Adjusted mean IPQ-R Personal control
Baseline
Time 2
Time 3
Intervention
Control


25
20
15
10
5
Adjusted mean IPQ-R Treatment control
Baseline
Time 2
Time 3
Intervention
Control


25
20
15
10
5
Adjusted mean BMQ Concern
Baseline
Time 2
Time 3
Intervention
Control


25
20
15
10
5
Adjusted mean BMQ Necessity
Baseline
Time 2
Time 3
Intervention
Control


5
4
3
2
1
0
Adjusted mean Treatment burden
Baseline
Time 2
Time 3
Intervention
Control


58
53
48
43
38
33
28
23
18
13
8
Adjusted mean Knowledge about methotrexate
Baseline
Time 2
Time 3
Intervention
Control

APPENDIX AA. QUALITATIVE CONSENT FORM

UCLH Project ID number 09/H0722/91

Patient Identification Number for this study:

CONFIDENTIAL

CONSENT FORM (INTERVIEW STUDY)

Title of Project: Self-monitoring of treatment with methotrexate alone or in combination with a self-injecting anti-tumour necrosis factor agent by patients with arthritis.

Name of Principal Investigator: Professor Stanton Newman

Please initial box

1. I confirm that I have read and understand the information sheet dated 08.10.10 (version 3) for the above study and have had the opportunity to ask questions ☐

2. I confirm that I have had sufficient time to consider whether or not I want to be included in the study ☐

3. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. ☐

4. I agree to take part in the above study. ☐

5. I understand that all the information I provide will be treated as confidential ☐

6. I understand that the interview will be tape recorded ☐

7. I understand that at the end of the study, the tape recording will be destroyed but an anonymous written copy of my interview will be kept for research purposes and potentially for teaching. ☐

CONSENT FORM

Title of Project: Self-monitoring of treatment with methotrexate alone or in combination with a self-injecting anti-tumour necrosis factor agent by patients with arthritis

Name of Principal Investigator: Professor Stanton Newman

_____	_____	_____
Name of patient	Date	Signature

_____	_____	_____
Name of Person taking consent (if different from researcher)	Date	Signature

_____	_____	_____
Researcher (to be contacted if there are any problems)	Date	Signature

Comments or concerns during the study

If you have any comments or concerns you may discuss these with the investigator. If you wish to go further and complain about any aspect of the way you have been approached or treated during the course of the study, you should write or get in touch with the Complaints Manager, UCL hospitals.
Please quote the UCLH project number at the top this consent form.