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A PATIENT-INITIATED DMARD SELF-MONITORING SERVICE FOR PEOPLE WITH RHEUMATOID OR PSORIATIC ARTHRITIS ON METHOTREXATE: A RANDOMISED CONTROLLED TRIAL.

Hayley McBain[1 2], Michael Shipley[3], Abigail Olaleye[3], Samantha Moore[3] & Stanton Newman[1]

[1] School of Health Sciences, City University London, UK
[2] East London Foundation Trust, UK
[3] Department of Rheumatology, University College London Hospital, UK

Corresponding author: Professor Stanton Newman, Myddleton Street Building, City University London, Myddleton Street, London, EC1V 0HB. Email: stanton.newman.1@city.ac.uk, Tel: 00 44 207 040 5755.

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ABSTRACT

Objective: To determine the effectiveness of a patient-initiated DMARD self-monitoring service for people with rheumatoid (RA) or psoriatic arthritis (PsA) on methotrexate.

Methods: A two-arm, single centre, randomised controlled trial assessing superiority in relation to healthcare utilisation, clinical and psychosocial outcomes. Participants were 100 adults with either RA or PsA on a stable dose of methotrexate, randomly assigned to usual care or the patient-initiated service. Intervention participants were trained how to understand and interpret their blood tests and use this information to initiate care from their clinical nurse specialist (CNS). The primary outcome was the number of outpatient visits to the CNS during the trial period. Differences between groups were analysed using Poisson regression models. Secondary outcomes were collected at baseline and after the 3rd and 6th blood tests. Disease activity was measured using either the DAS28 or PsARC, pain and fatigue using a visual numeric scale and the HAQII, HADS and SF12 were completed to assess disability, mood and quality of life, respectively. Differences between groups over time on secondary outcomes were analysed using multi-level models.

Results: The patient-initiated DMARD self-monitoring service was associated with 54.55% fewer visits to the CNS ($p<0.0001$), 6.80% fewer visits to the rheumatologist ($p=0.23$) and 38.80% fewer visits to the GP ($p=0.07$), compared with control participants. There was no association between trial arm and any of the clinical or psychosocial outcomes.

Conclusions: The results suggest that a patient-initiated service that incorporates patients self-monitoring DMARD therapy can lead to significant reductions in healthcare utilisation, whilst maintaining clinical and psychosocial well-being.

INTRODUCTION

Rheumatoid (RA) and psoriatic arthritis (PsA) are chronic inflammatory conditions. Both primarily affect the joints, and have a wide clinical spectrum from mild joint symptoms to severe inflammation and damage. In some cases drug-induced sustained remission is possible.[1-2] The prevalence of PsA ranges between 1 and 420 cases per 100,000, depending on country,[3] whilst the prevalence of RA in Western Europe is 0.44%.[4]

Rheumatology services have seen increasing numbers of patients with arthritis over the last 30 years. This in part reflects the increasing complexity of drug treatments and more intensive monitoring regimes. As a result the number of follow-up cases in rheumatologist outpatients service has increased.[5] The introduction of nurse-led care has reduced some of this demand and has been found to be equally as effective, as well as cost-effective, in managing disease activity as rheumatologist-led clinics.[6-7] Despite this, the monitoring requirements remain burdensome for both the health system and patients, with increased waiting times for new referrals and the lack of availability of urgent appointments for established patients. Data from the National Audit Office[8] in the UK indicated that 66% of healthcare trusts were unable to offer RA patients a timely follow-up appointment. Even when these appointments do occur, 30% lead to no investigation or other actions, 35% are seen to be problem free by rheumatologists and 42% completely unnecessary.[9] As a result, the focus is now on reducing unnecessary outpatient and follow-up appointments altogether, rather than simply redirecting care.[10]

One way in which this may be achieved is through the use of patient-initiated services, in which patients are encouraged to take an active role in initiating their own care. This approach is supported by over 40% of patients with arthritis, who feel they should be able to decide how frequently they need a check-up[11] and want to take responsibility for organizing their own DMARD monitoring appointments.[12] Whilst the traditional rheumatology system assumes that patients need to be seen on a regular basis as decided by clinicians, patient-initiated services allow the patient to access rheumatology services much like they do in primary care. A recent systematic review[13] concluded that UK policy is eager for evidence-based patient-initiated services to be implemented and evaluated qualitatively and quantitatively so that the time of both patients and healthcare professionals is not wasted and costs can be minimised. The trials reported within this systematic review[14-17] and subsequent evaluations[18-23] have found that patients with arthritis are able to appropriately self-refer, and that despite reducing hospital appointments, the clinical or psychological well-being of patients is not compromised.

To date this model of care has however, focused on the implementation of patient-initiated clinics in the context of rheumatologist-led services, as opposed to the nurse-led clinics where much of DMARD monitoring takes place.[24] In addition, previous patient-initiated services have used symptoms as triggers for contact[14-23] but, in order for this model of care to be implemented in a nurse-led monitoring clinic, patients would need to monitor their laboratory results, as well as their symptoms and any side effects, and use this information together to initiate care from their CNS.

The aim of this study is therefore to determine whether a patient-initiated DMARD self-monitoring follow-up service, in which patients monitor their symptoms and blood test results and used this information to initiate care from their CNS, reduces use of nurse-led rheumatology clinics, in comparison to treatment as usual and that any reduction is not offset by use of other healthcare services.

METHODS

Trial design

This was a two-arm, single centre, randomised controlled trial (RCT) with balanced randomisation (1:1), and conducted in the UK.

Participants

Participants were recruited from the Department of Rheumatology at University College Hospital, UK and were approached by postal invitation 2 weeks prior to their attendance at the nurse-led DMARD monitoring clinic. Inclusion criteria were those with diagnosed RA[25] or PsA[26] whose treatment was classified as stable. This was defined as treatment with methotrexate for at least 6 months, plus a further 3 months if the patient were receiving one of two self-injecting anti-TNF agents; adalimumab or etanercept. Exclusion criteria were patients with a significant co-morbidity (i.e. their predominant treatment was for another illness), those for whom blood tests and monitoring was undertaken by their GP and patients prescribed infliximab. Ethical approval was obtained (Camden and Islington Community Local Research Ethics Committee Ref. 09/H0722/91) and all participants

provided written informed consent and were enrolled into the study by the research assistant.

Intervention

All participants randomised to the intervention group took part in a group based training session to provide them with the knowledge, skills and resources required to self-monitor and initiate care. This one-off 2 hour training session was delivered by a rheumatologist and a Health Psychologist, with a group of between 2-6 patients. Participants were trained how to identify normal or "safe" ranges of blood levels, side effects and symptoms, decide if any action was necessary, and how to initiate care from their CNS. Participants were guided through example blood test scenarios and given practice materials to be completed during the session. The results of these tasks were then reviewed during group discussions led by the rheumatologist.

Participants interpreted markers of inflammation (CRP and ESR), plus haemoglobin, white blood cell count, liver function tests (ALP and ALT), platelets and neutrophils. Participants continued to receive routine care from their rheumatologist, defined as outpatient appointments every 6 months; had access to the emergency nurse helpline if necessary and continued with routine blood monitoring every 4-6 weeks depending on their dose of methotrexate.

Following 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, to enable calculation of change scores by the participant. Criteria for a significant change or out-of-range blood test were developed and agreed by the clinical team and shared with the patient (Table 1).

Table 1. 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

Participants also recorded, using a 17-item checklist developed by the authors, 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 indicated if the symptom had become worse, better or remained the same since their last blood test. The criteria for seeking a telephone consultation with the CNS are outlined in Figure 1.

Control group

Participants in the control group received standard care; this typically consisted of a blood test every 4-6 weeks and optimally outpatient appointments with their CNS every 3 months

and rheumatologist every 6 months. Advice was also freely available via the emergency nurse helpline when requested.

Participant safety

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 they were able to contact their clinical team by email or telephone. This included the CNS helpline or rheumatologist, where patients were responded to within 24-48 hours.

Outcomes

The primary outcome was visits to the nurse-led rheumatology clinic, and secondary outcomes visits to the rheumatologist and GP, disease activity, time between blood tests, pain, fatigue, disability, quality of life and mood. All patient reported outcomes measures were assessed at baseline, and after the 3rd and 6th blood tests.

Healthcare utilisation

Healthcare utilisation included outpatient visits to the CNS and rheumatologist, arthritis-related GP visits and telephone consultations with the CNS. Data on outpatient visits were taken from electronic patients records at the end of the trial period. Data on GP visits were provided by participants at each of the assessment points. A cumulative frequency of visits across the trial period was calculated for each participant, for each healthcare professional.

Disease activity

Disease activity was measured using the DAS28 (ESR)[27] for patients with RA and the PsARC[28] for patients with PsA. A response to treatment score was calculated using either the EULAR response criteria[29] or the PsARC[28]. The EULAR response criteria of 'moderate' and 'good' were recoded as a response; and 'none' as no response in order to correspond with the PsARC.

Pain and fatigue

Pain and fatigue were measured using two separate visual numeric scales which were displayed as histograms.[30] The histograms become larger in size and darker in colour as the severity of the pain or fatigue increases (from left to right). Scores ranged from 0 to 10, with the higher scores indicating greater pain or fatigue experienced in the past 2 weeks.

Functional disability

The Health Assessment Question-II (HAQ-II)[31] is a 10-item scale with responses from 'without any difficulty' (1) to 'unable to do' (4). The individual Likert scales range from 0-3, these items are then averaged, and hence the overall score for the scale is also 0-3 Higher scores represent greater levels of functional disability. The HAQ-II possess satisfactory reliability and correlates well with the full version of the HAQ,[32] quality of life and clinical outcomes.[33]

Mood

The Hospital Anxiety & Depression Scale (HADS)[34] is a 14-item self-screening questionnaire for depression and anxiety. 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. The scales possess excellent internal consistency[35] and high test-retest reliability.[36]

Quality of life

The SF-12v1[37] measures quality of life across two component summary scales - the Physical (SF-12v1® PCS) and Mental Component Summary (SF-12v1® MCS). Total scores range from 0-100 with higher scores representing better quality of life. The scale is responsive to change and has good test retest reliability.[38]

Sample size

An *a priori* power calculation was conducted using G-Power 3.1.[39] An initial power calculation was performed using data from a previous trial of patient-initiated services,[15] however, to make group comparisons on the primary outcome – outpatient visits to the nurse specialist, 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 a total sample size of 134 participants was required at 80% power (α=0.05), with a medium effect size of 0.50.

Randomisation

Participants were randomised with a randomization plan generator,[40] using randomly permuted blocks of 10 participants, by the research assistant. As with interventions of this type group allocation was not concealed. No stratification took place.

Blinding

Due to the nature of the intervention blinding of participants and treating healthcare professionals was not possible. The analysis was not performed blind to group allocation.

Statistical methods

The analysis followed a per-protocol and intention-to-treat approach for the primary outcomes. In order to test the robustness of the findings in relation to the secondary outcomes sensitivity analyses were performed for complete (i.e. all three administrations of the questionnaire) and available case cohorts. Univariate Poisson regressions were performed to explore if trial arm (independent variable) was associated with healthcare utilisation (dependant variable). Multi-level modelling was used to explore changes over time and differences between groups on pain, fatigue, functional disability, mood and quality of life. Interaction effects between group and time on disease activity were analysed using a mixed between-within participants ANOVA for the DAS28 and the individual subscales of the PsARC. An independent samples t-test was used to explore differences between trial arms on the time between laboratory tests.

Across the entire dataset there were 3.65% missing data, which was missing completely at random (p = 0.53). MLM allows for missing data, all other analyses were undertaken on the multiple imputed datasets. 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.[41] Analyses were performed on each of these 10 datasets and then pooled.

RESULTS

Of the 301 patients assessed for eligibility, 25% (n = 74) did not meet the eligibility criteria therefore, 227 patients were approached to take part (Figure 1). Of these 63% (n = 128) consented and were randomised. Of those who did not consent the most frequently reported reasons for refusal were 'too busy to participate' (n = 58, 59.09%) and a 'preference to see their CNS face-to-face' (n = 31, 31.82%). 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 and 3 (2.34%) participants were no longer eligible to take part in the trial. 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 (Figure 2). Analyses were performed on an ITT basis (n = 100) and repeated in complete cases only (n = 79), but with no differences; hence results for the whole sample (n = 100) are presented.

Sample characteristics

Participant characteristics at baseline can be found in Table 2.

Table 2 Sample characteristics

	Intervention (n=52)	**Control (n=49)**
Age, mean(SD)	54.83(11.22)	58.75(12.22)
Female, n(%)	24(46.15)	31(64.58)
Living status, n(%)		
Married or living with partner	37(71.15)	33(68.75)
Living alone	8(15.38)	10(20.83)
Living with friends or family	7(13.46)	5(10.42)
Ethnicity,† n(%)		
White	46(88.46)	43(89.58)
Indian	2(3.85)	2(4.17)
Other	3(5.77)	1(2.08)
Black-African	0(0.00)	1(2.08)
Black-Caribbean	1(1.92)	0(0.00)
Chinese	0(0.00)	1(2.08)
Disease type, n(%)		
Rheumatoid arthritis	33(63.46)	38(79.17)
Psoriatic arthritis	19(36.54)	10(20.83)
Disease duration in years, median(range)	8(1-40)	6(1-54)
No. of years on methotrexate, median(range)	4(1-20)	3.85(1-13)
Dose of methotrexate, median (range)	15(5-22.5)	15(5-25)
No. of medications, median(range)ǂ	4(1-10)	5(2-11)
Co-morbidities, n(%)		
Hypertension	9(17.31)	5(10.42)
Hypercholesterolemia	8(15.38)	5(10.42)
Hypothyroidism	2(3.85)	4(8.33)
Osteoporosis	2(3.85)	4(8.33)
Diabetes	2(3.85)	2(4.17)
Respiratory	1(1.92)	2(4.17)

Primary outcome

The intervention group initiated 54.6% fewer appointments with their CNS compared to control participants. Group was a significant predictor of outpatient visits to the CNS (Table 3). The intervention group attended 6.8% fewer reviews with their rheumatologist over the trial period compared to the control group participants (Table 3). Poisson regression indicated that group was not a significantly associated with visits to the rheumatologist

(Table 3). The intervention group initiated 38.8% fewer arthritis-related GP appointments than control group participants; this difference was also not statistically significant.

Table 3. Total number of face-to-face arthritis-related healthcare visits by trial arm for whole sample

Healthcare profession	**Total n=100**	**Intervention n=52**	**Control n=48**	**Difference between groups, AD(%) (C – I)**	**Statistic**
CNS	96	30	66	36(54.5%)	Exp(β) = 2.37 $\chi^2(1, n = 100) = 15.48$ $p < 0.0001$
Rheumatologist	199	96	103	7(6.80%)	Exp(β)=1.04 $\chi^2(1, n=100) = 1.16$ $p = 0.23$
GP	76	29	47	18(38.30%)	Exp(β) = 1.78 $\chi^2(1, n = 100) = 3.64$ $p = 0.07$

AD - actual difference; χ^2 - chi-squared test; Exp(β) – incident rate ratio

In the intervention group a total of 231 telephone consultations took place (mean per participant = 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 their six blood tests. For every seven telephone consultations one outpatient appointment was requested. Of these 231 telephone consultations, 74.7% were initiated appropriately by the patient in response to their results, and 25.3% were initiated by the CNS when abnormal blood results were detected, but not acted on by the patient. Two participants in the intervention were removed from the trial for safety reasons as they were deemed unable to self-monitor their laboratory results safely. Patients ability to safely

initiate care improved significantly over the trial period ($F_{1,278} = 9.24$, p = 0.003), from 65.4% of all decisions at blood test 1 to 89.1% at blood test 6.

Secondary outcomes

There was also no significant association between trial arm and disease response to treatment $\chi^2(1, n = 100) = 0.35$, $p = 0.77$, $\phi = -0.03$.

There were no statistically significant interaction effects between group and time on any of the laboratory results, see the online supplementary material Table S1.

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, $p = 0.001$, $\eta^2 = 0.12$). There were no statistically significant interaction effects on levels of disability, pain, fatigue or any of the psychosocial outcomes. (Table 4).

Table 4. 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)			
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; f/u – follow-up; MCS – Mental Component Score; PCS – Physical Component Score

DISCUSSION

This is the first evaluation of a patient-initiated service that has integrated patients self-monitoring their DMARD therapy and interpreting of their own laboratory results, and using this information along with their symptoms to seek care from rheumatology services. The primary findings of this RCT indicated that this novel model of care led to significant reductions in outpatient visits to the CNS and a reduction in visits to the GP, whilst maintaining the regularity with which patients saw their rheumatologist. Despite this reduction in attendance in primary and secondary care services, this new service was not inferior to standard practices in regards to disease activity, pain, fatigue, quality of life or mood. These results suggest that this model of care could be implemented without compromising the clinical or psychological well-being of patients with either RA or PsA on methotrexate, and are consistent with previous studies of patient-initiated services in the UK[14-16, 20-21] and Denmark.[18-19]

The significant reduction in CNS visits may indicate that a large proportion of follow-up appointments in nurse-led DMARD monitoring clinics are made habitually and may not be clinically necessary, reflecting previous reports.[9] A parallel reduction in GP attendance is encouraging, as this indicates that patients were not redirecting their care, but felt better able to manage their arthritis at home themselves rather than seek help in primary care, possibly because they knew rapid access to the CNS was available, as suggested elsewhere in the literature.[42] Further cost-effectiveness analyses needs to be performed in order to understand how these reductions translate into cost savings.

The clinical care and safety of participants in the intervention group was of high priority. 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 regarding participant safety, specifically in relation to deterioration of disease status, have been reported elsewhere in the literature.[14-16] 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.[14] In the study reported here the final blood test however, almost 90% of patients were safely initiating care from their CNS, with accuracy improving over time in response to the feedback given to patients at prior blood tests. This may indicate 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.

It is reassuring that an intervention that required patients to pay closer attention to their illness and reduced unnecessary healthcare visits did not have a detrimental impact on patients' psychosocial well-being. Contrary to the expectations of some rheumatology healthcare professionals[43] increasing patient knowledge, understanding and exposure to blood test results whilst at the same time decreasing healthcare utilisation was not associated with increased levels of anxiety. In fact there was tentative evidence to suggest that participants in receipt of the new service experienced improving levels of anxiety

compared to participants under control conditions, consistent with other trials of patient-initiated services.[14-15]

Increasing patients' understanding of and exposure to blood test results, and the use of these as triggers to access care from the CNS was a unique addition to the service. This, in addition to the provision of pre-filled blood test forms may explain why participants in the intervention group attended for their blood tests more frequently than control group participants, as theorized elsewhere in the literature.[44] Although frequency of attendance for blood tests does not necessarily reflect recommended scheduling, this finding is in contrast to other patient-initiated services, which have reported that patients initiating their own care are less adherent to their blood monitoring schedules than those monitored by a rheumatologist.[18]

Limitations of this trial relate to rates of refusal and study methodology. Data on the length of each telephone call was not available, an important factor when considering the capacity to take on such activities particularly as 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".[45] The costs of delivering a telephone consultation is, however, the same per patient irrespective of time.[46] Additionally, data were not available on the number of telephone calls made by the control group to the nurse helpline. Nor was data collected in either groups on use of other services such as physiotherapy, occupational therapy or podiatry.

A third of eligible patients preferred to have regular scheduled appointments with their CNS face-to-face, which has been reported as a reason for refusal in other patient-initiated trials.[18-19, 47] The increased level of involvement and additional responsibility for self-monitoring blood tests in this trial may explain the higher overall proportion of refusals in comparison to other trials.[47] Refusal to participate in trials that increase patient involvement in healthcare has been linked to a reluctance to disrupt services and relationships that are working well and are highly valued.[48] This may further account for the high rates of refusal found in the current trial, particularly as nurse-led services are associated with greater levels of satisfaction with care than consultant-led clinics.[49] In countries in which the role of the CNS in rheumatology is still in its infancy,[50-52] there is still much work to done to establish these services. In light of this study consideration may now be given to telephone as opposed to face-to-face follow-up.

Methodologically, random allocation was undertaken prior to baseline assessment, which may mean that participants reported poorer psychosocial well-being than if they had been randomised after baseline assessment.[53] Lack of allocation concealment and blinding may have also biased the effects of the service.[54-55] Finally, the single centre status of the trial has reduced the external validity of the findings,[56] and may have led to larger intervention effects on both the continuous[57] and binary outcomes.[58] A larger multi-centre RCT would therefore be required in order to test our hypothesis more robustly. Finally, although this trial suggests equivalence between the intervention and control arm on psychosocial outcomes, this study was not designed to test equivalence and hence these conclusions should be treated with caution.

CONCLUSION

This RCT demonstrated that a self-monitoring and patient-initiated service can lead to clear reductions in primary and secondary healthcare services, whilst at the same time maintaining patients' clinical and psychosocial well-being in comparison to nurse-led DMARD monitoring clinics. Further work is needed in order to establish the cost-effectiveness of the service.

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CONTRIBUTORS: SN and MS conceived the original idea and put the study team together. SN provided expertise in patient self-management, supervised the design and conduct of the trial, the study evaluation and reviewed the analyses by contributing towards the interpretation of the study findings. MS contributed to study design, co-delivered the intervention, and provided rheumatology expertise. HM led on the design and delivery of the trial, analyses and reporting, and drafted the manuscript. AO and SM provided clinical

expertise, assisted in the identification and recruitment of participants, and delivery of the intervention. All authors contributed to, reviewed and approved the final manuscript.

ETHICAL APPROVAL: This study was conducted with approval from Camden and Islington Community Local Research Ethics Committee (Ref. 09/H0722/91).

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- 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.

Figure 1. Criteria for patient action

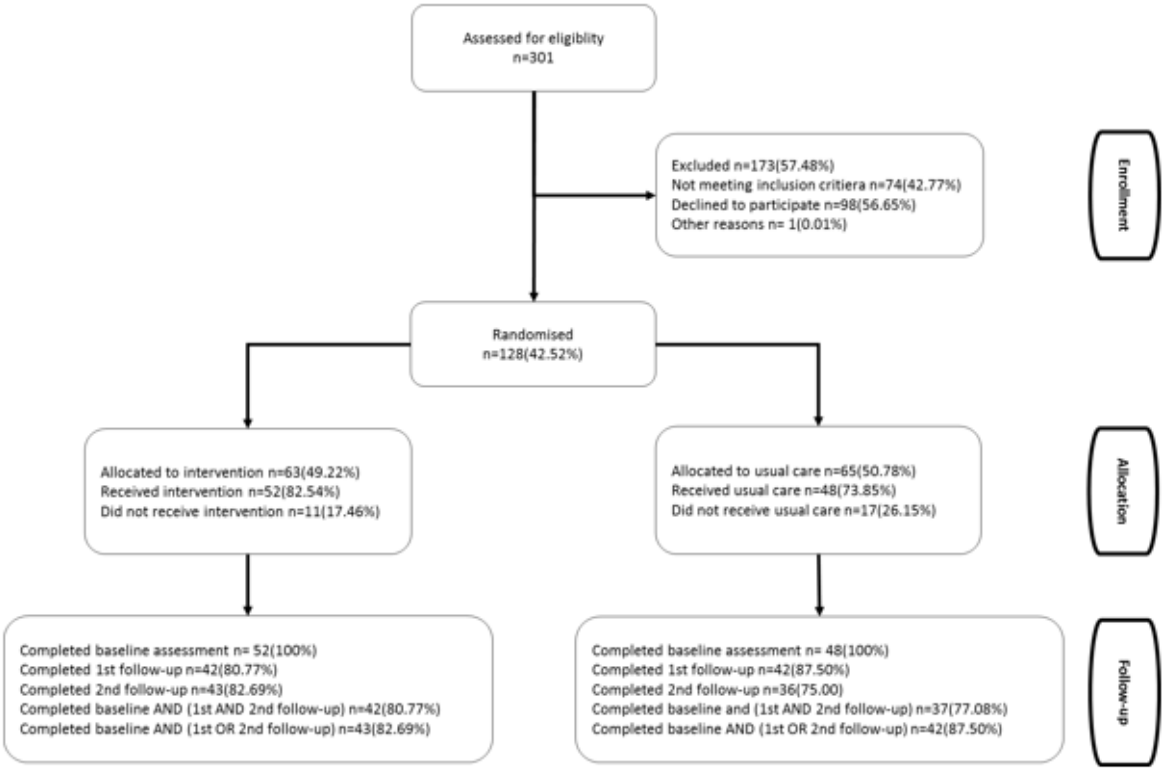

Figure 2. Consort flow chart

McBain, H., Shipley, M., Olaleye, A., Moore, S. & Newman, S. (accepted). A patient-initiated DMARD self-monitoring service for people with rheumatoid or psoriatic arthritis on methotrexate: a randomised controlled trial. Annals of Rheumatic Diseases.

Table S1. MLM analysis for laboratory tests (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)	**Group*Time**
	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)	$F_{6,302.56}$ = 0.75, p = 0.61
	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)	$F_{2,290.87}$ = 0.39, p = 0.89
	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)	$F_{6,288.13}$ = 1.33, p = 0.25
	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)	$F_{6,299.34}$ = 1.00, p = 0.43
	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)	$F_{6,297.91}$ = 1.19, p = 0.31
	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)	$F_{6,209.46}$ = 1.58, p = 0.15
	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)	$F_{6,300.96}$ = 0.35, p = 0.91
	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)	
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)	$F_{6,279.19}$ = 0.53, p = 0.78
	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	