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Investigating the mortality and morbidity burden from cardiovascular disease in the United Kingdom Armed Forces and optimising the screening for cardiac disease in potential British Army recruits

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Research Degree: PhD

3rd February 2020

DECLARATION

This body of work represents my original project. No portion of the work referred to in this thesis has been submitted in support of an application for another degree or qualification of this or any other University or other institute of learning.

This thesis forms the body of work upon which I expect to be examined for the degree of PhD.

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Dr Andrew Cox

Date: 02 February 2020

Dedication

To my wife Christina

The perfect woman – a balance of kind-hearted goddess, siren, true friend,

comedian and determined king! I am the luckiest man in the world!

And to my parents

They have always been there – supportive, kind and loving.

I am who and what I am because of them (it is their fault)!

Acknowledgments:

My thanks go out to my supervisory team:

Professor Sanjay Sharma, Professor Elijah Behr and Col Duncan Wilson.

This thesis has been a long time in the making and a lot of life has happened along the way. Thank you for your guidance, support, wisdom and of course endless patience.

Additional acknowledgements for the key team members involved in each chapter is also given at the end of each chapter

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List of abbreviations

ACC	Accuracy
AHA	American Heart Association
AR	Aortic regurgitation
ARVC	Arrhythmogenic right ventricular cardiomyopathy
AS	Aortic stenosis
ASD	Atrial septal defect
AV	Atrioventricular
BAV	Bicuspid aortic valve
BSE	British Society of Echo
CAD	Coronary artery disease
CMR	Cardiac Magnetic Resonance scan
CPVT	Catecholaminergic polymorphic ventricular tachycardia
CVA	Cerebrovascular accident
CVD	Cardiovascular disease
DCM	Dilated cardiomyopathy
DMICP	Defence Medical Information Capability Programme
DNBI	Disease and non-battle injury
ECG	Electrocardiogram
Echo	Echocardiogram
ESC	European Society of Cardiology
GIM	General and Internal Medicine
GMC	General Medical Council
GP	General Practitioner (primary care doctor)
HCM	Hypertrophic cardiomyopathy
IHD	Ischaemic heart disease
IRM	British Army Initial Recruit Medical
ISAF	International Security Assistance Force

JSP950	Joint Service Publication 950
LA	Left atrium
LBBB	Left bundle branch block
LQTS	Long QT syndrome
LR-	Negative likelihood ratio
LR+	Positive likelihood ratio
LV	Left ventricle
LVH	Left ventricular hypertrophy
LVOTO	Left ventricular outflow tract obstruction
MI	Myocardial infarction
MOD	Ministry of Defence
MoDREC	Ministry of Defence Research Ethics Committee
ms	Milliseconds
mV	millivolts
NATO	North Atlantic Treaty Organisation
MR	Mitral regurgitation
MVP	Mitral valve prolapse
NHS	National Heath Service
NPV	Negative Predictive Value
ONS	Office of National Statistics
PDA	Patent ductus arteriosus
PE	Pulmonary embolism
PFO	Patent foramen ovale
PPV	Positive Predictive Value
PR	Pulmonary regurgitation
PS	Pulmonary stenosis
PVC	Premature ventricular complex
RA	Right atrium
RAF	Royal Air Force

RBBB	Right bundle branch block
RG8 Part 1	Questionnaire section of the British Army Initial Recruit Medical
RG8 Part 2	Physical examination section of the British Army Initial Recruit Medical
RN	Royal Navy
RV	Right ventricle
RVOT	Right ventricular outflow tract
SADS	Sudden arrhythmic death syndrome
SCD	Sudden cardiac death
Sn	Sensitivity
Sp	Specificity
TR	Tricuspid regurgitation
UK	United Kingdom
US or USA	United States of America
VHD	Valvular heart disease
VSD	Ventricular septal defects
WHO	World Health Organisation

Abstract: Investigating the mortality and morbidity burden from cardiovascular disease in the UK Armed Forces and optimising the screening for cardiac disease in potential British Army recruits

Background: Inherited and congenital cardiac diseases are found in the general UK population and these conditions cause both disability and death. In those aged <35 years these diseases are the most frequent cause of sudden death and in a majority of cases present for the first time with a fatal event. As the population ages the risk of death from ischaemic heart disease (IHD) increases exponentially to become the most common cause of death. Neither the prevalence of cardiovascular disease (CVD), nor their impact more generally on the UK Armed Forces, is known.

Part 1: Investigating the mortality and morbidity burden from cardiovascular disease in the UK Armed Forces. This first part of this thesis investigates the epidemiology of CVD in the UK Armed Forces. It investigates the hypothesis, through three separate research studies, that the same CVDs that occur in the general population may also be found in the UK Armed Forces and that they cause a foreseeable and potentially preventable burden of morbidity and mortality.

Results: These studies show that 8.1% of admissions to the Role 3 Hospital in Afghanistan are due to confirmed CVD or symptoms suggestive of cardiovascular disease. They demonstrate that 9.2% of deaths (rate 7.41 per 100,000 Serviceperson years) in the UK Armed Forces result from CVD and that the incidence of medical discharges from service due to CVD occurs at a rate of 19.6 per 100,000 Serviceperson years.

Conclusions: These data provide compelling evidence that identifying these diseases before symptoms develop would identify individuals at a high risk of death or disability and present an opportunity for life-saving interventions to be delivered.

Section 2: Optimising cardiac screening of potential recruits to the British Army. Despite the deficiency in our understanding of the epidemiology of CVD in the Armed Forces there has long been a system in place to screen for occult CVD at the point of enlistment. The current system utilises a clinical history and examination to detect and exclude individuals in whom certain specified conditions are diagnosed. Evaluating the British Army's screening system is the first research project in this section of the thesis. Prospectively evaluating an alternative system, that includes an additional electrocardiogram (ECG) and when indicated, an echocardiogram (echo), is the second research project. This alternative system is hypothesised to be more sensitive and specific for CVD than the current system that does not utilise an ECG.

Results: The studies show that the current system misses a significant number of cases of potentially fatal or life-changing disease. Furthermore an additional ECG and echo, when indicated, reduce the false positive rate with screening and reduces the need for onward referral.

Conclusions: The addition of an ECG and echo when indicated results in an optimised screening system. A direct outcome of this research is the adoption of the research protocol for the routine screening of potential recruits into the British Army.

CHAPTER 1: INTRODUCTION

1.1 The epidemiology of cardiovascular disease in the UK Armed Forces

1.1.1 Cardiovascular disease in the general population

Cardiovascular disease accounts for 29.6% of deaths and is the leading cause of death worldwide[1]. The CVD mortality rate for the UK was 205.2 per 100,000 in 2010; this demonstrated an impressive reduction of 51% from the previous decade. These improvements were primarily due to better control of acquired risk factors[2] and improved outcomes in IHD, with incremental advances in the management of acute coronary syndromes and improvements in secondary prevention. Whilst mortality has decreased, morbidity has gradually risen with an increase in hospital admissions due to acute coronary syndromes as great as the decrease in mortality. These general population statistics are important starting blocks in examining and understanding the military population. It is from the general population that the Armed Forces are recruited and the factors affecting CVD in the wider society may also affect the Armed Forces.

1.1.2 The influence of demographics

There are obvious differences between the military and civilian populations. Firstly entry to the UK Armed Forces begins at the earliest in late adolescence and is truncated at a younger age than the general population as a whole; approximately 70% of Servicemen and women are under the age of 35 years and fewer than 3% are older than 50 years[3]. This means

children and young adolescents, with particularly high risk conditions such as severe congenital heart disease or the primary arrhythmic syndromes[4], may die or be disabled by their disease prior to the age they can enlist. It also means that deaths from IHD, a disease of exponentially increased incidence through middle-age and later life, should be under-represented relative to the general population[5]. Although the physical limitations associated with severe congenital cardiac diseases will effectively prevent military service, more mild forms of cardiac congenital conditions, which do not result in overt symptoms, might occur in similar proportions to the equivalent UK civilian population where the prevalence is approximately 1-2%.

Physical fitness and ongoing athletic training is integral to military life. The benefits of regular exercise on long term physical and mental health are well known[6], in particular with regards to the prevention of IHD. However sudden cardiac deaths (SCD) in athletes commonly occur during, or immediately following, intensive exercise and especially in sports involving intermittent explosive exercise, such as rugby, football or basketball, rather than in those participating in endurance running or cycling[7]. Athletes in Italy were observed to have an increased risk of SCD 2.8 times greater than sedentary controls[8]. This is in contrast to the general population where SCD primarily occurs in those at rest[9 10]. The UK Armed Forces are male dominated, with a male to female ratio of approximately 9:1; so conditions primarily affecting men are likely to be emphasised in any statistics. Males account for 90% of athletic deaths in the general population. Finally ethnicity appears to play a role in SCD in the young with black athletes 2.6 times more likely to die compared to Caucasians[11]; blacks and other ethnic minorities constitute 7.1% of the UK Regular Armed Forces.

1.1.3 Cardiac disease in populations comparable to the UK Armed Forces

In general, the hearts of both young athletic individuals, whether civilian or military, are undoubtedly healthy. This research relates not to these, but to the small minority of Servicemen and women who harbour unidentified inherited or congenital diseases, or that suffer from risk factors or lifestyle choices that put them at increased risk of death. Although excellent data relating specifically to the UK Armed Forces is available the most extensive research has involved other similar populations.

Given the large numbers participating in sport, deaths in athletes younger than 35 years are rare events. The exact prevalence is difficult to quantify and frequently studies of SCD incidence are methodologically biased and likely to under-represent the mortality rate i.e. reviewing media coverage of SCDs in order to derive the SCD rate[12]. Consequently estimates range between 1 per 23,000 and 1 per 300,000 person years[13].

The studies with some of the most rigorous methodology are US military figures where the entire subject population was reliably observed. The reported SCD rate in US military recruits was approximately 13 per 100 000 recruit years[14] - the highest rates reported in a cohort of the young and apparently well (at least at the point of enlistment). The leading autopsy findings were anomalous coronary artery origins (31.0%), structurally normal hearts (also known as the Sudden Arrhythmic Death Syndrome (SADS)) (34.9%), myocarditis (10.3%) and hypertrophic cardiomyopathy (HCM) (6.3%). A second study by the same authors[15] quantified deaths throughout the US Armed Forces, not exclusively in recruits, and

demonstrated an overall mortality rate of 5.9 per 100,000 service years and a higher rate in males compared with females (6.7 compared to 1.4 per 100,000 service years; p<0.0001). The most frequent autopsy findings in the <35 year cohort were SADS (41.3%), IHD (23.2%), HCM (12.8%), myocarditis (5.7%) and anomalous coronary arteries (4.0%).

Why the mortality rate in US recruits was so high is puzzling, but may be relevant to the UK Armed Forces, in which similar figures do not exist. One hypothesis is that the cohort studied may have consisted of relatively unfit individuals, exposed, for perhaps the first time, to routine, repetitive and arduous physical training. This sudden change in lifestyle may have unmasked otherwise asymptomatic latent disease with catastrophic consequences. Congenital anomalous coronary artery origins tend only to cause symptoms on strenuous physical exertion and are asymptomatic the remainder of the time. Specialist cardiac autopsy, including molecular and genetic analysis, has shown these SADS deaths to be predominantly the result of inherited cardiac conditions, particularly inherited ion channel and heart muscle diseases[16 17]. The most common ion channel diseases, also known as channelopathies, include the long QT syndrome (LQTS) and catecholaminergic polymorphic ventricular tachycardia (CPVT); ventricular arrhythmias in both of these diseases, as well as in the cardiomyopathies, are associated with adrenergic surges such as those that occur during competitive sports or military training[18]. Data looking at gender and mortality in cardiomyopathies within the general, rather than young and althetic, population, indicates a higher risk of death in males for cardiomyopathies associated with a lamin A/C mutation[19], in ARVC [20 21] and in HCM. There is also evidence of greater male penetrance in HCM (92% of males vs 67% of females in <40 year olds)[22 23]. Similar findings

with an increased risk of ventricular tachyarrhythmia is seen in males with LQTS. A particular aetiology pertinent to the Armed Forces is heat stroke; this accounts for a significant proportion of deaths in athletes[24] and although typically related to neurological symptoms fatal arrhythmias do occur.

With increasing age the incidence of disease changes as IHD becomes increasingly common. The incidence of death in the US military population due to IHD for those <35 years of age was 0.65 per 100,000 service years, increasing in those >35 years of age to 13.69 per 100,000 service years ($p < 0.001$). In the >50 years age group, the oldest in the US military, deaths due to IHD increased to 83.5 per 100,000 years. This trend is comparable to the increases in IHD incidence with age in the general population. In older civilian athletes there is also evidence that chronic athletic training increases the risk of atrial fibrillation[25], atrial flutter[26] and sinus node dysfunction[27], all of which may increase the symptoms, but non-fatal incidence, of cardiac disease in older Servicemen and women.

In general the distribution of diagnoses in UK and US civilian populations appears broadly similar to the general US military. It seems possible therefore that these may also be similar to the UK military. In both UK and US civilians HCM is the most frequent autopsy diagnosis in younger civilians[28 29] while coronary artery disease (CAD) increases in prevalence with increasing age, becoming the most common cause in those >35 years. The reasons for these differences may be due to different racial characteristics between the populations, as well as differences in disease

Congenital/inherited causes	
Myocardial disease	HCM, DCM, ARVC
Coronary artery disease / anomalies	Premature IHD in those aged <35 years, anomalous origins of the coronary arteries
Cardiac conductive tissue abnormalities and primary electrical diseases, including the channelopathies	WPW, LQTS, Brugada syndrome, CPVT, SQTS, Idiopathic VT, ERS
Valvular heart disease and disorders of the aorta	BAV, MVP, Marfan Syndrome
Acquired heart disease	
Atheromatous coronary artery disease	Myocardial ischaemia and infarction
Infections	Myocarditis, pericarditis, infectious endocarditis
Infiltrative disease	Sarcoid, amyloid
Other	Electrolyte disorders, drugs (drug-related long QT, cocaine, amphetamines, overdoses), hypothermia / hyperthermia, trauma (*commotio cordis*)

Table 1.1: Summary of potentially fatal cardiac conditions seen in young athletes and military populations. *HCM = Hypertrophic cardiomyopathy; DCM = dilated cardiomyopathy; ARVC = arrythmogenic ventricular cardiomyopathy; IHD = Ischaemic heart disease; WPW = Wolff-Parkinson-White syndrome; LQTS= Long-QT syndrome; Brugada syndrome; CPVT = Catecholaminergic polymorphic ventricular tachycardia; SQTS = Short-QT syndrome; VT = Ventricular tachycardia; ERS = Early repolarisation syndrome; BAV = Bicuspid aortic valve; MVP = mitral valve prolapse.*

classification and autopsy techniques. In both military and civilian groups inherited or congenital diseases are probably the most common culprit diagnoses (Table 1.1). Acquired conditions include myocarditis, *commotio cordis* (direct trauma to the chest, often during contact sports, that triggers ventricular fibrillation) and infiltrative disease, as well as non-cardiac disease in the form of venous and systemic thromboembolic disease. In addition to fatal events these conditions and others, such as hypertension, reflex syncope, orthostatic hypotension and supra-ventricular tachycardias, lead to an almost unseen burden of cardiac morbidity.

1.2 The burden of cardiovascular disease on the UK Armed Forces

1.2.1 Deaths from cardiovascular disease in the UK Armed Forces

The Office of National Statistics (ONS) is the government agency responsible for compiling population and health statistics in the United Kingdom (UK). Defence Statistics is the organisation within the Ministry of Defence (MOD) responsible for the compilation of defence related statistics, including those relating to morbidity and mortality within the Armed Forces. Defence Statistics brings together a combination of administrative systems used by the MOD and the ONS to produce several annual health related reports that are published on the agency's website, including an annual report of mortality figures. These mortality statistics show deaths from circulatory disease and neoplasms to consistently be the most frequent causes of death from disease in the UK Military. Thirty years ago rates of death in the UK Armed Forces from IHD were significantly greater amongst the enlisted ranks than that of the general population, while the rates amongst officers were lower[30]. Since then there appears to be a downward trend in military CVD deaths[31], in keeping with

societal lifestyle changes and medical advances, but no recent comparison of deaths due to IHD (or other CVD) rates in the general UK population has been made. Closer examination of these raw data demonstrates a likely signal of SADS deaths coded as unexplained sudden deaths, additional to the deaths categorised specifically as due to CVD. The total number of presumed and probable CVD deaths amounts to nearly as many deaths in absolute terms as those Servicemen and women that take their own lives. No more in depth interrogation of these deaths to discover the underlying diagnoses has been undertaken and undertaking this is a key project in this research degree.

1.2.2 Medical discharges due to cardiovascular disease in the UK Armed Forces

Many of these illnesses might not result in significant disability in most civilian environments, but in the Armed Forces benign, but distracting symptoms, can effectively terminate careers. Complicating the military employment environment are particular situations where a relatively untoward paroxysm of symptoms might result in disaster. These apply to drivers, air crew, divers, submariners and those remote to medical care or in particularly hostile environments, be that due to the environment or enemy action. For example, a disabling arrhythmia at the controls of a fast-jet, or during an infantry firefight with the enemy, may result in disaster. Even the resupply of regular medications may be impossible under certain circumstances. There are also conditions that occur primarily in soldiers, such as the development of myopericarditis following smallpox vaccination[32], or the cardiovascular complications of heat illness[33] or high altitude[34]. For these Servicemen there are currently few studies to allow an evidence-based risk-assessment to be made and occupational decisions are commonly based on informed common-sense and consensus

guidelines. Ultimately a decision may be made to discharge on medical grounds a Serviceman with a particular complaint as it prevents him safely undertaking his occupational role. Defence Statistics collect these numbers, but as yet no analysis of the cardiovascular diseases within this cohort has been undertaken. Undertaking this data collection and examining the underling cardiovascular diseases involved is a key project within this research degree.

1.2.3 The operational impact of cardiovascular disease in the UK Armed Forces

The main roles of the UK Armed Forces are to provide homeland security and to project force overseas, as required, in the national interest. While understanding the general burden of cardiac disease on the UK Armed Forces, through deaths and medical discharges, is itself useful, these data provide little information of the cost of caring for cardiac disease, in terms or manpower or material assets, during the execution of military operations. The little data on patients admitted to a UK Field hospital in Iraq during the 2003 OP TELIC campaign shows little differentiation in the conditions detected beyond that of the physiological system involved[35]. Furthermore the methodology of discriminating between different diseases is unclear. Data such as these and from other conflicts indicate that the overwhelmingly most frequent causes of hospital admission are due to infectious diseases and environmental injury[36 37 38], but that cardiac disease makes up a small but significant proportion of admissions, including up to 15% of admissions to the Intensive Care Unit. In addition to utilising limited hospital facilities, critically unwell patients put a strain on the limited medical and logistical resources available to evacuate a casualty to the hospital or to aeromedically evacuate a patient back to the UK.

As part of this degree a prospective study of admissions during the OP HERRICK Afghanistan campaign to the UK Role 3 Hospital in Camp Bastion, was undertaken. This examined all General Internal Medicine (GIM) admissions, but specifically those with cardiovascular disease, in order to identify potential public health interventions that may prevent similar admissions in the future, as well as training, diagnostics and therapeutic requirements.

There is recognition that there are a large number of aeromedical evacuations back to the UK for individuals deployed on operations. A total of 2566 servicemen were aeromedically evacuated to the UK with a primary 'Disease and non-battle injury' (DNBI) reason between 8 Oct 2007 and 15 Jun 2011. These data are collected by Defence Statistics but have never been examined in detail. An internal audit of a subgroup of disease cases identified 57 aeromedical evacuations of individuals with medical conditions between Jan 08 – Jul 09[39]. Of these 12 (21%) had a CVD diagnosis. These consisted of 7 arrhythmias, 3 acute coronary syndromes, 1 myocarditis and one 'obstetric' cardiology case; unfortunately further clinical details are unavailable. While there were no deaths within this group, the cost in financial terms to aeromedically evacuate a combatant is considerable (estimates range up to £200,000 per case if a critical care airframe is required).

A study to investigate aeromedical evacuations was approved by the Scientific Approval Committee and MoDREC with protocol number: 12/Gen/310. This was review of Armed Forces population data and therefore no consent from individuals was sought. Permission

to use these databases was provided by the Defence Medical Services Caldicott Guardian Committee for these data. Unfortunately once the necessary approvals were obtained it became apparent that the quality of the data was poor and interrogation of the military's primary care electronic patient record, known as Defence Medical Information Capability Programme (DMICP), to complete gaps in the record, was not going to be sufficient to enable any meaningful analysis or conclusions to be reached. The project was therefore abandoned.

1.2.4 Risk factors for cardiovascular disease in the UK Armed Forces

Currently the prevalence and management of relevant risk factors for IHD in the UK military population is poorly understood. There is evidence that younger Servicemen and women tend not to be overweight, but that body mass increases with age with as many as a quarter of males, aged greater than 35 years, reported as obese (defined as a Body Mass Index >30 kg/m2)[40]. Consumption of tobacco remains common in the Armed Forces with 26% of recruits admitting to be active smokers, a further 20% stating that they had discontinued the habit and only 54% denying they had ever regularly smoked[41]. It is less clear how the proportion of smokers changes as these recruits progress in their careers. No data on the prevalence of hypertension or dyslipidaemias in the Armed Forces are in the public domain.

Interrogation of the defence primary care electronic patient record, the DMICP appears an obvious method to identify risk factors, but this database is not validated as a research tool and has not previously been used for this purpose. Understanding the strengths and

limitations of DMICP may however provide a route to designing meaningful epidemiology studies, such as those aimed at identifying the numbers of Servicemen and women suffering from risk factors for IHD; particularly hypertension and dyslipidaemia, where highly effective primary prevention pharmacological therapies are available; but also for obesity and smoking, where better epidemiological understanding can inform improved public health policies, such as smoking cessation services.

Projects to validate this electronic patient record were designed and undertaken as part of this degree in order to design further epidemiology projects that might glean meaningful insights into cardiac risk factors in the UK military population and how they are currently managed. These were small projects and have been completed and published[42 43]. Unfortunately these two projects highlighted a number of data quality deficiencies in DMICP that meant more generalised research into CVD and risk factors using the database will need careful planning.

1.3 Cardiovascular disease screening in potential recruits to the British Army

1.3.1 Military medical screening

Formal medical screening was a military innovation by the US military who introduced screening for psychological disease in recruits in 1917[44]. The first formal definition for screening was developed by the United States Commission of Chronic Illness in 1951. It read: '*the presumptive identification of unrecognised disease or defect by the application of tests, examinations, or other procedures which can be applied rapidly. Screening tests sort out apparently well persons who probably have a disease from those who probably do not. A screening test is not intended to be diagnostic. Persons with positive or suspicious findings must be referred to their physicians for diagnosis and necessary treatment*'[45].

The aim of the selection process for potential recruits to the Armed Forces is to ensure they have the physical and intellectual aptitude to perform their duties. Part of this selection includes a health assessment designed to screen for disease or other health risks that could foreseeably result in death or significant disability to the individual, or affect the operational efficiency of their unit later. Currently the British Army Initial Recruit Medical (IRM) utilises a stereotyped methodology designed to identify disease affecting any of the physiological systems. Based on the current understanding of the natural history of CVD disease in the military population, including a system to identify disease prior to selection to the Armed Forces has therefore been considered justifiable and is included in the IRM. The goal of the British Army cardiac screening system may therefore be articulated as: 'to identify occult CVD prior to Army enlistment, in order to minimise morbidity and mortality from CVD in the trained soldier population'.

1.3.2 Pre-participation screening for cardiovascular disease

In 1968 the World Health Organisation (WHO) published their guidelines pertaining to what makes an effective screening program (Table 1.2)[46]. These principles relate primarily to the underlying diseases or the healthcare system within which the screening protocol sits. Only 4 points (numbers 5, 6, 9 and 10 in Table 2) actually relate to the screening system itself. In other words the context of the screening system is vital to producing an effective system. Once this context is valid however the screening test itself can be evaluated within this framework.

1.	The condition should be an important health problem.
2.	There should be a treatment for the condition.
3.	Facilities for diagnosis and treatment should be available.
4.	There should be a latent stage of the disease.
5.	There should be a test or examination for the condition.
6.	The test should be acceptable to the population.
7.	The natural history of the disease should be adequately understood.
8.	There should be an agreed policy on whom to treat.
9.	The total cost of finding a case should be economically balanced in relation to medical expenditure as a whole.
10.	Case-finding should be a continuous process, not just a "once and for all" project.

***Table 1.2: The World Health Organisation principles of early diseases detection*[41].**

1.3.3 Defining and measuring the efficacy of screening

Assessing the efficacy of a screening test is an important part of designing an effective screening system. The efficacy of a test is usually quantified by using a 2 x 2 table or confusion matrix to calculate a number of useful measurements that help investigators evaluate the test's utility (Figure 1.1).

The measurements of sensitivity (Sn), specificity (Sp) and Positive Predictive Value (PPV), Negative Predictive Value (NPV) and Accuracy (Acc) are the traditional measures used to assess the utility of a test, though other calculations are also used. The test Sn (or True Positive Rate), is defined as the probability that a test result will be positive when the disease is present. The test Sp (or True Negative Rate) is defined as the probability that a test result will be negative when the disease is not present. The PPV (or Precision) is the probability that the disease is present when the test is positive. The NPV is the probability that the disease is not present when the test is negative. The accuracy of a test is the overall probability that a patient will be correctly classified. These calculations are expressed as percentages.

A diagnostic test with a binary outcome is usually considered reasonable when both Sn and Sp are both >90%. This is less important in a screening system however where there should be a low threshold for doing further tests that in turn will make a definitive diagnosis. In these cases a high Sn is the most important measure as the clinician wants to know whether

they should be concerned enough by a positive test result to refer the individual for further investigation. Highly specific tests are better to confirm a diagnosis and are less important in screening programs.

In addition to Sn and Sp other calculations can be used to evaluate a test. The PPV and NPV are as much a function of the proportions of positive or negative cases in a population than an evaluation of the test itself and are of limited use in this regard. Better calculations are the accuracy, the F1 score and the Matthew Correlation Coefficient (MCC). Accuracy and F1 are less useful when the probability of a disease is either very high or very low. The MCC however takes account of the balance ratios of the four confusion matrix categories (true positives, true negatives, false positives, false negatives) so small groups are allowed. In this score a zero occurs when there is no correlation with a test result, -1 a perfect inverse correlation and 1 a perfect correlation.

Once the Sn and Sp are derived the positive (LR+) and negative likelihood ratios (LR-) can then be calculated (figure 1.1). The LR+ reflects the change from the pre-test to the post-test probability following a positive screening test. The LR- reflects the change from the pre-test to the post-test probability following a negative screening test. These calculations are useful in themselves as an indication of the change in probabilities (Table 1.3). Understanding the post-test probability is however of greater value and if the pre-test probability is known then this can be calculated (using a normogram or online calculator)[47]. Using this method a Sn and Sp of 90%, with a LR+ of 9, for ECG screening for HCM might appear a good test; given the prevalence of HCM is 1 in 500 (therefore the pre-test

	Disease	No disease	
Test positive	True Positive (TP)	False Positive (FP)	PPV = TP / TP + FP
Test negative	False Negative (FN)	True Negative (TN)	NPV = TN / FN + TN
	Sn = TP / TP + FN	Sp = TN / FP + TN	

Measurement	**Calculation equation**
Prevalence	TP + FN / Total population
Sensitivity (Sn)	Sn = TP / (TP + FN)
Specificity (Sp)	Sp = TN / (FP + TN)
Positive Predictive Value (PPV)	PPV = TP / (TP + FP)
Negative Predictive Value (NPV)	NPV = TN / (TN + FN)
Positive likelihood ratio (Ln+)	Ln+ = Sn / FPR
Negative likelihood ratio (LN-)	Ln- = FNR / TNR
False Positive Rate (FPR)	FPR = FP / (FP + TN)
False Discovery Rate (FDR)	FDR = FP / (FP + TP)
False Negative Rate (FNR)	FNR = FN / (FN + TP)
Accuracy (Acc)	ACC = (TP + TN) / (P + N) Worst value = 0; best value = 1
F1 Score (F1)	F1 = 2TP / (2TP + FP + FN) Worst value = 0; best value = 1
Matthew Correlation Coefficient (MCC)	TP*TN - FP*FN / sqrt((TP+FP)*(TP+FN)*(TN+FP)*(TN+FN)) Worst value = −1; best value = +1

Figure 1.3: A 2 x 2 table (above) used to calculate sensitivity, specificity, positive and negative predictive values*. The total that have the disease is TP + FN and the total with no disease is FP + TN and are usually generated from the 'gold standard' test or known prevalence to which the screening test is compared. The table (below) defines how these measurements are calculated.*

probability is 0.2%) in the general population, the probability of the test being a true positive after a positive screening result still remains only 1.8%[48]. This on its own might not seem like a high enough probability to justify a referral for numerous other tests that might be expensive, worrying to the patient and sometimes associated with complications.

1.3.4 The State of the Art of Cardiac Screening

There is controversy relating to the optimal method of cardiac screening within the WHO framework as any screening system will be a compromise between the potential benefits in

Likelihood ratio	Interpretation
>10	Large increase in the likelihood of disease
5 - 10	Moderate increase in the likelihood of disease
1-5	Trivial to small increase in the likelihood of disease
1	No change in the likelihood of disease
1-0.5	Trivial to small decrease in the likelihood of disease
0.1 - 0.2	Moderate decrease in the likelihood of disease
<0.1	Large decrease in the likelihood of disease

Table 1.4. Interpretation of likelihood ratios.

health or economic terms later, balanced against the acceptability, cost and efficacy of the screening system, at the point of screening. The most widely observed cardiac pre-participation screening programs are those that adhere to either the American Heart Association (AHA) guidelines[49] or the European Society of Cardiology (ESC) guidelines[50].

The history and examination have long been the cornerstone of screening for CVD and both guidelines recommend a structured history and physical examination is undertaken (Table 1.4). The history is targeted to elicit symptoms or family history that a patient has not previously recognised to be significant. The physical examination is primarily to identify structural heart diseases and although widely used, ensuring clinicians can detect significant abnormalities and that their findings are reproducible, remains a challenge[51].

Personal medical history
1. Exertional chest pain/discomfort
2. Unexplained syncope/near-syncope†
3. Excessive exertional and unexplained dyspnea/fatigue, associated with exercise
4. Prior recognition of a heart murmur
5. Elevated systemic blood pressure
Family medical history
6. Premature death (sudden and unexpected, or otherwise) before age 50 years due to heart disease, in ≥1 relative
7. Disability from heart disease in a close relative <50 years of age
8. Specific knowledge of certain cardiac conditions in family members: hypertrophic or dilated cardiomyopathy, long-QT syndrome or other ion channelopathies, Marfan syndrome, or clinically important arrhythmias
Physical examination
10. Femoral pulses to exclude aortic coarctation
11. Physical stigmata of Marfan syndrome
12. Brachial artery blood pressure (sitting position and in both arms)

Table 1.5. The recommended questions and physical examination outlined in the American Heart Association guidelines[42] *† Particularly during exertion and not thought to be neurocardiogenic in origin.*

1.3.5 To use an ECG or not in screening.

The AHA and ESC guidelines differ in that the former recommends that an ECG is not routinely acquired, while the latter recommends one is obtained. The reason for the difference in opinion is partly cultural, but also in part as there are no randomised clinical trials showing a benefit in outcome when an ECG is utilised. The most compelling evidence for inclusion of the ECG in screening protocols for young athletes is derived from a 90% reduction in SCD over a 25-year period in the Veneto region of Italy. In this study an original mortality rate of 3.6 per 100,000/year was reduced to 0.4 per 100,000/year[52]. Subsequent studies, notably from Israel and Minnesota in the US have since questioned the validity of this data[53 54]. The question being asked in the research study described in Chapter 6 is not relating specifically as to whether using an ECG is going to reduce the rate of SCD, but how best to screen the potential Army recruit population in order to most effectively exclude cardiac disease of military importance, but indirectly a reduction of SCD would be an desirable outcome.

Acquiring an ECG is relatively quick (approximately five minutes), though interpretation does require training and practice. Historically there has been considerable variability in the findings investigators describe as abnormal on the ECG, but more recent guidelines and research have concentrated on those ECG characteristics with a higher disease detection rate in order to reduce the rate of false positive findings[55 56 57]. These abnormalities are defined as ECG findings likely to be the result of athletic training rather than due to disease and are therefore considered acceptable (Group 1) or abnormalities that are closely associated with disease and are not training related that require further investigation

(Group 2) (Table 1.5). When the research projects described in this thesis were designed, the contemporary guidelines to interpret the ECG of an athlete were the 2010 ESC Guidelines that are summarised in table 1.5.

Group 1: Common and training-related ECG changes	**Group 2: Uncommon and training unrelated ECG changes**
• Sinus bradycardia • First-degree AV block • Incomplete RBBB • Early repolarisation • Isolated QRS voltage criteria for left ventricular hypertrophy	• T-wave inversion • ST-segment depression • Pathological Q-waves • Left atrial enlargement • Left-axis deviation / left anterior hemiblock • Right-axis deviation / left posterior hemiblock • Ventricular pre-excitation • Complete LBBB or RBBB • Brugada-like early repolarisation

Table 1.6. Classification of abnormalities of the athlete's electrocardiogram *(Corrado et al, 2010). AV = atrioventricular; RBBB = right bundle branch block; LBBB = left bundle branch block.*

In 2013 the consensus document that came to be known simply as the Seattle criteria[58] were released. These guidelines made a few refinements to the 2010 ESC guidelines: they removed RBBB as a pathological finding, lowered the lower QTc cut-off to 320ms from 360ms and increased the upper QTc limit to 470ms in males and 480ms in females and

required right axis deviation of 120 degrees as well as RVH by voltage criteria in order to diagnose RVH. These guidelines were designed to reduce the false positive rate of the test.

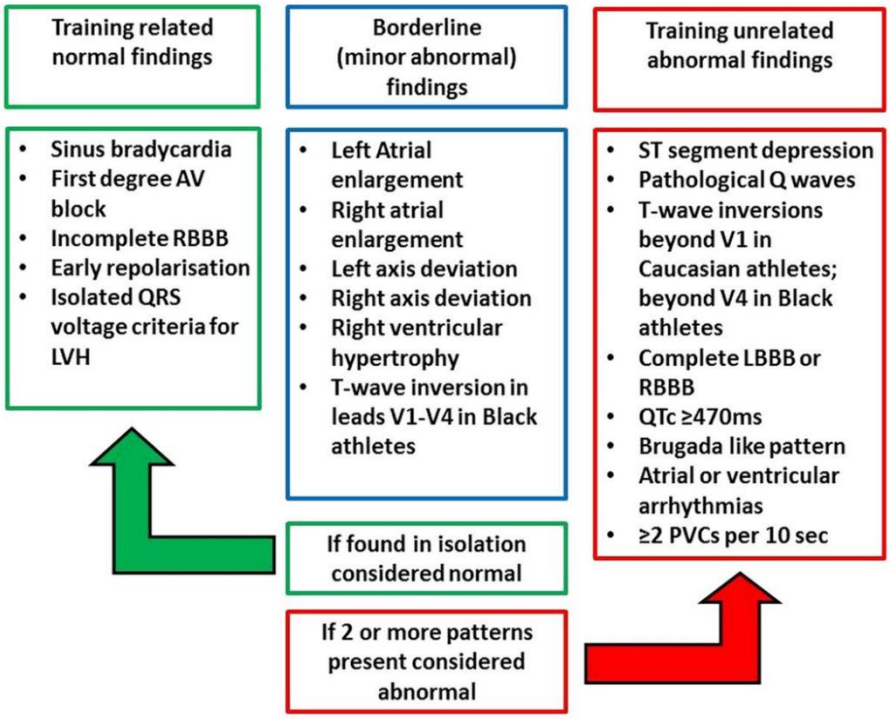


Figure 1.2. Definition of the 'refined criteria' used for ECG interpretation. *The previous European Society of Cardiology guidelines divided ECG changes into those likely to be due to athletic training and not disease (Group 1) and those ECG findings that are more likely to be due to disease and warrant further investigation (Group 2). The investigators proposing these new guidelines divided the Group 2 findings into those always likely to reflect disease and those that may be normal if not found with another abnormality. It was hoped that this will increase the sensitivity and reduce the false positive rate associated with ECG screening. Atrioventricular = AV, Right bundle branch block = RBBB, Left ventricular hypertrophy = LVH, Left bundle branch block = LBBB, Milliseconds = ms.*

These guidelines were then refined by Sheikh et al as 'refined guidelines' (figure 1.2) and these findings were integrated into the current International Guidelines published in 2017[59]. These guidelines made some further refinements; they removed the lower QTc cut-off

completely unless there was an abnormal ECG morphology identified, they integrated the borderline criteria from the 'refined guidelines'; they loosened the requirements for further investigations when isolated inferior T-wave inversions or ST depression were identified and raised the cut-off to 140ms for non-specific intraventricular conduction delay.

Another investigation occasionally used in cardiac screening is echo. Compared to other imaging modalities routine echo is relatively cheap and its portability makes it accessible. A standard scan takes approximately thirty minutes to perform and report so the numbers of patients that can be evaluated are smaller than with history, examination or ECG. The skill of acquiring echo is also specialised so integrating an echo into a screening program usually increases the cost of the screening system and reduces the number of patients that can be investigated. As a consequence echo tends only to be used routinely when cost is a less important factor and patient numbers are low, for example professional football clubs screening their players. Routine echo remains an unusual method of screening and is not recommended by either the AHA or ESC.

Additional tests, such as exercise testing, Holter monitors, other non-invasive imaging, invasive procedures and genetic screening may be indicated in specific groups of people with known risk factors, but they are not routinely used in asymptomatic populations on account of challenges relating to the time required, the high costs, limited accessibility, high levels of expertise required to interpret the tests, poor acceptability of the test by the population or simply because the test itself lacks utility as a screening tool.

Test	Likely to detect	May detect	Unlikely to detect
Physical examination	• Hypertension • Marfan's Syndrome† • VHD • VSD • Coarctation of the aorta	• Familial dyslipidaemia (with peripheral stigmata) • HCM (when LVOTO is present) • Other congenital heart disease • Heart rhythm disease (if present at the time)	• DCM • ARVC • Healed or subclinical myocarditis • Channelopathies‡ • Accessory pathways • ASD • Aortic dilatation • Anomalous coronary artery origins • IHD • Subclinical pericarditis
Resting 12 lead ECG	• HCM • DCM • ARVC • Healed or subclinical myocarditis • Accessory pathways • Heart rhythm disease (if present at the time)	• Hypertension (if severe) • Other congenital heart disease • Coarctation of the aorta • Channelopathies‡ • IHD (if previous MI or critical ischaemia)	• Marfan's Syndrome† • VHD • VSD • ASD • Aortic dilatation • Coarctation of the aorta • Anomalous coronary artery origins • Other congenital heart disease
Transthoracic echocardiography	• HCM • DCM • ARVC • VHD • ASD • VSD • Coarctation of the aorta • Other congenital heart disease • Aortic dilatation • Subclinical pericarditis	• Hypertension (if severe) • Marfan's Syndrome† (if characteristic echo findings only) • Heart rhythm disease (if present at the time) • Healed or subclinical myocarditis • Anomalous coronary artery origins • IHD (if previous MI)	• Familial dyslipidaemia • Channelopathies‡ • Accessory pathways

Table 1.7. The diseases that are frequently detected or missed with a physical examination, resting 12 lead ECG or echocardiogram in the young general population. *These likelihoods are subjective and based on the author's understanding of the test modality and the disease in question. There are several diseases not easily detected by any of these tests, for example anomalous coronary artery origins. Abbreviations: Valvular heart disease (including stenosis, incompetence or bicuspid aortic valve disease) = VHD, Ventricular septal defects (VSD), Hypertrophic cardiomyopathy = HCM, Left ventricular outflow tract obstruction = LVOTO, Dilated cardiomyopathy = DCM, Arrhythmogenic right ventricular cardiomyopathy = ARVC, Long QT Syndrome = LQTS, Catecholaminergic polymorphic ventricular tachycardia = CPVT, Atrial septal defects = ASD, Ischaemic heart disease = IHD, Myocardial infarction = MI. † and other connective tissue diseases. ‡ including LQTS, Brugada syndrome, CPVT, Short QT syndrome.*

The cardiac diseases being sought at cardiac screening are heterogenous and the history, physical examination and ECG each vary in their ability to identify disease (Table 1.6). A meta-analysis comparison of the Sn and Sp of history, physical examination and ECG shows that the ECG is the most sensitive test, in isolation, to detect potentially lethal disease (Table 1.7) but that in spite of this the positive post-test probability, assuming a 0.3% prevalence rate of disease, is still only 4.26%, a level where some clinicians might baulk at ordering further investigations. These figures may however be more of historic interest as they use relatively old studies with redundant ECG interpretation methods. Newer 'refined criteria' of ECG interpretation, published since the start of this research project, indicates that a LR+ as high as 22.8 is achievable, though this was a relatively small study with only a small number of disease cases detected (Figure 1.2)[57]. Unfortunately limited data exists for either a multiphasic screening system integrating all these tests, or for the Sn and Sp of these elements when diseases more likely to cause morbidity than mortality are included.

1.3.6 Screening for cardiac disease in the British Army

As a cardiac screening programme is already in place, the primary question in the Armed Forces is not whether screening should occur, but rather how best we should do it for reasons of cost-effectiveness, acceptability, and efficacy of the screening methods. The current screening programme has never been evaluated so whether the existing screening protocol in place for potential recruits to the British Army is the optimal method for detecting silent CVD is unknown. Appraising the current system and investigating alternative systems is the focus of the second part of this research degree.

Test	Sn (95% CI)	Sp (95% CI)	LR+ (95% CI)	LR- (95% CI)	Positive test post-test probability	Negative test post-test probability
History	20% (7%-98%)	94% (89%-96%)	3.22 (1.3-8.01)	0.85 (0.68-1.07)	0.96%	0.26%
Physical examination	9% (3%-24%)	97% (95%-98%)	2.93 (1.26-6.83)	0.93 (0.85-1.03)	0.87%	0.28%
Resting 12 lead ECG	94% (79%-98%)	93% (90%-96%)	14.8 (9.43-23.16)	0.055 (0.012-0.25)	4.26%	0.02%

Table 1.8. Showing the sensitivity (Sn), specificity (Sp), positive likelihood ratio (LR+) and negative likelihood ratio (LR-) of the different screening protocol components, on their own, to detect potentially lethal disease*. These Sn, Sp, LR+ and LR- figures are calculated by a meta-analysis of 15 pooled trials[60] and were published after this research degree was initiated. The post-test probabilities are calculated using a presumed pre-test probability of an individual having an occult, potentially lethal, disease of 0.3%. The combined effect of multiple screening tests is not assessed. It should be noted that diseases that may cause morbidity, but are rarely immediately lethal, were not included in this analysis, but are of relevance to the Armed Forces population. Furthermore the algorithms used to interpret the ECG findings varied between the studies used and these findings should be considered indicative rather than definitive. Published data on these non-lethal diseases is not available.*

The British Army cardiac screening programme for potential recruits is intended to ensure recruits meet a minimal set of medical employment standards. These are laid out in Joint Service Publication 950 (JSP950). These standards include the automatic exclusion of individuals with clearly defined CVD, such as a bicuspid aortic valve (BAV) or Marfan's syndrome. Individuals with a history of curative ablation therapy for accessory pathways

can be accepted following discussion with the single-Service Occupational Physician responsible for recruit selection. The eligibility for other diagnoses are less prescribed, such as mild valvular regurgitation where eligibility for service are dependent on the underlying anatomy, severity of dysfunction, functional capacity and predicted progression. Other findings may need further investigation using modalities that are not practical for a screening system, such as ambulatory monitoring or cardiac magnetic resonance imaging. The screening system should therefore provide, in addition to the identification of pathology, more information that can inform whether a candidate can be accepted immediately or should undergo additional investigation.

The current screening programme utilised in recruits applying to join the British Army consists of a questionnaire (RG8 Part 1) and physical examination (RG8 Part 2). The applicant's General Practitioner (GP) completes a questionnaire section in the RG8 Part 1 and this is reviewed by a military occupational physician. If this is acceptable then the candidate is booked onto the 2 day Army selection board, the first part of which is the IRM. The IRM includes a face-to-face consultation and physical examination (RG8 Part 2). If the RG8 Part 1 questionnaire identifies symptoms or a family history suggestive of CVD then the candidate is referred to a consultant cardiologist for further investigations. If these findings are found to be acceptable by the military occupational physician then the IRM is arranged. No additional cardiac specific investigations are routinely used with the exception of air-crew, Special Forces and divers who all have an additional 12 lead ECG taken. This paradigm therefore adheres to the AHA guidelines on Pre-participation screening in athletes, rather than those of the ESC.

If during the IRM a murmur is detected then the candidate is referred for investigation to a private company (Cardiac Report Ltd.) and an ECG, transthoracic echo, consultation and physical examination with a GMC specialist register accredited consultant cardiologist are undertaken through a MOD contract. This process run by Cardiac Report was in place from 2004 until the contract was taken over by another company (Capita Health and Wellbeing) in 2013. Until the contract changed each potential recruit underwent a consultation with a Consultant Cardiologist. During this period >11,000 individuals were screened by Cardiac Report with an age range of 17 – 29 years 11 months. The results of these investigations have never been collated. Investigating this asymptomatic cohort, in whom a murmur was detected, is a key project of this research degree.

A second part of this screening research is to prospectively recruit candidates undergoing the standard screening process into a study investigating comparing the effect of an additional ECG, as recommended by the ESC, with a standard history and examination alone. This is important in order to identify whether the current cardiac screening system should be innovated to routinely include an ECG, but will also allow different methods of ECG interpretation to be compared.

Having a rough understanding of the cost of screening has been calculated using a civilian screening program in the UK and this calculated the cost per athlete screened to the region of $90 per candidate and a cost of $28-30k per serious diagnosis made[61]. This analysis used the Seattle Criteria and refined criteria guidelines for ECG interpretation. This screening program was organised by a charity with screening partially self-funded and the estimated

costs were for the screening process and subsequent investigations only. A similar estimate of the current and alternative screening systems would be a useful planning tool for budget holders in commissioning an evidence-based and maximally cost effective screening system for the future. A modelling process to look at the cost of screening British Army using the current system and with alternative methodologies is also included.

Part 1: Investigating the mortality and morbidity burden from cardiovascular disease in the United Kingdom Armed Forces

Chapter 2: A review of deaths due to cardiovascular disease in the United Kingdom Armed Forces

2.1 Background

The population of the UK Armed Forces is selected from the general population. As such it can be supposed that Servicemen and women die from cardiovascular disease of a similar aetiology to the population of comparable demographics within the general population. All military deaths are reported to Defence Statistics where they are collated and incorporated into an annual health report. These deaths are not clearly characterised beyond broad aetiological grouping but from these reports it is apparent that approximately 10% of deaths in the UK Armed Forces result from cardiovascular disease. More detailed characterisation of the underlying diagnoses has never been performed, but might prove useful in identifying targets for preventative health interventions and allow the effect of these interventions to be observed.

The aim of this project is therefore to quantify the number and causes of deaths due to CVD in the Armed Forces in order to better identify who are at risk and how this risk has changed over time. It may allow us to identify groups that are at risk and whether deaths occur in low resource environments where there are limited medical facilities should personnel become critically unwell. Better describing these deaths will also allow us to confirm whether trends in the general population towards fewer deaths due to CVD or an increased

risk in males or of IHD with increasing age apply to the military population. A number of hypotheses will be tested.

2.1.1 Hypotheses

1. Individuals within the Armed Forces die suddenly from inherited CV diseases;
2. Deaths from IHD increases with age;
3. Males die more frequently than females;
4. Deaths occur during operational deployments;
5. Deaths occur while on duty in the UK / home base;
6. Death rates in general are reducing over time.

2.2 Methods

The cohort studied consists of the annual population of the UK Armed Forces between 1995 and 2013 inclusive. Demographic data of the Armed Forces during the study period has been compiled and includes age, rank, gender and Service (Royal Navy, including the Royal Marines, British Army and Royal Air Force). Rank was standardised using the NATO system (Table 2.1).

All deaths were captured and collated in order to obtain a complete mortality record for the UK Armed Forces. Death certificate and autopsy results (where applicable and available) were sought for all deaths and these were individually inspected. All diseases were

classified according to the WHO International Classification of Diseases 10 (ICD-10). The ICD10 Codes from 'Chapter I: Circulatory system disorders' (specifically codes: I00 - I99), 'Chapter R: Symptom, signs and abnormal clinical and laboratory findings, not elsewhere classified' (specifically codes R00, R01, R06, R07, R09, R55, R96, R98, R99) and the cardiovascular codes from 'Chapter C: Neoplasms' (specifically C38), 'Chapter Q: Congenital malformations, deformations and chromosomal abnormalities' (specifically Q20, Q21, Q22, Q23, Q24, Q25, Q26, Q27) and 'Chapter Z: Factors influencing health status' (Z941, Z950, Z951, Z952, Z954, Z958) were used as the basis of those deaths likely due to a cardiac cause.

Deaths were identified where the cause was due to an identified CVD or where the death was sudden. 'Sudden death' is defined as 'an unexpected and sudden cardiorespiratory collapse, with either death or terminal life support care taking place within 1 h from the onset of symptoms'. Sudden deaths were further sub-classified into either cardiovascular, non-cardiovascular (but classified according to a systemic cause) or idiopathic. All other deaths were classified as 'non-sudden'. Deaths were defined as cardiovascular in origin if the decedent had pathologically confirmed heart disease with clinical circumstances defined as probably cardiac in origin. Sudden Arrhythmic Death Syndrome was defined as any sudden death unexplained by pre-existing disease and without identifiable cause on a post-mortem examination that includes a toxicology screen. All deaths were collated with crude rates recorded per 100,000 Serviceperson years.

Subjects with stable or unstable medical conditions such as asthma and epilepsy could not be differentiated so all were included in the study. Deaths from accidental trauma (but not

that associated with enemy action), drug overdose or misuse, drowning, electrocution, burns, and suicide were included in the data capture, but excluded from the definition of sudden death. These were not included as due to cardiovascular death if there was not an underlying CVD state that contributed to the death. Deaths due to an ongoing chronic or malignant disease requiring hospitalization were also captured and sub-classified into cardiovascular and non- cardiovascular causes.

The Armed Forces is a large population, but unlike the general population where the population numbers are estimated between censuses, it is one where all deaths can be recorded with a fixed denominator population. We also have details of the population demographics for this period. Population numbers were taken from the Defence Statistics annual personnel reports; these were compiled annually and rates were based on the numbers on 1 April. Well differentiated ethnicity data was unavailable for the entire period so this was not evaluated.

This is a review of Armed Forces population data and therefore no consent from individuals was sought. This project was approved by the Scientific Approval Committee and MoDREC with protocol number: 12/Gen/310. Permission to use these databases was provided by the Defence Medical Services Caldicott Guardian Committee for these data.

NATO Code	Royal Navy	Royal Marines	Army	Royal Air Force
Officers				
OF-10	Admiral of the Fleet	-	Field Marshal	Marshal of the RAF
OF-9	Admiral	General	General	Air Chief Marshal
OF-8	Vice Admiral	Lieutenant General	Lieutenant General	Air Marshal
OF-7	Rear Admiral	Major General	Major General	Air Vice-Marshal
OF-6	Commodore	Brigadier	Brigadier	Air Commodore
OF-5	Captain	Colonel	Colonel	Group Captain
OF-4	Commander	Lieutenant Colonel	Lieutenant Colonel	Wing Commander
OF-3	Lieutenant Commander	Major	Major	Squadron Leader
OF-2	Lieutenant	Captain	Captain	Flight Lieutenant
OF-1	Sub-Lieutenant	Lieutenant/2nd Lieutenant	Lieutenant/2nd Lieutenant	Flying Officer/Pilot Officer
OF(D)	Midshipman	-	Officer Designate	Officer Designate
Other Ranks				
OR-9	Warrant Officer Class 1	Warrant Officer Class 1	Warrant Officer Class 1	Warrant Officer
OR-8	Warrant Officer Class 2	Warrant Officer Class 2	Warrant Officer Class 2	-
OR-7	Chief Petty Officer	Colour Sergeant	Staff Sergeant	Flight Sergeant/ Chief Technician
OR-6	Petty Officer	Sergeant	Sergeant	Sergeant
OR-4	Leading Rate	Corporal	Corporal	Corporal
OR-3	-	Lance Corporal	Lance Corporal	Lance Corporal
OR-2	Able Rating	Marine	Private	Junior Technician/ Leading Aircraftman/ Senior Aircraftman
OR-1	-	-	Junior	Aircraftman

Table 2.1: Standardisation of the different equivalent ranks was performed by NATO code. *This list of ranks is not exhaustive as different trades and Army regiments have ranks specific to them, for example a 'Trooper', a 'Sapper' and a 'Gunner' are all OR2 equivalent.*

2.3 Results

2.3.1 Population demographics

The population at risk over the period 1995-2013 inclusive was 3,764,517. The Army constituted a greater proportion of the overall Armed Forces with 2,033,114 (54.0%) of the manpower compared to the RAF with 959,661 (25.5%) personnel and the Royal Navy with 771,742 (20.5%) (figure 2.1).

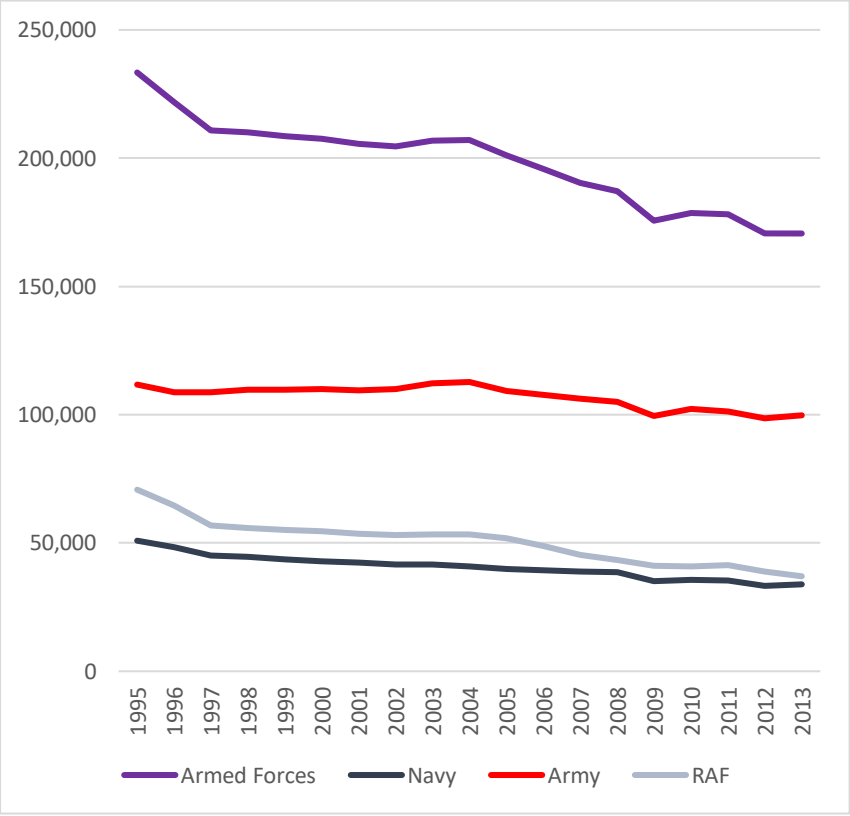


Figure 2.1: Graph illustrating the total numbers in the regular Armed forces and single Services annually from 1995 – 2013*. The Army make up the majority of the Armed Forces. Over the period studied the population of all three Services has decreased in line with changes in defence policy and funding.*

The Armed Forces were predominately male with only 324,881 (8.6%) Servicewomen in total. There were more females by proportion in the Officer cadre (10.3%) compared to the Other Ranks (8.3%) ($p<0.0001$). During the period studied the proportion of females gradually increased (figure 2.2) from 7.1% of the total in 1995 to 9.1% in 2013.

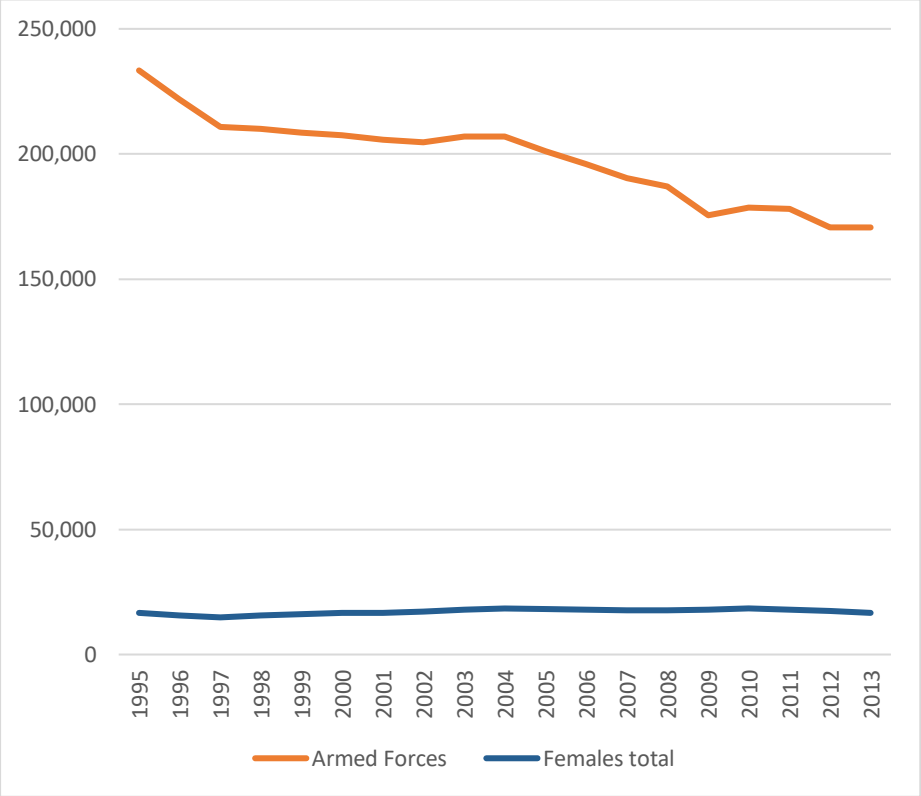


Figure 2.2: Graph showing the change in the numbers of females serving in the regular Armed Forces from 1995 – 2013. *The proportion of females increased consistently over the period in line with recruiting policy.*

Overall the mean age was 30 years but the median age group was 25-29 years (figure 2.3). Officers tended to be older than soldiers; their mean age was 37 years and 9.1% were aged 50 years or older; findings that reflect their higher educational levels, later age at

commissioning and later retirement age. The Other Ranks tended to be younger with a mean age of 29 years, a mode age group of 20-24 years and a median age group of 25-29 years.

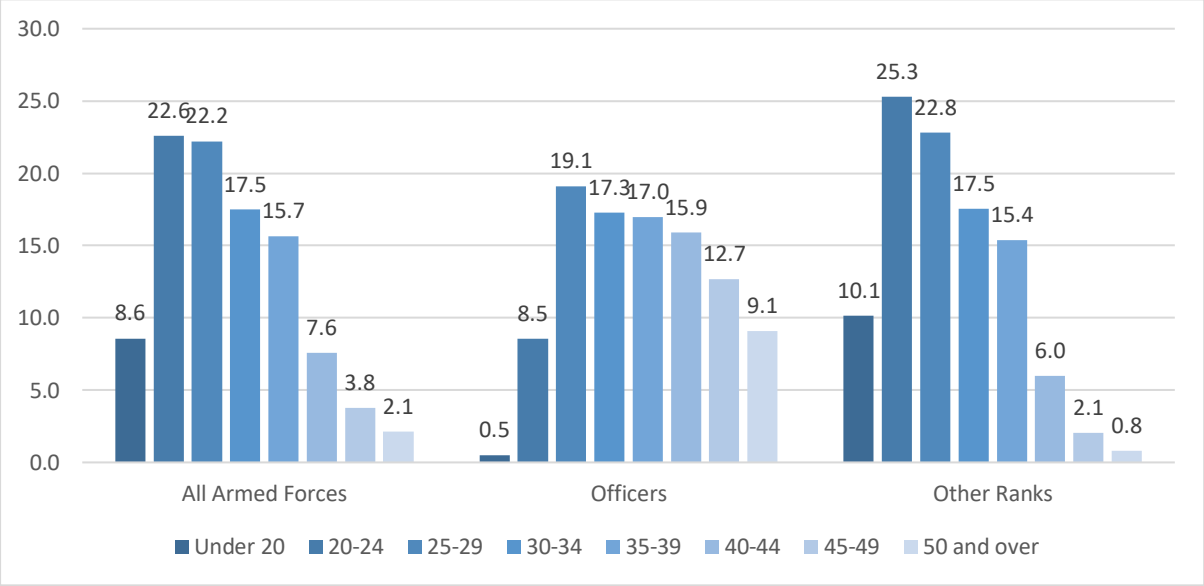


Figure 2.3: Graph illustrating the age distributions as percentages of the Armed Forces. *As a whole (left), Officers (middle) and Other Ranks (right).*

Officers made up a 16% minority of Servicemen and women (figure 2.4) with approximately 84% Other Ranks. As might be expected in a hierarchical organisation the more junior ranks in both Officer and Other Ranks groups were more numerous than those in higher ranks (figure 2.5).

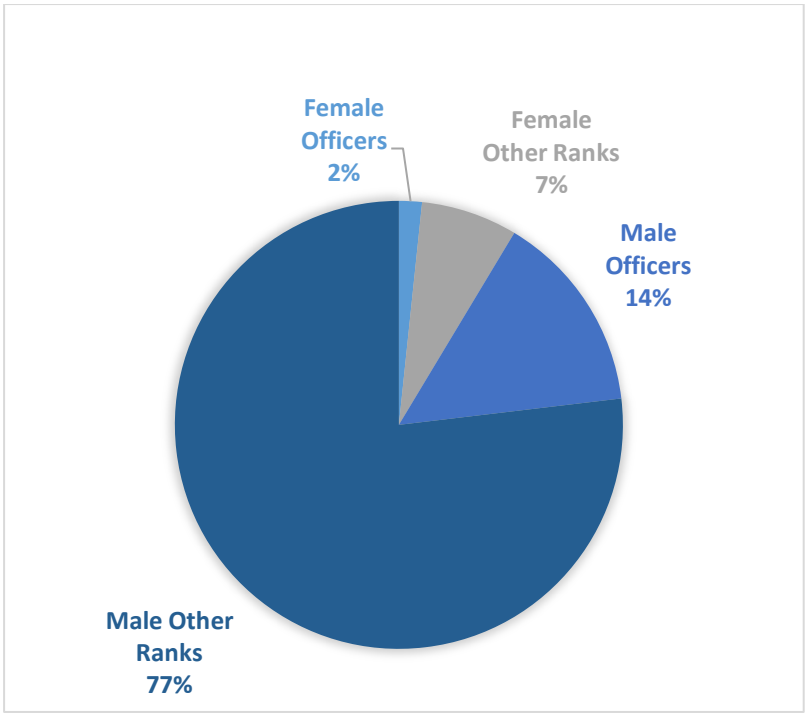


Figure 2.4: Chart illustrating the percentages of the Armed Forces by gender and rank structure.

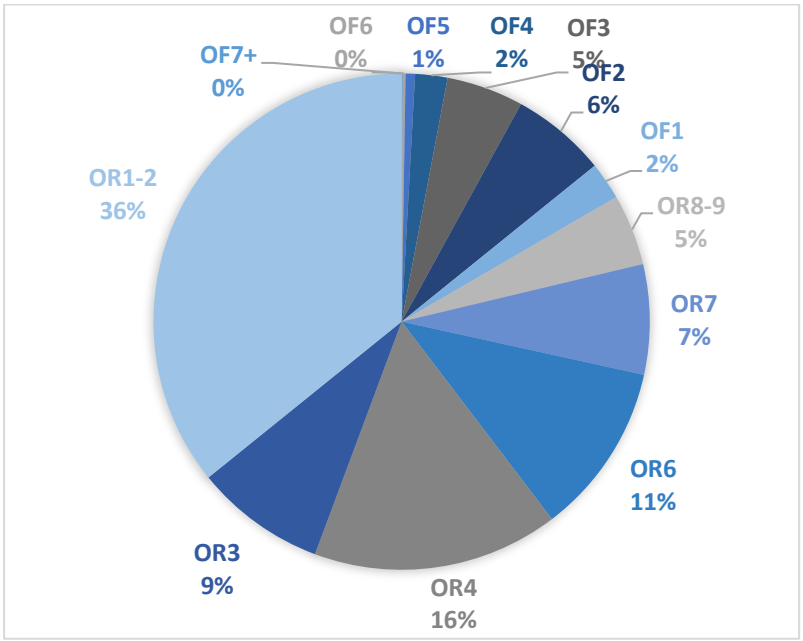


Figure 2.5: Chart illustrating the percentages of the Armed Forces by rank structure. OR1-2 ranks constituted over a third of the Armed Forces.

2.3.2 Overall deaths

During the period investigated there were 3037 deaths. Of these 851 fitted the inclusion criteria for more detailed examination to see if the cause of death was due to CVD or SADS.

2.3.3 Deaths unrelated to combat or cardiovascular disease:

Cancer accounted for 436 deaths in total, the largest single category of deaths with a crude rate of 11.5 per 100,000. The average age at death was 39 years (range 17-58 years). There were 27 (6.9%) female cancer deaths. These were not investigated or analysed further.

Accidents and suicide accounted for 1645 deaths with a crude rate of 43.7 and per 100,000. Accidents were varied and included road traffic accidents, helicopter and other aircraft crashes and deaths whilst participating in adventurous training, military exercises or on active operations. Within this total there were 29 drownings. These drownings were associated with alcohol intoxication in 4 cases and suicide in a single case; the remainder were whilst engaged in adventurous training (such as sailing, canoeing, caving and diving) or during military exercises or operations (such as during river crossings or in the case of several accidents, where vehicles overturned into water courses). None of these accidental or suicide deaths appeared to have an underlying cardiac cause.

Acute asthma resulting in death was infrequent, accounting for only 3 sudden deaths, all of whom were male.

There was a single death from heat stroke in a 25 year old off-duty male.

Epilepsy with status epilepticus, aspiration or asphyxiation accounted for 8 sudden deaths, all in males. One of these in 1997 occurred in a 23 year old male with no history of seizures who was found to be in cardiac arrest by paramedics on their arrival. Unfortunately no autopsy was performed. This was the only case that was suggestive of a possible alternative diagnosis of cardiac disease rather than epilepsy as the cause of death.

2.3.4 Deaths due to cardiovascular disease

There were 279 deaths due to cardiovascular disease, constituting 9.2% of all deaths in the Armed Forces (figure 2.6). Of all the CVD deaths 217 deaths were due to specific cardiac disease (figure 2.7). The death certificate was available for all cases. An autopsy was confirmed to have been performed in 161 cases (57.7%) and of these 60 were available for review (21.5%). The crude mortality rate was 7.41 per 100,000 Serviceperson years. Males made up 268 (96.06%; crude rate 7.79 per 100,000) of deaths and females 11 (3.94%; crude rate 3.39 per 100,000) deaths despite constituting 91.4% and 8.6% of the overall Armed Forces population respectively; males were more

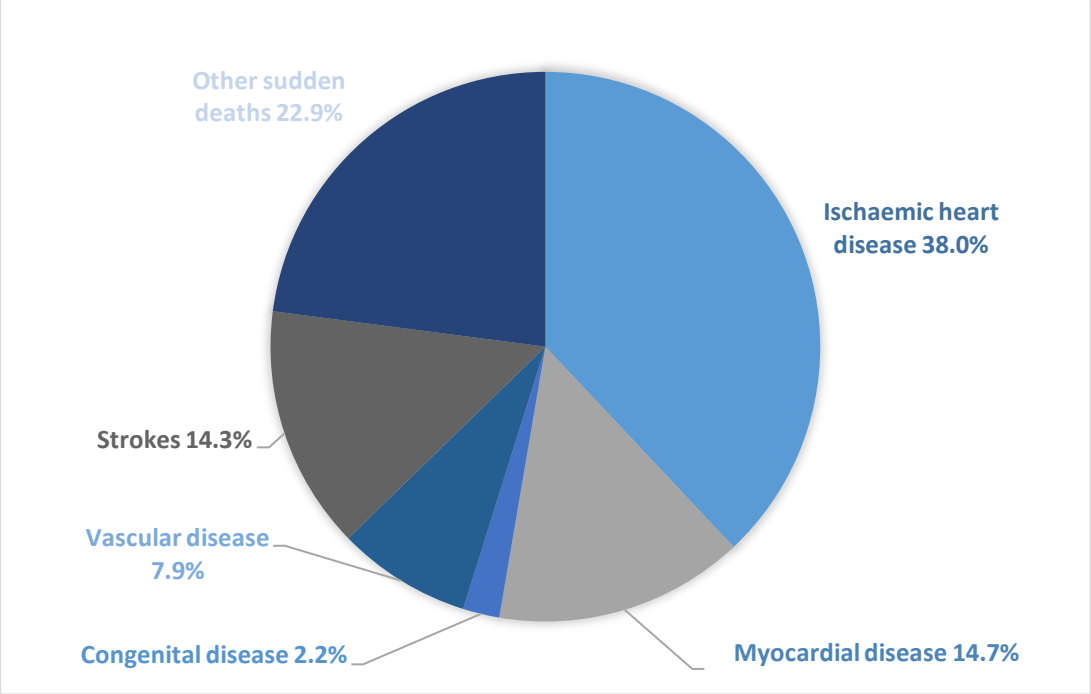


Figure2.6: Graph illustrating the proportions of deaths due to cardiovascular disease and different causes by group.

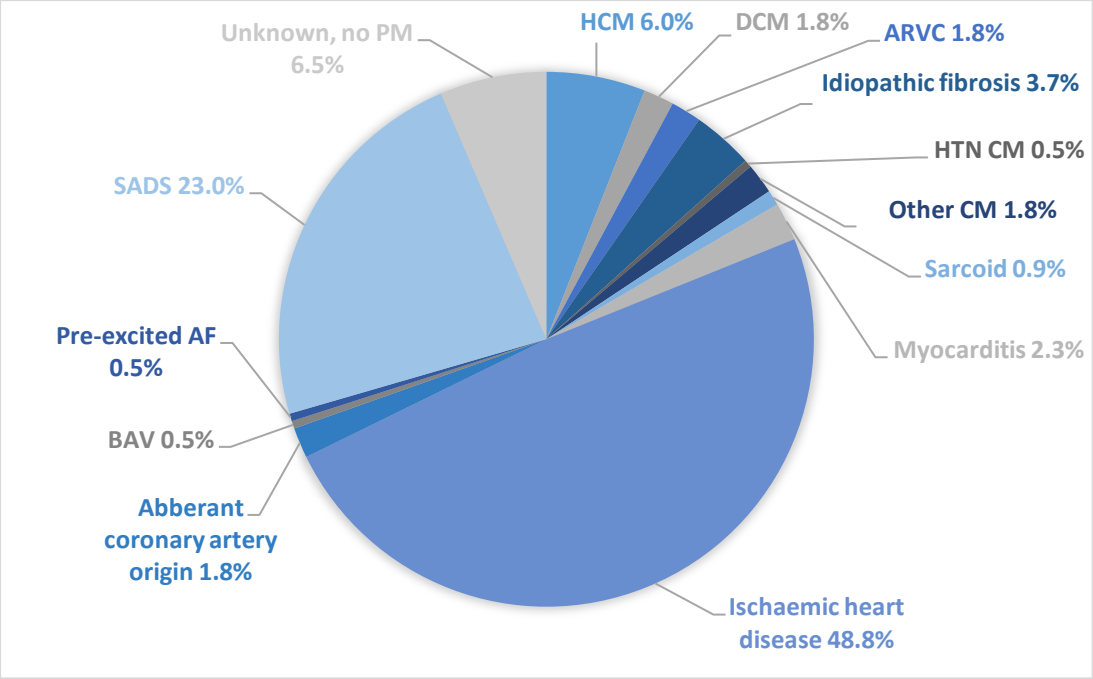


Figure 2.7: Graph illustrating the proportions of deaths due to cardiac diseases.

likely to die from CVD than females (p=0.005401). The cardiovascular deaths were due to a number of causes summarised in figure 2.6 where they are grouped by the type of CVD.

2.3.5 Locations of deaths

There were 213 deaths (76.3%) in the UK and 7 deaths in dependent territories (the Falklands, Gibraltar, Guernsey and Hong Kong prior to the handover to China). The remaining 61 deaths occurred in 21 different countries or at sea (2 deaths). Death occurred whilst an individual was on duty in 77 (27.6%) cases with 16 (5.7%) of these occurring whilst the individual was serving on active operations or whilst serving in the enduring overseas commitments in the British Sovereign Base Areas of Cyprus, Hong Kong, the Falkland Islands, Gibraltar or Brunei (16 deaths, 6.1%). The operational theatres that deaths occurred in were Northern Ireland, Cyprus, the Balkans, Iraq and Sierra Leone. Of these operational or overseas commitment deaths, IHD accounted for 11 deaths, cardiomyopathy for 8 deaths, SADS for 7 deaths, stroke for 2 deaths and one death each from aortic dissection, myocarditis, pre-excited atrial fibrillation and arterial thromboembolism. All these deaths occurred in males with the exception of the single myocarditis death.

2.3.6 Deaths by Service

There were differences in the crude mortality rates between the three Services with the Navy mortality rate at 8.2 per 100,000 Serviceperson years, the Army at 6.6 per 100,000 Serviceperson years and the RAF at 8.4 per 100,000 Serviceperson years. Although the crude rates appear different the Army's mortality rate was not significantly different than

the Navy (p=0.175) or RAF (p=0.87), nor were the Navy and RAF mortality rates significantly different (p=0.84). In total 71 Officers (25.4%, crude rate 11.5 per 100,000) died from CVD, a significantly greater rate than the 208 Other Ranks (74.6%, crude rate 6.5 per 100,000) who died from CVD (figure 2.8) (p<0.001). The mortality rate increased with age in both groups.

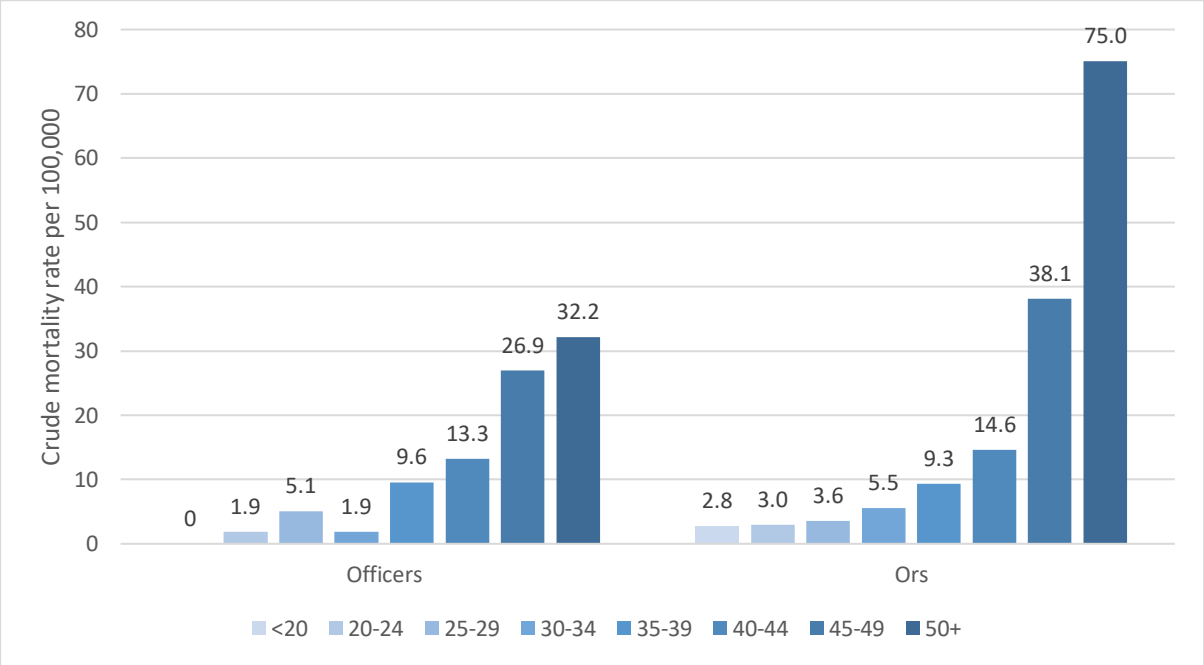
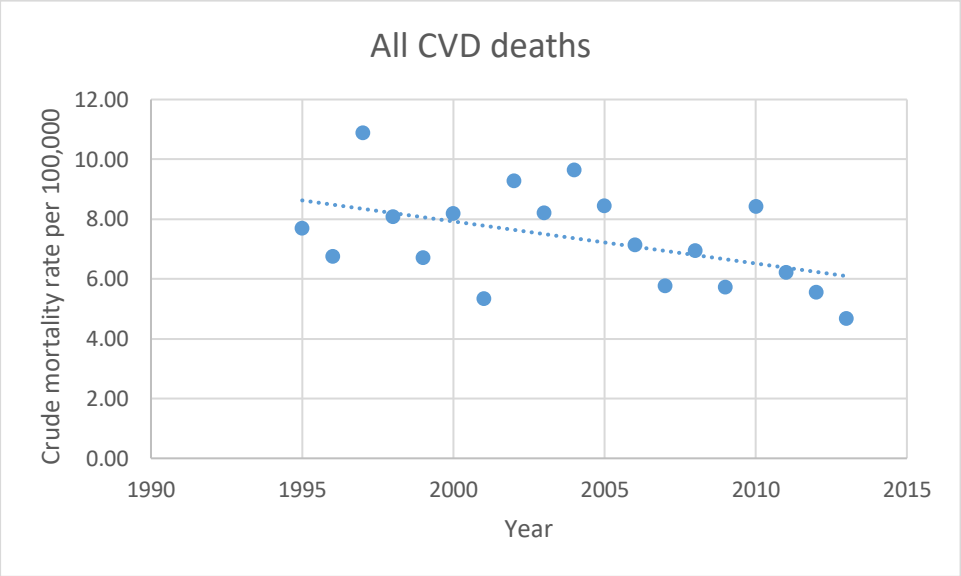


Figure 2.8*: *Graph illustrating the mortality rates per 100,000 at each age group for Officers and Other Ranks.

2.3.7 Deaths over time

The death rate from CVD has trended downwards over the study period in both absolute and crude mortality rate terms. This appears led by a decrease primarily in the incidence of deaths due to IHD that constituted almost 40% of the total deaths (figure 2.9). The numbers of deaths due to other diseases are low and it is therefore difficult to interpret the trends seen in other CVD (figure 2.10).



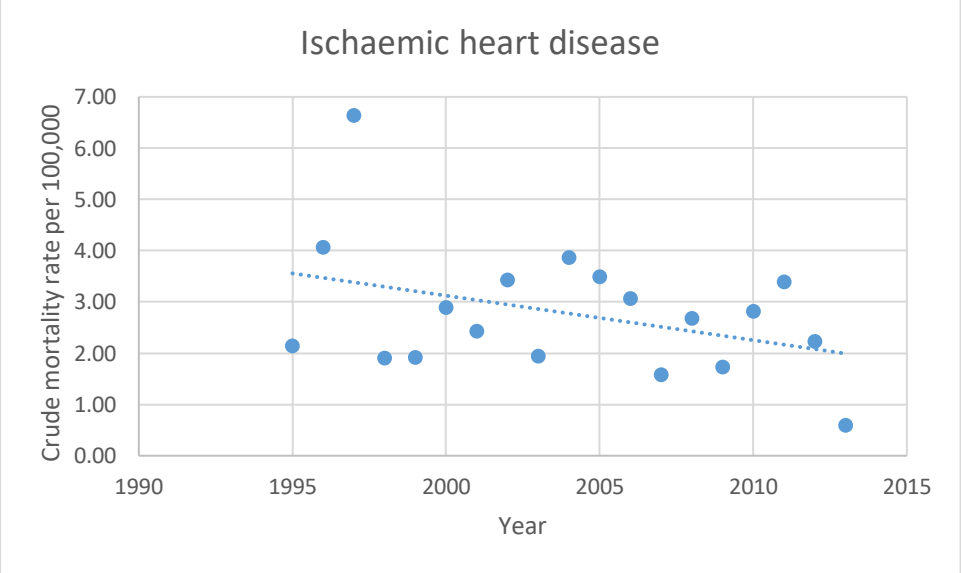


Figure 2.9 a (above) and b (below): *These graphs show the crude death rates due to all CVD (above) and the contribution of ischaemic heart disease (below) with the trends in both to lower rates over time.*

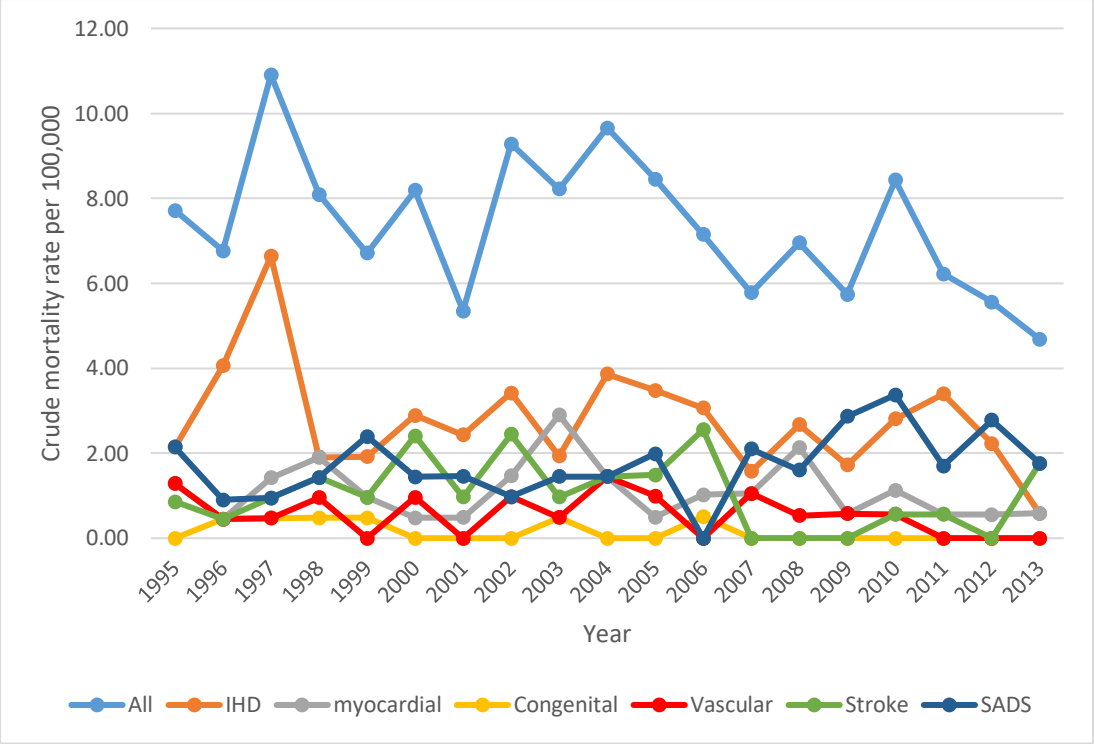


Figure 2.10: Graph illustrating the crude mortality rates of the different groups of cardiovascular disease over time.

2.3.8 Age and death due to cardiovascular disease

There was an association between increasing age and a significantly increased risk of death ($p<0.001$) from CVD with 99 deaths (35.5%; crude rate 3.71 per 100,000) in service personnel younger than 35 years and 180 deaths (64.5%; crude rate 16.41 per 100,000) in those 35 years or older. This difference was primarily due to the sharp increase in deaths due to IHD in those 35 years and older (table 2.2; figure 2.11), though small increases were also seen in deaths due to stroke, myocardial disease and SADS.

2.3.9 Cardiac disease deaths, including SADS

2.3.9.1 Ischaemic heart disease. There were 106 (crude rate 2.82 deaths per 100,000 Serviceperson years) deaths from IHD making it the most common cause of CVD death. All of these deaths were in males. As discussed above there was a decrease in mortality rate over the time period consistent with a similar drop in the general population. Mortality rates increased dramatically with increasing age (figure 2.11).

	IHD		Myocardial		Congenital		Vascular		Strokes		SADS	
	n	Rate	n	Rate	n	Rate	n	Rate	n	Rate	n	Rate
<20	0	0	0	0	1	0.31	0	0.00	3	0.92	5	1.53
20-24	2	0.23	6	0.70	1	0.12	2	0.23	2	0.23	12	1.39
25-29	4	0.47	9	1.06	2	0.24	1	0.12	2	0.24	14	1.65
30-34	5	0.75	3	0.45	1	0.15	5	0.75	7	1.05	12	1.80
35-39	22	3.69	12	2.01	1	0.17	4	0.67	11	1.84	7	1.17
40-44	21	7.26	3	1.04	0	0	7	2.42	3	1.04	6	2.07
45-49	27	18.8	3	2.09	0	0	3	2.09	9	6.27	4	2.79
50+	25	30.86	5	6.15	0	0	0	0	3	3.69	4	4.92
Totals	**106**		**41**		**6**		**22**		**40**		**64**	

Table 2.2: Cardiovascular deaths grouped by category and age group. *Crude rates expressed per 100,000 service person years.*

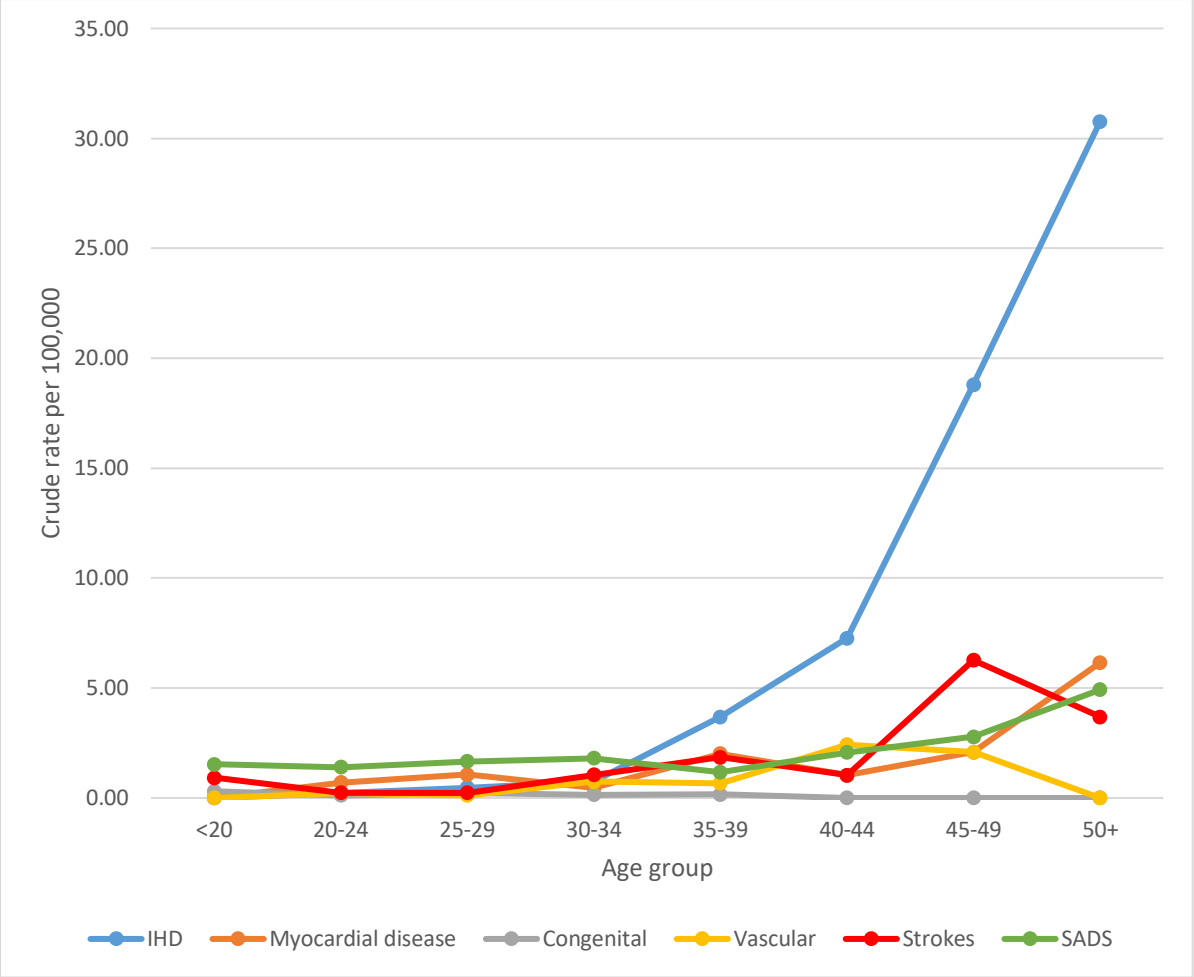


Figure 2.11: Graph illustrating the relationship between increasing age and crude mortality rate per 100,000.

2.3.9.2 Myocardial disease. In total 41 individuals died from myocardial diseases (crude rate 1.09 per 100,000 Serviceperson years), including cardiomyopathies, myocarditis and cardiac sarcoidosis (table). Of these 39 (95.1%) were males, a non-significantly higher proportion than females (p=0.394). The youngest death was at age 21 years and the oldest 56 years with a mean and median age of 35 years. Hypertrophic cardiomyopathy constituted 13 deaths and was the most common cause of death in this group of myocardial diseases (crude rate 0.35 per 100,000 Serviceperson years). There were 12 deaths where an

autopsy was unable to characterise the causative myocardial disease, but where interstitial fibrosis or other non-specific characteristics of cardiomyopathy were identified.

2.3.9.3 Congenital cardiac disease. These 6 deaths were due to aortic stenosis (AS) associated with a BAV, pre-excited AF or malignant aberrant origins to the coronary arteries and all were in males. More complex congenital structural disease were not associated with any of these cardiac deaths. Given the small numbers that died and the multiple diagnoses, it is difficult to make assumptions on gender differences in this group.

2.3.9.4 Sudden arrhythmic death syndrome and other unexplained deaths. There were 64 deaths due to SADS or other unexplained, but presumed cardiac causes (crude rate 1.7 per 100,000 Serviceperson years). This included 50 deaths due to SADS and 17 where the death was presumed to be cardiac, but no autopsy was performed. Two of these deaths were documented as due to heart failure of an unknown cause. Only 5 deaths due to cardiac causes were seen in those <20 years old and these were all SADS deaths. The majority of the SADS or other unexplained deaths were in males (62 cases, 96.9%) but there was no significant difference between genders (p=0.118).

2.3.10 Non-cardiac cardiovascular disease deaths

2.3.10.1 Vascular diseases. There were 10 cases of thoracic aortic dissection (crude rate 0.27 per 100,000 Serviceperson years). Aortic dissections are frequently due to the aortopathy associated with a congenital BAV, though whether a bicuspid valve was

associated was not recorded on the death certificates of these cases; 3 of these aortic dissection cases did undergo an autopsy and no comment was made of the aortic valve structure in any of these cases. There were 7 deaths due to pulmonary emboli with no other associated causes identified (crude rate 0.19 per 100,000 Serviceperson years). This was the only disease where there was a similar number of males (4 cases) to females (3 cases) but the numbers are low. No other associated risk factors or causes were documented. There were 4 cases of peripheral vascular disease (one each of bilateral carotid dissection, basilar artery thrombosis, systemic embolism where the emboli's source was unknown and arterial fibromuscular dysplasia) and a single case of primary pulmonary arterial hypertension.

2.3.10.2 Strokes. There were 40 deaths due to strokes (crude rate 1.06 per 100,000 Serviceperson years), 90% of which were in males with an overall crude rate of 1.06 per 100,000 Serviceperson years. There was no significant difference in the rates between genders (p=0.755). Three quarters of these deaths were due either to a subarachnoid haemorrhage (26 cases, crude rate 0.69 per 100,000 Serviceperson years) or another, unspecified non-traumatic intracranial bleed (4 cases, crude rate 0.19 per 100,000 Serviceperson years). The remaining 10 cases (crude rate 0.27 per 100,000 Serviceperson years) were due to arterial thrombosis or thromboembolic disease.

2.3.11 Inherited and congenital diseases.

Many of the conditions described above are either inherited or congenital in origin, or have a proportion of cases that are due to inherited or congenital disease and a proportion due to acquired factors. These conditions include HCM, ARVC, DCM, pre-excitation, BAV disease, aortic dissection and anomalous coronary artery origins as well as the SADS cases where the diagnosis was presumed to be cardiac in origin. In total there were 101 deaths (36.2% of all CVD; crude rate of 2.68 per 100,000 Serviceperson years) that fell into this category. It may well be that idiopathic myocardial fibrosis and the other non-specified cardiomyopathies may also have inherited causes; these conditions represented a further 12 deaths to this total and would increase the crude rate from possibly inherited or congenital disease to 3.0 per 100,000 Serviceperson years. Furthermore familial dyslipidaemias may have also played a role in some of the IHD deaths, particularly those in younger individuals. Therefore the estimate of a crude mortality rate of 2.68 per 100,000 Serviceperson years is likely to underestimate the contribution of inherited or congenital disease to the overall mortality rate.

	All deaths								Age <35			Age >35		
	n	rate	Male	%	rate	Female	%	rate	n	%	rate	n	%	rate
Ischaemic heart disease	**106**	**2.82**	**106**	**100**	**3.08**	**0**	**0**	**0**	**11**	**10.4**	**0.41**	**95**	**89.6**	**8.66**
Myocardial disease	**41**	**1.09**	**39**	**95.1**	**1.13**	2	4.9	0.62	**18**	**43.9**	**0.67**	**23**	**56.1**	**2.10**
HCM	13	0.35	13	100	0.38	0	0	0	8	61.5	0.30	5	38.5	0.46
DCM	4	0.11	4	100	0.12	0	0	0	1	25.0	0.04	3	75.0	0.27
ARVC	4	0.11	4	100	0.12	0	0	0	3	75.0	0.11	1	25.0	0.09
Idiopathic fibrosis	8	0.21	8	100	0.23	0	0	0	2	25.0	0.07	6	75.0	0.55
Hypertensive	1	0.03	1	100	0.03	0	0	0	0	0.0	0.00	1	100.0	0.09
Other cardiomyopathy	4	0.11	4	100	0.12	0	0	0	2	50.0	0.07	2	50.0	0.18
Cardiac sarcoid	2	0.05	2	100	0.06	0	0	0	0	0.0	0.00	2	100.0	0.18
Myocarditis	5	0.13	3	60	0.09	2	40	0.62	2	40.0	0.07	3	60.0	0.27
Congenital disease	**6**	**0.16**	**6**	**100**	**0.17**	**0**	**0**	**0**	**5**	**83.3**	**0.19**	**1**	**16.7**	**0.09**
Aberrant coronary artery	4	0.11	4	100	0.12	0	0	0	3	75.0	0.11	1	25.0	0.09
BAV	1	0.03	1	100	0.03	0	0	0	1	100.0	0.04	0	0.0	0.00
Pre-excited AF	1	0.03	1	100	0.03	0	0	0	1	100.0	0.04	0	0.0	0.00
Other sudden deaths	**64**	**1.70**	**62**	**96.8**	**1.80**	**2**	**3.1**	**0.62**	**43**	**67.2**	**1.61**	**21**	**32.8**	**1.91**
SADS	50	1.33	48	96	1.40	2	4	0.62	36	72.0	1.35	14	28.0	1.28
Unknown, no autopsy	12	0.32	12	100	0.35	0	0	0	6	50.0	0.22	6	50.0	0.55
All cardiac deaths	**217**	**5.76**	**213**	**98.2**	**6.19**	**4**	**1.8**	**1.23**	**77**	**35.4**	**2.89**	**140**	**64.5**	**12.76**

Table 2.3: Summary of the deaths due to cardiac-specific cardiovascular disease. *Rates are per 100,000 Serviceperson years.*

	All deaths								Age <35			Age >35		
	n	rate	Male	%	rate	Females	%	rate	n	%	rate	n	%	rate
Vascular disease	**22**	**0.58**	**19**	**86.4**	**0.55**	**3**	**13.6**	**0.92**	**8**	**36.4**	**0.30**	**14**	**63.6**	**1.28**
Aortic dissection	10	0.27	10	100	0.29	0	0.0	0.00	4	40.0	0.15	6	60.0	0.55
PE	7	0.19	4	57.1	0.12	3	42.9	0.92	2	28.6	0.07	5	71.4	0.46
PVD	4	0.11	4	100	0.12	0	0.0	0.00	2	50.0	0.07	2	50.0	0.18
Pulmonary HTN	1	0.03	1	100	0.03	0	0.0	0.00	0	0.0	0.00	1	100.0	0.09
Strokes	**40**	**1.06**	**36**	**90**	**1.05**	**4**	**10.0**	**1.23**	**14**	**35.0**	**0.52**	**26**	**65.0**	**2.37**
CVA	10	0.27	10	100	0.29	0	0.0	0.00	4	40.0	0.15	6	60.0	0.55
SAH	26	0.69	23	88.5	0.67	3	11.5	0.92	10	38.5	0.37	16	61.5	1.46
ICH	4	0.11	3	75	0.09	1	25.0	0.31	0	0.0	0.00	4	100	0.36
Non-cardiac CVD deaths	**62**	**1.65**	**55**	**88.7**	**1.60**	**7**	**11.3**	**2.16**	**22**	**35.5**	**0.82**	**40**	**64.5**	**3.65**
All CVD deaths	**279**	**7.41**	**268**	**96.1**	**7.79**	**11**	**3.94**	**3.39**	**99**	**35.5**	**3.71**	**180**	**64.5**	**16.41**

Table 2.4: Summary of the non-cardiac deaths due to cardiovascular disease. *Rates are per 100,000 Serviceperson years.*

2.4 Discussion

There were a number of strengths and limitations to this study. All deaths in the regular Armed Forces are recorded and the death certificate data was available. Similarly accurate manning data was also available so the numbers, ranks and genders of all serving personnel was also available. Unfortunately there were a significant number of autopsies not performed or unavailable for review, so a confirmation that the diagnosis was correct was not always possible.

Over the study period significant advances were made in autopsy quality and accuracy with trends including that of fewer deaths being attributed to CAD when, for example there was no evidence of plaque rupture or of infarction, and instead the alternative diagnosis of SADS being made. There is also a better understanding now of the underlying mechanisms and genetics of cardiomyopathies and ion channel diseases so family screening or molecular autopsies can illuminate cases where the previous investigations would have drawn no conclusion.

What this means for this study is that the numbers of deaths attributed to CAD might be higher in the earlier years of the study, where some deaths were due to other, unidentified causes and the numbers of deaths due to SADS, cardiomyopathies or ion channel diseases might be higher (and probably more accurate) in the more recent years. Whilst these advances might skew these mortality data over time it is also likely that most of the

diagnoses are correct when the findings at autopsy are likely to be gross, such as in aortic dissections, large pulmonary emboli, completed ST-elevation myocardial infarction or in advanced HCM; it is the more subtle diagnoses that are likely to be inaccurate. What is unmistakably accurate however are the numbers of overall CVD deaths in absolute terms, so the overall mortality trends have been accurately calculated.

This project sought to test a number of hypotheses and has succeeded in these respects. Cardiovascular diseases can be confirmed to cause a mortality burden on the UK regular Armed Forces with similar findings in this population to other similarly young and athletic populations. Every year CVD accounts for deaths numerically second only to cancers in those deaths due to disease in regular Armed Forces personnel.

2.4.1 Location and timing of deaths. Deaths occurred worldwide and both on operations and exercises as well as off duty. It was not possible to use these data to investigate whether these deaths were associated with exercise stressors, but this has been proposed as a trigger in many deaths. Despite this most deaths in the young general population occur during rest (though these individuals are not necessarily as athletic as those in the Armed Forces)[62]. This is important from the perspective of the institutional planning of medical cover to prevent these deaths, both by identifying individuals at risk before they become unwell and in treating cardiac casualties when they occur.

2.4.2 Service differences. There were no significant differences in the mortality rates between the three Services. Officers did have a higher mortality rate than ORs, though this is primarily due to the fact they are older on average. The increased mortality rate, primarily from IHD in those >40 years old, regardless of their rank, should focus preventative strategies primarily at this age group.

2.4.3 Gender differences. Males died from CVD more frequently than females in this population. Much of this was due to the entirely male population that died from IHD and these findings are consistent with other similar populations. Increased death rates in males (107 death) compared to females (4 deaths) with non-IHD deaths from cardiomyopathies, SADS and other diseases was not conclusively seen (p=0.060). These findings are not consistent with other similar athletic populations where the mortality rate is higher in males than females. In other populations where a gender difference is seen it has been proposed that there are physical differences between the genders in the diseases themselves and the increased risk of fatal arrhythmias in males over females with a similar disease. It may be that the military environment is similarly proarrhythmic for both genders in cardiomyopathy and ion channelopathy patients, perhaps due to the physical training element pushing individuals to a similar level.

2.4.4 Mortality over time. The small increase in deaths due to cardiomyopathy and SADS over the course of the study period is likely to be due to more accurate autopsies as these conditions are usually inherited and the prevalence of these conditions is unlikely to change dramatically in only one generation. Inherited cardiac conditions were conservatively

estimated to account for 2.68 deaths per 100,000 Serviceperson years. With current military manning this is likely to account for only a handful of deaths annually, but these are potentially preventable with early diagnosis and management. Effective screening might allow the early identification of individuals at risk and recruit screening is the focus of the second part of this thesis.

2.4.5 Ischaemic heart disease. The most common cause of CVD deaths were those due to IHD. These deaths occurred more frequently in males than females and with increasing frequency as the population aged, with a dramatic increase in the death rates in those over 35 years. Deaths due to IHD have dropped in the general population as the non-smoking proportion of the population increases and with better treatment of other risk factors, such as dyslipidaemia and hypertension. A general trend downward in the incidence of IHD is seen here in the military population. Whilst this might in part be due to better autopsy methods accurately identifying alternative diagnoses it is still likely to represent a true downward trend as the overall mortality rate reduced over time. Ischaemic heart disease deaths remain the most numerous of all CVD deaths and further measures should be considered to reduce the mortality rate further. These might include better identification and treatment of risk factors, including hypertension and smoking, but also inherited causes such as familial dyslipidaemias that are not currently screened for in the service population until personnel are middle aged.

Deaths occurred both on duty and on active operations and exercises at home in the UK and overseas. It is therefore important to identify conditions and individuals at risk prior to

deployment and to provide appropriate resuscitation and logistical facilities to investigate and manage potentially fatal events in remote and often austere locations. It is not known whether any of these deaths were the first presentation of a CVD, but Israeli soldiers presented with death as their first presentation in the majority of cases; it is no great leap to imagine most of these deaths in the UK military being the first presentation of a silently developing CVD.

It is possible that many individuals with underlying and silent CVD present first with symptoms other than death. The next chapters of this thesis will investigate the non-fatal incidence of CVD that either lead to discharge from the UK regular Armed Forces or in the presentation at a deployed hospital on active operations.

2.5 Key findings

1. The service population at risk over the period 1995-2013 inclusive was 3,764,517.
2. The Armed Forces were predominately male (93.4%) and the mean age was 30 years.
3. There were 279 deaths due to cardiovascular disease, constituting 9.2% of all deaths in the Armed Forces (crude mortality rate was 7.41 per 100,000 Serviceperson years).
4. Males were more likely to die from CVD than females.
5. There were 213 deaths (76.3%) in the UK and 7 deaths in dependent territories and 61 deaths in 21 different countries or at sea.

6. Death occurred whilst an individual was on duty in 77 (27.6%) cases with 16 (5.7%) occurring whilst the individual was serving on active operations or whilst in the enduring overseas commitments.
7. The death rate from CVD has trended downwards, led primarily by a drop in the incidence of deaths due to IHD.
8. There were 106 (crude rate 2.82 deaths per 100,000 Serviceperson years) deaths from IHD making it the most common cause of CVD death.
9. In total 41 individuals died from myocardial diseases (crude rate 1.09 per 100,000 Serviceperson years), including cardiomyopathies, myocarditis and cardiac sarcoidosis.
10. Hypertrophic cardiomyopathy accounted for 13 deaths and was the most common cause of death from myocardial disease (crude rate 0.35 per 100,000 Serviceperson years).
11. There were 6 deaths were due to aortic stenosis associated with a BAV, pre-excited AF or malignant aberrant origins to the coronary arteries.
12. There were 64 deaths due to SADS or other unexplained, but presumed cardiac causes (crude rate 1.7 per 100,000 Serviceperson years)

2.6 Acknowledgements

I am grateful to Mr Edd Byrne, Mrs Lisa Baird, Mr Ben Backholer, Dr Kate Harrison and in particular Mr Gavin Pratt, all from Defence Statistics, for their assistance in making this project possible.

Chapter 3: A review of discharges on medical grounds due to cardiovascular disease in the United Kingdom Armed Forces.

3.1 Background

Deaths due to CVD in the Armed Forces include many different aetiologies, including IHD, myocardial and structural inherited or congenital diseases, acquired cardiac diseases and non-cardiac diseases that include strokes and vascular disease. For methodological convenience investigations of CVD in young athletic populations usually attempt to quantify mortality as a proxy measurement of disease prevalence, but cardiovascular disability is also likely to be prevalent and this information is not captured. Most CVD presents with non-fatal outcomes, at least in the short-term[63 64 65 66 67 68], so it might be hypothesised that for every death due to CVD there are likely to be survivors from similar disease that are disabled. There may also be other CVD with disabling, but non-fatal symptoms, such as supraventricular tachycardias, recurrent pericarditis or neurocardiogenic syncope that produce an additional morbidity burden.

In servicemen and women CVD may preclude many of the activities required for normal military employment. The UK Armed Forces has specific medical employment requirements that enable service personnel to safely deploy to remote and isolated locations, with often arduous living and working conditions once deployed. There is a policy that individuals who are unable to safely deploy are discharged from service on medical grounds, usually after a thorough investigation of the patient and their disease. Quantifying the numbers and

diagnoses leading to medical discharge due to CVD may provide an insight into the underlying disease burden and suggest interventions to prevent it.

The aim of this chapter therefore is to quantify the number and causes of discharges due to CVD in the Armed Forces in order to potentially identify these individuals earlier in order to better manage and potentially prevent the progression of these diseases.

3.1.1 Hypotheses

1. Individuals are discharged from the military as a result of IHD.
2. Individuals are discharged from the military as a result of structural heart disease
3. Degenerative BAV disease leads to medical discharges
4. Individuals are discharged from the military as a result of non-fatal arrhythmic disease
5. Individuals are discharged from the military because of symptoms resulting from inherited cardiovascular diseases, particularly cardiomyopathies and ion channelopathies.
6. Cardiovascular diseases that are unlikely to result in death present with disabling symptoms that prevent ongoing military service.

3.2 Methods

The cohort studied consists of the annual population of the UK Armed Forces between 1995 and 2012 inclusive (note that this is one year less than the mortality data of the previous chapter). Demographic data of the Armed Forces during the study period has been compiled and includes age, rank, gender and Service (Royal Navy, including the Royal Marines, British Army and Royal Air Force). Military rank was standardised using the NATO system (Table 2.1).

All discharges on medical grounds are reported to Defence Statistics through a short medical report that summarises the underlying disease. These reports are categorised using the WHO ICD-10 system. The ICD10 Codes from 'Chapter I: Circulatory system disorders' (specifically codes: I00 - I99), 'Chapter R: Symptom, signs and abnormal clinical and laboratory findings, not elsewhere classified' (specifically codes R00, R01, R06, R07, R09, R55, R96, R98, R99) and the cardiovascular codes from 'Chapter C: Neoplasms' (specifically C38), 'Chapter Q: Congenital malformations, deformations and chromosomal abnormalities' (specifically Q20, Q21, Q22, Q23, Q24, Q25, Q26, Q27) and 'Chapter Z: Factors influencing health status' (Z941, Z950, Z951, Z952, Z954, Z958) were used as the basis of those discharges likely due to a cardiac cause. Discharges due to CVD have been collated with crude rates recorded per 100,000 service years.

This is a review of Armed Forces population data and therefore no consent from individuals was sought. This project was approved by the military Scientific Approval Committee and

MoDREC with protocol number: 12/Gen/310. Permission to use these databases was provided by the Defence Medical Services Caldicott Guardian Committee for these data.

3.3 Results

The regular Armed Forces population for the period of study was 3,599,857 individuals with 2,582,486 (71.7%) under the age of 35 years and 8.56% were female. The rank structure was similar to that described for the period of 1995-2013 inclusive (figure 2.4).

3.3.1 All medical discharges

There were 27,009 medical discharges during the study period (table 3.1). Of these 1092 cases (4.0%) had incomplete medical details and no discharge diagnosis was available. A further 46 cases (0.2%) withheld consent to have their details included in the Defence Statistics data. The most frequent ICD10 code chapter code was that of musculoskeletal disease and injuries that accounted for over two thirds of discharges with 17,297 medical discharges (64.1%; crude rate: 475.05 per 100,000 service person years). Cardiovascular diseases combined accounted for 707 medical discharges (2.6%; crude rate: 19.42 per 100,000 service person years).

ICD10 Chapter	ICD10 codes	n	%	rate
Infectious and parasitic diseases	A00 - B99	110	0.41	3.06
Neoplasms	C00 - D48	295	1.09	8.19
Blood disorders	D50 - D89	64	0.24	1.78
Endocrine, nutritional and metabolic diseases	E00 - E90	319	1.18	8.86
Mental and behavioural disorders	F00 - F99	2,833	10.49	78.70
Nervous system disorders	G00 - G99	1,117	4.14	31.03
Eye and adnexa diseases	H00 - H59	260	0.96	7.22
Ear and mastoid process diseases	H60 - H95	524	1.94	14.56
Circulatory system disorders	**I00 - I99**	**504**	**1.87**	**14.00**
Respiratory system disorders	J00 - J99	683	2.53	18.97
Digestive system disorders	K00 - K93	410	1.52	11.39
Skin and subcutaneous tissue diseases	L00 - L99	427	1.58	11.86
Musculoskeletal disorders and Injuries	M00 - M99 & S00 - T98	17,297	64.04	480.49
Genitourinary system diseases	N00 - N99	190	0.70	5.28
Pregnancy, Childbirth and the puerperium	O00 - O99	3	0.01	0.08
Congenital (non-cardiovascular) malformations	Q00 - Q19 & Q28-Q99	131	0.49	3.64
Congenital (cardiovascular) malformations	**Q20-Q27**	**23**	**0.09**	**0.64**
Clinical and laboratory (non-CVD) findings	R00 - R99	417	1.54	11.58
Clinical and laboratory (CVD) findings	**R00, R01, R06, R07, R09, R55, R96, R98, R99**	**177**	**0.66**	**4.92**
(Non-CVD) factors influencing health status	Z00 - Z99	84	0.31	2.33
(CVD) Factors influencing health status		**3**	**0.01**	**0.08**
Other Medical Discharges for which data are not available		1,092	4.04	30.33
Withheld consent		46	0.17	1.28
	Total	**27,009**		**750.28**
All cardiovascular codes		**707**	**2.62**	**19.64**

Table 3.1: Summary of the medical discharges from the UK Armed Forces from 1995 to 2012 inclusive by ICD10 Chapter. *The rate is the crude rate per 100,000 service years.*

3.3.2 Cardiovascular disease discharges

In total there were 707 individuals discharged with CVD (rate 19.6 per 100,000 service person years). There were 632 males (rate 19.2 per 100,000 service person years) and 75 females medically discharged (rate 24.3 per 100,000 service person years) due to CVD, with significantly more females discharged than males ($p<0.00001$). The discharges by Service were 175 individuals from the Royal Navy (rate 25.5 per 100,000 service person years), 376 individuals from the Army (rate 20.6 per 100,000 service person years) and 143 individuals from the RAF (rate 16.8 per 100,000 service person years). The Royal Navy CVD discharge rate was significantly greater than the Army ($p=0.021$) and in turn the CVD discharge rate of the Army was significantly higher than the Royal Air Force ($p=0.035$).

The distribution by age was of a U-shaped distribution, with higher rates soon after joining (younger service persons) and in the older groups (figure 3.1). Over a third of medical discharges occurred in the first three years of service with a median of 12 years and mean of 17 years of service (figure 3.2). In keeping with these findings it was more junior Officers and Other Ranks with higher CVD medical discharge rates with a drop in the middle ranks before an increase was seen with more senior rank, be that of an Officer or Other Rank (figure3.3).

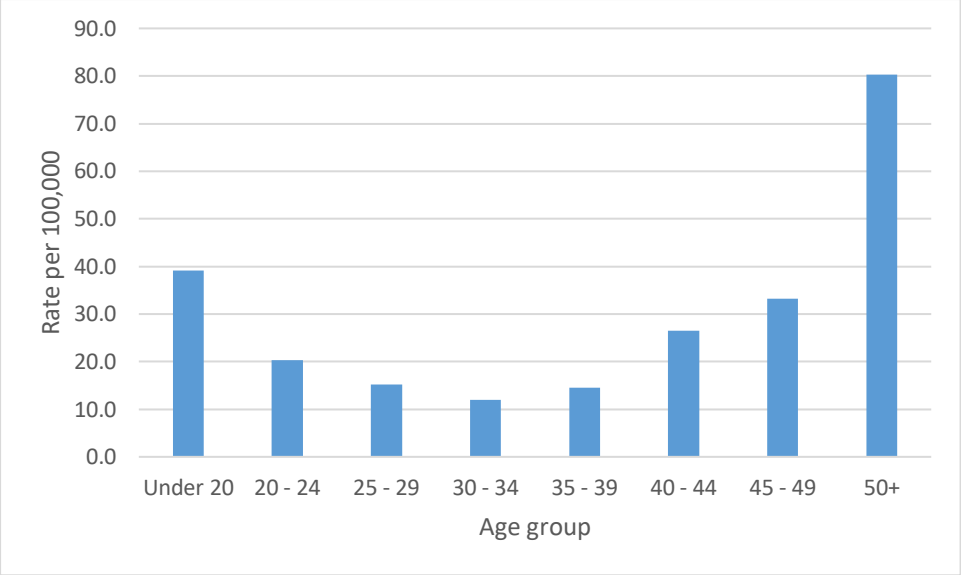


Figure 3.1: Graph showing a U-shaped distribution of CVD medical discharges by age. *Increasing CVD medical discharge rates are seen from age 35 years.*

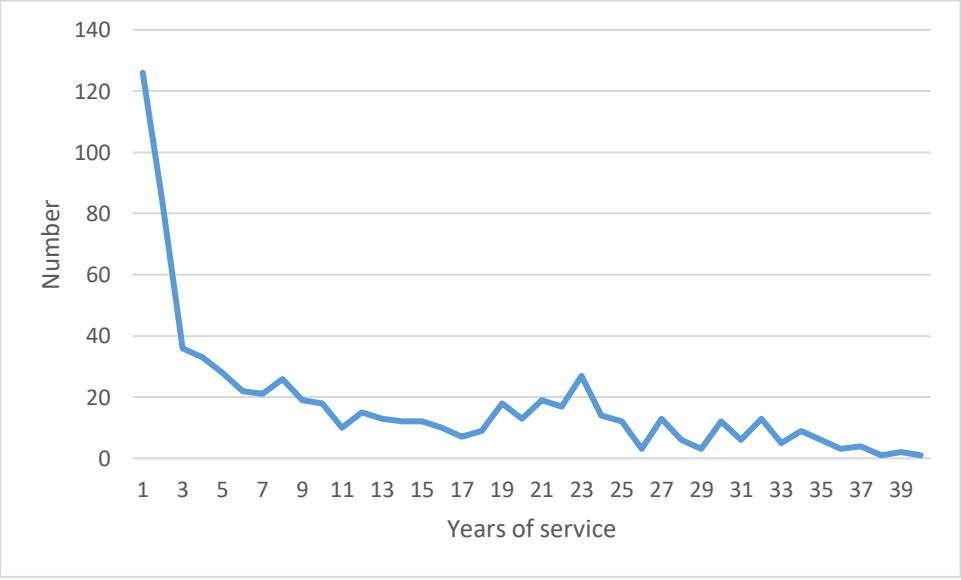


Figure3.2: Graph showing the absolute numbers of discharges by years served at the date of discharge. *Data identifying the denominator in each group is not available so calculating a crude rate is not possible.*

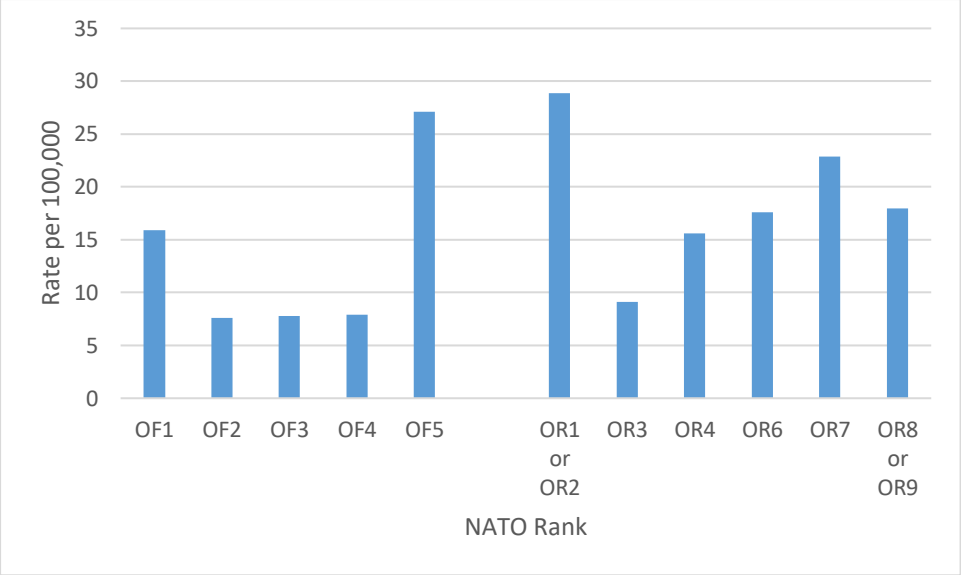


Figure 3.3: Graph showing the increases in CVD medical discharge rates by rank.

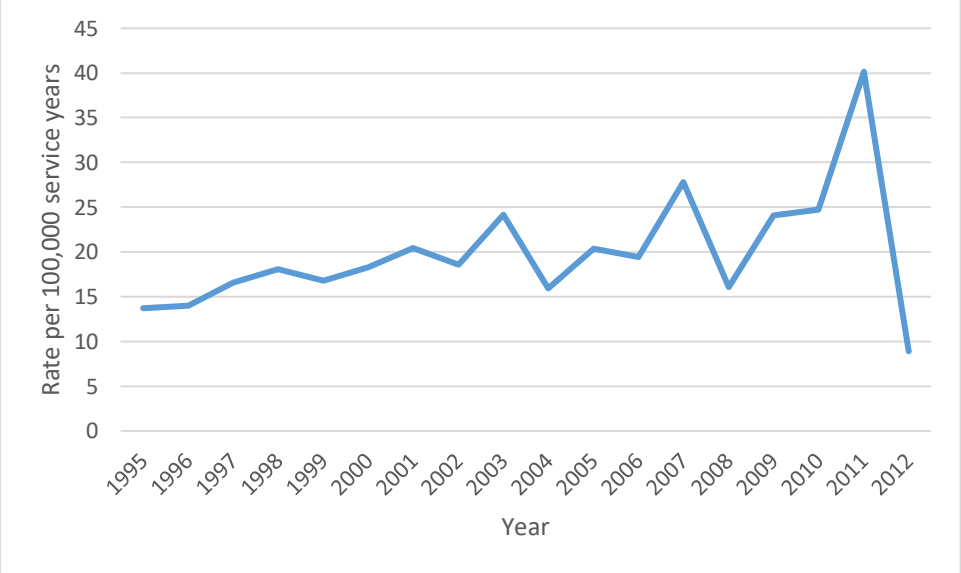


Figure 3.4: Graph showing the rate of discharges annually from 1995-2012 inclusive.

Over time there was a significant change in the rates of discharge (figure 3.4) with peaks seen in 2003 (rate 24.2 per 100,000 service person years), 2007 (rate 27.8 per 100,000 service person years) and 2011 (rate 40.1 per 100,000 service person years). In each of

these cases the rate dropped the following year to below the levels seen in the two years prior.

The causes of discharge were due broadly to cardiac disease (390 cases, rate 10.83 per 100,000 service person years), stroke (82 cases, rate 2.28 per 100,000 service person years) and vascular and thrombotic disease (191 cases, rate 5.31 per 100,000 service person years) (figure 3.5). Unfortunately 44 cases were codes as 'Other and unspecified disorders of circulatory system' with no further summary details available.

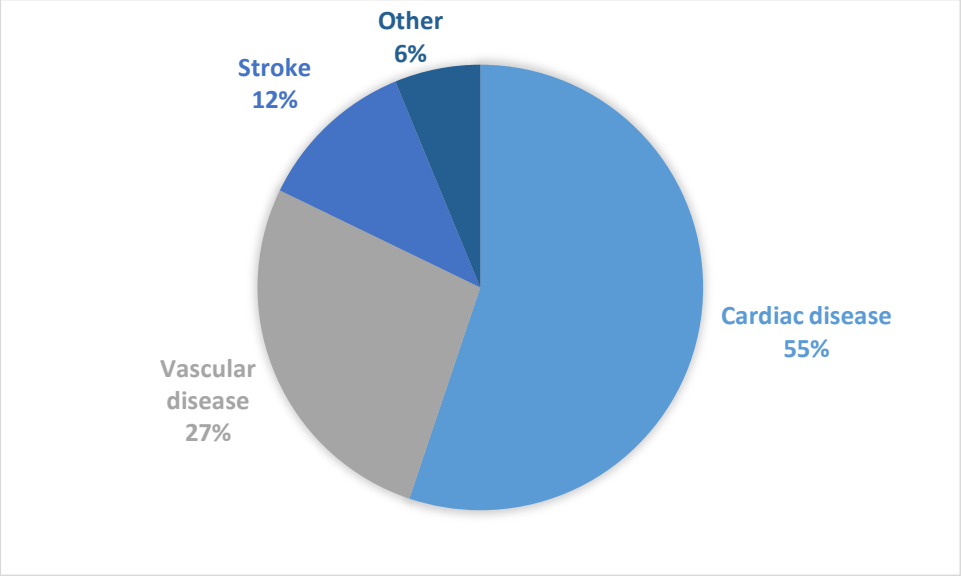


Figure 3.5: Chart illustrating the proportions of medical discharges due to different broad categories of CVD.

3.3.3 Cardiac disease. This group of cardiovascular diseases was the largest with 390 cases (55.2%) of all CVD discharges falling in this category (crude rate 10.83 medical discharges per 100,000 service years). Within this the diagnoses are subdivided by associated groupings (figure 3.6).

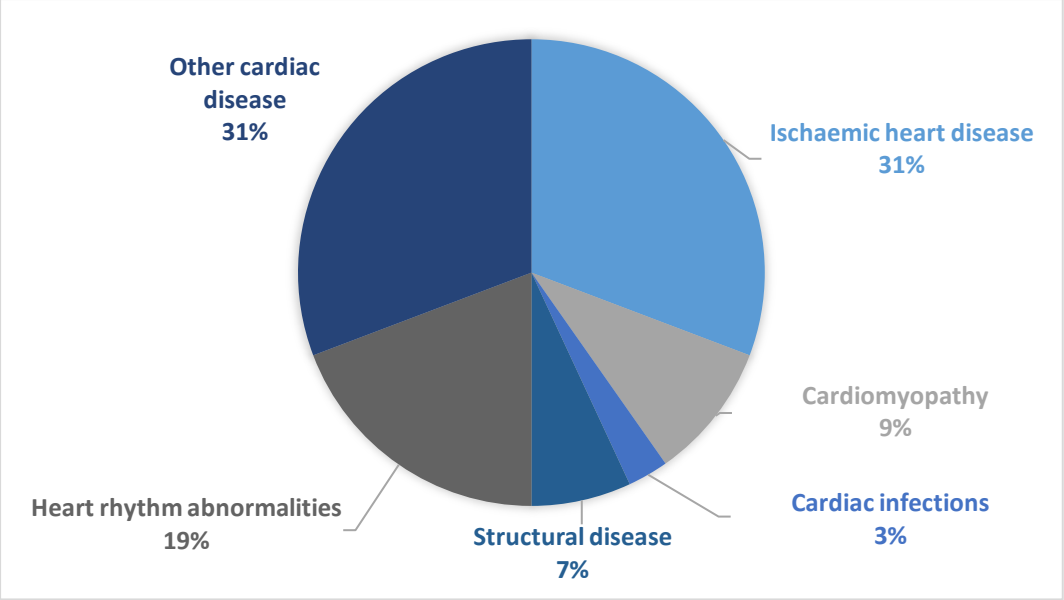
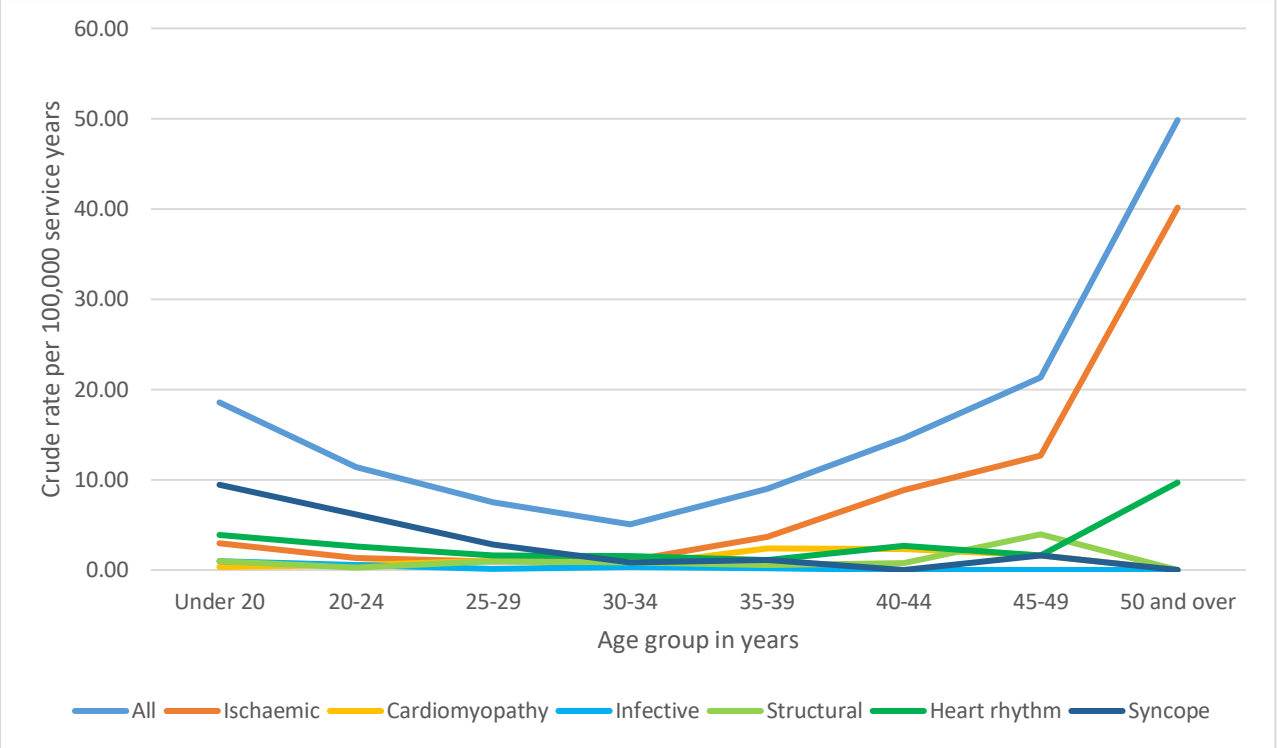


Figure 3.6: Chart illustrating the relative proportions of different diagnosis categories constituting the medical discharges due to cardiac disease.

3.3.4 Ischaemic heart disease. This was the most common cardiac cause for medical discharge, constituting 17% of all CVD disease with 120 cases (rate of 3.33 per 100,000 Serviceperson years). All but three of these cases were males and all three females were suffering from symptoms of angina. The mean age was 40 years (range 17-63 years) and the mean number of years served at discharge was 19.3 (range 0-38 years). An increasing incidence rate was observed with increasing age (figure 3.7a).



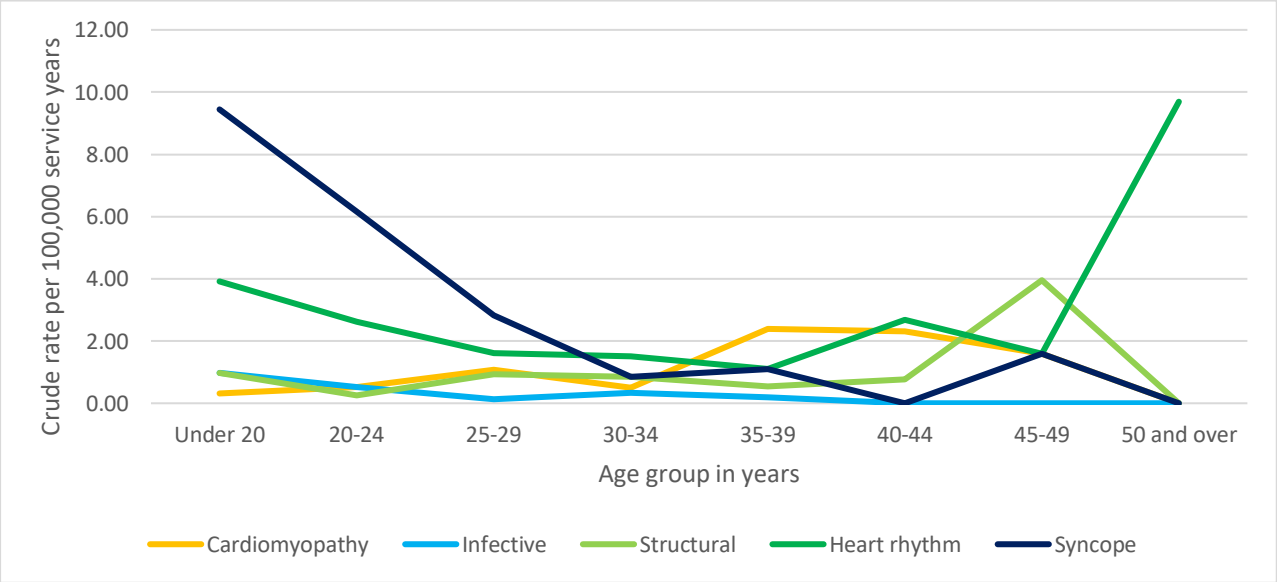


Figure 3.7a (above) and b (below): Graphs illustrating the crude rates of medical discharge due to cardiac disease by broad category. *Figure b is the same as figure a, but with the totals and ischaemic heart disease removed.*

Discharge diagnosis	n	%	Rate
Ischaemic heart disease	**120**	**17.0**	**3.33**
Angina pectoris	34	4.8	0.94
Acute myocardial infarction	28	4.0	0.78
Chronic ischaemic heart disease	58	8.2	1.61
Cardiomyopathy	**37**	**5.2**	**1.03**
DCM	17	2.4	0.47
HCM	15	2.1	0.42
Other CM	5	0.7	0.14
Cardiac infections	**11**	**1.6**	**0.31**
Pericardial disease	6	0.8	0.17
Myocarditis	1	0.1	0.03
Endocarditis	4	0.6	0.11
Structural disease	**27**	**3.8**	**0.75**
Aortic valve	16	2.0	0.39
Mitral valve	6	0.8	0.17
Septal defects	2	0.3	0.06
Other congenital malformations of the heart	3	0.4	0.08
Heart rhythm abnormalities	**75**	**10.6**	**2.08**
Atrial fibrillation and flutter	19	2.7	0.53
Other tachycardias	39	5.5	1.08
Inherited arrhythmic syndromes	4	0.6	0.11
Bradycardias	12	1.7	0.33
Cardiac pacemaker	1	0.1	0.03
Other cardiac disease	**120**	**17.0**	**3.33**
Syncope	110	15.6	3.06
Heart transplant	1	0.1	0.03
Survived cardiac arrest	2	0.3	0.06
Complications / ill-defined descriptions of heart disease	7	1.0	0.19
Total cardiac disease	**390**		**10.83**

Table 3.2: Summary of the medical discharges due to cardiac diseases. *Percentages relate to the total of all 707 discharges due to CVD diagnoses. Rates are crude rates per 100,000 Serviceperson years.*

The youngest individual to suffer an acute myocardial infarction (MI) that led to medical discharge, was 22 years old and he had served 6 years at discharge. In the Servicemen suffering from acute MI the mean age at discharge was 43 years (range 22 to 62) and the mean years served at discharge was 23 years (range 1 - 38 years).

A medical discharge diagnosis of angina was made in 34 individuals of whom 17 were recruits and at least partially untrained; only 4 of these had served for a year. The mean age range in the recruits was 23 (range 17-30).

3.3.5 Cardiomyopathy. There were 37 medical discharges resulting from a cardiomyopathy. Only one medical discharge secondary to a cardiomyopathy was female. The mean age at discharge was 34 years (range 20-49 years). The mean years served at discharge was 16 years (range 0-32 years). All but two discharges were trained.

Dilated cardiomyopathy (DCM) was the most frequent cardiomyopathy diagnosis with 17 cases. All these were trained males with a mean age of 34 years (range 20-49) and a mean duration of service at discharge of 16 years (range 1-32 years). Hypertrophic cardiomyopathy was the next most frequently seen cardiomyopathy diagnosis with 15 discharges. All these were trained males with a mean age of 35 years (range 23-47) and a mean length of service at discharge of 16 years (range 6-27 year). The type of cardiomyopathies in the remaining 5 cardiomyopathy discharges were not clear from the summary. These constituted 4 males and 1 female with two of these individuals untrained.

The average age was 29 years (range 20-39 years) and their mean length of service at discharge was 9 years (range 0-19 years).

3.3.6 Infective diseases of the heart. These were uncommon conditions. Only 4 individuals were discharged after being diagnosed with endocarditis; one of these was a female. Two of these were untrained and had been serving less than one year; the other two had served for 5 and 22 years. Further details, such as which valves were infected, the causative organism and whether there was an underlying structural abnormality that predisposed to the endocarditis was not specified. Pericarditis was more frequently seen with 6 individuals discharged with this disease. All six were males and 4 were recruits undergoing training. A single trained male was discharged following a diagnosis of myocarditis.

3.3.7 Structural heart disease. There were 27 individuals with structural heart disease incompatible with ongoing service that received a medical discharge.

The most common site of disease was the aortic valve with 16 cases of aortic valve disease, all of whom were male. Of these 11 were due to regurgitation, one due to pure stenosis and the remainder were mixed disease. One individual with mixed aortic valve disease also had an aortic coarctation. A BAV was confirmed as the underlying valve abnormality in 9 cases but was not stated in the remainder. Whether there was an associated aortopathy was not recorded in the data. The average age of those with aortic valve disease was 34 years (range 21 – 48 years) with 9 of these under 30 years. Their mean duration of service

was 14 years (range 2 – 31 years). One additional male individual was discharged due to a subvalvular aortic membrane leading to stenosis.

Mitral insufficiency of such severity as to require discharge from service occurred in 6 cases. Three of these cases were confirmed as due to mitral valve prolapse (MVP) and in the others the aetiology was not stated. All these individuals were males with a mean age of 29 years (range 19-38 years) and mean years served was 8 years (range 1 – 17 years).

The remaining 5 individuals had atrial septal defects (ASD) (2 cases) or abnormal venous anatomy draining into the heart. All these individuals were males with a mean age of 29 years (range 19-47 years) and a mean years served of 11 years (range 0-28 years) and all were trained except for one untrained recruit with an ASD.

3.3.8 Heart rhythm disease. In total 75 individuals were discharged due to arrhythmic disease that could be broadly divided into atrial fibrillation or flutter (19 cases), other tachyarrhythmias (39 cases), inherited arrhythmia syndromes (4 cases) and bradyarrhythmias (13 cases). There was an increase in the rate of discharge seen with increasing age (figure 3.7b).

Atrial fibrillation and flutter was responsible for 19 medical discharges. All but one of these were men. The mean age was 37 years (range 19 -60 years) with a mean of 15 years served at discharge (range 1 – 38 years).

Other paroxysmal tachycardias were the discharge diagnosis in 39 individuals, 13 of whom were untrained recruits and 9 of whom were female. The mean age at discharge was 27 years (range 18-44) and the mean years of service was 6 years (range 0-23 years).

A supraventricular tachycardia (SVT) was the identified arrhythmia in 19 individuals of which 3 were specifically a pre-excitation syndrome and 5 were female. The specific type of supraventricular tachycardia was not described in the remaining 16 cases. The mean age at discharge of these SVT patients was 26 years (range 18-40 years) and the mean years served was 7 years (range 0-23 years).

A ventricular tachycardia was described in 6 males and 1 female. The underlying type of ventricular tachycardia was not specified in these cases. The mean age at discharge was 29 years (range 19-42 years) and the mean years served was 9 years (range 0-22 years).

The remaining 13 paroxysmal tachycardias was not diagnostically characterised further and occurred in 6 untrained recruits and 7 trained individuals; ten were males and 3 were females. Their mean age at discharge was 26 years (range 18-39 years) and the mean years of service was 4 years (range 0-20 years).

3.3.9 Inherited arrhythmic syndromes. An inherited arrhythmic syndrome was responsible for 4 discharges in total, though the actual diagnoses was not available on the summary. Three of these were males and one was a female. Although the mean age was 31 years (range 20-55), the three youngest individuals were 30 years or younger.

3.3.10 Bradycardias. A bradycardia was described in 13 individuals with 6 cases of high degree AV block, 4 with sinus node disease, and three others with unspecified bradycardias, including one in whom a pacemaker was implanted. Only one of these individuals was female and all but one individual was trained. The mean age was 31 years (range 19-55 years) with 6 younger than 30 years. They had served for a mean of 12 years (range 1 – 26 years).

3.3.11 Syncope. After IHD, neurocardiogenic syncope was the next most frequent reason for discharge with 110 discharges with this diagnosis. Males constituted 90 (81.8%) of these cases, a significantly lower incidence than for females (P=0.0003). Approximately half of the discharges (54 cases, 49.1%) were in untrained recruits. The mean age at discharge was 24 years (range 17-48 years) with the mean length of service 4 years (range 0-22 years). The rate of syncope leading to medical discharge dropped with increasing age (figure 3.7b).

3.3.12 Vascular disease. This was a heterogeneous group of disorders that included pulmonary and systemic thromboembolic disease, varicose veins and hypertension amongst the various diagnoses; the most frequently diagnoses were Reynaud's disease and 'Phlebitis

and thrombophlebitis'. These discharges are summarised in table 3.3. The mean age of this group was 27 years (range 17-55 years) and the mean length of service was 7 years (range 0-37 years). Males constituted 167 cases (87.4%) of discharges, a significantly lower rate than females (p=0.0481).

Raynaud's disease accounted for 83 medical discharges. A total of 16 (19.3%) of these were in females, a significantly higher incidence (p=0.0005). The mean age at discharge was 24 years (range 17-43 years) and the mean length of service was 7 years (range 0-26 years).

Phlebitis and thrombophlebitis accounted for 28 medical discharges of which all but one case were males (96.4%). The mean age at discharge was 30 years (range 18-47 years) with the mean length of service 9 years (range 0-29 years).

3.3.13 Strokes. The most frequent cause of strokes leading to medical discharge were subarachnoid haemorrhage (28 cases, rate 0.78 per 100,000 Serviceperson years) with slightly fewer cerebral infarctions (16 cases, rate 0.44 per 100,000 Serviceperson years), though 25 strokes were unclear as to the underlying cause (table 3.4). Males constituted 71 cases (86.6%) and 5 were untrained recruits. The mean age was 39 years (range 19-57) with the mean length of service 19 years at discharge (range 0-41 years). There was an increase in overall stroke incidence with increasing age (figure 3.8).

Discharge diagnosis	n	%	Rate
Systemic arterial hypertension	17	2.4	0.47
Pulmonary arterial hypertension	4	0.6	0.11
Other disorders of arteries and arterioles	3	0.4	0.08
Aortic aneurysm and dissection	3	0.4	0.08
Arterial embolism and thrombosis	2	0.3	0.06
Pulmonary embolism	12	1.7	0.33
Phlebitis and thrombophlebitis	28	4.0	0.78
Varicose veins - lower extremities	7	1.0	0.19
Varicose veins - scrotal	17	2.4	0.47
Raynaud's disease	83	11.7	2.31
Other non-infective disorders of lymphatic vessels and lymph nodes	4	0.6	0.11
Other congenital malformations of peripheral vascular system	11	1.6	0.31
Total	**191**	**27.0**	**5.31**

Table 3.3: Summary of the vascular diagnoses leading to medical discharge. *Percentages relate to the total of all 707 discharges due to CVD diagnoses. Rates are crude rates per 100,000 Serviceperson years.*

Discharge diagnosis	n	%	Rate
Total stroke	**82**	**11.6**	**2.28**
Stroke, not specified as haemorrhage or infarction	25	3.5	0.69
Subarachnoid haemorrhage	28	4.0	0.78
Cerebral infarction	16	2.3	0.44
Other cerebrovascular diseases	7	1.0	0.19
Intracerebral haemorrhage	5	0.7	0.14
Other non-traumatic intracranial haemorrhage	1	0.1	0.03

Table 3.4: Summary of the medical discharges due to strokes. *Percentages relate to the total of all 707 discharges due to CVD diagnoses. Rates are crude rates per 100,000 Serviceperson years.*

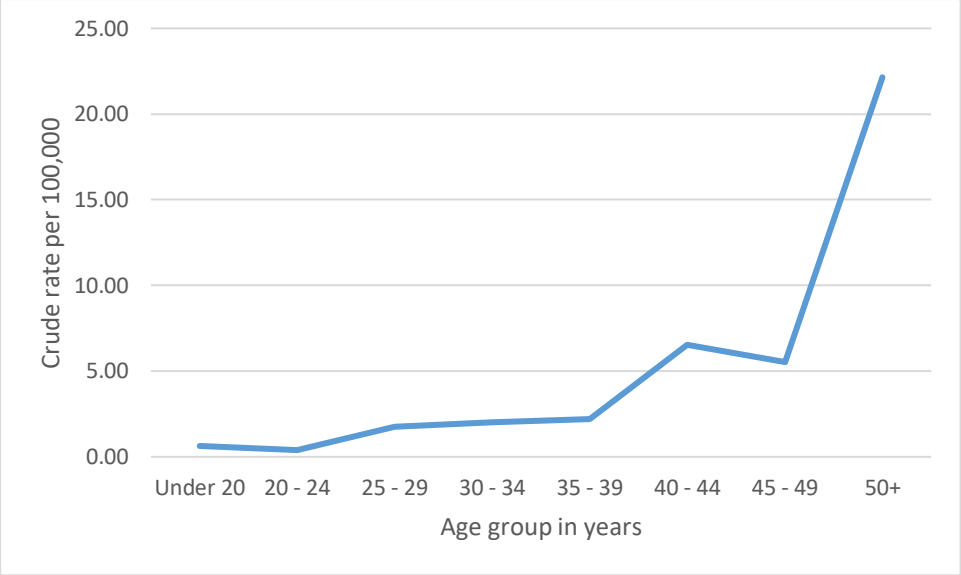


Figure 3.8: Graph showing the relationship between stroke incidence with age.

3.4 Discussion

A limitation of these data was that there were significant gaps in the usable records available for analysis. Out of all the medical discharges 4.2% did not have either a record as all, as the individuals had denied consent, or the record was missing the information required to categorise the underlying illness by system. Of those in whom a record was available the record was often vague, making accurate coding impossible. For example, within the group of patients in whom a tachycardia was described, a SVT was diagnosed in 19 individuals but the actual arrhythmia type itself was not specified in 16 cases. Also within the tachycardia group there were 13 other individuals in whom a tachycardia was recorded, but whether these were relatively benign SVTs or potentially fatal ventricular tachycardias is not known. It would be more worrying if we had identified 16 cases of ventricular tachycardia than 16 cases of SVT. These data therefore highlight a need for better data collection and clearer coding. Given the relatively small numbers of individuals discharged

annually due to cardiovascular disease, involving a cardiologist in the data-collection process could be justifiable.

A further limitation is that these data do not allow us to take further more meaningful information from the medical discharges seen. It is not for example going to be possible to see if any of the cases of infective endocarditis might have been prevented by better dental care or if they were due to infections sustained during training. These data are minimalist in nature and beyond crudely understanding the burden of disease in the military population they do not inform us further. These data will however allow us to focus future research on particular diseases and to try and better understand particular trends.

What is clear from these data is that the incidence of 19.8 medical discharges per 100,000 service years indicates that CVD causes a relatively unrecognised morbidity burden in the UK military. There are several main trends in the data:

1. There is a difference in the discharge rate between Services;
2. There is an increase in the discharge rate in the first few years of individuals joining the Armed Forces;
3. There is a higher discharge rate in females than in males
4. There is a trend to increasing discharges due to IHD and stroke with age;
5. There is a low level of heterogeneous CVD of many types in all groups by age.
6. Inherited and congenital cardiovascular diseases lead to discharge less frequently than might be expected from similar populations elsewhere.

3.4.1 Difference in discharge rate by Service. There were significant differences in the medical discharge rate on CVD grounds between the three Armed Services with the Royal Navy having the highest rate and the Royal Air Force the lowest. We can hypothesise on the reasons for this. From these data the differences could be between the populations themselves and their tendency to suffer from CVD or a consequence of policy decisions made at the single service level.

It is unlikely these differences are going to be due to different populations of people joining the Armed Services, but this cannot be excluded. Certainly there are population differences between the Services, for example the British Army's Brigade of Gurkhas is made up almost entirely of Nepali nationals (the only exceptions being some attached non-Nepali officers and soldiers), a nationality that is not recruited by the other two Services. All three services recruit from the British Commonwealth and therefore accept recruits from countries of predominantly different ethnicities, health backgrounds and beliefs, such as the British West Indies, Nigeria, Gambia, Sierra Leone and Fiji amongst others. The majority of these overseas recruits are accepted into the Army rather than the RAF or Royal Navy; as a consequence in 2013 the 'Black and minority ethnic' proportion of the Royal Navy was 3.5%, the Army 10.2% and the RAF 2.0%[69]. The Army's discharge rate is intermediate between the other two Services so it is unlikely that the differences in the proportion of ethnic minority soldiers accounts for this difference.

There is a difference between the three Services with respect to the proportion of serving females: during the period studied the Royal Navy were 6.3% female, the Army were 5.4% female and the Royal Air Force were 8.25% female. Given that females had a greater overall medical discharge rate, gender is unlikely to be responsible for the discrepancy in discharge rates between the three Services.

The most likely reason for the differences in discharge rates are the policy differences between the three Services. Their roles are rather different: the Army and Royal Marines (a branch of the Royal Navy) have a close combat role and in general their personnel need to be physically robust as on average they work in potentially more dangerous and physically arduous environments. The sailors of the Royal Navy have in general a less physical role to this. The Royal Air Force has a more 'arm's length' combat role where only a small proportion of their personnel are trained to close with the enemy, primarily their aircrew and the RAF Regiment (a formation of light infantry). Within these frameworks however the occupational medicine and political environments are also different.

Although the Surgeon General has historically set the minimum medical employment standards for the Armed Forces, each single Service has a separate occupational medicine policy with individual trades having specific employment standards. As a consequence a Serviceperson with the same phenotype might be managed differently depending on their trade. For example, imagine a 40 year old male who undergoes full coronary artery revascularisation after a MI and has residual moderate, but asymptomatic, left ventricular impairment. If this man is a Warrant Officer in the Royal Air Force responsible for

equipment stores then he might be retained by his Service as his role is sedentary and based in the UK with access to medical care. If instead this man is an Army Officer commanding an infantry battalion he might be medically discharged as his role would require that he can deploy to a highly kinetic combat environment where his disease would put him and the troops under his command at risk. This is a simplistic example, but one that hopefully makes the point that there are cultural and operational differences between the Services.

Furthermore, the political environment is such that the policy decisions made by each single Service might also differ considerably. In the last 25 years the Armed Forces have seen major deployments that include the Balkans, Northern Ireland, Cyprus, Sierra Leone, the Persian Gulf and Afghanistan. In 2001 the British joined the international coalition to fight 'the War on Terror' that involved fighting in Afghanistan; then in 2003 the UK took part in the invasion of Iraq; as a consequence the following decade saw constant high tempo combat operations in multiple theatres that were very different in their size and intensity to the operations of the decade before. In 2003 there was a recognition that there had been a relaxation in the medical standards of employment across the Services that were no longer fit for these new operational scenarios. It seems likely that this led to a peak in medical discharges that year and again in 2007, when the Afghanistan conflict reached a peak tempo.

The 'Strategic Defence and Security Review 2010' was a government review of the likely future requirements of the Armed Forces. The outcome of the review was that the Royal Navy was to have their numbers reduced by 5,000 to 30,000, the Army was to shrink from

102,500 to 82,000 and the RAF numbers were to be reduced by 5,000 to 33,000. Many of these personnel losses were through natural wastage, but there were also redundancies and a lower threshold to medically discharge personnel. It is likely that this review led to the peak in medical discharges in the following year. The differences in the effect this review had on individual Services was most significant for the Army and the Navy and the RAF were less effected. The combination of these different government and single Service policy decisions is the most likely cause of the differences in discharge rates across the Services.

3.4.2 Early discharges from service. A third trend in these data is that there is a higher rate of discharge from the Armed Forces in the first year of service with a gradual reduction over the next few years. This is likely to reflect the early identification of disease that makes a candidate unsuitable for service, yet is not always apparent from the history and examination at their entry medical. One of the most frequent diagnoses in this group was neurocardiogenic syncope, a relatively benign condition, but one that prevents recruits performing parade drill (such as standing upright, either at ease or to attention for prolonged periods). Also within this group are candidates in whom 'angina' was identified. This is an unlikely diagnosis in a relatively fit and young cohort and may reflect a low tolerance for illness during recruit basic training where a large volume of intensive physical, doctrinal and equipment training is crammed into the first six months of a military career; to miss out on a few weeks of this intensive course, whilst undertaking investigation for potentially serious symptoms, such as chest pain, rapidly results in a recruit falling behind his peers. For this reason there is a low threshold to discharge a recruit with a view to them

rejoining the Armed Forces later if their health allows it. In these cases the discharge diagnosis of 'angina' is likely to be presumptive rather than confirmed and the pains may be due to another cause, such as pericarditic or musculoskeletal pain. A similar phenomenon might be seen with the diagnosis of 'paroxysmal tachycardias' when investigation into an underlying arrhythmic disease prevents course attendance and precipitates an early discharge from training.

3.4.3 Gender differences. This incidence of medical discharge due to CVD is higher in females than males and the reason for this is unclear. There is a signal towards slightly higher discharge rates in females within many of the disease groups, but the numbers affected in each group were small and the statistics are consequent difficult to interpret e.g. 25% of the 4 discharges due to inherited arrhythmic syndromes were female. Only in the syncope and Raynaud's disease groups were there a clear gender difference with a higher incidence in women than men.

The causes of these gender differences are likely to be multifactorial, including physiological differences in the cardiac output during exertion e.g. women with smaller hearts are likely to have a lower cardiac output; differences in the peripheral vascular system or autonomic supply to the heart that might predispose to a greater risk of developing neurocardiogenic syncope; differences in the cardiac anatomy that leads to an increasing tendency to arrhythmia, in particular AVNRT; as well as social differences, such as different gender thresholds for medical discharge and possibly even discrimination. Similar gender differences have been seen within other disease systems, particularly due to

musculoskeletal disease. In the case of female recruits, who have a significantly higher rate of injury compared to men, this has led to the development of specific military research programs to identify the causes.

The relatively small numbers and heterogeneity of the CVD medical discharges makes gender based trends difficult to interpret. The syncope group is an exception though: these gender results, added to the numbers of recruits discharged from both genders, has led to the establishment of a funded doctoral degree student who is due to start investigating syncope and preventative treatments in the military.

3.4.4 Ischaemic heart disease and stroke. Much of the CVD discharge burden identified was due to the potentially lethal conditions of IHD and stroke, with increases in discharge rates with increasing age. This shows hypothesis 1 to be true. IHD and stroke have similar risk factors, such as hypertension, smoking and dyslipidaemia and they are the end result of the gradual progression of asymptomatic disease. The increasing incidence with age mirrors that of the general population in which this effect is also clearly observed. Whilst these conditions make up the largest groups of CVD discharges these are conditions that are well researched and have effective preventative management strategies to treat the risk factors and reduce the incidence of symptomatic disease. These data reinforce the need for systemised primary care preventative interventions in the Armed Forces. The current systems already include formalised smoking cessation programs, screening and treatment for hypertension, dyslipidaemia, diabetes and healthy lifestyle advice; these programs need continual revaluation to assess their efficacy.

3.4.5 Cardiomyopathies. There were 37 discharges due to an underlying cardiomyopathy; whilst this proves hypothesis 5 this seems a surprisingly small number of medical discharges due to a cardiomyopathy diagnosis. Both HCM and ARVC are primary cardiomyopathies with a prevalence of approximately 1 in 500 individuals[70],[71] and 1 in 2000-5000 individuals[72] respectively in the general population. Dilated cardiomyopathies are a heterogeneous group of conditions; whilst often due to an inherited cause they are frequently also the end result of diseases other than primary cardiomyopathies, such as valvular heart disease, IHD and persistent tachycardias, with an overall prevalence of approximately 1 in 2500 individuals[73], [74]. If an overall cardiomyopathy prevalence at the conservative limit of these estimates is taken we would derive a cardiomyopathy prevalence of approximately 13 in 5000 individuals. Annually approximately 12 730 to 24 490 individuals were recruited to the three Services in 2009-2011 and this was a lower number than at the beginning of the study when the Armed Forces were far larger. It might be reasonable therefore to assume that approximately 50 individuals are recruited annually with a cardiomyopathy. The reality is that some might be screened out prior to recruitment and others will only manifest phenotypically after they have left the Armed Forces. It may also be the case that these epidemiological estimates are over-estimating the burden of disease in this population. Even so these very rough calculations might lead us to hypothesise that there may be many servicemen and women that have undiagnosed cardiomyopathies or that there are individuals diagnosed with disease, but who are not discharged on medical grounds (they may be in roles with occupational restrictions or they may leave service without going down the medical discharge route). There may therefore be serving individuals who are at risk of developing more advanced heart failure or arrhythmic disease, including sudden death that

could be better managed. These estimates are no more accurate than rough calculations, but undoubtedly the possibility of an unseen burden of cardiomyopathies in the Armed Forces warrants further investigation.

3.5.6 Structural heart diseases. These were identified in low numbers and resulted in discharges from the Armed Forces, thus proving hypothesis 2 to be at least partially true. The specific diagnoses of BAV disease and MVP are discussed in more detail below; other structural diseases were seen at a low level. Mild congenital heart disease is increasing in the general population with an incidence of 10.2/ 1000 births in the US[75] (this estimate does not include BAV or MVP). Many of these are associated with other syndromes incompatible with military service, such as Down's Syndrome that accounts for approximately half of all septal defects. Septal defects in particular resulted in only a low incidence of medical discharges in this study. It is likely that the septal defects seen in the military populations are haemodynamically insignificant in most cases and are either accepted with limitations in permissible activities, for example with diving restrictions, or never identified in asymptomatic individuals. This may be important as individuals with septal defects have an increased, albeit still low, risk of infective endocarditis compared to the general population[76]. Although the medical discharges due to infective endocarditis were low it is possible that individuals were diagnosed and treated for endocarditis and did not require termination of their military service.

3.4.6 Bicuspid aortic valves and associated pathology. The BAV phenotype is the most common congenital heart defect in the general population. The prevalence in the general

population is estimated as 0.5 - 2% with a male to female ratio of about 3:1[77],[78],[79],[80]. The abnormality is usually asymptomatic in those younger than 30 with increased risk of intervention with increasing age or dysfunction of the valve. In this group of military medical discharges there were 9 cases of BAV disease described in the discharge summaries, though it should be suspected as being an underlying pathology in the other 7 cases of aortic valve disease, the 3 cases of aortic dissection and the 4 cases of endocarditis. Although hypothesis 3 could be considered as at least partially true, such as in the case of the cardiomyopathy medical discharges, these numbers appear low; a conservative estimate of the prevalence of a BAV in recruits is approximately 300 or more individuals annually. These low medical discharge numbers may be the result of several factors. Firstly the highest risk individuals, those who already have valve dysfunction on applying to join the Armed Forces, may have their disease identified by cardiac auscultation and therefore fail their military admission medical. Secondly most Servicemen and women will cease serving for non-medical reasons in their 4th decade and the risk of requiring an intervention to treat the aortic valve or aortic root dilation increases in incidence with increasing age; therefore the risk of intervention whilst serving is relatively low, even if the risk over a lifetime remains high. Thirdly individuals with a known BAV may be leaving the Armed Forces under terms other than that of a medical discharge, but because they know they have a medical condition that might limit their career in time. Finally it may be that individuals with a BAV in the Armed Forces have a particularly good prognosis compared to other population groups and the abnormality is never identified.

The natural history of BAV disease is relatively unknown in young, athletic cohorts and if this group was better characterised then it may be that the current policy preventing applicants with a BAV, even if normally functioning, from joining the Armed Services could be reconsidered. A potentially informative follow-on study to this would be to investigate the incidence of a BAV as a known diagnosis in the serving population through interrogation of their primary care record. These individuals can be formally followed-up during their careers and the progressive degeneration, or not, of their valves could be followed prospectively.

3.4.7 Mitral valve prolapse. This condition is present in as many as 4% of the general population with an increased prevalence in females. It is associated with a benign course in most patients, but can be complicated by mitral regurgitation (MR), atrial tachyarrhythmias, congestive heart failure, infective endocarditis, ventricular arrhythmias and SCD[81],[82],[83]. There were only three confirmed cases of medical discharge due to a MVP. Given that the condition is relatively common in the general population and that some studies indicated MVP may be responsible for as many as 11% of SCD in athletes, that MVP was responsible for so few discharges is highly surprising[84]. It leads us to hypothesise that either the condition is less common in this population than other groups studied or that it is less dangerous than supposed. As with other conditions described here, further investigation of the potential recruit and serving populations might provide a better understanding of the epidemiology of MVP in the Armed Forces.

3.4.8 Heart rhythm diseases. There were a number of discharges due to non-fatal arrhythmic diseases thus proving hypothesis 4 to be true. The observed increase in discharge rates with increasing age fits with the expectations of progressive disease, such cardiomyopathies that predispose to arrhythmias or atrial fibrillation, a condition primarily associated with increasing age.

3.4.9 Atrial fibrillation. Whilst atrial fibrillation is associated with an increased stroke risk and increased mortality, the arrhythmia itself does not lead to death. In many individuals symptoms resulting from the arrhythmia, such as fatigue, breathlessness and palpitations, may be incompatible with military service, while other individuals may be asymptomatic and remain potentially undiagnosed. Male gender, endurance training over many years[85],[86],[87],[88] as well as increased height and body mass[89],[90] (as might be expected in strength and aerobically trained Servicemen and women) are risk factors for the development of atrial fibrillation and flutter. Despite these the prevalence of AF in young populations is low, with estimates of 0.1% in those <50 years in US populations[91] and even lower rates in Spanish elite athletes[92]. In this military population there was a low observed discharge rate due to AF that fits with these experiences elsewhere. It would be interesting to investigate the serving population in more detail to investigate how those in whom AF is diagnosed are managed; it may be that some are 'cured' through lifestyle changes or ablation therapy and others are simply allowed to continue serving, potentially with employment restrictions.

Supraventricular tachycardia was identified as the disease leading to discharge in 19 individuals. This group of arrhythmias is not uncommon, but in the 21st century these

arrhythmias are almost always curable by catheter ablation. Whilst two of these individuals were discharged prior to the year 2000 the remainder were not. How these normally benign and curable arrhythmias led to medical discharge is a curiosity and unanswered in this study; it may be that some individuals were recruits, others might have declined an ablation procedure, whilst others still might have undergone catheter ablation but this had failed.

The few discharges due to ventricular tachycardias were primarily in younger individuals, as opposed to older patients in whom a previous MI was a more likely underlying cause. There are many underlying conditions that might predispose to ventricular tachyarrhythmias, including cardiomyopathies, myocarditis, sarcoidosis, or primary arrhythmic syndromes, as well as benign outflow tract VT. Whilst it is partially reassuring that these potentially dangerous arrhythmias are uncommon it might have been useful to have clearer information on the precise diagnoses, particularly as they may represent the progression of other conditions that might be detected earlier through focused screening.

Of the remaining paroxysmal tachycardias identified again only two were discharged prior to the year 2000. These arrhythmias were not clearly characterised in the records; due either a failure in the documentation or a failure in making a specific diagnosis.

In recruits undergoing their basic training, it may have been easier to discharge an individual without a definitive arrhythmia diagnosis. Even if a diagnosis was available then discharge might have been more practical than to wait to see whether a treatment, such as catheter

ablation, might have been successful. This explanation would go some way to explaining the discharges of 13 recruits, but would not explain the remaining 26 individuals discharged. It seems likely that incomplete data has been recorded or these individuals represent a diagnostic or treatment failure.

3.4.10 Inherited cardiac conditions. Numerous inherited or congenital conditions resulted in discharge from the Armed Forces, proving hypothesis 5 to be true. These included hypertrophic and arrhythmogenic cardiomyopathies, probably some dilated cardiomyopathies, aortic coartaction and dilatation, atrial and ventricular septal defects (VSD), BAV disease, MVP and a number of inherited arrhythmic syndromes. In addition to the disability identified in these patients all these conditions are associated with a mortality risk and as already discussed these disease have previously resulted in military deaths. Effective screening for inherited or congenital disorders at the point of recruit entry would allow early identification and intervention in these disorders.

3.4.11 Other cardiovascular conditions. There were a heterogeneous group of non-fatal but mildly to severely disabling diseases that resulted in medical discharge, thus proving hypothesis 6. This group includes varicose veins at various anatomical locations, Raynaud's disease and syncope (discussed above). Peripheral vasoconstriction in the cold is an important limitation to performing normal outdoor tasks for members of the Armed Forces and as such often results in a medical discharge. Primary Raynaud's disease is an interesting condition that when present has no occupational impact for most people and therefore

might have never have been perceived as a potential limitation to individuals joining the Armed Forces.

3.5 Key findings:

Points 5-10 relate to the hypotheses discussed in the introduction.

1. There are significant levels of incomplete data in the Defence Statistics record of medical discharges.
2. The single Services differ in their rates of CVD medical discharges.
3. Recruits undergoing basic training and individuals that have served for longer periods and are older have higher rates of medical discharge than trained Servicepersons who have served only a few years.
4. Women have a higher medical discharge rate due to CVD when compared to men.
5. Individuals are medically discharged from the military as a result of IHD.
6. Individuals are medically discharged from the military as a result of structural heart diseases. These include mild congenital heart disease, such as septal defects, MVP, and aortopathies.
7. Degenerative BAV disease leads to medical discharges.
8. Individuals are medically discharged from the military as a result of non-fatal arrhythmic disease, in particular atrial fibrillation and supraventricular tachycardias.
9. Individuals are medically discharged from the military because of symptoms resulting from inherited cardiovascular diseases, particularly cardiomyopathies and ion channelopathies, but this occurs less frequently than expected.

10. Cardiovascular diseases that are unlikely to result in death do present with disabling symptoms that prevent ongoing military service. In particular atrial fibrillation, supraventricular tachycardia, neurocardiogenic syncope and Raynaud's disease.
11. Individuals are medically discharged from the Armed Forces due to strokes.

3.6 Acknowledgements

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Chapter 4: A prospective evaluation of cardiology and general medical admissions to the British Role 3 Hospital in Camp Bastion

4.1 Background

Historically the majority of war casualties have resulted from disease or environmental factors as opposed to the wounds sustained in battle[93]. Osler made the observation that dysentery was "*more fatal to armies than powder or shot*"[94]. Accordingly, the historical narrative has been shaped by climate, illness and epidemic, as often as it has by great leaders or disruptive technologies. Disease during military campaigns has never prejudiced for status or rank, with senior commanders affected as frequently as the rank and file[95,96,97]. Whilst only a quiet and often unremarked footnote in history, disease has altered the outcomes of military campaigns; an example of this can be seen in French soldiers in the 1812 retreat from Russia where approximately a third were afflicted by the *Rickettsial* disease: Tick typhus[98].

Innovations in healthcare, such as vaccination, modern pharmaceuticals, better hygiene and other public health and occupational measures have transformed the health of the British Armed Forces over the last century and reduced the burden of infectious diseases. Despite this progress, acquired infectious disease and environmental stresses continue to produce a heavy burden on deployed troops during both exercises and on operations, reflecting the often remote and arduous conditions under which military operations take place. In addition to these acquired conditions, soldiers deploy on operations with either known and

managed chronic diseases, or unknown and asymptomatic diseases, including cardiovascular conditions. These diseases might be exacerbated by the conditions under which these servicemen and women work, such as extremes of heat, dehydration and high levels of psychological stress and fatigue. When new symptoms develop then affected individuals may be a long way geographically or temporally from medical provision and this provision may be inadequate for their needs. Predicting the variety and frequency of particular presentations is key for commanders to anticipate the medical requirements on operations.

Within NATO the background burden of disease and non-battle injury is known as DNBI. The term DNBI includes medical conditions, such as CVD, as well as any surgical disease that is not the result of battle injuries, including accidental injury and psychological illness. Whilst the DNBI acronym is useful at higher levels of planning, it lacks utility when it comes to preparing the teams of GIM doctors, nursing staff and support specialities for deployment or in the specific medical services provided in the field hospital, such as diagnostic equipment robust and portable enough for use 'in the field'.

Anticipating the range of probable presenting symptoms, diagnoses, length-of-stay and discharge destinations are important to predict the required scaling of specialist diagnostic investigations, provision of therapies and the speciality, grades and number of deployed staff, as well as informing the medical supply chains and allowing evacuation planning. Cardiac disease and stroke is traditionally managed by the deployed General Physician and their team in UK Role 3 hospitals. Training of the physician and nursing cadres will be

directly influenced by operational GIM epidemiology, such as climate, altitude or local infectious diseases, but more widely it will influence the deployment and training of all personnel involved in the treatment and transport of medical casualties on operations. An understanding of the epidemiology and planning is more important to the Armed Forces on Operations than similar planning in the UK where the NHS infrastructure can be generally relied upon to provide these clinical management functions.

The burden of CVD on Armed Forces deployed on operations has never been quantified but other data point to there being a burden of CVD in deployed personnel. The first two chapters of this thesis investigated the deaths and medical discharge due to CVD in the Armed Forces over a long period. The data identified a low level of CVD throughout the Armed Forces. Within the recorded deaths there were 32 deaths whilst individuals were deployed on enduring overseas commitments or whilst on active Operations. These occurred in ten different countries, though not during Operations in Afghanistan within this time period. The deaths were the result of IHD in 11 cases, cardiomyopathy in 8 cases, SADS in 7 cases, stroke in 2 cases and one death each from aortic dissection, myocarditis, pre-excited atrial fibrillation and arterial thromboembolism. It is likely that non-fatal symptoms from conditions such as these also occur wherever the affected individuals are located, including whilst deployed on Operations. Additional to these diseases other cardiovascular conditions, such as SVT and neurocardiogenic syncope, were identified that caused benign, but distracting, disabling and non-fatal symptoms so severe as to require discharge from service on medical grounds. The locations these symptoms presented is not known but it seems likely that there is an operational burden of cardiovascular disease.

The British Armed Forces have been deployed to either Iraq or Afghanistan, in a war-fighting or nation-building role, for over a decade. A summary of the overall GIM speciality burden of disease, as seen at the field hospital level, was collected in Iraq and is in the public domain[99]. These data were collected over a relatively short period and was neither prospectively collected nor systematically coded. Similar large scale cross-sectional surveys from United States military deployments are also available[100].

The Role 3 Treatment Facility, colloquially known as 'the Role 3 Hospital', in Camp Bastion, Helmand Province, was the British military hospital located in Afghanistan. The hospital was manned by military medical personnel from the UK, Denmark, the United States and Estonia. It provided secondary health care to the International Security Assistance Force, entitled civilian contractors and specified local nationals. Whilst Afghanistan campaign case reports and specific disease-focused research were collected by the deployed GIM cadre, no detailed information relating to the British forces deployed to Afghanistan had been formally recorded.

Whilst CVD is the focus of this thesis, a record of how CVD presentations fit within the greater spectrum of the medical disease managed by the GIM team would be helpful. The study described in this chapter therefore aimed to prospectively record the operational burden of medical illnesses, including CVD, over a prolonged period during the Afghanistan campaign. This work was designed to provide a reservoir of knowledge available to the

operational medical planners and commanders of the future by informing us about the burden of CVD and other medical presentations, on operations.

4.2 Methods

A record was collected of each consecutive admission under the GIM team to the Role 3 Hospital in Camp Bastion, Afghanistan. Data collection started in April 2011 and continued for a two year period. Data was prospectively collected by the author on initiating this study, then successive GIM doctors continued data collection with remote coordination by the author after he departed Afghanistan. All entries were cross-checked with the hospital electronic patient record and vice-versa to prevent omissions.

4.2.1 Inclusion and exclusion criteria. All GIM admissions were eligible including UK and allied military personnel, civilians and prisoners detained by the security forces. Patients only seen in the Emergency Department or as requested consultations to primary care, but who were not admitted, were excluded from the data collection. Patients admitted under the surgical teams that required a GIM opinion was also omitted.

4.2.2 Data collected. Demographic and clinical data were collected for all admissions. The details recorded for each case included gender, rank, age on admission, admission date, discharge date, presenting symptoms, discharge diagnosis and destination at disposal. Up to 4 different symptoms and diagnoses were recorded for each individual. All symptoms and diagnoses were coded using the WHO International Classification of Disease, version 10

(ICD-10)101. Coding was performed by two military physicians based on information entered into the database with access to the original electronic healthcare records if doubt existed about the most appropriate code. Data quantifying the population at risk and the total admissions were obtained from Defence Statistics.

Authorisation for this study was obtained from the Research Directorate at the Royal Centre for Defence Medicine (Protocol: RCDM/Res/Audit/1036/12/0305).

The findings are presented in descriptive form. Statistical analysis was carried out using commercially available software (SPSS PASW Statistics Release 18.0.0). Quartile-quartile plots and the Kolmogorov-Smirnov and Shapiro-Wilk tests were used to assess distribution normality. Significance testing was performed using the Student's T-test, the Mann-Whitney test or Fisher's exact test. A two-tailed $p<0.05$ was considered significant.

4.3 Results

4.3.1 General observations. Over the two year period there were 12,978 presentations to the Role 3 Hospital with 6838 (52.7%) admitted. In total 1,368 patients (20% of admissions; mean 1.87 patients / day) were admitted under the GIM team. The general demographics of these medical patients are summarised in table 4.1. Any GIM input into the care of any of the 5,470 non-GIM admissions (80% of admissions; mean 7.49 patients / day) was not recorded in this study.

The mean UK military population at risk was 10,941 per month over the two year period. The UK military population fluctuated during the six monthly handover periods during April and May and September and October, with increases in military personnel. The period of April and May were particularly associated with peaks in the total daily admissions (figure 4.2). Overall there were 612 UK military admissions with a mean GIM admission rate of 23.3 per 10,000 UK military per month, increasing to 42.2 per 10,000 UK military per month in the month of May ($p<0.005$) (figure 4.2).

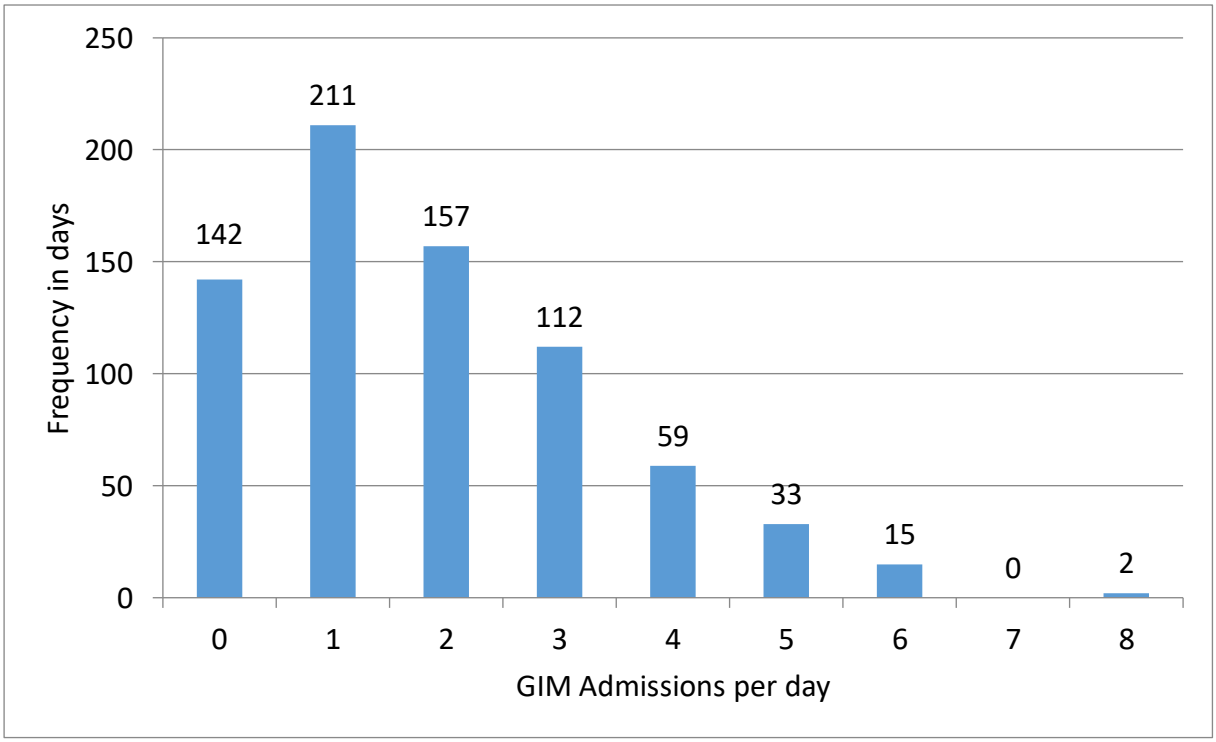

Figure 4.1. Numbers of admissions under the GIM team to the Role 3 Hospital per day

The military admissions mostly originated from 5 countries (figure 4.3) while civilian patients (figure 4.4) originated from 23 countries, including those neighbouring or close to Afghanistan in south and central Asia, as well as Europe, North America, Africa, the Middle East and Afghanistan itself. There were nearly 17 times more males than females admitted;

a reflection of the predominantly male population at risk, whether military or civilian contractors. Although the UK military population during the operational period was under 10% female[102], the number and proportion of females in the theatre was unknown, so meaningful comparison cannot be made. There was no significant difference between the ages of UK or non-UK military patients at 29 years (p=0.216). The civilian admissions were significantly older (p<0.001) and had a much greater age range. Five children (<18 years old) were admitted.

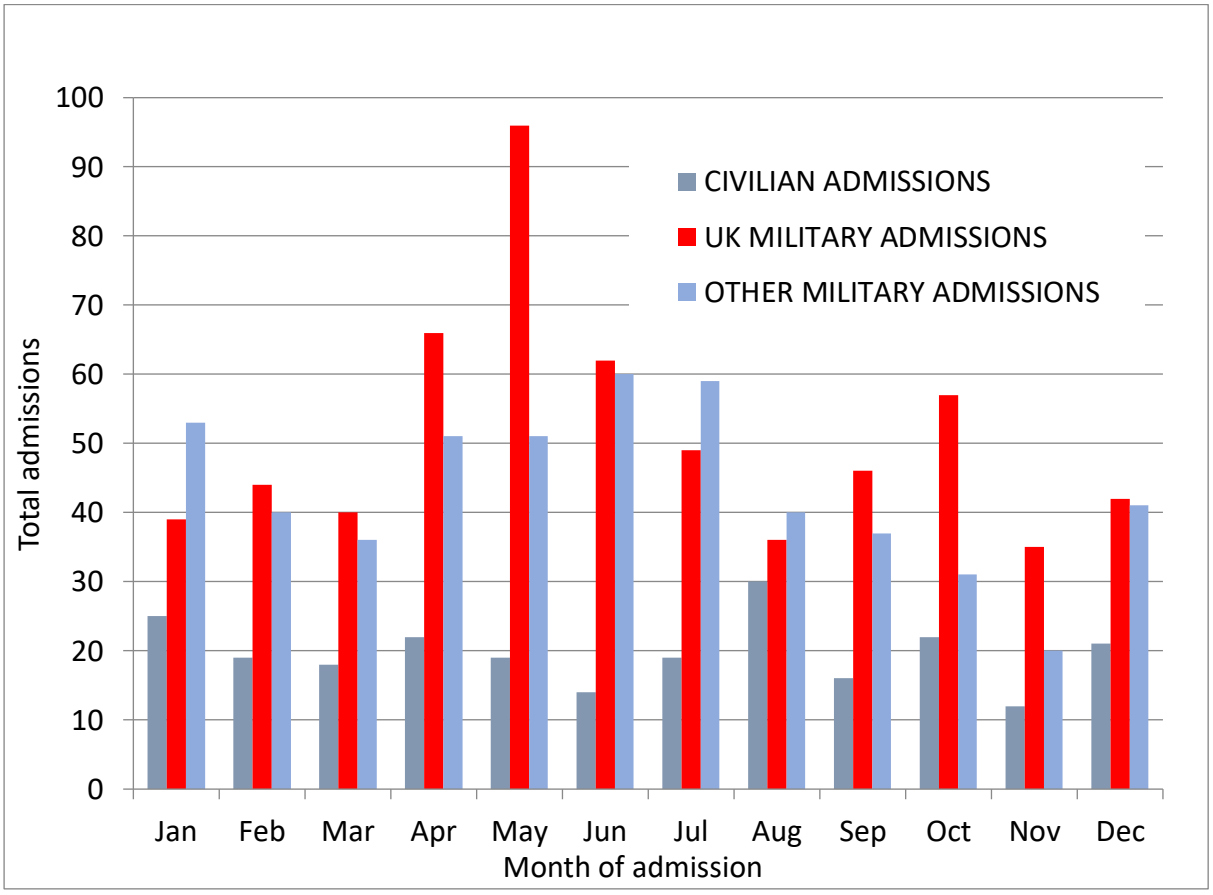

Figure 4.2: Chart illustrating the number of admissions for each month of the collection period.

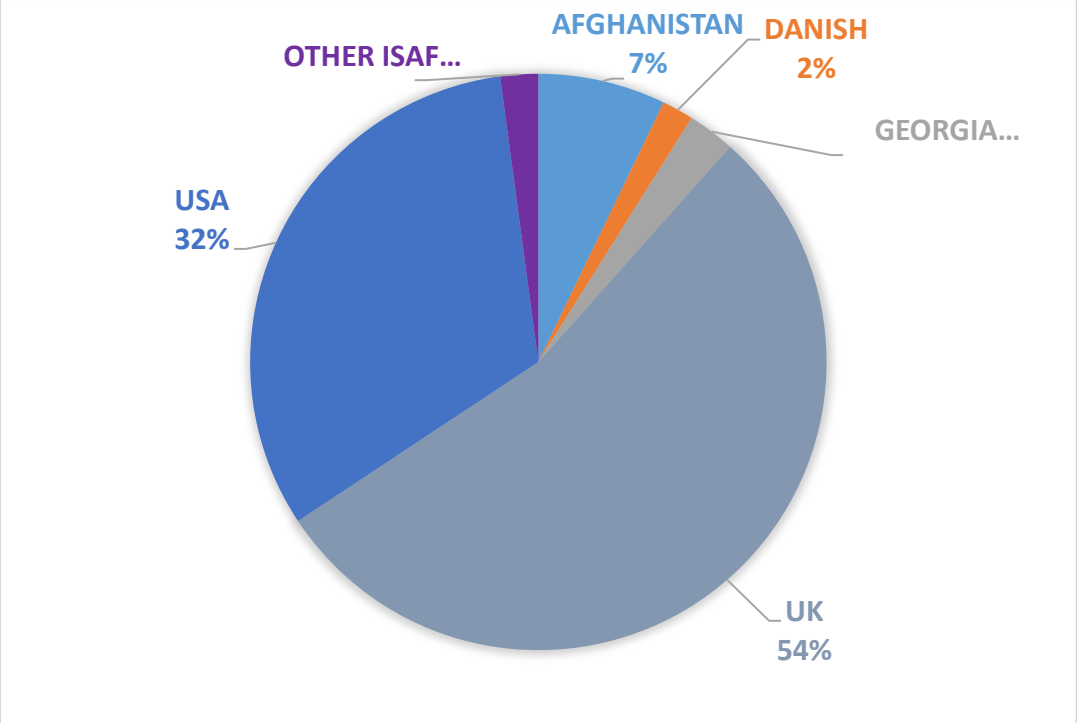

Figure 4.3. Military patients by nationality. *ISAF = International Security Assistance Force*

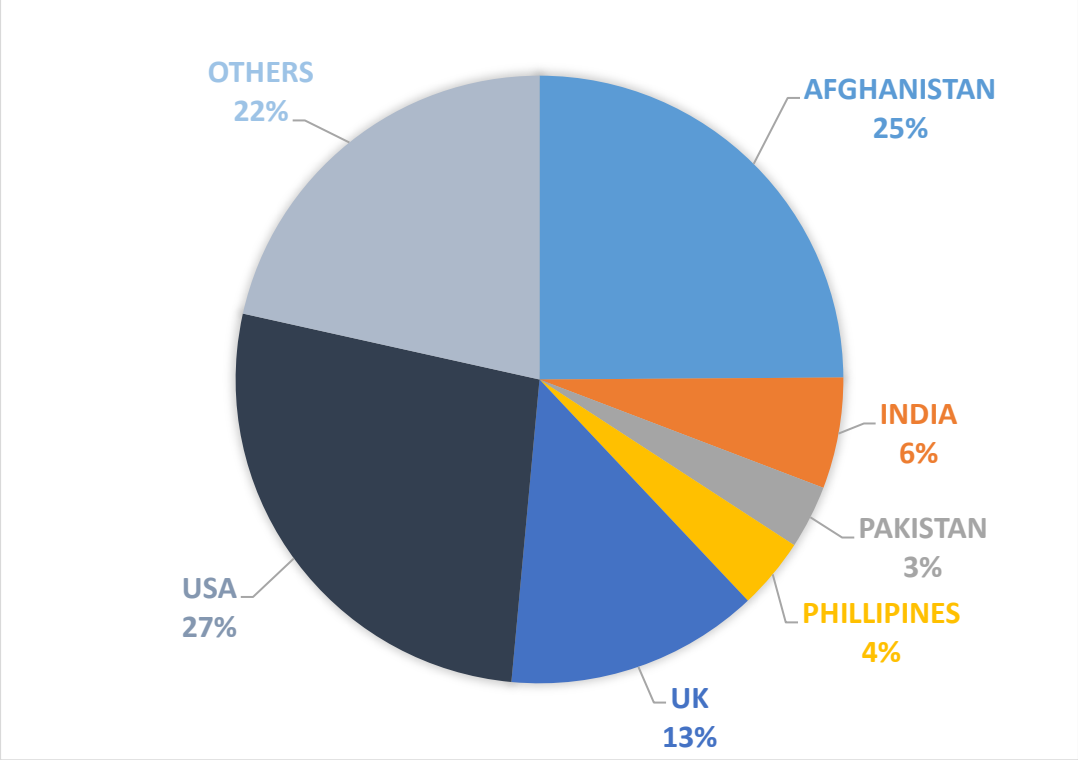

Figure 4.4. Civilian patients by nationality.

4.3.2 Length of stay and disposal. The length of stay was relatively short for all three patient groups at less than 2 days. The hospital stays for non-UK military patients were shorter than the UK military (p=0.001). The co-location of intermediate medical facilities in Camp Bastion, run by allied forces for their own personnel, may account for this difference. The length of stay for civilian patients was similar to UK Military personnel (p=0.276) despite a few long-staying outliers skewing the civilian pop to the right (maximum stay length of 21 days). The disposal rates overall are summarised in tables 1 and a more detailed summary for the UK military only is in table 3. Approaching three quarters of UK military patients were directly returned to their units (RTU) at discharge. These numbers are likely to be similar in the non-UK military cohort as a further 62% were directly discharged to their units and a further 10.7% were discharged to an intermediate facility to convalesce, but the data to confirm this was not available. The RTU rate for non-GIM admissions was 40.2%. The majority of the remainder were evacuated to their home nation or, in the case of local civilians, to an Afghan civilian hospital (role 4).

4.3.3 Deaths. No military died but three civilian GIM patients did die. Two deaths occurred in western contractors following acute MI and one death was in a locally employed civilian following the recreational ingestion of methanol.

4.3.4 Presenting symptoms. There were 1656 reported symptoms divided into 142 different presenting symptoms. The 20 most frequent symptoms for each of the three groups are summarised by frequency in table 4.2. There are striking similarities between

the three groups with symptoms of pain in the throat and chest (158 cases), diarrhoea (154 cases), fever (154 cases), syncope and collapse (139 cases), nausea and vomiting (126 cases), headache (105 cases), and rash (79 cases) all occurring in the top ten most frequent symptoms for all three groups. There were 22 cases of snake or non-human mammal bites, though none of these occurred in UK military patients, as well as a number of scorpion stings.

Table 4.1. Demographics of the GIM admissions to the Role 3 Hospital, Camp Bastion. *Abbreviations: Length of Stay = LOS; RTU = Returned to Unit or home; Detention = Det; Intermediate facility = IF; Other Afghanistan hospital = OAH; Role 4 = R4; number =n; Non-UK Military = Non-UK Mil. Role 4 was considered to be the home nation of non-Afghans or a local hospital (either military or civilian) for Afghan nationals.*

Group	**All**	**Males**	**Females**	**Age (years)**		**LOS (days)**		**Disposal destination**					
								RTU	Det	IF	OAH	R 4	Died
	n (%)	n (%)	n (%)	Median	Range	Median	Range	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
UK military	612 (44.7)	569 (93.0)	43 (7.0%)	29	19-58	1.6	0-10	443 (72.4)	0 (0)	0 (0)	3 (0.5)	166 (27.1)	0 (0)
Non-UK Mil	519 (37.9)	498 (96.0)	21 (4.0)	29	19-69	1.4	0-9	322 (62.0)	0 (0)	56 (10.7)	13 (2.5)	128 (24.7)	0 (0)
Civilians	237 (17.3)	223 (94.1)	14 (5.9)	40	2-72	1.8	0-21	178 (75.1)	5 (2.1)	4 (1.7)	0 (0)	47 (19.8)	3 (1.3)
All	1368	1290 (94.3)	78 (5.7)	30	2-72	1.6	0-21	942 (68.9)	5 (0.4)	60 (4.4)	16 (1.2)	342 (25.0)	3 (0.2)

Table 4.2. Summary of the 20 most frequent presenting symptoms by patient group.

	BRITISH MILITARY PATIENTS		NON-UK MILITARY PATIENTS		CIVILIANS ONLY	
	Total symptoms n=769 Different symptoms n=78		Total symptoms n=652 Different symptoms n=78		Total symptoms n=283 Different symptoms n=47	
Ranking by frequency	**Symptom**	**n (%)**	**Symptom**	**n (%)**	**Symptom**	**n (%)**
1	Diarrhoea	101 (16.5)	Pain in throat and chest	66 (12.7)	Pain in throat and chest	48 (20.3)
2	Fever	84 (13.7)	Syncope and collapse	52 (10.0)	Abnormalities of breathing	37 (15.6)
3	Nausea and vomiting	82 (13.4)	Fever	46 (8.9)	Syncope and collapse	28 (11.8)
4	Syncope and collapse	59 (9.6)	Headache	44 (8.5)	Fever	24 (10.1)
5	Pain in throat and chest	54 (8.8)	Diarrhoea	39 (7.5)	Abdominal and pelvic pain	14 (5.9)
6	Headache	48 (7.8)	Abnormalities of breathing	35 (6.7)	Diarrhoea	14 (5.9)
7	Rash	39 (6.4)	Nausea and vomiting	32 (6.2)	Rash	14 (5.9)
8	Malaise and fatigue	35 (5.7)	Psychiatric	30 (5.8)	Headache	13 (5.5)
9	Psychiatric symptoms	35 (5.7)	Convulsions	27 (5.2)	Convulsions	12 (5.1)
10	Abdominal and pelvic pain	33 (5.4)	Rash	26 (5.0)	Nausea and vomiting	12 (5.1)
11	Abnormalities of breathing	24 (3.9)	Malaise and fatigue	22 (4.2)	Hemiplegia	9 (3.8)
12	Dizziness and giddiness	14 (2.3)	Abdominal and pelvic pain	22 (4.2)	Cough	6 (2.5)
13	Hyperthermia	12 (2)	Palpitations	18 (3.5)	Malaise and fatigue	6 (2.5)
14	Acute pharyngitis	10 (1.6)	Snake or mammal bite	17 (3.3)	Snake or mammal bite	5 (2.1)
15	Palpitations	9 (1.5)	Scorpion sting	11 (2.1)	Dizziness and giddiness	5 (2.1)
16	Cough	8 (1.3)	Poisoning	11 (2.1)	Palpitations	4 (1.7)
17	Visual disturbances	8 (1.3)	Cough	8 (1.5)	Renal colic	4 (1.7)
18	Disorders of the eye and adnexa	8 (1.3)	Hemiplegia	7 (1.3)	Psychiatric symptoms	4 (1.7)
19	Scorpion sting	5 (0.8)	Acute pharyngitis	7 (1.3)	Haematemesis	2 (0.8)
20	Convulsions	3 (0.5)	Jaundice	6 (1.2)	Dysuria	2 (0.8)

Table 4.3: Summary of the 1368 primary diagnoses by ICD 10 chapter. *The categories with the 5 highest number of definitive GIM diagnoses for each group are highlighted in red. (table continued overleaf)* [†]*There was an additional internal transfer to another medical facility within theatre.* [‡]*In total 3 UK military patients were transferred to other medical facilities within the theatre.*

ICD Chapter	Disease category	Patient group				Disposal of UK military patients	
		UK Mil	Non-UK Mil	Civilian	Totals	RTU n (%)	Role 4 n (%)
A00-B99	Certain infectious and parasitic diseases	171	96	39	306	155 (90.6)	16 (9.4)
C00-97	Neoplasms	3	2	2	7	0 (0)	3 (100)
D00-89	Diseases of the blood and blood forming organs and certain disorders involving the immune mechanism	2	4	2	8	0 (0)	2 (100)
E00-90	Endocrine, nutritional and metabolic diseases	20	10	2	32	14 (70.0)	6 (30.0)
F00-99	Mental and behavioural disorders	31	20	9	60	11 (35.5)	20(64.5)
G00-99	Diseases of the nervous system	21	40	22	83	12 (57.1)	9 (42.9)
H00-59	Diseases of the eye and adnexa	10	4	2	16	4 (40.0)	5 (50.0)†
H60-95	Diseases of the ear and mastoid process	5	4	1	10	3 (60.0)	2 (40.0)
I00-99	Diseases of the circulatory system	29	46	36	111	13 (44.8)	15 (51.7)†
J00-99	Diseases of the respiratory system	38	39	28	105	31 (81.6)	7 (18.4)
K00-93	Diseases of the digestive system	23	22	21	67	9 (39.1)	13 (54.2)†
L00-99	Diseases of the skin and subcutaneous tissue	30	16	8	54	28 (93.3)	2 (6.7)
M00-99	Diseases of the musculoskeletal system and connective tissue	15	9	1	25	12 (80.0)	3 (20.0)
N00-99	Diseases of the genitourinary system	4	14	8	25	2 (50.0)	2 (50.0)

ICD Chapter	Disease category	Patient group				Disposal of UK military patients	
		UK Mil	Non-UK Mil	Civilian	Totals	RTU n (%)	Role 4 n (%)
Q00-99	Congenital malformations, deformations and chromosomal abnormalities	0	0	2	2	0 (0)	0 (0)
R00-99	Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified	120	95	37	252	92 (77.7)	28 (23.3)
S00-T98	Injury, poisoning and certain other consequences of external causes	80	80	13	173	49 (56.6)	31 (43.4)
V01-Y98	External causes of morbidity and mortality	5	12	1	18	3 (60.0)	2 (40.0)
Z00-99	Factors influencing health status	5	6	3	14	5 (100)	0 (0)
	Totals	**613**	**519**	**237**	**1368**	**443 (72.3)**	**166 (27.1)‡**

Table 3 continued.

Table 4.4. Summary of the discharge diagnoses occurring on three or more occasions and by patient group. *Abbreviations: Chronic obstructive pulmonary disease = COPD; Lower respiratory tract infection = LRTI; Transient ischaemic attacks = TIA (table continued overleaf)*

	BRITISH MILITARY PATIENTS		**NON-UK MILITARY PATIENTS**		**CIVILIANS ONLY**	
	Total discharge diagnoses n=716 Different discharge diagnoses n= 179		Total discharge diagnoses n= 627 Different discharge diagnoses n=178		Total discharge diagnoses n= 319 Different discharge diagnoses n= 124	
Ranking by frequency	**Discharge diagnosis**	**n (%)**	**Discharge diagnosis**	**n (%)**	**Discharge diagnosis**	**n (%)**
1	Infectious diarrhoea	138 (19.3)	Infectious diarrhoea	64 (10.2)	LRTI	41 (12.9)
2	Heat illness	44 (6.1)	Epilepsy (inc status epilepticus)	25 (4.0)	Infectious diarrhoea	16 (5.0)
3	Volume depletion	33 (4.6)	Volume depletion	16 (2.6)	Myocardial infarction or angina	15 (4.4)
4	Acute stress reaction	23 (3.2)	Myocardial infarction or angina	16 (2.6)	Epilepsy	11 (3.4)
5	Cellulitis	20 (2.8)	Envenomation	15(2.4)	Peptic ulcer disease& related	10 (3.1)
6	Migraine	13 (1.8)	Heat illness	14 (2.2)	Essential (primary) hypertension	8 (2.5)
7	Acute tonsillitis	9 (1.3)	LRTI	13 (2.1)	Stroke or TIA	8 (2.5)
8	LRTI	9 (1.3)	Peptic ulcer disease& related	13 (2.1)	Arrhythmia	7 (2.2)
9	Peptic ulcer disease& related	8 (1.1)	Acute stress reaction	11(1.8)	COPD	7 (2.2)
10	Arrhythmia	7 (1.0)	Cellulitis	11 (1.8)	Calculus of kidney and ureter	6 (1.9)
11	Q fever	6 (0.8)	Migraine	10 (1.61)	Cellulitis	6 (1.9)
12	Epilepsy	6 (0.8)	Arrhythmia	10 (1.61)	Diabetes	5 (1.6)

	BRITISH MILITARY PATIENTS		NON-UK MILITARY PATIENTS		CIVILIANS ONLY	
Ranking by frequency	**Discharge diagnosis**	**n (%)**	**Discharge diagnosis**	**n (%)**	**Discharge diagnosis**	**n (%)**
13	Inflammatory bowel disease	6 (0.8)	Acute tonsillitis	7 (1.1)	Migraine	5 (1.6)
14	Urticarial rash	5 (0.7)	Acute pericarditis	6 (1.0)	Asthma and status asthmaticus	4 (1.3)
15	Myocardial infarction or angina	4 (0.6)	Stroke	6 (1.0)	Pulmonary embolism	4 (1.3)
16	Acute renal failure	4 (0.6)	Asthma and status asthmaticus	6 (1.0)	Acute stress reaction	3 (0.9)
17	Dental abscess	4 (0.6)	Pleural effusion	6 (1.0)	Tuberculosis	3 (0.9)
18	Infectious mononucleosis	4 (0.6)	Unspecified septicaemia	5 (0.8)	Typhoid and paratyphoid fevers	3 (0.9)
19	Stroke and TIA	4 (0.6)	Unspecified acute hepatitis	5 (0.8)	-	-
20	Pulmonary embolism	3 (0.4)	Malaria	5 (0.8)	-	-
21	Acute pericarditis	3 (0.4)	Acute renal failure	4 (0.6)	-	-
22	Asthma	3 (0.4)	Tuberculosis	3 (0.5)	-	-
23	-	-	Pulmonary embolism	3 (0.5)	-	-

Table 4.4 continued.

Table 4.5. Summary of the discharge diagnoses occurring in ICD10 Chapter R00-99 'Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified'. *Summary of those codes present on three or more occasions by patient group.*

	BRITISH MILITARY PATIENTS		**NON-UK MILITARY PATIENTS**		**CIVILIANS ONLY**	
	Total discharge diagnoses n=716 Different discharge diagnoses n= 179		Total discharge diagnoses n= 627 Different discharge diagnoses n=178		Total discharge diagnoses n= 319 Different discharge diagnoses n= 124	
Ranking by frequency	**Discharge diagnosis**	**n (%)**	**Discharge diagnosis**	**n (%)**	**Discharge diagnosis**	**n (%)**
1	Fever of unknown origin	51 (7.1)	Syncope and collapse	24 (3.8)	Pain in throat and chest	12
2	Syncope and collapse	24 (3.4)	Fever of unknown origin	22 (3.5)	Syncope and collapse	12
3	Pain in throat and chest	14 (2.0)	Pain in throat and chest	20 (3.2)	Toxic effect of contact with venomous animals	5
4	Headache	7 (1.0)	Abnormalities of heart beat	5 (0.8)		
5	Abnormalities of heart beat	4 (0.6)	Headache	4 (0.6)		

4.3.5 Diagnoses. In the three patient groups the most frequently made diagnoses were similar (summarised in tables 4.3-4.5). Cardiovascular conditions, including acute MI and angina, arrhythmias, pericarditis and pulmonary emboli were reoccurring presentations but CVD were not the most frequently seen. Given the relative youth and healthy nature of the population at risk the group was perhaps unsurprisingly dominated by acquired infectious diseases, in particular infectious gastroenteritis, respiratory tract infections and cellulitis. Other notable infectious diagnoses included tuberculosis, Q-fever and malaria. Other frequent non-infectious diagnoses were neurological conditions, particularly migraines and epilepsy and respiratory disease, including asthma. For the military population heat illnesses, such as heat stroke, were particularly common environmental conditions and constituted the second greatest group of UK military patients. Adverse encounters with endemic fauna generated numerous admissions due to mammal bites, snake bites, with or without envenomation, and scorpion stings. There were a significant number of patients in whom no definitive diagnosis was made (table 5) and this was dominated by symptoms of undifferentiated febrile disease, chest pain, syncope, palpitations and headache. The full list of all 1626 discharge diagnoses are collated by system (tables 3).

4.3.5.1 A00-B99 - Certain infectious and parasitic diseases (table 4.6). There were 306 admissions (22.4%) whose primary diagnosis was in this category. These constituted the most frequent military diagnoses and were the second most frequent category in the civilian group. Infectious gastroenteritis accounted for 205 of all 350 infectious disease diagnoses and was more common than any other. These were the primary diagnosis in 15.0% of admissions and represented 12.6% of all diagnoses. The next most frequent infectious diagnoses were of undifferentiated fever (45 cases, 2.8% of diagnoses), Plasmodium vivax malaria (10 cases) and shigellosis, tuberculosis and infectious mononucleosis (each 6 cases). Of the remainder there were multiple cases of hepatitis (8 cases) and septicaemia (8 cases) where no specific pathogen was identified. Many identified infections would be familiar to a general physician working in the UK including one case of meningococcal meningitis, one of streptococcal septicaemia and two cases of chickenpox. There were sporadic cases of tropical diseases not commonly familiar to most physicians working in the UK including Q-fever, enteric fever, relapsing fever, Leishmaniasis, Dengue, Brucellosis, Amoebiasis, Echinococcosis and typhus as well as incidental findings of intestinal parasites. Two new cases of HIV were also identified; one in a British serviceperson and the other in a contractor.

Table 4.6: A00-B99 Certain infectious and parasitic diseases

Ranking	Diagnosis	n
1	Diarrhoea and gastroenteritis of presumed infectious origin	205
2	Viral infection of unspecified site	45
3	Plasmodium vivax malaria	10
4	Other acute viral hepatitis	8
5	Other septicaemia	8
6	Q fever	8
7	Infectious mononucleosis	6
8	Shigellosis	6
9	TB	6
10	Unspecified intestinal parasitism	4
11	Viral meningitis	4
12	Herpesviral [herpes simplex] infections	3
13	Other salmonella infections	3
14	Typhoid and paratyphoid fevers	3
15	Varicella [chickenpox]	3
16	Dengue fever [classical dengue]	2
17	Dermatophytosis	2
18	Echinococcosis	2
19	Other bacterial foodborne intoxications	2
20	Unspecified viral encephalitis	2
21	HIV	2
22	Amoebiasis	1
23	Anogenital herpesviral [herpes simplex] infections	1
24	Bacterial infection of unspecified site	1
25	Brucellosis	1
26	Leishmaniasis	1

Table 4.6 Cont

Ranking	Diagnosis	n
27	Meningococcal infection	1
28	Other bacterial intestinal infections	1
29	Other diseases caused by chlamydiae	1
30	Other protozoal intestinal diseases	1
31	Other viral encephalitis, not elsewhere classified	1
32	Rabies	1
33	Relapsing fevers	1
34	Streptococcal septicaemia	1
35	Typhus fever	1
36	Unspecified sexually transmitted disease	1
37	Zoster [herpes zoster]	1
	Total	**350**

4.3.5.2 C00-97 – Neoplasms (table 4.7). There were 7 neoplasms identified and all were the primary diagnosis. Three were intracranial masses, one presented with a seizure, one presenting with hemiplegia, and one with persistent headaches and nausea. Other neoplastic diseases included one multiple myeloma case presenting with back pain, a new acute leukaemia presenting with dyspnoea, metastatic oesophageal carcinoma presenting with chest pain and a malignant and locally invasive growth on the soft palate causing local pain. The multiple myeloma, leukaemia and palate mass occurred in British servicemen. Definitive histological diagnosis was not available in Afghanistan.

Table 4.7: C00-97 Neoplasms

Ranking	Diagnosis	n
1	Malignant neoplasm of brain	3
2	Malignant neoplasm of oesophagus	1
3	Malignant neoplasm of palate	1
4	Multiple myeloma and malignant plasma cell neoplasms	1
5	Neoplasm of uncertain or unknown behaviour of meninges	1
	Total	**7**

4.3.5.3 D00-89 - Diseases of the blood and blood forming organs and certain disorders involving the immune mechanism (table 4.8). In this group there were twelve cases of which eight were primary diagnoses. Most were iron deficiency anaemia or acquired haemolytic anaemia. There were two cases of sarcoid, one of Henoch-Schönlein purpura and one of methaemoglobinaemia.

Table 4.8: D00-89 Diseases of the blood and blood forming organs and certain disorders involving the immune mechanism

Ranking	Diagnosis	n
1	Iron deficiency anaemia	3
2	Acquired haemolytic anaemia	2
3	Other anaemias	2
4	Sarcoidosis	2
5	Agranulocytosis	1
6	Methaemoglobinaemia	1
7	Purpura and other haemorrhagic conditions	1
	Total	**12**

4.3.5.4 E00-90 - Endocrine, nutritional and metabolic diseases (table 4.9). There were 32 individuals (2.3% of admissions) with a primary diagnosis in this category. Of these 68 diagnoses 50 were of volume depletion as either a primary diagnosis (22 cases, 1.3%) or as an associated diagnosis (28 cases, 1.7%), usually with infectious gastroenteritis. There were 8 new cases of insulin-dependent diabetes and 3 new cases of non-insulin dependent diabetes. Insulin-dependent diabetes was newly diagnosed twice in British servicepersons.

Table 4.9: E00-90 Endocrine, nutritional and metabolic diseases

Ranking	Diagnosis	n
1	Volume depletion	50
2	Insulin dependent diabetes mellitus	8
3	Non-insulin dependent diabetes mellitus	3
4	Other disorders of fluid, electrolyte and acid-base balance	2
5	Disorders of porphyrin and bilirubin metabolism	1
6	Hyperaldosteronism	1
7	Obesity	1
8	Other disorders of adrenal gland	1
9	Unspecified protein-energy malnutrition	1
	Total	**68**

4.3.5.5 F00-99 - Mental and behavioural disorders (table 10). Psychiatry was not the focus of this study. Despite this patients admitted with mental health diagnoses were a significant minority of the patients seen (60 patients, 4.4% of admission). In the absence of a psychiatrist co-located at the hospital, any British patient with a primary psychiatric disorder, particularly when there were associated with safety issues (regarding their safety, or the safety of others) was admitted under the GIM team as a matter of policy. These referrals could originate from the emergency department, the field mental health team, or primary care. The majority were acute stress reactions. In total 60 patients were admitted with primary psychiatric symptoms (4.4% of admissions). Another 3 patients presented with organic symptoms and ultimately received a primary psychiatric diagnosis. A total of 66 diagnoses were made in this category.

Table 4.10: F00-99 Mental and behavioural disorders

Ranking	Diagnosis	n
1	Reaction to severe stress, and adjustment disorders	33
2	Mental disorder, not otherwise specified	9
3	Depressive episodes	8
4	Obsessive-compulsive disorder	4
5	Psychological and behavioural factors associated with disorders or diseases classified elsewhere	4
6	Other anxiety disorders	3
7	Unspecified nonorganic psychosis	3
8	Recurrent depressive disorder	2
9	Delirium, not induced by alcohol and other psychoactive substances	1
10	Dissociative [conversion] disorders	1
11	Eating disorders	1
12	Manic episode	1
13	Mental and behavioural disorders due to use of hallucinogens	1
14	Mental and behavioural disorders due to use of opioids	1
15	Nonorganic sleep disorders	1
16	Schizoaffective disorders	1
17	Somatoform disorders	1
18	Unspecified disorder of adult personality and behaviour	1
	Total	**76**

4.3.5.6 G00-99 - Diseases of the nervous system (table 4.11). There were 83 (6.1% of admissions) primary diagnoses in this category and in total 96 cases with disease of the nervous system were diagnosed. Two diagnoses were most common made: epilepsy (or a seizure suggestive of epilepsy) and migraine. There were 43 cases (2.6% of diagnoses) of epilepsy including one case of status epilepticus. Migraines or other headache syndromes constituted 29 (1.8% of diagnoses) presentations. Strokes are included in diseases of the cardiovascular system. However transient ischaemic attacks are included, and were diagnosed in 7 cases.

Table 4.11: G00-99 Diseases of the nervous system

Ranking	Diagnosis	n
1	Epilepsy	42
2	Migraine	24
3	Transient cerebral ischaemic attacks and related syndromes	7
4	Other headache syndromes	5
5	Facial nerve disorders	4
6	Inflammatory polyneuropathy	4
7	Disorders of myoneural junction and muscle in diseases classified elsewhere	1
8	Disorders of other cranial nerves	1
9	Encephalitis, myelitis and encephalomyelitis	1
10	Multiple sclerosis	1
11	Other disorders of brain	1
12	Other paralytic syndromes	1
13	Other polyneuropathies	1
14	Parkinsons disease	1
15	Sleep disorders	1
16	Status epilepticus	1
	Total	**96**

4.3.5.7 H00-59 - Diseases of the eye and adnexa (table 12). There were 16 primary diagnoses (1.2% of admissions) within this category. The diagnoses were most commonly infective in aetiology, including 6 cases of orbital cellulitis, 2 cases of conjunctivitis and one case of chalazion. Other medical eye disease included a single case of optic neuritis and two of iritis. There were also two retinal detachments.

Table 4.12: H00-59 Diseases of the eye and adnexa

Ranking	Diagnosis	n
1	Acute inflammation of orbit	6
2	Conjunctivitis	2
3	Keratitis	2
4	Other diseases of inner ear	2
5	Retinal detachments and breaks	2
6	Hordeolum and chalazion	1
7	Iridocyclitis	1
8	Optic neuritis	1
9	Other inflammation of eyelid	1
	Total	**18**

4.3.5.8 H60-95 - Diseases of the ear and mastoid process (table 4.13). There were 12 diagnoses within this category consisting primarily of otitis externa, otitis media and labyrinthitis.

Table 4.13: H60-95 Diseases of the ear and mastoid process

Ranking	Diagnosis		n
1	Otitis externa		3
2	Disorders of vestibular function		2
3	Other diseases of inner ear		2
4	Suppurative and unspecified otitis media		2
5	Nonsuppurative otitis media		1
6	Perforation of tympanic membrane		1
7		**Total**	**11**

4.3.5.9 I00-99 - Diseases of the circulatory system (table 4.14). There were 111 primary diagnoses (8.1% of admissions) in this category. Ischaemic heart disease was diagnosed in 40 admissions (2.4% of diagnoses), 20 of which were acute MI (1.2% of diagnoses) and 15 were new cases of unstable angina (1.0% of diagnoses). The majority of cases occurred in the group of older civilian contractors; only one case of MI and 3 cases of angina pectoris were diagnosed in UK military patients. The remainder were secondary to heart failure following previous MI in contractors. Two deaths occurred in the MI group and both were civilian contractors. There were 11 admissions with newly diagnosed atrial fibrillation and 13 admissions with supraventricular tachycardias, including one patient whose ECG demonstrated pre-excitation once cardioverted to sinus rhythm. Pericarditis was diagnosed in 11 patients. Venous thromboembolic disease was diagnosed in 19 patients (1.2% of diagnoses) of whom 6 were UK military. There were 13 strokes requiring admission, of which two were British military personnel. The remaining diagnoses were uncommon and included hypertrophic and DCM, conduction disease, and other vascular disease.

Table 4.14: I00-99 Diseases of the circulatory system

Ranking	Diagnosis	n
1	Acute myocardial infarction	20
2	Angina pectoris	15
3	Essential (primary) hypertension	14
4	Acute pericarditis	11
5	Atrial fibrillation and flutter	11
6	Cerebral infarction	10
7	Pulmonary embolism	10
8	Paroxysmal tachycardia	9
9	Phlebitis and thrombophlebitis	8
10	Hypotension	4
11	Other cardiac arrhythmias	4
12	Cardiomyopathy	3
13	Chronic ischaemic heart disease	3
14	Cardiac arrest	2
15	Haemorrhoids	2
16	Other cerebrovascular diseases	2
17	Atrioventricular and left bundle?branch block	1
18	Certain current complications following acute myocardial infarction	1
19	Heart failure	1
20	Hypertensive heart disease	1
21	Intracerebral haemorrhage	1
22	Other acute ischaemic heart diseases	1
23	Other conduction disorders	1
24	Other peripheral vascular diseases	1
25	Other venous embolism and thrombosis	1
26	Varicose veins of lower extremities	1
27	Varicose veins of other sites	1
	Total	**139**

4.3.5.10 J00-99 - Diseases of the respiratory system (table 4.15). There were 105 primary diagnoses (7.7% of admissions) of respiratory disease. Most of the 124 respiratory system diagnoses were due to infections. Lower respiratory tract infection, including pneumonia and bronchitis, was diagnosed in 59 cases (3.6% of diagnoses). Upper respiratory infections occurred in 29 cases including 16 cases of acute tonsillitis. Asthma was also frequently identified, with 11 diagnoses, including 4 admissions with of status asthmaticus. Within the UK Military group only 3 patients were diagnosed with asthma and these were concurrent with respiratory tract infections. Other diagnoses were sporadic and occurred at low frequencies (<5 cases per diagnosis).

Table 4.15: J00-99 Diseases of the respiratory system

Ranking	Diagnosis	n
1	Pneumonia, organism unspecified	41
2	Acute tonsillitis	16
3	Unspecified acute lower respiratory infection	11
4	Asthma	7
5	Influenza, virus not identified	5
6	Acute upper respiratory infections of multiple or unspecified sites	4
7	Other chronic obstructive pulmonary disease	4
8	Status asthmaticus	4
9	Acute bronchitis	3
10	Acute sinusitis	3
11	Other interstitial pulmonary diseases	3
12	Pleural effusion, not elsewhere classified	3
13	Respiratory conditions due to inhalation of chemicals, gases, fumes and vapours	3
14	Bronchitis, not specified as acute or chronic	2
15	Pleural effusion in conditions classified elsewhere	2
16	Bacterial pneumonia, not elsewhere classified	1
17	Diseases of vocal cords and larynx, not elsewhere classified	1
18	Dorsalgia	1
19	Emphysema	1
20	Other pleural conditions	1
21	Peritonsillar abscess	1
22	Pneumoconiosis due to asbestos and other mineral fibres	1
23	Pneumonia due to Streptococcus pneumoniae	1
24	Pneumonitis due to solids and liquids	1
25	Pneumothorax	1
26	Pulmonary eosinophilia, not elsewhere classified	1
27	Pulmonary oedema	1
28	Viral pneumonia, not elsewhere classified	1
	Total	**124**

4.3.5.11 K00-93 - Diseases of the digestive system (table 16). There were 67 primary diagnoses (4.9% of admissions) related to digestive system disease (excluding infectious gastroenteritis). There were 20 admissions (1.2% of diagnoses) with symptoms resulting from peptic ulceration or oesophageal reflux and this was the most frequent group of diagnoses. Hepatobiliary disease represented the next largest group of digestive system disease with 11 cases, but these were a heterogenous group of disorders. New inflammatory bowel disease was diagnosed in 4 cases, all of whom were UK military.

Table 4.16: K00-93 Diseases of the digestive system

Ranking	Diagnosis	n
1	Other diseases of oesophagus	10
2	Gastro?oesophageal reflux disease	9
3	Diseases of pulp and periapical tissues	6
4	Dyspepsia	5
5	Other functional intestinal disorders	5
6	Other diseases of digestive system	4
7	Other disorders of urinary system	4
8	Other inflammatory liver diseases	4
9	Other noninfective gastroenteritis and colitis	4
10	Peptic ulcer, site unspecified	3
11	Acute pancreatitis	2
12	Crohns disease [regional enteritis]	2
13	Gastric ulcer	2
14	Hepatic failure, not elsewhere classified	2
15	Other diseases of biliary tract	2
16	Toxic liver disease	2
17	Ulcerative colitis	2
18	Acute appendicitis	1
19	Cholelithiasis	1
20	Dental caries	1
21	Diverticular disease of intestine	1
22	Gastritis and duodenitis	1
23	Irritable bowel syndrome	1
	Total	**74**

4.3.5.12 L00-99 - Diseases of the skin and subcutaneous tissue (table 4.17). There were 54 patients (3.9% of admissions) with a primary diagnosis of skin and subcutaneous disease. Infectious cellulitis represented 37 of the diagnoses made (2.7%). The majority of the remainder of were diagnosed as dermatitis (7 cases) or urticaria (7 cases).

Table 17: L00-99 Diseases of the skin and subcutaneous

Ranking	Diagnosis	n
1	Cellulitis	37
2	Urticaria	7
3	Cutaneous abscess, furuncle and carbuncle	3
4	Dermatitis due to substances taken internally	3
5	Erythema multiforme	3
6	Other local infections of skin and subcutaneous tissue	2
7	Unspecified contact dermatitis	2
8	Atopic dermatitis	1
9	Other dermatitis	1
	Total	**59**

4.3.5.13 M00-99 - Diseases of the musculoskeletal system and connective tissue (table 4.18). There were 25 patients (1.8% of admissions) with a primary musculoskeletal diagnosis. Although 35 diagnoses were made, the group was varied with only non-specific diagnoses; dorsalgia was diagnosed in 8 cases, muscle disorders in 8 cases and cartilage disorders in 7 cases.

Table 4.18: M00-99 Diseases of the musculoskeletal system and connective tissue

Ranking	Diagnosis	n
1	Dorsalgia	8
2	Other disorders of muscle	8
3	Other disorders of cartilage	7
4	Soft tissue disorders related to use, overuse and pressure	3
5	Gout	2
6	Reactive arthropathies	2
7	Arthropathies in other diseases classified elsewhere	1
8	Other acquired deformities of limbs	1
9	Other intervertebral disc disorders	1
10	Other joint disorders, not elsewhere classified	1
11	Other systemic involvement of connective tissue	1
	Total	**35**

4.3.5.14 N00-99 - Diseases of the genitourinary system (table 19). There were 25 patients with a primary diagnosis in this disease category (1.8% of admissions). The most common abnormalities were urinary tract infect secondary to renal calculi (12 cases) or acute renal failure secondary to another diagnosis such as gastroenteritis or heat stroke (9 cases).

4.3.5.15 Q00-99 - Congenital malformations, deformations and chromosomal abnormalities (table 4.20). Both congenital abnormalities (dextrocardia and a leg deformity) identified were in Afghans and both were incidental findings.

Table 4.19: N00-99 Diseases of the genitourinary system

Ranking	Diagnosis	n
1	Calculus of kidney and ureter	12
2	Acute renal failure	9
3	Acute tubulo?interstitial nephritis	5
4	Unspecified renal colic	4
5	Other disorders of urinary system	3
6	Chronic renal failure	2
7	Chronic nephritic syndrome	1
8	Drug? and heavy?metal?induced tubulo?interstitial and tubular conditions	1
9	Inflammatory diseases of prostate	1
10	Orchitis and epididymitis	1
11	Other disorders of penis	1
	Total	**40**

Table 4.20: Q00-99 Congenital malformations, deformations and chromosomal abnormalities

Ranking	Diagnosis	n
1	Other congenital malformations of the heart (dextrocardia)	1
2	Congenital deformities of feet	1
	Total	**2**

4.3.5.16 R00-99 - Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified (table 4.21). There were 252 cases (18.4% of admissions) where no definitive diagnosis was made. These are important omissions to note as there were high numbers of unexplained fever (75 cases, 4.6% of diagnoses), syncope (60 cases, 3.7% of diagnoses), chest pain (46 cases, 2.8% of diagnoses), headache (13 cases) and palpitations (11 cases) amongst others.

Table 4.21: R00-99 Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified

Ranking	Diagnosis	n
1	Fever of unknown origin	75
2	Syncope and collapse	60
3	Pain in throat and chest	46
4	Symptoms and signs involving emotional state	16
5	Headache	13
6	Abnormalities of heart beat	11
7	Dizziness and giddiness	7
8	Unknown and unspecified causes of morbidity	7
9	Abnormalities of breathing	5
10	Enlarged lymph nodes	5
11	Abnormal involuntary movements	4
12	Abnormal results of function studies	4
13	Other symptoms and signs involving the circulatory and respiratory systems	4
14	Abdominal and pelvic pain	3
15	Convulsions, not elsewhere classified	3
16	Cough	3

Ranking	Diagnosis	n
17	Retention of urine	3
18	Haemorrhage from respiratory passages	2
19	Heartburn	2
20	Hepatomegaly and splenomegaly, not elsewhere classified	2
21	Disturbances of skin sensation	1
22	Dysphagia	1
23	Elevated blood glucose level	1
24	Hyperhidrosis	1
25	Nausea and vomiting	1
26	Other symptoms and signs involving cognitive functions and awareness	1
27	Other symptoms and signs involving the digestive system and abdomen	1
28	Other symptoms and signs involving the nervous and musculoskeletal systems	1
	Total	**283**

Table 4.21 cont.

4.3.5.17 S00-T98 - Injury, poisoning and certain other consequences of external causes (table 4.22). There were 173 patients (12.6% of admissions) with a primary diagnosis in this category. These diagnoses include heat illness, allergies, anaphylactic and angioedema reactions, poisoning and bites and stings. Heat illness occurred as the primary diagnosis (uncomplicated by concurrent infection) in 59 cases (4.3%) making it one of the most frequent causes of admission to hospital. Of these 38 cases were in UK military patients. There were 29 cases (1.9% of primary diagnoses) due to angioedema, allergic or anaphylactoid reactions.

There were 17 poisoning episodes that were most commonly accidental due to the recreational use of opiates (6 cases) or methanol consumption (4 cases) but there were also intentional paracetamol and non-steroidal anti-inflammatory drug overdose (4 cases). Importantly one of the methanol overdoses resulted in one of the only three fatalities following admission. This fatality was one of a small group of Afghan soldiers drinking methanol and two others in the group were dead or immediately died on reaching the emergency department so were not included in this study.

Animal bites and stings were an endemic hazard resulting in multiple admissions. Snake bites, with or without envenomation, resulted in 17 admissions, 9 with significant envenomation requiring antivenom and transfusion of blood products. There were 16 patients admitted with scorpion stings and three patients with severe local reactions to other insect bites or stings, including two that presenting with anaphylaxis. Five patients were admitted with mammal bites and required courses of rabies vaccination and antibiotics.

Table 4.22: S00-T98 Injury, poisoning and certain other consequences of external causes

Ranking	Diagnosis	n
1	Effects of heat and light	59
2	Adverse effects, not elsewhere classified	30
3	Toxic effect of contact with venomous animals	25
4	Intracranial injury	24
5	Injury of unspecified of body	6
6	Other and unspecified injuries of head	5

Table 4.22 cont

Ranking	Diagnosis	n
7	Toxic effect of other gases, fumes and vapours	5
8	Poisoning by agents primarily acting on smooth and skeletal muscles and the respiratory system	4
9	Poisoning by narcotics and psychodysleptics [hallucinogens]	4
10	Other complications of surgical and medical care, not elsewhere classified	3
11	Toxic effect of organic solvents	3
12	Hypothermia	2
13	Injury of eye and orbit	2
14	Poisoning by diuretics and other and unspecified drugs, medicaments and biological substances	2
15	Poisoning by nonopioid analgesics, antipyretics and antirheumatics	2
16	Superficial injury of thorax	2
17	Toxic effect of alcohol	2
18	Burn and corrosion confined to eye and adnexa	1
19	Certain early complications of trauma, not elsewhere classified	1
20	Dislocation, sprain and strain of joints and ligaments of knee	1
21	Dislocation, sprain and strain of joints and ligaments of shoulder girdle	1
22	Fracture of skull and facial bones	1
23	Injury of intra?abdominal organs	1
24	Injury of nerves and spinal cord at neck level	1
25	Injury of other and unspecified intrathoracic organs	1
26	Other effects of reduced temperature	1
27	Poisoning by agents primarily affecting the cardiovascular system	1
28	Poisoning by anaesthetics and therapeutic gases	1
29	Poisoning by antiepileptic, sedative?hypnotic and antiparkinsonism drugs	1
30	Poisoning by psychotropic drugs, not elsewhere classified	1
31	Sequelae of injuries of head	1
32	Superficial injury of ankle and foot	1

Ranking	Diagnosis	n
33	Superficial injury of neck	1
34	Superficial injury of shoulder and upper arm	1
35	Toxic effect of corrosive substances	1
	Total	**198**

Table 4.22 cont

4.3.5.18 V01-Z99 - External causes of morbidity and mortality and Factors influencing health status (tables 4.23 and 4.24). These two small groups were all related to other diagnoses and can really only be considered as co-diagnoses.

Table 4.23: V01-Y98 External causes of morbidity and mortality

Ranking	Diagnosis	n
1	Contact with unspecified venomous animal or plant	3
2	Other and unspecified vaccines and biological substances	3
3	Evidence of alcohol involvement determined by level of intoxication	2
4	Intentional self harm by unspecified means	2
5	Accidental poisoning by and exposure to nonopioid analgesics, antipyretics and antirheumatics	1
6	Bitten or stung by nonvenomous insect and other nonvenomous arthropods	1
7	Contact with hornets, wasps and bees	1
8	Foreign body or object entering through skin	1
9	Sexual assault by bodily force	1
10	Systemic antibiotics	1
	Total	**16**

Table 4.24: Z00-99 Factors influencing health status

Ranking	Diagnosis	n
1	Persons encountering health services for other counselling and medical advice, not elsewhere classified	9
2	Problems related to life management difficulty	4
3	Medical observation and evaluation for suspected diseases and conditions	1
4	Problems related to lifestyle	1
5	Problems related to physical environment	1
	Total	**16**

4.3.5.19 Children. Five children (all local Afghan civilians of age <18 years) were admitted under the GIM team. Three children presented following snake bite envenomation (two aged 10 and one aged 13 years), one with enteric fever (aged 13 years) and one following an accidental opiate overdose (aged 2 years). All five survived following appropriate and life-saving treatment. One of the snake bite patients used the hospital's entire supply of antivenom, required multiple clotting factor and blood product transfusions and spent several days on the intensive care unit.

4.4 Discussion

4.4.1 Limitations. The population of the UK Armed Forces were reasonably well characterised but for a number of reasons the remaining population at risk was difficult to quantify with accuracy. These reasons included the unknown numbers involved, the

different eligibility to access the Role 3 Hospital by different populations and differences between populations in their access to the hospital. This made the evaluation of disease incidence rates in the non-UK military population impossible to calculate with accuracy.

The total military population at risk fluctuated throughout the period of the study. Whilst the UK Armed Forces population was known in this regard the remainder (US, Georgian, Estonia etc) was not quantified for the purposes of this analysis.

UK and other foreign military personal were entitled to full medical care. Local civilians however were generally not eligible to access the Role 3 Hospital. Exceptions to this were emergencies with the aim of preserving 'life, limb and eye'. Civilian contractors providing logistics and infrastructure support varied in their eligibility to care depending on the contractual arrangements that had been made with the UK MOD.

Furthermore the pre-deployment medical standards for personnel of different nationalities were set and implemented at a national level. As a consequence it is likely that an individual with a defined pre-existing medical complaint might be deployed by one nation whilst another would state he was unfit to deploy. Each military therefore had their own doctrine and systems to provide health care. There were local differences in provision of both primary and secondary health care and intermediate discharge facilities. For example a Role 2 facility was available for many of the American casualties elsewhere in Helmand and the Danish, American and Afghan contingents all had intermediate facilities located

within Camp Bastion. Not all patients required the more advanced diagnostic and therapeutic facilities of the Role 4 hospital, particularly when the operational environment meant the transfer from a remote location could be dangerous.

The characterisation of the diseases may have varied between clinicians. The deployed physician was always trained in GIM, but usually practiced as an additional specialist in the UK. How much this specialist experience biased the diagnostic tests, risk assessment and ultimately the diagnosis made in each case was not able to be evaluated. In an attempt to overcome this the data collection was standardised and the coding of admissions was independently by two doctors. From the perspective of scientific purity it would have been interesting to have several clinicians individually evaluate patients to investigate differences in diagnosis and management, but given the relatively low numbers of patients and the limitations of the operational environment this was not possible. Practically speaking the uniformly high rates of recovery, short lengths of stay and low mortality rates indicate that the differences might have been trivial only.

4.4.2 Population differences. The relative numbers of patients admitted to the Role 3 Hospital differed between nations. As discussed above this is unlikely to accurately reflect the proportions of allied nations located in Helmand Province. It seems likely that British servicemen and women would have a lower threshold to present to the Role 3 Hospital as a significant proportion of the population were co-located in Camp Bastion. In addition to the logistical convenience, the cultural familiarity of a UK Field Hospital might have been more

comfortable to a British serviceperson than it might be to an Afghan or a Georgian soldier. As a consequence how different nations accessed the UK Role 3 Hospital varied.

The local intermediate healthcare facilities may, for example, account for the lower numbers of non-UK military presenting to the Role 3 Hospital with diarrhoeal disease as well as potentially enabling earlier discharge from hospital for non-UK military patients. This latter point might explain the shorter length of stay overall for non-UK military patients than UK military patients.

4.4.3 Peaks in admissions. Superficial comparison of the diagnoses with the most comparable set of historical data, to a different field hospital following the Iraq invasion[9], shows some similarities. These include high levels of infectious gastroenteritis and heat illness, and strikingly, a peak in admissions during the April/May rotations of UK military formations. This spike in admissions in May in Afghanistan has four likely explanations. Firstly more of the population at risk would be located close to the hospital prior to leaving Afghanistan to return to the UK, or to moving into their forward operational locations. Ordinarily, being located geographically distant from the hospital would mean that the majority of infectious gastroenteritis cases would be managed locally by primary care. Secondly, the population at risk was greatest during the Reinforcement-In-Place handover process providing the opportunity for the spread of contagious diseases to be facilitated by the dense living arrangements. Thirdly, the mobility of the military populations might expose them to pathogen strains to which they are immunologically naïve, with disease symptoms the result. Fourthly personnel newly arrived in Afghanistan and still un-

acclimatised might suffer from environmental disease due to the high temperature or acute asthma due to the dust-filled desert atmosphere.

4.4.4 Communication with patients. Admissions to the Role 3 Hospital came from a wide variety of countries and this may have presented potential communication problems. For the non-native English speaking military personnel a pool of interpreters was established. In my anecdotal experience communication between the medical staff and military patient was rarely a problem; however the civilian patients were a wide range of nationalities and often no official interpreter was available; reliable communication with this cohort could be challenging. This study did not investigate these potential issues associated with communications, but operating as part of a multi-national coalition with a large range of camp-followers providing support, has been the reality of all recent UK military operations. Adequate training on how to optimally work within this environment should be considered an essential part of the military physician's training.

4.4.5 Patient presentations. Whether a patient was admitted depended not only on the presenting complaint and clinical condition, but also on where they had arrived from and the time of their presentation to the hospital. Although arrival times were not recorded in this study, many patients from remote locations arrived late in the evening or during the night on helicopter transport (it was safer to fly at night due to the cooler temperatures and because the enemy were less able to engage aircraft they were unable to see). We might hypothesise that when the complaints in these patients were of a mild or ambulatory nature these patients may have been admitted to the hospital out of convenience, whereas had

they arrived during the day they would have been discharged to their unit. These admissions may have therefore biased the data in favour of mild complaints. It might also be true to say that the evacuating of a patient by helicopter, in a highly kinetic combat environment, might have required a higher threshold of illness in the patient for the local clinician to trigger an evacuation. As the data recorded neither the originating location, time of admission or method of transport to hospital, this can only be hypothesised.

4.4.6 Length of stay. It is reassuring that the mean length of stay was short for all groups. Ensuring a rapid turnover of patients meant the maximum number of beds and hospital staff were available in case of a major incident. The low daily admission rate, the good background health in most patients and the limited discharge options, enable us to hypothesise that it was possible to make easier and earlier decisions regarding discharge than in the busier UK National Health Service (NHS) hospital environment. The practice of at least twice daily ward rounds may have further facilitated rapid discharge.

The most striking figure relating to disposals is the fact that of the British military admissions the vast majority (72.2%) returned to their units and were able to continue in their operational roles. It was only just over a quarter of these patients who required evacuation back to the UK. When the infectious diseases admissions are examined in isolation this RTU rate increases to 90%. This is in particular contrast to the non-GIM admissions where the RTU rate was only 40.2%, in these cases due to the frequency and severity of the battle injuries and the prolonged recovery period following even relatively 'routine' surgery e.g. appendicectomy. What these data illustrate is that the majority of GIM complaints are

acutely debilitating but following appropriate diagnosis and treatment patients usually make a full recovery.

4.4.7 Non-cardiovascular diagnoses. Although this thesis was primarily to look at CVD in the Armed Forces it is impossible to provide care in a field hospital purely for patients with disease affecting a single system. This specific project was designed to provide a snapshot of all the conditions that a field hospital was likely to need to manage. Despite progress in hygiene and public health, infectious diseases and environmental illness were the most frequent diagnoses. The spectrum and variety of diagnoses was wide and varied however and as such requires a generalist to diagnose and manage these complaints.

4.4.8 Cardiovascular diagnoses. Diseases due to CVD were not common but were important for three main reasons. Firstly the provision of complex care for acutely unwell cardiac patients was not available. Secondly 2 of the 3 deaths were the result of cardiac disease. Thirdly the potential severity of cardiac disease was such that patients in whom significant coronary disease was identified were often flown back to the UK, at great expense, for further investigation and treatment.

Ischaemic heart disease was the most important diagnosis based on the subjective severity and frequency of symptoms. Ischaemic heart disease is highly associated with conditions such as the metabolic syndrome, familial dyslipidaemias and smoking, all of which can be managed aggressively with the aim to reduce the risk factors for CAD progression. However

inherited conditions such a cardiomyopathy and pre-excitation were also seen. Many of these inherited and congenital conditions could be identified prior to recruitment or deployment through focused screening efforts.

In addition to the patients with a relatively secure diagnosis of CVD a large number of patients presented with syncope, chest pain, and palpitations, all of which constituted the top six most frequently seen symptoms, with the implication that improved diagnostics might better characterise the underlying diagnoses in these individuals.

4.4.9 Implications for diagnostic testing, treatments and training. The range of diagnostic tests and therapies in the field hospital are limited when compared to the developed world hospitals; clinical decisions are by necessity often made based on the medical history and physical examination, tempered by clinical experience. Plans to extend and improve the 'diagnostic toolkit' available to a deployed military physician can be informed by these data and a side project investigating this was completed and published in conjunction with another military doctor[103]. Specific improvements implemented as a consequence of these data included the provision of training in basic echocardiography (to allow immediate assessment of ventricular filling and function) and basic thoracic ultrasound (to enable safe chest drain insertion) as well as improved microbiology diagnostics such as point-of-care PCR to rapidly identify pathogenic organisms.

For some conditions the 'gold standard' therapy was simply unavailable in the field hospital. An example of this was acute MI that resulted in the death of two of the three cases that died. Back in the UK an acute ST-elevation MI would be treated with primary percutaneous coronary intervention. This level of cardiology intervention was a logistical impossibility in Afghanistan, so the provision of thrombolysis, a therapy almost completely replaced in the UK, was reinforced by these data as a required capability. In situations such as acute MI, pre-deployment exercise to familiarise the team with the available protocols and equipment is important. Similarly specific clinical guidelines are essential to maintain operational efficiency. The outcome of this research was the development of training scenarios by the author that covered the conditions seen in the field hospital in preparation for other military operations.

In situations where a diagnosis cannot be made, or recovery from illness might not be complete, understanding the operational requirements of the patient following discharge enables an appropriate occupational risk assessment. Thus experience and knowledge of the occupational medicine implications of medical complaints remains a core competency differentiating the deployed military physician from their civilian counterpart.

The spectrum of symptoms and diagnoses in all three patient groups covered the complete range of general and internal medical disease. This finding reinforces the appropriateness of GIM trainees in the Armed Forces undertaking a broad training in addition to the acquisition of specialised skills. It reinforces the requirement for military physicians to

continue managing unselected acute medical patients, in order to maintain their clinical competencies, in their normal NHS-based posts.

The presenting complaints had a range similar, but distinctly different, to that seen by most UK-based physicians. A higher proportion of infectious diseases such as Q-fever, malaria and other undifferentiated fevers, as well as many cases of environmental illness, scorpion stings and snakebite were seen in Afghanistan. These findings inform the curriculum of the Defence Medical Services tropical medicine course, a compulsory level 2 course in infectious disease and tropical medicine that all physicians must remain accredited in and that has developed into an integral part of physician training. This course provides education in diagnosing and managing these conditions to clinicians throughout the UK Armed Forces.

The case mix also included a small number of children and psychiatric disease. Anecdotal reports of the management of paediatric cases highlighted a collaborative approach to the care of the child, particularly drawing on the knowledge and experience of the Emergency and intensive care departments. Psychiatric disease represented a significant minority of the case-load and in these patients close liaison with the deployed field mental health team was vital. An understanding of the clinical features and acute management of the most important psychiatric disorders should be included in the education of the GIM and Emergency Medicine cadres. These differences highlight that the deployed military physician requires additional training beyond that required of a purely civilian UK-based, physician.

4.4.10 Summary. In summary these data provide a record of the numbers of GIM admissions, including those due to cardiovascular disease, the UK military personnel admission rates, the spectrum of symptoms and diagnoses and the length of stay and disposal during a two year period in the UK Role 3 Hospital in Helmand, Afghanistan. These data inform future operational planning.

From the perspective of CVD it was seen that symptoms suggestive of CVD and firm diagnoses of CVD were observed. In particular syncope, chest pain and palpitations were all common presenting complaints. Important cardiovascular diagnoses included MI, atrial fibrillation, supra-ventricular tachycardias, cardiomyopathies and pericarditis.

Benefits identified from this study include the preparation of personnel, identifying training and material requirements prior to future military expeditions and in ensuring the resources in theatre most closely mirror clinical need.

4.5 Key findings.

1. This was a prospective cross-sectional record of all admissions under the general medical team to the Camp Bastion Role 3 Hospital commencing in April 2011 for a two year period.
2. In total 1,368 patients (20% of admissions; mean 1.87 patients / day) were admitted under the GIM team.
3. Overall there were 612 UK military admissions with a mean GIM admission rate of 23.3 per 10,000 UK military per month
4. Symptoms suggestive of cardiac disease and in particular chest pain, syncope, acute breathlessness and palpitations were common presentations.
5. The length of stay was relatively short for all three patient groups at less than 2 days.
6. There were 111 primary cardiac diagnoses (8.1% of admissions). The remaining diagnoses were a full range of non-cardiovascular diseases.
7. Ischaemic heart disease was diagnosed in 40 admissions (2.4% of diagnoses), 20 of which were acute MI (1.2% of diagnoses) and 15 were new cases of unstable angina (1.0% of diagnoses).
8. There were 11 admissions with newly diagnosed atrial fibrillation and 13 admissions with supraventricular tachycardias.
9. Uncommon cardiac diagnoses included hypertrophic and DCM and conduction disease.
10. Pericarditis was diagnosed in 11 patients.
11. No military died but three civilian GIM patients did die, two from acute MI.

12. This study resulted in changes to pre-deployment training and in the provision of cardiac echo on operations.

4.6 Acknowledgements

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Part 2: Optimising the screening for cardiac disease in potential British Army recruits

Chapter 5: A retrospective observational study of cardiac disease in potential recruits to the British Army in whom a murmur is detected during the Initial Recruit Medical

5.1 Background

When this study was designed there were >106,000 regular soldiers serving in the British Army. To maintain these numbers the army annually recruits about 10,000 soldiers although many more than this apply and are rejected on various grounds, but primarily for medical reasons detected during a two or three part screening process.

The cardiac screening of a potential recruit occurs in a two or three-step process (figure 5.1). This screening is performed in two or three stages and is a 'whole-person' screening system using the PULHHEEMS structure. The PULHHEEMS screening structure dates back to World War 2 when it was adopted into the British Armed Forces from the Canadian military[104]. Within this screening process the identification of cardiac or non-cardiac disease or disability, whether physical or psychological, that prevents service in the British Army, results in either a fail or a deferral of the decision to pass a candidate pending further investigation.

The first step of the screening process for a potential recruit is a questionnaire completed by the candidate's General Practitioner (GP). The completed questionnaire is reviewed by an

Army Occupational Medicine Physician. The questionnaire includes cardiac specific questions consistent with recognised international guidelines (Table1.4). If a finding suggestive of cardiac disease is identified then the candidate is deferred from further participation until assessed and cleared by a cardiologist. If a confirmed cardiac condition is disclosed then this will be evaluated based on an expert opinion and a decision made as to whether the candidate is suitable or unsuitable for service, or if further information is required. If no history suggestive of either cardiac or non-cardiac disease is identified then in this respect the candidate can proceed to the second stage.

Reasons for deferral therefore include:

1. A history of uninvestigated symptoms suggestive of cardiovascular disease;
2. A family history of premature death aged <50years in a first or second degree relative potentially due to a cardiovascular cause;
3. Confirmed CVD in a first or second degree relative that may be inherited;
4. The confirmed diagnosis of a condition, cardiac or non-cardiac that is a bar to service. These are listed in the military Joint Service Publication 346.

The second stage is the physical attendance of the candidate for the Initial Recruit Medical (IRM). In the majority of cases this occurs in one of 5 national selection centres, though a minority occur outside this framework. The IRM is performed by a doctor, but not a cardiologist; most commonly this is a GP with additional occupational medicine training. The IRM consists of a history and physical examination as well as assessments of spirometry,

visual acuity, colour perception, hearing and a urine dipstick. Similar to at the questionnaire stage, abnormal findings result in a fail or the deferral of a decision to pass or fail a candidate, pending investigations arranged through the candidate's GP. An exception to this is the finding of an isolated murmur on auscultation. All potential recruits to the British Army with an isolated murmur on auscultation and no other suspicion of cardiac disease, were referred for investigation to a private company (Cardiac Report Ltd., London) contracted by the MOD for stage three of the screening process.

All individuals referred to Cardiac Report underwent a consultation with an accredited Consultant Cardiologist. This evaluation included a stereotyped history, examination, resting 12 lead ECG and transthoracic echo (Figure 1). This was the only cardiac specific step in the screening system. This process resulted in three possible outcomes.

1. Recommendation to pass. If no cardiac abnormality was identified or suspected then a recommendation to the Army was made to pass the candidate.

2. Deferral. A proportion were referred back to their GP for further investigation to exclude or confirm suspected disease. The decision to pass or fail a candidate was deferred until this process was satisfactorily concluded. This decision would be based on further diagnostic tests or specialised opinion elsewhere to Cardiac Report. The ultimate decision on whether to pass or fail a candidate was made by the Army's Occupational Health physicians and this process did not involve the Cardiac Report cardiologists. The outcomes in these cases are not known.

3. Recommendation to fail. Certain cardiac diseases are listed as a bar to military service. In candidates in whom one of these diseases was identified then the outcome of the screening was a recommendation to the Army to fail the candidate on medical grounds. For these candidates a further plan was formulated to advise the candidate and their GP on how the condition should be managed going forwards.

5.2 Methods

This two or three step screening process was in place from 2004 to 2013 during which in excess of 11,000 individuals were screened by Cardiac Report with an age range of 16 – 32 years. The population of potential recruits screened by Cardiac Report Ltd are the subject of the study. None of these candidates had admitted to uninvestigated symptoms or a significant family history suggestive of cardiac disease at their IRM and they had all undergone a normal physical examination with the exception of a murmur detected at auscultation. Additionally no other non-cardiac disease had been identified at the IRM. All these candidates were seen by a Consultant Cardiologist working for Cardiac Report Ltd and underwent a history, physical examination, resting 12 lead ECG and transthoracic echo.

The history included questions to elicit symptoms suggestive of cardiac disease (chest pain, palpitations, syncope, breathlessness, as in table 1.4), a previous history of cardiac disease, whether treated or untreated and any family history suggestive of an inherited cardiac condition. The cardiovascular examination included, as a minimum, the measurement of

the heart rate and blood pressure and auscultation of the heart sounds. In addition other clinical signs, that might indicate a cardiac condition, were elicited if indicated to the examining cardiologist. All individuals referred to Cardiac Report for further assessment had a murmur detected at the physical examination at their IRM and a note was made as to whether a murmur was detected again at the Cardiac Report assessment.

All candidates referred to Cardiac Report had a resting 12 lead ECG recorded. The ECGs were performed using standard 12 lead ECG positions with a paper speed of 25 mm/s and amplification of 0.1 mV/mm. The interpretation of the ECG utilised the expert knowledge of the cardiologists examining the candidates, combined with contemporary ECG interpretation guidelines (as described in the introduction). In line with the guidelines, Bazett's correction was used by the examining cardiologist to correct the measured QT for heart rate (QTc). Leads II, V3 and V5 were the preferred leads for QT measurement. A lower QTc limit of 440ms in males and 460ms in females was originally used. In this analysis the 2018 guidelines are also utilised with the cut-offs at 470ms in males and 480ms in females. A QTc cut-off of 500ms makes a diagnosis of LQTS 'likely' and any candidates in this range are referred to as 'confirmed' cases, although they would still need formal confirmation.

All candidates referred to Cardiac Report had a transthoracic echo performed. All the echo departments in which these Cardiac Report screenings were undertaken were BSE accredited; the echos were performed using industry standard devices by British Society of

Echocardiography (BSE) accredited operators and they were reported according to the standard BSE protocol[105].

Due to the volume of investigations the ECGs and echo reports were not examined if no abnormality was highlighted in the cardiologist's letter. When an abnormality was identified however then the individuals ECG, as a pdf image and standardised echo report were individually examined. Discrepancies in the findings between the interpretation of the ECG by the examining cardiologist and the author were to be reviewed by a third party expert (Prof Sanjay Sharma or Prof Elijah Behr).

5.2.1 Hypotheses. By characterising the findings of this cardiac screening programme the minimum prevalence of inherited cardiac disease in this population can be estimated. In those whom an abnormality is discovered the specific investigation findings can be examined for the severity and presentation of disease. The following hypotheses are to be tested:

1. Asymptomatic congenital diseases, such as ion channelopathies, accessory pathways, cardiomyopathies and normally functioning bicuspid (non-tricuspid) aortic valves will be discovered as incidental findings when candidates with murmurs are investigated with a resting ECG and echo. This would imply that the current screening system results in the recruitment of many individuals with undetected occult CVD when no murmur is detected at the IRM.

2. Most murmurs detected at the initial recruit medical are innocent and do not represent disease (the positive predictive value of a murmur is low).

3. The non-pathological murmurs detected by non-cardiologists at the original screening might be undetectable on another day, under different physiological conditions, and when the auscultation is performed by a trained cardiologist.

4. A murmur heard by two different clinicians on two different days is more likely to represent disease than when a murmur was heard only at the IRM.

In other respects no further hypotheses relating to the screening will be tested, but the findings will be described in detail and may be hypothesis generating.

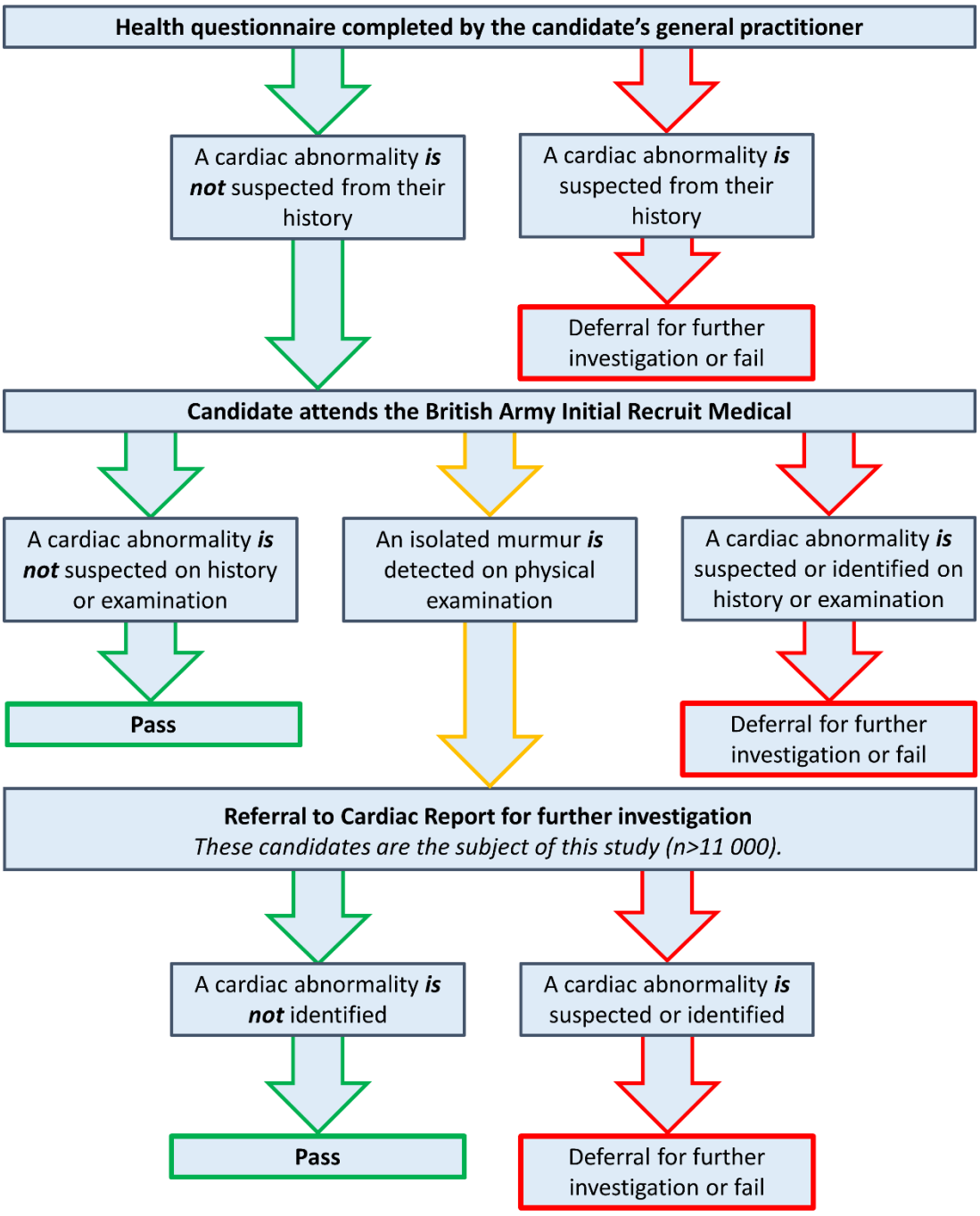

Figure 5.1: Diagram illustrating the process involved in the cardiac screening of potential recruits to the British Army.

This study group had already undergone a two-step screening process and no information on those candidates that had not been referred to Cardiac Report was available. This limits the possible utility of these data. The outcome measures of this study are:

1. To describe the demographics by age and gender.

2. To calculate the positive predictive value of the current screening process (for a normal questionnaire and clinical examination aside from the auscultation of a murmur).

3. To identify incidental disease that would not be diagnosed in this cohort without an additional ECG or echo; specifically diseases that would not account for a murmur, such as primary arrhythmic disorders or many cardiomyopathies.

4. To evaluate the minimum burden of occult CVD in this population.

For the purposes of this research study and the study in the following chapter the ESC guidelines on sport participation was adapted to the official (and restricted) policy outlined in JSP 950. These restrictions were discussed with all the military Cardiologists and agreed prior to the start of these studies and are summarised in appendix A. In general terms the military occupational guidelines for recruits are different to the ESC guidelines on sports

participation in the timeline they look at for participation; both guidelines presume that individuals will be followed clinically at appropriate intervals, but the ESC guidance evaluates the risk over a far shorter term than does the military. This is because the military recruit individuals for a full career that is 22 years for Other Ranks and to age 55 (or older in some cases) in Officers. An example pathology is that of a candidate with a known, normally functioning, BAV, who would not be recruited. This is because up to a third of BAV[106] will develop significant regurgitation, stenosis or aortic dilatation. This degeneration occurs in a bimodal distribution with a peak between 30-40 and another at age 50+ years. It is not possible to accurately predict which individuals with a BAV will develop significant and limiting disease during their military service. The cost of training these individuals is considerable, even though the risk of severe illness or death due to endocarditis, heart failure or aortic dissection is low and for the combination of these reasons enlistment is declined.

The scientific definition of positive predictive value is the ratio of true positives to combined true and false positives. The following definitions refer specifically to the evaluation by Cardiac Report, for either the ECG or echo:

1. A 'positive result' is an abnormality found that is consistent with any of the CV diseases outlined in JSP 950 and outlined in Appendix A . Positive findings will be further sub-classified by the investigation type (ECG and/or echo) and by specific abnormality.

2. A ‘negative result’ for either the ECG or echo is the absence of an abnormality consistent with any of the CV diseases outlined in JSP 950 and outlined in Appendix A .

The ‘gold standard’ by which the decision to classify the screening results as either a negative or positive is investigation with ECG, echo or other clinical investigations as indicated, including, but not exclusive to, additional ECG or functional testing (i.e. exercise stress testing, Holter monitoring, electrophysiological studies) and imaging modalities (cardiac magnetic resonance, computed tomography or other echocardiographic scanning). Unfortunately these subsequent investigations were not available for this study that included only an ECG and echo. I have therefore grouped the positive findings as ‘suspected’ or ‘confirmed’ categories depending of the firmness of the diagnosis and this constitutes a pragmatic ‘gold standard’, with acknowledgement that it might not correctly identify all disease or normality.

This group was already filtered by having had a murmur identified and therefore might not be representative of the potential recruit population. Therefore this study was not designed to characterise the ECGs of this cohort and detailed analysis of the ECGs was not undertaken. The study was also not designed to look at the normal range for specific echo parameters in potential recruits.

5.2.2 Statistical analysis. Categorical variables will be expressed as percentages. The Chi-squared test or Fisher's exact test will be used to compare categorical variables. Statistical significance will be defined as a two-sided P-value of <0.05 (95%CI of the mean and upper and lower 5% and 95% of the population). Given the nature of these data the only continuous variables are the ages of potential recruits.

5.2.3 Ethical considerations. As this is a retrospective review no consent from individuals was sought. Approval for this project was still sought and approved from the Ministry of Defence Research Ethics Committee with protocol 311gen12. All identifying information was restricted to the secure Cardiac Report server or secured using Trucrypt encryption software (www.trucrypt.org). Data was pseudo-anonymised by a unique candidate indicator once collected.

5.3 Results

The first Cardiac Report assessment was on 3 July 2006 and the final one was on 27 February 2014. In total the number of recruits aged 16-32 screened at the IRM during this period was 122,181, of which 110,803 (90.7%) were males. The median age was 19 years old and there was a peak at age 17, reflecting school-leaving age, with a gradual tapering downwards to the older end of the selection age range (figure 5.2). There were a number of 16 year olds screened; these were individuals applying to the Army Foundation College in Harrogate.

In total 11,070 candidates, constituting 9.1% of the total IRM population were assessed by Cardiac Report; of these 9,877 (89.2%) were male. Females were more likely to have a murmur detected at IRM than males. (P <0.0001). Candidates aged 16 were more likely to have a murmur detected at the IRM than the older groups (P <0.0001).

The majority of the referrals to Cardiac Report were from the 3 main recruit training centres in Pirbright, Glencorse and Lichfield and these accounted for 96.6% of all referrals with the smaller Belfast and Westbury selection centres and *ad hoc* selection for reservists contributing the remainder (table 5.1). These referrals were seen in 19 different hospitals used by Cardiac Report across the UK (table 2). Most of these centres saw a large volume of referrals with only 3 seeing fewer than 100 candidates.

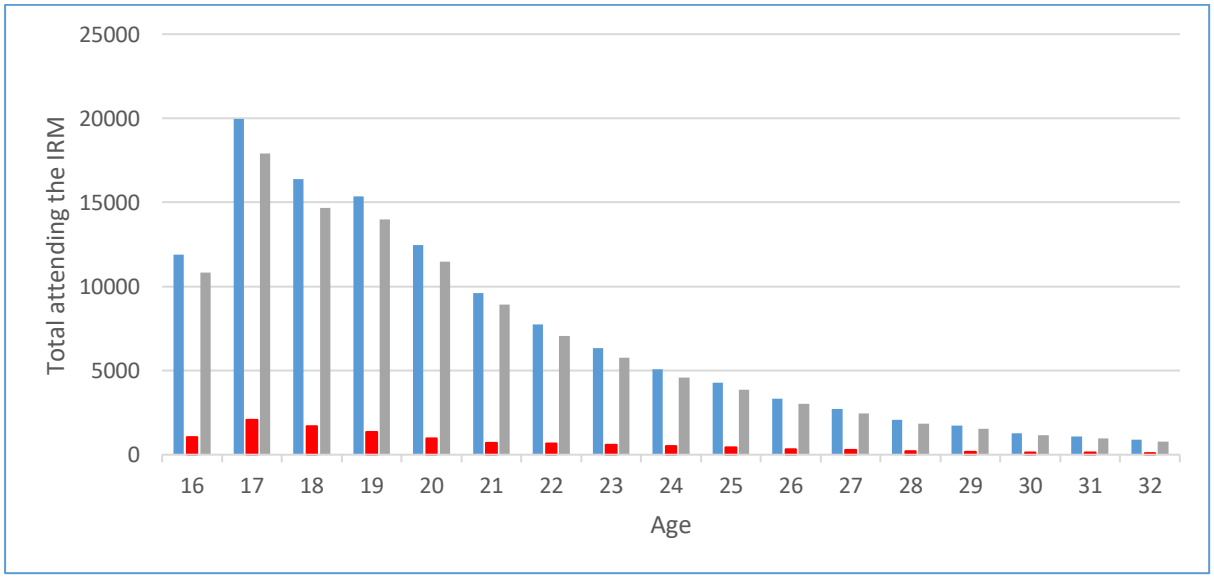

Figure 5.2: Age distribution of the potential recruits attending the Initial Recruit Medical (IRM).

Blue=total; Red = Females; Grey = Males.

5.3.1 ECG correlation. There was almost complete agreement in the ECG findings between the author and the Cardiac Report clinicians for the ECGs described as abnormal. The only exceptions to this were in the measurement of the QT interval. In 3 cases of a borderline long QTc, that resulted in deferral, the author and a second investigator both felt the QTc had been over-measured and was in fact normal. No cases were seen where the QTc appeared under-measured such that the candidate should have been deferred.

5.3.2 Summary of Cardiac Report findings

Of the 11,070 candidates assessed by Cardiac Report 469 (4.2%) candidates failed or were deferred for further investigations (table 5.3). A total of 9877 (89.2%) candidates were male of whom 9452 (95.7%) were passed. A total of 1193 (10.8%) candidates were female with 1149 passed (96.3%). There was no difference in the pass rate between genders in the candidates screened by Cardiac Report (p=0.248) as a proportion of all the candidates that attended the IRM (p=0.9588).

5.3.2 Summary of Cardiac Report findings

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Army Selection Centre	Total	%
ADSC Belfast	84	0.76
ADSC Glencorse	2322	20.98
ADSC Lichfield	3123	28.21
ADSC Pirbright	5245	47.38
AOSB Westbury	178	1.61
Other (ARTD, OTC and TA)	118	1.07
Total	**11070**	

Table 5.1: Numbers and percentages of the candidates evaluated by Cardiac Report and their referring selection centres. *ADSC = Army Development and Selection Centre; AOSB = Army Officer Selection Board; ARTD = Army Recruit Training and Development, the Army's main recruit occupation medicine department; OTC = Officer Training Corps; TA = Territorial Army (known now as the Army Reserve).*

A murmur was heard on the day in 2719 (24.6%) candidates of whom 2494 (91.7%) were passed. A murmur was not heard in 8351 (75.4%) candidates of whom 8107 (97.1%) were passed. A candidate in whom a murmur was heard by the Cardiac Report cardiologist was more likely to fail than a candidate in whom no murmur was heard ($p < 0.0001$). There was no difference between the genders in the detection rate of a murmur by a Cardiac Report cardiologist ($p=0.81$).

Screening Centre	Total	%
Belfast	51	0.5
Birmingham	358	3.2
Birmingham City	883	8.0
Cardiff	769	6.9
Exeter	365	3.3
Glasgow	677	6.1
Halifax	41	0.4
Leicester	711	6.4
London East (Princess Alexandra Hospital, Harlow)	768	6.9
London North West (Northwick Park Hospital, Harrow)	133	1.2
London South (St Helier Hospital, Carshalton)	442	4.0
London West (Charing Cross Hospital, Hammersmith)	2077	18.8
Manchester	1869	16.9
Newcastle	588	5.3
Norwich	243	2.2
Oxford	2	0.0
Plymouth	261	2.4
Portsmouth	287	2.6
Southampton	545	4.9
Total	**11070**	

Table 5.2: The Cardiac Report hospitals performing the screenings and the numbers of candidates evaluated at each.

The ECG was assessed as normal in 10,840 (97.9%) candidates, of whom 10,537 (97.2%) were passed. The ECG was abnormal in 230 candidates of whom 64 (27.8%) were passed. A candidate with a normal ECG was significantly more likely to be passed than a candidate in whom the ECG was abnormal ($p<0.0001$). A total of 209 (2.1%) male candidates and 21 females (1.8%) had an ECG abnormality with no difference in the proportions by gender ($p=0.48$).

5.3.3 Cardiac symptoms, history and family history

No candidates should have passed the initial vetting in the selection centre with any positive findings in their cardiac or family history; inevitably though a few either developed symptoms in the period between the IRM and their cardiology appointment and others only decided to disclose previously presenting symptoms once a murmur had been identified. In total 59 candidates (0.5%) declared one or more cardiac symptom.

5.3.3.1 Chest pain

A total of 10 candidates admitted to chest pain; the cardiologists examining decided that they were all non-cardiac in nature. One of these, a 16 year old male, was found to have a normally functioning BAV at echo and was failed; the remaining 9 were passed with no abnormalities found.

Gender	All candidates					
	Number		Pass	%	Fail	%
Males	9877	89.2	9452	95.7	425	4.3
Females	1193	10.8	1149	96.3	44	3.7
All	11070		10601	95.8	469	4.2

	No murmur and normal ECG						Murmur and normal ECG					
Gender	Number	%	Pass	%	Fail	%	Number	%	Pass	%	Fail	%
Males	7349	74.4	7221	98.3	128	1.7	2319	23.5	2174	93.7	145	6.3
Females	860	72.1	847	98.5	13	1.5	312	26.2	295	94.6	17	5.4
All	8209	74.2	8068	98.3	141	1.7	2631	23.8	2469	93.8	162	6.2

Gender	No murmur but ECG abnormal						Murmur and ECG abnormality					
	Number	%	Pass	%	Fail	%	Number	%	Pass	%	Fail	%
Males	127	1.3	37	29.1	90	70.9	82	0.8	20	24.4	62	75.6
Females	15	1.3	2	13.3	13	86.7	6	0.5	5	83.3	1	16.7
All	142	1.3	39	27.5	103	72.5	88	0.8	25	28.4	63	71.6

Table 5.3: *Summary of the numbers passed or failed by gender; whether there was a murmur heard on the day by the examining Cardiac Report cardiologist; whether the ECG was considered normal.*

5.3.3.2 Palpitations

Palpitation symptoms were described by 21 candidates; of these 15 were passed as the examining clinician felt them to be of no consequence and their physical examination and investigations were normal.

A 17 year old female gave an excellent history for a paroxysmal supraventricular tachycardia and despite a normal ECG and echo was referred for further investigation.

A 28 year old male with paroxysmal palpitations was found to have a ventricular septal defect and deferred. His ECG was entirely normal aside from right axis deviation. His echo demonstrated a dilated right ventricle (RVIDD 29x40 mm), borderline right atrial dilatation and a perimembranous ventricular septal defect with a small left to right shunt Qp:Qs 1.5. The peak VSD peak gradient was 82 mmHg and PASP 27-32 mmHg. There was also mild tricuspid regurgitation (TR).

A 22 year old male with palpitations was failed as he was found to have a preexcited ECG. His echo was normal. He also complained of a reduced exercise capacity.

A 19 year old male was deferred as he gave a history of palpitations and was found to have a run of a long RP narrow complex tachycardia during his echo. His ECG and echo were otherwise normal.

A 30 year old male with palpitations was found to have frequent monomorphic ectopy suggestive of a ventricular outflow tract focus. His echo was normal.

A 20 year old male with palpitations had developed several episodes of symptomatic atrial fibrillation in the context of alcohol intoxication and high caffeine content energy drinks. This had become persistent and required cardioversion. It was unclear how had been allowed to attend the IRM with this history and he was failed.

5.3.3.3 Presyncope

Presyncopal symptoms were described by 10 candidates; 9 of these were passed with no abnormalities found. One 18 year old male was deferred for further investigations on account of TWI in leads III and aVF. His echo was unremarkable.

5.3.3.4 Syncope

Syncopal symptoms were described by 19 candidates; 16 of these were considered by the examining clinicians to be of no consequence and in combination with normal ECG and echo were passed.

Of the remainder one of these was a 20 year old male with previous syncope. His ECGs showing persistent ventricular bigeminy with the monomorphic ectopic morphology suggestive of a single outflow tract focus. His echo showed mild left ventricular dilatation and systolic impairment. He was deferred for further investigation.

The second was a 17 year old female with runs of an atrial tachycardia on her ECGs and mild left ventricular dilatation on echo.

The third candidate with a syncopal history was an 18 year old female whose ECG was relatively normal though the QRS amplitude was generally low. Her echo however showed a dilated right ventricle with an abnormal apical regional wall motion abnormality. She was deferred for further investigations including a cardiac magnetic resonance scan (CMR).

5.3.3.5 Exertional dyspnoea

Exertional dypnoa was described by 5 candidates. One of these was the 18 year old male who was described above [in the presyncope section] that also had presyncope, reduced exercise tolerance and inferior TWIs on his ECG. He was deferred for further investigation. The remaining 4 candidates passed with normal investigations.

5.3.3.6 Reduced exercise tolerance

Reduced exercise tolerance was described by 5 candidates; 3 of which also complained of other symptoms. Two were otherwise normal but one was the 22 year old male with pre-excitation (described above).

The 5th candidate was failed due to moderate to severe pulmonary regurgitation (PR) and a borderline dilated right ventricle.

5.3.4 Cardiac history

A total of 66 candidates declared a previous cardiac history (0.59%); these are summarised in table 5.4.

A history of VHD was provided by 4 candidates including 1 with a BAV, which is usually a bar on joining the British Army. Unsurprisingly the candidate with a newly admitted history of a BAV had this diagnosis confirmed and was failed. Two candidates had trivial MR and a further candidate, previously diagnosed with mild PS as an infant, was found to have a normal pulmonary valve as a 17 year old; all three were passed.

A history of structural congenital heart disease was given in 44 candidates (0.39%) with the majority of these conditions consisting of atrial or VSD, most of which had not been repaired; though 14 of these had undergone childhood surgery. A total of 37 were passed as fit to join the Army and 5 were provisionally passed if further information regarding their surgery +/- a review by a congenital heart disease specialist, identified no additional contraindicated findings.

Table 5.4: Summary of cardiac conditions declared by the candidates attending their Cardiac Report assessment*. MVP = Mitral valve prolapse; PDA = Patent ductus arteriosus; ASD = Atrial septal defect; VSD = Ventricular septal defect; SVT = Supra-ventricular defect.*

Cardiac history	**Total**
No cardiac history	11,004 (99.4%)
History	66 (0.6%)
Valvular heart disease	
Bicuspid aortic valve	1
Mild MVP diagnosed previously	2
Mild pulmonary stenosis as a child	1
Other congenital heart disease	
PDA - repaired	4
Repair as an infant of anomalous pulmonary venous drainage	1
Septal defect - ASD previously repaired	3
Septal defect - VSD previously repaired	3
Septal defect - location not specified, previously repaired	1
Septal defect - location not specified, not repaired	22
Septal defect - VSD not repaired	8
Cardiac surgery as a child - unknown reason	2
Arrhythmic disease	
Possible SVT circuit - not confirmed or ablated	1
SVT - ablated	2
Infective disease	
Myocarditis - resolved	1
Pericarditis - resolved	2

Other cardiovascular disease	
Kawasaki disease	1
Borderline hypertension	10
Hypertension	1
Total	**11070**

A total of 30 candidates declared a previously diagnosed septal defect that had not required surgery. Of these were 25 were passed, despite the examination identifying 5 candidates with residual VSDs and 2 with ASDs, all of which were small and considered by the examining clinician to be insignificant. Two of these candidates were found to have VSDs that the examining cardiologist felt should undergo further evaluation by a congenital heart disease specialist. Two failed as they were found to have BAV and another was found to be hypertensive and required further investigation.

All 7 candidates with previous surgical repair of a septal defect were passed. There were small residual septal defects in two candidates (one with a previous ASD repair and one with a previous VSD repair) but the cardiologists examining felt these were trivial and of no major occupational consequence.

Four candidates had undergone surgery for a patent ductus arteriosus (PDA). All four had normal screenings aside from this history and were passed. A 16 year old male candidate who declared surgery as an infant for anomalous pulmonary venous drainage was found to have non-specific depolarisation abnormalities inferiorly, but the echo was within normal

limits. As a precaution he was referred for further investigations. Two further candidates who declared an unknown childhood cardiac surgery were provisionally passed pending further information regarding their operations being evaluated. One of these was found to have a normal examination, ECG and echo and the other a small ASD but normal examination, ECG and echo otherwise.

Three individuals declared previous ablations for SVT. All three were asymptomatic, had normal findings on ECG and echo and were passed.

Three candidates admitted to previous myocarditis or pericarditis. One 16 year old male with a history of pericarditis was found to have a QTc of 488ms and was referred for investigations to exclude familial LQTS. Aside from this there were no other ECG or echo abnormalities seen in these candidates. The other two candidates were passed.

Eleven candidates (0.1%) admitted to a history of hypertension or borderline hypertension. Of these 3 were found to be significantly hypertensive on the day, but with no ECG or echo abnormalities and another was found to have concentric LVH on echo, suggestive of either poorly controlled hypertension or HCM. All were referred for further investigation prior to being passed.

A single case of childhood Kawasaki disease was declared and although this candidate had a normal examination, ECG and echo he was deferred pending further investigation of his coronary arteries.

No candidates admitted to a history of IHD, diabetes or dyslipidaemia.

5.3.5 Family history

A total of 165 candidates (1.5%) declared a family history of specific or non-specific cardiac disease (table 5.5). Of these 26 candidates (15.8%) had an abnormal screening medical.

Of the 9 candidates with a hypertensive parent 2 were also found to have hypertension requiring further investigation. One was a 26 year old male with a normal ECG, but mild concentric LVH (maximum wall thickness of 13mm in the septum). The other was a 28 year old black female who on examination had a BP of 168/101 over serial readings, her ECG showed 1mm deep TWI in V1-2 and moderate TR with mild RV dilatation.

One candidate declared a family history of dyslipidaemia. Screening for dyslipidaemia was not part of the protocol, but rather a condition to be cleared in the community prior to attending the IRM. It was not known whether this had been undertaken prior to the IRM.

A family history of IHD was identified in only 63 individuals and although 10 of these had abnormal investigations most were mild, none were associated with IHD and only 2 failed the screening medical (one due to MVP and the other hypertension).

A family history of cardiomyopathy was described in 12 candidates. Two of these failed pending further investigation for ARVC and DCM. One was a 21 year old male with a cousin diagnosed with ARVC. His ECG demonstrated subtle repolarisation abnormalities laterally and his echo was normal. As a precaution further investigations were advised by the examining clinician including a Holter, exercise test and CMR as well as correlation with the cousin's history and genetic testing if appropriate. The second was a 20 year old male with a two generation history of 'an enlarged heart'. His ECG was normal and his echo had a hypertrabeculated appearance. The examining clinician advised further investigation and correlation with the candidate's relatives' medical history.

A family history of BAV was described in two candidates. One had a normal screening, but the other was found to have a BAV with no significant stenosis, regurgitation or aortopathy; this candidate was failed.

Marfan's Syndrome was described in the family history of 4 candidates, none of whom had any features of this condition. A single candidate gave a history of a second degree relative having a thoracic aortic aneurysm. Their screening was normal and they were passed.

Family history	Total	%
Hypertension - parent(s)	9	0.08
Dyslipidaemia - first degree relative	1	0.01
IHD <55 in 2nd degree relative(s)	27	0.24
IHD <55 in a parent(s)	36	0.33
Cardiomyopathy - parent(s)	7	0.06
Cardiomyopathy - second degree relative	5	0.05
Bicuspid aortic valve - parent(s)	1	0.01
Bicuspid aortic valve - second degree relative	1	0.01
Marfan syndrome first degree relative	4	0.04
Thoracic aneurysm - second degree relative	1	0.01
Vasculitis - first degree relative	1	0.01
Epilepsy - first degree relative	1	0.01
SCD in a sibling(s) or parent(s) <50years	5	0.05
SCD in second degree relative(s) <50 years	10	0.09
FH of other unspecified heart disease	56	0.51
Total	**165**	

Table 5.5: *Summary of the declarations of a potentially significant family history identified at the Cardiac Report assessment. IHD = Ischaemic heart disease; SCD = Sudden Cardiac death; FH = Family history.*

Sudden cardiac death in either a first or second degree relative aged <50 years was described by 15 candidates. Of these 3 (20%) were failed. One, a 21 year old male, was found on ECG to have a RSR QRS pattern with a slightly 'coved' ST-segment and TWI. This was felt suggestive of a Brugada type 2 pattern and he was failed pending the results of additional investigations, including an ajmaline test. The outcome of this is not known. A second was a 22 year old black male with a BP measured as 169/101 in the context of high levels of anxiety. His ECG showed widespread repolarisation abnormalities suggestive of a

myopathic process. His echo was normal. The third candidate to fail was a 16 year old female whose ECG showed a borderline prolonged QTc and normal echo.

The two candidates with a family history of vasculitis and epilepsy respectively had normal screenings and both were passed.

A further 56 candidates described a non-specific CVD in one of their first or second degree relatives. Four candidates were failed. These were a 21 year old male with a functionally normal BAV; a 19 year old female with normal ECG and a left to right shunt through an ASD with mild RV dilatation; a 23 year old male with a small ASD but otherwise normal ECG and echo; and a 17 year old male with LVH by voltage, early repolarisation and inferior fractionation on his ECG, and echo features of left ventricular non-compaction affecting the anterior, lateral, inferoposterior and inferoseptal walls. An inherited element to these could not be confirmed.

5.3.6 Auscultation findings by Cardiac Report cardiologists

It was a pre-requisite that all the candidates referred to Cardiac Report needed to have had a murmur detected at their IRM. Despite this 8351 (75.4%) were not found to have a murmur at their Cardiac Report appointment (table 5.6). Of those found to have a murmur the overwhelming majority were systolic with only 22 diastolic murmurs documented.

Auscultation findings	Number	%
Normal - no murmur	8351	75.44
Innocent systolic murmur	161	1.45
ESM - AV	82	0.74
ESM - AV and PV	16	0.14
ESM - PV	64	0.58
ESM - valve not-specific	508	4.59
PSM	1	0.01
PSM - MV	11	0.10
PSM - TV	21	0.19
PSM - valve not specified	34	0.31
LSM – suspected MVP	3	0.03
Systolic murmur – suspected VSD	2	0.02
Systolic murmur - non-specific	1794	16.21
Both systolic and diastolic murmur	10	0.09
Diastolic murmur - no valve specified	4	0.04
Diastolic murmur -AR	6	0.05
Diastolic murmur -PR	2	0.02
Total	**11070**	

Table 5.6: Summary of the descriptions of the murmurs heard by the examining Cardiac Report cardiologist and localised to specific likely culprit valves. *ESM = Ejection systolic murmur; AV = aortic valve; PV = Pulmonary valve; PSM + Pan-systolic murmur; MV = Mitral valve; TV = Tricuspid valve; LSM = Late-systolic murmur; VSD = Ventricular septal defect; AR = Aortic regurgitation; PR = Pulmonary regurgitation.*

There were 2707 systolic murmurs described. Of these 161 were considered 'innocent' by the examining clinician; 670 murmurs were thought due to ventricular outflow tract

turbulence; 70 were considered to be due to a tricuspid or mitral origin and 2 were thought associated with a VSD.

Innocent murmurs should, by definition, not be associated with pathological disease, but could conceivably be confused with a murmur caused by disease. Of the candidates with an innocent murmur, 152 (94.4%) had no obvious cause for a systolic murmur on echo (table 5.7). Of the 9 candidates with a discernible cause for a murmur only 5 were not passed; 4 candidates had BAV and a further candidate had a possible non-compaction cardiomyopathy.

A murmur not explicitly described as innocent was heard in 2546 candidates. Of these 2251 (88.4%) candidates, including 22 who were hypertensive on the day, had no pathological or other clear structural explanation for their murmur (table 5.8). Often hyper-dynamic and turbulent flow, perhaps associated with anxiety regarding the medical itself, was seen on colour Doppler at echo, but this was noted as a comment by a few echocardiographers only and the overall frequency cannot be quantified. In total 209 (8.2%) candidates were failed or went on to have further investigations and 2337 (91.8%) were passed. An 'abnormal' finding was identified in 350 (13.7%) cases. A structural abnormality was seen in 295 candidates plus an incidental finding of a PFO in 16 candidates. Hypertension was the only abnormal finding in 22 candidates and 17 had an incidental finding on ECG either demonstrating an arrhythmia or suggestive of an underlying arrhythmic substrate, such as a suspiciously long QT interval, an ECG suggestive of the Brugada Syndrome, pre-excitation or frequent atrial or ventricular ectopics.

Finding possibly consistent with a systolic murmur	Total	%
BAV with mild stenosis	1	0.62
BAV without stenosis	3	1.86
Non-compaction suspected and mild TR and MR	1	0.62
Mild MR	2	1.24
Mild / Moderate TR	1	0.62
Minor sub-aortic stenosis	1	0.62
Small Gradient in LVOT	1	0.62
Findings inconsistent with a systolic murmur		
No abnormality seen	140	86.96
ASD	1	0.62
Mild AR	4	2.48
Brugada Syndrome suspected	2	1.24
HTN	1	0.62
PFO	1	0.62
Other arrhythmia	2	1.24
Grand Total	**161**	

Table 5.7: Summary of the findings for those candidates described by the Cardiac Report cardiologist as having an innocent systolic murmur on auscultation. *The candidates highlighted in red were not passed on the day. BAV = Bicuspid aortic valve; TR = Tricuspid regurgitation; MR = Mitral regurgitation; LVOT = Left ventricular outflow tract; ASD = Atrial septal defect; AR =Aortic regurgitation; HTN = Systemic hypertension; PFO = Patent foramen ovale.*

Of 22 diastolic murmurs 20 correlated with a significant echocardiographic finding (table 5.9). The positive predictive value of a diastolic murmur was 90.1%. There were 9 BAV with 6 demonstrating moderate regurgitation and 3 severe regurgitation. Several had associated aortopathies, including one aortic coarctation. A further 5 candidates had regurgitation through a tricuspid aortic valve, one of which was severe enough to precipitate an

Condition†	Number	%
Normal	2196	86.25
HTN	22	0.86
Incidental ECG only abnormality		
Brugada suspected	1	0.04
LQTS suspected	2	0.08
Frequent atrial or ventricular ectopy	10	0.39
Pre-excitation	4	0.16
Structural abnormalities		
Aortic dilatation	2	0.08
ASD	27	1.06
AV disease	31	1.22
BAV	60	2.36
Cardiomyopathy (confirmed or suspected)	43	1.69
Coarctation of the aorta	8	0.31
Mitral valve prolapse	8	0.31
Mitral valve disease - other	39	1.53
PFO (incidental)	16	0.63
Pulmonary valve disease	26	1.02
Tricuspid valve disease	19	0.75
VSD	9	0.35
Other structural disease	23	0.90
Total	**2546**	

Table 5.8. Summary of the screening findings in the candidates in whom a non-innocent systolic murmur was auscultated on physical examination. *The conditions highlighted in red are conditions associated with an incidental ECG finding, rather than a structural disease that might account for a murmur. A Patent foramen ovale (PFO) is not strictly an abnormality, rather a normal variant, but is included here for completeness. † note some candidates had 2 conditions. LQTS = Long QT syndrome; HTN = Systemic hypertension; ASD = Atrial septal defect; AV = Aortic valve; BAV = Bicuspid aortic valve; VSD = Ventricular septal defect.*

No	Explanation for the diastolic murmur	Outcome
1	BAV with moderate regurgitation, no stenosis, mild LV dilatation, normal root	Fail
2	BAV with moderate aortic regurgitation, mild stenosis, normal LV and root	Fail
3	BAV with moderate aortic regurgitation, no stenosis, normal LV, mildly dilated root, coarctation noted	Fail
4	BAV with moderate regurgitation, no stenosis, mildly dilated LV, normal root	Fail
5	BAV with moderate regurgitation, no stenosis, normal LV, normal root	Fail
6	BAV, moderate regurgitation, mild stenosis, normal LV, normal root	Fail
7	BAV, severe aortic regurgitation, no stenosis, LV dilatation and dysfunction, normal root	Fail
8	BAV, severe regurgitation, no stenosis, dilated LV, mild aortopathy	Fail
9	BAV, severe regurgitation, no stenosis, mild LV dilatation, severely dilated aortic root	Fail
10	Tricuspid aortic valve with mild regurgitation	Pass
11	Tricuspid aortic valve with mild regurgitation	Pass
12	Tricuspid aortic valve with moderate regurgitation and stenosis	Fail
13	Tricuspid aortic valve with moderate regurgitation, dilated LV with mildly impaired function Mild mitral and tricuspid regurgitation	Fail
14	Tricuspid aortic valve with severe regurgitation, moderate stenosis, LV dilatation	Fail
15	Mild pulmonary valve prolapse with moderate pulmonary regurgitation	FI
16	Mild pulmonary regurgitation Mild mitral regurgitation	Pass
17	Mild pulmonary regurgitation PFO	Pass
18	Patent ductus arteriosus	FI
19	Probable coronary artery to RV fistula	FI
20	Diastolic tricuspid inflow murmur due to elongated anterosuperior leaflet Cardiomyopathy suspected (abnormal ECG, biventricular dilatation)	FI
21	No pathology seen	Pass
22	No pathology seen	Pass

Table 5.9. Summary of the screening findings in the 22 candidates in whom a diastolic murmur was auscultated on physical examination. *FI = Further investigation / treatment required*

immediate referral for consideration of valve surgery. Mild or moderate PR was seen in 3 cases of which one also had moderate MR and another a PFO. A PDA was seen in one case and a fistula between the right coronary artery to the right ventricle was seen in one candidate. No explanation for the diastolic murmur was heard in 2 cases.

5.3.7 Candidates in whom no murmur was detected.

There were 8351 (75.4%) candidates examined by Cardiac Report in whom no murmur was detected (table 5.10). A total of 411 candidates were found to have a cardiac abnormality with 225 of these passed and 243 failed or referred for further investigation. In total 8107 (97.1%) were passed with no cardiac abnormality discovered. Males accounted for 7476 (89.5%) candidates without a murmur of whom 7258 (97.1) were passed. Females accounted for 875 (10.5%) candidates without a murmur of whom 849 (97.0) were passed. A cardiac condition identified because of an incidental ECG abnormality, that would not explain why a murmur might be detected, was identified in 58 (0.7%) candidates in this group. A cardiac condition identified on echo alone, but that would be unlikely to explain the finding of a murmur at the IRM, was seen in 81 cases and included anomalous coronary arteries, aortic dilatation, ASD and PFO. Interestingly diseases that might be expected to cause a murmur, such as a VSD or valvular heart disease, were identified by echo in at least 129 candidates.

5.3.8 The use of a murmur as a screening tool

Using these data we can calculate the Positive Predictive Value of screening for cardiac abnormalities in an otherwise normal potential recruit, but in whom a murmur is detected at the IRM. The pragmatic 'gold standard' in this case includes a resting 12 lead ECG and an echo. A 'positive' is a confirmed or suspected finding for CVD that requires further investigation. The figures used in the confusion matrix are: True Positive = 469; False Positive = 10,604 and True and false negative value are unknown but number a total of 111,108. With these figures the Positive Predictive Value = 4.24%.

Using these data available we can evaluate the utility of using auscultation for a murmur by a cardiologist as a screening tool in a young potential recruit with a normal history and physical examination, when an isolated murmur has previously been identified by a non-cardiologist on another day (table 11). The pragmatic 'gold standard' in this case includes a resting 12 lead ECG and an echo. A 'positive' is a confirmed or suspected finding for CVD that requires further investigation. The figures used in the confusion matrix are: True Positive = 225; False negative = 243; False Positive = 2494 and True negative = 8108.

Condition†	Total	(%)
Normal	7940	94.94
HTN	34	0.41
Incidental ECG only abnormality	**58**	**0.6935**
Brugada suspected	3	0.04
LQTS suspected	16	0.19
LQTS diagnostic	1	0.01
Frequent atrial or ventricular ectopy	24	0.29
Pre-excitation	14	0.17
Structural abnormalities	**331**	**3.96**
Aortic dilatation	1	0.01
Anomalous coronary artery origin	3	0.04
ASD	50	0.60
AV disease	24	0.29
BAV	52	0.62
Cardiomyopathy confirmed	4	0.05
Cardiomyopathy suspected	71	0.85
Double aortic arch	1	0.01
Mitral valve prolapse	5	0.06
Mitral valve disease - other	26	0.31
PFO (incidental)	46	0.55
Pulmonary valve disease	8	0.10
Tricuspid valve disease	10	0.12
VSD	4	0.05
Other structural disease	26	0.31
Total	**8363**	

Table 5.10. This is a summary of the conditions seen in the group of candidates that had a murmur identified at their IRM, but in whom a murmur was not detected by a Cardiac Report cardiologist*. Many of the conditions (highlighted in red) are incidental findings identified based on the ECG. A number of the suspected cardiomyopathy cases were also identified this way (see section on suspected cardiomyopathy). Other conditions such as the anomalous (continued)*

(continued) coronary arteries and some of the asymptomatic congenital disease were only detected because of the echo examination and would have otherwise remained undetected. The 'Other structural disease' is a heterogeneous collection of conditions described in more detail below. There were 13 candidates with two diagnoses. ASD = Atrial septal defect; AV= Aortic valve; BAV= Bicuspid aortic valve; HTN = Systemic hypertension; LQTS = Long QT Syndrome; MVP = Mitral valve prolapse; PFO = Patent foramen ovale; VSD=Ventricular septal defect.

Measurement	Value
Prevalence	4.18%
Sensitivity	48.1%
Specificity	76.5%
Positive Predictive Value	8.3%
Negative Predictive Value	97.1%
Positive likelihood ratio	2.04
Negative likelihood ratio	0.68
False Positive Rate	0.235
False Discovery Rate	0.917
False Negative Rate	0.519
Accuracy	0.753
F1 Score	0.141
Matthew Correlation Coefficient	0.115

Table 5.11: Outcomes from a 2 x 2 confusion matrix when using the detection of a murmur on two separate days as a screening test. *Abbreviations: PPV = Positive Predictive Value; FDR = False discovery rate; FOR = False omission rate; NPV = Negative Predictive Value; TPR = True Positive Rate; Sn = Sensitivity; FPR = False Positive Rate; LR+ Positive Predictive Value; DOR = Diagnostic Odds Ratio; FNR = False Negative Rate; TNR = True Negative Rate; Sp = Specificity; LR- = Negative Likelihood Ratio.*

5.3.9 Diseases discovered

In total 726 (6.6%) abnormalities (including the incidental finding of a PFO) were identified (table 12) and of these 312 (43.0%) were passed; 414 (3.7%) were deferred. There was no difference between genders in the likelihood of failure (p=0.635). Valvular heart disease was the most frequently identified group of abnormalities but importantly there were nearly 200 cases of either suspected or confirmed cardiomyopathy or primary electrical disease and 201 cases of other non-valvular congenital structural diseases. These groups are described in more detail below.

	All			Males				Female			
CVD conditions	**n**	**Pass**	**%**	**n**	**%**	**Pass**	**%**	**n**	**%**	**Pass**	**%**
Cardiomyopathy	123	0	0	108	87.8	0	0	15	12.2	0	0
Electrical disease	70	10	14.3	62	88.6	8	12.9	8	11.4	2	25.0
Valvular heart disease	332	163	49.1	292	88.0	137	46.9	40	12.0	26	65.0
Septal defects	154	121	78.6	136	88.3	112	82.4	18	11.7	9	50.0
Other structural disease	47	18	38.3	47	100	18	38.3	0	0	-	-
Total	**726**	**312**	**43.0**	**645**	**89**	**275**	**42.6**	**81**	**11**	**37**	**45.7**

Table 5.12: Summary of the cardiovascular conditions identified or suspected and their pass rates overall and by gender.

5.3.10 Cardiomyopathy

A total of 123 candidates (1.1%) had a cardiomyopathy diagnosis confirmed (17 candidates; 0.15%) or suspected (106 candidates, 0.96%) by Cardiac Report (table 14).

Hypertrophic cardiomyopathy was provisionally confirmed in 13 asymptomatic candidates (0.12%) though alternative causes of the diagnostic ECG and echo findings were not completed as part of the screening protocol. In these candidates no hypertension was identified on the day. All these candidates were male. In the candidates with provisionally confirmed HCM a murmur was detected in 6 cases and of these 3 had ECGs that would be identified as normal using screening criteria. In 7 candidates with confirmed HCM no murmur was detected; of these 5 had abnormal ECGs and one had an ECG that would not be identified as abnormal using the contemporary ECG screening criteria. All these confirmed cases were failed.

Findings that were non-diagnostic, but highly suggestive of HCM were seen in another 10 candidates. All had mild LVH on echo. A murmur was identified in 6 of these, all of which were found to have LVH by voltage on ECG, but no findings that would trigger further investigation using ECG screening criteria. No murmur was detected in 4 candidates, 2 of which had ECG abnormalities that would be identified using contemporary screening criteria. Although the phenotype of these candidates could be the result of athletic adaptations, the assessing clinicians felt this was unlikely given the history of only light physical training that these individuals described.

There were 2 asymptomatic male candidates (0.02%) who reached task force criteria for ARVC/D and a further 13 in whom it was suspected. One case had a murmur detected and

the other did not. Both cases met the task force criteria on account of at least two major criteria: each had a dilated RV with regional wall motion abnormalities and repolarisation abnormalities on the ECG. One case had a likely epsilon wave. Both cases were also noted to have frequent premature ventricular contractions of a LBBB morphology. The case with a murmur detected had no pathological echocardiographic features that would account for the auscultation finding.

A further 13 candidates were considered to have findings suspicious for ARVC; all but 4 had ECG abnormalities that would be identified using screening criteria and all had subtle findings on echo that would satisfy the ARVC 'minor criteria' definition. A murmur was detected in 3 of these candidates with no obvious pathological cause identified on echo.

An asymptomatic hypokinetic, non-dilated or DCM was considered highly likely in 5 candidates (0.05%), all of which were male. Of these only one was found to have a murmur and all five had ECGs that would be passed using screening criteria. All 5 had a normal LV wall thickness, 2 had a dilated LV and RV and all 5 had at least moderately impaired LV function without a clear RWMA. There were 5 further candidates who had mildly dilated or mildly hypokinetic LV function at echo that the screening cardiologist felt would not be due to athletic adaptation. Two had abnormal ECGs that would be identified using screening criteria.

Findings non-diagnostic, but suspicious for cardiomyopathy, racial variation or athletic adaptations that required further investigation, were identified in 75 candidates. Candidates with findings in the grey zone between a cardiomyopathy and an athletic heart were described by the examining clinicians in 30 cases (0.27%). Although race was not recorded in the demographics, this was reported in the summaries of the examining clinicians as a possible explanation for particular ECG findings in 14 candidates, all of which had ECG findings suggestive of normal racial variation combined with possible athletic adaptation. The specific race was not described in any of these cases. Findings more suspicious for a cardiomyopathy, rather that athletic adaptation or racial variation, were detected in 45 (0.4%) candidates. The overwhelming ECG findings were of TWI >2mm in 2 or more adjacent leads from V2-6, I, II, III, avF with no significant echo abnormalities identified. In those without ECG abnormalities chamber dilatation or hypertrabeculation were the main findings.

5.3.11 Primary electrical disease of the heart

There were 70 candidates (0.6%) in whom a primary arrhythmic condition was identified or suspected (table 14). Of these 62 were men and 8 were women; there was no difference in the incidence by gender (p=0.86).

5.3.12 Sinus tachycardia. Sinus tachycardia was identified in 4 cases. These candidates all had sinus tachycardia at rest despite repeating the ECG after a period of calm. All their ECGs

were normal aside from the sinus tachycardia. All 4 were all deferred in order to exclude non-cardiac conditions such as anaemia or endocrine disease.

5.3.13 Accessory pathways. An accessory pathway was identified in 21 candidates based on the presence of a short PR interval and a delta wave. One candidate had been symptomatic of palpitations and exertional dyspnoea (discussed above) but the remainder were asymptomatic. One candidate was found to have moderate TR and an apically displaced tricuspid valve; a provisional diagnosis of Ebstein's anomaly was made (discussed below). All 21 candidates were deferred.

5.3.14 Ion channel diseases. An ion channelopathy was suspected or provisionally confirmed in 21 candidates. These included suspected Brugada and LQTS only.

5.3.15 Long QT Syndrome. There were 19 candidates in whom LQTS was considered and all were deferred or failed. On re-examination of the ECGs for this study 3 candidates (1 x female and 2 x males) were felt to have been over-measured by the examining cardiologist and were closer to 420ms in each case; they are mentioned here for completeness. Using the 2010 ECG interpretation guidelines 16 candidates would have tested positive for suspected LQTS (2 x females and 14 x males) but the 2017 guidance would have reduced this to only 11 candidates (1 x female and 10 x males). Of these 16 candidates a QTc > 500ms was identified in 4 males (QTc measurements: 505ms, 523ms, 563ms and 584ms)

and all were failed. The 23 year old candidate with the longest QTc also had TWI in V1-3 in addition to the prolonged QTc and his echo was normal.

5.3.16 Brugada Syndrome. All 4 candidates in whom the Brugada syndrome was suspected had type 2 (1 candidates) or type 3 (3 candidates) Brugada pattern changes on ECG. All were asymptomatic but one 21 year old male with a Type 3 Brugada pattern had a family history of sudden death in a young second degree relative. All four candidates were deferred for further investigation. No Type 1 Brugada pattern was identified.

5.3.17 Ectopy. Atrial or ventricular ectopy or both was seen in 14 candidates. One 17 year old female candidate had previously syncopal symptoms and her ECG showed runs of likely atrial tachycardia with a probable right atrial focus and her echo showed borderline, at worst mild, left ventricular dilatation. She was documented as a 'pass', but the cardiologist recommended that she undergo routine blood tests to exclude hyperthyroidism or anaemia. The other candidates with occasional atrial ectopics were all asymptomatic, all had normal echos and all were passed.

Diagnosis	All candidates			Murmur heard on the day						No murmur heard on the day						
	Total	Male		Total	Normal ECG		Abnormal ECG		Male		Total	Normal ECG		Abnormal ECG		Male	
		n	%		n	%	n	%	n	%		n	%	n	%	n	%
HCM	13	13	*100*	7	3	*42.9*	4	*57.1*	7	*53.8*	6	5	*83.3*	1	*16.7*	6	*100*
Sp HCM	10	10	*100*	6	3	*50.0*	3	*50.0*	6	*60.0*	4	2	*50.0*	2	*50.0*	4	*100*
ARVC	2	2	*100*	1	0	*0.0*	1	*100*	1	*50.0*	1	0	*0.0*	1	*100*	1	*100*
Sp ARVC	13	10	*76.9*	3	0	*0.0*	3	*100*	0	*0.0*	10	4	*40.0*	6	*60.0*	10	*100*
DCM	5	5	*100*	1	1	*100*	0	*0.0*	1	*20.0*	4	4	*100*	0	*0.0*	4	*100*
Sp DCM	5	5	*100*	2	1	*50.0*	1	*50.0*	2	*40.0*	3	2	*66.7*	1	*33.3*	3	*100.0*
Sp CM	45	40	*88.9*	16	4	*25.0*	11	*68.8*	15	*33.3*	29	9	*31.0*	20	*69.0*	25	*86.2*
Overlap	30	23	*76.7*	12	6	*50.0*	6	*50.0*	5	*16.7*	18	11	*61.1*	7	*38.9*	18	*100*
Totals	**123**	**108**	***87.8***	**48**	**18**	***37.5***	**29**	***60.4***	**37**	***30.1***	**75**	**37**	***49.3***	**38**	***50.7***	**71**	***94.7***

Table 5.13: Summary of the suspected or confirmed cardiomyopathy cases identified and whether they were associated with a murmur. *All cases were deferred or failed. 'Overlap' refers to cases in the overlapping zone between a cardiomyopathy and either an athletic heart or normal racial variation. HCM = Hypertrophic cardiomyopathy; Sp = Suspected; ARVC = Arrhythmogenic right ventricular cardiomyopathy; DCM = Hypokinetic/dilated cardiomyopathy; CM = Non-specified Cardiomyopathy.*

In contrast the 7 candidates with ventricular ectopy and 1 with both atrial and ventricular ectopy were all deferred for further investigation. All 8 of these candidates were male. The candidate with both atrial and ventricular ectopy was an asymptomatic 16 year old and he actually had a normal 12 lead ECG, but atrial ectopics and two different broad complex ectopics were frequently seen during the echo. The echo parameters were all within the normal range. The 7 candidates with frequent ventricular ectopics all had monomorphic ectopy that in 4 cases was a RVOT bigeminy pattern; in 1 case a RVOT trigeminy pattern; in 1 case a LVOT bigeminy pattern; in the final case the origin was probably arising in the outflow tracts but the morphology was not specific to one particular side and was seen only in leads I, II, III, V4-6. All had structurally normal hearts except for a 19 year old male whose LV was borderline dilated.

5.3.18 Conduction abnormalities. Conduction abnormalities were seen in 9 candidates. Three candidates were found to have sinus bradycardia and first degree heart block and intermittent Mobitz type 1 AV block and two candidates had first degree block with sinus bradycardia and runs of isorhythmic AV dissociation. All five candidates were asymptomatic and athletic with normal echos so it was felt that these findings were all secondary to high vagal tone. One 22 year old male with Mobitz type 1 AV block was deferred as unlike the others his AV conduction did not normalise with light exercise; the other 4 were passed. A bifascicular block (RBBB and right axis deviation) was described in 2 asymptomatic male candidates whose echos were both normal. They were deferred for further monitoring and CMR. One further asymptomatic candidate was deferred as he was found to have junctional escape beats competing with his sinus rhythm; his echo was normal. The cardiologist that

deferred him felt the rhythm was probably due to vagal tone, but wanted a Holter and exercise test to exclude significant conduction disease.

Finally one candidate was found to have Mobitz type 2 AV block. He admitted to childhood surgery to treat transposition of the great arteries and is described in the structural heart disease section below; he had significant structural and functional disease and was failed.

5.3.19 Valvular heart disease

A total of 332 cases of VHD were identified. These have been categorised according to the main pathology found, though only a handful were found to have disease of more than one valve.

5.3.20 Aortic valve disease

The cohort containing the 169 cases of aortic valve disease is divided here into valves with a normal, tricuspid morphology (49 cases) and BAV (120 cases). This differentiation is in part because of the risk for early degeneration of the BAV, the aortopathy associated with BAV that results in an increased risk of dissection and the

	All				Murmur				No murmur			
ECG finding	**Number**	**%**	**Pass**	**%**	**Number**	**%**	**Pass**	**%**	**Number**	**%**	**Pass**	**%**
Sinus tachycardia	4	0.04	0	0	2	50	0	0	2	50	0	0
WPW	21	0.19	0	0	6	25	0	0	15	75	0	0
LQTS	4	0.04	0	0	1	25	0	0	3	75	0	0
Suspected LQTS	12	0.11	0	0	1	6.7	0	0	14	93.3	0	0
Suspected Brugada	6	0.05	0	0	3	50	0	0	3	50	0	0
Atrial ectopy	6	0.05	6	100	2	33.3	2	100	4	66.7	4	100
Ventricular ectopy	7	0.06	0	0	3	42.9	0	0	4	57.1	0	0
Atrial and ventricular ectopy	1	0.01	0	0	1	100	0	0	0	0	-	-
Mobitz Type 1 AV block	3	0.03	2	33.3	0	0	-	-	3	100	2	66.7
Mobitz Type 2 AV block	1	0.01	0	0	1	100	0	0	0	0	-	-
Isorhythmic AV dissociation	2	0.02	2	100	1	50	1	100	1	50	1	100
Other conduction disease	3	0.03	0	0	0	0	-	-	3	100	0	0
Total	**73**	**0.62**	**10**	**13.7**	**21**	**28.8**	**3**	**0.14**	**52**	**71.2**	**7**	**13.5**

Table 5.14: *Summary of the candidates in whom a primary electrical condition was confirmed or suspected from the ECG.*

consequential bar to service for those candidates in whom a BAV is found. No other morphological forms of the aortic valve were seen.

Disease of a structurally tricuspid aortic valve was identified in 49 candidates of which males constituted 45 candidates (table 15). There was no difference in the frequency between males and females (p=0.7185). The vast majority of the valve dysfunction identified was isolated mild AR (44 cases, 89.8%) in the context of an otherwise normal aortic valve (table 16). Mixed aortic valve disease was seen in 5 candidates and stenosis was not seen without regurgitation. Two cases of AR were discovered with moderate MR and in both cases the mitral and aortic valves were noted to be morphologically normal. One case with moderate AR was also found to have a globular and dilated left ventricle that appeared out of proportion to the degree of regurgitation; consequently the possibility of a cardiomyopathy was raised by the examining cardiologist. The ECG in this case was normal.

A murmur was heard in 32 of the 49 candidates (63.3%) and was more likely to be heard in those who were passed than those that were not (p= 0.0187). Despite the finding that most disease seen was mild AR the majority of the murmurs heard (87.1%) were systolic in nature.

The only case associated with an abnormal ECG was a candidate with mixed stenotic and regurgitant disease. His echo demonstrated a calcified aortic valve with at least moderate AR; a pressure half time between 292 ms and 414 ms and moderate to severe AS, with a

pressure gradient of 70 mmHg and valve area calculated 0.9-1 cm^2. This candidate was failed and referred onwards for a surgical review. No other cases were found to have an ECG abnormality that would have allowed detection using an ECG as the only screening tool and this was the only case severe enough to require a surgical referral. In total nine cases were failed.

There were 120 candidates (1.08%) in whom a BAV was discovered (table 5.17). Of these 113 (94.16%) of these were males. There was no difference between the prevalence of BAV between the male and female populations (p= 0.1113). All these candidates were failed as a known BAV is a bar to military recruitment regardless of whether the BAV is functionally normal and irrespective of the aortic anatomy.

In 52 candidates with a BAV no murmur was heard and in 50 of these the ECG was also normal (41.7% of all BAV) indicating that screening without an echo would detect only about 3 in 5 cases in this already screened cohort. An ECG added little value in the detection of a BAV as only 6 of these 120 (5%) cases would have been identified had the ECG been the only screening tool.

Almost half of the BAV cases identified were functionally normal with a normal aorta on echo (table 18). Despite this 22 of these 56 cases (39.2%) were found to have a murmur on auscultation. The remaining 64 candidates (53.3%) had at least mild valvular

	All aortic valve dysfunction (non-BAV)				Normal ECG				Abnormal ECG			
Murmur description	n	%	Pass	%	n	%	Pass	%	n	%	Pass	%
Normal	18	36.7	17	94.4	18	37.5	17	94.4	0	0	0	0
Any murmur	31	63.3	23	74.2	30	62.5	23	76.7	0	0	0	0
Innocent systolic murmur	3	6.1	3	100.0	3	6.3	3	100	0	0	0	0
Unspecified Systolic murmur	14	28.6	12	85.7	14	29.2	12	85.7	0	0	0	0
ESM	10	20.4	7	70.0	10	20.8	7	70	0	0	0	0
Diastolic murmur	2	4.1	1	50.0	2	4.2	1	50	0	0	0	0
Both systolic and diastolic murmur	2	4.1	0	0.0	1	2.1	0	0	1	50.0	0	0
Total	**49**		**40**	**81.6**	**48**	**98.0**	**40**	**83.3**	**0**	**0.0**	**0**	

Table 5.15: Summary of the aortic valve dysfunction detected in candidates with a structurally tricuspid aortic valve and the pass rates in those with a normal or abnormal ECG.

	All AV disease		Normal ECG		Abnormal ECG	
AS Severity	**Total**	**%**	**Total**	**%**	**Total**	**%**
None	44	36.7	44	38.6	0	0
Mild	1	0.8	1	0.9	0	0
Moderate	4	3.3	4	3.5	1	16.7
AR Severity						
None	0	0	0	0	0	0
Mild	44	36.7	44	38.6	0	0
Moderate	5	4.2	5	4.4	1	16.7
Aortic dilatation?						
No	47	39.2	47	41.2	0	0
Yes	2	1.7	2	1.8	0	0
Mixed AV disease						
No	44	36.7	44	38.6	0	0
Yes	5	4.2	5	4.4	1	16.7

Table 5.16: Summary of the severity of aortic valve dysfunction seen in those candidates with structurally tricuspid aortic valve disease. *The 9 candidates that were failed were those with moderate stenosis or regurgitation on echo and this included all 5 candidates with mixed stenotic and regurgitant disease.*

dysfunction, aortic root dilatation or rarely, aortic coarctation. Of these candidates 46 (71.9%) were found to have a murmur on auscultation. Unsurprisingly it was more likely for a murmur to be detected when valvular dysfunction or coartation of the aorta were present (p=0.0004).

5.3.21 Mitral valve disease

A total of 96 candidates were found to have either morphological mitral valve disease or at least mild MR with a structurally normal valve (table 19); no candidates were found to have

mitral stenosis. Within this group the underlying pathology was of MVP, a condition thought to predispose some people to SCD, or other causes of regurgitation, usually due to a subtle failure of leaflet coaptation in an otherwise apparently normal valve. There was no difference in incidence between genders in either the non-MVP group where 62 (83.8%) were males (p=0.1859) or in the 22 cases of MVP where 18 (81.8%) male cases were identified (p= 0.4370).

The vast majority of MV disease not due to MVP resulted in mild MR only and of these 69 (93.2%) were passed. A small minority had other pathology detected. One candidate was found to have a large primum VSD and associated cleft MV and he was referred directly for a surgical opinion. Another two candidates were found to have moderate MR and moderate AR through a tricuspid aortic valve; both were failed.

Candidates with MVP and no regurgitation can be passed for service and 7 candidates within these limits were passed; the remaining 15 candidates were failed (table 5.20). One candidate with MVP and severe MR was referred for a surgical review.

Of all the candidates with mitral valve disease almost a third had no murmur on auscultation and 67.7% of these cases would have been identified on auscultation. Only one candidate had an abnormal 12 lead ECG that showed frequent multifocal ectopics;

Murmur described	All		ECG normal		ECG abnormal	
	Total	%	Total	%	Total	%
No murmur	52	43.3	50	96.2	2	3.8
All murmurs						
Innocent systolic murmur	4	3.3	4	100	0	0
ESM - aortic valve	18	15.0	17	94.4	1	5.6
Non-specific systolic murmur	37	30.8	35	95	2	5.4
Diastolic murmur - aortic regurgitation	3	2.5	3	100	0	0
Diastolic murmur - no valve specified	1	0.8	1	100	0	0
Both systolic and diastolic murmur	5	4.2	4	80	1	20
Total	**120**		**114**	**95**	**6**	**5**

Table 5.17: *Summary of the 120 candidates in whom a BAV was detected by auscultation and ECG findings.*

	All BAVs		Normal ECG		Abnormal ECG	
Normal AV function & aorta	Total	%	Total	%	Total	%
No	64	53.3	60	93.8	4	6.3
Yes	56	46.7	54	96.4	2	3.6
AS Severity						
None	98	81.7	95	83.3	3	50.0
Mild	17	14.2	15	13.2	2	33.3
Moderate	5	4.2	4	3.5	1	16.7
AR Severity						
None	65	54.2	63	55.3	2	33.3
Mild	38	31.7	37	32.5	1	16.7
Moderate	13	10.8	10	8.8	3	50.0
Severe	4	3.3	4	3.5	0	0.0
Aortic dilatation						
No	114	95.0	108	94.7	6	100.0
Yes	6	5.0	6	5.3	0	0.0
Coarctation						
No	117	97.5	111	97.4	6	100.0
Yes	3	2.5	3	2.6	0	0.0
Mixed AV disease						
No	106	88.3	103	90.4	3	50.0
Yes	14	11.7	11	9.6	3	50.0

Table 5.18: *Summary of aortic valve function and associated abnormalities in the aorta in those candidates in whom a BAV was identified.*

he also had a run of bigeminy noted during his echo. This candidate had a late systolic murmur and mild regurgitation through a prolapsing mitral valve and was failed.

5.3.22 Pulmonary valve disease

A total of 36 people were identified with more than trivial physiological pulmonary valve regurgitation or PS (table 21). Of these 33 (91.7%) individuals were male and there was no difference in the incidence between genders (p=0.8380). The majority of cases were found to have a murmur and of the 11 cases that were failed only 3 (27.3%) had no murmur detected. All the ECGs were normal in this cohort. Of the three cases with 'moderate' PR that were passed the examiner had in each case evaluated the severity of the PR as 'mild-moderate' rather than a clear 'moderate' severity. Although 30.6% of these cases were failed only one was severe enough to trigger a surgical review – this was a 26 year old man with severe PR with an abnormal valve structure that the echo report described as 'ballooning'.

5.3.23 Tricuspid valve disease

A total of 31 candidates were found to have more than trivial, physiological tricuspid valve regurgitation (table 22). There were no cases of tricuspid stenosis. Of these 31 cases males accounted for 23 (74.2%) with no difference in incidence between genders (p=0.0164). Of the 9 candidates that were failed 2 (22.2%), with moderate regurgitation, did not have a murmur detected; this was not significantly different to the group that were passed (p=0.6770).

Whilst most of the echos showed morphologically normal tricuspid valves, two cases were highly suggestive of Ebstein's anomaly. In one of these two cases, a 20 year old

	All Mitral valve disease				Non-MVP disease				MVP			
Murmur description	**Total**	**%**	**Pass**	**%**	**Total**	**%**	**Pass**	**%**	**Total**	**%**	**Pass**	**%**
Normal	31	32.3	25	80.6	23	74.2	21	91.3	8	25.8	4	50
Any murmur	65	67.7	54	83.1	51	78.5	48	94.1	14	21.5	4	28.6
Innocent systolic murmur	2	2.1	2	100	2	100	2	100	0	0	0	-
Non-specific systolic murmur	40	41.7	31	77.5	32	80.0	30	93.8	8	20	2	25
ESM	3	3.1	3	100	3	100	3	100	0	0	0	-
LSM	3	3.1	3	100	0	0	0	-	3	100	0	0
PSM	16	16.7	14	87.5	13	81.3	12	92.3	3	18.8	2	66.7
Both systolic and diastolic murmur	1	1.0	1	100	1	100	1	100	0	0	0	-
Total	**96**		**79**	**82.3**	**74**	**77.1**	**69**	**93.2**	**22**	**22.9**	**8**	**36.4**

Table 5.19: Summary of the mitral valve disease cases grouped together as a whole or separated by those with or without mitral valve prolapse with regards to whether a murmur was auscultated by a cardiologist on the day. *The pass mark relates to the candidates in that subgroup with the same murmur description. MVP = Mitral valve prolapse; ESM = End-systolic murmur; LSM = Late systolic murmur; PSM = Pan-systolic murmur.*

	All Mitral valve disease				Non-MVP disease				MVP			
MR Severity	**Total**	**%**	**Pass**	**%**	**Total**	**%**	**Pass**	**%**	**Total**	**%**	**Pass**	**%**
None	7	7.3	7	6.1	0	0	-	-	7	100	7	100
Mild	82	85.4	70	61.4	72	87.8	69	60.5	10	12.2	1	1.0
Moderate	6	6.3	0	0	2	33.3	0	0	4	66.7	0	0
Severe	1	1.0	0	0	0	0	-	-	1	100	0	0
Total	96		77	67.5	74		69	60.5	22		8	36.4

Table 5.20: Summary of the mitral valve disease cases grouped together as a whole or separated by those with or without mitral valve prolapse with regards to the severity of the mitral regurgitation identified. *MVP = Mitral valve prolapse*

	Pulmonary valve disease			
Murmur description	**Total**	**%**	**Pass**	**%**
Normal	8	22.2	5	62.5
All murmurs	28	77.8	20	71.4
Systolic murmur - non-specific	12	33.3	8	66.7
ESM	14	38.9	11	78.6
Diastolic murmur	1	2.8	1	100.0
Systolic and diastolic murmur	1	2.8	0	0.0
Total	**36**		**25**	**69.4**
Regurgitation severity	**Total**	**%**	**Pass**	**%**
Mild	4	28.6	3	75.0
Moderate	9	64.3	3	33.3
Severe	1	7.1	0	0.0
	14		**6**	**42.9**
Stenosis severity	**Total**	**%**	**Pass**	**%**
Mild	22	100.0	17	77.3

Table 5.21: *Summary of the 36 cases of identified pulmonary valve disease.*

asymptomatic male, the only abnormal ECG seen in the group showed a short PR interval with a LBBB and LAD pattern suggestive of either ventricular pre-excitation or a conduction abnormality. The echo also visualised right ventricular dilatation and impaired systolic function with a dysplastic and apically displaced tricuspid valve with severe regurgitation.

The second candidate with likely Ebstein's anomaly was a 16 year old asymptomatic male with moderate regurgitation through an apically displaced and dysplastic valve with preserved RV size and function.

	Tricuspid valve disease			
Murmur description	**Total**	**%**	**Pass**	**%**
Normal	10	32.3	8	80.0
All murmurs	21	67.7	14	66.7
Innocent systolic murmur	1	3.2	1	100.0
Unspecified systolic murmur	10	32.3	7	70.0
ESM	2	6.5	1	50.0
PSM	8	25.8	5	62.5
Total	**31**		**22**	**71.0**
Regurgitation severity	**Total**	**%**	**Pass**	**%**
Mild	19	61.3	18	94.7
Moderate	10	32.3	4	40.0
Severe	2	6.5	0	0.0
Total	**31**		**22**	**71.0**

Table 5.22: *Summary of the candidates in whom tricuspid regurgitation was identified. Two of these cases were suspected of Ebstein's anomaly.*

The only other candidate with isolated severe TR, an asymptomatic 22 year old male, was noted to have an abnormal valve with an unusual tricuspid valve appearance. The cardiologist examining him suggested that referral for a transoesophageal echo was indicated.

Another candidate with a history of previous childhood surgery for transposition of the great vessels had moderate TR but in the context of significant other abnormalities and was failed (see section on other structural heart disease below).

5.3.24 Cardiac septal defects

A cardiac septal defect, differentiated into patent foramen ovale (PFO), and ASD or VSD, were seen in 154 cases. They are described here by the site of the defect.

5.3.25 Patent foramen ovale

An incidental finding of a PFO was identified in 62 (0.56%) cases of which 58 were male (table 23). There was no difference in the proportion of males to females (p=0.3702). Two candidates in whom a PFO was found were failed for reasons separate to the PFO finding; one was found to have TWI in the lateral leads and an otherwise normal echo and the other had frequent ventricular ectopy, including ventricular bigeminy, during his echo, which was otherwise normal. A PFO is considered a normal variant but has occupational medicine relevance with regards to diving in the military population.

5.3.26 Atrial Septal Defect

There were 77 ASD identified (table 24) of which 67 were male (87%). There was no difference in the proportion of males to females with an ASD (p=0.66). Almost two thirds were passed as their defects were small and of no significant haemodynamic consequence.

The remaining candidates were failed pending further assessment and potentially treatment.

There was a large secundum defect with right ventricular dilatation in 7 candidates and the consulting cardiologist advised in each case that these defects would need referral for closure. One 16 year old female candidate was found to have a large primum defect with an associated VSD and cleft mitral valve with moderate regurgitation; she was referred directly to a congenital heart disease specialist for consideration for surgery; she consequently failed selection. The remaining 20 candidates that were deferred had defects of intermediate severity, some with significant shunts, but no ventricular dilation or other acutely high risk features.

5.3.27 Ventricular septal defects

There were 15 VSDs identified (table 25) of which 11 (73.3%) were male. There was no difference in the proportion of males to females (p= 0.1623). Of the VSDs identified 11 (73.3%) were considered small with no high risk features and the candidates were passed. Of the 4 candidates failed on the day three were considered borderline and referred for further evaluation and one had an associated ASD and valvular disease and was referred for a specialised surgical opinion.

Murmur identified	Total				ECG normal				ECG abnormal			
	n	%	Pass	%	n	%	Pass	%	n	%	Pass	%
Normal	44	71.0	43	97.7	42	95.5	42	100.0	2	4.5	1	50.0
Any murmur	18	29.0	17	94.4	18	100	17	94.4	0	0	0	0
Innocent systolic murmur	1	1.6	1	100	1	100	1	100	0	0	0	0
ESM	3	4.8	3	100	3	100	3	100	0	0	0	0
PSM	0	0.0	0	0	0	0.0	0	0	0	0	0	0
Non-specific systolic murmur	13	21.0	12	92.3	13	100	12	92.3	0	0	0	0
Diastolic murmur - aortic regurgitation	0	0.0	0	0	1	0.0	1	100	0	0	0	0
Diastolic murmur - no valve specified	1	1.6	1	100	0	0.0	0	0	0	0	0	0
Both systolic and diastolic murmur	0	0.0	0	0	0	0.0	0	0	0	0	0	0
Total	62		60	96.8	60	96.8	59	98.3	2	3.2	1	50.0

Table 5.23: *Summary of the PFO cases identified*.

Murmur identified	**Total**				**ECG normal**				**ECG abnormal**			
	n	**%**	**Pass**	**%**	**n**	**%**	**Pass**	**%**	**n**	**%**	**Pass**	**%**
Normal	49	63.6	36	73.5	44	89.8	34	77.3	5	10.2	2	40.0
Any murmur	28	36.4	13	46.4	27	96.4	13	48.1	1	3.6	1	100.0
Innocent systolic murmur	1	1.3	1	100.0	1	100.0	1	100.0	0	0.0	0	0.0
ESM	8	10.4	4	50.0	8	100.0	4	50.0	0	0.0	0	0.0
PSM	1	1.3	0	0.0	0	0.0	0	0.0	1	100.0	1	100.0
Non-specific systolic murmur	18	23.4	8	44.4	18	100.0	8	44.4	0	0.0	0	0.0
Total	**77**		**49**	**63.6**	**71**	**92.2**	**47**	**66.2**	**6**	**7.8**	**3**	**50.0**

Table 5.24. *Summary of the atrial septal defects identified.*

5.3.28 Other structural heart disease

In addition to the conditions above 47 candidates were identified or suspected of other, mostly congenital cardiac disease (table 5.26). Of these 19 (40.4%) had a murmur identified at auscultation and only 2 candidates had an abnormal ECG.

Many of these conditions appeared mild and without any significant cardiovascular effects, such as at most mild obstruction of the pulmonary or aortic outflow tracts by sub-pulmonary or sub-aortic membranes respectively and in these cases the candidates were passed; where the obstruction was more than mild though (2 of 8 cases)the candidates were deferred. A persistent left-sided superior vena cava was identified in 8 cases and these candidates were passed. Other congenital heart diseases, such as co-tritriatum (2 cases), a double aortic arch (1 case), a PDA (8 cases) and Ebstein's anomaly (2 cases described above under the section on tricuspid valve disease) were all deferred for further investigation or failed.

There were two cases of previously operated congenital heart disease. One 16 year old male had undergone surgery as an infant for anomalous pulmonary venous drainage. He was found to have a pan-systolic murmur on examination; a borderline inferior repolarisation abnormality (that did not reach the threshold of 1mm of TWI in adjacent leads) on the ECG that was passed as acceptable; and mild MR and a dilated left atrium (LA) at echo. This candidate was deferred for further investigation.

	Total				ECG normal				ECG abnormal			
Murmur identified	**n**	**%**	**Pass**	**%**	**n**	**%**	**Pass**	**%**	**n**	**%**	**Pass**	**%**
Normal	4	26.7	3	75.0	3	75.0	2	66.7	1	25.0	1	100.0
Any murmur	11	73.3	8	72.7	11	100.0	8	72.7	0	0.0	0	0.0
ESM	1	6.7	0	0.0	1	100.0	0	0.0	0	0.0	0	0.0
PSM	8	53.3	7	87.5	8	100.0	7	0.0	0	0.0	0	0.0
Non-specific systolic murmur	2	13.3	1	50.0	2	100.0	1	50.0	0	0.0	0	0.0
Total	**15**		**11**	**73.3**	**14**	**93.3**	**10**	**71.4**	**1**	**6.7**	**1**	**100.0**

Table 5.25. *Summary of the VSDs identified*

The second candidate with previously operated congenital heart disease had a history of transposition of the great vessels that he only admitted after his ECG and echo were found to be grossly abnormal. This 17 year old male had a pan-systolic murmur detected at physical examination. His ECG was grossly abnormal with sinus rhythm, intermittent 2:1 atrioventricular block, a broad QRS complex with a non-specific intraventricular delay and left axis deviation. His echo identified a systemic right ventricle and severely impaired systolic function, with the LVEF estimated at 28% and at least moderate TR. He was failed and referred directly from clinic for a congenital cardiology opinion.

There were three incidental findings on echo of anomalous coronary arteries in asymptomatic male candidates aged 16, 18 and 27; none of these had murmurs or ECG abnormalities at rest. Two of these were right coronary arteries arising from the left coronary cusp and one was thought to be a circumflex artery arising from the right coronary cusp. All three candidates were referred for more detailed coronary artery imaging with either cardiac CT or magnetic resonance imaging.

Two male candidates aged 16 and 17 had examination findings suggestive of Marfan Syndrome, including a positive wrist and thumb sign, high-arched palate and wide arm-span; neither had ectopia lentis. In neither case was there a murmur or ECG abnormality. The echo for both was unremarkable, with no MVP or aortic dilatation that might suggest Marfan syndrome. Based on the examination and echo findings neither candidate was clearly diagnostic for Marfan syndrome using the 2010 Revised Ghent Nosology. The examining cardiologists in both cases felt a specialist opinion was indicated though and both candidates were deferred.

Condition		Total	%	Pass	%		Normal ECG	%	Pass	%
Double aortic arch	All	1		0	0		1	0	0	0
	Murmur	0	0	-	-		-	-	-	-
	No murmur	1	100	0	0		1	100	0	0
Subaortic membrane	All	8		6	75		8	100	6	75
	Murmur	4	50	4	100		4	100	4	100
	No murmur	4	50	2	50		4	100	2	50
Subpulmonary membrane	All	5		4	80		5	100	4	80
	Murmur	5	100	4	80		5	100	4	80
	No murmur	0	0	-	-		-	-	-	-
Co-triatriatum	All	2		0	0		2	100	0	0
	Murmur	0	0	-	-		-	-	-	-
	No murmur	2	100	0	0		2	100	0	0
Persistent left-sided SVC	All	8		8	100		8	100	8	100
	Murmur	1	12.5	1	100		1	100	1	100
	No murmur	7	87.5	7	100		7	100	7	100
Patent ductus arteriosus	All	8		0	0		8	100	0	0
	Murmur	5	62.5	0	0		5	100	0	0
	No murmur	3	37.5	0	0		3	100	0	0
Ebstein's anomaly	All	2		0	0		1	50	0	0
	Murmur	2	100	0	0		1	50	0	0
	No murmur	0	0	-	-		-	-	-	-
Previously operated congenital heart disease	All	2		0	0		1	50	0	0
	Murmur	2	100	0	0		1	50	0	0
	No murmur	0	0	-	-		-	-	-	-
Anomalous coronary artery origin	All	3		0	0		3	100	0	0
	Murmur	0	0	-	-		-	-	-	-
	No murmur	3	100	0	0		3	100	0	0
Kawasaki disease	All	1		0	0		1	100	0	0
	Murmur	0	0	-	-		-	-	-	-
	No murmur	1	100	0	0		1	100	0	0
Suspected PAH	All	3		0	0		3	100	0	0
	Murmur	1	33.3	0	0		1	100	0	0
	No murmur	2	66.7	0	0		2	100	0	0
Suspected Marfan's Syndrome	All	2		0	0		2	100	0	0
	Murmur	0	-	-	-		-	-	-	-
	No murmur	2	100	0	0		2	100	0	0
Suspected congenital heart disease	All	2		1	100		2	100	1	100
	Murmur	1	50	0	0		1	100	0	0
	No murmur	1	50	1	100		1	100	1	100

Table 5.26: Summary of the other structural disease identified.

There were two further cases of suspected congenital disease. Both were 18 year old males, one with an unspecified systolic murmur and the other with no murmur on auscultation. Both had a normal ECG. One candidate had a jet of diastolic colour flow seen at pulmonary artery bifurcation that appeared in the incorrect location for a PDA. The examining cardiologist felt a CMR would better characterise the anatomy and the candidate was deferred. The second candidate had isolated and significant right atrial dilatation but no other abnormality was identified on echo. The cardiologist requested a CMR to better characterise the anatomy in case of anomalous pulmonary drainage and the candidate was deferred.

There were 4 candidates in whom non-congenital disease was identified or suspected. One 16 year old male candidate admitted to a history of Kawasaki' disease of the coronary arteries as a six year old infant. He had a normal examination, ECG and echo but was deferred for imaging of the coronary arteries in order to exclude significant pathology.

Three candidates were deferred for investigation of suspected pulmonary artery hypertension. All three were males ages 16, 22 and 32 years. The 22 year old had a murmur on auscultation whereas the other two did not and all three had normal ECGs. In all three cases the pulmonary artery pressure estimates were only minimally raised (reported respectively as 34-36mmHg, 41-46mmHg and 40-45mmHg) on resting echo and there were no other abnormalities detected.

5.4 Discussion

The British Army recruit screening program is the largest occupational screening programme of its kind in the UK, as defined by the numbers screened annually. Over the approximately seven and a half years that the Cardiac Report screening contract was in place in the region of 122,000 potential recruits were assessed at the IRM and 9.1% of these underwent enhanced cardiac screening by Cardiac Report.

This study is the first to look at untrained British Army recruits with no previous known CVD and a murmur heard at auscultation. It is the largest British study of this kind. In total 11,070 candidates (9.1% of the total screened) fitted these criteria and were evaluated by cardiac report. Understanding these data is important in order to better understand the epidemiology of the diseases studied and to design a more effective screening system.

5.4.1 Limitations to this study

This is a retrospective, observational and cross-sectional investigation of the historical screening system. This system was a practical, real-life system and it was not designed to adhere to a well-defined research protocol. As a consequence these data contain multiple potential biases and limitations that we need to consider when weighing the significance of the results.

5.4.2 Limitations in the study population

There are a number of unknowns regarding the population of potential recruits that the cohort seen by Cardiac Report was derived from:

1. We do not know how many candidates were failed at the initial questionnaire stage;
2. We do not know for what reasons candidates were failed at initial questionnaire stage and whether they were for cardiac or non-cardiac reasons;
3. We do not know the drop-out rate of those passed at the initial questionnaire stage, but before the IRM;
4. We do not know how many candidates were failed at the IRM stage;
5. We do not know the reasons candidates were failed at the IRM stage, or the proportions that were due to cardiac or non-cardiac reasons;
6. We do not know the drop-out rate of candidates between being identified with a murmur but otherwise cleared at the IRM and their appointment with Cardiac Report.
7. We do not know the outcome of the candidates deferred for further investigation by Cardiac report.
8. We do not know the health outcomes of the candidates screened.

For example, understanding the voluntary drop-out and medical or other fail rates at each stage of the screening process would be helpful in designing an improved system. Anecdotally many candidates are failed prior to attending the IRM and some of these are for

cardiac reasons; as such the figures for the number of candidates that attended the IRM is undoubtedly fewer than those that originally applied to join the Army. Many candidates drop out voluntarily during the recruitment process and the reasons for this almost certainly varies between individuals. For example, a dramatic increase in the dropout rate was seen following well documented administrative delays to British Army recruiting in 2017 due to computer system and other failures: 47% of applicants voluntarily dropped out during the recruiting process and only 11% went on to join the Army. This effect on the ultimately inadequate recruitment into the British Army was significant enough that a parliamentary inquiry was undertaken with the National Audit Office to address the underlying issues. A reversal to this effect, where candidate drop-out rates were reduced to near-zero, might be easily absorbed by the existing screening infrastructure, but if there were too many candidates it might alternatively overwhelm the screening system; which of these outcomes is likely to occur is unknown without the additional data.

I did look at the feasibility of collecting more information on the larger population from which this Cardiac Report cohort was derived. For logistical reasons analysis of these data was not possible. This was because the data was recorded in different, primarily paper based formats and these were held in multiple locations; it was also unclear whether all these data were still available. For these reasons the analysis was restricted to this relatively clear data set only.

5.4.3 Limitations with the Cardiac Report dataset

5.4.3.1 Screening locations. The majority of referrals arose at the three main recruit selection centres of ADSC Glencourse, ADSC Pirbright and ADSC Lichfield where the majority of candidates undergo selection. In excess of 50 doctors are responsible for the section medicals in these centres. These data cannot differentiate between referring doctors as the referrals were generic, but coded by the originating location. The quality of the examinations performed by individual doctors and the rates of referral were not examined in this study and it is therefore impossible to comment further on this aspect of the data.

The candidates were reviewed in 19 different hospital locations by accredited consultant cardiologists. No analysis of the screenings based on which cardiologist saw the candidate was performed so further analysis of the consultations is not possible.

5.4.3.2 Demographics. These data were clear and accurate with regards to the age and gender of the candidates. Ethnicity plays an important role in the normal cardiac phenotype and this was not routinely recorded in the Cardiac Report clinical summaries. Race was sometimes documented in the cardiologist's report, but only when the cardiologist felt it to be relevant. There were only 14 candidates, all with a suspected cardiomyopathy, where the examining cardiologist thought the phenotype overlapped with a normal racial variant. Ethnic minorities constitute approximately 7.1% of the British Army and understanding more about how race influences screening is important. Unfortunately these data allow no

inferences to be made in this regard and additional research will need to be designed to look specifically at this.

5.4.3.3 Auscultation of murmurs. The identification of a murmur at the IRM occurred with a minimum incidence of 9.1% that on first impression appears high. Historical studies from the 1960s described murmur detection rates in paediatric populations that are far higher than those seen here – up to 60% in one study of 3797 participants and 18.9% in another of 49,573 participants. Smaller but more contemporary studies in athletes have also indicated higher murmur rates such as 13%. Despite this though the results of further investigations still highlighted a high false positive rate. The IRM was a single doctor auscultating for murmurs without corroboration at the time by another clinician. To understand whether this detection rate was reasonable or not would require a prospective study to assess examination technique and interpretation. Furthermore this group was pre-screened based on medical and family history prior to attending the IRM as well as a self-selecting group of candidates that believed they might be physically capable to become soldiers. It is therefore likely that the burden of CVD was lower in this population that the general population.

Cardiologists have been shown to be better at discerning the presence and character of murmurs than other doctors and are the only group of doctors to recognise the majority of heart murmurs. In this study though the reporting of the presence of a murmur and when present its character, by the examining consultant cardiologist, was open to bias. The examining cardiologist already knew that a murmur had been heard by another doctor and might even know the results of the ECG and echo that, for logistical reasons, may have been

performed prior to the physical examination. Furthermore these examination findings were retrospectively reported by the cardiologist at the end of the consultation. No other clinician routinely corroborated the examination findings. So while it is interesting to evaluate these data pertaining to the description of any murmurs present, these results need to be treated with a greater degree of caution than the other results in this study.

5.4.3.4 ECG analysis. The interpretation of the ECG at the time of these screenings was not standardised and the primary resource to judge whether an ECG was normal was the training and experience of the cardiologists performing the screening. This is not an objective system, though it is likely to be relatively better than non-cardiologists examining the ECGs. Until 2010 there were no consensus guidelines on how to interpret the ECG in an objective and systematic manner in young athletes and only since these candidates were screened has this been honed to further minimise the false positive rate. Furthermore it is difficult to justify delving deeper into this set of ECGs as, although they are a large collection from a well phenotyped cohort, they come from the group of candidates in whom a murmur was detected at the IRM. This group only makes up 9.1% of the total population screened at the IRM. While it is important to understand what the 'normal ECG' in the wider screening population looks like and the incidence of abnormalities, this should come from a prospective data collection rather than this dataset.

5.4.3.5 Echocardiography. These scans were performed to the standardised BSE protocol in BSE accredited departments. The images were locally peer-reviewed in cases of pathology or ambiguity by other experts in cardiology and echocardiography. Although no quality

control was performed as a part of this study we can be reasonably confident that these echo studies were performed and reported to a high standard.

5.4.4 Study findings

5.4.4.1 Demographics

There was a predominance of younger males in this group consistent with candidates joining the British Army at school leaving age. The mode age for recruitment was at 17 years, after school-leaving at 16 years of age, with a median of 19 years and a distribution skewed to the right and truncated at 32 years. This cohort was not completely similar to other screening populations in the literature, including amateur school, collegiate and professional athletes in the UK, Europe and the USA, but at the same time it covered a similar spectrum of ages. However, this was a pre-filtered group based on the exclusion of known cardiac disease or a significant family history and the prior detection of a murmur, so consequently the incidence of disease cannot be compared meaningfully with other studies.

Females compared to males and 16 year old adolescents compared with older candidates, had higher murmur detection rates at the IRM. It is unclear why this might be the case, but might be related to their smaller body mass or to a different, more juvenile physiological response to the anticipation of the stressful IRM examination. There was no significant difference in murmur rates at the Cardiac Report medical and no difference in the pass rate between genders.

Male athletes are recognised in other young athletic groups to have a higher mortality rate than females. In this analysis females were found to have a higher murmur detection rate than males at the IRM. Despite this when these candidates were investigated by Cardiac Report there was no difference between genders in the incidence of disease when a murmur was present. This implies that there are gender factors beyond the obvious pathological effects of the disease that might result in males sustaining potentially fatal arrhythmias.

The new developments of symptoms or family history that were not previously declared at the IRM may reflect new symptoms or familial findings. However, the Cardiac Report assessments were arranged to be performed within a fortnight of the IRM and it may be that candidates failed to make these declarations prior to or at the IRM for fear that it might compromise their application. As detailed knowledge of the application was not provided to the Cardiac Report cardiologists it may also be that some candidates with a significant family history or symptoms had declared these and previously undergone investigation elsewhere for which they were cleared by a military occupation medicine doctor to apply to the British Army.

5.4.4.2 Pathological findings

The prevalence of a life-threatening cardiac condition in the general population has been estimated at approximately 0.4%. The prevalence of cardiac disease not associated with sudden death is less well characterised. We know that cardiomyopathy and primary

electrical disease account for the majority of sudden death in young populations and these are arguably the most important conditions to identify through screening. In this cohort, in whom a murmur had previously been identified, the disease detection rate was 6.6%. A large proportion of this disease was not clinically or occupationally significant and 43% of these candidates were passed. In total 3.7% of candidates were deferred or failed.

Primary electrical disease was identified in 0.6% of cases (only 10 of 70 cases were passed) and cardiomyopathies in 1.1% of cases (all of whom were deferred), a surprisingly large proportion given few of these conditions produce a murmur on auscultation and these were pre-screened candidates with minimal or no symptoms or relevant personal or family history. It should be considered though that not all of these cases were confirmed and many candidates required further investigation that might ultimately have excluded disease, but even so these numbers are surprisingly high.

Most of the conditions identified by Cardiac Report were unlikely to present with sudden death; the majority of the structural and congenital disease seen here are more likely to present gradually with heart failure symptoms. Structural disease was found in 4.8% of candidates. Whilst this is a high proportion it is easy to understand why these findings occurred given a murmur had previously been detected in all these candidates. Most of these identified conditions are associated with regurgitant, accelerated or turbulent forward flow or other abnormal heart sounds.

5.4.4.3 Missed cardiac diseases

If we are to interpret the data on the cross-sectional incidence of occult CVD in this population then not knowing the disease that has been missed at the questionnaire and IRM stages means that the data recorded in the results section is the minimum disease burden in the overall potential recruit population. It is unlikely that there was no significant occult CVD in the candidates who were not referred to Cardiac Report. It is also difficult to extrapolate the findings in this cohort, who had a murmur detected at their IRM, to those candidates in whom a murmur was not detected, as the mere fact a murmur was heard presumably selected these candidates into a higher risk group. For example, of the 120 candidates in whom a BAV was diagnosed 52 cases (43.3%) of these had no murmur described by the examining cardiologist, over 80% had less than mild AS and just over half had less than mild AR. It seems possible though that the turbulence of blood flow caused by the anatomically abnormal BAV could cause a murmur given the right loading conditions, so extrapolating the incidence seen in this Cardiac Report group across the whole screened population is not realistic.

In some conditions though, such as those of a solely electrical nature such as LQTS or pre-excitation, where there was no structural disease, such as Ebstein's Anomaly, the incidence of disease is unlikely to be affected by whether a murmur is incidentally found. The incidence of electrical disease in the Cardiac Report population who had no structural abnormality that might cause a murmur, was 66 (0.60%) candidates. Extrapolating this to the whole population of 122,181 candidates screened, an estimate of 728 candidates that might have a primary electrical disease of the heart can be calculated. Whilst in reality the

figure is likely be different to this, it has to make the observer question how many candidates with potentially significant CVD is missed by the recruit screening program and perhaps explains why around 11% of military deaths have a cardiovascular or presumed cardiovascular cause.

5.4.4.4 Hypothesis testing

Hypothesis 1 stated that 'asymptomatic congenital diseases, such as ion channelopathies, accessory pathways, cardiomyopathies and normally functioning bicuspid (non-tricuspid) aortic valves will be discovered as incidental findings when candidates with murmurs are investigated with a resting ECG and echo'. In total 123 candidates had a cardiomyopathy suspected or confirmed and 38 (30.9%) of these had no murmur heard on the day. Of 73 candidates identified with a suspected or confirmed arrhythmia, accessory pathway or ion channelopathy, 52 candidates (71.2%) had no murmur heard on the day. Of 120 candidates found to have a BAV 52 (43.3%) had no murmur heard on the day. These data have therefore shown this hypothesis to be true, thus implying that the current screening system results in the recruitment of many individuals with undetected occult cardiovascular disease. These findings allow us to hypothesise that an ECG and echo may add incremental benefits over a physical examination alone. It seems likely that many candidates that do not have a murmur detected at their IRM successfully pass the medical and are subsequently recruited into the British Army with occult cardiac disease.

Hypothesis 2 stated that 'most murmurs detected at the initial recruit medical are innocent and do not represent disease (the positive predictive value of a murmur is low)'. In this population of potential army recruits a murmur was not heard in 75.4% when examined by a Cardiac Report cardiologist and 1.45% of the murmurs that were heard were described as innocent. The positive predictive value of a murmur detected at the IRM was only 8.3% and as already demonstrated, many of these are incidental findings of cardiomyopathies, anomalous coronary artery or electrical diseases that would not cause a murmur. We can conclude from this finding that a physical examination may have a place in a screening program, but that as a sole test in additional to a medical history, it has a limited utility. The addition of an ECG and echo might potentially improve the Sn and Sp of the British Army screening system.

Hypothesis 3 stated that 'the non-pathological murmurs detected by non-cardiologists at the original screening might be undetectable on another day, under different physiological conditions, and when the auscultation is performed by a trained cardiologist'. We knew in advance of this study that athletes in whom a physical examination is performed have a high rate of detected murmurs, most of which do not represent underlying disease. The finding here that three quarters of murmurs heard at the IRM were no longer detected at the Cardiac Report medical allows us to conclude that the physical examination for a murmur is a poorly reproduced test when the individual examined is under different physiological conditions.

Hypothesis 4 stated that 'A murmur heard by two different clinicians on two different days is more likely to represent disease than a murmur detected at the IRM alone'. These data found the failure rate was 8.2% in those found to have a murmur when examined by the Cardiac Report cardiologist and this was greater than the 5.0% failure rate when a murmur was not heard by the Cardiac Report cardiologist (p=0.0001). This finding is consistent with the hypothesis that an underlying pathology that causes a murmur will be more likely to lead to a detectable murmur on different occasions and under different physiological conditions. What is also notable is that the failure rate remained low in both groups, further emphasising the high false positive rates of cardiac auscultation.

5.4.4.5 The use of a murmur as a screening tool

Without evaluating those candidates at the IRM in whom a murmur was not heard, it was not possible to truly evaluate the utility of using a murmur alone to screen recruits. Despite this drawback though these findings show this test to be a poor screening tool. The NPV is high, but this is likely a reflection of the low prevalence of disease, rather than an indicator that the test is a good test. Given the low disease prevalence the accuracy is unlikely to be a useful measurement and the Matthews Correlation Coefficient is a better assessment of the test. Although a somewhat artificial calculation in this context, the Matthews Correlation Coefficient was only 0.1148; this is a poor score.

In addition to the benefits to the British Army in understanding better the utility of this screening programme, this study has wider benefits. The British Army recruits from the

general population, albeit the candidates are self-selected and as such are in the main able-bodied, athletically fitter than much of the population and generally healthy. Furthermore the first part of the screening programme filters out many of those who are not able-bodied and healthy. Despite these limitations the programme does reflect the wider British society and is pertinent from the perspective of examining the athletic young adult population.

5.4.4.6 Implications to recruit cardiac screening in the British Army

The cardiac component of the recruiting process is a particularly important aspect of the screening programme for several reasons. Most importantly the conditions sought are medically important as some lead to sudden death whilst others put candidates at a higher risk of disease progression or other complications, such as infective endocarditis. The finding of a murmur is also important because of the additional financial costs to the screening program. Individuals with a murmur are not allowed to proceed to the physical assessment components of the selection process and are therefore sent home, leaving a vacancy in the downstream selection process. This vacancy is obviously a lost or delayed opportunity to recruit someone into the Army and as the candidate might have passed the IRM the personnel and additional catering facilities must be available for the remainder of their selection stay. Although the economics of this screening system was not investigated, these factors cannot be a negligible expense when >11,000 candidates are deferred on account of a murmur. When a murmur is identified there is the further expense to the Army of the investigations and consultation with a cardiologist; the costs in rail and other transportation fares to attend the appointment and to then return to reattempt selection, as well as an administrative burden to coordinate these. If added to this a number of

candidates drop out because the inconvenience of the screening outweighs their motivation to join the Army, then these already sunk costs are lost completely. Candidates in whom a murmur is detected may also be worried about what this represents from both a health and recruiting perspective; in most cases this concern is likely to be unwarranted.

Despite these high costs, as it stands this system has a high false positive rate and consequently results in unnecessary delays and worry to many candidates undergoing the IRM. The system is also likely to fail to identify most of the candidates applying to the British Army with functionally normal BAV, occult electrical diseases, asymptomatic cardiomyopathies and other asymptomatic diseases that do not cause a murmur to develop. The epidemiology studies in the first part of this thesis clearly illustrate a low level of cardiac morbidity and mortality as a consequence of these diseases. Identifying these currently undetected and untreated cardiac diseases could be partially improved by optimising the screening system used at the IRM.

The taxpayer should expect that any costs are reduced as far as possible and this applies this screening programme as much as any other area of public expenditure. These costs can be justified if a serious disease is diagnosed, but as this only occurs in 4.2% of all the candidates seen by Cardiac Report this system is likely to be expensive and yet also remain ineffective. Identifying and applying interventions to this screening system to improve the efficacy of the system and the efficiency in which it is run is therefore important.

Based on these data we were able to propose a number of changes to the selection system that allowed it to be streamlined. These included a better system to perform the selection process, so the cognition tests and candidate interview were performed prior to a candidate being sent home. This meant candidates passed by Cardiac Report could return only for an abbreviated medical assessment (they had been cleared aside from an isolated murmur at their first IRM) and physical testing. These simple improvement measures did not however alter the finding that 9.1% of candidates were found to have a murmur and were deferred for further investigation. Nor did it change the fact that screening for a murmur alone failed to identify most candidates with a cardiomyopathy or primary electrical disease.

I therefore proposed a new system where all candidates received a resting 12 lead ECG and the interpretation of this was standardised against clearly defined, evidence-based, contemporary criteria. Based on the examination and ECG findings those candidates in whom an echo was indicated would then have an echo performed on the day at the selection centre. This new system was to be prospectively studied and is the focus of the next section of this doctoral thesis.

5.5 Key findings

1. The potential army recruits examined were aged 16 to 32 years, the majority were male (90.7%).

2. The detection of a murmur in asymptomatic Army recruits with no medical or family history is at least 9.1% at the IRM.

3. Females compared to males and 16 year old adolescents compared with older candidates, had higher murmur detection rates at the IRM.

4. On re-examination by a Cardiac Report cardiologist, on a different day, a murmur was not detected in 75.4% of candidates.

5. There was the potential for bias in the reporting of murmurs by the Cardiac Report cardiologists.

6. Most murmurs detected by a Cardiac Report cardiologist were described as systolic rather than diastolic.

7. Systolic murmurs detected by a Cardiac Report cardiologist and described as 'innocent' were predominantly in candidates in whom no cardiac disease was identified (94.4%).

8. Candidates in whom a non-innocent systolic murmurs was detected by a Cardiac Report cardiologist had a higher detection rate for underlying cardiac disease, but even so the majority (88.4%) were passed with no significant cardiac disease identified.

9. Murmurs described as diastolic by a Cardiac Report cardiologist were rare but the positive predictive value of detecting a cardiac disease when present was 90.1%.

10. The majority of candidates (97.1%) in whom no murmur was detected by the Cardiac Report cardiologist were passed with no underlying cardiac disease detected. Therefore most murmurs detected at the initial recruit medical were innocent and did not represent disease.

11. A murmur heard by two different clinicians, on two different days, appears more likely to represent disease than a murmur detected at the IRM alone.

12. Screening asymptomatic candidates, with no medical or family history of cardiac disease, with a physical examination that identifies a murmur on two occasions, has a low positive predictive value of 8.3%. Although a somewhat artificial calculation due to the incomplete data, an estimate of the Sp (76.5%) and Sn (48.1%) indicate that this test alone has a poor utility for screening.

13. Following investigation by Cardiac Report there was no difference between genders in the incidence of disease when a murmur was detected at the IRM.

14. Following investigation by Cardiac Report 6.6% of candidates, in whom a murmur was detected at the IRM, were found to have a confirmed or suspected abnormality. Of these 43% were passed. In total 3.7% of candidates investigated by Cardiac Report were deferred or failed due to the detection or suspicion of cardiac disease.

15. Of candidates in whom a murmur was detected at the IRM, 4.8% had a structural disease (valvular disease, septal defects, other abnormalities) identified.

16. Of candidates in whom a murmur was detected at the IRM, cardiomyopathy was suspected or diagnosed in 1.1% of cases, a rate higher than expected from the epidemiology of the general population. All these candidates were deferred or failed.

17. Of candidates in whom a murmur was detected at the IRM, primary electrical disease was suspected or diagnosed in 0.6% of cases; 85.7% of these candidates were deferred or failed.

18. Of candidates in whom a murmur was detected at the IRM, non-valvular congenital structural disease was identified in 201 candidates (1.8%).

19. Inherited or congenital diseases were identified in asymptomatic candidates in whom there was minimal medical or family history of cardiac disease.

20. Of the 120 candidates in whom a BAV was identified 43.3% had no murmur heard by the examining Cardiac Report cardiologist.

21. When a BAV was identified 53.3% had at least mild BAV dysfunction, aortic root dilatation or rarely, aortic coarctation; the remaining 46.7% were functionally normal.

22. The ECG was not a useful investigation to identify a BAV and was normal in 95% of cases.

23. Mitral valve prolapse was only seen in 0.2% of cases.

24. It is likely that most of the cardiomyopathy and primary electrical disease cases were identified as incidental findings as in most cases no murmur was detected by the Cardiac Report cardiologist.

25. It is likely that candidates in whom no murmur was detected at the IRM will also have a low prevalence of cardiomyopathy and primary electrical disease that is not detected prior to their recruitment into the British Army. The current screening system is therefore likely to fail to identify a large proportion of potentially life-threatening cardiac disease.

26. Cardiac auscultation alone appears to delay the recruiting process, may potentially worry candidates in whom a murmur is detected and requires an expensive and complex administrative, logistical and medical system to ultimately clear most candidates of any significant cardiac disease.

27. Effective cardiac screening might be better achieved with additional ECG and echo, both of which add incremental benefits over a physical examination alone.

28. Although not formally evaluated only 2.8% of ECGs were considered to be abnormal by the Cardiac Report cardiologists. This is lower than studies published in the literature. Further systematic investigation into the ECGs seen in this population needs undertaking.

5.6 Acknowledgements

I must acknowledge the help of Dr Richard Bogle from Cardiac Report Ltd and Cardiology registrar Dr Douglas Cannie whose assistance enabled this study to take place.

Chapter 6: Screening for cardiovascular disease in British Army potential recruits with or without an additional electrocardiogram and echocardiography

6.1 Background

As described in the previous chapter the IRM includes a history and physical examination consistent with the AHA guidelines on pre-participation screening for cardiac disease in athletes. Evaluating the third part of this system, associated with the further investigation by Cardiac Report of candidates in whom a murmur is detected, demonstrated that the use of auscultation to detect a murmur with no other investigations performed unless a murmur was detected, was inefficient, ineffective and presumably expensive.

The ESC guidelines on pre-participation screening for cardiac disease in athletes recommend the integration of an ECG into the pre-participation evaluation, but this recommendation is not universally accepted due to the perception that it increases the cost of screening and requires the screening doctors to process an additional competency in ECG interpretation whilst still being associated with poor Sn and Sp and in particular a high false positive rate. Echo is not recommended by any sports or cardiology association for the routine pre-participation screening of all athletes, primarily because of the increased time and resources required to perform the screening. Anecdotally the routine use of echo is used in some situations though, such as to screen high value sportsmen where there is a large financial

consequence to a disease being found. Furthermore, echo is a first line follow-up investigation for many of the physical examination or ECG abnormalities detected and in itself can be used to exclude disease in many patients.

I hypothesised that in this population of potential British Army recruits the addition of an ECG to the screening system would identify more primary electrical disease and cardiomyopathy than the existing system. These are probably the highest value diseases to detect as they account for the majority of deaths in young populations. They are not usually thought to be associated with a murmur on examination.

Ideally a screening system would bring the utility of echo to the candidates on the day of their screening; the intention being to accelerate the screening process as candidates would undergo echoes for the investigation of murmurs when detected during the physical examination or when indicated by pre-defined ECG findings. This would reduce the number of candidates deferred on the day of their screening, thus allowing more candidates to immediately progress to the physical evaluation of recruit selection. It would also eliminate the cost of transporting them to the Cardiac Report screening location, the costs associated with processing those passed by Cardiac Report and the cost of transporting them back to the selection centre for ongoing assessment. Overall this might reduce the costs of screening whilst increasing the Sn and Sp of the cardiac screening process.

The costs involved in the pre-existing screening system, (including the IRM and Cardiac Report when indicated) are not accurately calculable. The British Army finances the total cost of the screening process, including the cardiac screening elements. These costs include transport to and from the recruiting centre, the IRM itself and in the event of a deferral requiring investigation by Cardiac Report, the transport costs of attending the Cardiac Report consultation, the investigation and consultation and of reattending the IRM. These costs themselves are opaque. For example, candidates may be deferred for more than one reason; they may have an isolated murmur detected, but also need an opinion for another medical query unrelated to their cardiovascular system; the number of candidates in whom this occurs is unknown. There are additional costs for the overnight accommodation, meals and administration. All these costs are integrated into the entire selection process that the IRM constitutes only a part. In the event a candidate is deferred there is an opportunity cost in that there is a space in the follow-on selection process involving assessment of educational level, interviews and physical assessments that need to be financed whether a candidate is present or absent following deferral. In addition the cost of the Cardiac Report consultation and investigation is commercially confidential and not released for the purposes of this research. Similarly the transport costs were not available, but involved train fares that could be in excess of £100 to attend the selection centre or Cardiac Report consultation or be met by the candidate who made their way at their own expense.

The cost of screening is also not only restricted to the screening process itself and also integrates the costs of subsequently investigating candidates in whom an abnormality was identified. Depending on the abnormality detected this might just require a normal echo to

pass the screening or in a suspected cardiomyopathy it might include multiple expensive investigations. For abnormalities that need an invasive procedure, such as an electrophysiology study, this could add considerably to the cost. A cost-effectiveness analysis would be helpful in evaluating the different systems available for screening.

6.1.1 Hypotheses. The following hypotheses were to be tested:

1. In potential recruits to the British Army, attending the Initial Recruit Medical, the addition of a 12 lead ECG to the physical examination improves the Sn and Sp of pre-participation cardiac screening, when compared to physical examination only.

2. The use of more contemporaneous guidelines on ECG interpretation reduces the false positive rate whilst not increasing the false negative rate.

3. An alternative system of screening that utilised a physical examination and an ECG for all candidates and when indicated an echo at the selection centre on the day of the IRM would be more cost effective than the current system.

In addition this project set out to show that the placement of an echo service at the recruit selection centre was feasible in order to facilitate the efficient progression of most recruits through the recruit selection process.

6.2 Methods

6.2.1 Inclusion and exclusion criteria

All candidates aged between 15 and 32 years attending the IRM for British Army selection at the Pirbright recruiting centre were provisionally eligible to be recruited into this study, irrespective of their race or gender. All candidates attending the IRM had undergone the first part of the medical screening that included the completion of a questionnaire excluding cardiac symptoms, a history of cardiac disease, or a family history of sudden death or premature cardiac disease in a first degree relative. Infrequently candidates with previously managed cardiac disease attended for the IRM. Prior to attending these candidates had been assessed by an Army occupational medicine physician, usually in correspondence with a specialist in the condition and it was felt their cardiac condition would not pose a bar to service. In order to concentrate on detecting asymptomatic and unknown disease in this population these candidates were excluded from this study. The standard selection days were either all male or all female candidates with the method of candidate selection within each day's IRM followed the same pattern regardless of gender.

6.2.2 Study recruitment

Candidates were aware in advance of their arrival that this research project was underway and had advance opportunity to read the briefing material. The standard protocol for the IRM began with the candidates arriving at the medical centre for their medical. They were sat down in the waiting room and were called forward in turn for each aspect of the standard screening protocol that included visual acuity and colour vision assessment, urine

dipstick sampling, height, weight, blood pressure, audiology and spirometry. These 'work-ups' were performed prior to their consultation with a doctor. Due to the difficulties of recruiting into a research study without disturbing the normal daily operations of the already busy selection process, the first candidate not immediately involved in any of these aspects of the screening program was selected at the beginning of each day and given the opportunity to participate in the research. A verbal briefing was provided by the investigator and there was an opportunity for the candidate to ask questions. Candidates were questioned to ensure they had no new symptoms of cardiac disease or new family history; they were not recruited into the study if either of these were positive. If they were happy to participate then written consent was obtained. Once the study investigations on this candidate were completed they were returned to the waiting room and they continued with their standard screening work-ups. The next available candidate awaiting their work-ups was then given the opportunity to participate in the same way as the previous candidate. Successive candidates were offered entry to the study until the end of each recruiting day. Candidates recruited into the research were therefore recruited prior to their consultation with the occupational physician.

6.2.3 Study investigations and protocol

All candidates recruited into the research project underwent a physical examination that included a record of their height and weight, a blood pressure measurement, palpation of their peripheral pulses, assessment for the stigmata of Marfan Syndrome and the auscultation of the heart sounds. The blood pressure measurement was performed using an arm cuff with a calibrated automatic Omron M6 Comfort Digital Blood Pressure Monitor

(Omron Healthcare, Hoofddorp, Netherlands). The blood pressure was measured with the candidate lying at rest and angled at 30 degrees on the examination couch. The stigmata of Marfan Syndrome specifically sought are detailed in the 2010 Revised Ghent Nosology[107] and included long digits and limbs, a tall and thin body habitus, pectus excavatum or chest asymmetry, scoliosis or thoracolumbar kyphosis, reduced elbow extension, flexible joints, flat feet, crowded teeth and skin striae.

Auscultation of the heart sounds was performed by a trained investigator using a stethoscope (Littmann Cardiology IV, 3M United Kingdom PLC, Bracknell, UK) and the outcome recorded. Auscultation was performed both standing and supine with all areas of the anterior chest wall auscultated. A repeat examination of the heart sounds was performed during the physical examination performed by the occupational physician undertaking the standard screening process. If either examiner detected a murmur then this was considered as a positive murmur detection. These candidates would have undergone an ECG and echo by Cardiac Report under the standard screening process. A chaperone was routinely offered for all candidates and as the investigator was male, the chaperone was always present for female candidates.

The primary investigator, a cardiology registrar trained in the interpretation of screening ECGs, acquired the ECG in all cases. In all candidates a resting 12 lead ECG was undertaken with either a Mac 3000 or Mac 5500 ECG recording device (GE Healthcare, Chicago, USA) using adhesive stickers attached to prepared skin and in the standard positions. Patients were at rest and lying supine at 30 degrees for the ECG recording. The ECGs were printed at

25mm/s and amplification of 0.1 mV/mm. Candidates who were tachycardiac or hypertensive at rest were allowed to rest with the lights dimmed for up to 20 minutes before the tests were repeated.

The automatic measurements performed by the GE Mac software for the heart rate, PR, QRS and QT durations and QRS axis were visually checked to avoid gross mistakes and these were recorded. These values were used primarily as they would be reproducible in a future scaled-up screening programme. The QTc was manually measured in all cases using the 'teach the tangent' method[108] with the longest QTc in any lead considered the absolute QT. ECG interpretation was undertaken by the primary investigator, a cardiology registrar, at the time with a real-time visual review of the ECG by the cardiac physiologist performing the echo who was trained in the interpretation of these screening ECGs. In cases of diagnostic uncertainty the ECG was reviewed in real time by Prof Sanjay Sharma or Prof Elijah Behr. A second cardiology registrar performed a further review of the ECG later in order to corroborate any normal or abnormal findings. Inter-observer and intra-observer variability was calculated using the Cohen's kappa coefficient (κ) method[109] for those variables that contributed to the abnormal findings within each screening system. Electrocardiograms were analysed according to published criteria: the guidelines used were the ESC 2010 Guidelines that were the only published guidelines when this study was initiated. Comparison was later made with the Seattle criteria and the 2017 International recommendations.

Although the 2010 guidelines were used for analysis there were several differences in the protocol used from the perspective of allowing candidates to pass on the day. Firstly there was no lower cut-off for a short QTc that would require deferral. Secondly the upper QTc cut-off for deferrals was set longer than the 2010 guidelines: for males it was set at 470ms and for females 480ms. These decisions were based on published a high false positive rate and poor evidence of efficacy at the levels set in the then 3 year old guidelines with a view of balancing the needs of this research study with the practical operational recruit screening process that this study was operating alongside. It was felt these criteria were justifiable as in the former case of the short QTc, no lower cut-off had been convincingly ascertained as pathological[110 111 112]. In the latter case of a prolonged QTc, it was felt that the weight of evidence was for this longer duration to reduce the false positive rate on the day[113 114 115 116 117].

***Figure 6.1: Image of the research room at Pirbright selection centre**. The Vivid I echo machine and GE Mac 5500 ECG machine used for the study are seen along with a laptop computer on the desk that was used to upload the echo studies onto the Ultralinq website.*

A transthoracic echo was prospectively performed in all volunteers by a BSE accredited sonographer using a Vivid I portable echo machine (GE Healthcare, Chicago, USA). Echos were performed with candidates primarily in the left lateral position to optimise the imaging quality, but other positions were used as required. Measurements were performed simultaneously and corroborated with the investigator immediately following the case. All the standard BSE measurements were recorded as well as additional measurements of the right ventricle. All images were uploaded in real-time onto an encrypted online system

(UltraLinq Healthcare Solutions,New York, USA) that allowed remote image review. In studies where there was disagreement or uncertainty about the findings the images were reviewed online by an echo specialist (Dr Rajan Sharma, Consultant Cardiologist at St George's Hospital). The room used for acquiring the ECG and echo is shown in figure 6.1.

At the end of this consultation with the examining occupational physician the candidate was discussed and if a murmur had been detected then this was recorded. Candidates in whom a murmur was detected and that had a normal ECG and echo, were passed without referral to Cardiac Report. If a finding in the cardiac screening was suspicious for, or detected a cardiac pathology that would be a bar to service, then this was discussed with the candidate who was appropriately counselled. A plan for further investigation and management was made and this was communicated verbally and as a letter to the candidate's GP that was given to the candidate. The GP referral letter was also posted directly by the investigator to the candidate's GP.

6.2.4 Additional investigations

Further investigations were determined by ECG indication or when a diagnosis was made, the clinical indication. Candidates requiring further investigation were referred to their GP for these to be arranged. Where possible they were assessed at St George's Hospital by the clinical team of Prof Sanjay Sharma or Prof Elijah Behr. For candidates assessed at St George's Hospital an appointment within two weeks was arranged before the candidate departed the recruiting centre. Many candidates requested to be seen at a centre local to

them as Pirbright was the recruiting centre for the southeast, south and south west of England. When investigations were performed in a hospital other that St George's Hospital then the outcome was requested from their clinical team with the consent of the candidate.

The 'pragmatic' gold standard to detect or exclude cardiac disease included a resting 12 lead ECG, high lead ECG, echo (at the recruit training centre) and other investigations elsewhere, when clinically indicated. These additional investigations included, but were not exclusive to, additional ECG or functional testing (i.e. exercise stress testing, Holter monitoring, electrophysiological studies) and imaging modalities (cardiac magnetic resonance, computed tomography or other echocardiographic scanning). Table 6.1 provides a summary of the investigations requested depending on the ECG findings.

Any additional clinical investigations that the investigator felt were indicated was specified in the individualised deferral letter to the candidate's GP. The interpretation of additional tests was undertaken by the relevant specialist and not necessarily the investigators. Eligibility for enlistment was decided using the military occupational medicine consensus guideline as described in Appendix A.

6.2.5 Cost effectiveness analysis

The cost of the screening can be calculated as a cost to the British Army or as a cost overall to the British taxpayer who finances both the NHS and the British Army. The investigations generally indicated for specific screening abnormalities are described in table 6.1. A

comparison of the costs of screening using the current system utilising Cardiac Report was made with i) examination only, but the ECG and echo in those with a murmur performed at the selection centre and the responsibility for decision making moved from Cardiac Report to the occupational physicians performing the IRM; ii) ECG interpretation using the different international recommendations only and iii) a combination of examination and ECG interpretation.

The costs of the physical examination at the recruiting centre was calculated at £30. This was calculated as the cost of an occupational physician paid at £80 per hour (a rate of 3 examinations per hour) plus consumables and other miscellaneous costs. The cost of the original health questionnaire was not included as it was already integrated into the multi-system screening process.

The cost of the ECG at the selection centre was calculated at £5. This was calculated based on an equivalent NHS band 4 practitioner (approximately £22k per annum) recording 36 x ECGs in the morning and for a third of their working day, plus the cost of an ECG machine at £2500 each over 4 years (£625 per annum) and consumables. The NHS tariff for an ECG was £5.

The cost of an echo at the selection centre was calculated at £65 each, but this did not include the hosting of images or the governance mechanisms needed to ensure quality. This £65 cost per study was calculated as the salary of an NHS equivalent band 7 physiologist

with BSE accreditation (approximately £40k per annum) working 4 days per week and performing 7 echos daily for 40 weeks per annum, plus the cost of an echo machine (estimated at £40k over 4 years; £10k per annum) and approximately £10 per study for administration, governance and web hosting of the recorded images. The NHS tariff was greater than this at £75 per study.

The costs for the secondary care investigations were calculated using the 2014-15 NHS Tariff payments system in Great British Pounds (£). The cost for genetic testing was obtained from the national molecular centre for clinical genetics in Oxford, UK. The costs of the IRM physical examination and investigations are difficult to calculate, but for the purposes of this modelling the tariffs were estimated.

The costs presumed that the ECG and echo would be repeated by the cardiologist at the hospital following referral. The actual cost of a consultation with Cardiac Report was unknown so the additive cost of a consultation, ECG and echo was combined using the NHS tariffs at £410. As this was a private sector contract it might have been greater than this. The costs for all consultations and investigations are summarised in table 6.2.

6.2.6 Statistical analysis

Data collected for each candidate included: gender, ethnicity, date of birth, height, weight, whether a murmur was auscultated and ECG and echo findings. Analysis of the screening test efficacy was performed using a standard 2 x 2 table. Comparison between screening

with and without an ECG was made. Furthermore a review of candidates undergoing further investigation was also performed to obtain the positive predictive valve of using an additional echo on the day of the screening. Descriptive statistics of the ECG and echo findings were obtained. Categorical variables are expressed as percentages. The Chi-squared test or Fisher's exact test were used to compare categorical variables. Continuous variables were expressed as means and standard deviation. Sensitivity, Sp, negative and positive predictive valve were expressed as percentages. Statistical significance are defined as a two-sided P-value of <0.05 (95% CI of the mean and upper and lower 5% and 95% of the population).

ECG Finding	Exercise ECG	Echo	Holter	ETT	CMR scan	CT / Angio	Genetics	EPS
Sinus bradycardia rate <30 bpm	PIN	NNR	NNR	NNR	NNR	NNR	NNR	NNR
First degree heart block	NNR	NNR	NNR	NNR	NNR	NNR	NNR	NNR
Second-degree Mobitz Type 1	PIN	NNR	NNR	NNR	NNR	NNR	NNR	NNR
Second-degree Mobitz Type 2	MBN	MBN	MBN	MBN	S	S	S	S
Complete AV block	MBN	MBN	MBN	MBN	S	S	S	S
Premature ventricular contractions	C	C	C	C	C	S	S	S
Atrial tachycardia (SVT, typical flutter, Afib)	C	C	C	C	NNR	S	S	S
Ventricular arrhythmia (>2 x PVCs or NSVT)	C	C	C	C	C	S	S	S
Right or left atrial enlargement	NNR	PIN	NNR	NNR	NNR	NNR	NNR	NNR
Right- or left-axis deviation	NNR	PIN	NNR	NNR	NNR	NNR	NNR	NNR
Pathological Q waves	NNR	MBN	MBN	MBN	MBN	S	S	NNR
Ventricular pre-excitation	NNR	MBN	NNR	NNR	NNR	NNR	NNR	MBN
Isolated LVH by voltage	NNR	PIN	NNR	NNR	NNR	NNR	NNR	NNR
RVH by voltage	NNR	PIN	NNR	NNR	NNR	NNR	NNR	NNR
Incomplete RBBB	NNR	PIN	NNR	NNR	NNR	NNR	NNR	NNR
Complete right bundle branch block	NNR	PIN	NNR	NNR	NNR	NNR	NNR	NNR
Complete left bundle branch block	NNR	MBN	C	C	C	S	S	NNR
Nonspecific intraventricular delay	NNR	MBN	MBN	MBN	MBN	S	S	S
ST-segment depression	NNR	MBN	MBN	MBN	MBN	S	S	NNR
Early repolarisation	NNR	PIN	NNR	NNR	NNR	NNR	NNR	NNR
Brugada-like early repolarization pattern	NNR	MBN	S	S	S	NNR	S	S

Long-QT interval	NNR	MBN	MBN	MBN	MBN	NNR	S	NNR
Short-QT interval	NNR	NNR	NNR	NNR	NNR	NNR	NNR	NNR
T-wave inversion	NNR	MBN	MBN	MBN	MBN	S	S	NNR

Table 6.1: General summary of the diagnostic tests required given a specific ECG finding. *Some findings (green) could be passed directly on the day if an isolated finding with either an exercise ECG and / or echo if they were normal. Other findings, such as a Type 1 Brugada pattern would always result in a fail. The outcome depended on the diagnosis, treatment and individual context. PVC = Premature ventricular complex; NSVT = Non-sustained VT; PIN = Pass if normal; NNR = Not Normally Required; MBN = Must be normal; C = To be considered in context; S = Specialist decision.*

6.2.7 Ethical considerations

Informed consent was obtained as described. Approval from the MOD REC committee was obtained for this study (Protocol 12/gen/312). All identifying information was secured using Trucrypt encryption software (www.trucrypt.org). Data was pseudo-anonymised by a unique candidate indicator once collected.

Expense	Cost
Occupational medicine consultation at IRM	£30
Cardiac Report consultation	£410
ECG at IRM	£5
Echo at IRM	£65
Hospital appointment and follow-up	£660
ECG in hospital outpatients	£5
Echo in hospital outpatients	£75
ETT	£170
Holter	£170
CMR	£210
Cath lab procedure (PDA closure or EPS)	£2,000
Genetics	£600
TOE	£290

Table 6.2: Summary of the costs of different elements of the cardiac screening and subsequent investigations in secondary care.

6.3 Results

6.3.1 General characteristics

Recruiting for the study took place between 14 Jan 2013 to 16 Dec 2014. There were logistical restrictions in accessing candidates, unrelated to this study, resulting suspension of recruiting between 4 April 2013 and 30 July 2013 and then limited to only a few candidates per day thereafter.

A total of 834 volunteers were recruited into the study and all underwent a physical examination, an ECG and an echo. Males constituted the majority of participants with a total of 735 (88.1%) candidates, reflecting the predominance of male applicants to join the British Army (table 6.3, figure 6.2). The ages ranged from 15 to 32 years with a median age of 19 years (tables 6.3 and 6.4). The majority of volunteers were White British (83.3%) but a large number of nationalities and ethnicities were represented (table 6.5). There was no difference in the self-reported training time between genders.

6.3.2 Physical examination findings

On average males were taller and heavier than females, but there was no difference in the mean body mass index. Although the heart rate on examination and the diastolic blood pressure did not differ between genders the systolic blood pressure was higher in males. Comparison of white and black males showed the black males were slightly older and had a higher BMI and diastolic blood pressure than white candidates. None of the candidates examined had a radio-femoral delay detected. One 23 year old male candidate was

deferred due to stigmata suggestive of Marfan Syndrome (high-arched palate, pectus excavatum, long limbs). This candidate was assessed in a specialist Marfan's clinic where the condition was excluded. His echo images were poor quality but a CMR was acceptable and ultimately he passed selection into the Army.

Characteristic	Males	Females	p-value	Total
Median age	20	21	-	20
Gender (%)	735 (88.1)	99 (11.9)	-	834
Ethnicity (%)				
White	612 (88.2)	82 (11.8)	-	694 (83.3)
Black -African or African Caribbean	81 (88.0)	11 (12.0)	-	92 (11.0)
South Asian	29 (93.5)	2 (6.5)	-	31 (3.8)
Others	14 (82.5)	4 (23.5)	-	17 (2.0)
Mean hours training / week (SD)	7.1 (5.1)	6.8 (4.8)	0.64	7.1 (5.1)
Mean preparation time – weeks (SD)	24.6 (26.2)	27.0 (35.1)	0.49	24.8 (27.3)

Table 6.3: Summary of participant characteristics by gender.

Age	Males (% of males)		Females (% of females)		Total (%)	
15	5	(100)	0	(0)	5	(0.6)
16	93	(92.1)	8	(8.0)	101	(12.2)
17	69	(90.8)	7	(9.3)	76	(9.2)
18	91	(90.1)	10	(10.0)	101	(12.2)
19	102	(91.9)	9	(8.2)	111	(13.4)
20	49	(87.5)	7	(12.5)	56	(6.8)
21	61	(84.8)	11	(15.3)	72	(8.7)
22	52	(88.2)	7	(11.9)	59	(7.1)
23	42	(87.5)	6	(12.5)	48	(5.8)
24	36	(80.0)	9	(20.0)	45	(5.4)
25	35	(83.4)	7	(16.7)	42	(5.1)
26	17	(85.0)	3	(15.0)	20	(2.4)
27	22	(75.9)	7	(24.2)	29	(3.5)
28	10	(91.0)	1	(9.1)	11	(1.4)
29	8	(100)	0	(0)	8	(1.0)
30	14	(87.5)	2	(12.5)	16	(2.0)
31	14	(87.5)	2	(12.5)	16	(2.0)
32	16	(88.9)	2	(11.2)	18	(2.2)
Totals:	**735**	**(88.1)**	**99**	**(11.9)**	**834**	

Table 6.4: Distribution of study participants by age and gender.

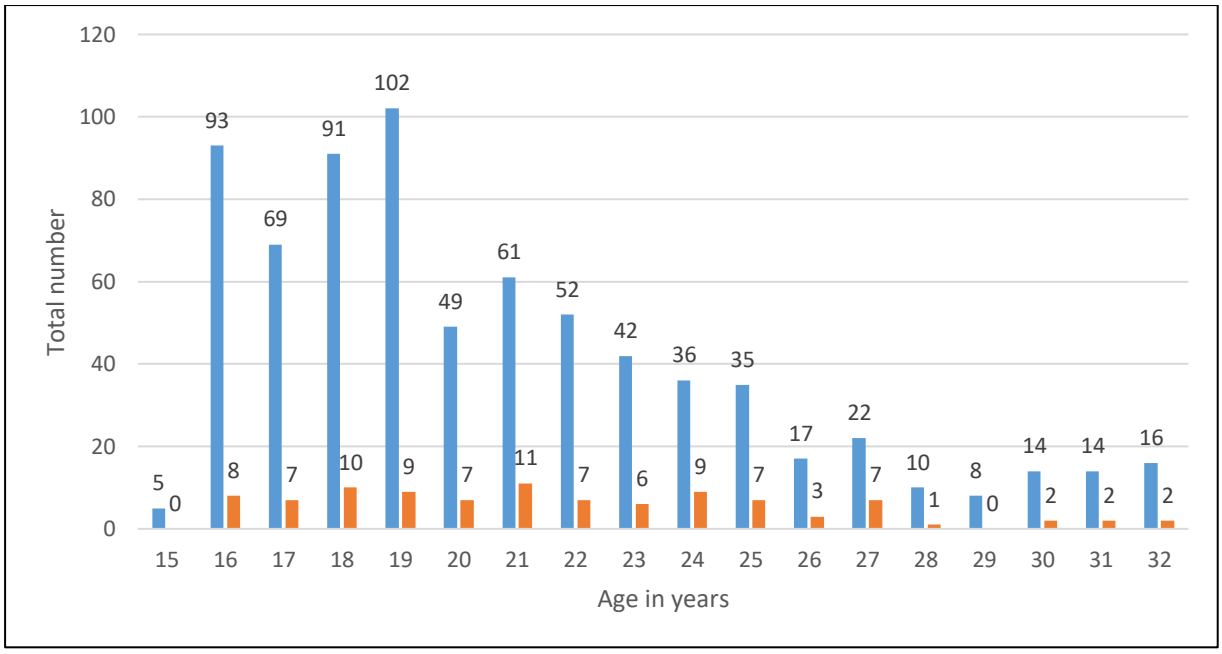

Figure 6.2: Distribution of study participants but age and gender (males in blue; females in red).

A murmur was detected in 136 (16.3%) candidates. Of these the investigator felt 76 cases were likely to be innocent flow murmurs leaving only 7.2% of candidates with a potentially pathological murmur clinically. There was no difference between genders in the proportions of candidates with a murmur though a murmur was detected more frequently in black males than white males.

6.3.3 ECG quality and interpretation reproducibility

The ECG was of good diagnostic quality in all cases. In some candidates the skin preparation needed to be repeated and meticulous to order to obtain a high quality ECG trace, but it was generally achievable with little effort or extra time. Inter-observer (table 6.8) and intra-observer (table 6.9) variability was generally good. For the more obvious abnormalities, such as detected extra-PVCs, complete RBBB or T-wave inversions in consecutive leads, there was perfect reproducibility. For the slightly more subjective

interpretations, such as left atrial abnormalities or QTc prolongation there was moderate or substantial reproducibility.

6.3.4 Echo quality and interpretation

The quality of the echo images was usually outstanding, presumably as the candidates were young with normal lungs and normal BMIs. In only one case were the images non-diagnostic; this candidate had pectus excavatum and he was deferred in order to exclude Marfan Syndrome. Subsequently a CMR showed a normal heart aside from RV compression by the anterior thoracic wall. All the echo images were acquired by a BSE accredited sonographer and the measurements were visually checked by the primary investigator at the time of the study. A 10% peer review by another sonographer was also undertaken routinely as part of the standard governance of this echo program. Any borderline findings or significant abnormalities were reviewed and confirmed / excluded by a dedicated imaging cardiologist.

6.3.5 ECG findings.

6.3.5.1 Automatic calculations. The GE ECG software automatically calculated several parameters including the heart rate, PR interval, QRS axis and duration, as well as the absolute QT and QTc using the Bazett Formula[118]. These findings are summarised in table6.9. As a check I manually measured the absolute QT and QTc. The two sets of readings were slightly different in that on average the manual measurement was 7.8ms less than the computer calculated reading ($p< 0.0001$) with a similar standard deviation. For the

purposes of this study the automatic calculations were used unless they were clearly incorrect because this would allow reproducibility later.

Ethnicity	Number	Males	Females	Totals (%)
White				**694** (83.3)
White British	*687*	*607*	*80*	
One each of: Jersey (Channel Islands), German, Armenian, Polish, Turkish and two South Africans	*7*	*6*	*1*	
Hispanic				**2** (0.3)
One each of: Colombian and Ecuador	*2*	*1*	*1*	
African-Caribbean				**32** (3.9)
Jamaica	*17*	*13*	*4*	
Grenada	*5*	*4*	*1*	
St Lucia	*3*	*2*	*1*	
St Vincent	*3*	*3*	*0*	
Mixed Caribbean	*2*	*2*	*0*	
Dominique	*1*	*1*	*0*	
Trinidad	*1*	*0*	*1*	
Black African				**60** (7.2)
Cameroon	*6*	*5*	*1*	
Gambia	*3*	*3*	*0*	
Ghana	*22*	*21*	*1*	
Kenya	*6*	*5*	*1*	
Nigerian	*10*	*10*	*0*	
Sierra Leone	*2*	*2*	*0*	
Uganda	*3*	*2*	*1*	
Zambia	*2*	*2*	*0*	
Zimbabwe	*2*	*2*	*0*	
One each of Angola, Congo, Somalia, South Africa	*4*	*4*	*0*	
South Asian				**31** (3.8)
India	*10*	*8*	*2*	
Mauritius	*2*	*2*	*0*	
Nepal	*17*	*17*	*0*	
One each of Bangladesh and Indian Kenyan	*2*	*2*	*0*	

East Asian				**4** (0.5)
One each of Hong Kong, Malaysia, Philippines, Thailand	*4*	*3*	*1*	
Polynesian				**4** (0.5)
Fiji	*4*	*3*	*1*	
Other				**4** (0.5)
One each of: Iraq, Kazakhstan, St Helena, United Arab Emirates	*4*	*4*	*0*	
Mixed				**3** (0.4)
One each of: Greek/Malaysian, South African 'coloured' and Black Jamaican/White British	*3*	*2*	*1*	
			Total:	**834**

Table 6.5: Ethnicity by self-declaration of the study volunteers.

Examination finding	All (n=834)		Males (n=735)		Females (n=99)		
	mean		mean		mean		p value
Age (SD)	21.5	(4.14)	20.8	(4.14)	22.3	(4.03)	0.0014
Height mean cm (SD)	175.7	(7.56)	177.0	(6.85)	166	(5.91)	< 0.0001
Weight kg (SD)	71.5	(10.7)	72.5	(10.48)	62.9	(8.59)	< 0.0001
BMI (SD)	22.6	(2.73)	22.6	(2.75)	22.2	(2.55)	0.1711
BSA Mosteller formula m2 (SD)	1.9	(0.17)	1.9	(0.16)	1.7	(0.13)	< 0.0001
BSA Du Bois formula m2 (SD)	1.9	(0.16)	1.9	(0.15)	1.7	(0.13)	< 0.0001
Systolic BP mean mmHg (SD)	130.3	(13.02)	131.2	(12.93)	123.5	(11.22)	< 0.0001
Diastolic BP mean mmHg (SD)	71	(9.79)	71.1	(9.73)	70.9	(10.39)	0.8490
Asymmetrical brachial BP (%)	0	(0)	0	(0)	0	(0)	na
Radial-femoral delay (%)	0	(0)	0	(0)	0	(0)	na
Stigmata of Marfan's disease (%)	1	(0.12)	1	(0.14)	0	(0)	1.00
Auscultation of a systolic murmur (%)	137	(16.4)	119	(16.2)	18	(18.2)	0.6644
Auscultation of a non-innocent murmur (%)	60	(7.2)	50	(6.8)	10	(10.1)	0.2182

Table 6.6. Summary of the physical examination findings and comparison of all males and all females. *BP = Blood Pressure; SD = standard deviation; BMI = Body mass index; BSA =Body surface Area*

Examination finding	Males (n=735)		White Males (n=735)		Black Males (n=99)		
	mean		mean		mean		p value
Age (SD)	20.8	(4.14)	20.7	3.82	24.0	4.51	< 0.0001
Height mean cm (SD)	177.0	(6.85)	177.3	6.78	176.4	6.41	0.259
Weight kg (SD)	72.5	(10.48)	72.4	10.69	74	8.7	0.197
BMI (SD)	22.6	(2.75)	22.5	2.78	23.3	2.43	0.0138
BSA Mosteller formula m2 (SD)	1.9	(0.16)	1.9	0.16	1.9	0.13	1.00
BSA Du Bois formula m2 (SD)	1.9	(0.15)	1.9	0.15	1.9	0.13	1.00
Systolic BP mean mmHg (SD)	131.2	(12.93)	131.2	12.79	132.1	14.51	0.5584
Diastolic BP mean mmHg (SD)	71.1	(9.73)	70.4	9.7	75.5	8.3	< 0.0001
Asymmetrical brachial BP (%)	0	(0)	0	0	0	0	na
Radial-femoral delay (%)	0	(0)	0	0	0	0	na
Stigmata of Marfan's disease (%)	1	(0.14)	1	0.16	0	0	1.00
Auscultation of a systolic murmur (%)	119	(16.2)	98	16	21	26	0.04
Auscultation of a non-innocent murmur (%)	50	(6.8)	43	7	7	8.6	0.6456

Table 6.7. Summary of the physical examination findings and comparison of white males and black males. *BP = Blood Pressure; SD = standard deviation;*

ECG Finding	Inter-observer variability		
	% agreement	Kappa	Interpretation
Pre-excitation	100	1	Perfect agreement
Right atrial abnormality	99.6	0.878	Almost perfect agreement
Left atrial abnormality	98.8	0.793	Substantial agreement
Complete RBBB	100	1	Perfect agreement
Non-specific intraventricular block (*QRSd>110*)	99	0.709	Substantial agreement
RVH	99.3	0.959	Almost perfect agreement
TWI >1mm in 2 consecutive leads - %	100	1	Perfect agreement
Inferior TWI >1mm	100	1	Perfect agreement
ST-depression >0.5mm in 2 consecutive leads	100	1	Perfect agreement
Gender specific QTc prolongation - Seattle or 2017	99.4	0.526	Moderate agreement
≥2 PVCs per 10 s tracing	100	1	Perfect agreement

Table 6.8: ***Summary of the Cohen's kappa coefficient statistics for Inter-observer variability for the non-calculated characteristic and for QTc prolongation using the Seattle criteria / 2017 guideline cut-off values.*** These comparisons were between two cardiology registrars trained in the interpretation of screening ECGs with the exception of the QTc which was a comparison of the primary investigator and the GE Mac algorithm.

ECG Finding	Intra-observer variability		
	% agreement	Kappa	Interpretation
Pre-excitation	100	1	Perfect agreement
Right atrial abnormality	99.5	0.816	Almost perfect agreement
Left atrial abnormality	98.0	0.656	Substantial agreement
Complete RBBB	100	1	Perfect agreement
Non-specific intraventricular block (*QRSd>110*)	98.4	0.756	Substantial agreement
RVH (*RV1 + SV5 > 10.5mm*	98.8	0.930	Almost perfect agreement
TWI >1mm in 2 consecutive leads	100	1	Perfect agreement
Inferior TWI >1mm	100	1	Perfect agreement
ST-depression >0.5mm in 2 consecutive leads	100	1	Perfect agreement
≥2 PVCs per 10 s tracing	100	1	Perfect agreement

Table 6.9: ***Summary of the Cohen's kappa coefficient statistics for intra-observer variability***. These comparisons were between the initial interpretation by the primary investigator and a second occasion at least 6 months apart.

6.3.5 ECG findings.

6.3.5.1 Automatic calculations. The GE ECG software automatically calculated several parameters including the heart rate, PR interval, QRS axis and duration, as well as the absolute QT and QTc using the Bazett Formula[119]. These findings are summarised in table6.9. As a check I manually measured the absolute QT and QTc. The two sets of readings were slightly different in that on average the manual measurement was 7.8ms less than the computer calculated reading ($p< 0.0001$) with a similar standard deviation. For the purposes of this study the automatic calculations were used unless they were clearly incorrect because this would allow reproducibility later.

6.3.5.2 Cardiac conduction. All the candidates studied were found to be in sinus rhythm as their underlying rhythm. The characteristics of their cardiac rate and AV conduction are summarised in table 6.10. In this population sinus arrhythmia was more commonly seen than not seen and around a quarter of candidates were bradycardic at rest. First degree AV block is well described as an athletic adaptation but was only seen in 1.9% of candidates. Indeed a short PR duration of <120ms with no delta wave was seen in 55 candidates (6.6%). There was no higher degree AV block seen. As discussed below there were 3 candidates with pre-excitation on their ECG. No difference was seen between genders or between white and black males.

6.3.5.3 Borderline abnormal ECG findings. The 2017 ECG interpretation Guidelines consider complete right bundle branch block (RBBB), left or right axis deviation or left or right atrial

abnormalities to be of 'borderline' significance. The frequency these findings were seen in this group is summarised in table 6.11.

6.3.5.4 Atrial abnormalities. A right atrial abnormality was seen in 1.3% of candidates. None of these were associated with cardiac pathology. A left atrial abnormality was seen in 3.1% of candidates and in a greater proportion of candidates within the black male population where 12.3% were found to have this finding. This was a significantly great proportion than in the white male group. The finding of a left atrial abnormality was not frequently associated with disease. One white male candidate with mild MR had a leftward axis and a black male with anterior T-wave inversions also had a leftward axis. The former was passed on the day and the latter was deferred and underwent investigation at our institution that did not identify any disease.

6.3.5.5 Deviation of the QRS axis. Left axis deviation was seen in 3.2% of candidates. The finding of a left axis deviation was not commonly associated with disease. It was only seen in a single case: a 19 year old white male with a VSD. Another white male candidate with T-wave inversions confined to the inferior leads also had a left axis deviation. Following further investigations he was passed. Right axis deviation is less well defined. The classical teaching of >90 degrees would have resulted in a detection rate of 11.9% in this group and this was seen particularly in the white males where 12.9% of candidates had a rightward axis and normal echo. Increasing the cut off to >110 degrees, as suggested in the 2010 guidelines, reduced the positive rate to 2% and if increased further still to >120 degrees the

positive rate dropped to 1%. None of the candidates with a QRS axis >110 degrees was found to have any pathology.

ECG Finding	All n=834		
	Mean	Range	SD
Heart rate bpm	69	41-111	11.86
PR interval - ms	147.9	67-280	23
QRS axis - degrees	59.1	-88 - 256	36.6
QRS duration - ms	94.7	70-152	11.04
Automatic QTc - ms	407.9	322-558	31.72
Manual QTc - ms	400.1	320-561	32.54

ECG Finding	Males n=735			Females n=99			p-value
	Mean	Range	SD	Mean	Range	SD	
Heart rate bpm	68.7	44-111	11.73	70.8	45-112	12.58	0.0978
PR interval - ms	148	67-280	23.18	145	96-210	21.18	0.2225
QRS axis - degrees	59.4	-88 - 256	37.53	55.6	-66 - 108	27.24	0.3307
QRS duration - ms	95.8	70-152	10.44	85.7	72-110	8.06	< 0.0001
Automatic QTc - ms	407.2	334-558	23.5	394.6	322-462	28.01	< 0.0001
Manual QTc - ms	399.5	328-561	35.01	386.2	320-460	30.17	0.0003

ECG Finding	White Males n=613			Black Males n=81			p-value
	Mean	Range	SD	Mean	Range	SD	
Heart rate bpm	69.0	41-111	11.96	66.9	47-91	10.56	0.1329
PR interval - ms	147.6	77-280	22.96	153	92-238	24.3	0.0486
QRS axis - degrees	61.4	-88 - 256	37.85	43.2	-79 - 85	33.41	< 0.0001
QRS duration - ms	96.7	74-152	10.2	89.7	70-124	10.3	< 0.0001
Automatic QTc - ms	409	337-558	23.19	394.3	334-458	23.13	< 0.0001
Manual QTc - ms	401.1	328-561	24.73	387.6	334-458	24.67	< 0.0001

Table 6.10: Summary of the ECG values calculated by the GE Mac software. *Comparison is made between males and females and between white males with black males where appropriate. SD = standard deviation; ms = milliseconds*

ECG Finding	Males n=735		Females n=99			All n=834	
	Positive	%	Positive	%	p-value	Positive	%
Sinus arrhythmia	410	55.8	56	65.9	0.9145	466	55.9
Sinus bradycardia <60bpm	188	25.6	31	31.3	0.0812	219	26.3
Profound sinus bradycardia <30bpm or sinus pauses ≥ 3s	0	0	0	0	na	0	0
First degree AV block	15	2.0	1	1.2	0.7088	16	1.9
Mobitz type 2 AV block or complete heart block	0	0	0	0	na	0	0
Pre-excitation	3	0.4	1	1.2	0.3974	4	0.5

ECG Finding	White Males n=613		Black Males n=81		p-value
	Positive	%	Positive	%	
Sinus arrythmia	349	56.9	39	48.1	0.1532
Sinus bradycardia <60bpm	155	25.28548124	24	29.6	0.4183
Profound sinus bradycardia <30bpm or sinus pauses ≥ 3s	0	0	0	0	na
First degree AV block	13	2.1	2	2.5	0.6911
Mobitz type 2 AV block or complete heart block	0	0	0	0	na
Pre-excitation	3	0.5	0	0	1.00

Table 6.11: Summary of the numbers and percentages of candidates in whom specific ECG findings were identified. *The p-values compare either males to females or white males to black males. The other ethnicities were not included as their numbers were low in this study. na = not applicable*

ECG Finding	Males n=735		Females n=99			All n=834	
	Positive	%	Positive	%	p-value	Positive	%
Right atrial abnormality	11	1.5	0	0	0.3789	11	1.3
Left atrial abnormality	24	3.3	2	2.4	0.7585	26	3.1
Left axis deviation <-30 degrees	25	3.4	2	2.4	0.7606	27	3.2
Right axis deviation >90 degrees	95	12.9	4	4.7	0.0076	99	11.9
Right axis deviation >110 degrees	17	2.3	0	0	0.2463	17	2.0
Right axis deviation >120 degrees	8	1.1	0	0	0.6059	8	1.0
Partial RBBB	68	9.3	1	1.2		69	8.3
Complete RBBB	7	1.0	0	0	1	7	0.8

ECG Finding	White Males n=613		Black Males n=81		p-value
	Positive	%	Positive	%	
Right atrial abnormality	9	1.5	2	2.5	0.374
Left atrial abnormality	13	2.1	10	12.3	<0.0001
Left axis deviation <-30 degrees	22	3.6	2	2.5	1
Right axis deviation >90 degrees	90	14.7	0	0	<0.0001
Right axis deviation >110 degrees	16	2.6	0	0	0.2392
Right axis deviation >120 degrees	8	1.3	0	0	0.6059
Partial RBBB	63	10.3	3	3.7	
Complete RBBB	6	1.0	1	1.2	0.5822

Table 6.12: Summary of the 'borderline' ECG characteristics. *The p-values compare either males to females or white males to black males. The other ethnicities were not included as their numbers were low in this study.*

6.3.5.6 Ventricular depolarisation.

6.3.5.7 Intraventricular conduction delay. A partial RBBB was a frequent finding and was identified in 8.3% of cases. It is not recognised as associated with disease. Complete RBBB is associated with athletic training and in this group was seen in only 0.8% of cases. Two cases of pathology were found to have a complete RBBB: one was a case of probably ARVC discussed below and the other was in fact not a true RBBB but rather a manifestation of the delta wave seen in a pre-excited QRS. No candidates were seen with a complete left bundle branch block (LBBB). A non-specific intraventricular conduction delay of >110ms but <140ms was seen in 1.6% of candidates and all of these were normal aside from a single case of ventricular pre-excitation. There were no candidates with a non-specific intraventricular conduction delay of >140ms.

6.3.5.8 Ventricular hypertrophy. Both left and right ventricular hypertrophy by voltage were seen. Using the Sokolow–Lyon criteria of the sum of the S wave in V1 and R wave in V5 >3.5mV (35mm at standard calibration of 10mm = 1mV), LVH was seen in over a quarter of males and one in ten females. It was also more common in white males than black males (27.2 vs 10.6%)[120]. If the 94 candidates with LVH detected by the alternative Sokolow–Lyon criteria (calculation of the sum of the S wave in V1 to the R wave in V6), all but one of these were also positive for the S wave in V1 to the R wave in V5. Using the Cornell score for LVH did reduce the positive rate to 4.3% if used in isolation. Neither method was correlated with the echo measurements of LVH as it was felt there was little to gain scientifically. Right ventricular hypertrophy by voltage criteria was identified in 9.7% of candidates and was more frequently seen in males than in females (10.9% vs 1.2%). Either RVH or LVH was

detected in 272 candidates (32.6%) and of these 16 candidates were found to have disease of some severity, albeit not significant enough to always result in a screening failure. As a test for pathology this provided a Sn of 21.05%, Sp of 66.23% and positive predictive value of only 5.88% and was therefore a poor test in isolation.

6.3.5.9 Early repolarisation and ST segment abnormalities. The ECG findings due to early repolarisation, the Brugada pattern and epsilon waves are summarised in table 6.14. Early repolarisation, seen as J-point elevation was highly prevalent in leads V2-V4 with >1mm of elevation seen in 70.6% of males and 18.8% of females ($p<0.0001$). Either a slurred or notched ER, seen at the termination of the QRS complex, was seen in 24.6% of the candidates. Both J-point elevation in V2-4 and the slurred or notched element of the QRS in the inferolateral leads were more frequently seen in black males than in white males. Further analysis was not performed as none of the consensus guidelines incorporate the finding of ER within the screening criteria as it is so prevalent in young, athletic populations.

Biphasic T-waves with preceding j-point elevation and convex ST-segment elevation in leads V2-4 have been associated with athletic training and are particularly prevalent in black athletes [121] [122]. In this population it was seen infrequently with a rate of 1.2% in males and 3.5% (n=3) in females. It was not more frequently seen in black males than white males.

ECG Finding	Males n=735		Females n=99			All n=834	
	+ve	%	+ve	%	p-value	+ve	%
Complete LBBB	0	0	0	0	na	0	0
NSIVD *QRSd>110*	13	1.8	0	0	0.3839	13	1.6
NSIVD QRSd>140	0	0	0	0	na	0	0
LVH - SLC (SV1 + RV5>35)	200	27.2	9	10.6	<0.0001	209	25.1
LVH - SLC (SV1 + RV6>35)	94	12.8	1	1.2	<0.0001	95	11.4
LVH by Cornell criteria	30	4.1	6	7.1	na	36	4.3
RVH	80	10.9	1	1.2	0.0004	81	9.7

ECG Finding	White Males n=613		Black Males n=81		
	+ve	%	+ve	%	+ve
NSIVD *QRSd>110*	13	1.8	0	0	0.3839
NSIVD QRSd>140	0	0	0	0	na
Pathological q-waves	0	0	0	0	na
LVH - SLC (SV1 + RV5>35)	200	27.2	9	10.6	<0.0001
LVH - SLC (SV1 + RV6>35)	94	12.8	1	1.2	<0.0001
LVH by Cornell criteria	30	4.1	6	7.1	na
RVH (*RV1 + SV5 > 10.5mm*)	67	10.9	7	8.6	0.7013

Table 6.13: Summary of the ECG findings with ventricular depolarisation abnormalities. *Partial and complete RBBB are included in table 6.12. The p-values compare either males to females or white males to black males. The other ethnicities were not included as their numbers were low in this study.* NSIVD = Non-specific intraventricular delay; SLC = Sokolow–Lyon criteria; LVH by Cornell criteria uses gender specific cutoffs; RVH calculated: *RV1 + SV5 > 10.5mm*

ECG Finding	Males n=735		Females n=99			All n=834	
	Positive	%	Positive	%	p-value	Positive	%
ER - J point elevation >1mm	519	70.6	16	18.8	<0.0001	535	64.1
ER - slurred or notched	182	24.8	23	27.1	0.8044	205	24.6
Biphasic T waves anteriorly	9	1.2	3	3.5	0.1616	12	1.4
ST-depression >0.5mm in 2 consecutive leads	3	0..4	0	0	1	3	0.4
Type 1 Brugada pattern	0	0	0	0	na	0	0
Epsilon waves	0	0	0	0	na	0	0

ECG Finding	White Males n=613		Black Males n=81		p-value
	Positive	%	Positive	%	
ER - J point elevation >1mm	424	69.2	30	37.0	<0.0001
ER - slurred or notched	139	22.7	7	8.6	0.0022
Biphasic T waves anteriorly	6	1.0	2	2.5	0.2374
ST-depression >0.5mm in 2 consecutive leads	1	0.2	1	1.2	0.22

Table 6.14: Early repolarisation and ST segment abnormalities. *The p-values compare either males to females or white males to black males. The other ethnicities were not included as their numbers were low in this study.*

Neither a spontaneous type 1 Brugada pattern nor an epsilon wave was seen on the ECG of any candidate.

6.3.5.10 T-wave changes.

Inverted T-waves of >0.1mV (1mm at standard calibration of 10mm = 1mV) in 2 consecutive leads were seen in 23 candidates (2.8%) and all of these candidates were deferred (table 6.15). Two of these candidates were found to have HCM (discussed below). Of the remainder 8 candidates had inferior T-wave inversion only, significant as using the 2017 guidelines these candidates without symptoms, previous cardiac or family history and a normal examination and echo, could potentially be passed. They all had normal echos on the day and went on to have normal CMR, Holter and exercise tests as well. The 3 females with anterior TWI were all suspected as having a possible juvenile pattern ECG; two of these were aged 16 but the third was 18 years old and this latter case was therefore more suspicious. All these candidates were cleared after further investigation failed to detect disease.

6.3.5.11 Long and short QTc intervals. There were 52 cases of suspected LQTS identified using the 2010 criteria, all in asymptomatic individuals (table 6.15). Although this study was initiated in 2013, the screening protocol used for the study had a pragmatic QTc cut-off in males of 470ms and in females 480ms (as discussed in the methods and later introduced in the Seattle criteria guidelines). Using this cut-off 8 candidates were measured by the GE Mac ECG interpretation algorithm as prolonged. One candidate's prolonged QTc was

associated with pre-excitation and appeared to be inappropriately measured. Another candidate also appeared to be measured incorrectly by the machine on account of ventricular bigeminy. These two candidates were deferred for their pre-excitation and outflow tract ectopy rather than the prolonged QTc. Of the remaining 6 candidates 3 were deferred and 3 borderline cases were passed following manual measurement and adjudication by Professor Sharma or Professor Behr. One case of LQTS was identified as described below.

The study protocol did not have a cut-off for the QTc that was considered so short as to require exclusion, though the investigators did examine the ECGs when the QTc was measured at <380ms in case of other characteristics associated with the short QT syndrome (a short or absent ST-segment and morphologically tall, narrow, and symmetrical T-waves in the precordial leads). In no cases were any of these characteristics seen.

Had the 2010 guideline cut-off been used then a large number of candidates would have required consideration for exclusion as the QTc of 10.8% of the males and 2.4% of the females were measured at <380ms. Females had a lower percentage of short QTc durations than males and fewer white males had a QTc <380ms than black males (8.5% vs 27.2%) Using the Seattle criteria, in which the cut-off was lowered to <320ms, only 4 males would have been considered for deferral.

ECG Finding	Males n=735		Females n=99			All n=834	
	Positive	%	Positive	%	p-value	Positive	%
TWI >1mm in 2 consecutive leads	19	2.585	4	4.04	0.3395	23	2.8
Only Inferior TWI >1mm	8	1.088	1	1.01	1	9	1.1
Inferior TWI >1mm	13	1.769	1	1.01	1.00	14	1.7
Lateral TWI >1mm	2	0.272	0	0	1.00	2	0.2
Inferolateral TWI >1mm in inferior leads and V4-V6, I, aVL	5	0.68	0	0	1.00	5	0.6
Anterior TWI V1-V3	4	0.544	3	3.03	0.0398	7	0.8
Possible juvenile pattern	0	0	3	3.03	0.0016	3	0.4

ECG Finding	White Males n=613		Black Males n=81		
	Positive	%	Positive	%	p-value
TWI >1mm in 2 consecutive leads	15	2.4	2	2.5	1.00
Only Inferior TWI >1mm	7	1.1	0	0	1.00
Inferior TWI >1mm	13	2.1	0	0	0.3820
Lateral TWI >1mm	1	0.2	1	1.2	0.2197
Inferolateral TWI >1mm in inferior leads and V4-V6, I, aVL	5	0.8	0	0	1.00
Anterior TWI V1-V3	2	0.3	1	1.2	0.3113

Table 6.15: Summary of the candidates in whom T-wave inversions (TWI) were seen. *The p-values compare either males to females or white males to black males. The other ethnicities were not included as their numbers were low in this study.*

ECG Finding	Males n=735		Females n=99		p-value	All n=834	
	Positive	%	Positive	%		Positive	%
Gender specific long QTc 2010	45	6.6	6	7.1	na	51	6.1
Gender specific long QTc Seattle	2	0.7	1	3.5	na	3	1.0
QTc >500ms	1	0.4	0	0	1.00	1	0.4
QTc <380ms	78	10.6	2	2.4	0.0033	80	9.6
QTc <320ms	4	0.5	0	0	1.00	4	0.5

ECG Finding	White Males n=613		Black Males n=81		p-value
	Positive	%	Positive	%	
QTc>440ms	41	6.7	4	4.9	0.8093
QTc >470ms	2	0.8	0	0	1.00
QTc >500ms	1	0.5	0	0	1
QTc <380ms	52	8.5	22	27.2	0.0001
QTc <320ms	3	0.5	1	1.2	0.392

Table 6.16: Summary of the QTc measurements for the different groups. *The 2010 guidelines used 440ms for males and 460ms for females as the upper cut-off of normal. Both Seattle and 2017 guidelines used 470ms for males and 480ms for females as the upper cut-off for normal. The p-values compare either males to females or white males to black males. The other ethnicities were not included as their numbers were low in this study.*

ECG Finding	Males n=735		Females n=99		p-value	All n=834	
	Positive	%	Positive	%		Positive	%
Atrial tachyarrhythmias	0	0	0	0	na	0	0
≥2 PVCs per 10 s tracing	2	0.3	0	0	1.00	2	0.2
Ventricular tachycardia	0	0	0	0	na	0	0

ECG Finding	White Males n=613		Black Males n=81		p-value
	Positive	%	Positive	%	
Atrial tachyarrhythmias	0	0	0	0	na
≥2 PVCs per 10 s tracing	2	0.3	0	0	1.00
Ventricular tachycardia	0	0	0	0	na

Table 6.17: Summary of the Atrial and ventricular arrhythmias. *Given the low incidence of positive findings the p values are of limited utility.*

6.3.5.12 Atrial and ventricular arrhythmias. No atrial or ventricular tachycardias were detected, as summarised in table 6.16. Two male candidates were deferred following the discovery of a monomorphic ventricular ectopy suggestive of a right ventricular outflow tract origin.

6.3.6 Pathological findings

In total 60 candidates (7.2%) were suspected or identified with disease using the study protocol (table 6.17). Of these 45 were male (75% of the total and 6.1% of the males) and 15 were female (25% of the total and 15.1%). The incidence of any cardiac disease, including clinically irrelevant disease, was 4.31%. The incidence of disease leading to a failure from screening was 1.92%. Following investigation 16 candidates (13 males and 3 females) were failed or lost to follow-up. The two candidates lost to follow-up were a male with monomorphic ventricular bigeminy consistent with a RVOT focus and a female with a VSD referred for an ACHD opinion (see below). In total 14 (1.9%) candidates were formally failed.

In total 41 candidates (4.9%) were deferred on the day (34 males and 7 females) and 19 were passed on the day as their disease diagnosis was clinically insignificant. The largest category of abnormalities seen were of 19 VHD cases (2.3% of candidates), though 14 of these were mild enough to be passed on the day.

6.3.6.1 Congenital heart diseases. There were 6 candidates diagnosed with simple congenital heart diseases. Three females ages 18, 19 and 24 years old and one male aged 31 years old all were all found to have a VSD. Two had loud murmurs suggestive of the diagnosis but two had no murmur over the anterior chest

Category	Condition suspected	Total	Outcome on the day		Ultimate outcome		
			Passed	Deferral	Passed	Failed	Lost
Congenital	VSD	4	3	1	0	0	1
	PDA	1	0	1	0	1	0
	Anomalous coronary artery origin	1	1	0	1	0	0
Aortopathy	Marfan - suspected	1	0	1	1	0	0
Electrical	RVOT ectopy	2	0	2	1	0	1
	Pre-excitation	4	0	4	0	4	0
	LQTS	3	0	3	2	1	0
CM	HCM	2	0	2	0	2	0
	ARVC	1	0	1	0	1	0
	ST-depression	1	0	1	1	0	0
	TWI	21	1	20	20	0	0
Valvular	BAV	3	0	3	0	3	0
	MVP	1	0	1	0	1	0
	PS	1	0	1	0	1	0
	Other mild valvular disease	14	14	0	0	0	0
	Totals	**60**	**19**	**41**	**25**	**14**	**2**

Table 6.18: Summary of the 60 candidates in whom a pathological finding was identified or suspected on the day of their IRM and their ultimate outcome. *This table includes candidates in whom minor disease was identified and that were passed on the day, as well as those deferred candidates who underwent further investigation. VSD = Ventricular septal defect; PDA = Patent Ductus Arteriosus; RVOT = Right Ventricular Outflow Tract; LQTS = Long QT Syndrome; CM = Cardiomyopathy; HCM = Hypertrophic Cardiomyopathy; ARVC = Arrhythmogenic Right Ventricular Cardiomyopathy; TWI = T-wave inversions in two consecutive leads; BAV = Bicuspid Aortic Valve; PS = Pulmonary stenosis*

wall. All 4 were discussed and 3 were passed as the murmurs were felt to be of no clinical consequence aside from a small increase in the risk of infectious endocarditis. The ECGs in these candidates were normal. The 4th, a 19 year old female, had a loud PSM heard throughout her precordium and left axis deviation on ECG. She was referred for an Adult Congenital Heart Disease opinion as her septal defect appeared significant and was associated with moderate MR. She was unfortunately lost to follow-up.

One 21 year old male was identified with a PDA. He had a systolic murmur detected and a normal ECG. He was deferred for an Adult Congenital Heart Disease opinion regarding PDA closure and was consequently failed.

One 21 year old female candidate was found to have anomalous coronary artery origins with dual origins of the LMS and Circumflex arteries arising from the left coronary cusp. This was considered to be a benign abnormality and passed. Her ECG had isolated RVH by voltage and was otherwise normal.

6.3.6.2 Marfan Syndrome. As discussed above, a single individual was deferred for possible Marfan syndrome based on his physical examination alone. He was investigated at this institution in a specialist clinic and the disease was excluded.

6.3.6.2 Primary electrical diseases

6.3.6.3 Pre-excitation. There were 4 cases of asymptomatic pre-excitation on the ECG. These were identified in 3 males aged 16, 18 and 22 and 1 17 year old female. The female had an innocent sounding murmur on auscultation and the examinations of all the males were normal. Echo examination was normal in all cases. All 4 cases were failed and referred to a cardiac electrophysiologist. The outcome of the female was that she underwent an invasive electrophysiology study and curative ablation at our institution, but when followed up she had not decided if she wanted to proceed with her Army application. The 3 males were managed elsewhere.

6.3.6.4 Outflow tract ectopy. There were two cases of monomorphic ventricular ectopy seen as a bigeminy pattern on ECG with a suspected right ventricular outflow tract (RVOT) origin. Both were in males of ages 18 and 25 and both were asymptomatic with a normal echo. The 18 year old underwent investigation with a CMR and Holter; the CMR was normal with no evidence of a cardiomyopathy and the Holter showed only a low burden of ectopy. He was therefore passed and ultimately he went on to join the Army. The second candidate did not attend for further investigation and was unfortunately lost to follow-up.

6.3.6.5 Long QT Syndrome. Only three candidates were deferred for further investigation because of a prolonged QTc duration. One 24 year old male candidate's QTc measured 561ms and was referred to this institution where LQTS was confirmed and managed. The second candidate, an 18 year old female with a QTc of 485ms was deferred. The LQTS was excluded at this institution and she was passed for selection. A third candidate, an 18 year old male with a measured QTc 484ms was also deferred and again LQTS was excluded at another centre.

6.3.6.6 Cardiomyopathy or other myocardial disease

6.3.6.7 Hypertrophic cardiomyopathy. There were two cases deferred due to a suspicion of HCM that were later confirmed. One was a 28 year old asymptomatic female with an ejection systolic murmur and biphasic then deep inverted T-waves in leads V1-4. Her echo detected a 15mm thick septum in the PLAX view and systolic anterior movement of the mitral valve. There was also calcification of her aortic valve with a suspicion of it being at

least functionally bicuspid. The second case was a 19 year old asymptomatic male with no murmur on physical examination. His ECG showed sinus rhythm with a QRS axis of 99 degrees, RVH but no LVH by voltage criteria and T-wave inversions and ST depression in leads II, III, aVF. His echo was borderline with a maximum left ventricular wall thickness of 11mm with a false tendon and increased left ventricular trabeculation. He was deferred and the diagnosis of HCM was confirmed by his local hospital. In neither case was there any family history suspicious for an inherited cardiomyopathy. Both cases were identified using all three ECG criteria.

6.3.6.8 Arrhythmogenic right ventricular cardiomyopathy. One case of probable ARVC was detected. This was in a 23 year old asymptomatic male who had no murmur on physical examination. His ECG was only mildly abnormal, showing sinus rhythm, a complete RBBB morphology and a QRS duration of 125ms; aside from this it was normal with no atrial abnormalities, QRS axis deviation (it was 70 degrees) or T-wave inversions. His echo demonstrated moderate RV dilatation, mild TR, abnormal ventricular septal movement and an aneurysmal atrial septum with no shunt measured or seen. He was deferred and investigated at his local hospital where a CMR confirmed the findings at echo as well as localised late-gadolinium enhancement and RV regional wall motion abnormalities. A provisional diagnosis of ARVC was made by the investigating cardiologists. This young man habitually exercised for approximately one hour daily without any limitations and had no family history suspicious for an inherited cardiomyopathy. Although he would have been detected with the 2010 ECG criteria he would not have been detected using either the

Seattle criteria or 2017 consensus guidelines for ECG interpretation where RBBB was removed as a trigger for further investigation.

6.3.6.9 Suspected cardiomyopathy. In total 22 candidates (18 males and 4 females) were suspected of having an underlying cardiomyopathy based on suspicious ECG abnormalities (table 6.18) . Only one of these had a murmur. All went on to have unremarkable echos. One, a white 19 year old male was passed on the day as his ECG showed biphasic T-waves in V1 and V2 with early repolarisation more suggestive of athletic adaptation than a cardiomyopathy. This individual also had the only murmur detected in this group. The remaining 21 candidates were deferred for further investigation. All of these were subsequently passed following normal findings at exercise test, CMR and Holter testing. Of note 9 candidates deferred using either the 2010 or Seattle criteria guidelines could have been deferred had the 2017 guidelines been in use as they had either inferior TWI or ST-depression only.

6.3.6.10 Valvular heart disease.

There were 19 candidates in whom a valvular abnormality was detected (table 6.18). Of these 14 candidates had at most mild disease and were passed on the day. A total of 5 candidates were failed.

6.3.6.11 Bicuspid aortic valves. A BAV was identified in three cases, all of which were asymptomatic white males. Two of these cases had murmurs detected; one had established

disease with mild stenosis and moderate regurgitation on echo and the other mild stenosis and mild regurgitation. The third case had no murmur detected and at most mild regurgitation. None of the three had any aortic root dilatation. The ECGs in all three cases were normal. All three were failed as a BAV is a bar to service.

6.3.6.12 Mitral valve prolapse. One asymptomatic 16 year old male was found to have a pan-systolic murmur and mild MR associated with a bileaflet MVP. His ECG was normal. He was failed as MVP with associated regurgitation is a bar to service.

6.3.6.13 Pulmonary stenosis. A single case of moderate PS and mild TR was identified in an asymptomatic 28 year old male with an ejection systolic murmur. He was failed as moderate PS is a bar to service.

6.3.7 Comparison of the different ECG interpretation criteria

The three most widely used criteria can be used to interpret the ECG independently of the physical exam. This section examines the positive findings with each screening protocol in general terms and in isolation (in these candidates who were pre-screened and negative for symptoms, cardiac and family history and without the findings of physical examination) in order to estimate the deferral rate for ECG changes in a large screening programme if implemented permanently by the British Army. An evaluation of the sensitivities and specificities of the ECG alone or in combination with a physical examination are examined in the next section.

Number	Age	Gender	Ethnicity	Murmur	ECG findings
1	23	Male	South Asian	No	ST depression
2	31	Male	Black African	No	Anterior TWI
3	16	Female	White European	No	Anterior TWI
4	18	Female	White European	No	Anterior TWI
5	16	Female	White European	No	Anterior TWI
6	19	Male	White European	No	Inferior and anterior TWI
7	17	Male	White European	No	Inferior TWI
8	24	Male	White European	No	Inferior TWI
9	24	Male	White European	No	Inferior TWI
10	22	Male	White European	No	Inferior TWI
11	16	Female	White European	No	Inferior TWI
12	19	Male	White European	No	Inferior TWI
13	26	Male	White European	No	Inferior TWI
14	17	Male	White European	No	Inferior TWI
15	29	Male	South Asian	No	Inferolateral TWI
16	18	Male	White European	No	Inferolateral TWI
17	23	Male	White European	No	Inferolateral TWI
18	16	Male	White European	No	Inferolateral TWI
19	18	Male	White European	No	Inferolateral TWI
20	17	Male	White European	No	Lateral TWI
21	29	Male	Black African	No	Lateral TWI

Table 6.19: *Summary of the candidates in whom a myocardial disease was suspected from ECG. Using the 2017 ECG interpretation guidelines candidates a further 9 of these asymptomatic candidates with isolated ST-depression or inferior T-wave inversions and normal echos might have also been passed on the day (orange). All of these candidates were ultimately passed as no disease was detected.*

6.3.7.1 The 2010 Guidelines. At the time of this study these were the dominant ECG interpretation guidelines internationally. The findings of physiological type 1 changes on the ECG are summarised in table 6.20 and the findings associated with cardiac pathology are

summarised in tables 6.18 and 6.19. The type 1 findings were seen more frequently than not seen with a minority of candidates exhibiting 4 or 5 of these ECG characteristics. Males candidates were more likely than female candidates to exhibit type 1 changes. Almost 40% of candidates presented with a type 2 ECG finding on screening and these were also more prevalent in males than in females. Particularly high proportions would have required deferral for either long or short QT durations, axis deviation, non-specific intra-ventricular conduction delay and T-wave inversions.

6.3.7.2 The Seattle criteria. The Seattle criteria increased the upper QTc duration cut-off and reduced the lower QTc duration cut-off; they removed isolated RVH by voltage from the criteria; increased the tolerated rightward axis to 120 degrees and increased the allowed duration of a non-specific intraventricular delay to 140ms. Using the Seattle criteria there were 11.9% of study candidates in whom the ECG would trigger further investigation (tables 6.21 and 6.22). There was no difference in rates between males and females or between white males and black males.

6.3.7.3 The 2017 Guidelines. The criteria in the Seattle guidelines and updated 2017 Guidelines were similar, but with the added refinements of creating 'borderline' criteria and removing the lower QTc limit. This resulted in a total positive rate of 5.2% in the study population of which almost half could be cleared with echo alone (table 6.24). Proportionally there were more females than males that could not be cleared by echo. No differences between the white males and black males was observed.

2010 Guideline	Males n=735		Females n=99			All n=834	
	Positive	%	Positive	%	p-value	Positive	%
Type 1 +ve	595	80.95	43	43.43	<0.0001	638	76.5
No type 1	140	19.05	56	56.57		196	23.5
1 x type 1	256	34.83	26	26.26		282	33.8
2 x type 1	191	25.99	13	13.13		204	24.5
3 x type 1	115	15.65	3	3.03		118	14.1
4 x type 1	30	4.082	1	1.01		31	3.7
5 x type 1	3	0.408	0	0		3	0.4
2010 Guideline	**White Males n=613**		**Black Males n=81**		p-value		
	Positive	%	Positive	%			
Type 1 +ve	497	81.08	72	88.9	0.0918		
No type 1	116	18.92	9	11.1			
1 x type 1	223	36.38	18	22.2			
2 x type 1	155	25.29	24	29.6			
3 x type 1	87	14.19	23	28.4			
4 x type 1	30	4.894	6	7.4			

Table 6.20: Summary of the proportions of screened candidates that would have tested positive for the Type 1 ECG findings as defined in the 2010 ESC guidelines. *The p-values compare either males to females or white males to black males. The other ethnicities were not included as their numbers were low in this study.*

2010 Guideline ECG Type 2 findings	All n=834	
	Positive finding	%
Profound sinus bradycardia <30bpm or sinus pauses ≥ 3s	0	0
Mobitz type 2 AV block or complete heart block	0	0
Pre-excitation - %	4	0.5
Right atrial abnormality	11	1.3
Left atrial abnormality	26	3.1
Left axis deviation <-30 degrees	27	3.2
Right axis deviation >110 degrees	17	2.0
Complete RBBB	7	0.8
Complete LBBB	0	0
Non-specific intraventricular block (*QRSd>110*)	13	1.6
Pathological q-waves in 2 consecutive leads	0	0
ST-depression >0.5mm in 2 consucutive leads - %	3	0.4
Type 1 Brugada pattern	0	0
Epsilon waves	0	0
TWI >1mm in 2 consecutive leads - %	23	2.8
Machine measured gender long QTc 2010 - %	80	9.6
Machine measured QTc >380ms - %	51	6.1
Atrial tachyarrhythmias - %	0	0
≥2 PVCs per 10 s tracing - %	2	0.2
Ventricular arrhythmias -%	0	0

Table 6.21: Types and number of the positive type 2 ECG findings using the 2010 guidelines for all 834 candidates recruited into this study.

2010 Guideline	Males n=735		Females n=99			All n=834	
Finding	Positive	%	Positive	%	p-value	Positive	%
Type 2 +ve	306	41.63	20	20.2	<0.0001	326	39.1
No type 2	428	58.23	79	79.8		507	60.8
1 x type 2	236	32.11	20	20.2		256	30.7
2 x type 2	52	7.075	0	0		52	6.2
3 x type 2	16	2.177	0	0		16	1.9
4 x type 2	2	0.272	0	0		2	0.2
5 x type 2	1	0.136	0	0		1	0.1
2010 Guideline	**White Males n=613**		**Black Males n=81**				
Finding	Positive	%	Positive	%	p-value		
Type 2 +ve	228	37.19	48	59.3	0.0002		
No type 2	385	62.81	33	40.7			
1 x type 2	175	28.55	36	44.4			
2 x type 2	38	6.199	10	12.3			
3 x type 2	12	1.958	2	2.5			
4 x type 2	2	0.326	0	0.0			

Table 6.22: Summary of the proportions of screened candidates that would have tested positive for the Type 2 ECG findings as defined in the 2010 ESC guidelines. *The p-values compare either males to females or white males to black males. The other ethnicities were not included as their numbers were low in this study.*

Seattle Criteria and 2017 Guidelines abnormal findings	All n=834 Positive	%
Profound sinus bradycardia <30bpm or sinus pauses ≥ 3s	0	0
Mobitz type 2 AV block or complete heart block	0	0
Pre-excitation - %	4	0.5
Right atrial abnormality	11	1.3
Left atrial abnormality	26	3.1
Left axis deviation <-30 degrees	27	3.2
Right axis deviation >120 degrees	8	1.0
Complete RBBB	7	0.8
Complete LBBB	0	0
Non-specific intraventricular block (QRSd>140)	0	0
Pathological q-waves in 2 consecutive leads	0	0
ST-depression >0.5mm in 2 consecutive leads	3	0.4
Type 1 Brugada pattern	0	0
Epsilon waves	0	0
TWI >1mm in 2 consecutive leads	23	2.8
TWI >1mm inferior leads only	14	1.7
Gender-specific prolonged QTc	3	1.0
Machine measured QTc <320ms	4	0.5
Atrial tachyarrhythmias	0	0
≥2 PVCs per 10 s tracing	2	0.2
Ventricular arrhythmias	0	0

Table 6.23: Summary of the different ECG criteria included in either the Seattle or 2017 guidelines and their incidence in this study group.

Seattle Criteria Finding	***Males n=735***		**Females n=99**			**All n=834**	
	Positive	*%*	Positive	%	p-value	Positive	%
Abnormal +ve - %	*87*	*11.8*	12	12.1	0.8698	99	11.9
No abnormalities - %	*648*	*88.2*	87	87.9		735	88.1
1 x abnormal - %	*71*	*9.7*	11	11.1		82	9.8
2 x abnormal - %	*16*	*2.2*	1	1.0		17	2.0
Seattle Criteria Finding	***White Males n=613***		**Black Males n=81**				
	Positive	*%*	Positive	%	p-value		
Abnormal +ve - %	*61*	*10.0*	14	17.3	0.0559		
No abnormalities - %	*552*	*90.0*	67	82.7			
1 x abnormal - %	*55*	*9.0*	12	14.8			
2 x abnormal - %	*6*	*1.0*	2	2.5			

Table 6.24: Summary of the proportions of screened candidates that would have been identified as potentially abnormal as defined in the Seattle consensus guidelines. *The p-values compare either males to females or white males to black males. The other ethnicities were not included as their numbers were low in this study.*

6.3.8 Combining the physical examination with the ECG interpretation guidelines

A comparison was made of the 3 different ECG interpretation guidelines with and without a physical examination to evaluate the key test characteristics (table 6.26). This also estimates of the burden of additional tests that would be required, in particular echocardiography. The incidence of any cardiac disease, including clinically irrelevant disease, in this study was 4.31%, with the incidence of disease leading to a failure from

screening was 1.92%. All the screening systems had a good NPV. For the purposes of evaluating these tests the whole study population was used, rather than subgroups and the clinically insignificant disease was ignored.

Joint 2017 recommendations	Males n=735		Females n=99			All n=834	
	Positive	%	Positive	%	p-value	Positive	%
Abnormal +ve	33	4.49	10	10.1	0.027	43	5.2
1 or more borderline	75	10.2	4	4.0	0.0648	79	9.5
2 x borderline abnormalities	3	0.408	0	0.0	1	3	0.4
Could be cleared by echo	20	2.721	1	1.0	0.4974	21	2.5
Could not be cleared by echo	13	1.769	9	9.1	0.0004	22	2.6
Joint 2017 recommendations	**White Males n=613**		**Black Males n=81**				
	Positive	%	Positive	%	p-value		
Abnormal +ve	27	4.405	4	4.9	0.775		
1 or more borderline	54	8.809	15	18.5	0.0098		
2 x borderline abnormalities	2	0.326	1	1.2	0.3113		
Could be cleared by echo	16	2.61	2	2.5	1		
Could not be cleared by echo	11	1.794	2	2.5	0.6562		

Table 6.25: Summary of the outcomes interpreting these candidates using the 2017 International Recommendations on ECG interpretation. *The p-values compare either males to females or white males to black males. The other ethnicities were not included as their numbers were low in this study.*

	A: Exam only and no ECG		B: 2010 ECG and no exam	
	All findings	Disease fails	All findings	Disease fails
Sensitivity	52.78	50.00	58.33	68.75
Specificity	85.23	84.25	63.20	62.88
PPV	13.87	5.84	6.67	3.49
NPV	97.56	98.85	97.12	99.04
+ LR	3.57	3.17	1.59	1.85
- LR	0.55	0.59	0.66	0.50
	C: 2010 ECG and exam		**D: Seattle ECG and no exam**	
	All findings	Disease fails	All findings	Disease fails
Sensitivity	88.89	93.75	30.56	56.25
Specificity	54.44	53.48	89.99	89.99
PPV	8.08	3.79	12.09	9.89
NPV	99.09	99.77	96.64	99.06
+ LR	1.95	2.02	3.05	5.62
- LR	0.20	0.12	0.77	0.49
	E: Seattle ECG and exam		**F: 2017 ECG and no exam**	
	All findings	Disease fails	All findings	Disease fails
Sensitivity	69.44	87.50	30.56	62.50
Specificity	76.35	75.58	95.87	95.85
PPV	11.68	6.54	25.00	22.73
NPV	98.23	99.68	96.84	99.24
+ LR	2.94	3.58	7.40	15.06
- LR	0.40	0.17	0.72	0.39
	G: 2017 ECG and exam		**H: 2017 ECG and exam +/- echo**	
	All findings	Disease fails	All findings	Disease fails
Sensitivity	72.22	87.50	38.89	87.50
Specificity	81.48	80.46	98.12	98.17
PPV	14.94	8.05	48.28	48.28
NPV	98.49	99.70	97.27	99.75
+ LR	3.90	4.48	20.71	47.77
- LR	0.34	0.16	0.62	0.13

***Table 6.26 : Test characteristics of different screening strategies (n=834)**: **Method A:** with a physical examination alone (the status quo); **Method B:** screening with no examination, but with an*

*[**Table 6.24 continued]** ECG and using the 2010 guidelines to interpret this; **Method C:** screening with both a physical examination and an ECG and using the 2010 guidelines to interpret this; **Method D:** screening with no examination, but with an ECG and using the Seattle guidelines to interpret this; **Method E:** screening with both a physical examination and an ECG and using the Seattle guidelines to interpret this; **Method F:** screening with no examination, but with an ECG and using the 2017 guidelines to interpret this; **Method G:** screening with both a physical examination and an ECG and using the 2017 guidelines to interpret this; **Method H**: Using method G with an echo immediately if indicated.*

6.3.8.1 Physical examination without an ECG. This was the pre-existing method of screening. It has both a poor Sn and Sp as well as low positive and negative likelihood ratios. Using this system would require 16.1% of candidates to undergo an echo. Of the diseases that lead to fails, screening with just a physical examination would have failed to detect 3 cases of pre-excitation, 1 case of ventricular bigeminy, 1 case of HCM, 1 case of ARVC, 1 case of LQTS and a BAV. This means this screening system would have missed all the potential causes of sudden death identified in this population with the exception of a single case of HCM.

6.3.8.2 Screening without a physical examination but with an ECG interpreted using the 2010 guidelines. Using this system would require 37.7% of candidates to undergo an echo. Of the diseases that led to fails, screening with this system would have failed to detect any of the VHD that included 1 case of MVP, 3 cases with BAV and the case of moderate PS. It

would have detected all the diseases discovered that were most likely to cause a sudden death.

6.3.8.3 Screening with both a physical examination and an ECG interpreted using the 2010 guidelines. This system also has a much higher Sn but the Sp and positive likelihood ratios remained poor. Using this system would require 47.4% of candidates to undergo an echo. Of the diseases that led to fails, screening with this system would have failed to detect one case of BAV, but would have detected all the diseases identified that might cause sudden death.

6.3.8.4 Screening without a physical examination but with an ECG interpreted using the Seattle criteria. The Sp of this screening system is approaching 90% but the other test parameters remained poor. Using this system would require 10.9% of candidates to undergo an echo. Of the diseases that led to fails, screening with this system would have failed to detect the case of ARVC (the only ECG abnormality in that case was a complete RBBB) as well as the same valvular heart diseases also missed by using the 2010 guidelines and not performing a physical examination, as they all had normal ECGs. It detected all the diseases identified that might cause a SCD with the exception of the ARVC case.

6.3.8.5 Screening with both a physical examination and an ECG interpreted using the Seattle criteria. The Sn and Sp of this screening strategy was improved relative to the methods above with Sn 87.5% and Sp 75.5%. Using this system would require 25.6% of

candidates to undergo an echo. It would fail to detect one case of BAV and the candidate with ARVC, but would detect the other conditions associated with SCD.

6.3.8.6 Screening without a physical examination but with an ECG interpreted using the 2017 guidelines. With a value of 15.06 this system has the best positive likelihood ratio of the methods so far discussed but the Sn was still only 62.5%. Using this system would require only 5.3% of candidates to undergo an echo. This system would miss the same disease cases as using the Seattle criteria and no physical examination (the case of ARVC, the candidate with a PDA, 3 BAV cases and a case of moderate PS).

6.3.8.7 Screening with both a physical examination and an ECG interpreted using the 2017 guidelines. This system would have a higher Sn than using the ECG with the same interpretation guidelines without a physical examination (Sn 87.50% cf 62.5%) but has a lower Sp. Using this system would require 20.8% of candidates to undergo an echo. This system would only miss the case of ARVC and a BAV and would detect all the other cases that might cause a SCD.

6.3.8.8 Screening with both a physical examination and an ECG interpreted using the 2017 guidelines and an echo on the day when indicated. The previous protocol, utilising the most contemporary ECG interpretation guideline system and a physical examination has a Sp of 80.46. For all the systems that utilise both an ECG and physical examination this is a problem because of the high deferral rate due to TWI on the ECG and because so many

candidates have a murmur detected. The two tests do not identify the same pathologies but complement each other in spanning most of the full range of pathologies. Combined they unfortunately generate a high false positive and therefore high deferral rate in candidates in whom no disease will be found to be present. Reducing this 'fail on the day', rate is important to the British Army from a logistics perspective as it is expensive because it comes with the opportunity cost of any deferred candidates not participating in the physical elements of the screening process, worries the individual affected, requires expensive tests to ultimately exclude disease (albeit these are paid through the NHS system) and results in many candidates dropping out of the recruiting process completely.

To mitigate these problems performing an echo on the day is desirable as it would allow the majority of candidates with murmurs, but no underlying cardiac disease, to be passed. The false positives associated with TWI inferiorly can also be passed in the absence of any echo abnormalities or other abnormal findings, as can candidates with axis deviation or other 'borderline' abnormalities. There is no difference in the cases detected using the Seattle and 2017 criteria, but the echo rate with the 2017 criteria is almost 5% lower and there are more cases that can be passed if the echo is normal i.e isolated inferior T-wave inversions.

It is a somewhat artificial evaluation to calculate the test performance statistics with a physical examination, ECG using the 2017 guidelines and an echo on the day if it is indicated, because this was the pragmatic 'gold standard' of the trial. However to illustrate the utility of this methodology (summarised as Method H in table 6.26) it increased the Sp from 80.5% to 98.17% and increased the positive likelihood ratio from 4.48 to 47.77. This methodology

would have resulted in 14 candidates being appropriately failed due to significant cardiac disease and 15 candidates being investigated for an abnormal finding, but in whom no disease was diagnosed following extensive further investigations. So if a candidate was deferred on the day they would have a 48.3% probability that they would have an underlying cardiac disease.

6.3.9 **Cost effectiveness.** The breakdown of the different components of the screening and ongoing investigation are summarised in Table 6.27. The cost to the British Army to use the current Cardiac Report system, with each candidate referred to this private provider, was the most expensive of all the screening methods and more than twice the cost per candidate than many of the other screening possibilities. Bringing the ECG and echo to the selection centre and moving the responsibility away from a consultant cardiologist to the occupational physician, significantly reduced the overall cost. The cost of either physical examination or ECG alone was less expensive than both combined. The cost to use the 2017 ECG interpretation guidance was lower than the previous guidelines as the number of false positive results requiring further investigation was reduced.

Table 6.27: ***Costs associated with the different screening strategies.*** Upper table: Summary of the consultation, investigation or procedures identified using different screening strategies. Red type: costs incurred by the British Army. Green type: costs incurred by the NHS. Lower table: summary of the total costs and costs per candidate using each screening system.

Expense	Cardiac Report		Exam only		2010 only		Seattle only		2017 only		Exam + 2010		Exam + Seattle		Exam + 2017	
	n	Cost	n	Cost	n	Cost	n	Cost	n	Cost	n	Cost	n	Cost	n	Cost
IRM consult	834	£25,020	834	£25,020	834	£25,020	834	£25,020	834	£25,020	834	£25,020	834	£25,020	834	£25,020
Cardiac report	137	£56,170														
ECG at IRM			137	£685	834	£4,170	834	£4,170	834	£4,170	834	£4,170	834	£4,170	834	£4,170
Echo at IRM			137	£8,905	326	£21,190	91	£5,915	43	£2,795	407	£26,455	212	£13,780	175	£11,375
ECG in hospital	10	£50	9	£45	326	£1,630	91	£455	43	£215	407	£2,035	212	£1,060	175	£875
Echo in hospital	10	£750	9	£675	163	£12,225	43	£3,225	31	£2,325	170	£12,750	50	£3,750	38	£2,850
ETT	1	£170	1	£170	163	£27,710	43	£7,310	31	£5,270	163	£27,710	43	£7,310	31	£5,270
Holter	1	£170	1	£170	163	£27,710	43	£7,310	31	£5,270	163	£27,710	43	£7,310	31	£5,270
CMR	2	£420	2	£420	27	£5,670	27	£5,670	19	£3,990	31	£6,510	31	£6,510	23	£4,830

Expense	Cardiac Report		Exam only		2010 only		Seattle only		2017 only		Exam + 2010		Exam + Seattle		Exam + 2017	
	n	Cost	n	Cost	n	Cost	n	Cost	n	Cost	n	Cost	n	Cost	n	Cost
Genetics	1	£600	1	£600	4	£2,400	4	£2,400	4	£2,400	5	£3,000	5	£3,000	5	£3,000
Procedure	2	£4,000	1	£2,000	4	£8,000	4	£8,000	4	£8,000	5	£10,000	5	£10,000	5	£10,000
TOE	1	£290	1	£290	0	£0	0	£0	0	£0	1	£290	1	£290	1	£290
OP consultation	10	£6,600	9	£5,940	163	£107,580	43	£28,380	31	£20,460	170	£112,200	50	£33,000	38	£25,080

	Cardiac Report	Exam only	2010 only	Seattle only	2017 only	Exam + 2010	Exam + Seattle	Exam + 2017
Total Army cost	**£81,190**	**£34,610**	**£50,380**	**£35,105**	**£31,985**	**£55,645**	**£42,970**	**£40,565**
Army cost per candidate	**£97**	**£41**	**£60**	**£42**	**£38**	**£67**	**£52**	**£49**
Total NHS cost	**£13,050**	**£10,310**	**£192,925**	**£62,750**	**£47,930**	**£202,205**	**£72,230**	**£57,465**
NHS cost per candidate	**£16**	**£13**	**£231**	**£75**	**£57**	**£242**	**£87**	**£69**
Total cost	**£94,240**	**£44,920**	**£243,305**	**£97,855**	**£79,915**	**£257,850**	**£115,200**	**£98,030**
Cost per candidate	**£113**	**£62**	**£292**	**£117**	**£96**	**£309**	**£138**	**£118**

6.4 Discussion

6.4.1 Limitations

6.4.1.1 Defining the 'Gold Standard' in disease detection. Firstly the ideal 'gold standard' of cardiac investigations to compare the screening protocol to is impossible to define. With additional diagnostic tests the detection of disease approaches 100%, but in reality this is an asymptote and the 100% mark will never be met with complete certainty. In an ideal world with unlimited time, clinicians and financial resources and with no risks from invasive procedures or radiation exposure, a gold standard might include all the tests outlined in table 6.1 as well as high lead and signal averaged ECGs, pharmacological provocation tests, long duration cardiac monitoring and family screening. Without this full battery of investigations though we are reliant on more pragmatic protocols, such as the protocol used in this and other similar studies. When interpreting these data it is important to understanding that the gold standard used is therefore not perfect. There was a single case of aberrant origins to the coronary arteries identified with echo, but this was a relatively unexpected finding as although the coronary artery origins can often be visualised, the echo modality is not going to detect as many cases of aberrant coronary artery origins as is CT coronary angiography, or taken to the extreme: an autopsy. For this reason the test results of Method H in table 6.26 are not easy to rely on as we don't know if there was disease that remained undetected, potentially because the test that would have identified it was not performed. We are therefore comparing the test to what is essentially itself for the vast majority of individuals.

6.4.1.2 Study design. This study was a cross-sectional design without longer term follow-up. For the reasons described in the earlier epidemiology chapters, the Armed Forces are uniquely placed in the UK to follow-up personnel for at least as long as they are serving. Despite these advantages a cross-sectional design was used. This is because the cardiac mortality rate in the UK Armed Forces is low and given the small size of this study population a single cardiac death (or no deaths at all) would be meaningless and as likely the result of chance as due to the a deficiency in the study investigations. For this reason it was decided not to include follow-up in the original design of the study;

6.4.1.3 Limitations in the study size. The study was limited by the number of candidates recruited. When the prevalence of many of the diseases is low, as is the case for arrhythmic cardiomyopathies, ion channel diseases or congenital diseases, then the numbers that are likely to be detected are also low. The presentation of the single probable ARVC case in this series is also interesting in that it was an atypical ECG presentation with a RBBB only. Most ARVC of the severity seen in this case is likely to be detected based on changes in the T wave or the development of an epsilon wave. The presence or absence of unlikely events, such as this ARVC example, can skew the results in a way a far larger study, with many tens of thousands of candidates, would partially avoid. That study however would be breathtakingly expensive and logistically difficult to achieve.

One way to partially get around this problem is to study the phenotypes of a large cohort of a particular disease in order to better understand the spectrum of possible presentations. So for example, by investigating a cohort of 114 young HCM patients it was ascertained that

approximately 10% of patients with HCM did not have ECG changes that would be detected using the 2010 ESC interpretation guidelines[123]. Approaching the detection of disease from different directions can therefore improve our understanding of how to detect the disease as well as provide additional insights, such as to the natural history. In this case recognising that a significant minority of HCM is likely to be missed by ECG screening reinforces the requirement for screening to be a process repeated at intervals and not a one-off event, as described in the WHO screening framework.

6.4.1.4 Gender and ethnicity limitations. The majority of recruits in this study were male. In part this reflects the British Army population as a whole and the nature of the recruiting system, where there was usually only a single day dedicated to recruiting females each fortnight. However it was also more difficult to recruit females to the study from a practical perspective as a chaperone was essential for the physical examination and ECG and to perform the echo. Unfortunately it wasn't always possible for a female member of the recruiting staff to assist in this regard and recruiting was slower as a consequence. These lower female numbers mean that the conclusions from the screening need to be considered within this context and chance anomalies may skew the data.

The study location at Pirbright in Surrey parforms a larger number of IRMs in black recruits than the other recruiting centres, though the precise figures relating to this were not known. The reason for this is that most of the Black African and West Indian recruits from British Commonwealth countries enter the UK via a London airport and therefore undergo their IRM at the Pirbright recruiting centre. In the decade prior to this study the British

Army extensively recruited from Fiji and these recruits were screened at Pirbright on their arrival to the UK. As a consequence a significant proportion of the British Army are of Fijian ethnicity. The Defence Statistics demographic data describes this population as a minority ethnicity and does not differentiate Fijians specifically, but they probably constitute >5% of many 'tooth arm' combat units, such as the infantry, armoured regiments and the close combat support units such as the Royal Artillery and Royal Engineers. Fijian potential recruits were also were more likely to present at Pirbright for their IRM for the same reasons that other British Commonwealth potentiall recruits did. Unfortunately immediately prior to this study the recruiting policy was changed as the British Army was reduced in size and these groups were no longer actively recruited. Commonwealth Black recruits and Fijians in particular, were therefore under-represented relative to their proportions in the British Army and fewer were recruited into this study than anticipated when the study was designed. Interestingly this policy of not recruiting from the Commonwealth was reversed soon after the recruiting for this study was completed.

Another ethnicity barely represented in this study were Nepalis. For over 200 years the British Army has recruited Nepali mercenaries into units consisting almost entirely of Nepali soldiers with only a few non-Nepali Officers or attached soldiers. Currently the Brigade of Gurkhas consists of approximately 3000 Nepali soldiers. They were not represented in this study as they undergo a Gurkha specific selection process in Nepal and are therefore recruited using a system that does not involve the Pirbright selection centre.

The numbers of non-white ethnicities recruited into this study was unfortunately lower than anticipated. To take meaningful insights from these small numbers into the differences between the normal and abnormal cardiac phenotypes of these groups is therefore difficult; the few observed similarities and differences need to be considered through this prism. It is for this reason that the evaluation of the different screening methodologies in sections 6.3.7 and 6.3.8 were not differentiated along racial or gender lines. The better phenotypic characterisation of these ethnic groups might form the basis of future screening research.

6.4.1.5 Limitations in the cost-effectiveness analysis. There are limitations to this cost-effectiveness analysis. Firstly many of the conditions sought are rare and are unlikely to be representatively identified in a sample size of only 834 candidates in a way that accurately reflects a system that screens approximately 20,000 candidates annually. The costs used for modelling are estimated rather than accurate, though for the purposes of this study conservative costs were used. For example, it is likely that the cost for a consultation, ECG and echo by Cardiac Report would have cost in excess of the £410 used in the modelling. Furthermore individual tariffs are not always used in the current NHS where a block fee system may be in place. The additional costs of transport, administration, dining and other costs are also not included in the calculations. In a real life screening system the costs are also likely to be greater than estimated due to real-life issues such as missed appointments, administration errors, staff or candidate illness and clinical errors that misdiagnose ECGs as normal when they are not or as abnormal when they are normal, with a knock on effect in the cost of further investigations. The proposal to move the ECG and echo and interpretation of the results into the clinical responsibilities of the occupational physicians,

rather than outsourced to a highly trained and experienced consultant cardiologists, also presents risk and if implemented would need appropriate training and governance structures to be introduced; these would come with clinical risk and financial costs that this modelling does not take into account.

This cost-effectiveness analysis looked only at the screening and original investigation and treatment and was intentionally short-term in nature. One reason is that there are costs associated with longer-term follow-up of progressive but not severe conditions such as mildly dysfunctional bicuspid aortic valves. Beyond this though the details relating to cardiac screening in the military are not straight-forward as in addition to the costs of the screening process and the investigations that are required as a consequence of it, there are additional costs from not screening that must be considered, such as the cost of investigating adverse events, the cost of evacuating an serviceperson with an adverse event from a remote and potentially hostile location and the in-service and medical discharge and pension costs of not diagnosing a disease prior to enlistment. These costs are not easily evaluated and for this reason the analysis avoided them completely.

6.5.1 Population characteristics. The study population was weighted to the younger part of the age spectrum with 450 candidates (54%) aged 20 or younger. This reflected the random nature of candidate recruitment and mirrored the age of the potential recruits attending the IRM and consequently joining the British Army. As a consequence cardiac diseases that progress over time, such as degeneration of a BAV or HCM might be less likely to be

detected at age 18 than at age 30 with an ECG or echo and the findings described might be different to what might be diagnosed had the study been conducted in only 30 year olds.

Black males appeared to have a higher rate of ECG changes consistent with a LAA. There was also a difference in the mean and distribution of the QRS axis (mean in white males was 61 degrees versus 34 degrees in black males). This distribution resulted in more white males with RAD and more black males with LAD whilst still having normal cardiac structure and function on echo. Why this might be could be any of a combination of reasons. The blacks were older and had a higher BMI, which might result in leftward axis rotation. They also had a higher diastolic blood pressure that might lead to adaptive hypertrophy changes in the left ventricle, albeit changes not detectable with echo or clinically meaningful.

6.5.2 Repeat screening and the passage of time. Many of the conditions that screening seeks to identify are progressive, such as in HCM or BAV degeneration and in these conditions the mild, earlier phenotype tends to be less associated with adverse events. It is likely that the first time an individual is screened the easiest to identify disease will be detected and these individuals will be removed from the pool that is exposed to further screening. The first screening is likely to detect the more severe congenital phenotypes, pre-excitation and the higher risk myocardial or ion channel conditions that may already be evident as electrocardiographic abnormalities in the second decade of life. Whilst the milder phenotypes of the same disease are more likely to be missed at screening these individuals are likely to be lower risk patients. An example of this is HCM where risk factors for sudden death include increasing age, left atrial thickness, ventricular wall thickness and

left ventricular outflow tract obstruction, all characteristics that develop gradually over time. An 18 year old asymptomatic individual with none of these structural features will on average be at far lower risk of adverse events than an 18 year old asymptomatic individual with a 30mm thick left ventricular wall, dilated LA and elevated outflow tract gradients. What this means practically is that for a screening at any point in time the higher risk disease will be preferentially detected over lower risk disease and some disease is likely to be missed.

Creating a system to detect this missed disease, much of which is progressive, poses a challenge. Re-screening would need to be staggered in time to allow any disease to progress in order to become detectable, but not so delayed as to allow symptoms to develop. In the case of this study there were 21 candidates in whom T wave inversions were identified and yet no disease was identified. It may be that these individuals are simply variants of the normal human phenotype that happens to have suspicious ECG changes, but no underlying disease, or it could be that these T-wave changes are the first manifestations of an underlying disease that is not yet diagnostically apparent. Certainly at the time of this screening and their follow-up investigations, no disease was identified and all these candidates were passed, albeit with a 'flag' on their medical record to trigger follow-up investigations after 2-3 years, or before if they develop symptoms. This is a pragmatic clinical approach to this difficulty and understanding the optimal time for rescreening is therefore not clear and could be the focus of future study.

This therefore introduces the passage of time as another factor that might be associated with screening yield. This study has investigated potential recruits, most of whom are aged 15-20 years. Of the important cardiac conditions sought by screening, probably only pre-excitation is likely to improve with the passing of time, as conduction through accessory pathways often degenerates with increasing age. Most important conditions, such as HCM as discussed immediately above, are likely to progress with time and might have been undetectable using the methods utilised here, at the point of this screening, but will become apparent over the coming decades. With the passing of time additional acquired conditions, most obviously IHD, become increasingly prevalent and these pose further difficulties for screening beyond the scope of this thesis.

6.5.3 Athletic conditioning. It is fair to state that most newly trained soldiers are athletically conditioned by the nature of the compulsory physical training in which they are persistently engaged over their first year of training. As soldiers progress in their careers persistent adaptation cannot be taken for granted as their roles can become increasingly sedentary and chronic disability due to injuries and obesity become more prevalent[124]. The purpose of this study was to investigate screening for cardiac disease in a standard cohort of potential recruits. It was not to evaluate changes in athletic physiology, nor to extrapolate these results onto another population. Therefore the purpose of questioning study participants on how many hours they trained each week and for how long they had been training at that level, was to merely ascertain whether this cohort should also be considered collectively as athletes. The self-declared training times described by the candidates were neither well standardised nor validated and as such they were not used to subdivide the

screened population into more or less athletic groups. On average the candidates declared that they were training on average for one hour daily and had been for 6 months. Even if this proportion suffers from a high degree of over-reporting it does indicate that the majority of applicants have prepared in anticipation of the fitness assessment that is a component of the selection process.

That some degree of athletic adaptation may have occurred was provided by the high proportion of type 1 ECG changes identified using the 2010 ECG interpretation guidelines. In this cohort 76.5% of candidates exhibited at least one type 1 ECG characteristic. This compares similarly to a larger cohort of similarly aged athletes that using the same 2010 criteria exhibited type 1 changes in 84.7% of cases compared to non-athletes where type 1 changes were seen in 49.1% [125]. These athletic changes were seen more frequently in males that in females.

6.5.4 ECG and echo findings. These data demonstrate some similarities and differences to other datasets. For example, in a study investigating 510 US college athletes[126], using a similar study design to this, a LAA was seen in 5.1% (compared to 3.1% in this study), a RAA was seen in 1.0% (compared to 1.3% in this study), a leftward axis was detected in 0.6% (compared to 3.2% in this study) and a rightward axis >120 degrees in 0.2% (compared to 1% in this study). The college athletes had a higher rate of RBBB compared to this group (13% versus 0.8%) and 2 cases presented with a LBBB, a characteristic not seen at all in this group. There were T-wave inversions in 3 cases (5.8%). An echo characterised 6 cases of

valvular heart disease, one case of HCM and one case of DCM, possibly following an episode of viral myocarditis.

Another similar study of 964 college athletes interpreting the ECGs using a different (less well defined) protocol[127], detected a LAA in 4.8%, RBBB in 1.1% and an accessory pathway in 7 cases (compared with 4 cases in this study) and one of these had Ebstein's anomaly. There was also a single diagnosis of LQTS. Repolarisation abnormalities were seen in 2.1% of candidates compared to 2.8% in this study. Valvular or structural disease was identified on echo in 7 cases. No cardiomyopathy was diagnosed.

The relatively low prevalence of the different ECG findings and the different patient populations prevents a meaningful comparison between studies. However the observations in this study do not appear significantly different to the expected prevalence of ECG and echo findings or of cardiac disease.

6.5.5 Pathological findings. The majority of VHD found in this study were trivial and of no clinical consequence; most were mild mitral or TR and this constituted 14 of the 19 cases. Of the remaining 5 cases none were physically limiting at the time of discovery. Bicuspid aortic valves without significant stenosis or regurgitation and in the absence of aortic dilatation do not usually restrict participation in sport. Nor would MVP with only mild MR. However the Armed Forces recruit for a full career of 22 years and the speed of disease progression in a 20 year old is not foreseeable. For this reason both conditions were a bar to service.

A number of potentially fatal conditions were identified by screening. These included three cardiomyopathies, a case of LQTS and 4 cases of ventricular pre-excitation. To the casual observer that these potentially fatal conditions are lurking asymptomatic and unnoticed in otherwise fit and well people might be surprising. That these were discovered at these rates is not unsurprising given the known prevalence of these diseases as we have discussed previously. The key role of the screening options was to therefore identify these conditions as effectively as possible.

6.5.6 Screening system efficacy. The analysis of the different screening systems utilising either a physical examination or ECG (with one of three guidelines on interpretation) or both, show a clear evolution in the test efficacy. However interpretation of the results isn't straightforward as the physical examination and ECG identify different disease conditions, some of which have an overlap and both create the complication of false positive results. There is little overlap in the two tests that allow a false positive in one test to be excluded by the other. The key false positives are the 9 in every 10 murmurs that are physiological in origin and the low individual rates of ECG findings (T-wave inversions, axis deviation, left and right atrial abnormalities and so on) that cumulatively add up to significant false positive rates. The introduction of an echo does however exclude disease in a great many of these candidates.

The evolution in ECG guidelines showed a decrease in the requirement for echo from 37.7% using the 2010 guidelines, to 10.9% with the Seattle guidelines and 5.3% with the 2017 guidelines. The three guidelines identified all the likely causes of SCD aside from the atypically presenting case of probable ARVC. Unfortunately they missed the structural and VHD in most cases.

The existing system of deferral to Cardiac Report whenever a murmur was identified has been shown in the last chapter to be flawed because it is expensive, logistically inefficient and still probably misses most of the potentially life-threatening disease. In this study screening with only a physical examination resulted in an echo rate of 16.1% - higher than the historical average referral rate to Cardiac Report. Why this was the case is uncertain. The cardiology registrar auscultating for a murmur heard a murmur in 7.2% of cases and yet almost 9% more cases were reported to have a murmur by the examining occupational physician. It may be that a Hawthorne-like effect occurred with the examining occupational doctors, who knew that their patients were enrolled in a trial and they didn't want to appear as though they had missed a murmur. Despite the high murmur detection rate, auscultation alone missed almost all of the potentially fatal disease cases aside from one case of HCM.

Combining the two tests did improve the Sn and Sp, especially when the 2017 guidelines were adopted. Unfortunately 20.8% of candidates still required an echo. This would have been logistically impossible and very expensive if all these candidates were referred on to Cardiac Report for echo. It was therefore proposed by the primary investigator that we

bring the echo service to the point-of-care and those candidates that needed an echo could get this on the day in their IRM. By introducing this 'Method H' from above the deferral rate could be reduced to 29 candidates (3.5%) or whom 48.3% are likely to have a significant cardiac condition. This would increase the detection rate of disease and reduce the deferral rate, thus streamlining the IRM.

An automated and manually measured QT was recorded for all ECGs. The QT measurement is regarded as a more subjective measurement in ECG analysis than other parameters and although it can be reliably taught[128], expertise in measurement generally is not highly reproducible. Automated measurement algorithms are prone to errors when arrythmias such are premature atrial or ventricular complexes, atrial fibrillation or even pronounced sinus arrythmia are present. Reproducibility using manual and automated methods has been shown to be poor in normal subjects[129 130]. The automated algorithm measured the QT duration as longer than the manual measurement in this study. This does not however mean that one measurement is better than the other for screening and it is possible that a hybrid of manual and automated measurement, to act as a self-checking mechanism, is likely to be best strategy. The question of whether one individually or both combined might be better was not investigated. The methodology for this would require a greater number of analysing clinicians and a variety of expertise levels.

6.5.7 Cost effectiveness. The costs for the screening investigations themselves were similar to the analysis performed by Dhutia et al in their 2017 analysis[61] – both consultation, physical examination and ECG were approximately £35 for each candidate despite the British Army costs not being subsidised, but rather because it was integrated into a larger

multi-system screening system. The cost of the British Army system was therefore reproducible as a 'real-life' screening system should another organisation in the UK want to reproduce it within a similar multi-system screening context.

The main cost to the British Army of the screening is the cost of the occupational medicine opinion at the IRM, of which the multi-system physical examination is a part, and of the consultations by Cardiac Report. Even if the cardiac aspects of the IRM examination were to be removed it would not significantly alter the time taken for the IRM consultation. Accelerating the consultation is not required to increase efficiency operationally as the limitation to the numbers of candidates screened daily at the selection centres is the accommodation capacity provided and most IRMs are completed early in the day. Removing the cardiac physical examination would be inconsistent with the other aspects of the physical examination looking for non-cardiac disease and is unlikely to be an acceptable strategy to the occupational medicine doctors running the recruiting medical. This is because the physical examination clearly detects so many cases of structural disease, even if most are not likely to be life-threatening and as a downside there is a high false positive rate. This is confirmed as the system in place currently accepts these limitations.

When a physical examination only strategy is used then bringing the ECG and echo to the IRM would significantly reduce the cost of cardiac screening by 57.7% per candidate to the British Army (£97 compared to £41). This innovation alone would be highly cost-effective and with the adoption of appropriate governance structures, such as a cardiology specialist opinion in cases of uncertainty, it is unlikely to result in a reduction in the quality of care.

This saving is before the additional costs of transport to and from the Cardiac Report appointment, the costs of returning to the selection centre for the majority that are passed and the opportunity cost in deferring candidates who would have been passed on the day; the reality is therefore likely to be an even greater cost savings.

The use of an ECG alone adds to the cost of screening and the newer guidelines reduce the false positive rate and consequently the cost compared to the older guidelines. The most cost-effective ECG strategy would be to use the 2017 guidelines regardless of whether a physical examination was used or not.

The combination of both physical examination and ECG improves the quality of the screening itself as previously discussed. Screening with a physical examination and ECG each have their benefits and drawbacks and the two modalities complement each other. The drawback of the strategy is that of cost, but this analysis shows that the cost to the British Army of physically examining and recording an ECG routinely in all candidates, then performing an echo when required in the selection centre at the time of the IRM, would be nearly 50% cheaper than the current system utilising Cardiac Report.

If the echos were moved into the selection centre and performed on the day, it would be only £8 more expensive to the British Army per candidate to add an ECG for all candidates (using the 2017 ECG interpretation guidelines). There would be an increased cost to the NHS and overall to investigate the additional abnormalities detected, but this cost seems

reasonable at only £118 per candidate overall compared to £113 per candidate overall using the current system, as this combined system would detect the potentially life threatening diseases that were essentially all missed under the current system.

Despite the limitations in the methodology of this cost-effectiveness analysis, these data provide a compelling argument to change the current system on cost grounds. An integrated screening system that uses a physical examination and ECG in all candidates and an echo on the day of the ILR in the selection centre, in those in whom a murmur or ECG abnormality (using the 2017 ECG interpretation guidelines) is detected would be cheaper than the current system to the British Army and only £6 more expensive per candidate overall whilst also detecting the more dangerous cardiac conditions that the current system misses.

6.5.8 Modelling a proposed new system (Method H in table 6.26). The three main selection centres had a capacity to perform the IRM and onward selection process, on 36-38 candidates each day. This was limited primarily by restrictions on the available accommodation. In a small sample of 50 ECGs we showed that acquiring an ECG took <4 minutes in almost all cases (results not included in this thesis). In performing this study at Pirbright I had proven that up to twelve echos could be performed daily without significantly delaying the operational screening of the IRM. Any further echos caused delays that had proven unacceptable to the screening team. This study was performed under conditions more strict than the normal screening process and the ECG interpretation was performed by a cardiac specialist trained in ECG interpretation and how it would perform in the 'real

world' was uncertain. I hypothesised that the murmur detection rate would deviate to the long term mean rate of approximately 9% but that the detection rate for ECG abnormalities might increase when ECGs were interpreted by non-cardiologists.

By applying different echo rates, including the study rate of 20.8%, the probability of requiring to perform up to and including 10 or 12 echos in a day was modelled using a binomial distribution (table 6.28). At the study echo rate of 20.8% of candidates undergoing echo the probability of requiring to perform >12 echos in a day was only 3.9%. In these cases candidates could have their echo first thing in the morning the following day.

Probability of an echo	Probability of >12 echos	Probability of >10 echos
0.150	0.003	0.021
0.208	0.039	0.150
0.250	0.132	0.345

Table 6.28: Probabilities of undertaking >12 or >10 echos daily at different echo rates per candidate.

Appropriate clinical governance policies were also proposed and a screening system using the study ECG interpretation protocol was developed and implemented over a one year period by the primary investigator as the new British Army screening program. Since the introduction of the system approximately 20,000 potential recruits to the British Army have been annually screened using this system. The savings of converting to this system is £48 per candidate to the British Army. This represents an annual saving of approximately

£960,000 to the British Army whilst improving the detection rate of serious disease and increasing the efficiency of the screening system.

6.5 Key findings

1. 834 potential recruits to the British Army volunteered to participate in this study.
2. Candidates were excluded if they had any cardiac symptoms, history or family history.
3. All candidates underwent screening by physical examination, 12 lead ECG and echo.
4. The ECG was interpreted using three guidelines and the different guidelines, with and without a physical examination were evaluated. The ECG interpretation guidelines were the ESC 2010 guidelines, the Seattle criteria and the 2017 International Guidelines.
5. In total 60 candidates had either a pathological cardiac condition or a suspicion of one that required further investigation.
6. The incidence of any cardiac disease, including clinically irrelevant disease, was 4.31%.
7. Following investigation 16 candidates were failed (a prevalence of 1.92%) of which 14 were 'officially' failed and 2 with confirmed disease dropped out of the application process and were lost to follow-up.
8. The physical examination alone missed all the disease that was likely to cause SCD with the exception of one case of HCM.
9. The ECG interpreted using the 2010 guidelines detected all the cardiac disease that might cause a SCD but had an unacceptably high false positive rate.

10. The Seattle criteria and 2017 guidelines detected all the disease that could cause SCD except for an unusual presentation of probable ARVC.
11. The combination of physical examination and ECG interpretation using the 2017 guidelines detected all the disease with exception of one case of a BAV and the ARVC case. The echo rate for this strategy though remained 20.8%.
12. The addition to an echo on the day, when indicated, allowed most of the false positive screening results from the physical examination or ECG to be passed. With this system 29 candidates would have been deferred on the day; 14 of these would have cardiac disease that would result in a fail outcome from their IRM and 15 were false positive tests.
13. Performing the ECG and echo on the day of the IRM at the selection centre, , in the case of a murmur being detected, and moving the responsibility for decision making to the occupational physicians instead of outsourcing to Cardiac Report, would reduce the cost per candidate of screening by 57.7% compared to the current system.
14. The cost of performing a physical examination and ECG with the 2017 ECG interpretation guidelines utilised on all candidates, an echo if indicated at the selection centre, on the day of the IRM and moving the responsibility for decision making from the Cardiac Report cardiologists to the occupation physicians performing the IRM, would reduce the cost to the British Army by 49.5% per candidate compared to the current system and detect more potentially fatal cardiac conditions.
15. This system was proposed as a new system to improve the cardiac screening of potential recruits and it has since been introduced as the British Army's cardiac screening system nationally. This new system will have saved the British Army

approximately £960,000 annually whilst improving the detection of serious cardiac disease.

6.6 Acknowledgements

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Chapter 7: Summary and conclusions

This thesis explores cardiac disease in the UK Armed forces both from an epidemiology perspective and from the viewpoint of developing a system to identify disease early. The first section, consisting of Chapters 2-4, looks at the epidemiology of deaths and morbidity resulting from CVD in general. The second section, consisting of Chapters 5 and 6, focuses on how to detect disease through the systematic screening of potential recruits to the British Army.

7.1 Cardiac mortality in the UK Armed Forces

The first research project, described in Chapter 2, investigates cardiovascular mortality. This is a retrospective review of the 279 deaths (9.2% of all in-service deaths, crude mortality rate of 7.41 per 100,000 Serviceperson years) due to CVD deaths in the UK Armed Forces over a 17 year period. Through a systematic examination of the death certificates and autopsy findings, a picture of the underlying diagnoses that led to death is gained. It shows that males were more likely to die than females and that deaths in the service population occurred worldwide. In particular 27.6% of deaths occurred whilst on duty and 5.7% occurred whilst the decedent was serving on active operations or in the UK's enduring overseas commitments.

The main cause of cardiovascular death was from IHD; this accounted for 106 of the deaths. These were all in males and death rates increased rapidly in incidence from the fourth

decade of life onwards. The death rates due to IHD trended downwards over the course of the study period. This finding is a reflection of downward mortality trends due to IHD in the general population. The downward mortality trends are likely to be due to a drop in the proportion of the population smoking tobacco, improved primary prevention treatments to manage risk factors-such as dyslipidaemia and hypertension- and better acute treatments and secondary prevention therapies.

Myocardial diseases were an important cause of death and included cardiomyopathies, myocarditis and cardiac sarcoidosis. Hypertrophic cardiomyopathy accounted for 13 deaths and was the most common cause of death from myocardial disease (crude rate 0.35 per 100,000 Serviceperson years).

In 64 cases and constituting approximately a third of all cardiovascular deaths, the cause of death was presumed to be a cardiac arrhythmia but no underlying pathology was found. We know from other cardiac epidemiology research that these SADS deaths are usually due to a combination of several inherited cardiac diseases including ion channelopathies and cardiomyopathies. In 6 cases congenital heart disease was the cause of death, including cases due to AS associated with a BAV, pre-excited AF or malignant aberrant origins to the coronary arteries.

7.2 Discharges from the UK Armed Forces due to cardiovascular disease

The employment requirements of military service include robust health and in cases where CVD is diagnosed, individuals are often discharged on medical grounds. Chapter 3 of this thesis describes a retrospective investigation of the burden of CVD leading to medical discharges over a 17 year span. During this period cardiovascular diseases combined accounted for 707 medical discharges (crude rate: 19.42 per 100,000 service person years). There were differences in the rates of discharge by Service. There were also year-to-year differences in the rates of discharge. These differences reflect policy changes and the varying tolerance of the Armed Forces to retain personnel with restrictions to their employment.

Similar cardiac conditions to those that were found leading to death, were also found to lead to medical discharges. In addition conditions associated with disabling symptoms, but not death were also identified as a reason for medical discharge. These included discharges due to IHD, structural and mild congenital heart diseases, such as septal defects, MVP, aortopathies and degenerative BAV. Other important reasons for discharge were myocardial diseases, including inherited cardiomyopathies such as HCM. Primary arrhythmic complaints that resulted in discharge included disabling atrial fibrillation and supraventricular tachycardias as well as potentially fatal ion channelopathies.

7.3 Operational medicine and cardiology

Chapter 4, the third epidemiology chapter investigates the admissions, under GIM team, to the British Role 3 Hospital in Camp Bastion during combat operations in Helmand Province,

Afghanistan. This was a 2 year prospective, cross-sectional study designed to identify epidemiological patterns, preventable admissions and diagnostic, treatment or training deficiencies in operational general medicine. In addition to the general medicine data collected, it also identified important operational insights into cardiovascular disease.

In total 1,368 patients (20% of admissions; mean 1.87 patients / day) were admitted under the GIM team. The length of stay was relatively short: less than 2 days before patients were evacuated back to their home country or discharged back to their units. Symptoms suggestive of cardiac disease and in particular chest pain, syncope, acute breathlessness and palpitations were all common presentations. There were 111 primary cardiac diagnoses (8.1% of admissions) made. Ischaemic heart disease was diagnosed in 40 admissions (2.4% of diagnoses), 20 of which were acute MI (1.2% of diagnoses) and 15 were new cases of unstable angina (1.0% of diagnoses). There were 11 admissions with newly diagnosed atrial fibrillation and 13 admissions with supraventricular tachycardias. Uncommon cardiac diagnoses included HCM and DCM and conduction disease and pericarditis, the latter was diagnosed in 11 patients. No military patients died from cardiac disease, but two civilian contractors died from acute MI. This study resulted in changes to pre-deployment training and in the provision of cardiac echo on operations.

The combination of findings from these three studies demonstrates that cardiac disease presents an ongoing problem in the UK Armed Forces. The cardiac diseases that are most important militarily are acquired conditions, in particular IHD and inherited conditions, such as cardiomyopathies and the wide range of conditions that underlie deaths due to SADS.

With regards to IHD, deaths occur later in life and have been trending downwards as a consequence of advances in prevention and treatment. Detection of high risk individuals prior to their acute event is difficult and prevention is primarily focused around the management of risk factors in primary care.

With regards to inherited cardiac conditions, many individuals die as the first presentation of their underlying disease that until the terminal event was unknown. These diseases can be and are screened for by the UK Armed Forces and the second section of this thesis investigates the screening system in place and the options of introducing an ECG to the screening system in order to improve the detection rates of militarily important cardiac disease.

7.4 The existing screening programme

Chapter 5 describes an evaluation of the pre-existing screening system. This is a retrospective study investigating in particular the findings of Cardiac Report Ltd. They were contracted by the British Army to provide a consultation with a cardiology consultant and perform an ECG and echo on all potential recruits found to be normal at their IRM, aside from the discovery of a murmur on auscultation.

In total the number of recruits aged 16-32 screened at the IRM during this period was 122,181. Of these 11,070 candidates, constituting 9.1% of the total IRM population, were

assessed by Cardiac Report. On re-examination by a Cardiac Report cardiologist, on a different day to their IRM, a murmur was not detected in 75.4% of candidates in whom a murmur had been detected at the IRM. The majority of candidates (97.1%) in whom no murmur was detected by the Cardiac Report cardiologist were passed with no underlying cardiac disease detected. Therefore most murmurs detected at the initial recruit medical were innocent and did not represent disease. Murmurs described as diastolic by a Cardiac Report cardiologist were rare, but the positive predictive value of detecting a cardiac disease when a diastolic murmur was detected was 90.1%.

Following investigation by Cardiac Report 6.6% of candidates were found to have a confirmed or suspected abnormality and 43% of these were passed. The most frequent abnormalities identified were of structural diseases (valvular disease, septal defects, and other abnormalities) seen in 4.8% of candidates. A BAV was identified in 120 candidates of which 53.3% had at least mild BAV dysfunction, aortic root dilatation or rarely, aortic coarctation; the remaining 46.7% were functionally normal. An ECG was not a useful investigation to identify a BAV and was normal in 95% of cases. A cardiomyopathy was suspected or diagnosed in 1.1% and a primary electrical disease was suspected or diagnosed in 0.6% of cases. In total 3.7% of candidates investigated by Cardiac Report were deferred or failed due to the detection or suspicion of cardiac disease.

These findings showed that the screening system of referring only candidates in whom a murmur was heard had a high false positive rate and created a speedbump to the efficiency of the recruiting system. Whilst it did identify candidates with significant structural diseases

it is likely that most of the cardiomyopathy and primary electrical disease cases were identified as incidental findings, as in most cases no murmur was detected by the Cardiac Report cardiologist. These conclusions led the primary investigator to believe an alternative screening system should be evaluated and this forms the subject of Chapter 6.

7.5 Study screening potential recruits with an additional ECG

The final research chapter describes a prospective cross-sectional study where 834 potential recruits to the British Army volunteered to undergo an ECG and echo in addition to the standard screening system of a clinical history and physical examination. Screening with and without a physical examination and with and without an ECG were compared. The ECG when included was interpreted using three different interpretation guidelines (the ESC 2010 guidelines, the Seattle criteria and the 2017 International guidelines). Comparison was against a pragmatic 'gold standard' of a history, physical examination, ECG, echo and any other clinically indicated tests.

In total 60 candidates were either suspected or diagnosed with cardiac disease on the day of screening. Candidates with suspected disease were deferred for further investigation. The incidence of cardiac disease, including clinically irrelevant disease, was 4.31% and 16 candidates were failed (a prevalence of 1.92%) of which 14 were 'officially' failed and 2 with confirmed disease dropped out of the application process and were lost to follow-up. The diseases identified with the potential to cause SCD included 2 cases of HCM, 1 case of ARVC, 4 candidates with ventricular pre-excitation and a case of LQTS. Other important diseases

included 3 cases of BAV disease, one case of MVP, one PDA and a VSD with associated AV valve regurgitation.

With the exception of one case of HCM the physical examination alone missed all the disease that was likely to cause SCD, but it did detect most structural disease. Using an ECG interpreted using the 2010 guidelines enabled the detection of all the cardiac disease that might cause a SCD but had an unacceptably high false positive rate. Using an ECG interpreted using the Seattle criteria or 2017 guidelines detected all the disease that could cause SCD except for an unusual presentation of probable ARVC but missed most of the structural disease. The combination of physical examination and ECG interpretation using the 2017 guidelines detected all the disease with the exception of one case of a BAV and the ARVC case. The echo rate for this strategy remained 20.8%, over twice the rate of referral to Cardiac Report under the existing system.

The addition of an echo on the day, when indicated, allowed most of the false positive screening results from the physical examination or ECG to have disease excluded and be passed. With this system 29 candidates (3.5%) would have been deferred on the day; however 14 of these would have had confirmed cardiac disease that would result in a fail outcome from their IRM and 15 would have been false positive tests.

A cost-effectiveness analysis of the different screening systems indicated that significant savings would be made through implementing an enhanced screening system that utilised

an ECG. As a consequence of this study, implementation of this system was proposed in order to improve the cardiac screening of potential recruits and it has since been introduced as the British Army's screening system nationally.

7.6 The current situation with screening in the UK Armed Forces

Since the completion of this research and the successful introduction of this enhanced screening system across the UK based Army selection, the primary investigator has also facilitated the expansion of this system to the selection of the recruits into the Brigade of Gurkhas in Nepal.

Unfortunately the three Armed Services all operate separate recruiting systems with individual single-Service policies relating to how recruit screening is undertaken. In particular the infrastructure for recruitment into the RN and RAF is far less developed or centralised than the Army system. As a consequence the adoption of the British Army's screening method by the other Services is not simple, albeit that both Services have declared that it is their desired direction of travel. Currently both the RN and the RAF entry medicals consist of a medical history and physical examination and further investigations only if there is an abnormality detected.

7.7 Future directions

There has never been a randomised controlled trial of screening with or without an ECG. As discussed in the introduction, the best evidence of benefit is the data from northern Italy

demonstrating a reduction in the mortality rate in athletes to that similar to the baseline level of non-athletes following the introduction of the screening programme that utilised an ECG. The current difference in screening methodologies between the British Army on one hand, who now utilise the ECG routinely, and RN and RAF on the other, provides the opportunity of comparing the mortality rates in each group over the same period. This study is planned by the author.

The operationally active current screening system results is approximately 20,000 IRMs being performed annually and this provides an opportunity for the recruit population to be selectively studied. There is a need to validate the system that is not run by cardiologists, but rather by occupational physicians, most of whom have a background in general practice and this ongoing governance work is undertaken by Capita, the contractor that currently owns the recruiting contract for the British Army. As described in the discussion of the previous chapter, there are gaps in our knowledge regarding the female, Nepali, Fijian and Black, as well as mixed race recruit populations. Currently the author is engaged in a study looking at Gurkha recruits undergoing selection at the British Army camp in Pokhara, Nepal but these other groups also present an opportunity for study.

Further exciting areas that could improve the screening process involve using machine learning to digitally analyse the heart sounds recorded through an electronic stethoscope. This has the potential to improve the referrals for echo in the presence of a murmur and has the potential to reduce the false positive rate from this element of the screening system.

There may also be the potential for a similar use of artificial intelligence in the interpretation of the ECG.

Screening for cardiac disease has evolved a great deal in the last decade but there are still false positives and potentially false negatives with the system currently in use. There are also unknowns in the natural history of the different important diseases and even what constitutes a normal phenotype for several sub-groups of the military population. With the current systems in place there is now a wonderful opportunity to fill in some of these gaps in order to make the already good screening system even better.

The end. Of a beginning.

Appendix A – Military consensus guidance on eligibility criteria for the screening study

Appendix A: Table 1 - Congenital diseases

Lesion	Common definition criteria	Action for recruits
ASD (closed or small, unoperated)	<6 mm defect, or 6 months post-closure, with normal pulmonary artery pressure, no significant arrhythmia or ventricular dysfunction	Likely to be eligible. Need ref for further cardiology assessment prior to joining (or qualifying correspondence). Discuss with military occupational medicine +/- consultant cardiologist
Patent foramen ovale	May need a bubble echo to diagnose but this should not prevent immediate eligibility	Eligible. Percutaneous closure may be considered before regular scuba diving
VSD (closed or small unoperated)	Restrictive defect (left-to-right gradient >64 mmHg) or >6 months post-closure, no pulmonary hypertension	Likely to be eligible. Need ref for further cardiology assessment prior to joining (or qualifying correspondence). Discuss with military occupational medicine +/- consultant cardiologist
Other VSD	More severe than above	Not eligible
AVSD	Individual review based on defects above	Likely to not be eligible. Need ref for further cardiology assessment prior to joining (or qualifying correspondence). Discuss with military occupational medicine +/- consultant cardiologist
Partial or complete anomalous pulmonary venous connection	No significant pulmonary or systemic venous obstruction, no pulmonary hypertension or exercise-induced atrial arrhythmia	Likely to not be eligible. Need ref for further cardiology assessment prior to joining (or qualifying correspondence). Discuss with military occupational medicine +/- consultant cardiologist
Persistent ductus arteriosus (operated)	6 months post-closure and no residual pulmonary hypertension	Likely to be eligible. Need ref for further cardiology assessment prior to joining (or qualifying correspondence). Discuss with military occupational medicine +/- consultant cardiologist
Persistent ductus arteriosus (not operated)	Any imaging modality	Need ref for further cardiology assessment prior to joining (or qualifying correspondence). Discuss with military occupational medicine +/- consultant cardiologist

Appendix A: Table 1 - Congenital diseases continued

Lesion	Common definition criteria	Action for recruits
Pulmonary stenosis (mild native or treated)	Native or 6 months post-interventional/post-surgical; normal RV, normal ECG or only mild RV hypertrophy, no significant arrhythmias	Likely to be eligible. Need ref for further cardiology assessment prior to joining (or qualifying correspondence). Discuss with military occupational medicine +/- consultant cardiologist
Pulmonary stenosis (moderate or severe native or treated)	Peak transvalvular gradient ,>3 $msec^{-1}$, ECG changes	Not eligible
Non-tricuspid aortic valve	Any diagnosis	Not eligible
Coarctation of the aorta (native or repaired)	Any diagnosis	Not eligible
Tetralogy of Fallot	Any diagnosis	Not eligible
Transposition of the great arteries (arterial switch)	Any diagnosis	Not eligible
Malignant coronary artery origins or proximal LMS tunnelled coronary artery	Will need CTA / CMR to confirm	Not eligible
Familial hypercholestrolaemia	Any diagnosis	Need ref for further cardiology / chemical biology assessment prior to joining (or qualifying correspondence). Usually not eligible if treated or should be treated with a statin (increased risk of rhabdomyolysis) Discuss with military occupational medicine +/- consultant cardiologist
Marfan's Syndrome	Any diagnosis	Not eligible
Other connective tissue disease	Any diagnosis	Likely to not be eligible. Need ref for further cardiology assessment prior to joining (or qualifying correspondence). Discuss with military occupational medicine +/- consultant cardiologist

Appendix A, Table 2 - Valvular heart disease

Lesion	Definition criteria	Action for recruits
Mitral Valve Stenosis (any severity)	Any diagnosis criteria (multiple modalities)	Likely to be ineligible. Need ref for further cardiology assessment prior to joining (or qualifying correspondence). Discuss with military consultant cardiologist and occupational medicine
Mitral valve Regurgitation (mild-moderate)	Jet area / LA <20% Vena contracta <0.3cm PISA radius <0.4 Regurgitant volume <30mL Regurgitant fraction <30% Regurgitant orifice area <0.2cm2 No atrial fibrillation	Likely to be eligible Discuss with military consultant cardiologist and occupational medicine
Mitral valve prolapse	Mitral leaflet thickening >5 mm and leaflet displacement >2 mm (one or both valves)	Discuss with military consultant cardiologist and occupational medicine Usually eligible if complete absence of: unexplained syncope, family history of sudden death, complex supraventricular or ventricular arrhythmias or long QT interval or moderate-severe mitral regurgitation
Aortic stenosis (mild)	Mean transvalvular gradient <25 mmHg, no history of arrhythmia, no syncope, dizziness, or angina pectoris	Likely to be ineligible Need ref for further cardiology assessment prior to joining (or qualifying correspondence). Discuss with military consultant cardiologist and occupational medicine
Aortic stenosis (moderate to severe)	Mean transvalvular gradient between >25 mmHg, no history of arrhythmia, no syncope, dizziness or angina pectoris	Not eligible

Appendix A: Table 2 - Valvular heart disease continued

Lesion	Definition criteria	Action for recruits
Aortic valve regurgitation (mild)	Vena contracta <0.3cm Jet width/LVOT diam <25% Regurgitant volume <30mL Regurgitant fraction <30% Regurgitant orifice area <0.1cm2 Pressure half-time <500ms normal LV size and function, no significant arrhythmia	Usually eligible if a structurally normal valve Discuss with military consultant cardiologist and occupational medicine
Aortic valve regurgitation (moderate to severe)	As for mild but with one or more worse measure	Likely to be ineligible. Need ref for further cardiology assessment prior to joining (or qualifying correspondence). Will require an ETT. Discuss with military consultant cardiologist and occupational medicine
Tricuspid valve stenosis (mild)	Valve area <7cm2 but normal RA pressure	Usually eligible Discuss with military consultant cardiologist and occupational medicine
Tricuspid valve stenosis (moderate or severe)	Valve area <7cm2 and elevated RA pressure	Likely to be ineligible Need ref for further cardiology assessment prior to joining (or qualifying correspondence). Discuss with military consultant cardiologist and occupational medicine
Tricuspid valve regurgitation (mild)	Jet area <5cm2; PISA radius <0.5cm; CW jet contour soft and parabolic; RV/RA/IVC normal sized	Eligible Discuss with military consultant cardiologist and occupational medicine
Tricuspid valve regurgitation (moderate or severe)	More severe than above	Likely to be ineligible Need ref for further cardiology assessment prior to joining (or qualifying correspondence). Discuss with military consultant cardiologist and occupational medicine
Poly-valvular diseases	See most relevant valve	See most relevant valve
Prosthetic valve or valvuloplasty	Any diagnosis	Not eligible

Appendix A: Table 3 - Heart muscle and pericardial disease

Lesion	Definition criteria	Action for recruits
Hypertrophic cardiomyopathy	Will need additional investigations to confirm screening suspicions (ETT, CMR, Holter)	Not eligible Discuss with military consultant cardiologist and occupational medicine if there is doubt regarding the diagnosis
Dilated cardiomyopathy	Will need additional investigations to confirm screening suspicions (ETT, CMR, Holter)	Not eligible Discuss with military consultant cardiologist and occupational medicine if there is doubt regarding the diagnosis
Arrythmogenic right ventricular cardiomyopathy	Will need additional investigations to confirm screening suspicions (ETT, CMR, Holter)	Not eligible Discuss with military consultant cardiologist and occupational medicine if there is doubt regarding the diagnosis
Infiltrative disease	Will need additional investigations to confirm screening suspicions (ETT, CMR, Holter)	Usually ineligible Need ref for further cardiology assessment prior to joining (or qualifying correspondence). Discuss with military consultant cardiologist and occupational medicine
Myocarditis	If symptoms completely resolved and ECG, echo, Holter +/- CMR normal	Sometimes eligible Discuss with military consultant cardiologist and occupational medicine
Pericarditis - single episode	If symptoms completely resolved for 2 years and ECG and echo normal	Usually eligible Discuss with military consultant cardiologist and occupational medicine
Recurrent pericarditis	Recurrent disease	Usually ineligible

Appendix A: Table 4 - Primary electrical disease

Lesion	Definition criteria	Action for recruits
Marked sinus bradycardia (<40 b.p.m.) and/or sinus pauses >3 s with symptoms	ECG	Unusual finding but can be related with extreme endurance training. Need ref for further cardiology assessment prior to joining (or qualifying correspondence). Chronotropic competence annd normal cardiac structure needs to be confirmed. Discuss with military consultant cardiologist and occupational medicine
Asymptomatic partial RBBB, AV block first and second degree, type 1	ECG	Eligible
Mobitz type 2 second degree AV block or complete heart block	ECG	Usually ineligible Need ref for further cardiology assessment prior to joining (or qualifying correspondence). Discuss with military consultant cardiologist and occupational medicine
Supraventricular premature beats	Asymptomatic, no thyroid disease	Eligible
Paroxysmal supraventricular tachycardia (AVNRT or AVRT over a concealed accessory pathway)	ECG	EPS and ablation is required with no reoccurrence off medication for 6 months. Discuss with military consultant cardiologist and occupational medicine
Ventricular pre-excitation (WPW syndrome) with symptoms thought due to a) Paroxysmal AV reentry tachycardia b) Atrial fibrillation or atrial flutter	ECG	Ablation is required with no reoccurrence off medication for 6 months. Discuss with military consultant cardiologist and occupational medicine

Appendix A: Table 4 - Primary electrical disease continued

Lesion	Definition criteria	Action for recruits
Asymptomatic pre-excitation pattern	Short-PR and delta wave with no evidence of symptoms or documented SVT	EPS +/- ablation is required with no symptoms off medication for 6 months post-procedure Discuss with military consultant cardiologist and occupational medicine
Atrial fibrillation (paroxysmal, persistent)	ECG	Usually ineligible Discuss with military consultant cardiologist and occupational medicine
Atrial flutter	ECG	Ablation is required with no reoccurrence off medication for 6 months. Discuss with military consultant cardiologist and occupational medicine
PVCs	Frequent ectopy detected on palpation of the pulse and >2 PVBs detected on a 10s ECG,	Eligible if <2000 PVB/24 hours excluded on Holter and no structural disease Need ref for further cardiology assessment prior to joining (or qualifying correspondence). Discuss with military consultant cardiologist and occupational medicine
Nonsustained ventricular tachycardia	In the absence of: cardiac disease or arrhythmogenic condition, symptoms, family history of SD, relation with exercise, multiple episodes of NSVT with short RR interval. Define as 3 or more beats for <30 seconds for >120 bpm	Often eligible but likely to require EPS +/- ablation Need ref for further cardiology assessment prior to joining (or qualifying correspondence). Discuss with military consultant cardiologist and occupational medicine
Slow ventricular tachycardia, fascicular ventricular tachycardia, RV outflow tachycardia	In the absence of: cardiac disease or arrhythmogenic condition, family history of SD, symptoms	Often eligible but likely to require EPS +/- ablation Need ref for further cardiology assessment prior to joining (or qualifying correspondence). Discuss with military consultant cardiologist and occupational medicine
Neurocardiogenic syncope	Once arrhythmia excluded and a single episode only	Eligible but needs Ix if multiple episodes Discuss with military consultant cardiologist and occupational medicine
Long QT syndrome	ECG	Not eligible
Brugada syndrome	ECG	Not eligible

Appendix A: Table 4 - Primary electrical disease continued

Lesion	Definition criteria	Action for recruits
Other channelopathies	ECG	Not eligible
Implanted pacemaker for bradycardia indication	Any diagnosis	Not eligible
Implanted cardiac defibrillator	Any diagnosis	Not eligible
Implanted cardiac resynchronisation therapy device	Any diagnosis	Not eligible

Appendix A: Table 5 - HTN and CAD

Lesion	Definition criteria	Action for recruits
Primary systemic hypertension	No ECG or echo abnormalities and effectively treated on medications	Probably eligible at stage 1 Discuss with occupational medicine
Secondary systemic hypertension	Depends on the underlying cause	Depends on underlying condition, response to treatment. Discuss with occupational medicine and relevant specialist
Stable angina secondary to confirmed atheromatous coronary artery disease, even if treated	Any diagnosis	Ineligible
Post myocardial infarction due to confirmed atheromatous coronary artery disease	Any diagnosis	Ineligible

REFERENCES

1 Lozano R, Naghavi M, Foreman K et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet. 2012 15;380(9859):2095-128.

2 Nichols M, Townsend N, Scarborough P, Rayner M. Cardiovascular disease in Europe 2014: epidemiological update. Eur Heart J. 2014 7;35(42):2950-9.

3 https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/312539/uk_af_annual_personnel_report_2014.pdf accessed 4 December 2014.

4 Arnestad M, Crotti L, Rognum TO et al. Prevalence of long-QT syndrome gene variants in sudden infant death syndrome. Circulation. 2007 23;115(3):361-7.

5 Nichols M, Townsend N, Scarborough P, Rayner M. Trends in age-specific coronary heart disease mortality in the European Union over three decades: 1980-2009. Eur Heart J. 2013 34(39):3017-27.

6 Thompson PD, Buchner D, Pina IL et al. Exercise and physical activity in the prevention and treatment of atherosclerotic cardiovascular disease: a statement from the Council on Clinical Cardiology (Subcommittee on Exercise, Rehabilitation, and Prevention) and the Council on Nutrition, Physical Activity, and Metabolism (Subcommittee on Physical Activity). Circulation. 2003 24;107(24):3109-16.

7 Harmon KG, Asif IM, Klossner D, Drezner JA. Incidence of sudden cardiac death in national collegiate athletic association athletes. Circulation. 2011 19;123(15):1594-600.

8 Corrado D, Basso C, Rizzoli G, et al. Does Sports Activity Enhance the Risk of Sudden Death in Adolescents and Young Adults? J Am Coll Cardiol 2003;42-1959-63

9 Pilmer CM, Porter B, Kirsh JA et al. Scope and nature of sudden cardiac death before age 40 in Ontario: A report from the Cardiac Death Advisory Committee of the Office of the Chief Coroner. Heart Rhythm. 2013 10(4):517-23.

10 de Noronha SV, Behr ER, Papadakis M et al. The importance of specialist cardiac histopathological examination in the investigation of young sudden cardiac deaths. Europace. 2014 16(6):899-907.

11 Maron BJ, Carney KP, Lever HM, et al. Relationship of race to sudden cardiac death in competitive athletes with hypertrophic cardiomyopathy. J Am Coll Cardiol 2003;41: 974-80.

12 Maron BJ, Doerer JJ, Haas TS et al. Sudden deaths in young competitive athletes: analysis of 1866 deaths in the United States, 1980-2006. Circulation. 2009 3;119(8):1085-92.

13 Sheikh N, Sharma S. Overview of sudden cardiac death in young athletes. Phys Sportsmed. 2011 39(4):22-36.

14 Eckart RE, Scoville SL, Campbell CL. Sudden Death in Young Adults: A 25-Year Review of Autopsies in Military Recruits. Ann Intern Med. 2004;141:829-834

15 Eckart RE, Shry EA, Burke AP et al. Sudden death in young adults: an autopsy-based series of a population undergoing active surveillance. J Am Coll Cardiol. 2011 13;58(12):1254-61.

16 Tan HL, Hofman N, van Langen IM, et al. Sudden unexplained death: heritability and diagnostic yield of cardiological and genetic examination in surviving relatives. Circulation. 2005 12;112(2):207-13.

17 Behr ER, Dalageorgou C, Christiansen M et al. Sudden arrhythmic death syndrome: familial evaluation identifies inheritable heart disease in the majority of families. Eur Heart J. 2008 29(13):1670-80.

18 Kaufman ES. Mechanisms and clinical management of inherited channelopathies: long QT syndrome, Brugada syndrome, catecholaminergic polymorphic ventricular tachycardia, and short QT syndrome. Heart Rhythm. 2009 6(8 Suppl):S51-5.

19 van Rijsingen IA, Nannenberg EA, Arbustini E, Elliott PM, Mogensen J, Hermans-van Ast JF, van der Kooi AJ, van Tintelen JP, van den Berg MP, Grasso M, Serio A, Jenkins S, Rowland C, Richard P, Wilde AA, Perrot A, Pankuweit S, Zwinderman AH, Charron P, Christiaans I, Pinto YM. Gender-specific differences in major cardiac events and mortality in lamin A/C mutation carriers. Eur J Heart Fail. 2013 Apr;15(4):376-84. doi: 10.1093/eurjhf/hfs191.

20 Protonotarios A, Anastasakis A, Panagiotakos DB, Antoniades L, Syrris P, Vouliotis A, Stefanadis C, Tsatsopoulou A, McKenna WJ, Protonotarios N Arrhythmic risk assessment in genotyped families with arrhythmogenic right ventricular cardiomyopathy. Europace. 2016 Apr;18(4):610-6. doi: 10.1093/europace/euv061.

21 Bhonsale A, James CA, Tichnell C, Murray B, Madhavan S, Philips B, Russell SD, Abraham T, Tandri H, Judge DP, Calkins H. Risk stratification in arrhythmogenic right ventricular dysplasia/cardiomyopathy-associated desmosomal mutation carriers. Circ Arrhythm Electrophysiol. 2013 Jun;6(3):569-78. doi: 10.1161/CIRCEP.113.000233.

22 Terauchi Y, Kubo T, Baba Y, Hirota T, Tanioka K, Yamasaki N, Furuno T, Kitaoka H. Gender differences in the clinical features of hypertrophic cardiomyopathy caused by cardiac myosin-binding protein C gene mutations. J Cardiol. 2015 May;65(5):423-8. doi: 10.1016/j.jjcc.2014.07.010.

23 Christiaans I, Birnie E, Bonsel GJ, Mannens MM, Michels M, Majoor-Krakauer D, Dooijes D, van Tintelen JP, van den Berg MP, Volders PG, Arens YH, van den Wijngaard A, Atsma DE, Helderman-van den Enden AT, Houweling AC, de Boer K, van der Smagt JJ, Hauer RN, Marcelis CL, Timmermans J, van Langen IM, Wilde AA. Manifest disease, risk factors for

sudden cardiac death, and cardiac events in a large nationwide cohort of predictively tested hypertrophic cardiomyopathy mutation carriers: determining the best cardiological screening strategy. Eur Heart J. 2011 May;32(9):1161-70. doi: 10.1093/eurheartj/ehr092.

24 Yankelson L, Sadeh B, Gershovitz L et al. Life-threatening events during endurance sports: is heat stroke more prevalent than arrhythmic death? J Am Coll Cardiol. 2014 5;64(5):463-9

25 Mont L, Sambola A, Brugada J, et al. Long-lasting sport practice and lone atrial fibrillation. Eur Heart J. 2002 Mar;23(6):477-82.

26 Mont L, Elosua R, Brugada J. Endurance sport practice as a risk factor for atrial fibrillation and atrial flutter. Europace. 2009 Jan;11(1):11-7.

27 Baldesberger S, Bauersfeld U, Candinas R et al. Sinus node disease and arrhythmias in the long-term follow-up of former professional cyclists. Eur Heart J. 2008 Jan;29(1):71-8.

28 de Noronha SV, Sharma S, Papadakis M et al. Aetiology of sudden cardiac death in athletes in the United Kingdom: a pathological study. Heart. 2009 95(17):1409-14.

29 Maron BJ, Haas TS, Ahluwalia A, Rutten-Ramos SC. Incidence of cardiovascular sudden deaths in Minnesota high school athletes. Heart Rhythm. 2013 10(3):374-7.

30 Gray J. Mortality from ischaemic heart disease in the Armed Forces 1973-1984. J R Army Med Corps. 1987 Jun;133(2):106-12.

31 https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/295835/20140327_UKAF_deaths_National_Statistic_2013.pdf Accessed 3 December 2014.

32 Eckart RE, Love SS, Atwood JE et al. Incidence and follow-up of inflammatory cardiac complications after smallpox vaccination. J Am Coll Cardiol. 2004 7;44(1):201-5.

33 Stacey M, Woods D, Ross D and Wilson D. Heat illness in military populations: asking the right questions for research. J R Army Med Corps. 2014 160(2):121-4.

34 Woods DR, Boos C, Roberts PR. Cardiac arrhythmias at high altitude. J R Army Med Corps. 2011 157(1):59-62. Review.

35 Grainge C, Heber M. The role of the physician in modern military operations: 12 months experience in Southern Iraq. J R Army Med Corps. 2005 Jun;151(2):101-4.

36 Smallman-Raynor MR, Cliff AD. Impact of infectious diseases on war. Infect Dis Clin North Am. 2004;18:341–68

37 Raoult D, Dutour O, Houhamdi L et al. Evidence for louse-transmitted diseases in soldiers of Napoleon's Grand Army in Vilnius. G. J Infect Dis. 2006 Jan 1;193(1):112-20.

38 Sanders J, Putnam S, Frankart C, et al. Impact of illness and non-combat injury during operations Iraqi Freedom and Enduring Freedom (Afghanistan). Am J Trop Med Hyg 2005;73:713-9.

39 Personal communication with Sqn Ldr C Patterson RAF.

40 Fear NT, Sundin J, Rona RJ. Obesity in the United Kingdom Armed Forces: prevalence based on measured and self-reported data. Mil Med. 2011 176(1):44-9.

41 Casey A, Hughes J, Izard RM and Greeves JP. Supplement use by UK-based British Army soldiers in training. Br J Nutr. 2014 14;112(7):1175-84.

42 Cox AT, Linton T, et al. A review of the documentation in the British Armed Forces electronic patient record following discharge from the Role 3 Hospital in Camp Bastion. J R Army Med Corps. 2015 Jun;161(2):132-4.

43 Cox AT, Gillingham S et al. An assessment of the accuracy and utility of the primary care electronic medical record as used by the British Army. J R Army Med Corps. 2015 Nov 25.

44 Yoakum CS, Yerkes RM. Army mental tests. New York: Henry Holt And Company, 1920

45 Commission on Chronic Illness. Chronic illness in the United States. Vol I. Prevention of chronic illness. Cambridge, MA: Harvard University Press, 1957;1:45

46 Wilson JMG, Jungner G. Principles and practice of screening for diseases. Geneva: World Health Organisation, 1968.

47 Fagan TJ. Nomogram for Bayes theorem. N Engl J Med. 1975;293:257.

48 Bolin E, Lam W. A review of sensitivity, specificity, and likelihood ratios: evaluating the utility of the electrocardiogram as a screening tool in hypertrophic cardiomyopathy. Congenit Heart Dis. 2013 Sep-Oct;8(5):406-10.

49 Maron BJ, Thompson PD, Ackerman MJ et al. Recommendations and considerations related to preparticipation screening for cardiovascular abnormalities in competitive athletes: 2007 update: A scientific statement from the American Heart Association Council on Nutrition, Physical Activity, and Metabolism: Endorsed by the American College of Cardiology Foundation. Circulation 2007;115:1643–5.

50 Corrado D, Pelliccia A, Bjørnstad HH et al. Cardiovascular pre-participation screening of young competitive athletes for prevention of sudden death: proposal for a common European protocol. Consensus Statement of the Study Group of Sport Cardiology of the Working Group of Cardiac Rehabilitation and Exercise Physiology and the Working Group of Myocardial and Pericardial Diseases of the European Society of Cardiology. Eur Heart J. 2005 Mar;26(5):516-24.

51 O'Connor FG, Johnson JD, Chapin M, Oriscello RG, Taylor DC. A pilot study of clinical agreement in cardiovascular preparticipation examinations: how good is the standard of care? Clin J Sport Med. 2005 May;15(3):177-9.

52 Corrado D, Basso C, Pavei A, Michieli P, Schiavon M, Thiene G. Trends in sudden cardiovascular death in young competitive athletes after implementation of a preparticipation screening program. JAMA. 2006;296(13):1593-601

53 Steinvil A, Chundadze T, Zeltser D, Rogowski O, Halkin A, Galily Y, Perluk H, Viskin S. Mandatory electrocardiographic screening of athletes to reduce their risk for sudden death proven fact or wishful thinking? J Am Coll Cardiol. 2011 Mar 15;57(11):1291-6. doi: 10.1016/j.jacc.2010.10.037.

54 Maron BJ, Haas TS, Doerer JJ, Thompson PD, Hodges JS. Comparison of U.S. and Italian experiences with sudden cardiac deaths in young competitive athletes and implications for preparticipation screening strategies. The American journal of cardiology. 2009;104(2):276-80.

55 Corrado D, Pelliccia A, Heidbuchel H, Sharma S et al. Recommendations for interpretation of 12-lead electrocardiogram in the athlete. Eur Heart J. 2010 Jan;31(2):243-59.

56 Drezner JA, Ackerman MJ, Anderson J, Ashley E, et al. Electrocardiographic interpretation in athletes: the 'Seattle criteria'. Br J Sports Med. 2013 Feb;47(3):122-4.

57 Riding NR, Sheikh N, Adamuz C et al. Comparison of three current sets of electrocardiographic interpretation criteria for use in screening athletes. Heart. 2015 Mar;101(5):384-90.

58 Drezner JA, Ackerman MJ, Anderson J, Ashley E, Asplund CA, Baggish AL, Börjesson M, Cannon BC, Corrado D, DiFiori JP, Fischbach P, Froelicher V, Harmon KG, Heidbuchel H, Marek J, Owens DS, Paul S, Pelliccia A, Prutkin JM, Salerno JC, Schmied CM, Sharma S, Stein R, Vetter VL, Wilson MG. Electrocardiographic interpretation in athletes: the 'Seattle criteria'. Br J Sports Med. 2013 Feb;47(3):122-4. doi: 10.1136/bjsports-2012-092067

[59] Sharma S, Drezner JA, Baggish A, Papadakis M, Wilson MG, Prutkin JM, La Gerche A, Ackerman MJ, Borjesson M, Salerno JC, Asif IM, Owens DS, Chung EH, Emery MS, Froelicher VF, Heidbuchel H, Adamuz C, Asplund CA, Cohen G, Harmon KG, Marek JC, Molossi S, Niebauer J, Pelto HF, Perez MV, Riding NR, Saarel T, Schmied CM, Shipon DM, Stein R, Vetter VL, Pelliccia A, Corrado D. International recommendations for electrocardiographic interpretation in athletes. Eur Heart J. 2018 Apr 21;39(16):1466-1480. doi: 10.1093/eurheartj/ehw631.

60 Harmon KG, Zigman M2, Drezner JA. The effectiveness of screening history, physical exam, and ECG to detect potentially lethal cardiac disorders in athletes: a systematic review/meta-analysis. J Electrocardiol. 2015 May-Jun;48(3):329-38.

[61] Dhutia H, Malhotra A, Gabus V, Merghani A, Finocchiaro G, Millar L, Narain R, Papadakis M, Naci H, Tome M, Sharma S.Cost Implications of Using Different ECG Criteria for Screening Young Athletes in the United Kingdom. J Am Coll Cardiol. 2016 Aug 16;68(7):702-11. doi: 10.1016/j.jacc.2016.05.076.

[62] Bagnall RD, Weintraub RG, Ingles J, Duflou J, Yeates L, Lam L, Davis AM, Thompson T, Connell V, Wallace J, Naylor C, Crawford J, Love DR, Hallam L, White J, Lawrence C, Lynch M, Morgan N, James P, du Sart D, Puranik R, Langlois N, Vohra J, Winship I, Atherton J, McGaughran J, Skinner JR, Semsarian CA Prospective Study of Sudden Cardiac Death among Children and Young Adults. N Engl J Med. 2016 Jun 23;374(25):2441-52. doi: 10.1056/NEJMoa1510687.

[63] Thomas A, Papoutsidakis N, Spatz E, Testani J, Soucier R, Chou J, Ahmad T, Darr U, Hu X, Li F, Chen ME, Bellumkonda L, Sumathipala A, Jacoby D. Access and Outcomes Among Hypertrophic Cardiomyopathy Patients in a Large Integrated Health System J Am Heart Assoc. 2020 Feb 4;9(3):e014095. doi: 10.1161/JAHA.119.014095. Epub 2020 Jan 24.

[64] Lu DY, Ventoulis I, Liu H, Kudchadkar SM, Greenland GV, Yalcin H, Kontari E, Goyal S, Corona-Villalobos CP, Vakrou S, Zimmerman SL, Abraham TP, Abraham MR. Sex-specific cardiac phenotype and clinical outcomes in patients with hypertrophic cardiomyopathy. Am Heart J. 2020 Jan;219:58-69. doi: 10.1016/j.ahj.2019.10.004. Epub 2019 Oct 20.

[65] Halliday BP, Gulati A, Ali A, Newsome S, Lota A, Tayal U, Vassiliou VS, Arzanauskaite M, Izgi C, Krishnathasan K, Singhal A, Chiew K, Gregson J, Frenneaux MP, Cook SA, Pennell DJ, Collins P, Cleland JGF, Prasad SK Sex- and age-based differences in the natural history and outcome of dilated cardiomyopathy. Eur J Heart Fail. 2018 Oct;20(10):1392-1400. doi: 10.1002/ejhf.1216. Epub 2018 Jun 3.

[66] Goff ZD, Calkins H. Sudden death related cardiomyopathies - Arrhythmogenic right ventricular cardiomyopathy, arrhythmogenic cardiomyopathy, and exercise-induced cardiomyopathy. Prog Cardiovasc Dis. 2019 May - Jun;62(3):217-226. doi: 10.1016/j.pcad.2019.04.002. Epub 2019 Apr 17.

[67] Rohatgi RK, Sugrue A, Bos JM, Cannon BC, Asirvatham SJ, Moir C, Owen HJ, Bos KM, Kruisselbrink T, Ackerman MJ. Contemporary Outcomes in Patients With Long QT Syndrome. J Am Coll Cardiol. 2017 Jul 25;70(4):453-462. doi: 10.1016/j.jacc.2017.05.046.

[68] Chung SC, Gedeborg R, Nicholas O, James S, Jeppsson A, Wolfe C, Heuschmann P, Wallentin L, Deanfield J, Timmis A, Jernberg T, Hemingway H. Acute myocardial infarction: a comparison of short-term survival in national outcome registries in Sweden and the UK. Lancet. 2014 Apr 12;383(9925):1305-12. doi: 10.1016/S0140-6736(13)62070-X. Epub 2014 Jan 23.

[69] Defence Statistics UK Defence Statistics Compendium 2013 https://webarchive.nationalarchives.gov.uk/20140116145018/http://www.dasa.mod.uk/publications/UK-defence-statistics-compendium/2013/2013.pdf accessed 30 March 2019

[70] Frisso G1, Limongelli G, Pacileo G, Del Giudice A, Forgione L, Calabrò P, Iacomino M, Detta N, Di Fonzo LM, Maddaloni V, Calabrò R, Salvatore F. A child cohort study from southern Italy enlarges the genetic spectrum of hypertrophic cardiomyopathy. Clin Genet. 2009 Jul;76(1):91-101. doi: 10.1111/j.1399-0004.2009.01190.x.

[71] Maron BJ1, Gardin JM, Flack JM, Gidding SS, Kurosaki TT, Bild DE. Prevalence of hypertrophic cardiomyopathy in a general population of young adults. Echocardiographic analysis of 4111 subjects in the CARDIA Study. Coronary Artery Risk Development in (Young) Adults. Circulation. 1995 Aug 15;92(4):785-9.

[72] Oomen AWGJ, Semsarian C, Puranik R, Sy RW. Diagnosis of Arrhythmogenic Right Ventricular Cardiomyopathy: Progress and Pitfalls. Heart Lung Circ. 2018 Nov;27(11):1310-1317. doi: 10.1016/j.hlc.2018.03.023. Epub 2018 Apr 4.

[73] Gillum RF. Idiopathic cardiomyopathy in the United States, 1970-1982. *Am Heart J*. 1986;111:752–755.

[74] Manolio TA, Baughman KL, Rodeheffer R, Pearson TA, Bristow JD, Michels VV, Abelmann WH, Harlan WR. Prevalence and etiology of idiopathic dilated cardiomyopathy (summary of a National Heart, Lung, and Blood Institute workshop. *Am J Cardiol*. 1992;69:1458–1466.

[75] Egbe A, Uppu S, Lee S, Stroustrup A, Ho D, Srivastava S Temporal variation of birth prevalence of congenital heart disease in the United States. Congenit Heart Dis. 2015 Jan-Feb;10(1):43-50. doi: 10.1111/chd.12176. Epub 2014 Feb 24.

[76] Lee PT, Uy FM, Foo JS, Tan JL Increased incidence of infective endocarditis in patients with ventricular septal defect. Congenit Heart Dis. 2018 Nov;13(6):1005-1011. doi: 10.1111/chd.12667. Epub 2018 Sep 27.

[77] Basso C, Boschello M, Perrone C, et al. An echocardiographic survey of primary school children for bicuspid aortic valve. Am J Cardiol 2004;93:661–3.

[78] Roberts WC. The congenitally bicuspid aortic valve. A study of 85 autopsy cases. Am J Cardiol 1970;26:72– 83

[79] Michelena HI, Desjardins VA, Avierinos JF, et al. Natural history of asymptomatic patients with normally functioning or minimally dysfunctional bicuspid aortic valve in the community. Circulation 2008; 117:2776–84.

[80] Tzemos N, Therrien J, Yip J, et al. Outcomes in adults with bicuspid aortic valves. JAMA 2008;300:1317–25.

[81] Delling FN, Vasan RS. Epidemiology and pathophysiology of mitral valve prolapse: New insights into disease progression, genetics, and molecular basis. Circulation. 2014;129:2158–70

[82] Pelliccia A, Caselli S, Sharma S, Basso C, Bax JJ, Corrado D, et al. European Association of Preventive Cardiology (EAPC) and European Association of Cardiovascular Imaging (EACVI) Joint Position Statement: Recommendations for the indication and interpretation of cardiovascular imaging in the evaluation of the athlete's heart. Eur Heart J. 2018;39:1949–69.

[83] Basso C, Perazzolo Marra M, Rizzo S, De Lazzari M, Giorgi B, Cipriani A, Frigo AC, Rigato I, Migliore F, Pilichou K, Bertaglia E, Cacciavillani L, Bauce B, Corrado D, Thiene G, Iliceto S. Arrhythmic Mitral Valve Prolapse and Sudden Cardiac Death. Circulation. 2015 Aug 18;132(7):556-66. doi: 10.1161/CIRCULATIONAHA.115.016291. Epub 2015 Jul 9.

[84] Corrado D, Basso C, Rizzoli G, Schiavon M, Thiene G. Does sports activity enhance the risk of sudden death in adolescents and young adults? J Am Coll Cardiol. 2003;42:1959–63.

[85] Karjalainen J, Kujala UM, Kaprio J, Sarna S, Viitasalo M. Lone atrial fibrillation in vigorously exercising middle aged men: case-control study.BMJ. 1998 Jun 13;316(7147):1784-5.

[86] Elosua R, Arquer A, Mont L, Sambola A, Molina L, García-Morán E, Brugada J, Marrugat J. Sport practice and the risk of lone atrial fibrillation: a case-control study. Int J Cardiol. 2006 Apr 14;108(3):332-7

[87] Mont L, Elosua R, Brugada J Endurance sport practice as a risk factor for atrial fibrillation and atrial flutter. Europace. 2009 Jan;11(1):11-7. doi: 10.1093/europace/eun289. Epub 2008 Nov 6.

[88] Molina L, Mont L, Marrugat J, Berruezo A, Brugada J, Bruguera J, Rebato C, Elosua R. Long-term endurance sport practice increases the incidence of lone atrial fibrillation in men: a follow-up study. Europace. 2008 May;10(5):618-23

[89] Andersen K, Rasmussen F, Neovius M, Tynelius P, Sundström J Body size and risk of atrial fibrillation: a cohort study of 1.1 million young men. J Intern Med. 2018 Apr;283(4):346-355. doi: 10.1111/joim.12717. Epub 2017 Dec 25.

[90] Persson CE, Adiels M, Björck L, Rosengren A.Young women, body size and risk of atrial fibrillation.
Eur J Prev Cardiol. 2018 Jan;25(2):173-180. doi: 10.1177/2047487317740644. Epub 2017 Nov 2.

[91] Go AS, Hylek EM, Phillips KA, Chang Y, Henault LE, Selby JV, Singer DE. Prevalence of diagnosed atrial fibrillation in adults: national implications for rhythm management and stroke prevention: the AnTicoagulation and Risk Factors in Atrial Fibrillation (ATRIA) Study. JAMA. 2001 May 9;285(18):2370-5.

[92] Boraita A, Santos-Lozano A, Heras ME, González-Amigo F, López-Ortiz S, Villacastín JP, Lucia A Incidence of Atrial Fibrillation in Elite Athletes.JAMA Cardiol. 2018 Oct 31. doi: 10.1001/jamacardio.2018.3482.

93 Smallman-Raynor MR, Cliff AD. Impact of infectious diseases on war. Infect Dis Clin North Am. 2004;18:341–68

94 Osler W. The Principles and Practice of Medicine. New York: Appleton, 1892: 130

95 Warren, W. Lewis. (1991) King John. London: Methuen. ISBN 0-413-45520-3.

96 Macnalty AS. The illness of Edward the Black Prince. Br Med J. 1955 Feb 12;1(4910):411.

97 Fears JR. The plague under Marcus Aurelius and the decline and fall of the Roman Empire. Infect Dis Clin North Am. 2004 Mar;18(1):65-77.

98 Raoult D, Dutour O, Houhamdi L *et al*. Evidence for louse-transmitted diseases in soldiers of Napoleon's Grand Army in Vilnius. G. J Infect Dis. 2006 Jan 1;193(1):112-20.

99 Grainge C, Heber M. The role of the physician in modern military operations: 12 months experience in Southern Iraq. J R Army Med Corps. 2005 Jun;151(2):101-4.

100 Sanders J, Putnam S, Frankart C, *et al*. Impact of illness and non-combat injury during operations Iraqi Freedom and Enduring Freedom (Afghanistan). Am J Trop Med Hyg 2005;73:713-9.

101 http://apps.who.int/classifications/icd10/browse/2010/en - accessed Nov 2013

102 https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/280407/1_april_2012.pdf - accessed 24 Sep 2012

[103] Parsons I, Hutley EJ, Gibb I, Lentaigne J, Wilson D, Cox AT. Deployed military general internal physician's toolkit: the recent past and near future. J R Army Med Corps. 2018 Aug;164(4):230-234.

[104] Finnegan TP. Fifty years of PULHHEEMS--the British Army's system of medical classification. Ann Acad Med Singapore. 2001 Sep;30(5):556-7.

[105] Wharton G, Steeds R, Allen J, Phillips H, Jones R, Kanagala P, Lloyd G, Masani N, Mathew T, Oxborough D, Rana B, Sandoval J, Wheeler R, O'Gallagher K, Sharma V. A minimum dataset for a standard adult transthoracic echocardiogram: a guideline protocol from the British Society of Echocardiography. Echo Res Pract. 2015 Mar 1;2(1):G9-G24. doi: 10.1530/ERP-14-0079.

[106] Masri A, Svensson LG, Griffin BP, Desai MY. Contemporary natural history of bicuspid aortic valve disease: a systematic review. Heart. 2017 Sep;103(17):1323-1330. doi: 10.1136/heartjnl-2016-309916.

[107] Loeys BL et al. The revised Ghent nosology for the Marfan syndrome. J Med Genet. 2010 Jul;47(7):476-85. doi: 10.1136/jmg.2009.072785.

[108] Postema PG, De Jong JS, Van der Bilt IA, Wilde AA. Accurate electrocardiographic assessment of the QT interval: teach the tangent. Heart Rhythm 2008;5:1015–8

[109] Landis JR, Koch GG. The measurement of observer agreement for categorical data. Biometrics. 1977 Mar;33(1):159-74.

[110] Dhutia H, Malhotra A, Parpia S, et al. The prevalence and significance of a short QT interval in 18 825 low-risk individuals including athletes. Br J Sports Med 2016;50:124–9.

[111] Basavarajaiah S, Wilson M, Whyte G, Shah A, Behr E, Sharma S. Prevalence and significance of an isolated long QT interval in elite athletes. Eur Heart J 2007;28:2944–9

[112] Gollob MH, Redpath CJ, Roberts JD. The short QT syndrome: proposed diagnostic criteria. J Am Coll Cardiol 2011;57:802–12

[113] Uberoi A, Stein R, Perez MV, et al. Interpretation of the electrocardiogram of young athletes. Circulation 2011;124:746–57.

[114] Ackerman MJ, Zipes DP, Kovacs RJ, Maron BJ. Eligibility and disqualification recommendations for competitive athletes with cardiovascular abnormalities: Task Force 10: The cardiac channelo- pathies: a scientific statement from the American Heart Association and American College of Cardiology. J Am Coll Cardiol 2015;66:2424–8.

[115] Schwartz PJ, Crotti L. QTc behavior during exercise and genetic testing for the long-QT syndrome. Circulation 2011;124:2181–4

[116] Schwartz PJ, Moss AJ, Vincent GM, Crampton RS. Diagnostic criteria for the long QT syndrome. An update. Circulation 1993;88:782–4.

[117] Ackerman MJ, Priori SG, Willems S, et al. HRS/ EHRA expert consensus statement on the state of genetic testing for the channelopathies and car- diomyopathies this document was developed as a partnership between the Heart Rhythm Society (HRS) and the European Heart Rhythm Association (EHRA). Heart Rhythm 2011;8:1308–39.

[118] Bazett HC. An analysis of the time-relations of electrocardiograms. Heart 1920; (7): 353–37.

[119] Bazett HC. An analysis of the time-relations of electrocardiograms. Heart 1920; (7): 353–37.

[120] Pelliccia A, Maron BJ, Culasso F, Di Paolo FM, Spataro A, Biffi A, Caselli G, Piovano P. Clinical significance of abnormal electrocardiographic patterns in trained athletes. Circulation 2000;102:278–284

[121] Brosnan M, La Gerche A, Kalman J, et al. Comparison of frequency of significant electro-cardiographic abnormalities in endurance versus nonendurance athletes. Am J Cardiol 2014;113: 1567–73.

[122] Calore C, Zorzi A, Sheikh N, et al. Electrocardiographic anterior T-wave inversion in athletes of different ethnicities: differential diagnosis between athlete's heart and cardiomyopathy. Eur Heart J 2015;37:2515–27.

[123] Rowin EJ, Maron BJ, Appelbaum E, Link MS, Gibson CM, Lesser JR, Haas TS, Udelson JE, Manning WJ, Maron MS. Significance of false negative electrocardiograms in preparticipation screening of athletes for hypertrophic cardiomyopathy. Am J Cardiol. 2012 Oct 1;110(7):1027-32. doi: 10.1016/j.amjcard.2012.05.035. Epub 2012 Jul 16.

[124] Fear NT, Sundin J, Rona RJ. Obesity in the United Kingdom Armed Forces: prevalence based on measured and self-reported data. Mil Med. 2011 Jan;176(1):44-9.

[125] Chandra N, Bastiaenen R, Papadakis M, Panoulas VF, Ghani S, Duschl J, Foldes D, Raju H, Osborne R, Sharma S. Prevalence of electrocardiographic anomalies in young individuals: relevance to a nationwide cardiac screening program. J Am Coll Cardiol. 2014 May 20;63(19):2028-34. doi: 10.1016/j.jacc.2014.01.046.

[126] Baggish AL, Hutter AM Jr, Wang F, Yared K, Weiner RB, Kupperman E, Picard MH, Wood MJ. Cardiovascular screening in college athletes with and without electrocardiography: A cross-sectional study. Ann Intern Med. 2010 Mar 2;152(5):269-75.

[127] Magalski A, McCoy M, Zabel M, Magee LM, Goeke J, Main ML, Bunten L, Reid KJ, Ramza BM. Cardiovascular screening with electrocardiography and echocardiography in collegiate athletes. Am J Med. 2011 Jun;124(6):511-8. doi: 10.1016/j.amjmed.2011.01.009.

[128] Postema PG , De Jong JSSG, Van der Bilt IAC, Wilde AAM. Accurate electrocardiographic assessment of the QT interval: teach the tangent Heart Rhythm
. 2008 Jul;5(7):1015-8. doi: 10.1016/j.hrthm.2008.03.037.

[129] Savelieva I, Guo GYX, Hnatkova K, Malik M. Agreement and reproducibility of automatic versus manual measurement of QT interval and QT dispersion. Am J Cardiol. 1998 Feb 15;81(4):471-7. doi: 10.1016/s0002-9149(97)00927-2.

[130] Kautzner J, G Yi, Camm AJ, Malik M. Short and long-term reproducibility of QT, QTc, and QT dispersion measurement in healthy subjects. Pacing Clin Electrophysiol. 1994 May;17(5 Pt 1):928-37. doi: 10.1111/j.1540-8159.1994.tb01435.x. DOI: 10.1111/j.1540-8159.1994.tb01435.x