Cardiac death in the young in Scotland: Implications for screening

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Abstract

Cardiovascular pre-participation screening in sport remains a controversial area. The general consensus is that it should be available given the increased risk of sudden cardiac death with exercise, but debate exists to the format of this screening. Part 1 of this thesis examines the incidence and epidemiology of death in young people to set the context; Part 2 evaluates the results of the Cardiac Assessment in Young Athletes (CAYA) programme in Scotland.

Part 1 investigated a database of 41,049 deaths in those aged 0-35 years in Scotland from 1986-2008. Information such as location of death, whether a PM had taken place and cause of death was examined for all subjects with deaths categorised as those which occurred in-hospital or out-of-hospital and by age category and sex. Cardiac deaths (n=2084) were then investigated further.

Analysis showed that the majority of deaths in young people in Scotland are due to accidents (27%), self-harm (16.2%) and cancers (11.8%). Coronary artery disease is the largest contributor of cardiac deaths in young people in Scotland (30%) with the greatest number occurring out-of-hospital (55.3%). Only a relatively small number of deaths (0.9% of total) were due to conditions that would be identified and potentially prevented by a cardiac screening programme.

Part 2: The CAYA study was based on the Italian Model of screening by personal and family history, physical examination and resting 12-lead ECG, with the addition of an echocardiogram for all participants. Data was available for 1713 subjects from the CAYA study from October 2009-December 2012. Results showed a high incidence of hypertension in this young, athletic population, with a pilot study suggesting that this is likely to be 'white

coat hypertension'. Screening with ECG identified 3 subjects with Wolff Parkinson-White syndrome and 1 with Long QT syndrome. Around 5% of subjects demonstrated left ventricular hypertrophy out with normal limits on echo (>13mm), but no structural abnormalities such as cardiomyopathy were diagnosed. Use of the ECG in cardiac screening remains controversial but these results suggest that, although the ECG is not a useful diagnostic tool for identifying those with left ventricular hypertrophy, it has a high negative predictive value meaning it can identify those without pathology.

In conclusion, these results do not support the inclusion of echocardiography as a tool in cardiovascular screening in Scotland. The majority of cardiovascular deaths identified in this study were due to undiagnosed coronary heart disease which would not be identified by screening. Other causes of sudden cardiac death which may be identified by screening, such as familial arrhythmias and cardiomyopathies, are rare in Scotland. A screening service with ECG should be available to athletes and young people in Scotland but this should remain voluntary for those with symptoms or a positive family history. Improved first aid education and provision of defibrillators at sporting facilities would perhaps help to reduce the number of fatalities that occur in young athletes.

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This thesis is dedicated to Professor W Stewart Hillis who sadly passed away before final publication.

Authors Declaration

I declare that, except where reference is made to the contribution of others, this thesis is the result of my own work and has not been submitted for any other degree at the University of Glasgow or any other institution.

Katy L Stewart

Contents

List of Abbreviations

ABP	Ambulatory blood pressure
AED	Automatic external defibrillator
AF	Atrial fibrillation
AHA	American Heart Association
ARVC	Arrhythmogenic right ventricular cardiomyopathy
ASD	Atrial septal defect
A-V	Atrio-ventricular
BP	Blood pressure
BPM	Beats per minute
BSA	Body surface area
CAD	Coronary artery disease
CAYA	Cardiac Assessment in Young Athletes
CHD	Coronary heart disease
CI	Confidence interval
CMRI	Cardiac magnetic resonance imaging
CO	Cardiac output
CPVT	Catecholaminergic polymorphic ventricular tachycardia
CRY	Cardiac Risk in the Young
DBP	Domiciliary blood pressure
DCM	Dilated cardiomyopathy
ECG	Electrocardiogram
Echo	Echocardiogram

ESC	European Society of Cardiology
GRO	General Register Office
GI	Gastro-intestinal
GU	Genito-urinary
HCM	Hypertrophic cardiomyopathy
HD	Heart disease
HR	Heart rate
IAS	Mobile inter atrial septum
ICD	Implantable cardioverter defibrillator
IRBBB	Incomplete right bundle branch block
ISD	Information Services Division
IVSd	Inter-ventricular septal thickness
LBBB	Left bundle branch block
LQTS	Long QT syndrome
LV	Left ventricle
LVH	Left ventricular hypertrophy
LVID	Left ventricular internal diameter
LVPWd	Left ventricular posterior wall thickness
MI	Myocardial infarction
MVP	Mitral valve prolapse
NICE	National Institute for Clinical Evidence
NPV	Negative predictive value
NSC	National Screening Committee
OOH	Out-of-hospital
ONS	Office National Statistics

PDA	Patent ductus arteriosus
PE	Physical examination
PFO	Patent forearm ovale
PM	Post mortem
PPV	Positive predictive value
QTc	Corrected QT interval
RBBB	Right bundle branch block
SADS	Sudden arrhythmic death syndrome
SCD	Sudden cardiac death
SD	Standard deviation
SMR	Scottish Morbidity Records
SQTS	Short QT syndrome
SV	Stroke volume
SVT	Supraventricular tachycardia
TTE	Trans-thoracic echocardiography
VF	Ventricular fibrillation
VO_{2max}	Maximal oxygen uptake
VT	Ventricular tachycardia
WHO	World Health Organisation
WPW	Wolff-Parkinson-White

List of Figures

List of Tables

Chapter 1 - Introduction

The death of any young person is tragic, but the death of an athlete who is deemed to be at the peak of physical health is a larger shock and often receives a great deal of media interest. In 2012 several high profile sports stars suffered from fatal cardiac events including Norwegian swimmer Alexander Dale Oen, Italian footballer Piermario Morosini and a sudden death during the London Marathon. In addition to this, in the UK there was added media attention following the cardiac arrest of Fabrice Muamba whilst playing for Bolton Wanderers. Whether the number of such deaths is increasing, or whether these are just being reported more frequently remains unknown, because there is a lack of an international database to record these deaths and the circumstances surrounding them.

It has been identified that up to 80% of these deaths are due to cardiac causes[1]. This suggests that athletes may be put at an increased risk as a result of undiagnosed predisposing cardiac conditions, for example structural heart disease such as cardiomyopathies or familial arrhythmias such as long QT syndrome (LQTS).

The consensus opinion is that some form of cardiovascular screening should be available to identify such problems; however controversy currently exists surrounding the efficacy of ways to identify these conditions. In Europe, the gold standard protocol is the Italian Model which includes personal and family history questionnaire, physical examination (PE) and resting ECG[2]. In America, the American Heart Association (AHA) guidelines rely on a 12-point personal and family history questionnaire and PE[3]. They have resisted the use of ECG on the basis of cost, doubts over the knowledge base of ECG morphology in athletes and fear of increasing anxiety in false positive results.

Until now the advice of the National Screening Committee (NSC) in the UK is that pre-participation screening should not become a national programme for the general population, because of a lack of evidence of effectiveness of existing screening tests[4], but should instead be targeted at those at high risk of cardiac complications with exercise.

1.1. What is Sudden Cardiac Death (SCD)?

Sudden cardiac death (SCD) is not a new phenomenon. Greek mythology suggests that in 490BC, Pheidippides suffered a SCD after running from Marathon into Athens to announce the Greek victory over its invaders. However an exact definition of SCD is hard to apply with only two thirds being witnessed[5 6].

The World Health Organisation (WHO) definition of sudden cardiac death includes instantaneous deaths and all deaths from cardiac cause occurring within 24 hours of an acute collapse[7] and this definition has been used in many studies[8 9 10]; however other studies have used a shorter cut off such as 1 hour[11 12], 6 hours or 12 hours[13 14]. The definition of SCD used influences the data generated and affects the proportion of natural deaths due to cardiac cause. Zipes et al[15] report this as being 13% of natural deaths when using a 1 hour cut off. This percentage will increase depending on the time cut off used as has been reported to be as high as 18.5% in a study using a 24 hour time period in The Netherlands[16].

Due to the way data is recorded in many countries including Scotland, and the fact that the time of symptom onset is not recorded on the death certificate, it is impossible to use these exact time cut offs. Therefore, the definition which has been commonly used instead is 'out-of-hospital deaths' (OOH deaths) which can be attributed to be sudden or unexpected death which occurs outside of hospital, within the emergency room or if subjects are pronounced dead on arrival to hospital[17 18]. The definition used has an impact on the figures recorded for

the incidence of deaths. The incidence is also dependent on the study population with age, ethnicity and sex all being influential factors.

Whether sudden death in sport is becoming increasingly frequent or is merely better reported remains an important question; are athletes really at greater risk than the general population? A prospective study by Corrado et al[2] aimed to answer that question by evaluating the incidence of sudden death in both the athletic population and the general population in Italy from 1979-1999. This study identified 300 cases of sudden death in 12-35 year olds during the 21 year study period, giving an incidence of 1 death per 100, 000 person years. Fifty five deaths occurred in athletes, with 245 occurring in the general population ($p=0.002$) which gave incidences of as 2.3 sudden death per 100,000 person years in athletes compared with 0.9 sudden deaths per 100,000 person years in the general population. These results suggest that being an athlete, and therefore undertaking high levels of vigorous physical training, could be a risk factor for SCD.

So, are athletes more 'at risk'? Evidence suggests exercise can act as a trigger for cardiac arrest[15 19 20] but this can only happen if there is an underlying cardiac problem predisposing the athlete to an arrhythmia. However, there are few prospective studies in this area [20 21 22] with most being retrospective[23 24 25] including newspaper articles and Google searches to identify the study population. This highlights the need for a more reliable recording system of such deaths universally so that we can correctly identify how wide-scale the incidence for SCD is. Often studies include deaths in athletes which do not occur during exercise and this may also affect the data[23], as it is not possible to know if these are linked to sports participation.

Table 1-1 shows papers which have examined sudden death in young populations. It demonstrates that the incidence of sudden death ranges from 0.3-0.6 per 100,000 in high school athletes to 13.2 deaths per 100,000 in army recruits. Some of this variation can be

attributed to the way that data was collected and the age group monitored but it suggests that better recording of such deaths could lead to a uniform comparison between countries and athletes/non-athletes.

Table 1-1: Studies that have investigated the incidence of sudden deaths in young populations

Study	Population	Age	Methodology/Study Design	Incidence (person years)
Maron (1998)	High school athletes Minnesota	13-19 years	Retrospective cohort	0.5 per 100,000
Corrado (2006)	Competitive athletes, Italy	12-35 years	Mandatory Register for SCD	3.6 per 100,000
Eckhart (2004)	Young Military recruits, USA	18-35 years	Autopsy based	13.2 per 100,000
Behr et al (2007)	White Caucasians, UK	4-64 years	SADS cases identified by Coroner	1.34 per 100,000
Vaartjes et al (2009)	Young people, Netherlands	1-40 years	Death certificate out of hospital cardiac deaths	1.62 per 100 000
Shen et al (1995)	Young adults, Minnesota	20-40years	Retrospective analysis of death certificates	6.2 per 100,000
Harmon et al (2011)	National Collegiate Athletic Association (NCAA) Athletes	17-24 years	NCAA database, insurance company claims, media reports	2.3 per 100,000
Van Camp et al (1995)	High school and college athletes	12-19 years	Prospective 10 year study of non-traumatic deaths	0.3 per 100,000
Maron et al (2009)	1866 deaths in athletes	15-39 years	Retrospective analysis using specialist database and Google/Yahoo searches	0.6 per 100,000
Steinvil et al (2011)	Deaths of competitive Israeli male athletes	12-44 years	Retrospective analysis of media sources	2.6 per 100,000
Holst et al (2010)	Sports related SCD in Denmark	12-35 years	Retrospective analysis of death certificates and public media reports	1.21 per 100,000

SCD-Sudden cardiac death, SADS-Sudden arrhythmic death syndrome

1.2. Causes of SCD

Cardiac deaths in older adults (>35years) are generally accepted as being largely attributed to coronary heart disease (CHD). However the cause of death in younger people (1-35 years) are harder to identify. This is made more difficult due to the fact 25-40% of deaths in those aged 1-40 years are described as having a 'negative autopsy' where there is a lack of evidence to assign a definite known cause of death[26]. Here, undiagnosed arrhythmias are often thought to be responsible with the heart appearing structurally normal at post mortem (PM) examination although this is difficult to prove without a diagnosis prior to death.

SCD in the young are mainly due to structural abnormalities, such as coronary artery disease (CAD) and inherited cardiomyopathies, or familial arrhythmias such as long QT syndrome (LQTS) and Brugada syndrome. There are also a number of other causes of deaths which have been reported as potentially having a cardiac origin. These have been classed as 'class B' cardiac deaths as post mortem is negative and include unexplained car accidents and unexplained drowning and submersion in natural water[27]. This is due to the fact that the drowning or other incident such as epileptic seizure may have been caused by a primary myocardial disorder.

Although in many cases of SCD, the underlying cause is structural or due to an electrical abnormality, the final event which leads to cardiac arrest is always an arrhythmia such as ventricular fibrillation (VF) or ventricular tachycardia (VT). There are a number of mechanisms that result in arrhythmia: 1) automaticity 2) triggered activity - delayed after-depolarisation or early after-depolarisation and 3) re-entry[28]. In electrical abnormalities ventricular arrhythmia may be caused by triggered activity whereas structural abnormalities such as CAD and cardiomyopathies are commonly caused by re-entry arrhythmia as a result of scarring, tissue damage and fibrosis.

1.2.1. Cardiomyopathies

The term 'cardiomyopathy' covers a number of conditions, broadly categorised as heart muscle disease. There are 3 main types of cardiomyopathy that affect the young: hypertrophic cardiomyopathy (HCM), dilated cardiomyopathy (DCM), and arrhythmogenic right ventricular cardiomyopathy (ARVC).

1.2.1.1. Hypertrophic Cardiomyopathy (HCM)

Hypertrophic cardiomyopathy is defined as heart muscle disease characterised by unexplained hypertrophy of the left (and sometimes the right) ventricle. This hypertrophy is asymmetric and affects the inter-ventricular septum more than the left ventricular free wall. HCM is an inherited autosomal dominant disease, most common in males of black origin. Histologically it is characterised by myocyte disarray which predisposes the subject to cardiac arrhythmias particularly ventricular fibrillation (VF) and ventricular tachycardia (VT). Patients can complain of chest pain, palpitation and blackouts with diagnosis being through ECG, echo and MRI. Surgical treatments include ablation, myectomy or coronary artery injection and, in patients at high risk of SCD, fitting of an implantable cardioverter defibrillator (ICD).

1.2.1.2. Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC)

Arrhythmogenic right ventricular cardiomyopathy is reported as one of the most common causes of SCD in the young, particularly in Italy[2]. The exact prevalence of ARVC is unknown but is estimated at 1 in 10,000, meaning there are approximately 5000 affected individuals in the UK[29]. The condition is hereditary and has been reported to affect males and females equally.

ARVC is characterised by a progressive replacement of normal right ventricular muscle cells by fibrous tissue and fat which can lead to ventricular arrhythmia and heart failure. Regrettably, in many cases SCD is the first manifestation of the disease with diagnosis made at post mortem but live diagnosis can be made using ECG, echo, MRI and electro-physiological studies. Treatment includes lifestyle modification to reduce the risks of SCD, beta-blockers, anti-arrhythmic drugs, surgical ablation or implantation of an ICD.

1.2.1.3. Dilated Cardiomyopathy (DCM)

Dilated cardiomyopathy causes the ventricles to become enlarged causing poor contraction which can lead to heart failure. It occurs when the myocardium becomes damaged which can be familial or can be due to existing cardiac disease, toxins or infection. It causes shortness of breath, ankle swelling and palpitations and would be diagnosed using ECG, echo and possibly an exercise test. Treatments include diuretics, ACE inhibitors, implantation of an ICD or heart transplantation.

1.2.2. Familial Arrhythmias

Familial arrhythmias are a group of conditions that are characterised by inherited electrical abnormalities in the heart. These abnormalities cause irregular heart rhythms which may be the cause of death, and may be the cause of SCD particularly where there is no structural abnormality found at post mortem[30]. Cardiac arrhythmia may be the first sign of any cardiac disease and may prove fatal.

1.2.2.1. Long QT Syndrome (LQTS)

Long QT syndrome is a disease that mainly effects children and young adults and is recognised as the leading arrhythmic cause of death in this population[31]. It is now estimated to affect 1 in 2000 people[32]. LQTS is caused by one of several gene mutations which prolong

the ventricular action potential causing the QT interval of the ECG to be lengthened (>440ms). The cause of death is polymorphic ventricular tachycardia ("torsades des pointes") or VF. Exercise is a recognised trigger for arrhythmia in some genotypes (e.g. LQT1). Patients with LQTS are advised to avoid drugs which prolong the QT interval such as anti-histamines, and may be advised to avoid competitive sports. Treatments include beta blockers and high risk patients are fitted with an ICD[33].

1.2.2.2. Short QT Syndrome (SQTS)

Short QT syndrome is uncommon and occurs when the ventricle takes a shorter time than normal to repolarise so that the QT interval is <300ms. This occurs due to increased activity of potassium channels causing a shortening of the action-potential phase and makes the subject prone to ventricular arrhythmias. Treatment is with anti-arrhythmic drugs and ICD[34].

1.2.2.3. Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT)

Catecholaminergic polymorphic ventricular tachycardia is an inherited arrhythmogenic disorder which is estimated to affect 1 in 10,000 people worldwide mainly in adolescent males. It occurs when there are increased levels of calcium inside the heart cells which leads to arrhythmia. Diagnosis is made using exercise testing as it is characterised by ventricular tachycardia (VT) on exercise. Treatment is with beta blockers and ICD implantation[30].

1.2.2.4. Brugada Syndrome

Brugada syndrome is characterised by a distinctive ECG pattern including right bundle branch block (RBBB) and ST segment elevation. This can lead to ventricular fibrillation (VF) with symptoms including blackouts and palpitations. It is caused by a mutation in the sodium channels and is most common in South East Asia. Death due to Brugada syndrome is not

thought to be associated with exercise and occurs more commonly during sleep[30]. Treatment requires implantation of an ICD.

1.2.3. Other Conditions

1.2.3.1. Coronary Heart Disease (CHD)

The commonest cause of cardiac death in the Western World in all ages is acute myocardial infarction (MI) which is caused by acute thrombotic occlusion of a coronary artery at the site of an atherosclerotic plaque[35]. Statistics from the British Heart Foundation suggest that in 2008, as many as 35 people a day died from CHD in the UK[36]. Although the numbers of deaths due to MI have reduced in recent years due to surgery and new therapeutic interventions, poor diet, smoking and an inactive lifestyle all contribute to make CHD a major problem, particularly in Scotland. Age is also seen as an important risk factor but CHD does manifest itself in younger people who can remain asymptomatic for many years. In 2008, CHD was responsible for 25.4% of deaths in those under 75 years in Scotland compared with 15.0% in England and 14.5% in Wales[36]. Coronary heart disease cannot always be diagnosed using ECG and echocardiography alone (unless there has been a prior event) and instead would be require the use of exercise testing and angiography.

1.2.3.2. Wolff-Parkinson White (WPW) Syndrome

In 1930, Wolff, Parkinson and White described a series of patients who presented with a bundle branch pattern on ECG, a short PR interval and evidence of tachycardia[37]. This pre-excitation pattern is caused by an additional electrical connection (accessory pathway) between the atria and ventricles thus shortening the PR interval and predisposing the patient to arrhythmia. It is estimated that WPW syndrome occurs in approximately 1 in 1000 athletes[38]. Risk of sudden death occurs if the pathway has a short refractory period and the onset of atrial fibrillation (AF) can lead to VF. It is detected using ECG, with palpitation being the main symptom.

Table 1-2 details the cardiac conditions that commonly lead to SCD and details how these conditions can be identified. None of the conditions can be identified using physical examination (PE) and although family history can be useful; this is normally in symptomatic subjects. Table 1-2 suggests the ECG as the most useful diagnostic tool in identifying both structural and electrical abnormalities with further tests often required before a diagnosis is made.

Table 1-2: Conditions that can pre-dispose to sudden cardiac death with potential diagnostic tools

Condition	Family History	Symptoms	PE	ECG	Echocardiogram	Other
Long QT Syndrome	√	√		√		24 hour holter monitor Ajmaline Provocation
Short QT Syndrome	√	√		√		24 hour holter monitor
CPVT	√	√		√		Exercise Test
Brugada Syndrome	√	√		√		Ajmaline Provocation
Hypertrophic Cardiomyopathy	√	√	√	√	√	Exercise Test CMRI
ARVC	√	√	√	√	√	CMRI EP studies
Dilated Cardiomyopathy	√	√	√	√	√	Exercise Test
Wolff-Parkinson White Syndrome	√	√		√		EP Studies
Coronary Heart Disease	√	√		√	√ (if previous MI)	Exercise Test Angiography

(CPVT= catecholaminergic polymorphic ventricular tachycardia; ARVC= arrhythmogenic right ventricular cardiomyopathy; PE= physical examination; CMRI= cardiac magnetic resonance imaging; EP=electro-physiological)

1.3. Sex and Gender Differences

SCD has been found to be more common in male athletes than females with studies showing up to a 9:1 ratio[2 39]. Perhaps this is due to the larger male participation rates and the types and intensity of sports undertaken, or maybe there is an underling hormonal cause?

Studies agree that there appears to be a genetic/ethnicity bias towards SCD with black athletes being more at risk of SCD than Caucasian athletes, however there is disparity across studies as to the incidence of this. In America, most SCD are due to HCM with these being more common in black athletes whereas arrhythmias were found to be more common in non-black athletes[40]. In Italy, the leading cause of SCD is ARVC[2]; however this is not replicated anywhere else in the world. This suggests that there may be a genetic predisposition to certain conditions which are attributable to the geographic distribution or ethnicity.

1.4. Cardiovascular Adaptations to Exercise

It is well documented that the heart undergoes a series of changes in response to exercise or physical training[41 42]. These physiological adaptations induced by chronic exercise increase both preload and afterload on the heart and lead to a form of cardiac remodelling. This comprises of ventricular hypertrophy, an increase in cardiac chamber size and enhanced diastolic ventricular filling, which provides an increase in stroke volume (SV)[41]. These cardiovascular changes are produced by a complex interaction of central and peripheral mechanisms, which operate at structural, biochemical and metabolic levels[42].

The 'Morganroth hypothesis' was first presented by Joel Morganroth and colleagues in 1975 to suggest the theory that different types of exercise training elicit different structural changes within the heart[43]. This theory proposed that endurance training elicits eccentric forms of hypertrophy characterised by increased LV cavity size and LV mass. Strength training elicits concentric hypertrophy including increased wall thickness but no alterations in cavity size. However, this theory remains controversial.

The 26th Bethesda Conference defined endurance or dynamic sports as those that involve "changes in muscle length and joint movement with rhythmic contractions which develop a relatively small intramuscular force", whilst strength or static training was referred to as activities that "develop relatively large intramuscular forces with little or no change in muscle length or joint movement[44]. However, most modern sports require a combination of both strength and endurance training meaning athletes are exposed to both static and dynamic demands.

Dynamic exercise requires large muscle mass use and causes a marked increase in oxygen consumption generating a volume overload on the ventricle. Therefore, dynamic sports result in larger absolute LV mass and chamber size[45]. These adaptations of the athlete's heart are of major importance in the maximal oxygen uptake (VO_{2max}) improvement that is described[46]. During progressive dynamic exercise, oxygen uptake increases from the resting value until maximal VO_{2max} is achieved. During this exercise, both heart rate (HR) and SV increase causing an increase in cardiac output. The increase in SV is achieved by both an increase in end diastolic volume and a decrease in end systolic volume. By contrast, static exercise induces a small increase in VO_{2max}, HR and cardiac output (CO) and no change in SV[46]. These adaptations to static exercise generate an increase in LV mass without an increase in chamber size[45].

Although exercise is well documented to be able to lower blood pressure in hypertensive patients[47] and reduce cardiovascular risk, hypertension or high blood pressure is not an uncommon finding in athletes due to the increased size of the left ventricle[48].

1.5. Athlete's Heart vs Hypertrophic Cardiomyopathy

Around half of highly trained athletes will demonstrate some form of cardiac remodelling[49]. These changes are more evident in the left ventricle (LV) which can show cavity enlargement, and increments in wall thickness. The traditional physiological adaptation seen following a period of exercise is left ventricular hypertrophy (LVH), which can be eccentric or concentric in nature. Eccentric changes are normally associated with endurance training due to the volume load on the left ventricle whereas concentric changes are related to power training due to the pressure load[45 50]. LVH is affected by sport, training intensity and duration but is also influenced by intrinsic factors such as age, sex, ethnicity and BSA.

These physiological cardiac adaptations which occur following a period of high intensity exercise training are acknowledged and referred to as 'athlete's heart'. However, these changes can mimic those of hypertrophic cardiomyopathy (HCM), and mis-diagnosis would lead to the athlete being strongly advised against participating in competitive sport. This has led to a so-called 'grey area' in the literature identified in Figure 1-1[49].

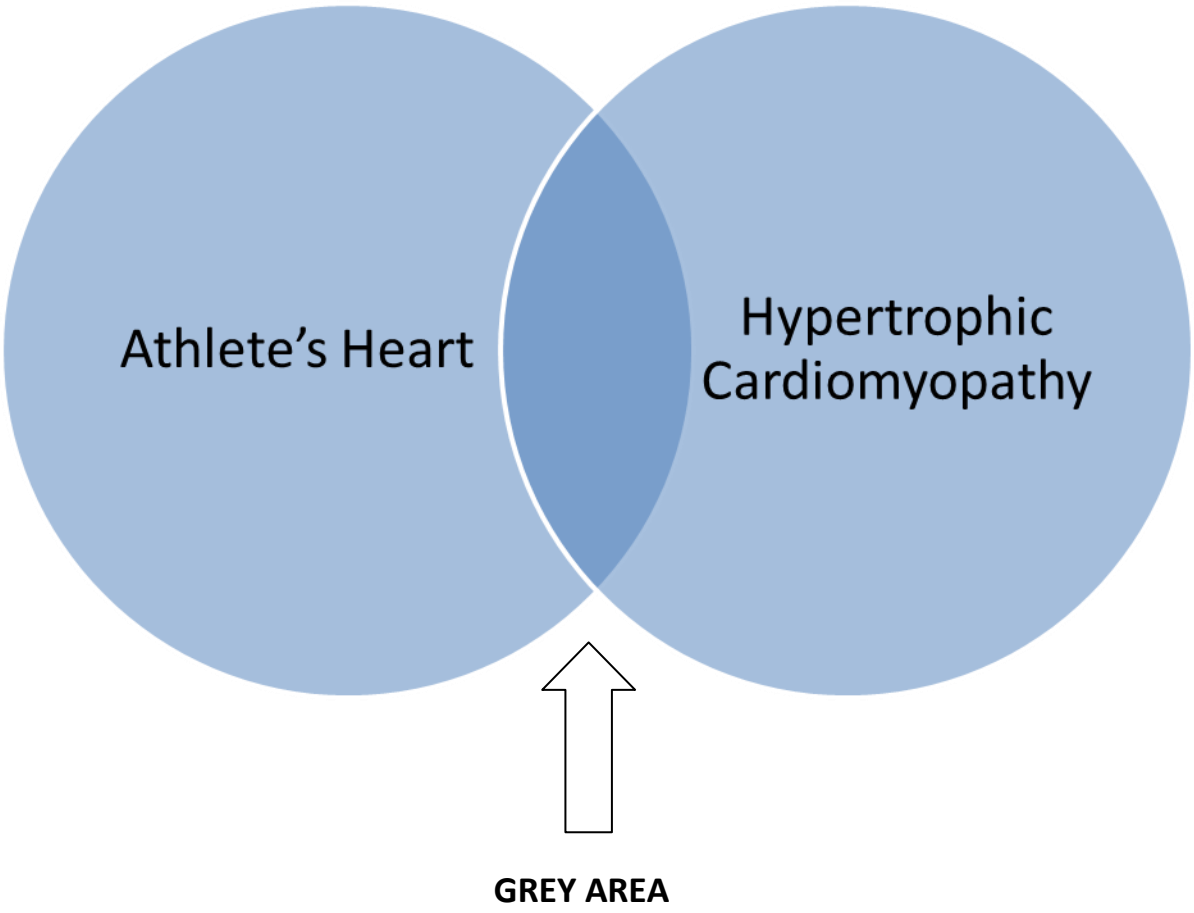


Figure 1-1: The so-called 'grey area' described by Maron between physiological athlete's heart and pathological hypertrophic cardiomyopathy[49]

Research questions whether these changes are solely physiological due to training, or whether they may be due to underlying pathological causes. In order to measure this, an echocardiogram is necessary to assess levels of hypertrophy on the left ventricular posterior wall thickness (LVPWd) and the inter-ventricular septal diameter (IVSd) as well as assessing the size of the left ventricular cavity. The physiological changes associated with athletes heart can be reversed following a period of de-training.

In addition to changes in wall thickness, the LV cavity can also be enlarged in athletes. This enlargement can be mistaken for dilated cardiomyopathy and so it is important to recognise the upper limits of normal. It is also recognised that cavity enlargement can exist without an increase in wall thickness due to the remodelling. Reference values have been published for LV cavity size and this has been suggested as the most important discriminator between physiological LVH and pathological disease such as HCM[51].

As discussed, different sports place different demands upon the body, which have been reported to cause variation in the degree of hypertrophy demonstrated. Most athletes in modern sport combine aerobic training with strength training which makes research difficult but ultra-endurance sports such as cycling, rowing and skiing have been shown to elicit the greatest increases in LVPWd measures[52].

Normal limits of physiological LVH have been discussed in the literature[42 53] and upper limits of normal are generally accepted as 13mm with measurements higher than this restricted to athletes such as rowers and cyclists[53] . Subjects with LV wall measurements greater than 13mm, should undergo further tests to rule out any pathology.

A study was conducted on Scottish footballers to try to establish the degree of LVH found in this population[54]. Footballers were compared with age matched controls and were found to have significantly greater left ventricular posterior wall thickness (9.2 v 8.5mm) and septal thickness (10.4 v 9.1mm). Only 17 footballers (12.1%) had a septal or wall thickness greater than 12mm. This research agrees with previous work[53] that footballers generally fall within normal limits for LV measurements. This suggests that perhaps footballers as a group are not as aerobically fit as athletes who participate in sports such as cycling and rowing.

1.6. Hypertension in Athletes

Regular exercise is associated with decreased blood pressure, but elevated BP has been found to be the most common abnormality found during athletic pre-participation screening[48]. Whelton et al showed cardiorespiratory fitness to be inversely related to BP[55].

A BP greater than 140/90mmHg is considered as 'hypertension' in adults (those greater than 18 years)[56]. In those under 18, hypertension is defined as an average BP greater than or equal to the 95th percentile for gender, age and height[57]. Task Force 5 from the 36th Bethesda Conference accept that young people who plan to participate in sport should have their BP routinely checked. It states that athletes with high readings should have 'additional recordings outside the office' to exclude elevated anxiety readings or 'white coat hypertension' readings[58].

The National Institute of Clinical Evidence (NICE) has stated that white coat hypertension may exist in up to 25% of patients[56]. There is sparse longitudinal data to suggest that young people with 'pre-hypertension' will develop hypertension in later life. The prevalence of hypertension in the physically active has been shown to be approximately 50% lower than that of the general population (Lehmann et al 1990).

Kouidi et al[59] conducted a study on 410 footballers, and found 10% (41 athletes) had blood pressure recordings above accepted normal limits after 2 or more measurements. Following ambulatory 24hour monitoring, only 2 athletes had BP >140 or 90mmHg. Another study did show that 80% of young athletes identified as having a BP greater than 142/92mmHg at pre-participation screening developed chronically elevated BP after 1 year[60].

No clear correlations have been found between hypertension and SCD in young athletes[61]. However, a link does exist between hypertension and LVH though it is not apparent if this is a

cause and effect relationship. Isolated systolic BP has been shown to be associated with athlete's heart based on the mechanism of high resting SV and CO, and low HR with a wide pulse pressure[62].

Reims et al[63] have suggested that one-off BP measurements are higher than ambulatory BP (ABP) measurements. A study of footballers in Norway revealed a significant relationship between high BP, LV mass and HR[64]. A further study by Berge et al[65] aimed to investigate the incidence of high ABP in male professional footballers in Norway. Based on BP recordings carried out during routine pre-participation screening in 2008, a case control study recorded ABP from October 2010 to February 2011. Players (mean age=28.3 years) with untreated high BP (n=28) were compared with age/ethnicity matched control with optimal BP (n=26). A weak but significant correlation ($r=0.21$, $p<0.01$) was found between screening BP and mean arterial pressure. Of the 26 cases, 58% were found to have sustained hypertension with 42% having white coat hypertension. In the control group, only 65% were found to be truly normotensive while the remaining 35% has masked hypertension. The hypertension in this study would only be classed as 'pre-hypertension' according to our study and current guidelines with a mean ABP of 138/82.

1.7. The Adolescent Athlete

The majority of studies in this area have been conducted in adults, with few in adolescents. Studies have shown[66 67] that adolescent athletes display a form of LVH, with a greater IVSd and LVPWd than control subjects, but that these values still fall within normal limits. Questions remain regarding at what age the heart is fully developed in terms of size and structure. Corrado et al[68] suggest that screening children less than 12 years old reduces the sensitivity of the tests with most conditions including HCM and DCM not manifesting themselves until adolescence. American and European guidelines suggest that screening should begin between 12 and 14 years old and that it should be repeated every 2 years. In Italy, screening is mandatory for athletes aged 12-35 years[2].

Young athletes, particularly footballers tend to have similar training patterns but variation exists in body size and biological maturation[69]. Skeletal age has been shown to be a better predictor of athletic performance than chronological age suggesting it is this instead of age that should indicate when athletes should be screened. Fat free mass has been shown to be a strong determinant of left ventricular mass but Daniels et al[70] argue lean body mass to be a better predictor. This study did not find an independent relationship between sexual maturity and left ventricular mass suggesting it manifests itself through body size[70].

1.8. Implications for Screening

Fabrice Muamba, who suffered a cardiac arrest while playing football for Bolton Wanderers in March 2012, had reportedly been screened 4 times[71]. This does not support the argument for cardiovascular screening and suggests that it may not be an effective way to prevent a cardiac event if an underlying condition exists.

The National Screening Committee in the UK established a set of criteria (Table 1-3) to assess the effectiveness and appropriateness of any potential screening programme[72]. These criteria state that the targeted condition should be a significant public health issue, which can be targeted by a safe and effective and inexpensive treatment strategy.

Table 1-3: National Screening Committee Criteria for assessing effectiveness of a screening programme[72]

1. The condition should be an important health problem
2. The epidemiology and natural history of the condition should be adequately understood and there should be a detectable risk factor, disease marker or latent period
3. There should be a simple, safe and precise validated screening test
4. The test should be acceptable to the population
5. There should be an effective treatment or intervention for patients identified through early detection, with evidence of early treatment leading to better outcomes than late treatment
6. There should be evidence that the screening programme is effective in reducing mortality or morbidity
7. The benefit from the screening programme should outweigh the physical and psychological harm (caused by the test, diagnostic procedure and treatment)
8. The opportunity cost of the programme (including testing, diagnosis and treatment, administration, training and quality assurance) should be economically balanced in relation to expenditure on medical care as a whole (that is, value for money)

In the United States, this has been modified by the US Preventive Services Task Force suggesting such a programme must improve specific health outcomes such as mortality, quality of life or pain[73]. The main issue that is argued by the UK's National Screening Committee (NSC) is that cardiovascular screening of athletes does not 'fit' the above criteria. However, it is not designed to screen for only one condition. These criteria suggest that cardiovascular screening would need to reduce the incidence of SCD to be worthwhile, and there have been no randomised control trials conducted to show this. Instead, a comprehensive cardiovascular assessment is able to detect a number of different conditions, some of which are not life threatening, but will be a long term burden to both patient and NHS. There are also ethical considerations involved with making screening mandatory, which is especially problematic in younger people.

The lack of a national register of SCD in the UK makes it hard to quantify the true incidence of this problem in the general population and also the numbers of deaths in athletes or those who die during or following exercise. One study[74] attempted to confirm the aetiology of SCD in athletes in the UK by examining 118 cases of SD in people participating in sport between January 1996 and July 2008. All these cases had been referred to the Cardiac Risk in the Young (CRY) Centre for Cardiac Pathology at the Royal Brompton Hospital in London by local coroners and pathologists for further investigation. Pathological analysis of the heart included measurements of left and right ventricular wall thickness and internal cavity dimensions, while histological investigation for any myocardial fibrosis or myocyte disarray was also carried out. The coronary arteries were also studied. Abnormal cardiac pathology was identified in 91 cases (77%) with the remaining 23% having morphologically normal hearts. Left ventricular hypertrophy was discovered in 49 cases (42%) of athletes suggesting possible HCM; however only 13 out of 49 cases (27%) displayed associated myocyte disarray on histology which would confirm the presence of HCM. Arrhythmogenic right ventricular hypertrophy was discovered in 16 subjects (14%) with evidence of biventricular involvement in 50% cases. Coronary artery pathology was identified in 9% (11 cases). Somewhat surprisingly, 96% of cases in this study were Caucasian which may be due to the population in the UK as other countries (USA) have found SCD and in particular those due to HCM are more prevalent in those with African-American origin. The number of morphologically normal hearts in this study (23%) is considerably higher than in previous studies, but we must look at this with caution as these figures were prior to introduction of pre-participation screening which may potentially have identified some electrical abnormalities in these cases.

An American Heart Association (AHA) Scientific Statement[3] advised the screening of children aged 12-18 years with an 8 point health questionnaire and a four point clinical examination. However, Wilson et al[75] concluded from their study that “family history and personal symptom questionnaires alone are inadequate to identify people with disease associated with sudden cardiac death”. This suggests further tests are required in addition to the questionnaire and physical examination to make the screening process more reliable. The Lausanne Recommendations (2004) led to a common world screening protocol for Olympic

sports based on a personal and family history questionnaire, physical examination and 12-lead ECG[76].

The concept that cardiovascular screening can significantly reduce SCD in athletes is largely based on information from the Veneto Region of Italy[2]. This study suggests an 89% reduction in cases of SCD from 3.6 deaths per 100,000 person years before screening (1979 to 1982) to 0.4 deaths per 100,000 person-years at the end after the introduction of mandatory screening. However, these results have not been replicated in similar studies[25], calling into question the general application to different populations. Some rationale for the significant reduction in SCD comes when we further evaluate the pre-screening data. This data only encompassed deaths from the 2 years prior to the introduction of screening. The number of deaths during these years was high and it could be that this caused a misrepresentation of the scale of the problem. The high numbers could also have been the trigger for the introduction of mandatory screening.

The only other European country which has introduced mandatory screening is Israel. A study was carried out in Israel to evaluate whether the Italian data could be replicated in a different population[25]. This study, which included an exercise test in addition to the Italian model, found no difference in the incidence of SCD before and after the implementation of a mandatory screening programme (1997). Instead it found the average incidence of SCD to increase from 2.54 deaths to 2.66 deaths per 100,000 person years[25]. So, how did these results differ so greatly from the Italian data?

The positive results found in Italy could be due to an unusually high number of deaths in the years preceding the screening, with Israel using a 12 year pre-screening period which could have eliminated annual variation. However, Italy used a National Register to calculate the number of deaths in preceding years whereas Israel relied on newspaper and media reports.

In both studies the number of competitive athletes was difficult to quantify. Israel extrapolated their data to allow for growth in the population, but there was no discussion of this in the Italian paper. It is very difficult to generalise the Italian data as the population was mainly composed of white males and the lead cause of death was ARVC which has not been seen in any other studies and suggests this condition is more prevalent in the Veneto region of Italy. The death rate in Italy after implementing screening (0.43 deaths per 100,000 person years)[2] is similar to that of the USA (0.5 deaths per 100,000 person years)[77] who do not have a mandatory programme so perhaps SCD is more common in Italy? Potentially it may also be related to the high prevalence of ARVC which can be detected using ECG screening.

1.9. The Cost of Screening

Elston & Stein[78] attempted to quantify the impact of establishing a similar screening programme to Italy in the UK for athletes aged 12-35 years. By using the data from Italy, it was calculated that 38,151 athletes would need to be screened to prevent 1 SCD. This suggests that if screening had a 100% uptake, 1.5 million athletes in the UK would be screened, with 140,000 being referred for further investigations such as echocardiography and exercise testing and with 31,522 being disqualified from sport. This suggests that to prevent 1 SCD, 800 athletes would have to be disqualified. This would incur a great deal of unnecessary anxiety placed on young athletes due to false positive results. While in some countries screening is mandatory, it is voluntary in others including the UK. This leads to questions about consent and whether this is something that an athlete wants to undertake. A recent study in Switzerland[79] surveyed 1047 athletes and only 47% expressed an interest in undergoing screening. Eighty percent of these athletes were symptomatic or had concerns leading to a selection bias in the research. There are also questions to be answered over the ethics of offering screening to those involved in sport alone and what we class as an 'athlete'. There is also a possibility that by screening all involved in sport, we are creating a new vulnerable population who may be affected by the outcomes of positive tests.

1.10. Use of the ECG in Screening

As well as significant debate regarding the implementation of cardiac screening as mandatory, controversy also exists in what format this screening process should take and the inclusion or exclusion of the electrocardiogram (ECG). American experts acknowledge the benefits of ECG for diagnosing a breadth of potentially fatal cardiac disorders[3] however they also question the implications of a high number of false positive results and needless further tests and potential disqualification. Their European counterparts suggest this is not the case and that screening should always include an ECG.

In an athletic population the ECG can suggest evidence of both structural and electrical remodelling of the heart as a result of intense physical training. Therefore, the ECG pattern in an athlete often looks abnormal, particularly in black athletes and it is this that the Americans worry will cause false positive findings. Pelliccia et al[38] reported that up to 60% of athletes present with abnormal ECG changes including sinus bradycardia, sinus arrhythmia, 1st degree atrio-ventricular (AV) block, early repolarisation, incomplete right bundle branch block (IRBBB) and high voltage criteria. Increased vagal tone in athletes often elicits a lower resting heart rate (HR) with more HR variability. Sinus bradycardia is thought to be present in around 80% of trained athletes[80] but this disappears on exercise. This low HR can also affect the corrected QT interval (QTc) as Bazett's formula has been known to be unreliable at low HR's.

Early repolarisation has recently been suggested as a potential marker for risk of sudden cardiac death[81]. This phenomenon which describes J point elevation (or notching of the QRS terminal) is reportedly commonly found in young, physically active men. Early repolarisation can be misinterpreted by the computer as pericarditis or a myocardial infarction[82] and high voltage criteria can be suggestive of structural abnormalities, both of which are more common in black athletes. This highlights the necessity of an experienced cardiologist to

oversee the results. Other common ECG changes found in athletes include incomplete and complete right bundle branch block (RBBB) which has been postulated to be a reflection of right ventricular adaptations following exercise (Table 1-4)[82].

Table 1-4: Normal ECG findings associated with an athletic population with the abnormal values in this population

Sinus bradycardia	Up to 80%
Sinus arrhythmia	Up to 55%
Ectopic atrial rhythm	Unknown
Junctional escape rhythm	8%
1st° AV block	4.5-7%
Mobitz type I (Wenckeback) 2nd ° AV block	Unknown
Incomplete RBBB	12-32%
Voltage criteria for LVH	45% males, 10% females
Early repolarisation	Up to 45% (higher in black athletes)
Complex ST segment elevation with T wave inversion	2-3% (13% in black athletes)

(AV-atrioventricular, RBBB-right bundle branch block, LVH-left ventricular hypertrophy)

There are also a number of abnormalities we can expect to see on an athlete's ECG which are not considered 'normal' and are unrelated to athletic training. These may suggest an underlying pathology and would require further assessment (see Table 1-5).

ECG abnormalities had been the subject of much debate and controversy before these guidelines, the Seattle Criteria (Table 1-4 and 1-5), were drawn up[82 83]. These criteria are a refinement of previous ESC guidelines which aim to further reduce the false positive rate of the ECG in an athletic population. The main difference in the new criteria is the lengthening of the abnormal QT interval. Previously, the QTc was thought to be abnormal at 440ms but

recent studies have increased this to 470ms (480ms in females). Previous QT cut offs have been derived from a non-athletic population and debate exists as to how accurate Bazett's formula is in calculating the QTc at low heart rates, which are common in an athletic population. The predictive value of the QTc in detection of LQTS is >500ms which exceeds the new criteria.

Table 1-5: The Seattle Criteria for Abnormal ECG findings in athletes which would suggest further investigation[83]

Abnormal Finding	Definition
T wave inversion	>1mm in 2 or more leads
ST-segment depression	>0.5mm in 2 or more leads
Pathologic Q waves	>3mm or >40ms in duration in 2 or more leads
Complete LBBB	QRS >120ms, predominantly negative QRS complex in V1
IV conduction delay	Any QRS duration >140ms
Left axis deviation	-30° to -90°
Left atrial enlargement	Prolonged P wave duration of >120ms in leads I or II with negative portion of P wave>1mm and >40ms in V1
Right ventricular hypertrophy pattern	R-V1+S-V5>10.5mm and right axis deviation >120°
Ventricular pre-excitation	PR interval <120ms with delta wave and wide QRS (>120ms)
Long QT interval	QTc >470ms (male)/ QTc > 480ms (female) QTc > 500ms (marked QT prolongation)
Short QT interval	QTc <320ms
Brugada-like ECG pattern	High take off and down-sloping ST segment elevation followed by negative T wave in 2 leads (V1-V3)
Profound sinus bradycardia	<30bpm or sinus pauses
Atrial tachyarrhythmias	Supraventricular tachycardia, atrial fibrillation, atrial flutter
Premature ventricular contractions	>2 premature ventricular contractions per 10sec tracing
Ventricular arrhythmias	Couplets, triplets and non-sustained ventricular tachycardia

A study by O'Connor & Knoblauch[84] aimed to investigate the population benefit and effectiveness of adding routine ECG to the AHA protocol. The study was based on a complex scientific model which predicted that 16% of all athletes would be expected to have an abnormal ECG, whereas only 2% would have been abnormal with the current questionnaire and PE. However, with follow up only 1.3% of these athletes would have a cardiac problem which suggested ECG was an expensive tool to use in the cardiac assessment of athletes due to the number of potential false positive tests which are not cost effective and could place undue psychological stress on the athlete.

The benefit of adding ECG to personal and family history and PE was examined by Baggish et al[85]. This study screened 508 university athletes with personal and family history, PE, ECG and transthoracic echocardiogram (TTE). History and PE alone did not detect any of the abnormalities that were found on ECG and/or echocardiogram suggesting history and PE alone is not a useful screening tool. However, the positive predictive value (PPV) of the ECG in identifying LVH was only 10.4% suggesting that ECG does not add significant useful information although it could be argued that it is useful in those with no abnormality (negative predictive value (NPV)=99.8%).

A landmark study by Pelliccia et al[62] on 1005 athletes suggested that new ECG recommendations reduced the number of athletes who were initially thought to have CV disease from 40% to 11% and increased specificity of the ECG to 95%. This study suggests that the ECG can be a useful tool in cardiovascular screening if interpreted with caution.

1.11. Sex and Ethnic Differences in ECG and Echocardiogram

Differences in the ECG and echocardiogram in Caucasian and black athletes have been widely reported[86 87]. The prevalence of ECG abnormalities including repolarisation changes and T wave inversion are far more common in athletes of black origin however differences do exist amongst races.

Basavarajaiah et al[87] conducted a study in the UK comparing ECG and echo data in 300 asymptomatic black male athletes (42% Afro-Caribbean, 40% West African, 18% East African) and 300 white male athletes. This also included control groups of 150 sedentary black males and 150 sedentary white males. They found T wave inversion was only prevalent in black athletes (12% v 0%). Left ventricular wall thickness (LVPWd) was significantly greater in black athletes (11.3mm±1.6 v 10.0mm±1.5) with only 4% of white athletes demonstrating LVPWd greater than 13mm. Interestingly, there were no differences ($p>0.05$) in LVWT between black and white control groups (9.0mm±1.2 v 8.8mm±1.3). With HCM being more common in black athletes, it raises the question of upper limits of normal on echo in this population.

Gender differences can also be identified on ECG and echocardiogram. Females have been shown to have a slower rate of repolarisation[88] have a longer QT interval, and higher HR. Some other differences in the QRS complex are due to females having a smaller LV mass than males and smaller cavity size[41] which is shown on echocardiogram.

1.12. Secondary Prevention

Maron included information on survivors of cardiac arrest in one of his studies[23]. This is an important factor as without successful defibrillation, these would have been recorded as sudden cardiac deaths. It has been shown that early defibrillation in the event of cardiac arrest provides the greatest survival chances[89]. The UK survival rate for out-of-hospital cardiac arrest remains low at between 2 and 12%[90]. This is much lower than that reported in both Norway and the USA[91].

A previous study by Schmied et al[92] investigated the occurrence of cardiac events in football and assessed what preventative measures were taken by individual member nations of FIFA. This was a questionnaire based study which asked about the occurrence of any sudden cardiac arrest, SCD or sports-related death with further questions regarding resuscitation protocols and whether pre-participation screening was carried out. The response rate was 74.1% (126 of 170 questionnaires) with 107 sudden cardiac arrests/SCD reported (as well as 5 additional sports related deaths) from 52 of the 103 responding nations. Only 20.5% survived (23 out of 112 SCD) with only 22 being treated with an AED on the pitch of whom 12 survived (54.5%).

1.13. Conclusions

Sudden cardiac death remains an unknown quantity in terms of incidence and cause. We need to establish mandatory reporting of sudden deaths due to cardiac causes worldwide both in the general population and an athletic population to analyse the true incidence of this problem.

Many of the previous studies discussed here[2] [25] [77] have introduced the concept of cardiovascular screening to reduce the incidence of SCD in young athletes given that they are thought to be more at risk than the general population. The results of such screening studies are mixed, with reductions in SCD shown in Italy but not in Israel. Controversy also exists as to whether the Italian Model is truly the 'gold standard' programme.

In 2008, the Scottish Government (in conjunction with the Scottish Football Association and University of Glasgow) established a cardiovascular screening programme in Scotland. This programme was designed to establish whether the Italian Model was transferable to a Scottish population and to investigate the addition of echocardiography to the Model in terms of diagnosis of conditions.

1.14. Aims and Objectives

This thesis will be presented in 2 parts with separate aims and objectives.

The aim of Part One of this thesis was:

- To investigate the incidence and causes of cardiac death in the young in Scotland

This was the translated into the following objectives:

- To use a national database provided by ISD to:
  - investigate what young people in Scotland die from
  - determine the incidence of cardiac death in the young in Scotland
  - Investigate the causes of cardiac death in the young in Scotland
- To assess the proportion of these deaths for which the causes may be identified using cardiac screening

The aim of Part Two of this thesis was:

- To assess whether the addition of ECG and echocardiography adds benefit to current screening practice

This was the translated into the following objectives:

- To use the results of the Cardiac Assessment in Young Athletes (CAYA) programme to:
  - determine the incidence of left ventricular hypertrophy in a sporting population in Scotland
  - evaluate the sensitivity and specificity of ECG and echocardiography in identifying LVH in those undertaking athletic training
  - identify conditions such as LQTS, WPW and HCM in a young athletic population

Chapter 2 - Methodology

This thesis is written in two parts. Part one examines the epidemiology of sudden cardiac death in the young in Scotland and aims to provide information regarding the magnitude and causes of this problem. Part two of the thesis analyses the results of the CAYA (Cardiac Assessment in Young Athletes) study to investigate the use of routine echocardiography in cardiovascular screening.

2.1. Part One-Epidemiology

Part one of the study aimed to examine the incidence of all deaths in the young with special consideration given to out of hospital (OOH) deaths, particularly those with a cardiac cause. Data was requested from and collated by the Information Services Division (ISD), a division of National Services Scotland, part of NHS Scotland. The ISD provides health information, health intelligence, and statistical services to support the NHS in Scotland.

2.1.1. Data Source

ISD were asked to provide information for the period 1986 to 2008 (inclusive) on deaths in individuals aged 0-35 years at time of death. For each death they supplied the following data:

- Unique identifier
- Date of death (dd/mm/yyyy)
- Age at death
- Sex
- Institution
- Post Mortem
- Postcode Sector
- Health Board of Residence
- Primary cause of death
- All Secondary causes
- Nature of injury marker

- Place of occurrence marker
- Supplementary code for place of occurrence
- Local government region
- Health Board area
- Year of death

This information was generated by ISD from death certificate data which is collated by the General Register Office for Scotland (GRO). The death certificate includes information on the place of onset of the clinical event, the location of death as well as the cause of death. For each death primary cause of death is provided, with additional secondary causes if recorded.

ISD were also asked to look back to SMR (Scottish Morbidity Records) to see if the individuals had any specific diagnoses and to create a marker flag (0-no, 1-yes) for each:

a) at any time since 1981
b) within 1 year of their death
c) within 5 years of their death

Data regarding the health of patients in Scotland is collated as a catalogue of Scottish Morbidity Records (SMR's). These records identify the type of treatment received during an episode, recording all discharges following an acute hospital admission (SMR01) which was used in this research to record prior hospitalisation. The SMR01 relates to all in-patient or day case discharges, associated with both elective and emergency admissions. This record is generated following discharge from hospital to home, to another hospital or specialty or death. SMR and death registration records, belonging to the same patient in Scotland, have been linked together in the Scottish Record Linkage System. Each patient receives a primary diagnosis at discharge, which was used in this study.

For each of the above hospitalisations, ISD were asked to supply the following information:

- Date of admission (dd/mm/yyyy)
- Date of discharge
- Hospital code
- Age
- Sex
- Type of admission
- Type of facility
- Specialty
- Length of stay
- Year of admission

This data was presented to us by ISD in an SPSS spreadsheet with 1001 variables on 41,049 deaths.

2.1.2. Coding of Data

The cause of death was analysed from the International Clinical Diagnostic classification (ICD code) used in epidemiological research to classify diseases in clinical records such as medical notes and death certificates. ICD is the universally applied classification system for coding illness, medical diagnoses and external causes of injury.

Causes of death in the current study were registered according to the International Classification of Diseases-9 (ICD-9), previous to year 1994, and the International Classification of Diseases-10 (ICD-10) from 1994 onwards. ICD-9 has a total of 6969 codes, while there are 12,420 ICD-10 codes, meaning deaths from 1994 onwards are coded into more distinct categories. Doctors do not assign codes on the death certificate; instead the responsibility for the recording of codes for each death is undertaken by specialist clinical coders working within Medical Records departments. Errors in recording have been reported to be as high as 20% for various reasons such as accuracy of diagnosis and human error as interpretation of information may vary[93].

The General Register Office (GRO) for Scotland records and stores the cause of death for all patients based on information from the medical certificate issued at time of death. Due to there being no information concerning the time from onset of symptoms to death available on the death certificate, I was unable to study 'sudden death'. This thesis will analyse deaths which occurred in-hospital and out-of-hospital.

2.1.3. Location

Information was available on the location of the initial clinical event. These were chosen from one of the standard locations below:

- Home
- Farm
- Mine/Quarry
- Place of Industry
- Sport/Recreation Area
- Street/Highway
- Public Building
- Residential Institution
- Other Specified Place
- Unspecified Place

Deaths were then categorised into those which occurred 'in hospital' and those which occurred 'out-of-hospital' (Table 2-1).

Table 2-1: Locations of in and out-of-hospital death according to ISD information

In-Hospital	Out-of-Hospital
NHS hospital	Administration office
Joint User hospital	Health Centre/GP surgery
Contractual hospital	Clinic premises
Non NHS Maternity	Non-institutional e.g. home
Private hospital	School
	Prison
	Home for the elderly
	Miscellaneous premises

2.1.4. Post Mortem Results

For each death, information was provided on whether a post mortem (PM) had been carried out. No further information was available from the PM. In Scotland, the post mortem examination is generally requested by the Procurator Fiscal where a death is sudden and/or unexplained, or the cause of death is not obvious. Deaths were classified into 6 categories as stated below:

1. Post mortem was performed
2. Post mortem was not proposed
3. Post mortem may have been performed
4. Post mortem was proposed and performed later
5. Post mortem was proposed and not performed
6. Post mortem was not proposed but was later performed

These were than grouped as those which had undergone a PM examination (1, 4 and 6) and those which did not undergo a PM (2 and 5). For the remaining deaths, it is not clear whether a PM took place (3).

2.1.5. Primary Cause of Death

In this study, the primary cause of death from the death certificate was provided. Deaths were then categorised according to classifications from the World Health Organisation (WHO) coding system (Table 2-2). Additional secondary causes were available but were not studied in this thesis.

Table 2-2: Causes of death according to WHO classifications with associated ICD-9 and ICD-10 Codes

Cause	ICD-9 Codes	ICD-10 Codes
Infection	001-139	A00-B99
Cancers	140-239	C00-D48
Blood Diseases	280-289	D50-D89
Endocrine/Metabolic Diseases	240-279	E00-E90
Mental/Behavioral Disorders	290-319	F00-F99
Diseases of Nervous System	320-389	G00=G99
Circulatory Disease	390-459	I00-I99
Respiratory Disease	460-519	J00-J99
Diseases of GI System	520-579	K00-K93
Diseases of Skin/Connective Tissue	680-739	L00-M99
Diseases of GU System	580-629	N00-N99
Pregnancy/Childbirth	630-679	O00-O99
Perinatal Conditions	760-779	P00-P96
Congenital Malformations	740-759	Q00-Q99
Symptoms/Ill Defined Causes	780-799	R00-R99
Accidents	E800-E929	V01-X59
Drugs	304, 305, E850-E858	T36-T50
Self Harm	E950-E959, 960-979	X60-X84
Assault	E960-E69	X85-Y09
Alcohol	980	Y15, F10, K70

(GI=gastro-intestinal, GU=genito-urinary)

2.1.6. Cardiac Deaths

Cardiac deaths were identified from ICD coding for circulatory causes of death (ICD-9 codes 390-459, ICD-10 codes I00-I99) shown in Table 2-3.

Table 2-3; Circulatory causes of death with associated ICD codes

Chapter	ICD 9 Codes	ICD 10 Codes
Acute Rheumatic Fever	390-392	I00-I02
Chronic Rheumatic HD	393-398	I05-I09
Hypertensive HD	401-405	I10-I15
Ischaemic HD	410-414	I20-I25
Pulmonary HD	415-417	I26-I28
Other forms of HD	420-429	I30-I52
Cerebrovascular disease	430-438	I60-I69
Diseases of arteries, arterioles and capillaries	440-449	I70-I79
Diseases of veins, lymphatic vessels and lymph nodes	451-459	I80-I89
Other and unspecified disorders of circulatory system	-	I90-I99

Cerebrovascular disease was excluded (ICD-9 codes 430-438, ICD-10 codes I60-I69). Congenital heart defects and Marfans syndrome were included (745-747, 759.82, Q20-Q28, Q87.4). 'Sudden death, unknown' was also included (ICD codes 798.1, 798.2 and R96). Sudden death unknown (798, R96) is later categorised within cardiac dysrhythmia due to the small numbers. Table 2-4 presents the causes of cardiac death as described by the ICD system with the associated ICD codes.

Table 2-4: Cardiac Causes of Death with ICD Codes

Cause	ICD-9 Codes	ICD-10 Codes
Congenital	745-747	Q20-Q28,Q87.4
Coronary HD	410-414	I20-I25
Cardiomyopathies	425	I42-I43
Hypertensive HD	401-405	I10-I15
Pulmonary HD	415-417	I26-I28
Conduction Disorders	426	I44-I45
Cardiac Dysrhythmias	427	I46-I49
Heart Failure	428	I50
Diseases of arteries	440-449	I70-I79
Diseases of veins	451-459	I80-I89, I95
Other	394-398, 420,423, 429	I05-I09, I30-I32, I34-I37, I51-I52, I97-I98
Endocarditis	421, 424	I33,I38-I39
Myocarditis	422	I40-I41
Sudden Death unknown	798	R96

(HD=heart disease. Other includes includes valvular disease, pericarditis and diseases of pericardium and complications and ill-defined descriptions of HD)

2.1.7. Previous Cardiovascular Diagnosis and Hospitalisation

Previous diagnoses of cardiovascular disease were provided for analysis and were coded as in Table 2-5. Data on any previous hospitalisations was available in the spreadsheet from SMR01 records.

Table 2-5: Classification of previous cardiac diagnosis according to ICD coding

Diagnosis	ICD-9 Codes	ICD-10 Codes
Cardiovascular Disease	390-459	I00-99
Coronary HD	410-414	I20-25
Chest Pain	786.5	R07
Angina	411, 413	I20, I24.9

(HD=coronary heart disease)

The date of admission and discharge were noted along with the clinical specialty. Any history of cardiac surgery was also detailed. Diagnosis, admissions and surgery were categorised into:

a) All diagnoses since 1981
b) Within 5 years of death
c) Within 1 year of death

Admissions for cardiac causes and previous diagnosis of cardiac disease were identified and cross tabulated with the primary cause of death to establish if a death was caused by a 'known cardiac condition'.

2.1.8. Population and Calculation of Incidence of Death

In order to calculate the incidence of death in this population, information on population size of Scotland for those aged 0-35 years was obtained using the mid-year population estimates from the General Register Office (GRO) for Scotland[94]. These were calculated for each year (1986-2008) to allow calculations on the incidence of deaths.

Annual mortality incidence was calculated per 100,000 of the population by:

(*Number of deaths /estimated population size for each year) x 100,000*

The overall incidence of death in this population was calculated as:

(Total no. deaths / sum of estimated populations over 23 years) x 100,000

2.1.9. Analysis by Age

Data was further analysed according to age and gender, in order to identify any trends or differences within groups. Age categories were: 0 years (which were then excluded from analysis), 1-4 years, 5-9 years, 10-14 years, 15-19 years, 20-24 years, 25-29 years, 30-35 years.

2.1.10. Statistical Analysis

All data was stored and analysed using SPSS 19.0, with graphs drawn using Microsoft Excel 2010. Data is presented as absolute numbers, percentages and incidences per 100,000 person years. Results are presented with corresponding standard deviations (SD) and proportional 95% confidence intervals (CI).

The incidence and causes (with corresponding 95% CI) of both in-hospital and out of-hospital deaths were reported by age and sex. Person-years were based on the number of persons in Scotland in the relevant age category from 1986 to 2008.

2.2. Part Two-Screening of Young Athletes

Part 2 of the project aimed to evaluate the Scottish cardiovascular screening service, Cardiac Assessment in Young Athletes (CAYA). The CAYA Study is a joint project between the Scottish Executive, the University of Glasgow and the Scottish Football Association. This is a voluntary service available to the public which is based at the Sports Medicine Centre at the National Stadium, Hampden Park. The programme also runs a number of Satellite sessions at other sites at a distance to make the testing available to a larger outlying population and to avoid postcode bias. The programme is based on the Italian Model, which is regarded as the Gold Standard screening protocol, but with the inclusion of an echocardiogram for all subjects.

Each subject underwent the following tests as part of the screening protocol:

- Personal and family history questionnaire
- Physical examination
- Resting 12-lead ECG
- Echocardiogram

I was responsible for administering all of the above with the exception of the echocardiogram which was carried out by a trained clinical physiologist. An experienced consultant cardiologist (Professor W. Stewart Hillis) was responsible for overseeing and reporting all results. A copy of all results were sent to the subject's GP and/or referring doctor with any necessary follow up arranged locally. Communication was also made with the patient following any positive results.

2.2.1. Subjects

Cardiovascular screening in Scotland is a voluntary service available to the general public upon appointment free of charge. This service was initially set up to screen those aged 16-18, however younger ages were included due to demand and The uptake of this service was poor amongst the general public with the majority of participants recruited from football clubs affiliated to the Scottish Leagues. Footballers competing in European competition must be screened according to UEFA laws but no domestic laws exist below the Premier League.

Subjects were recruited from 3 main sources:

1. Volunteers from the general public who participate in organised sport (aged 12-19 years)
2. Members of the Scottish Institute and regional Institutes for sport (aged 12-19 years; 20-24 years; 25-29 years and 30-35 years)
3. Footballers from Scottish Premier League and Scottish Football Leagues who required screening as part of mandatory licensing for team activities (aged 12-14 years; 15-19 years; 20-24 years; 25-29 years and 30-35 years)

Subjects completed a consent form which outlined potential implications regarding future employment, insurance and possible restriction from sporting competition.

2.2.2. Personal and Family History Questionnaire

Adapted versions of the personal and family history questionnaires detailed in the Lausanne Recommendations[76] were completed by each participant. This included a symptomatic enquiry of the cardiovascular system and a family history of cardiovascular events as well as general health questions including any prescribed medications (see Appendix A).

2.2.3. Physical Examination

Physical examination was carried out in accordance with the Lausanne Recommendations[76], including examination of radial and femoral pulses and auscultation of the heart at all 4 areas. If a suspected murmur was heard, this was further investigated during the echocardiogram and a referral made if necessary.

Height and weight were measured to the nearest 0.1cm/kg in bare feet and minimal clothing. Body surface area (BSA) was then calculated using the equation from Du Bois & Du Bois[95].

2.2.3.1. Blood Pressure Measurement

The blood pressure was recorded on the right arm using an automated blood pressure cuff (Omron M7) once the subject was quietly in a supine position for 5 minutes. At least two measurements were taken for each subject, with the lowest value being recorded. Blood pressure was then categorised as in Table 2-6. Blood pressure machines were replaced every 6 months to avoid any calibration issues.

Table 2-6: Blood pressure classifications with associated systolic and diastolic measurements

Classification	Systolic Value	Diastolic Value
Normal	<120mmHg	<80mmHg
Pre-Hypertension	120-139mmHg	80-89mmHg
Stage I Hypertension	140-159mmHg	90-99mmHg
Stage II Hypertension	>160mmHg	>100mmHg

2.2.3.2. Blood Pressure Sub-study

Due to the high incidence of hypertension found, a small sub-study was undertaken following data collection to establish if the hypertension found in the CAYA study (stage I and II) was true hypertension or was due to 'white coat' syndrome. Subjects with stage I or stage II hypertension as per Table 2-6 were identified using the CAYA database from clubs with matched normal controls (BP below 120/80mmHg). These 2 groups were then re-tested with domiciliary BP (DBP) to assess the prevalence of white coat hypertension in this population.

Players were identified from the CAYA database and contacted via their Club Doctor before being provided with an additional information sheet and consent form (Appendix E). Standard Omron M7 digital blood pressure monitors were then issued to players and they were instructed on taking their blood pressure twice daily for 4 days according to NICE guidelines.

2.2.4. Electrocardiogram

A resting 12 lead electrocardiogram was recorded on all participants at 25mm/s and 0.5mV/mm using a Mac 800 machine (GE Healthcare, UK). This provided automatic measurement of all standard intervals (QTc, PR and HR) (Figure 2-1) and gave qualitative reports. The assessment of LVH criteria were made by direct measurements using the Sokolow Lyon criteria (sum of S wave in V1 + R wave in V5 >35mm indicative of LVH)[96] which was manually counted by an experienced cardiologist (WSH). The QT interval and corrected QT (QTc) were generated by the ECG machine according to Bazett's formula[97]. ECG changes were determined as significant abnormalities following The European Society of Cardiology's (ESC) criteria (see Table 2-7).

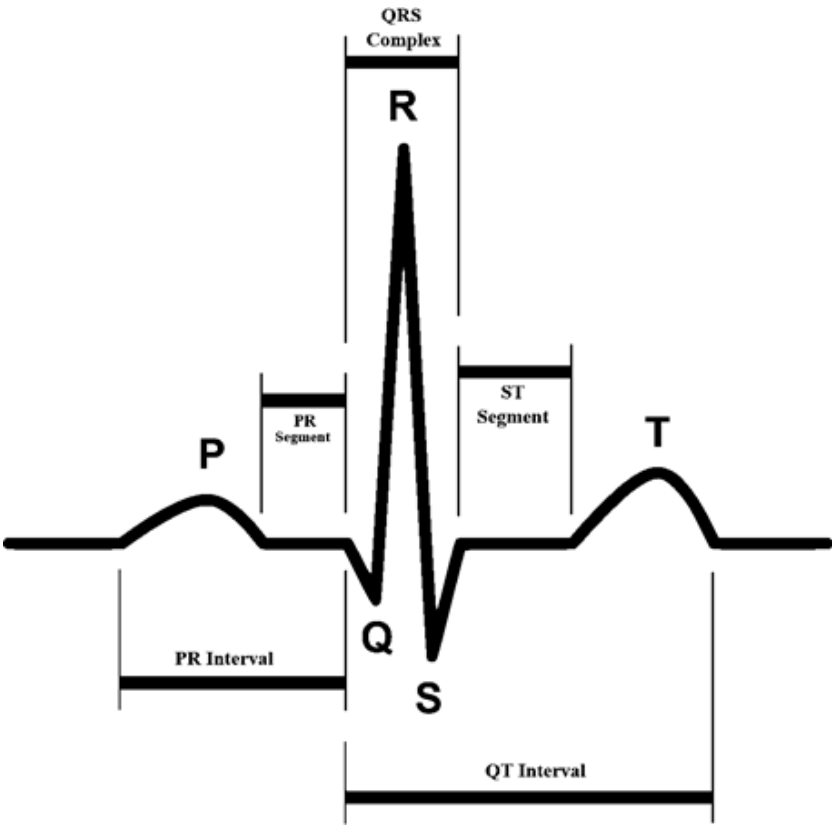


Figure 2-1: Diagram of the QRS complex from ECG illustrating the measured PR and QT intervals (adapted from wikipedia)

Table 2-7: ECG Abnormalities determined as significant according to ESC criteria[98]

P Wave -Left atrial enlargement: negative portion of the P wave in V1>0.1mV in depth and >0.4s in duration - Right atrial enlargement: peaked P wave in leads II and III or V1>0.25mV in amplitude - Prolonged PR interval >0.20s - Short PR interval <0.12s
QRS Axis - Right axis deviation ≥ 120º - Left axis deviation -30 º to -90 º
QRS Voltage (Sokolov Lyon Criteria for LVH) - S wave in V_1+R wave in V_5>35mm
QRS Morphology - Partial RBBB (QRS>100ms) - RBBB (QRS>120ms) - LBBB (QRS>120ms) - Inter-ventricular conduction defect
ST Segment and T Wave - Early repolarisation (ST elevation ≥2mm in>2 leads) - T wave flattening or inversion in >2 leads - Repolarisation pattern with particularly tall T waves (>15mm)
Intervals - Prolonged QTc (using Bazett's formula) (>440ms in men; 460ms in women)
Arrhythmia and Conduction Defects **-** Ectopic atrial rhythms - Atrial fibrillation or flutter - 1st degree heart block - 2nd degree heart block - Complete heart block

(LVH=left ventricular hypertrophy, RBBB-right bundle branch block, LBBB-left bundle branch block, QTc=corrected QT interval)

2.2.5. Echocardiogram

Echocardiography was performed using standard 2D and M-mode trans-thoracic echocardiography (TTE) with Doppler measurements using an Acuson P50 or an Acuson CV70 machine (Siemens, USA), and performed by 1 of 9 trained clinical physiologists. All physiologists were registered members of the British Society of Echocardiography and were working within the NHS. Results were overseen by Professor W S Hillis and reports sent to the GP and/or club doctor depending on the referral source.

Left ventricular dimensions were assessed by measuring inter-ventricular septal diameter (IVSd), posterior wall diameter (LVPWd) and left ventricular internal diameter (LVIDd) - all at end of diastole. These measurements were taken using M-mode from a 2D parasternal long axis view (see Figure 2-2).

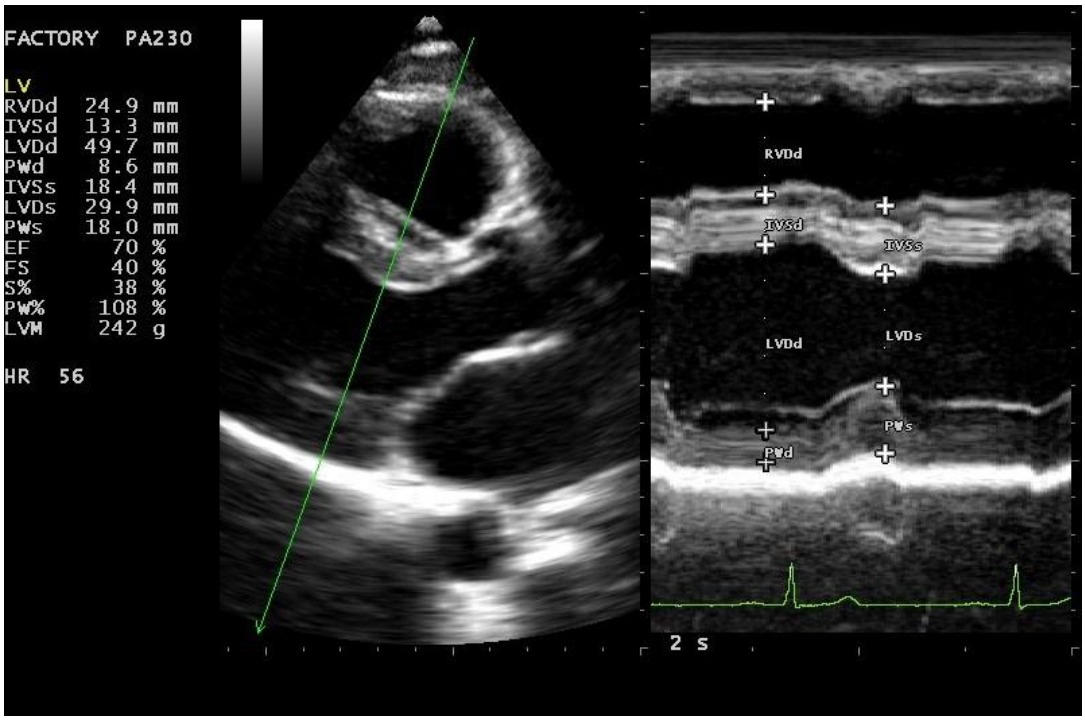


Figure 2-2: Diagram illustrating the measurements taken in M-mode during echocardiogram for intra-ventricular septal thickness (IVSd), left ventricular internal diameter dimension (LVIDd) and left ventricular posterior wall thickness (LVPWd)

All valves (pulmonary, tricuspid, mitral and aortic) were assessed for structural and functional abnormalities using short axis views at their respective levels with colour Doppler to illustrate flow. An apical 4 chamber view with Doppler measurements was also used. All subjects were then assigned to one of three categories following TTE – those with no abnormal findings, those that could be considered abnormal but consistent with physiological remodeling and those that were abnormal and suggestive of underlying pathology according to left

ventricular dimension measurements (see Table 2-8). All echocardiographic studies were performed to the Guidelines of British Society of Echocardiography and appropriate European Guidelines[99].

The right ventricle was visually assessed by the physiologist to ensure it was smaller than the left ventricle and eliminate any doubts over ARVC[100]. Measurements were taken if appropriate. Clinical comments on ventricular function were made by the physiologists and cardiologist looking to exclude appearance of HCM.

Table 2-8: Transthoracic echocardiography measurements used for diagnosis of left ventricular hypertrophy[85]

Finding	Males	Females
NORMAL ECHO		
Normal LV Wall Thickness	IVSd or LVPWd <11mm	IVSd or LVPWd <10mm
MILDLY ABNORMAL: CONSISTENT WITH PHYSIOLOGICAL REMODELLING		
Mild LV Hypertrophy	IVSd or LVPWd 11-13mm	IVSd or LVPWd 10-12mm
ABNORMAL: SUGGESTIVE OF PATHOLOGY		
LV Hypertrophy	IVSd or LVPWd >13mm	IVSd or LVPWd >12mm

(IVSd= intra-ventricular septal thickness, LVPWd=left ventricular posterior wall thickness)

2.2.6. Ethical Approval

Ethical approval was granted by University of Glasgow Medical Faculty Ethics Committee (Appendix B). An information sheet (Appendix C) was provided to all interested participants detailing the procedures involved with all subjects then being asked to sign a written consent form (Appendix D) prior to inclusion in the study, which were countersigned by a parent or guardian if under 16 years.

2.2.7. Statistical Analysis

All data was securely stored within a custom made CAYA database from which data was exported to SPSS 19.0. Continuous data is presented as means (±SD). Graphs were presented using SPSS and Microsoft Excel.

Pearson correlations were undertaken for all continuous data with Spearman Rank correlations used for categorical data. Paired t-tests were used to compare results in the blood pressure sub study. The level of significance was accepted as $p<0.05$.

Screening test statistics including sensitivity and specificity and negative and positive predictive values were calculated using 2x2 contingency tables based on the ability of each technique (ECG and echo) to identify athletes with left ventricular hypertrophy.

Chapter 3 - Results Part 1

3.1.1. All Deaths aged 0-35 years in Scotland 1986-2008

A total of 41,049 deaths were recorded in the young (ages 0-35 years) in Scotland between 1986 and 2008. The mean age of these deaths was 19.2 years (±12.5). Of these deaths, 27,748 (67.6%) were male, and 13,299 (32.4%) were female. This gives a ratio of 2.1 male: 1 female deceased. The absolute number of deaths can be seen to decrease from 2045 deaths in 1986 to 1482 deaths in 2008 (27.5% decrease) (Figure 3-1). Similar decreases are seen for both sexes although the number of deaths occurring in males always exceeds the number in females, and also shows more variation.

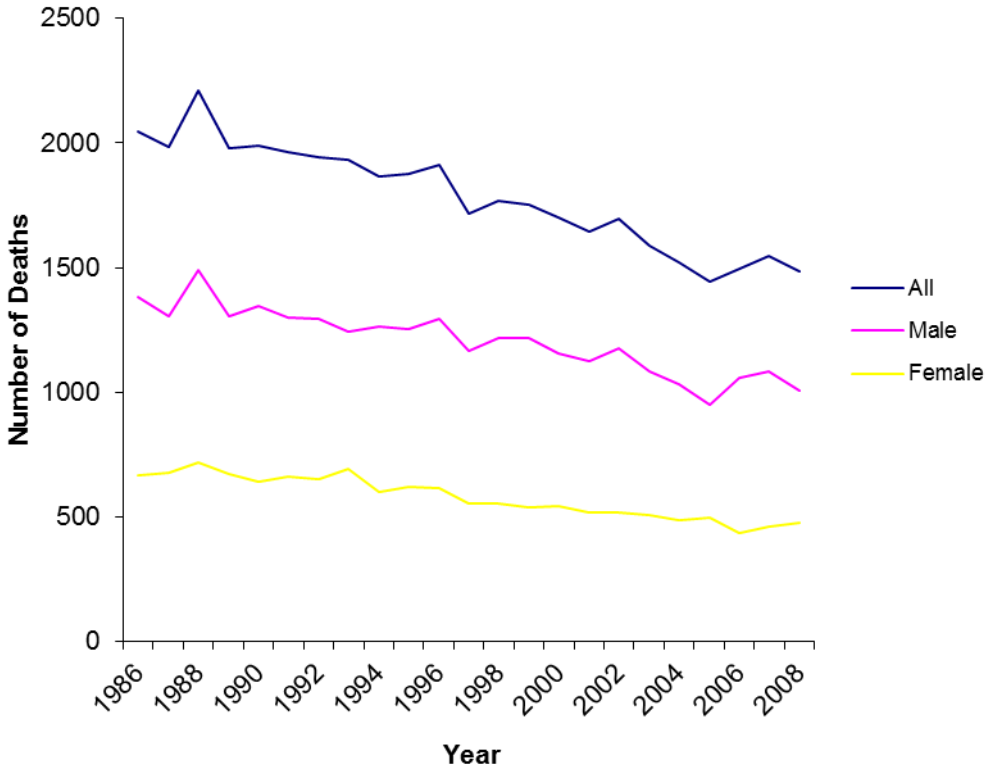


Figure 3-1: Numbers of deaths per year in 0-35 year olds in Scotland 1986-2008

According to the mid-year population estimates (GRO Scotland), there was a 15.7% decrease in the size of the population of 0-35 year olds in Scotland between 1986 and 2008 (Figure 3-2). Similar declines were seen for both male (15.8% decrease) and female (15.7% decrease) sexes.

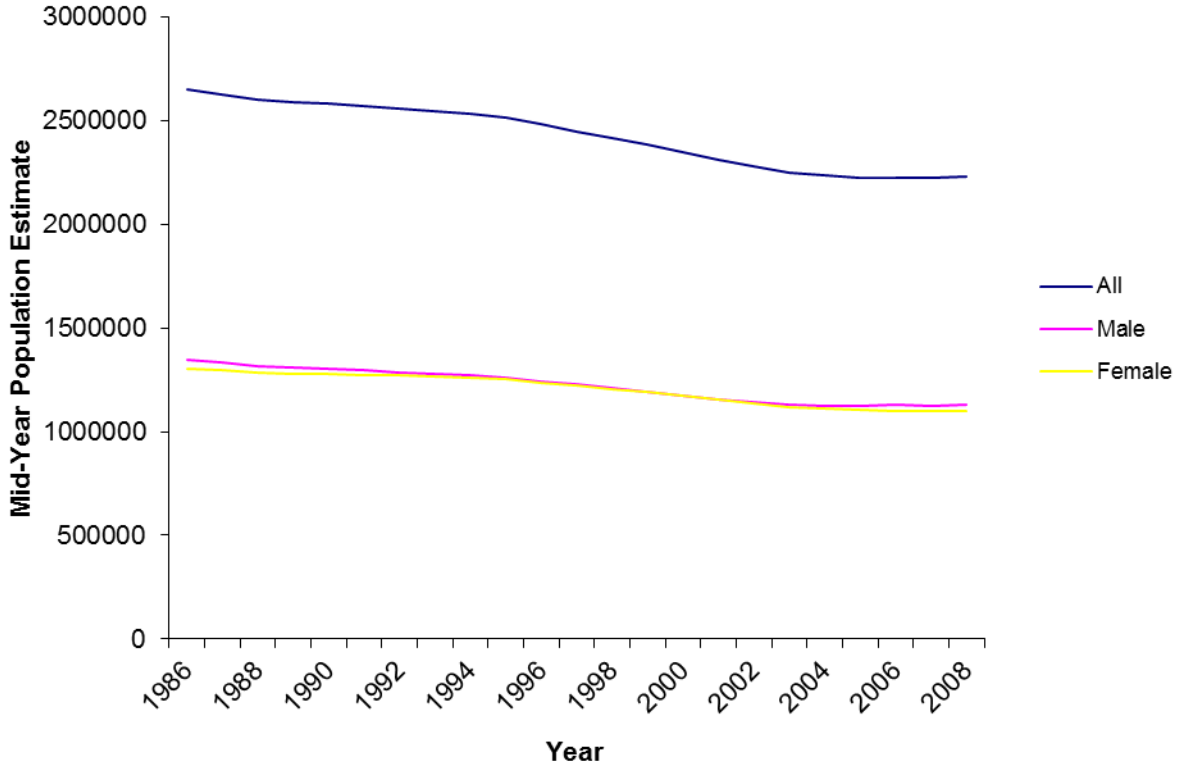


Figure 3-2: Changes in mid-year population estimates for 0-35 year olds in Scotland 1986-2008

Despite this decrease in the population size, Figure 3-3 shows a 14.0% decrease in incidence of mortality between 1986 (77.2 deaths per 100,000 population) and 2008 (66.4 deaths per 100,000 population) and comparative declines in both sexes (male 13.6% v female 14.8%). The slight 'peak' that can be seen in 1988 can be accounted for by the Lockerbie Disaster (270 fatalities), with a smaller peak seen in 1996 being attributed to the Dunblane tragedy (18 deaths including 16 children).

Figure 3-3: All-cause mortality rates (per 100,000 of population) for men and women aged 0-35 years during 1986-2008

3.1.2. Post Mortem Examination

Table 3-1 shows the number of dead who did or did not undergo a post mortem examination. Over half of all deaths (57.2%) had a post mortem carried out, with 11,641 deaths not having a post mortem requested. There are a number of deaths (2089 deaths, 5.1%) where we cannot confirm if a PM took place or not.

Table 3-1: Performance of a post mortem in all dead aged 0-35 years

Post Mortem	No. of Deaths	% of Deaths
Was performed	23,500	57.2
May have been performed	2089	5.1
Not proposed	11,641	28.4
Proposed & performed later	2876	7
Proposed & not performed later	910	2.2
Not proposed but performed later	33	0.1

3.1.3. Place of Occurrence of Symptoms

For the majority of deaths, the initial onset of symptoms were recorded to occur at home (37,426 deaths) (Table 3-2). On initial examination a number of collapses which lead to death (n=180, 0.4%) were found to occur on the sports field. This was of particular interest to part 2 of this study; however on closer examination we find that none of these were sports-related and were instead due to self-harm and assault.

Table 3-2: Place of occurrence of onset of symptoms with absolute numbers and percentages

Place of Occurrence	No. of Deaths	% of Deaths
Home	37,426	91.2
Farm	79	0.2
Mine/Quarry	57	0.1
Place of Industry	229	0.6
Sport/Recreation Area	180	0.4
Street/Highway	97	0.2
Public Building	93	0.2
Residential Institution	62	0.2
Other Specified Place	1416	3.5
Unspecified	1410	3.4

3.1.4. Location of Death

The majority of deaths in 0-35 year olds (21,475 deaths, 52.3%) were found to have occurred in-hospital. Of the 19,574 deaths that occurred out-of-hospital, 19,363 (47.2%) were recorded to occur in the home with deaths also occurring in nursing homes, prison and clinic premises (Table 3-3).

Table 3-3: Location of deaths aged 0-35 years with absolute numbers and percentages

Location of Death	No. of Deaths	% of Deaths
Prison	143	0.3
NHS Hospital	20,849	50.8
Other Home (medical facility)	54	0.1
Private Nursing Home/hospital	452	1.1
Contractual Hospital	172	0.4
Health Centre/GP Surgery	3	<0.1
Home for the Elderly	9	<0.1
Joint User Hospital	2	<0.1
Non Institutional e.g. home	19,363	47.2
Non NHS Maternity	1	<0.1
Clinic Premises	1	<0.1

Table 3-3 also identified 452 deaths occurred in private nursing homes and hospitals. This is an abnormally high number for a young population and warranted further investigation. On examination, the majority of deaths (n=260) were in those aged 30-35 years. The main cause of death within these private homes was cancer suggesting patients with terminal illness who were admitted for palliative treatment.

3.1.5. Deaths According to Age Category

With the exception of a large number of deaths which occurred in infants (8514 deaths, 21%), Figure 3-4 shows that the number of deaths increases with increasing age with the highest number of deaths occurring in the 30-35 year age category (10,887 deaths, 27%).

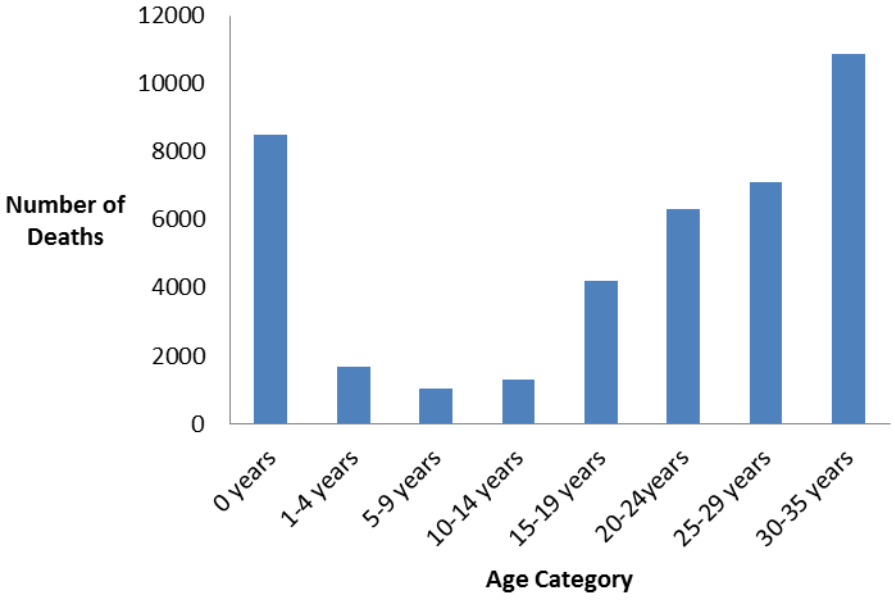


Figure 3-4: All 41,049 deaths in the young (0-35 years) according to age category

Figure 3-5 shows the numbers of deaths over time according to each age category. The largest change in deaths is those in infants (0 years). This has significantly decreased from 569 deaths in 1986 to 240 deaths in 2008. This led to these infant deaths being removed from the remaining analysis. All other age categories show variation in numbers of deaths over time, with the largest fluctuation seen in deaths in 30-35 year olds.

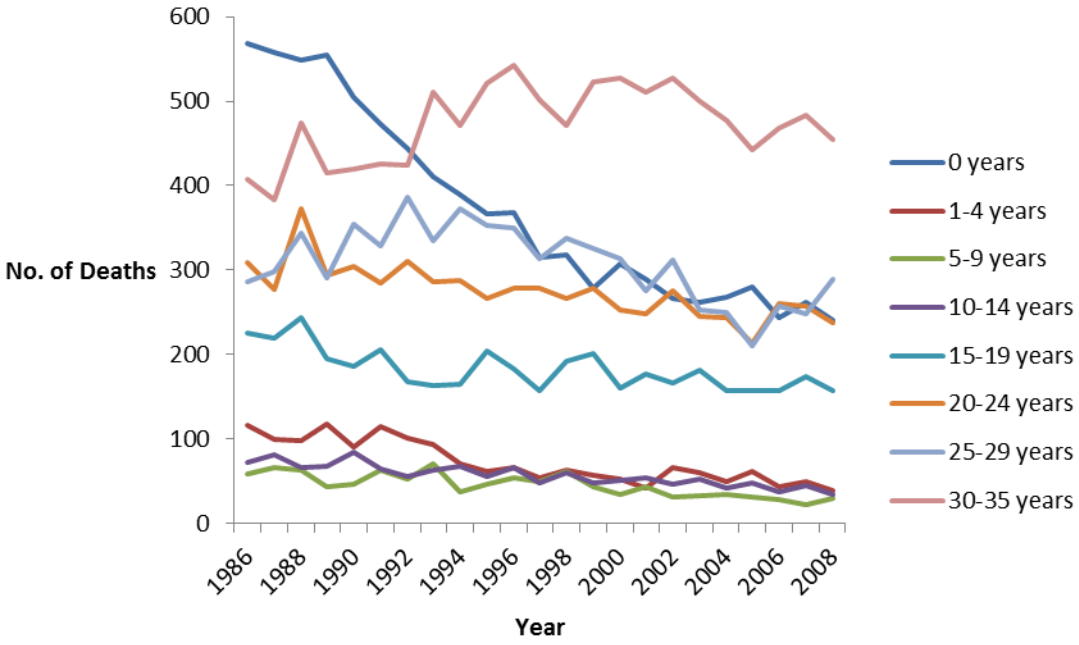


Figure 3-5: Line graph showing the absolute number of deaths according to age category over time

3.1.6. Primary Cause of Death in 0-35 year olds

Figure 3-6 illustrates the primary causes of death in the young between 1986 and 2008 according to ICD classifications. The largest causes of deaths are by accidents (8908 deaths, 21.7%) and self-harm (5281 deaths, 12.9%). The majority of medical related deaths are perinatal causes (4042 deaths, 9.8%), cancers (3894 deaths, 9.5%) and congenital defects (3153 deaths, 7.7%). Table 3-4 shows the total number of deaths for each cause alongside the percentage of deaths for each category with associated 95% confidence interval.

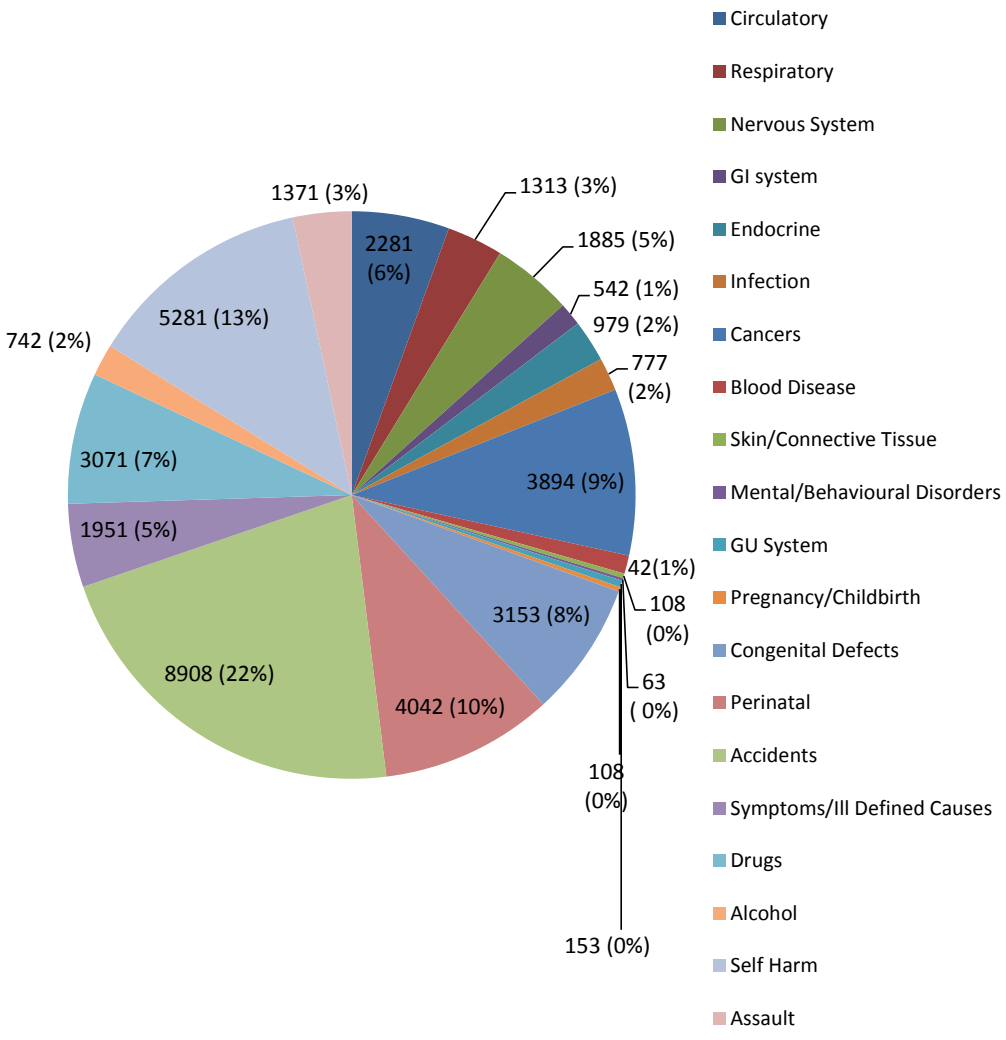


Figure 3-6: Primary Causes of Death in the Young from 1986-2008

Table 3-4: Prevalence of Primary Causes of Death in the Young 1986-2008

classified according to ICD-9 and ICD-10 coding with proportional 95% CI

Cause of Death	Total No. of Deaths	Percentage (with 95% CI)
Circulatory	2281	5.6% (5.3-5.8)
Respiratory	1313	3.2% (3.0-3.4)
Nervous System	1885	4.6% (4.4-4.8)
GI System	542	1.3% (1.2-1.4)
Endocrine	979	2.4% (2.2-2.5)
Infection	777	1.9% (1.8-2.0)
Cancer	3894	9.5% (9.2-9.8)
Blood Disease	427	1.0% (0.9-1.1)
Skin/Connective Tissue	108	0.3% (0.2-0.3)
Mental/Behavioural Disorders	63	0.2% (0.1-0.2)
GU System	153	0.4% (0.3-0.4)
Pregnancy/Childbirth	108	0.3% (0.2-0.3)
Congenital Defects	3153	7.7% (7.4-7.9)
Perinatal	4042	9.8% (9.6-10.1)
Accidents	8908	21.7% (21.3-22.1)
Symptoms/Ill Defined Causes	1951	4.8% (4.6-5.0)
Drugs	3071	7.5% (7.2-7.7)
Alcohol	742	1.8% (1.7-1.9)
Self-Harm	5281	12.9% (12.6-13.2)
Assault	1371	3.3% (3.2-3.5

3.2. Infant Deaths

Twenty one percent (8514 deaths) of all deaths in the young from 1986-2008 were in infants (0-1 years). Of these deaths, the majority of these were due to perinatal causes (47 %) and congenital malformations (25%) (Figure 3-7).

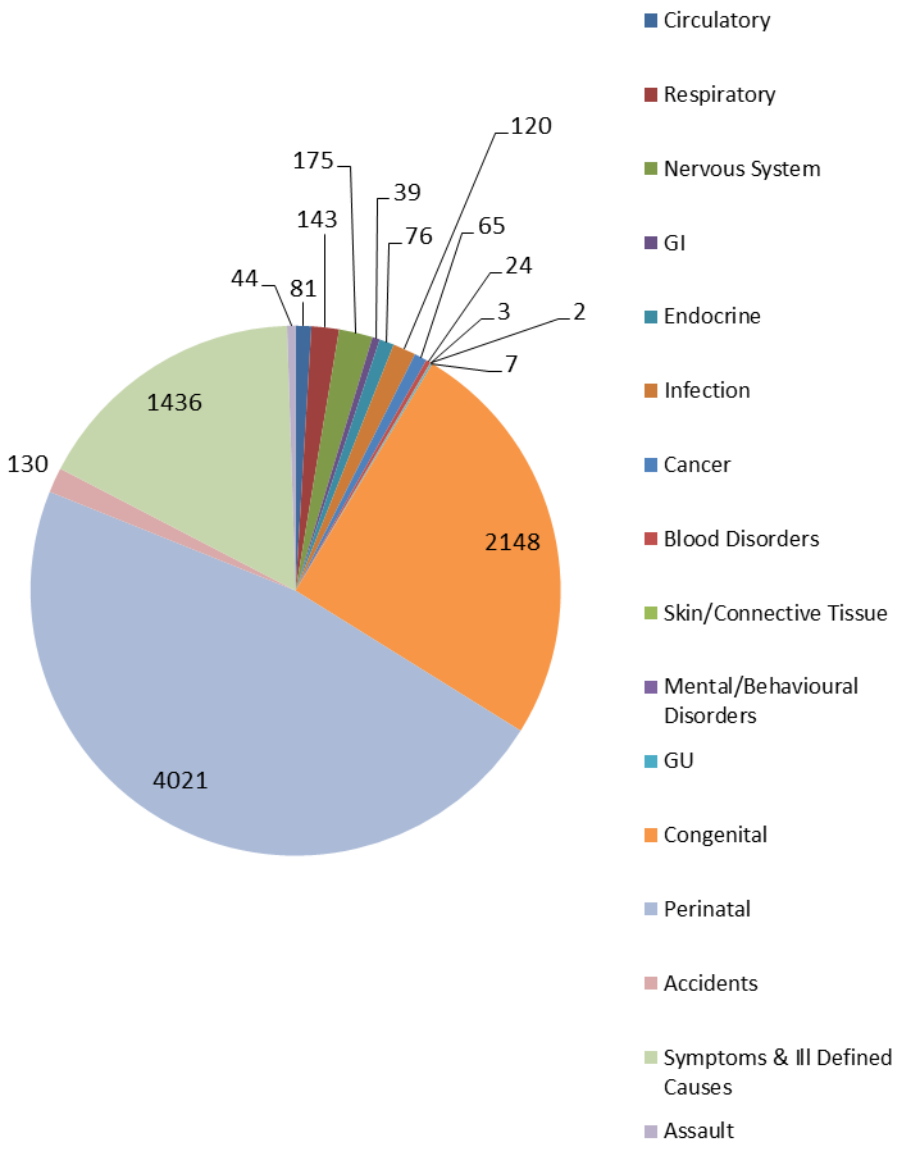


Figure 3-7: Primary causes of death in infants (0 years) between 1986 and 2008

3.3. All Deaths aged 1-35 years in Scotland 1986-2008

Of the 41,049 deaths, 8514 (20.7%) were infant deaths (0 years), which were excluded from further analysis. The remainder of this thesis includes 32,535 deaths which occurred in those aged 1-35 years. The mean age of these deaths was 24.2 years (±8.7). Of the deceased, 22,823 were males, and 9712 were females. This gives a ratio of 3.2 male: 1 female deceased.

The overall incidence of deaths in this population is 12 per 100,000 people. The number of deaths in 1-35 year olds is seen to be variable over time although a decrease can be seen from 1476 deaths in 1986 to 1242 deaths in 2008 (15.9% decrease), with a peak of 1664 deaths in 1988 attributable to the Lockerbie Disaster (Figure 3-8). A similar pattern can be seen for male deaths (decrease of 17.1% from 1053 deaths in 1986 to 873 deaths in 2008) whereas the total decrease is less for deaths in females (decrease of 12.8% from 423 deaths in 1986 to 369 deaths in 2008).

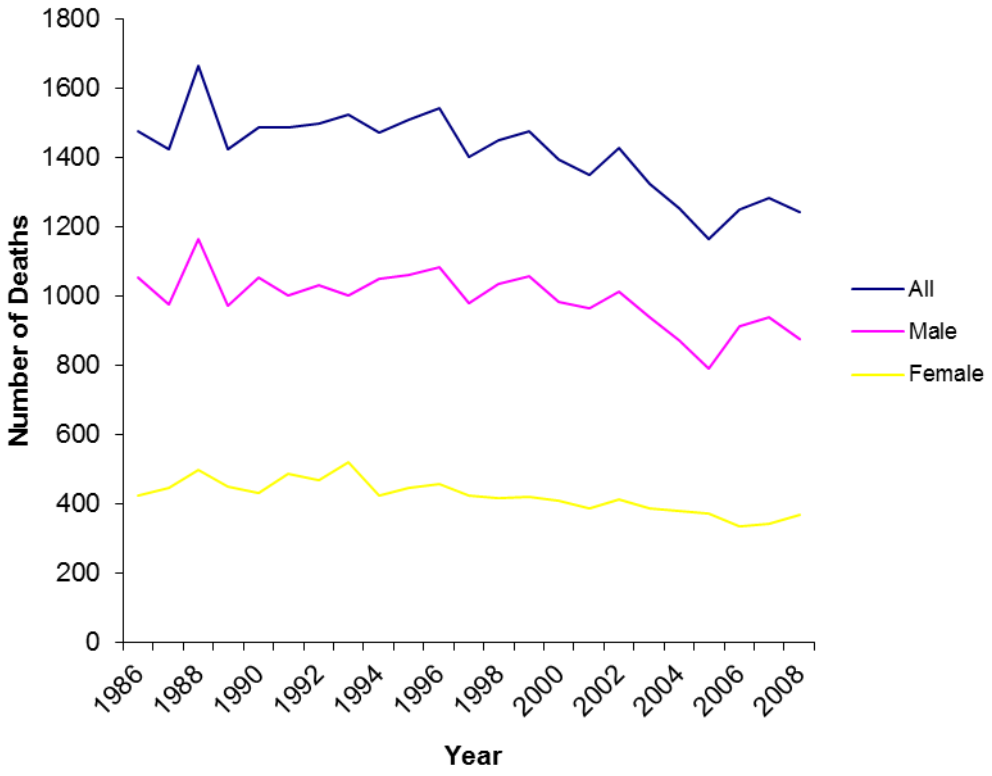


Figure 3-8: Number of deaths per year in 1-35 year olds in Scotland 1986-2008

Despite the decrease in population size, results suggest there has been little change in the overall annual incidence of death in this age category when expressed per 100,000 of the population, with a visible peak in 1988 due to the Lockerbie Disaster (Figure 3-9).

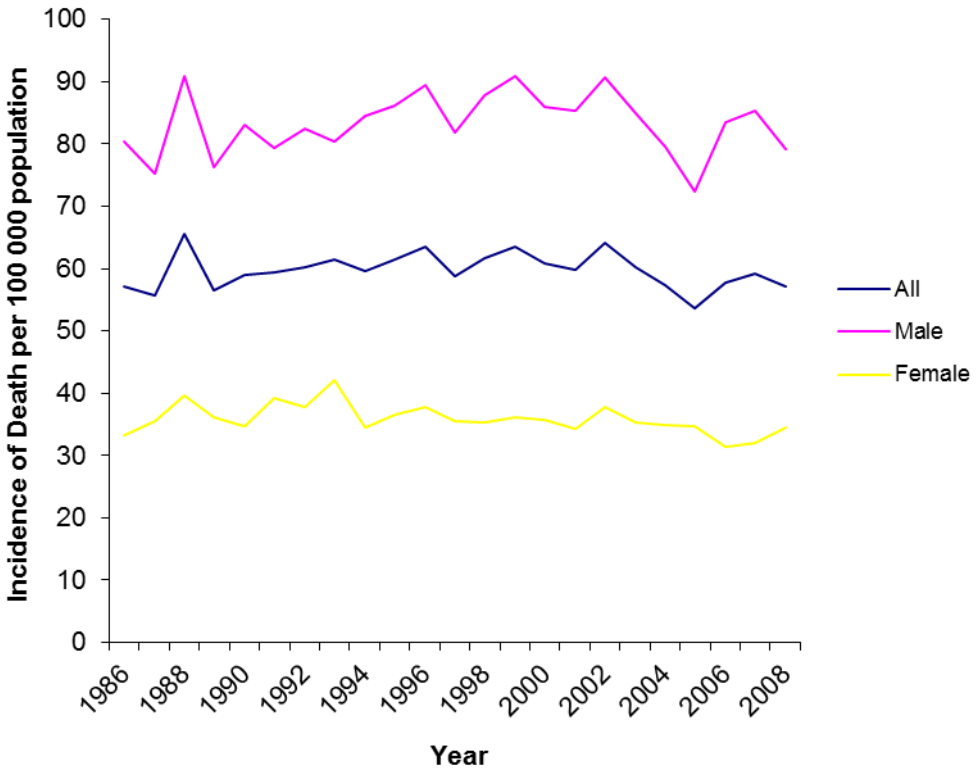


Figure 3-9: Incidence per 100,000 population for those aged 1-35 years in Scotland 1986-2008

Variation in the incidence of death can be seen over time within age categories, but the highest incidence remains in the 30-35 year category (mean 107.3 deaths per 100 000), followed by 25-29 year category (mean 86.3 deaths per 100,000). The lowest incidence is seen in aged 5-9 years (14.8 deaths per 100,000), followed by 10-14 years (18.7 deaths per 100,000) and 1-4years (29.8 deaths per 100,000) (Figure 3-10).

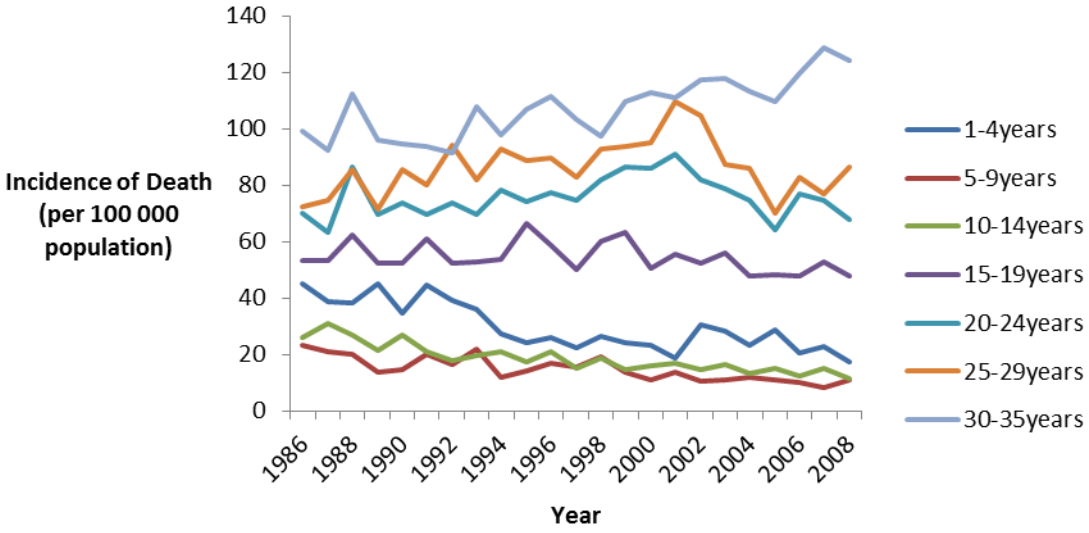


Figure 3-10: The incidence of death per 100 000 population according to age category

3.3.1. Location of Death in 1-35 year olds

By removing the infant deaths, it can be seen that majority of deaths in the young (1-35 year olds) were found to occur out-of-hospital, with 17,998 occurring in the home (55.3%) and 143 deaths (0.4%) in prison. Of the remaining deaths, 13,898 occurred in-hospital with 494 deaths occurring in nursing/residential homes (1.5%) and 2 deaths in clinic premises/GP surgery (<0.1%).

3.3.2. Primary Cause of Death in 1-35 year olds

Figure 3-11 illustrates the primary causes of death in those aged 1-35 years. Nearly a third of deaths are due to accidents (8778 deaths, 27%), with the other highest causes being self-harm (5281 deaths, 16.2%), cancer (11.8%) and drugs (2459 deaths, 9.4%).

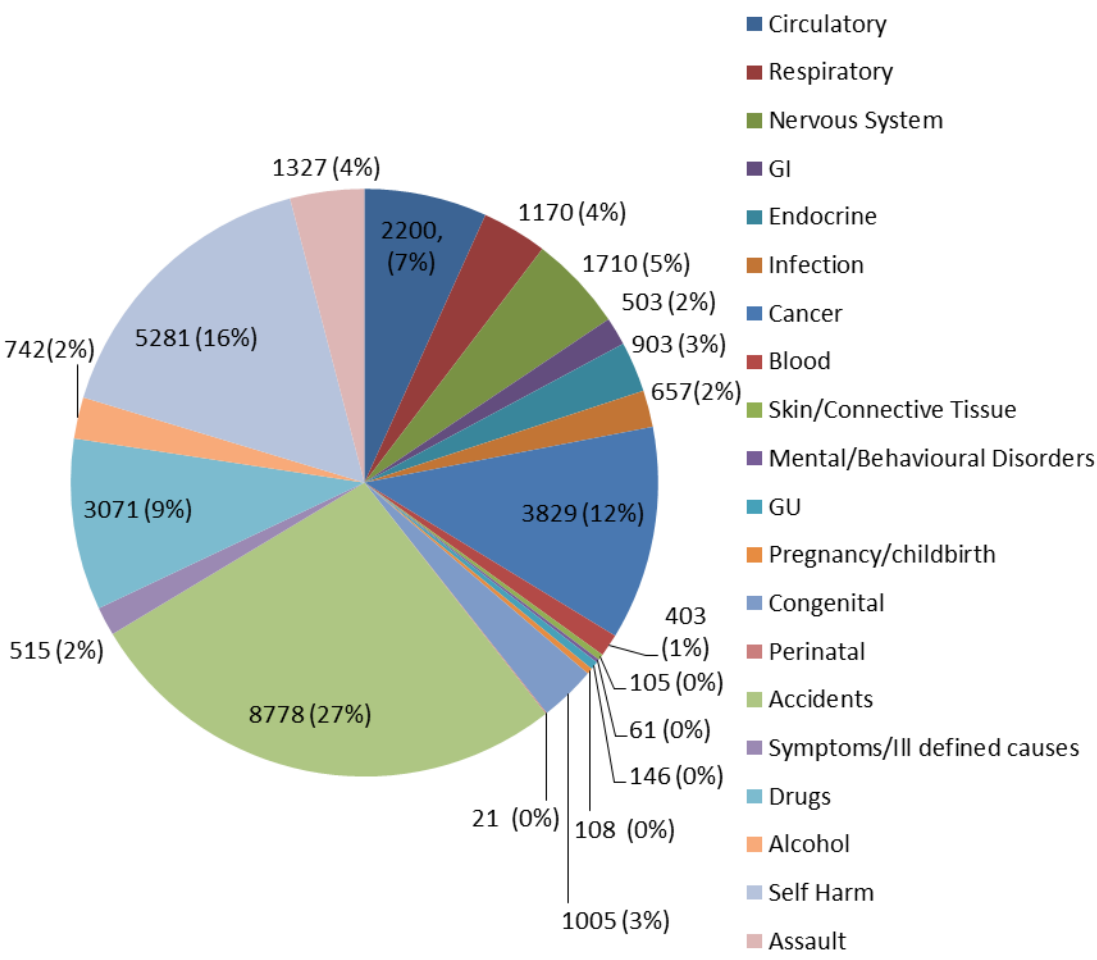


Figure 3-11: Primary causes of death in ages 1-35years

3.4. Changing Causes of Death in 1-35 year olds

On closer examination of the primary causes of death in this age group, we can see some variation over time (Table 3-5). The incidence of many causes of death (cancer, accidents, congenital) can be seen to decrease over time possibly due to improved healthcare providing better outcomes. The incidence of deaths due to circulatory disease has also decreased from 5.0 per 100,000 in 1986 to 3.3 per 100,000 in 2008.

Table 3-5: The changing incidence of death for primary causes (according to ICD coding) per 100,000 of the population throughout the study period

Cause	1986	1996	2008
Circulatory	5.0	4.5	3.3
Respiratory	3.1	2.4	1.7
Nervous System	3.5	3.3	3.9
GI	0.9	1.6	1.1
Endocrine	2.8	1.3	1.5
Infection	1.0	3.0	1.0
Cancer	7.5	7.6	4.9
Blood	0.5	0.2	0.2
Skin/Connective Tissue	0.3	0.2	0.1
Mental/Behaviour Disorders	0.2	>0.1	0.2
GU	0.5	0.3	0.3
Pregnancy/Childbirth	0.3	0.2	0
Congenital	6.8	5.6	4.3
Accidents	20.4	15.6	12.6
Symptoms/Ill-Defined Causes	6.0	2.6	7.6
Drugs	0.6	6.7	7.6
Alcohol	0.6	0.8	1.9
Self-Harm	7.0	10.7	7.8
Assault	1.4	3.3	1.2

One of the largest decreases in incidence of death is from cancer. Recent research compiled by Cancer Research UK has shown that since 1990, deaths from the 4 most common cancers (breast, bowel, lung and prostate) have fallen by almost a third in the UK.

3.5. Social Causes of Death in 1-35 years

Analysis of the causes of death in 1-35 year age group highlighted a large number of deaths due to drugs and alcohol in Scotland (Table 3-5). Figure 3-12 illustrates the increasing trend from 1986-2008 in the incidence of deaths due to drugs (0.6-7.6 per 100,000 with peak of 11.8 per 100,000 in 2002) and alcohol (0.6-1.9 per 100,000 with peak 2.7 per 100,000 in 2004) from 1986-2008, whereas the incidence of deaths due to cardiac cause has remained steady (3. 9 per 100,000 in 1986 and 3.8 per 100,000 in 2008).

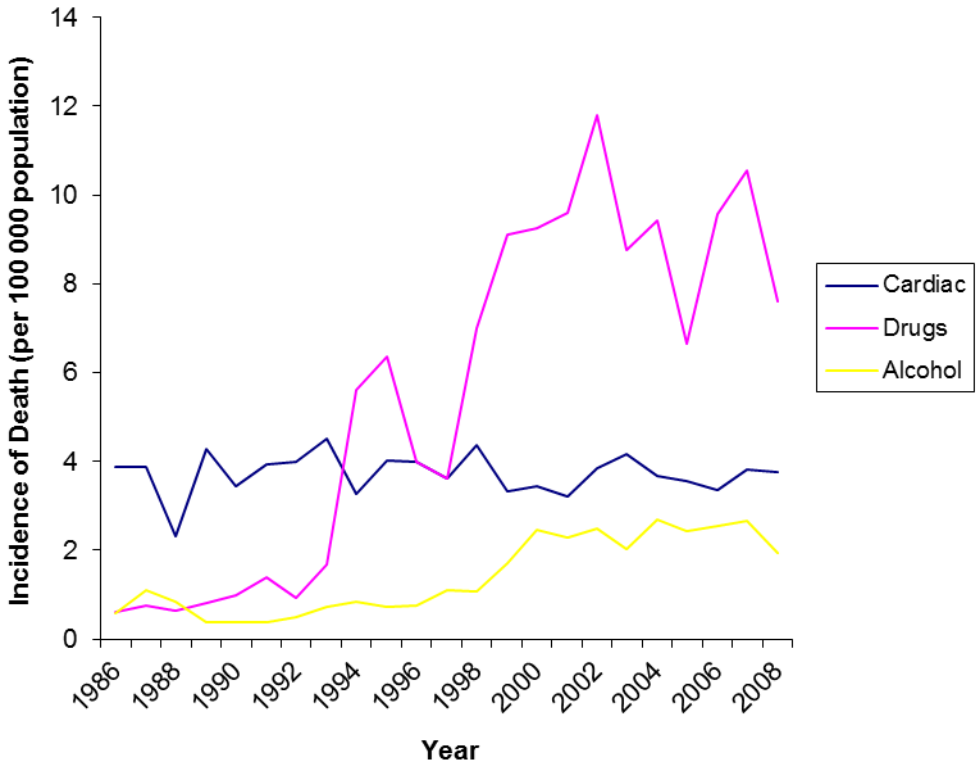


Figure 3-12: Incidence of death per 100,000 population over time for social causes (alcohol and drugs) and cardiac causes of death

3.6. All In and Out-of-Hospital (OOH) Deaths in 1-35 years

Of the total 32,535 deaths recorded in those aged 1-35 years from 1986-2008, 18,204 deaths (56.0%) occurred out-of-hospital (OOH), and 14,331 deaths (44.0%) occurred in-hospital. Table 3-6 shows the mean age of out-of-hospital deaths is 25.0 years which is higher than in-hospital deaths (23.1 years). The number of male deaths is higher for both in and out-of-hospital deaths.

Table 3-6: Demographics of all deaths aged 1- 35 year old in Scotland 1986-2008

	All Deaths	In Hospital	Out of Hospital
Total Number	32,535	14,331 (44.0%)	18,204 (56.0%)
Mean Age	24.2	23.1	25.0
Males	22,823	8992 (39.4%)	13,831 (60.6%)
Females	9712	5339 (55.0%)	4373 (45.0%)

3.6.1. Post Mortem Examination

In total, 22,421 post mortems were carried out (71.0%) in 1-35 year olds who died from 1986-2008. Deaths which occurred out-of hospital had a higher rate of post mortem (83.6% deaths) examinations than those that occurred in-hospital (54.7% deaths) (Table 3-7).

Table 3-7: Numbers of In and Out-of-Hospital Post Mortems

	Post Mortem	No Post Mortem	Totals
In Hospital	7518 (54.7%)	6225 (45.3%)	13,743
Out of Hospital	14,903 (83.6%)	2913 (16.4%)	17,816
Totals	22,421 (71.0%)	9138 (29.0%)	31,559

An additional 976 deaths may have had a post mortem, but further information was not available from our source (588 in-hospitals and 388 out-of-hospitals).

3.6.2. In and Out-of Hospital Death according to Age Category

Deaths in younger age groups (1-4, 5-9 and 10-14 years) were found to occur more frequently in-hospital. With increasing age (15years+), the number of out-of-hospital deaths exceeds the number of in-hospital deaths in the young (Figure 3-13). This is greater in 25-29 age group (2725 deaths v 4360 OOH deaths), and is greater still in 30-35 year category (4762 deaths v 6125 OOH deaths).

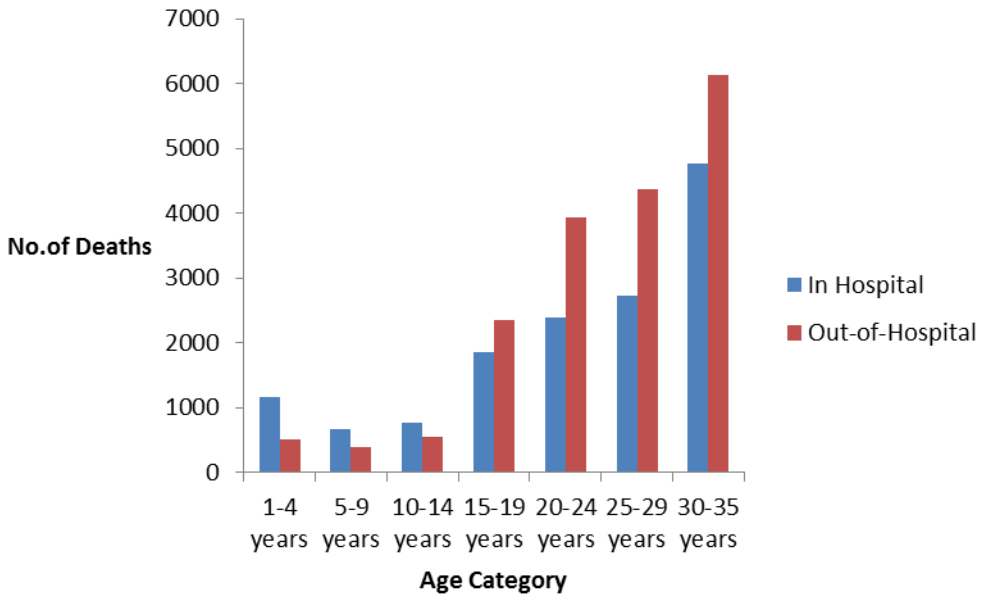


Figure 3-13: Number of in-hospital and out-of-hospital deaths according to age category

3.6.3. Primary Causes of In and Out-of-Hospital Death in 1-35 year olds

In total, 18,204 deaths occurred outside-of-hospital (OOH) (56.0%), with 14,331 deaths occurring inside hospital. Most medical causes of death were found to occur more frequently in-hospital, whereas deaths due to accidents, self-harm and drugs occurred more frequently out-of-hospital (Table 3-8).

Table 3-8: Primary causes of in and out-of-hospital death aged 1-35 years according to ICD coding

Cause of Death	Total Number of Deaths	In-Hospital Deaths	Out-of-Hospital Deaths
Circulatory	2200	1393 (63.3%)	807 (36.7%)
Respiratory	1170	747 (63.8%)	423 (36.2%)
Nervous System	1710	933 (54.6%)	777 (45.4%)
GI System	503	351 (69.8%)	152 (29.2%)
Endocrine	903	491 (54.4%)	412 (45.6%)
Infection	657	543 (82.6%)	114 (17.4%)
Cancer	3829	2510 (65.6%)	1319 (34.4%)
Blood Disease	403	321 (79.7%)	82 (19.3%)
Skin/Connective Tissue	105	91 (86.7%)	14 (13.3%)
Mental/Behavioural Disorders	61	43 (70.5%)	18 (29.5%)
GU System	146	119 (81.5%)	27 (18.5%)
Pregnancy/Childbirth	108	91 (84.3%)	17 (15.7%)
Congenital Defects	1005	781 (77.7%)	224 (22.3%)
Perinatal	21	19 (90.5%)	2 (9.5%)
Accidents	8722	3288 (37.5%)	5434 (62.5%)
Symptoms/Ill Defined Causes	515	131 (25.4%)	384 (74.6%)
Drugs	3127	668 (21.8%)	2459 (78.2%)
Alcohol	742	391 (52.7%)	351 (47.3%)
Self- Harm	5281	789 (14.9%)	4492 (85.1%)
Assault	1327	631 (47.6%)	696 (52.4%)
Total Number	**32,535**	**14,331**	**18,204**

3.7. All Cardiac Deaths aged 1-35 years

From circulatory ICD codes, cerebrovascular causes were excluded and congenital cardiac defects were included to create 'cardiac' causes of death. A total of 2084 cardiac deaths occurred in those aged between 1 and 35 years old from 1986-2008. Of these, 1405 were male and 679 were female, giving a ratio of 2.1 male: 1 female deceased. In total, 1317 deaths occurred in-hospitals (63.2%), and 767 deaths occurred out-of-hospital.

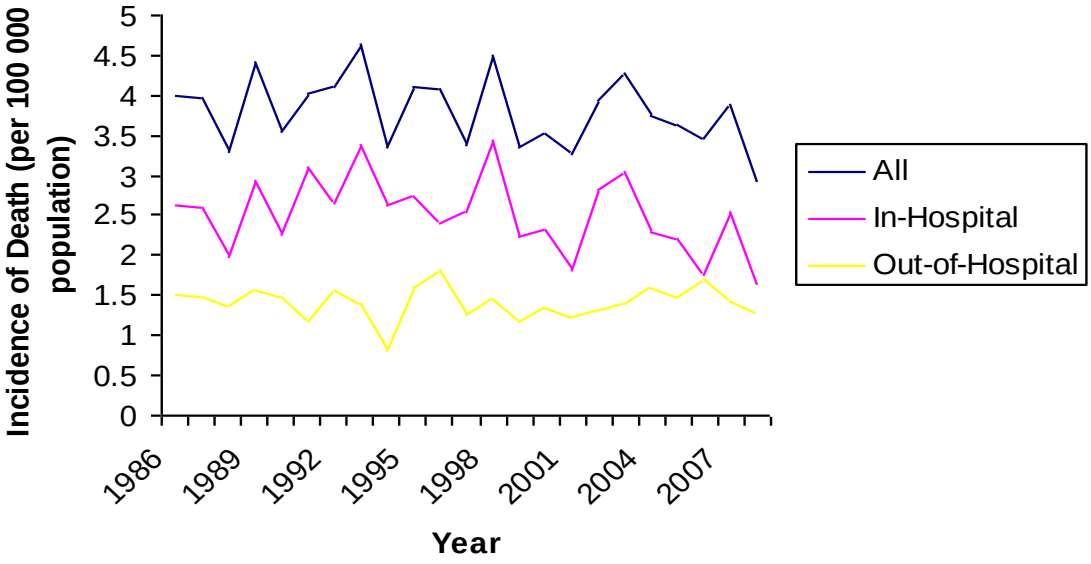


Figure 3-14: Incidence of cardiac death, in-hospital and out-of-hospital per 100,000 population

Figure 3-14 illustrates that the overall incidence of cardiac death has both increased and decreased between 1986 and 2008, with the 2008 figure being lower (4.0 per 100,000 in 1986-2.9 per 100,000 in 2008). This is also true for in-hospital deaths which have decreased over the 23 year study period (2.6 per 100,000 to 1.6 per 100,000). However, the number of OOH cardiac deaths remains steadier over time with a smaller reduction (1.5 per 100,000 to 1.3 per 100,000).

3.7.1. All Cardiac Deaths aged 1-35 years according to Age Category

The number of deaths attributed to a cardiac cause, were found to increase with increasing age. Figure 3-15 shows the incidence to be highest in those aged 30-35years (909 deaths, 44%), following by those aged 25-29years (373 deaths, 18%).

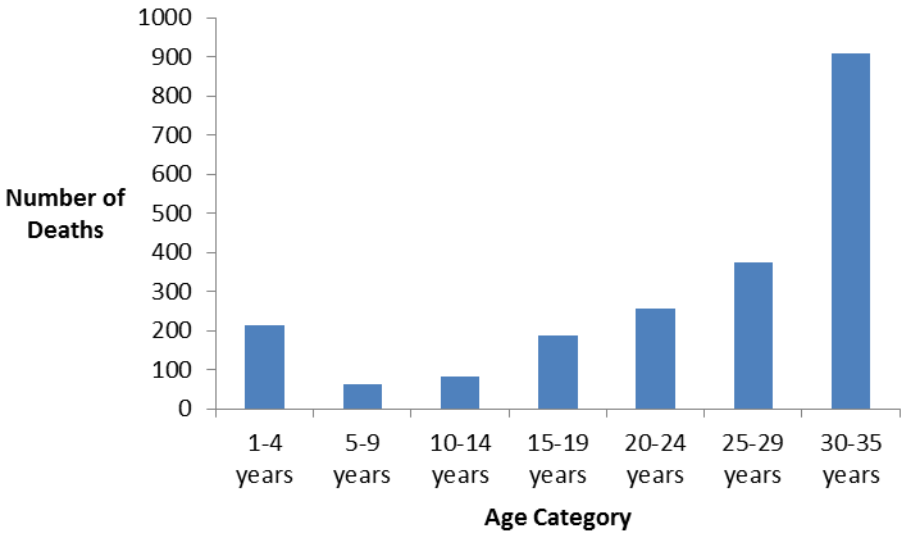


Figure 3-15: All 2087 cardiac deaths aged 1-35 years according to age category

3.7.2. Primary Cause of Cardiac Death in 1-35 year olds

Of the 2084 cardiac deaths, 30% (624 deaths) were due to coronary heart disease. 24.8% were due to congenital heart defects (516 deaths) and 9.8% were due to cardiomyopathies (205 deaths) (Figure 3-16).

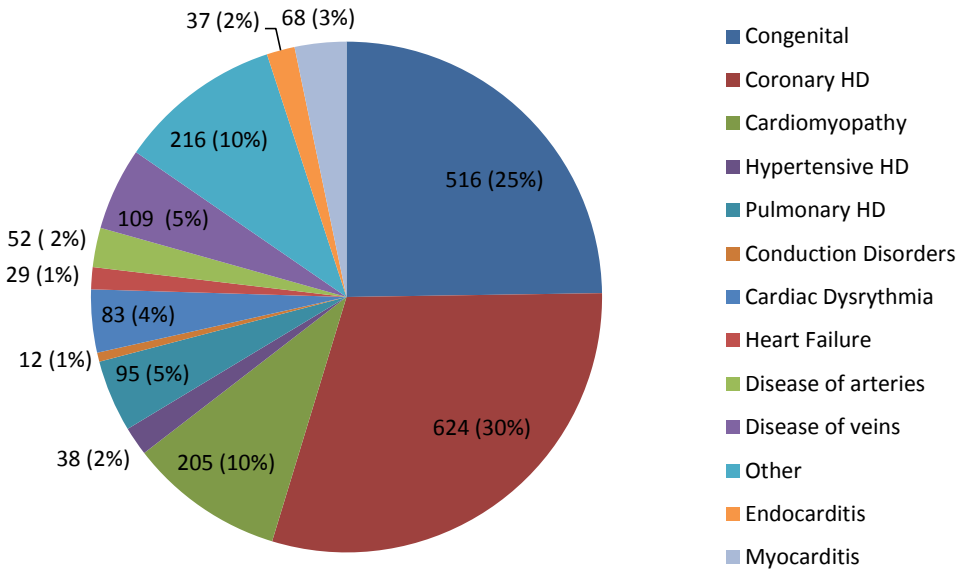


Figure 3-16: Primary causes of cardiac death in 1-35 year olds in Scotland 1986-2008

3.7.3. Post Mortem Examination for Cardiac Deaths

Not all cardiac deaths were confirmed by post mortem examination, with some information on whether a PM was carried out not available (527 deaths, 25.3%). In total, 69.1% of cardiac deaths had a PM carried out (1441 deaths) to confirm a cardiac cause of death (Table 3-9).

Table 3-9: Numbers of post mortems carried out to confirm cardiac death

Cause of Death	No. of Deaths	No. of PM	Percentage of Deaths with PM
Congenital	516	236	45.7%
Coronary HD	624	531	85.1%
Cardiomyopathy	205	130	63.4%
Hypertensive HD	38	22	57.9%
Pulmonary HD	95	54	56.8%
Conduction Disorders	12	7	58.3%
Cardiac Dysrhythmia	83	52	62.7%
Heart Failure	29	21	72.4%
Diseases of Arteries	53	35	66.0%
Diseases of Veins	109	90	82.6%
Other	216	182	84.7%
Endocarditis	37	20	54.1%
Myocarditis	68	61	89.7%

3.7.4. In and Out-of-Hospital Cardiac Deaths by Age Category

The number of in-hospital deaths is found to be high in the 1-4 year age category and then decreases before it increases steadily from aged 5-35 years. OOH deaths increase steadily with age with the largest increase being seen 30-35 year age category (Figure 3-17).

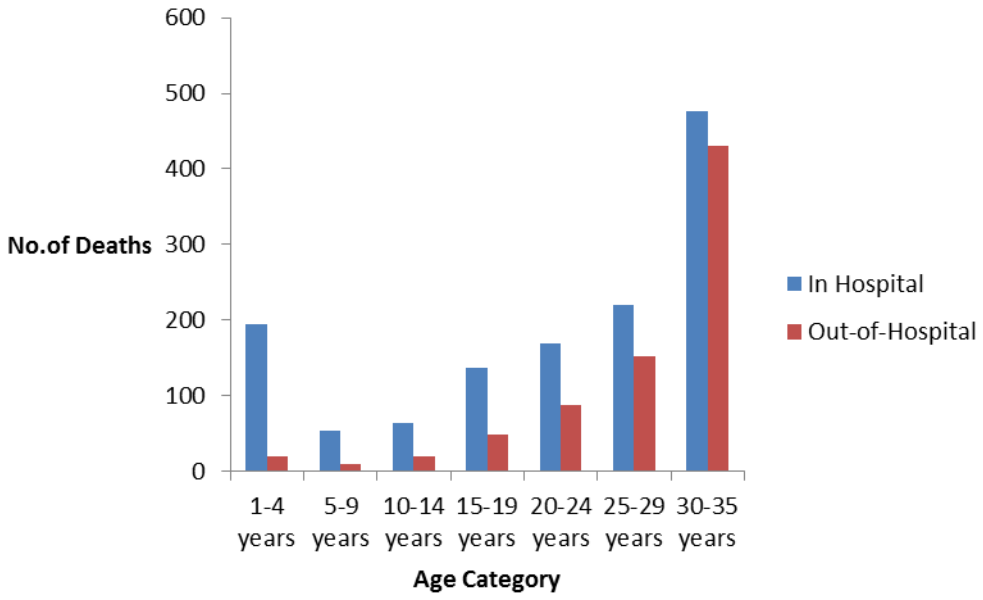


Figure 3-17: Numbers of in-hospital and out-of-hospital cardiac deaths

3.7.5. Causes of In and Out-of-Hospital Cardiac Death

Table 3-10 provides information of the total number of deaths per cause as well as information regarding the numbers of in and out-of-hospital cardiac deaths by cause. The majority of deaths are attributable to coronary heart disease (629 deaths, 30.0 %) and congenital malformations (516 deaths, 24.8 %).

Table 3-10: Numbers of in and out-of-hospital cardiac deaths 1-35 years with according ICD codes

Cause of Death	ICD-9 Codes	ICD-10 Codes	All Deaths	No. In Hospital Deaths	No. Out-of-Hospital Deaths
Congenital	745-747 759.82	Q20-28, Q87.4	516 (24.8%)	439 (85.1%)	77 (14.9%)
Coronary HD	410-414	I20-25	624 (30.0%)	279 (44.7%)	345 (55.3%)
Cardiomyopathy	425	I42-43	205 (9.8%)	122 (59.5%)	83 (40.5%)
Hypertensive HD	401-405	I10-15	38 (1.8%)	20 (52.6%)	18 (47.4%)
Pulmonary HD	415-417	I26-28	95 (4.6%)	80 (84.2%)	15 (15.8%)
Conduction Disorders	426	I44-45	12 (0.6%)	8 (66.7%)	4 (33.3%)
Cardiac Dysrhythmia	427	I46-49	83 (4.0%)	58 (69.9%)	25 (30.1%)
Heart Failure	428	I50	29 (1.4%)	14 (48.3%)	15 (51.7%)
Disease of arteries	440-449	I70-79	53 (2.5%)	48 (92.3%)	5 (7.7%)
Disease of veins	451-459	I80-89, I95	109 (5.2%)	75 (68.8%)	34 (31.2%)
Other	394-398, 420, 423, 429	I05-09, I30-32, I34-37, I51-52, I97-98	215 (10.3%)	91 (42.6%)	124 (57.4%)
Endocarditis	421, 424	I33, I38-39	37 (1.8%)	32 (86.5%)	5 (13.5%)
Myocarditis	422	I40-41	68 (3.3%)	51 (75.0%)	17 (25.0%)

(CHD: coronary heart disease, HD: heart disease)

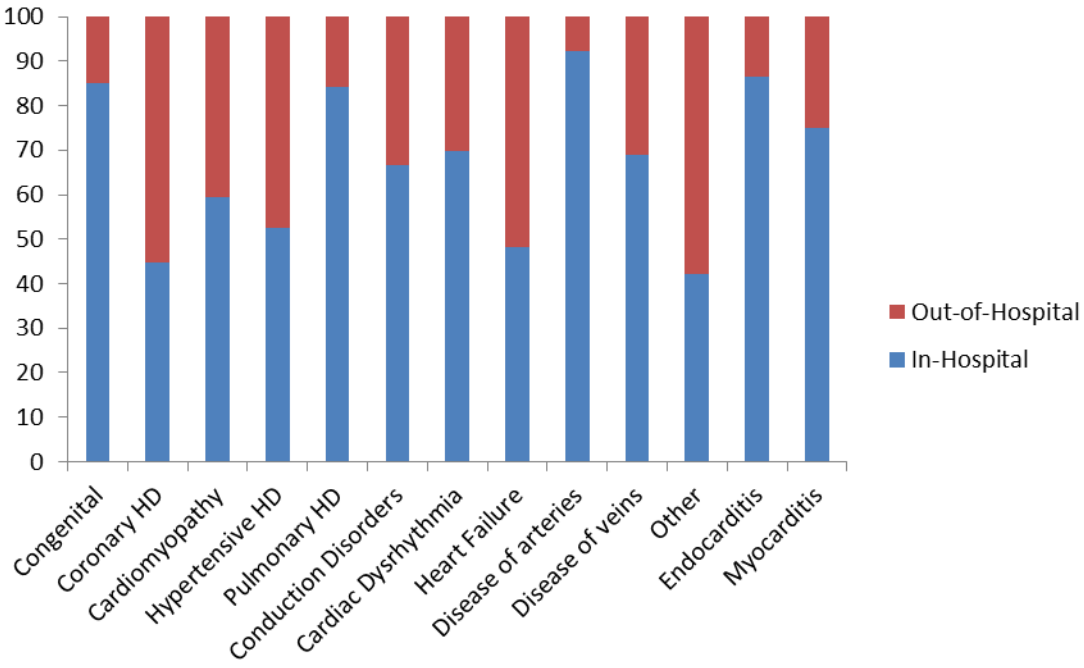
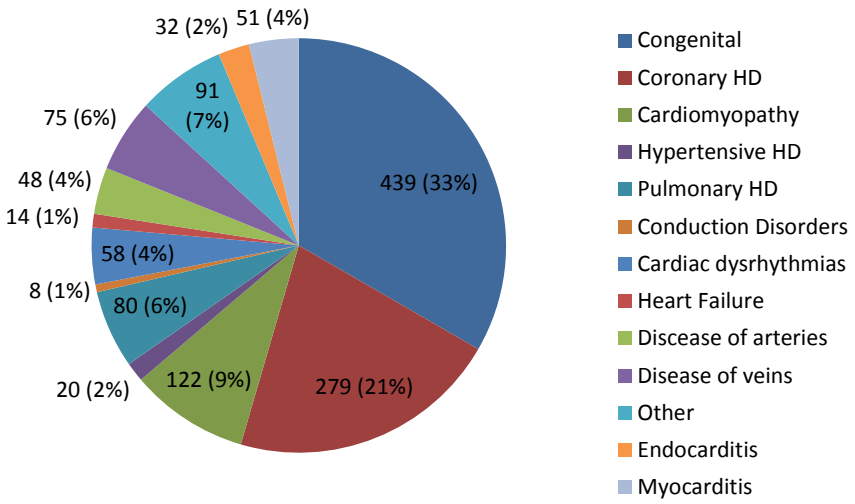


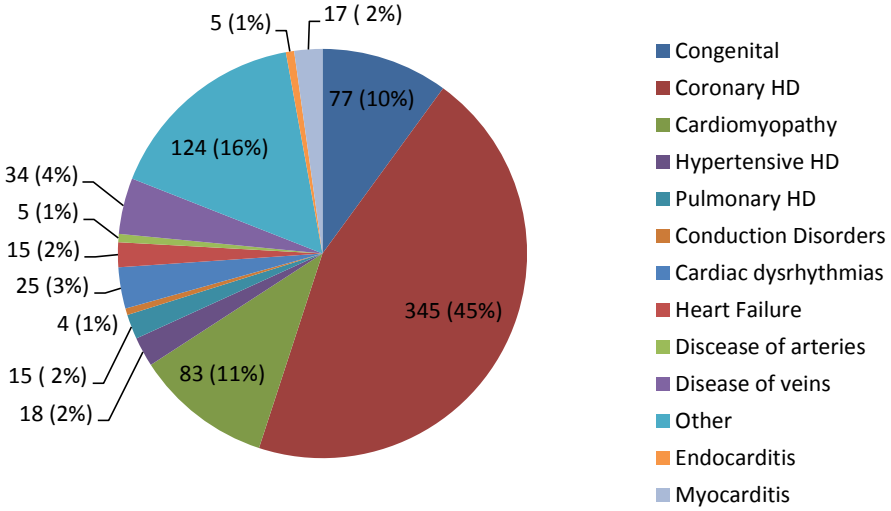
Figure 3-18: Histogram showing proportional %'s of in and out-of-hospital deaths for each cardiac cause of death

With the exception of CHD and heart failure, the majority of each cause of cardiac death occur in hospital (see table 3-10 and figure 3-18) The split for CHD is 44.7% in-hospital (279 deaths) and 55.3% (345 deaths) with heart failure deaths being more evenly split at 48.3% in-hospital and 51.7% out-of-hospital.

Figure 3-19 illustrates that the main 3 primary causes of cardiac death are the same for both in-hospital and out-of-hospital deaths but that the incidence is different. The main cause of in-hospital cardiac death is from congenital malformations (439 deaths), followed by CHD (279 deaths) and cardiomyopathy (122 deaths). The majority of out-of-hospital deaths are due to CHD (345 deaths), followed by cardiomyopathy (83 deaths) and congenital malformations (77 deaths).



a) Primary Cause of In-Hospital Cardiac Deaths aged 1-35years



b) Primary Cause of Out-of-Hospital Cardiac Deaths aged 1-35years

Figure 3-19: Primary causes of in-hospital and out-of-hospital cardiac death in those aged 1-35 years (CHD=coronary heart disease, HD=heart disease)

The causes of cardiac death vary amongst age categories (Figure 3-20), with congenital deaths being most common in the 1-4 year age group (171 deaths, 79.2%) and then decreasing steadily to smaller numbers (62 deaths, 6.8%) in the 30-35 year age category. Deaths due to CHD are more apparent in older age categories, particularly 30-35 year group (458 deaths, 50.4%) and the 25-29 years group (125 deaths, 33.5%). The number of deaths due to cardiomyopathies appear to vary most across the age categories with the highest number in those aged 15-19 years (35 death; 18.8%) and similar percentages of deaths in those aged 10-14 (9 deaths, 10.7%) years and 20-24 years (30 deaths, 11.7%).

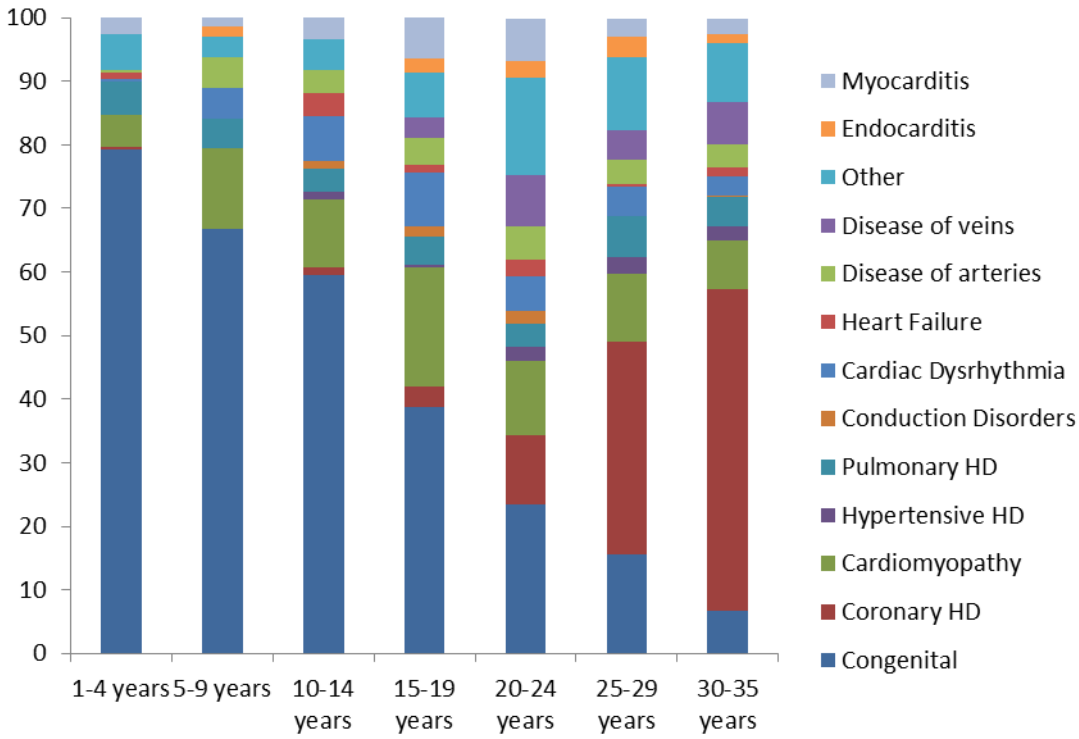


Figure 3-20: Proportional % causes of OOH cardiac deaths by age category

(CHD=coronary heart disease, HD=heart disease)

3.8. Out-of-Hospital Cardiac Death

Of the 2084 deaths attributable to a cardiac cause, 767 (36.8%) occurred out-of-hospital and so could be considered to be 'sudden' in nature. Results show that the main causes of out-of-hospital death are similar to those which occurred in-hospital, but differences do exist in the ages of these deaths.

3.9. Confirmed Cardiac Death

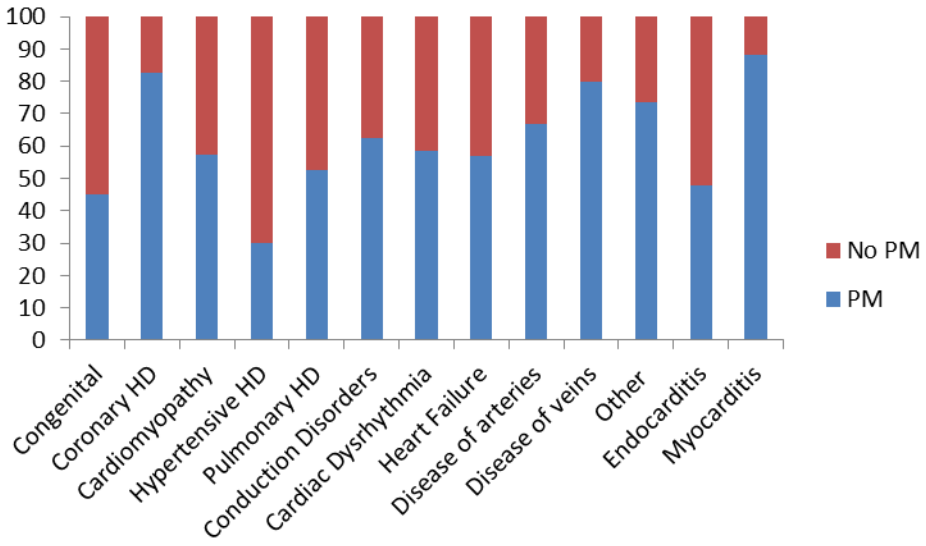
For a death to be confirmed as due to a cardiac cause, a post mortem examination must have taken place. Of the 2083 cardiac deaths analysed, 1442 had undergone a PM (69.2%) Of the 767 out-of-hospital cardiac deaths, 629 had undergone post mortem (82%), with 813 of 1316 (61.8%) of in-hospital deaths having undergone PM.

Table 14 and Figure 3-21 show that with the exception of conduction disorders and diseases of the arteries, there are a higher percentage of PM's carried out for deaths which occur out of hospital (OOH). All deaths that occurred OOH caused by endocarditis had a PM, compared to less than half (47.9%) that occurred in-hospital. However, it also shows that there are a large number of deaths (both in and out-of-hospital) which received a cardiac diagnosis without post mortem.

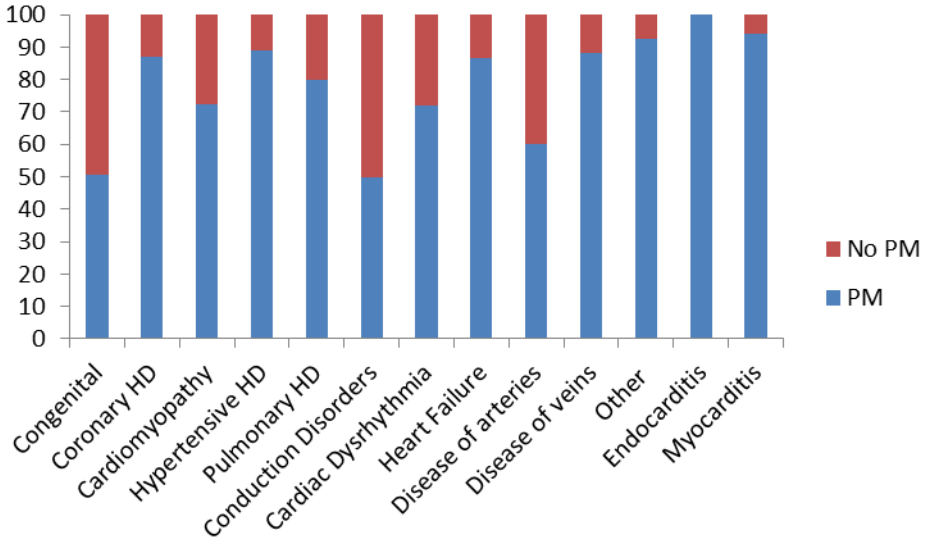
Table 3-11: Numbers of deaths which underwent PM for a confirmed cardiac diagnosis

Cardiac Cause of Death	In-Hospital Cardiac Deaths	No. In Hospital Deaths with PM	OOH Cardiac Deaths	No. Out-of-Hospital Deaths With PM
Congenital	439	197 (44.9%)	77	39 (50.6%)
Cornonary HD	279	231 (82.8%)	345	300 (87.0%)
Cardiomyopathy	122	70(57.4%)	83	60 (72.3%)
Hypertensive HD	20	6 (30.0%)	18	16 (88.9%)
Pulmonary HD	80	42 (52.5%)	15	12 (80.0%)
Conduction Disorders	8	5 (62.5%)	4	2 (50.0%)
Cardiac Dysrhythmia	58	34 (58.6%)	25	18 (72.0%)
Heart Failure	14	8 (57.1%)	15	13 (86.7%)
Disease of arteries	48	32 (66.7%)	5	3 (60.0%)
Disease of veins	75	60 (80.0%)	34	30 (88.2%)
Other	92	67 (73.6%)	124	115 (92.7%)
Endocarditis	32	15 (47.9%)	5	5 (100.0%)
Myocarditis	51	45 (88.2%)	17	16 (94.1%)

(OOH=out-of-hospital, PM=post mortem)



a) In-hospital deaths



b) Out-of-hospital deaths

Figure 3-21: Histogram showing percentage proportions of a) in-hospital and b) out-of-hospital deaths which underwent post mortem examination (PM=post mortem)

3.10. OOH Cardiac Death with No Prior History of Cardiovascular Disease

Out of hospital cardiac deaths which had been confirmed by PM were investigated to see whether there had been any previous cardiac diagnosis or history of hospital admission. Figure 3-22 shows the incidence of OOH cardiac death to be variable throughout the study period.

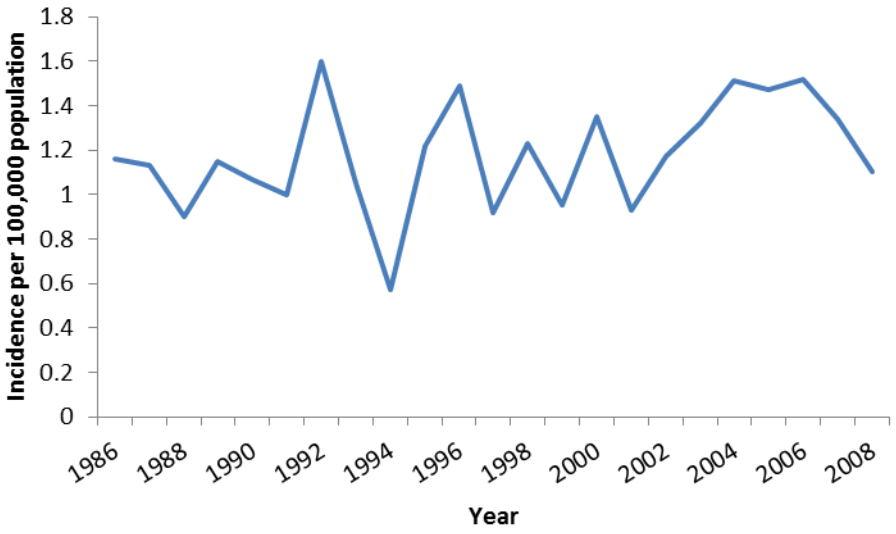


Figure 3-22: Incidence of OOH cardiac death as confirmed by PM per 100,000 of the population

Results showed 629 confirmed OOH cardiac deaths following PM examination (30.2% of all cardiac deaths). Of these 629 confirmed OOH cardiac deaths, 462 were male (73.4%) and 167 were female. Figure 3-23 shows that the number of these deaths increases with age, with 59.1% of deaths (372 deaths) occurring in the 30-35 year category.

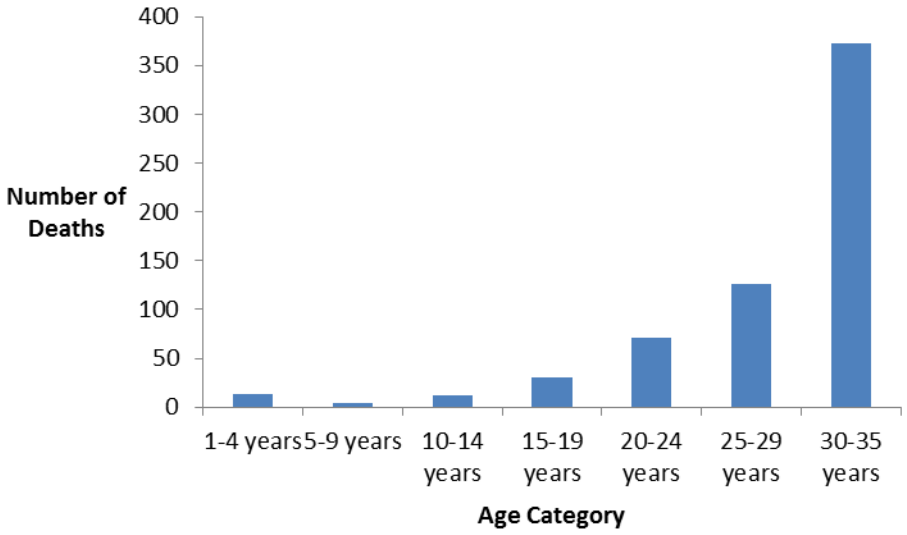


Figure 3-23: Number of confirmed OOH cardiac deaths according to age category

The majority of OOH cardiac deaths confirmed by PM examination are due to coronary heart disease (300 deaths, 47.7%), followed by 'other' category which includes valvular disease, pericarditis and diseases of pericardium and complications and ill-defined descriptions of HD (115 deaths, 18.3%), and cardiomyopathy (60 deaths, 9.5%) (Figure 3-24).

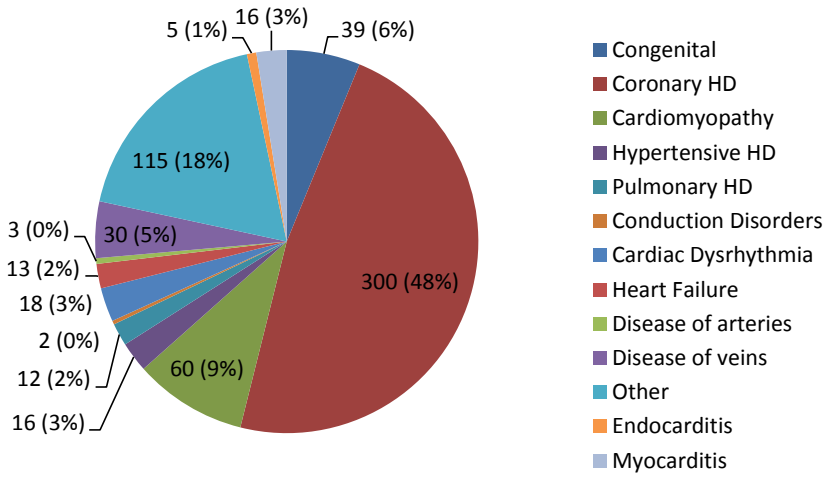


Figure 3-24: Primary causes of confirmed OOH Cardiac Deaths

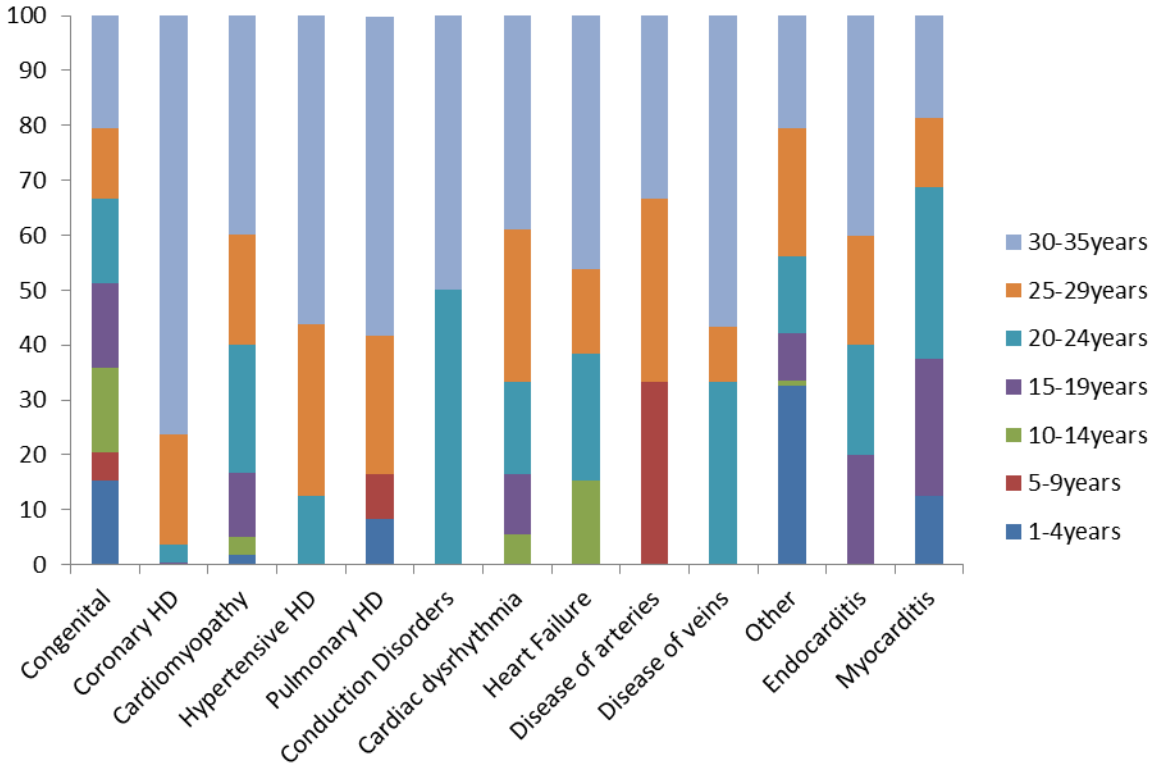


Figure 3-25: Causes of confirmed cardiac death according to age category

3.11. OOH Deaths due to Coronary Heart Disease

There were 300 deaths due to coronary heart disease that were confirmed by PM examination. According to our data, only 13 of these 300 (4.3%) had a previous diagnosis of coronary heart disease, with 10 (76.9%) of these being diagnosed in the year leading up to death.

3.12. OOH Deaths due to Congenital Heart Disease

There were 39 deaths due to congenital heart disease that were confirmed by PM examination. Results show that only 14 (35.9%) of these deaths had a prior diagnosis of congenital heart disease, with 11 (28.2%) being noted as having a diagnosis of cardiovascular disease.

3.13. OOH Deaths due to Cardiomyopathy

There were 60 deaths due to cardiomyopathy that were confirmed by PM examination. Data shows that only 17 of these 60 (28.3%) had a previous diagnosis of cardiovascular disease, with 7 (41.2%) of these being diagnosed in the year leading up to death. From the information available, it is not possible for us to differentiate between types of cardiomyopathy such as DCM or HCM.

3.14. OOH Deaths due to Dysrhythmia

It has been discussed that deaths due to arrhythmia cannot be diagnosed at PM without an ECG prior to death. Therefore we can assume that those with a dysrhythmia as primary cause of death have either had a prior diagnosis or a negative PM. Only 2 deaths were

identified as having a dysrhythmia as cause of death and both of these deaths had a prior diagnosis of cardiovascular disease and atrial fibrillation.

3.15. Potential Cardiac Deaths

There are an additional number of deaths which could be attributed to cardiac causes (Class B cardiac deaths). Table 3-12 identifies 1012 deaths which according to Cardiac Risk in the Young (CRY) [27]could be attributed to cardiac causes. CRY suggest that in the cases outlined in Table 3-12, could be due to an underlying undiagnosed cardiac arrhythmia which would present a negative PM.

Table 3-12: Details of the 1012 deaths (age 1-35 years) which according to CRY, could be attributable to cardiac causes

ICD Codes	Cause	No. of Deaths
345.9, G40.9	Epilepsy, unspecified	573
345.3, G41.9	Status epilepticus	82
493.1, J46	Status asthmaticus	53
E910, W69, W65, W67, W69, W70	Accidental drowning	266
W73	Other specified drowning	2
W74	Unspecified drowning	21
E913.0, W75	Accidental suffocation in bed	15

Chapter 4 -Discussion Part 1

This is the first study to investigate the incidence and all causes of death in a young population (1-35 years) in Scotland. Previous studies have examined drugs deaths[101], suicides[102] and medical causes[103 104] individually in this age group but this study will put these into a wider context. Deaths that occurred both in and out-of-hospital were then investigated, before focussing on those due to a cardiac cause, particularly those which occurred out-of-hospital and those which could have potentially been identified by cardiac screening.

4.1. All Deaths in Scotland 1986-2008

In total there were 41,049 deaths in those aged 0-35 years in Scotland between 1986 and 2008. During this 23 year period, there was a 14% reduction in overall mortality with similar results being seen in both sexes (Figure 3-1). Previous evidence suggests Scotland has one of the worst mortality rates in Western Europe, and that the reductions seen in this study are lower in comparison to other countries[105-107]. Most evidence in this area features those of working age (15-74 years) which makes direct comparisons with our younger cohort difficult [18 107 108].

A large number of deaths occurred in infants (21%, 8514 deaths) with perinatal deaths shown to significantly decrease over the study period. This is a positive indication that pre and post natal care has improved over recent years with advances in neo-natal care and surgical techniques. The greatest number of deaths occurred in those aged 30-35 years (10,887 deaths, 27%). The majority of deaths in this study occurred following a collapse in the home (91.2%) with 51.7% of these leading to death in the home. No information was available on

the circumstances surrounding the deaths in this study and the time from the subject being well, to collapse and death so it is impossible to ascertain which deaths can be deemed 'sudden'. This led to us focusing on OOH deaths in this study which had been used in previous studies[17].

4.1.1. Use of Post Mortem

In Scotland, a post mortem (PM) will be carried out when the procurator fiscal feels it is required to establish the cause of death particularly if the death was sudden and/or unexpected. A PM may also be requested by the hospital in which case consent must be obtained by the next of kin. Without a post mortem, cause of death can be wrong in up to 30% of cases[109], but even after a PM the exact cause of death may remain unknown. Our results show that in 68.9% of deaths in 1-35 year olds, a PM took place. We would expect this rate to be higher than that of the entire population as PM's are more routinely undertaken in young, previously healthy subjects who die suddenly. The post mortem rate in England and Wales is reported to be almost double the rate in Scotland, possibly due to the fact that the option exists in Scotland for an external examination of a body before dissection[110].

Eighty two percent of OOH cardiac deaths underwent PM. Due to the nature of the study, results of the PM were not available and cause of death was taken from the death certificate. If the post mortem is negative, the pathologist should review the patient history and conduct pathological and histological testing. Tissue should also be kept for genetic and DNA sampling under the Tissue Act; however this remains controversial. We have no information regarding whether the recording of a specific cause of death was following the result of histology and in some cases such as HCM, diagnosis should not be made without this additional testing.

4.2. Incidence and Causes of Cardiac Death

In the current study, 6.4% of deaths in those aged 1-35 years (n=2084) were due to cardiac causes giving an annual incidence of 0.33 deaths per 100,000 population. Although Scotland is a smaller country, this figure is much lower incidence than is quoted by Cardiac Risk in the Young (CRY) who have suggested that there are 12 SCD every day in the UK. Papadakis et al[27] found the incidence of SCD in England and Wales to be 1.8 deaths (±0.08) per 100,000 per year (3409 deaths) over a 4 year period (2002-2005) in those aged 1-34 years in a study based on governmental data. In the Netherlands, an incidence of 1.62 deaths per 100,000 person years was found but SCD was based on an ICD code for acute MI only and included deaths up to the age of 40 years[17].

As in previous studies[17 23 111], a higher incidence of OOH death was found in males, with a ratio of 2.1male: 1 female death. It is accepted that the incidence of SCD increases with age due to a rise in the prevalence of coronary artery disease[61 111-113]. Almost a third of our cardiac deaths were due to CHD (n=624; 29.9%), with 24.8% due to congenital heart disease (n=516) and 9.8% due to cardiomyopathies (n=205). These proportions are the same as in the rest of the UK where a study by Papadakis et al[27] found approximately one third of deaths were due to ischaemic HD (33.5%), with 56% of these due to acute MI. Cardiomyopathies were the second commonest cause (27% of all deaths) of definite cardiac deaths (12% of all deaths DCM and 5% HCM) with SADS accounting for 14% of deaths[27]. A study in Ireland which only included cases with a confirmed cardiac cause of death following PM, found the leading cause of death in 15-35 year olds to be SADS (26.7%) followed by CAD (20.7%) and HCM (14.7%)[114]. The remaining deaths were due to idiopathic LVH (10.3%), myocarditis (6.0%), congenital HD (8.6%), DCM (2.7%), ARVC (1.7%) and a number of conditions with only 1 death[114].

In Italy the largest cause of SCD in the young has been shown to be ARVC[2], a condition which is relatively rare elsewhere in the world suggesting a geographical link to this condition. In America it is HCM[23] is the largest cause of SCD but they have a large black population who are more susceptible to this condition due to genetics, Our different results suggest that the main causes of SCD in the young are changeable depending on geographical location and ethnic factors. Our population were mainly white, whereas HCM is more common in blacks and ARVC is not a common cause of death outside Italy. Cardiovascular screening in these countries is designed to target those at risk from SCD from structural conditions such as HCM and ARVC. Our results show that these conditions are not as prevalent in Scotland and that perhaps our causes of death do not support the introduction of such screening models.

4.3. Prior Diagnosis of Cardiovascular Disease

Some causes of cardiac death such as conduction disorders or cardiac dysrhythmias cannot be identified using PM unless an abnormal ECG has been performed prior to death. In this study, only 4 deaths were due to cardiac dysrhythmia with 2 (both of which occurred OOH) undergoing PM with a prior diagnosis of AF. Of 83 deaths due to conduction disorders, only 30.1% occurred OOH none of them having a previous cardiovascular diagnosis. Seventeen OOH cardiomyopathy deaths (20.5%) with post mortem had a previous diagnosis of cardiovascular disease.

4.4. Cardiac Deaths identifiable by Screening

The introduction of cardiac screening is designed to reduce the number of SCD's from conditions which can be identified by cardiac investigations. In Italy the rate of SCD has been reduced from 3.6 deaths per 100,000 person years to 0.43 deaths per 100,000 person years after the introduction of a mandatory screening service[2] although these results have not

been replicated in any other countries. In this study, there are very few deaths (0.9% of total) which could potentially have been identified through screening (205 cardiomyopathies, 12 conduction disorders and 83 cardiac dysrhythmias).

The commonest cause of cardiac death in this study was CHD (29.9%). Although family history can be an important factor in the development of CHD, this condition would not be identified by ECG or echocardiogram in asymptomatic patients. This would require additional tests such as exercise testing or angiography which would not be cost effective or practical. The low number of arrhythmic deaths in this study may be an under-representation of the truth as any evidence of CAD could lead to a mis-diagnosis at PM.

The aim of screening is to identify those with a previously undiagnosed condition. This study found that the majority of cardiomyopathy deaths occur in those age 15-19 years with Papadakis et al[27] finding a greater proportion of these deaths in those aged 10-19 years. This suggests that cardiac screening should be carried out at around 14 years old for maximal disease identification.

4.5. Reliability of the Data

The lack of a national register to record sudden deaths means that using data from ISD is the most accurate way to analyse such deaths. It is acknowledged that the biggest limitation to this epidemiological study is that we were unable to examine the death certificates or post mortem reports ourselves and are reliant on the information provided by ISD. Misclassification of deaths is possible but given the high incidence of PM in this study (approximately 70%) we assume this would reduce this problem. Given the ambiguity surrounding many sudden cardiac deaths, some arrhythmic deaths may have been mis-coded.

The robustness of the ICD coding system determines the reliability of the data. Codes are assigned by clinical coders employed within medical records departments within hospitals. This information is processed from information in hospital case notes and death certificates. There is no mechanism for us to confirm the reliability of the data. We know for certain who died (unique identifier only), at what age and on what date but we do not know how accurate the rest of the information is. For example, we know that during the research period (1986-2008) there was one high profile death where the initial collapse happened during a football match (Phil O'Donnell playing for Motherwell on 29th December 2007), yet when we investigate this further this collapse is coded as happening at home.

Some of the ICD codes are also unclear. There is no distinct code for ARVC and instead it is coded under 'other cardiomyopathies'. The term 'sudden adult death syndrome' or SADS is now commonly used for deaths where there are no signs or illness or injury at PM and the heart remains morphologically normal (negative PM). However, until 2012 there was no guidance for pathologists how these deaths should be coded (now these are coded as I49.9 cardiac arrhythmia, unspecified), meaning that these deaths could be assigned to a variety of different codes making analysis of true numbers difficult.

In Ireland, a SCD in the Young Registry was established in 2007 by the Health Services Executive to identify all sudden deaths in those aged 15-35 years (1-14 years are held on a paediatric mortality register). A similar Register exists in Italy whereas other studies[23 25] have relied on newspaper and media reports to calculate numbers of deaths.

4.6. Limitations

The initial study set out to examine causes of sudden cardiac death and smoking was not thought to be an important factor. Given the high prevalence of CHD found, it would be reasonable to have examined this and other lifestyle factors or to introduce this in future screenings. The study was limited by the retrospective nature and the reliance on correct information being placed on death certificates by clinical coders, and this information being reliably transferred to the ISD database. A more accurate study would have examined death certificates itself, or collected data prospectively from procurator fiscal offices.

The choices of which ICD codes to include for cardiac deaths could be questioned and may be different between studies. Errors can occur in communication between the attending doctor and the clinical coder in the cause of death recorded as this is open to individual interpretation with the coders' experience often a major influence[93]. Some causes of death could be deemed different by 2 pathologists depending on the circumstances of the death and information available. To improve reliability of the data, it would have been useful to access the death certificates myself, to reduce any error and validate the database but this was not possible.

4.7. Summary

The majority of deaths in young people in Scotland were found to be due to accidents, cancer, self-harm and drugs identifying a social problem in Scotland. Cardiac deaths compose a small number of deaths in this age group (6.4%) with most occurring in-hospital (63.2%). Due to the nature of the data, the most workable definition of unexplained death in this study was 'out-of-hospital' death. These OOH deaths, where the deceased has not previously been diagnosed with cardiovascular disease are the ones which would be targeted by a screening programme.

The majority of OOH cardiac deaths occurred in those aged 30-35 years and were due to coronary artery disease which cannot be identified by cardiovascular screening. Other causes of SCD which may be identified by screening such as familial arrhythmias and cardiomyopathies were rare. This study did not include survivors of cardiac arrest and so we cannot comment on survival rates following successful defibrillation which may affect the numbers of deaths.

Results suggest that a screening model for all in Scotland may not be cost effective and instead should be targeted to those at risk due to family history or personal symptoms. Part 2 of this thesis will evaluate the Cardiac Assessment in Young Athletes (CAYA) programme which was established in 2008. This study is unique in that it includes echocardiography for all subjects in addition to the gold standard Italian Model.

Chapter 5 - Results Part 2

Between November 2009 and December 2012, 1955 subjects took part in the Cardiac Assessment in Young Athletes programme. Of these, complete data on those aged 10-35 years was available on 1713 subjects with the remaining 242 excluded from analysis due to technical issues leading to incomplete results.

5.1. Demographic Data

One thousand seven hundred and thirteen subjects aged between 10-35 years with a mean age of 19.8 years were included in this analysis. Subject demographics can be seen in Table 5-1. The distribution of ages is represented graphically in Figure 5-1. The majority of subjects were male (1429 subjects) with most (87%) being footballers. Ninety eight percent of subjects were white (n=1679).

Table 5-1: Demographic data from 1713 subjects from Cardiac Assessment in Young Athletes (CAYA) programme

	Total	Males	Females
Numbers	1713	1429	284
Mean Age	19.8 (±4.6) years	19.8 (±4.4) years	19.6 (±5.5) years
Mean Height	174.8 (±9.1) cm	176.7 (±8.4) cm	165.6 (±6.5) cm
Mean Weight	69.3 (±11.7)kg	70.8 (±11.4) kg	62.0 (±10.1) kg
Mean Body Surface Area	1.83 (±0.2)	1.86 (±0.2)	1.68 (±0.2)

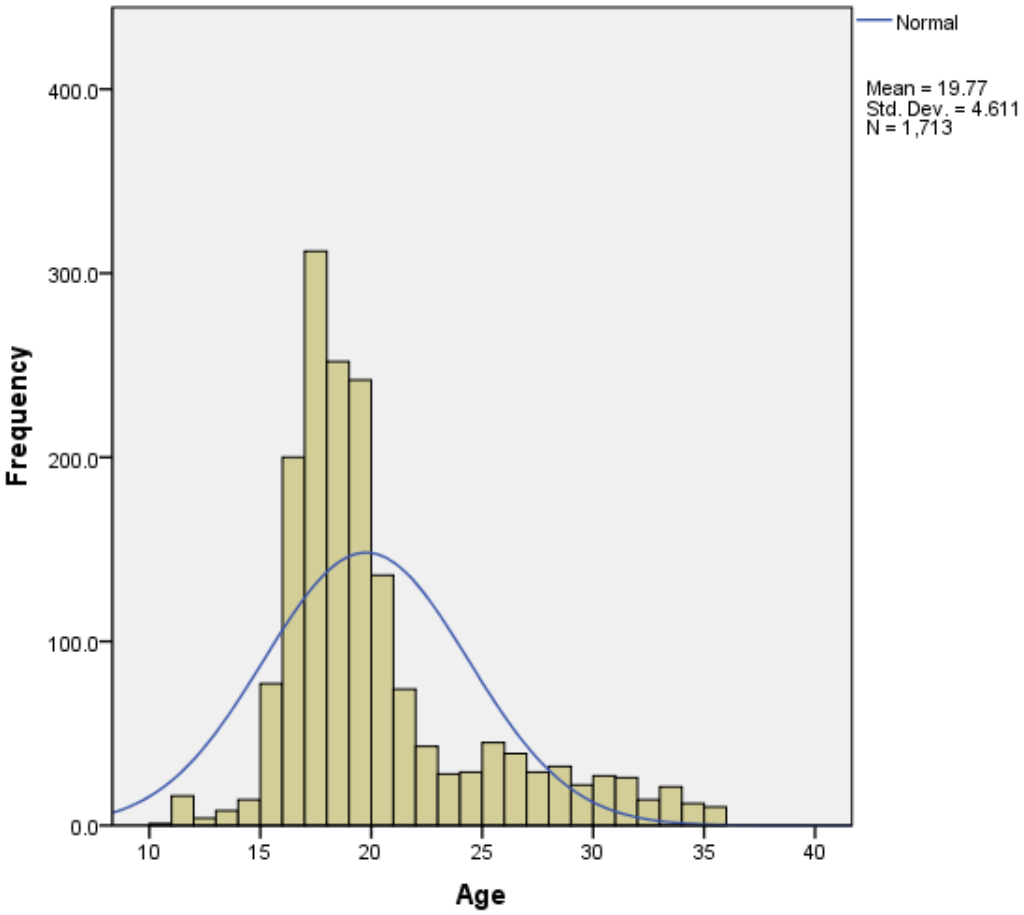


Figure 5-1: Histogram showing distribution of age of all subjects

The 1713 subjects were then split into 5 age category groups for further analysis of these mean values. The number of subjects in each category can be seen in Figure 5-2, with the majority being 15-19 years old (63%).

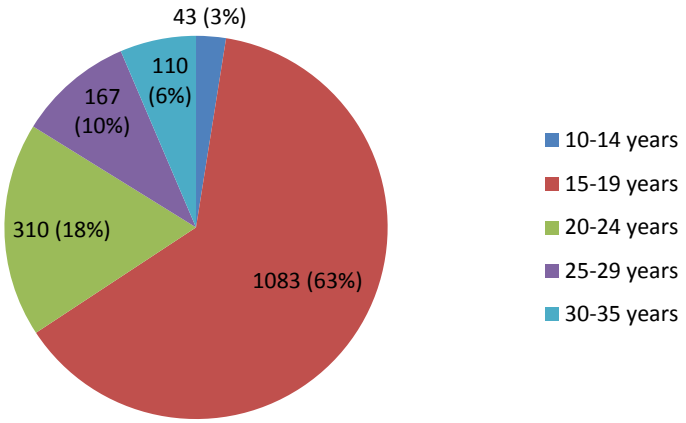


Figure 5-2: 1713 subjects of the CAYA programme separated into age categories for further analysis

5.2. Personal and Family History

Subjects were asked to complete the personal and family history questionnaire (Appendix A) in advance of their appointment, and were then questioned on any positive responses to gain more information. The numbers of positive responses can be seen in Table 5-2.

Table 5-2: Results of the personal history and family history questionnaire based on the Lausanne Recommendations

PERSONAL HISTORY	N	%
Have you ever been told that you have a heart condition?	14	0.8
Have you ever had chest tightness at rest/exertion?	115	6.7
Have you ever fainted during exercise?	22	1.3
Have you ever been told you have asthma?	307	17.9
Have you ever been told you have raised/high blood pressure?	23	1.3
Have you ever been told to give up sports because of a health problem?	3	0.2
Have you ever been diagnosed with a heart murmur?	35	2.0
Have you ever experienced irregular heart beat (palpitations)?	56	3.3
Do you become breathless/tired far more quickly than your team mates?	35	2.0
Have you ever felt dizzy/faint after exercise/exertion?	106	6.2
Have you ever had a seizure or been diagnosed with epilepsy?	13	0.8
Have you routinely taken medication in the past two years?	74	4.3

Has anyone in your family:	N	%
Died suddenly or unexpectedly?	178	10.4
Been treated for recurrent fainting?	9	0.5
Had unexplained seizure problems?	9	0.5
Had an unexplained drowning whilst swimming?	0	0
Had an unexplained car accident?	5	0.3
Had heart surgery?	205	12.0
Had a pacemaker implanted?	65	3.8
Had a defibrillator implanted?	1	0.05
Been treated for an irregular heartbeat?	72	4.2
Has anyone in your family been told they have vascular disease?	10	0.6
Has anyone in your family been told they have Marfan Syndrome?	0	0

The largest positive response on the personal medical history was those suffering from asthma (17.9%) although a large number of this group were asymptomatic and did not take medication. Those who answered positively for medication use were for asthma or skin problems such as acne. Those who had been told they had a heart condition were found to be murmurs diagnosed at birth which had given no further health problems.

Of the subjects who had been told to give up sport (n=3), none of these were due to cardiac problems and all had resumed sport following a period of illness with appropriate medical advice.

5.3. Physical Examination

112 subjects had a murmur heard on auscultation (6.5%), this included 24 who had previously been told they had a heart murmur. No subjects presented with physical characteristics of Marfan syndrome and none of them had a diminished femoral pulse.

5.3.1. Blood Pressure

The mean blood pressures recorded were 129.3mmHg systolic and 75.0mmHg diastolic. They were then categorised by age in Table 5-3. Mean values can be seen to increase with age (Table 5-3).

Table 5-3: Mean systolic and diastolic blood pressure values according to age category

	10-14 years	15-19 years	20-24 years	25-29 years	30-35 years
Mean Systolic (±SD) mmHg	122.3 (±14.7)	128.5 (±12.2)	131.1 (±13.5)	131.0 (±13.5)	133.2 (± 12.8)
Mean Diastolic (±SD) mmHg	72.7 (±9.7)	74.1 (±9.9)	75.5 (±9.4)	77.4 (±9.8)	80.1 (± 7.8)

The box plot illustrated in Figure 5-3 and 5-4 show an increase in both systolic (Figure 5-3) and diastolic (Figure 5-4) blood pressure with increasing age category but with no significant differences found.

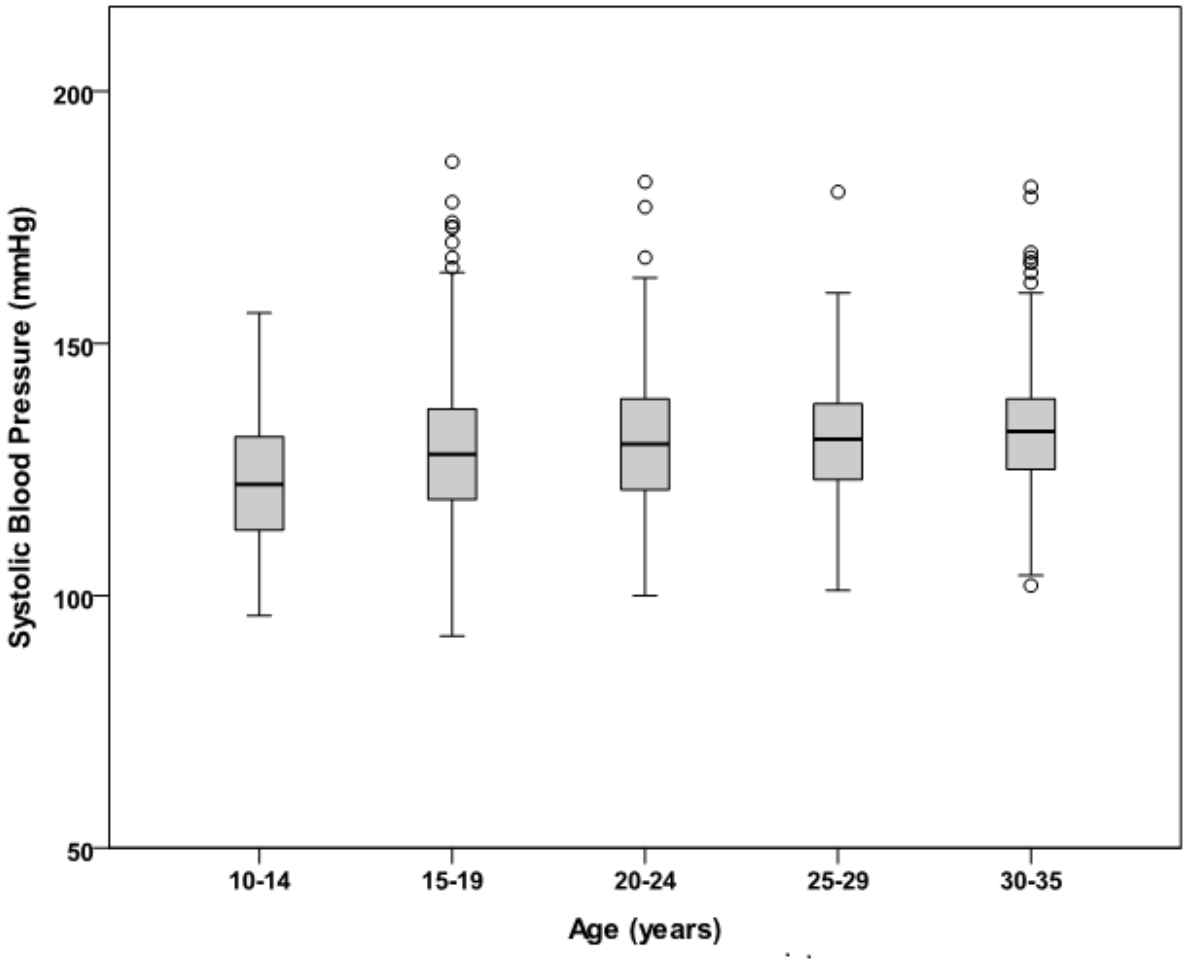


Figure 5-3: Boxplot illustrating relationship between age and systolic blood pressure

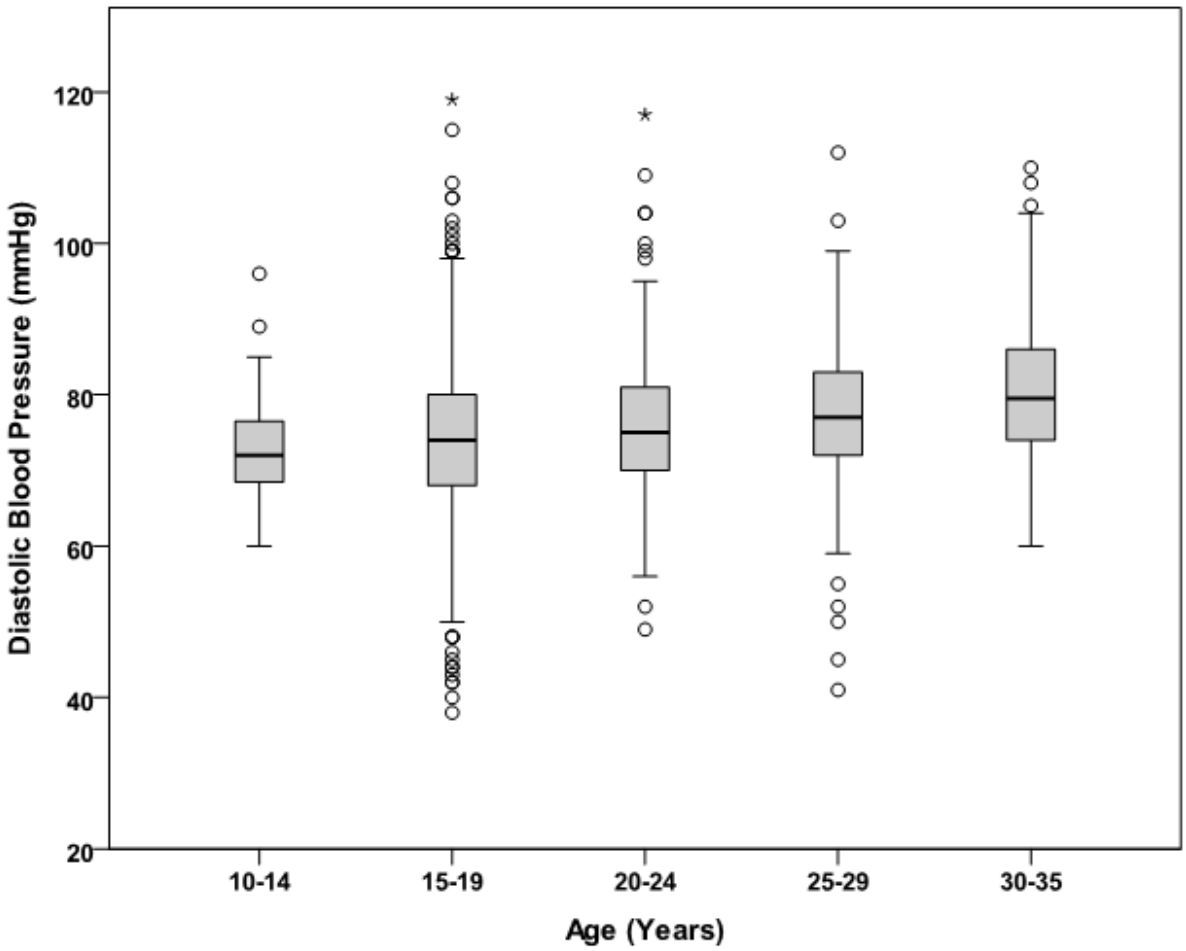


Figure 5-4: Boxplot illustrating relationship between age and diastolic blood pressure

Spearman rank correlation coefficient was r=0.125 suggesting a weak correlation but this was statistically significant ($p<0.0001$). Linear regression suggests that age category is a significant predictor of blood pressure ($p<0.001$) and that systolic BP increases by a factor of 1.783mmHg for each age category.

Blood pressure results were then categorised into 4 groups as per Table 2-5 (in methodology) which can be seen in Figure 5-5.

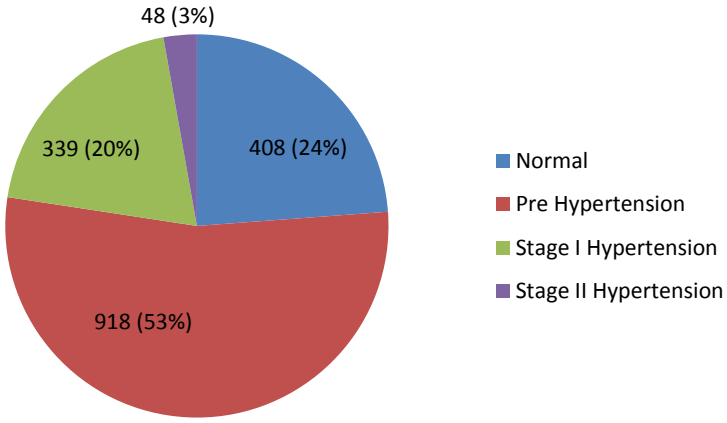


Figure 5-5: Percentages of subjects within each of the blood pressure category

The majority of subjects in our study (318 athletes, 18.6%) with hypertension were found to have systolic hypertension (>140mmHg) with only 14 athletes having a diastolic BP greater than 100mmHg.

Table 5-3 shows that the majority of subjects with more severe hypertension (Stage 2) are in the older age category (30-35 years). When analysed with age (Figure 5-6) we can see a large proportion of 'normal' blood pressure in the younger age categories. Stage I hypertension appears to be common in all age groups, with a fairly broad rise in higher BP (Stage II hypertension) in those aged 30-35 years.

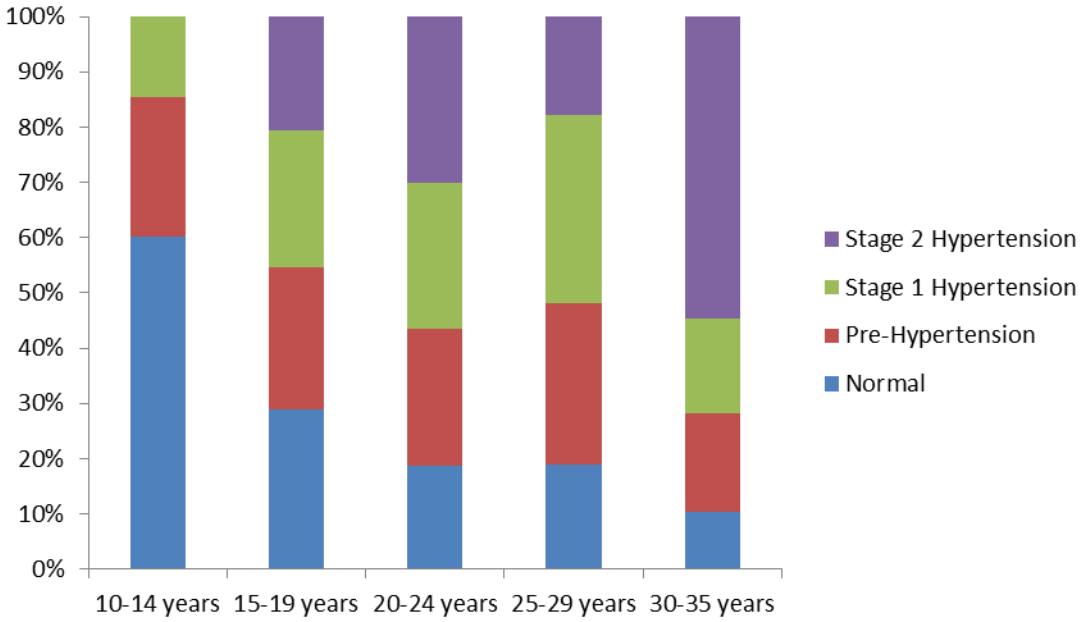


Figure 5-6: Distribution of BP across age category shown as percentages of each BP code

We investigated whether blood pressure could be correlated with age but the correlation coefficients remained low (systolic v age r=0.142, diastolic v age r=0.176) although statistically significant ($p<0.001$).

Figure 5-7 illustrates the relationship between BSA and BP category. When comparing body surface area (BSA) with BP, there is a small trend of higher blood pressure with increased BSA. The Pearson correlation coefficient is 0.344 when comparing BSA and systolic BP ($p<0.001$) but is not as strong for diastolic BP ($r=0.066$ and $p=0.006$). A Spearman Rank correlation was carried out to assess the relationship between BSA and BP code and this found $r=0.302$ ($p<0.001$).

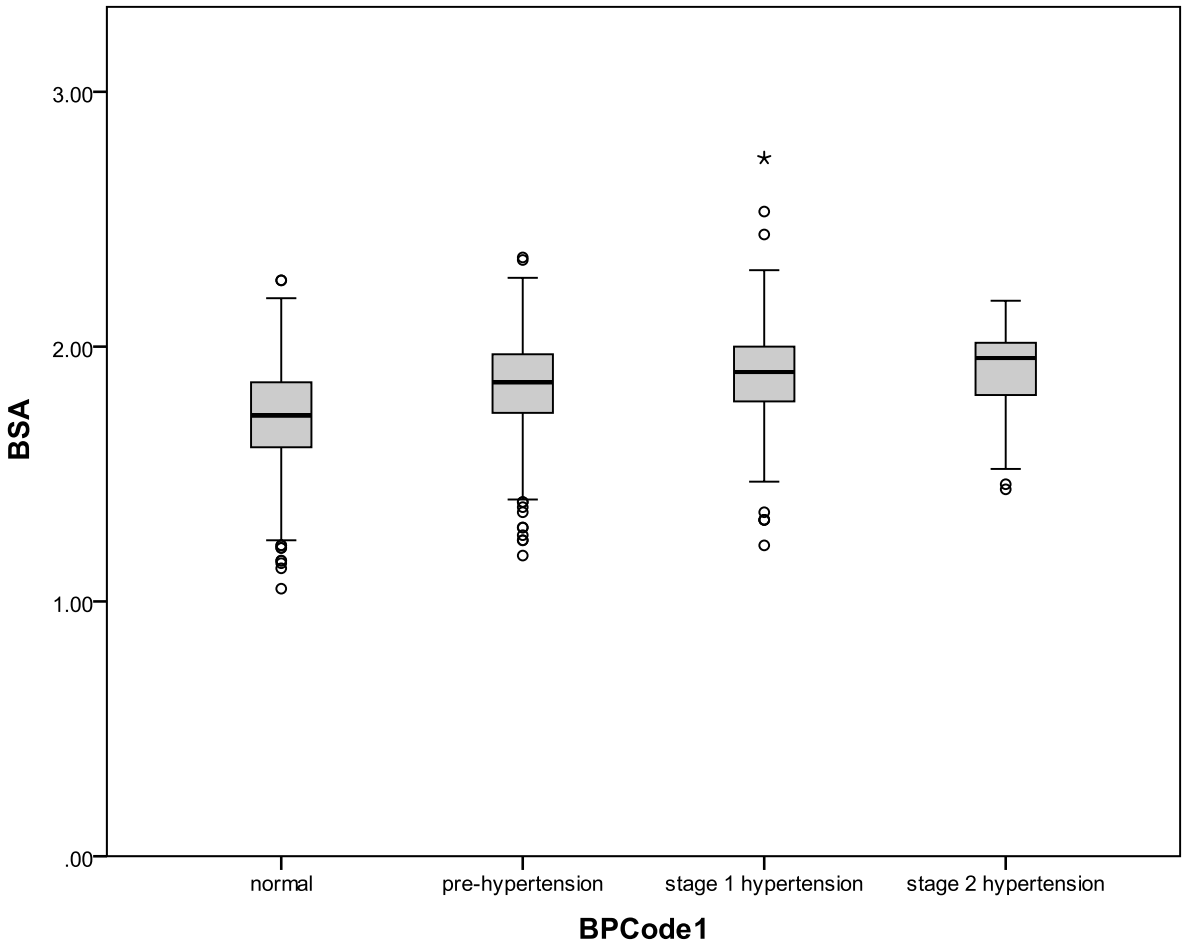


Figure 5-7: Boxplot examining the relationship between body surface area (BSA) and BP category

5.3.1.1. Blood Pressure Sub-study

Thirty five male Caucasian footballers were identified and invited to participate in this sub-study (17 in study group with stage I or stage II hypertension, 18 as control). The mean systolic BP in the hypertensive footballers was significantly reduced from 148.6mmHg to 130.2mmHg ($p<0.001$) with mean diastolic being significantly reduced from 83.4mmHg to 79.7mmHg ($p=0.007$). Control readings did not alter ($p>0.05$). These initial results suggest that the original high blood pressure recordings have been caused by anxiety and/or other stress as home BP monitoring has provided normal or pre-hypertensive readings for all subjects (Table 5-4).

Table 5-4: Initial BP results with follow up home BP measures for the 17 subjects in the BP sub-study

Initial BP Recording	Initial BP Code	Average Home BP Result	Follow up BP Code
150/73	Stage I hypertension	124/68	Pre-hypertensive
150/72	Stage I hypertension	134/70	Pre-hypertensive
142/88	Stage I hypertension	126/78	Pre-hypertensive
141/83	Stage I hypertension	127/81	Pre-hypertensive
139/93	Stage I hypertension	118/79	Normal
145/82	Stage I hypertension	132/80	Pre-hypertensive
154/79	Stage I hypertension	138/86	Pre-hypertensive
143/80	Stage I hypertension	133/80	Pre-hypertensive
147/81	Stage I hypertension	136/79	Pre-hypertensive
139/91	Stage I hypertension	128/84	Pre-hypertensive
144/77	Stage I hypertension	131/78	Pre-hypertensive
141/85	Stage I hypertension	127/79	Pre-hypertensive
142/83	Stage I hypertension	131/81	Pre-hypertensive
156/89	Stage I hypertension	139/82	Pre-hypertensive
171/88	Stage II hypertension	124/81	Pre-hypertensive
162/91	Stage II hypertension	129/86	Pre-hypertensive
160/82	Stage II hypertension	137/88	Pre-hypertensive

5.4. Electrocardiogram (ECG)

The main clinical finding on ECG was bradycardia with 426 subjects (24.9%) having a heart rate lower than 55bpm (mean 62.8 (±11.5) bpm). The mean QT interval was 402.1ms (±35.7) with the mean corrected QT (QTc) being 409.0ms (±24.5). One hundred and thirty two subjects (82 male and 50 female) had a QTc longer than 440ms which was previously considered prolonged according to the ESC criteria. Table 5-5 provides the mean values for measured intervals as well as providing the numbers of subjects with what would be deemed 'abnormal' measures according to the Seattle Criteria[82].

Table 5-5: Mean ECG values with abnormal values according to the Seattle Criteria[82]

Measure	Mean Value (±SD)	Abnormal range	Number of abnormal
Heart Rate	62.8bpm (±11.5)	<55bpm	426 (24.9%)
QTc	409.0 (±24.5)	Male >470ms Female >480ms	3 3
PR interval	146.7 (±28.3)	<120ms	177 (10.3%)
Voltage criteria (V1+V5)	33.8 (±10.1)	>35mm	700 (40.9%)

Of the 1713 ECG's recorded, only 250 (14.6%) could be considered to have abnormal findings according to the Seattle criteria (Table 5-6)[82].

Table 5-6: Numbers of abnormal ECG's in the current study according to the Seattle criteria[82]

Abnormal Finding	Numbers in CAYA Study
T wave inversion	62 (3.6%)
ST-segment depression	139 (8.1%)
Pathologic Q waves	0
Complete LBBB	0
IV conduction delay	31 (1.8%)
Left axis deviation	0
Left atrial enlargement	0
Right ventricular hypertrophy pattern	7 (0.4%)
Ventricular pre-excitation	3 (0.2%)
Long QT interval (>470ms in males or >480ms in females)	6 (0.4%)
Short QT interval (<320ms)	2 (0.1%)
Brugada-like ECG pattern	0
Profound sinus bradycardia	0
Atrial tachyarrhythmias	0
Premature ventricular contractions	0
Ventricular arrhythmias	0

Additional ECG findings included 3 subjects with Wolff-Parkinson White syndrome (ventricular pre-excitation), only 1 of whom was symptomatic (occasional palpitations and dizziness) which would have been identified on questionnaire. One subject was also diagnosed with LQTS who had been symptomatic with dizziness.

5.4.1. Left Ventricular Hypertrophy on ECG (V1+V5)

Seven hundred subjects (40.9%) were found to have voltage criteria for LVH on ECG (V1+V5 >35mm). There was a very weak but statistically significant correlation (r=0.1, p<0.001) between voltage criteria and age as can be seen in Figure 5-8.

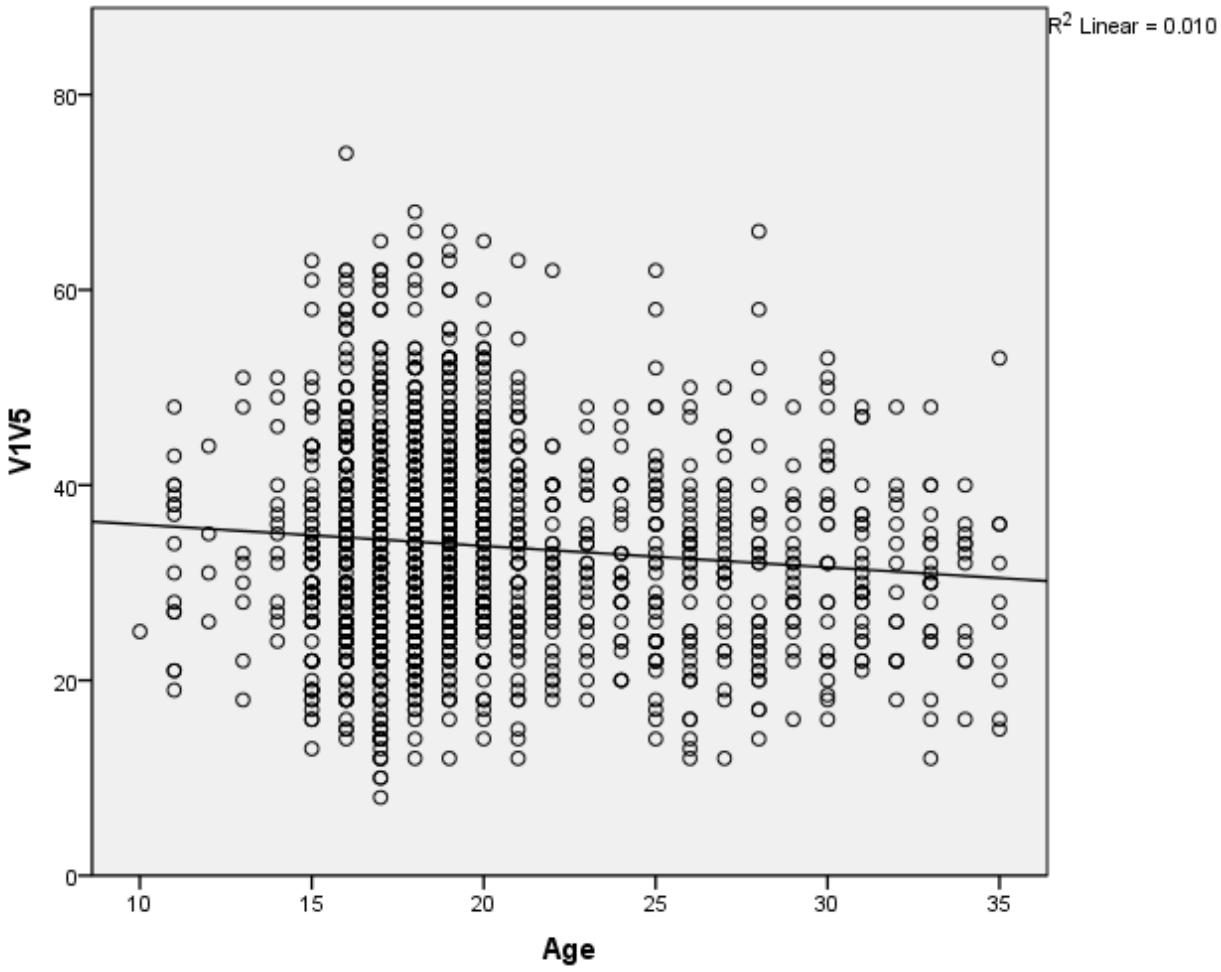


Figure 5-8: Scatter plot illustrating the relationship between age and left ventricular hypertrophy (V1+V5) on ECG (r=0.1, p<0.001)

5.5. Echocardiogram

5.5.1. Left Ventricular Wall Measurements

The mean left ventricular posterior wall thickness (LVPWd) was 10.1 (±1.6) mm. Four hundred and twelve subjects (24.0%) were found to have a LVPWd greater than 11mm, with 74 subjects (4.3%) found to have a LVPWd of 13mm or greater. Figure 5-9 suggests a higher percentage of older athletes with increased wall thickness.

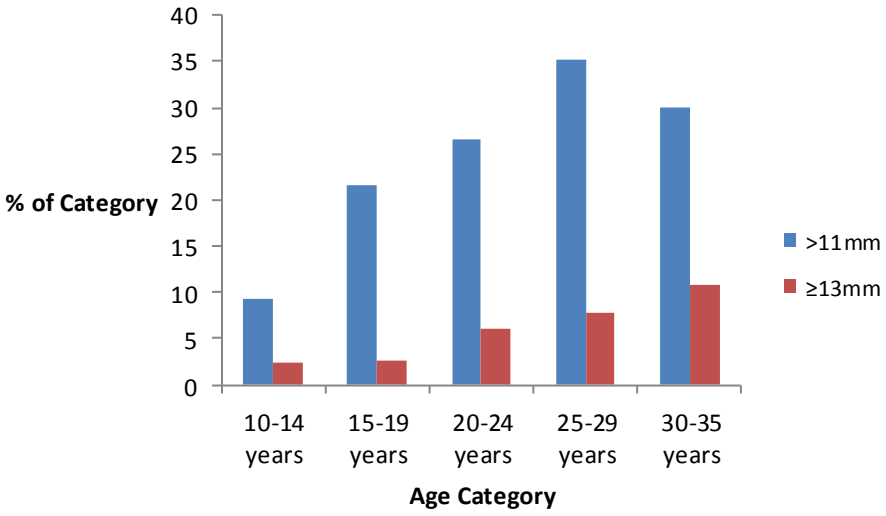


Figure 5-9: Percentage of age category with left ventricular posterior wall thickness (LVPWd) greater than 11 and ≥13mm

A very weak but statistically significant correlation was found between left ventricular wall thickness and age (r=0.170, p<0.001) which is illustrated in Figure 5-10.

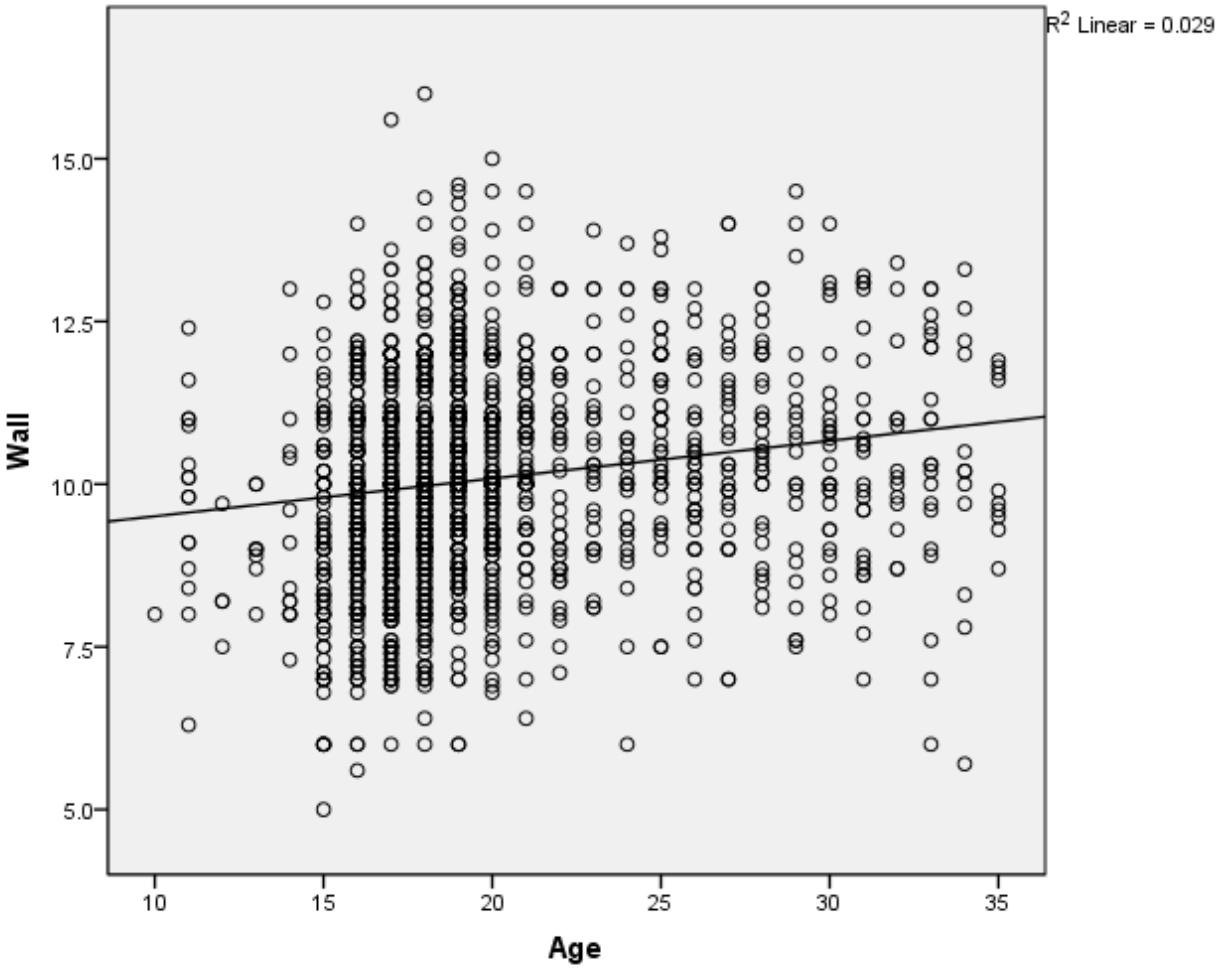


Figure 5-10: Scatter plot of left ventricular wall thickness with age (Pearson correlation r=0.170, p<0.001)

5.5.2. Septal Measurements

The mean inter-ventricular septal thickness (IVSd) was 10.2 (±1.6) mm. Four hundred and sixty three subjects (27.0%) were found to have a IVSd greater than 11mm, with 87 subjects (5.1%) found to have a IVSd of 13mm or greater. Figure 5-11 shows an increase in the number of subjects with septal thickness greater than 11mm per age category.

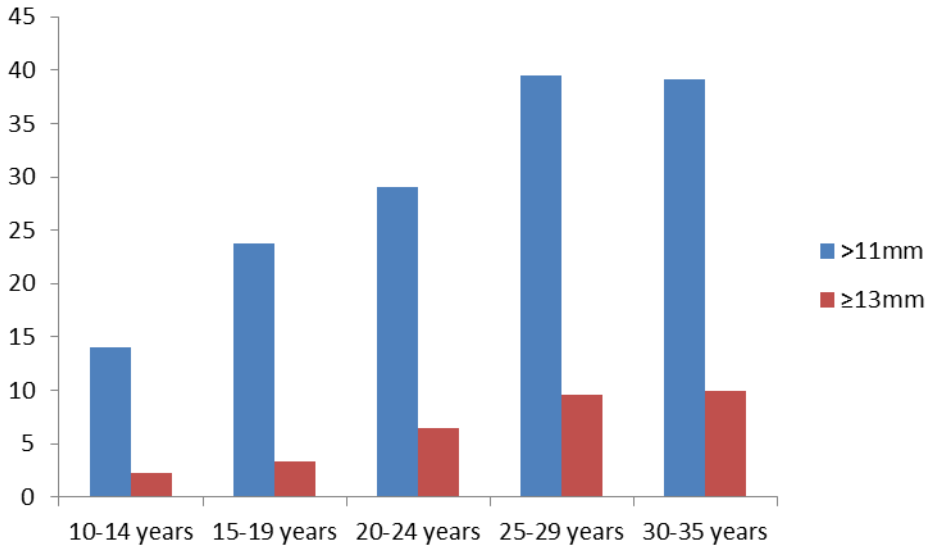


Figure 5-11: Percentage of age category with intra- ventricular septal diameter (IVSd) greater than 11 and ≥ 13mm

A very weak correlation was found between age and septal thickness ($r=0.189$, $p<0.001$) showing no direct relationship (Figure 5-12).

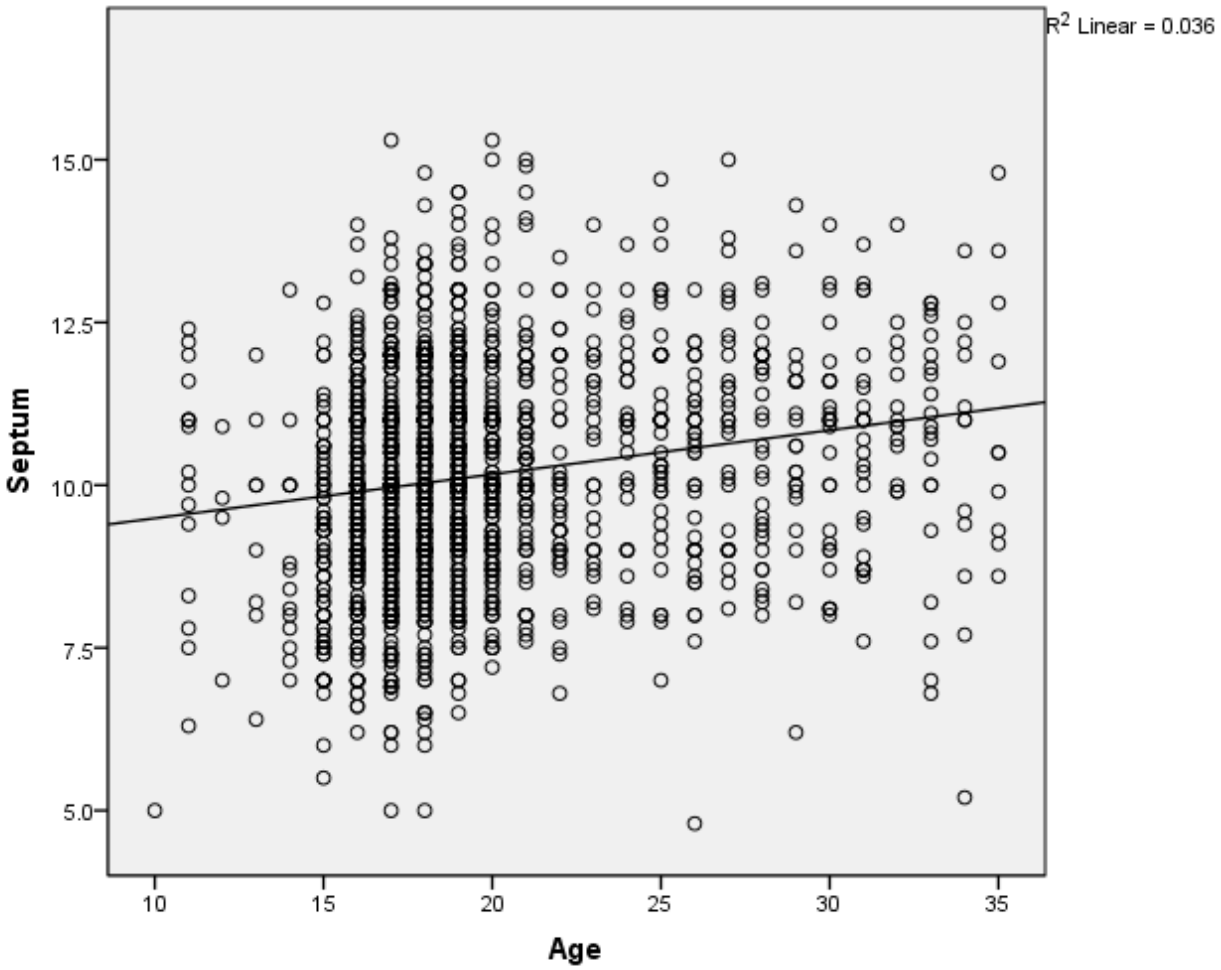


Figure 5-12: Scatterplot of septal thickness and age (r=0.189, p<0.001)

5.5.3. Relationship between left ventricular wall thickness and septal thickness

Analysis was carried out to establish whether there was a relationship between septal thickness and posterior wall thickness which gave us a Pearson correlation coefficient of r=0.6 (p<0.001) suggesting a linear relationship which can be seen in Figure 5-13. The finding of a linear relationship between IVSd and LVPWd provides evidence of symmetrical hypertrophy in this population which is suggestive of athlete's heart rather than HCM where the hypertrophy is normally asymmetrical.

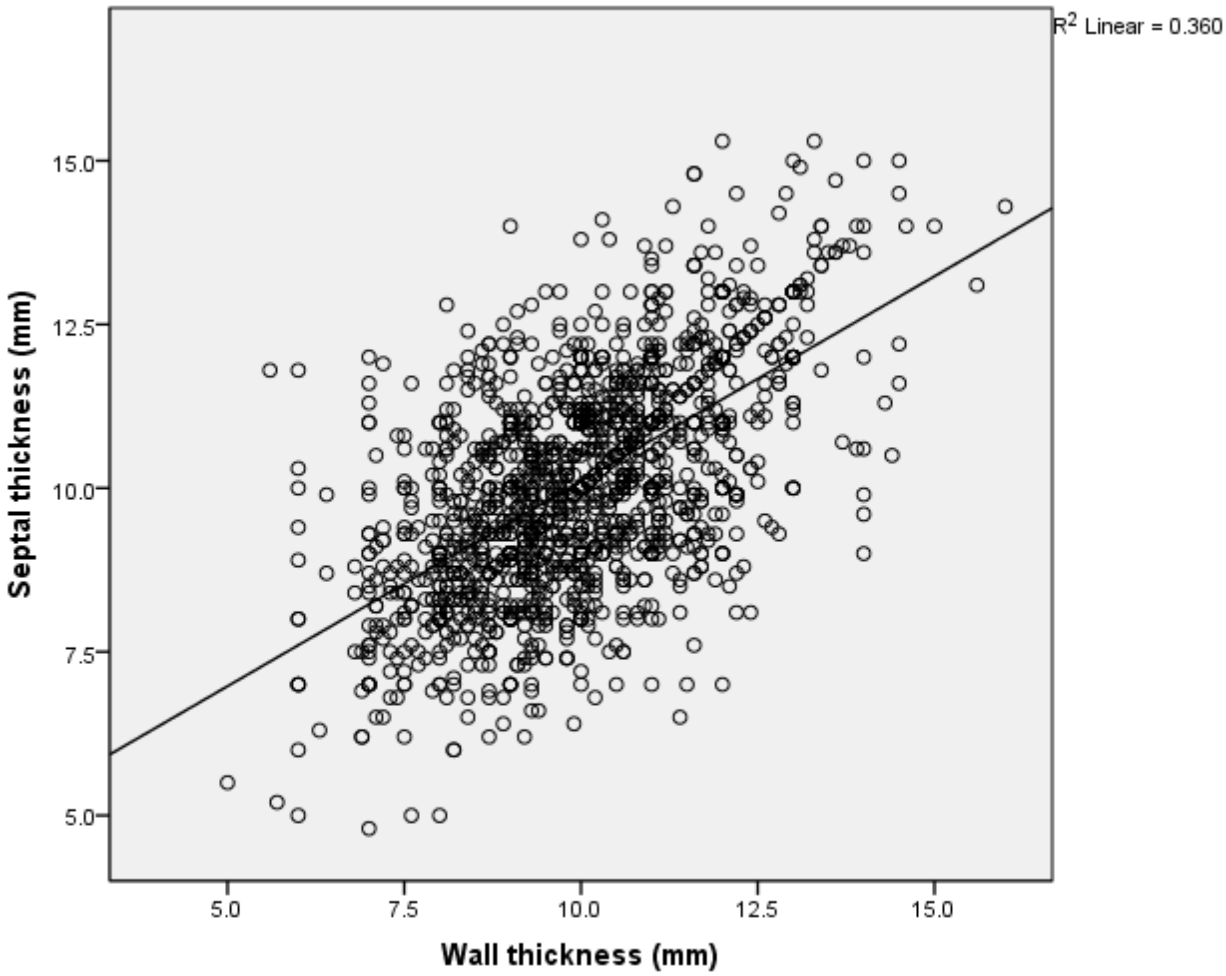


Figure 5-13: Scatter plot of wall thickness v septal thickness showing the Pearson correlation coefficient of r= 0.6 (p<0.05)

5.5.4. Valvular Function

Valves were visually assessed using Doppler echocardiogram. Any regurgitation was noted and is recorded in Table 5-7.

Table 5-7: Numbers of subjects with regurgitation at each of the 4 heart valves

Valve	Number of Subjects	%
Pulmonary	238	15.6
Tricuspid	433	25.3
Aortic	30	1.8
Mitral	213	12.4

The majority of the regurgitation above is trivial or mild suggesting it is physiological. Previous studies[115] have found up to 45% of normals to have mitral regurgitation and up to 80% to show pulmonary regurgitation. Only 26 subjects had more serious regurgitation and requiring follow up.

5.5.5. Additional Diagnosis

Forty six additional diagnoses were made on echocardiography which would not have been identified with ECG alone (Table 5-8).

Table 5-8: Additional diagnoses made with echocardiography which would not be identified using the other screening tools

Diagnosis	Number Identified
Bicuspid Aortic Valve	10
Suspected Patent Forearm Ovale (PFO)	12
Mitral Valve Prolapse (MVP)	2
Atrial Septal Defect (ASD)	2
Patent Ductus Arteriosus (PDA)	2
Aneurysmal Septum	4
Mobile/Prominent Chiari Network	4
Flattened tricuspid leaflet	1
Right Ventricular Enlargement	2
Mobile Inter-Atrial Septum (IAS)	3
Non-Compaction cardiomyopathy	2
Coarctation	2

5.6. Diagnosis of LVH on ECG and Echocardiogram

According to the Sokolow-Lyon criteria, LVH can be diagnosed on ECG if the sum total of S wave in V1+ R wave in V5 is greater than 35mm. Seven hundred subjects in this study (40.6%) were found to have voltage criteria for LVH (V1+V5 >35mm). Voltage criteria was correlated with LVPWd with $r=0.137$ ($p<0.05$). This positive but weak relationship can be seen in Figure 5-14.

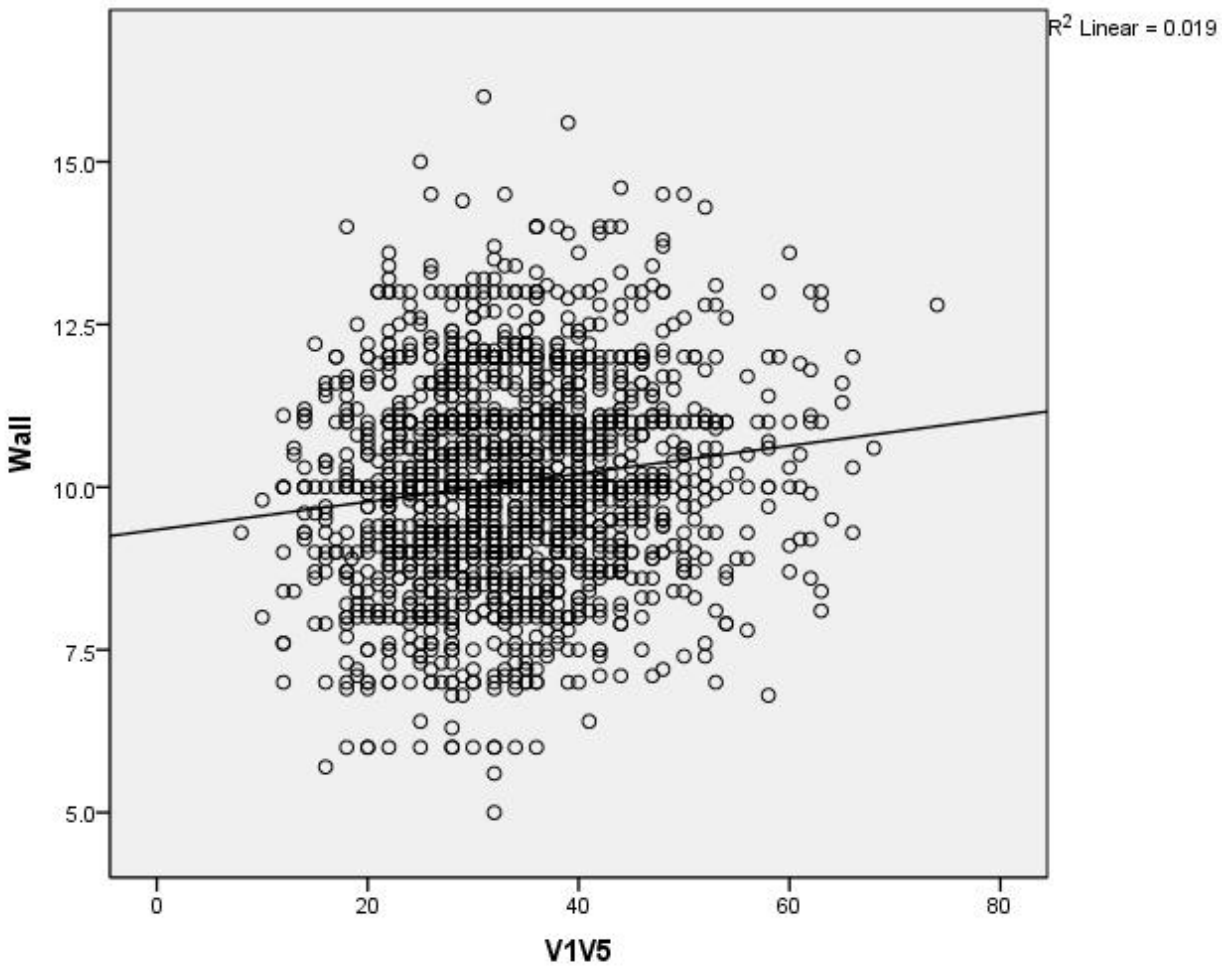


Figure 5-14: Scatter plot showing the relationship between LVH diagnosis on ECG (V1+V5) and left ventricular wall thickness on echocardiogram (r=0.137, p<0.05)

Voltage criteria was also correlated with septal thickness which again showed a very weak but significant correlation r=0.141 (p<0.05). This is illustrated in the scatter plot in Figure 5-15 with no obvious relationship apparent.

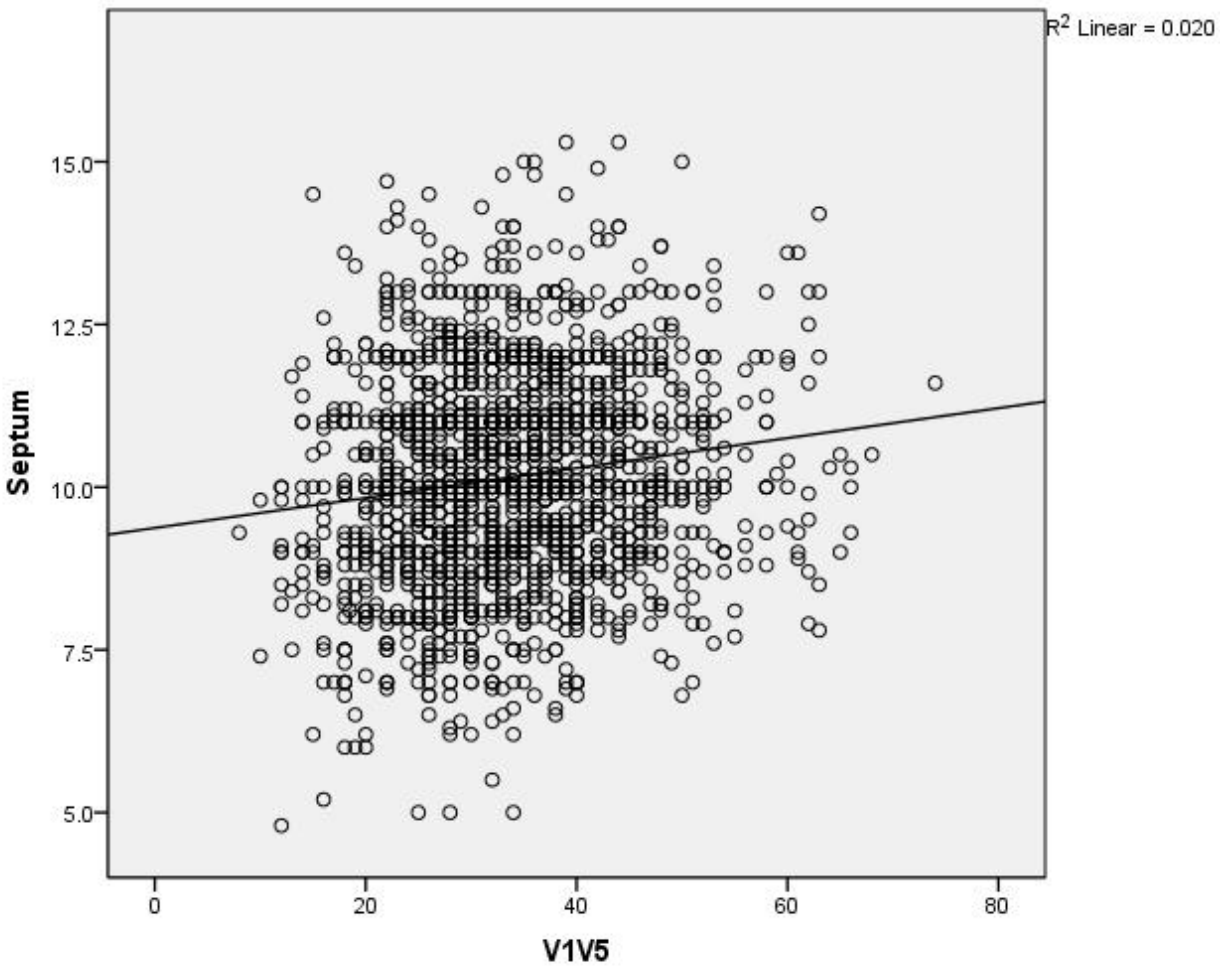


Figure 5-15: Scatter plot showing the relationship between LVH diagnosis on ECG (V1+V5) and septal thickness on echocardiogram (r=0.141, p<0.05)

5.7. Relationship between Heart Rate and Echo Parameters

Heart rate was correlated with both septal thickness (r=0.082, p=0.070) and wall thickness (r=0.094, p=0.038). The significant but weak correlation with wall thickness can be seen in Figure 5-16.

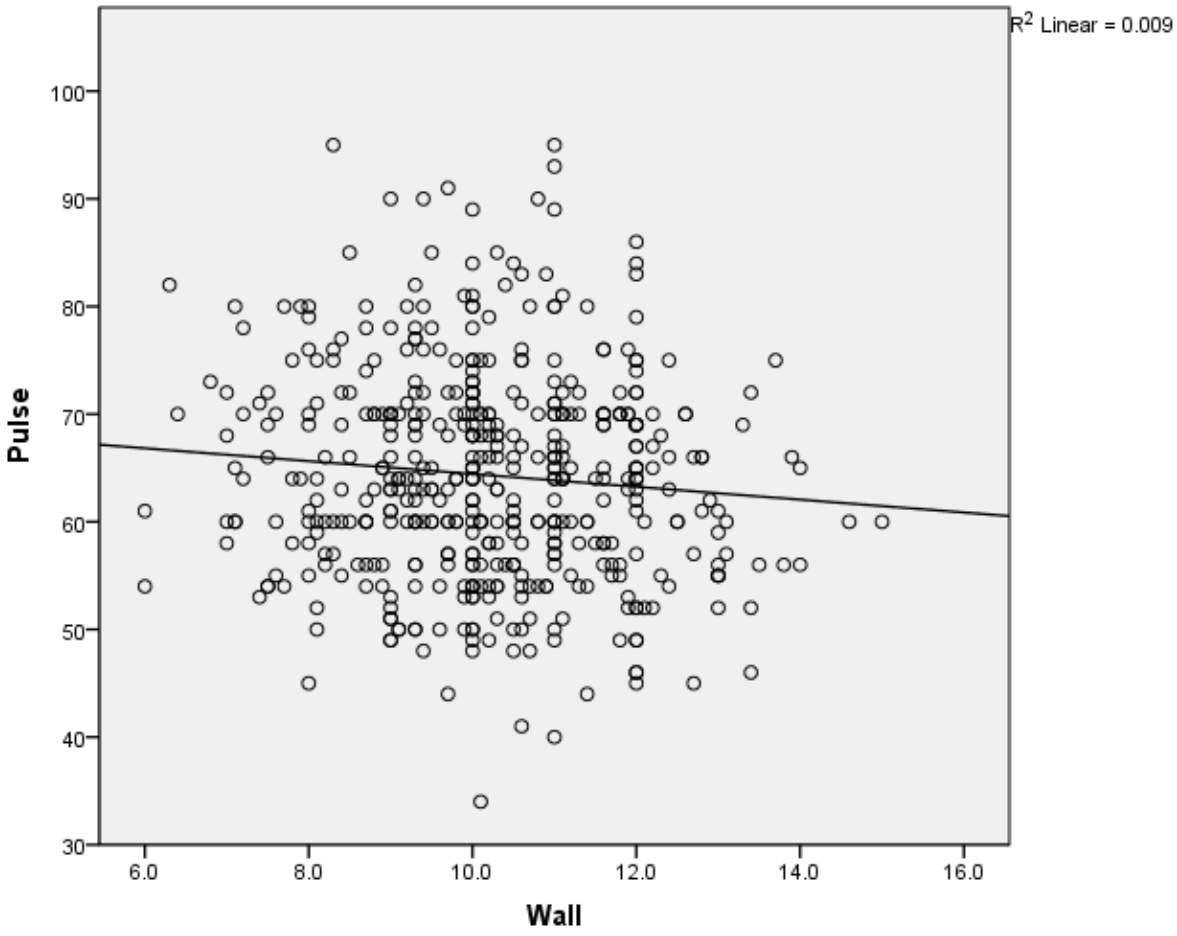


Figure 5-16: Scatter plot of heart rate and left ventricular wall thickness (r=0.094, p=0.038)

5.8. Sensitivity and Specificity of Screening Tools for LVH

In order to calculate how sensitive and specific the screening tools used were in diagnosing LVH, we used 2x2 contingency tables to calculate the positive predictive value (PPV) and negative predictive value (NPV). These were calculated based on echocardiographic cut offs of 11mm and 13mm of hypertrophy for septum and left ventricular wall.

Table 5-9 shows the 2x2 contingency table for detecting left ventricular hypertrophy (>11mm) using ECG and echocardiogram. It shows only 189 subjects with hypertrophy of the left ventricular wall (LVPWd) would have been identified using Sokolov-Lyon criteria on ECG. This gives a sensitivity of 0.49 (95% CI= 0.416-0.502) and specificity of 0.39 (95% CI=0.379-0.406).

Table 5-9: 2x2 contingency table comparing ECG and echocardiogram in identifying subjects with LVH with wall thickness >11mm

	LVPWd > 11mm	LVPWd ≤ 11mm	Total
With V1+V5>35mm	189	511	**700**
Without V1+V5 ≤ 35mm	223	790	**1013**
Total	**412**	**1301**	**1713**

This table then gives us a positive predictive value (PPV) of 27.0% (95% CI=0.245-0.295) and a negative predictive value (NPV) of 78.0% (95% CI=0.763-0.797). This suggests that the ECG is not a useful diagnostic test for left ventricular hypertrophy of posterior wall, but that it can identify those without LVH.

A 2x2 contingency table was then completed for wall thickness greater than 13mm which could be suggestive of pathology. Table 5-10 shows a sensitivity of 0.514 (95% CI: 0.398-0.628) and specificity of 0.596 (95% CI: 0.591-0.601). The PPV is extremely low at 5.4% (95% CI: 0.042-0.066) but NPV is extremely high at 96.4% (95% CI: 0.956-0.973).

Table 5-10: 2x2 contingency table comparing ECG and echocardiogram in identifying subjects with LVH with wall thickness ≥ 13mm

	LVPWd ≥13mm	LVPWd <13mm	Total
With V1+V5>35mm	38	662	**700**
Without V1+V5 ≤ 35mm	36	977	**1013**
Total	**74**	**1639**	**1713**

The sensitivity and specificity of ECG in identifying septal hypertrophy was also computed using 2 x 2 contingency tables. Table 5-11 shows a sensitivity of 0.47 (95% CI: 0.429-0.508) and specificity of 0.61 (95% CI: 0.599-0.628) for septal hypertrophy of greater than 11mm. The PPV of the ECG is 31.0% (95% CI: 0.284-0.336) and the NPV is 75.7% (95% CI: 0.739-0.775).

Table 5-11: 2x2 contingency table comparing ECG and echocardiogram in identifying subjects with LVH with septal thickness >11mm

	IVSd >11mm	IVSd ≤11mm	Total
With V1+V5>35mm	217	483	**700**
Without V1+V5 ≤ 35mm	246	767	**1013**
Total	**463**	**1250**	**1713**

The ECG and echo were then evaluated for septal hypertrophy greater than or equal to 13mm which may be suggestive of underlying pathology. Table 5-12 shows the 2x2 contingency table which gives a sensitivity of 0.471 (95% CI: 0.367-0.578) and a specificity of 0.595 (95% CI: 0.589-0.600). The PPV was only 5.9% (95% CI: 0.046-0.072) but the NPV was 95.5% (95% CI: 0.946-0.964).

Table 5-12: 2x2 contingency table comparing ECG and echocardiogram in identifying subjects with LVH with septal thickness ≤13mm

	IVSd ≥13mm	IVSd <13mm	Total
With V1+V5>35mm	41	659	**700**
Without V1+V5≤ 35mm	46	979	**1013**
Total	**87**	**1638**	**1713**

5.9. Relationship between Hypertension and Left Ventricular Hypertrophy

Three hundred and eighty seven subjects were identified as being hypertensive (339 with stage I hypertension and 48 with stage II hypertension). Of these 387 subjects, 174 were identified as having LVH on the ECG (V1+V5>35mm) with 87 of these also having LVH on echo (>11mm) (40 of wall and 47 of septum)

Pearson correlations were carried out to examine whether there was a relationship between LVH and BP code but no associations were found (V1V5 r=0.125, wall r=0.158, septum r=0.170, p<0.001). Results from a Pearson correlation showed a significant but weak

relationship between LVPWd and diastolic blood pressure (r=0.051, p=0.034) which is illustrated in the scatter plot in Figure 5-16.

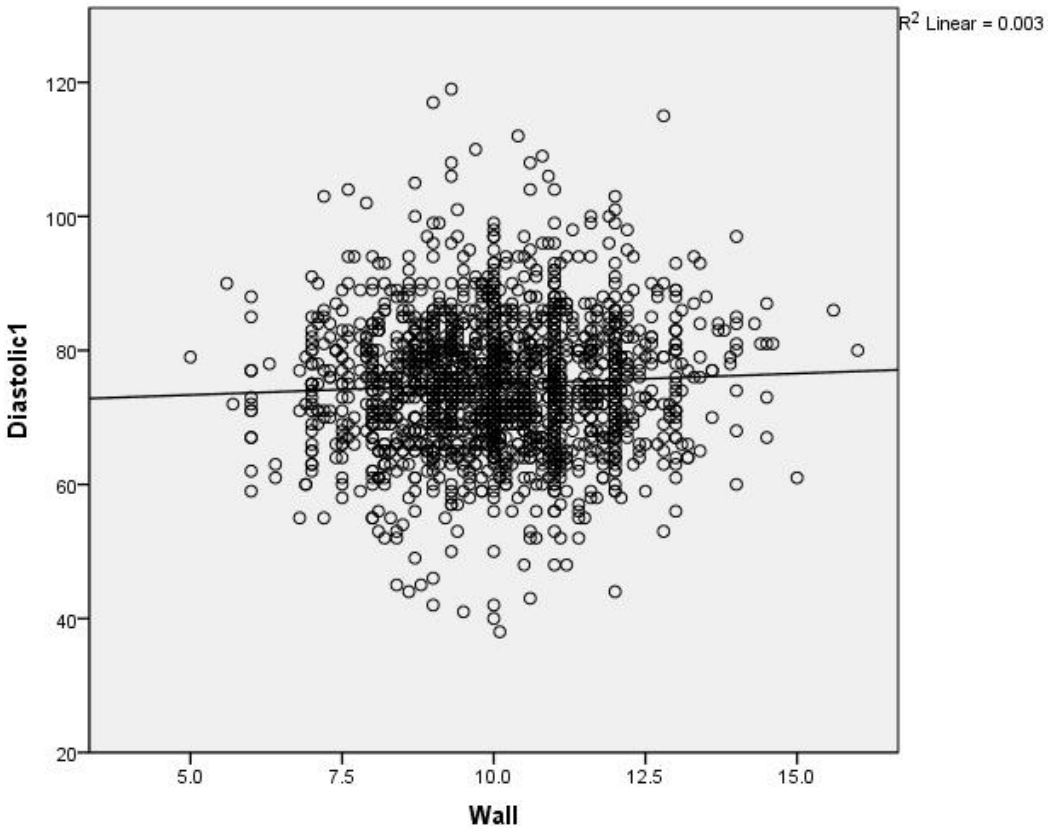


Figure 5-17: Scatter plot of correlation between LVPWd and diastolic BP suggesting a weak but significant relationship (r=0.051, p+0.034)

Chapter 6 -Discussion Part 2

Consensus opinion is that cardiovascular screening should be made available for those participating in sport, but debate remains about what form this screening should take, whether it should be mandatory or voluntary and to whom it should be offered. This study is the only UK research to date which has provided echocardiography for all subjects in order to evaluate whether the Italian Model of family and personal history, physical examination and ECG is sufficient in a Scottish population or whether the addition of echocardiography reduces the numbers of false positives provided by ECG and provides further useful information on the subjects health.

6.1. Personal and Family History and Physical Examination

6.1.1. Patient Demographics

The majority of subjects in the current study were 15-19 years old (n=1083, 63.2%). Maron et al[23] suggest that 65% of young athletes who die are of school age (<17 years old) suggesting that perhaps screening should take place when subjects are 15-16 years old in order to prevent potential SCD. Previous studies[2 23] have shown males to be at higher risk of SCD. We screened more male than female athletes but this reflects participation rates particularly when the majority of our subjects were footballers.

We did not ask our athletes regarding personal social habits such as smoking which may affect their health. This was because it was felt it may make our athletes feel uncomfortable as this information was to be shared with the clubs.

6.1.2. Blood Pressure

Systolic hypertension is more common than diastolic hypertension in our population (318 athletes v 14 athletes). This pattern is in keeping with the physiological changes associated with athlete's heart. These high numbers of hypertensive readings may be reflective of the cardiac adaptations to physical training but results may also suggest a number of subjects with possible 'white coat hypertension'.

A number of possible explanations could account for the high BP readings in our study. Anxiety is a common problem, particularly when measuring BP in a clinical area. The recent media attention surrounding screening and the potential implications of a positive finding may also cause worry. Previous research[59] has suggested a prevalence of the 'white coat' phenomenon of 4.4% in adolescent athletes. Following domiciliary BP monitoring this was reduced to 0.5% in a cohort of 410 athletes. The pilot study carried out on a small number of our hypertensive subjects does support ambulatory or home monitoring to rule out true hypertension.

The significant relationship that we found between BSA and BP could be an important one as it could provide a marker for risk stratification in the future. There is a trend with a significant r-value of 0.302 ($p<0.001$) which suggests that the larger the athlete, the higher the blood pressure is likely to be. This would be similar to the general population whereas overweight or obese subjects would tend to have higher BP measurements.

The pilot sub-study suggests that the hypertension seen in this population is mainly 'white coat' with all readings being normal or pre-hypertensive on follow up. This has led to GP's and club doctors being asked to follow up subjects with unexplained high blood pressure routinely with a copy of results passed on to us for records.

The prevalence of high BP in this population is worrying and may reflect on the fitness and environment our athletes are in. Scotland traditionally has a high incidence of inactivity and poor social status (smoking and diet) with the Scottish Health Survey estimating that a third of young Scots (aged 16-34) are hypertensive. It could be said that although our population are participating in sport, they are not as aerobically fit and healthy as counterparts from other countries and sports.

6.2. Electrocardiogram

Debate exists surrounding the use of ECG in cardiac screening due to concerns about its high false positive rate and low specificity for the diagnosis of LVH. Results from the Italian screening model suggest that ECG should be included as standard practise in the cardiac assessment of athletes[2], but that they must be interpreted with caution, whereas America have resisted it's use due to the supposed false positive results[116].

The most common ECG finding in this study is sinus bradycardia, which was present in 24.9% of our cohort (n=426). This is accepted as a 'normal' finding in an athletic population with the incidence being as high as 60% in previous studies[38]. Sixty two subjects (3.6%) were found to have T-wave inversion. Although non-specific in our athletes, this finding in V1-V3 could be consistent with a diagnosis of ARVC. Previously a QT interval above 440ms was considered abnormal but recent guidelines[82] have seen this be changed to an abnormal value greater than 470ms (480ms in females) due to the QTc being based on a HR of 60bpm and athletes generally having lower pulses.

Voltage criteria for LVH (V1+V5>35mm) has been shown to be present in approximately 45% of male athletes and 10% female athletes[80 117]. Figures in our study are very similar to these

with 47.2% of males (n=675) and 8.8% females (n=25) being identified as having a voltage criteria for LVH using Sokolov-Lyon criteria.

Early research suggested that false positive rates with ECG could be as high as 40%[62] but using the new ESC criteria, this was reduced to 11% increasing the specificity of the test. Using the Seattle criteria[82], only 14.6% of ECG's in this study (n=250) would be considered abnormal warranting further investigation. Previous data[66 86 118] suggest that abnormal ECG patterns are more common in black athletes but the current study did not have a large enough cohort of these subjects for separate analysis.

Studies[2 77] have shown that there is large geographical variation in the incidence and causes of cardiac death in young people which can be identified by ECG. Both ARVC and HCM which are the leading causes of SCD in Italy and America can be identified by ECG, whereas this is not a tool which can identify CAD and so is not so useful in a Scottish population.

6.3. Echocardiogram

In the current study, 1081 (63.1%) subjects had normal echo findings, 632 (36.9%) had signs of physiological LVH and 39 (2.3%) had evidence of potential pathology. None of the subjects in our study were diagnosed with HCM or were disqualified from sport. Similar results were found in the only other study which has included echocardiography for all subjects[85]. This study categorised echo findings into 3 groups: normal (n=387, 76%), mildly abnormal (physiological remodelling) (n=110, 22%) and abnormal (n=11, 2.2%). Of the 11 subjects who were deemed to have 'abnormal' echo findings, 3 required sport participation restriction including 1 subject with hypertrophic cardiomyopathy.

Physiological LVH is symmetrical in athletes[119]. Most of the subjects in our study (n=632) demonstrated symmetrical hypertrophy with a statistically significant positive correlation

(r=0.6, p<0.05) found between septal and left ventricular wall thickness. This is more suggestive of physiological remodelling as a result of physical training than any underlying pathological condition. Levy et al[120] found LVH on echocardiogram to increase with age, as in the current study but no strong correlation was found (r=0.170, p<0.001).

The addition of echocardiography to a standard screening programme is unique to CAYA. This was routinely introduced to investigate whether it would reduce the number of 'abnormal' screenings identified on ECG and prevent further investigation. Unfortunately, echocardiogram cannot identify patients with CHD (unless there has been a previous coronary event) and so similar to the ECG, it is perhaps not a useful tool for cardiovascular screening in Scotland.

The prevalence of HCM in the UK is around 1 in 500[4] which would suggest when screening over 1700 subjects, at least 3 participants would be identified as having the condition. From this, we can deduct that either HCM is not as prevalent in Scotland, or that subjects with this condition, self-select out of sport at a younger age. Although the echocardiogram is not able to diagnose CHD, it was useful in identifying 'other' cardiac abnormalities which could become problematic in later life. Many of these conditions were non-specific such as PFO and bicuspid aortic valve which have a high incidence in the normal population[121]. Other conditions such as atrial septal defects and non-compaction cardiomyopathy are more serious and require further consultation with a cardiologist. By identifying these conditions and referring subjects into the NHS system, it could be argued that echocardiogram should be routinely used in a Scottish population in terms of long-term follow up.

6.4. Relationship between Heart Rate and Echo Parameters

Bradycardia is a common finding in this study with almost a quarter of athletes presenting with heart rates less than 55bpm. There was a weak but significant correlation between HR and both wall thickness (r=0.094, p=0.038) and septal thickness (r=0,082, p=0.070). It could be postulated that the lower heart rates associated with this population relate to fitness levels and an increased proportion of LVH compared to a normal population.

6.5. Sensitivity and Specificity in Diagnosing Left Ventricular Hypertrophy

Previous studies[85] [122] have found echocardiography to have good sensitivity and specificity in diagnosing LVH. Our results show that the ECG has a good NPV suggesting it is useful to diagnose those without LVH (particularly that greater than 13mm), but a low PPV suggests it is not a useful diagnostic tool. The PPV for posterior wall hypertrophy when examining physiological LVH (>11mm) is only 19.3% which increases to 31.0% when looking at potential pathological hypertrophy (≥13mm). The NPV also increases from 69.6% to 75.7% suggesting the echocardiogram is a much better identifier of posterior wall hypertrophy than the ECG.

When comparing the Sokolov Lyon criteria with septal hypertrophy on echo, the PPV is as low as 5.9% for potential pathological LVH (≥13mm) which increases to 31.0% for physiological LVH (>11mm). This means that the ECG alone cannot be used to diagnose those with septal hypertrophy but a NPV of 75.7% for >11mm and 95.5% for ≥13mm suggests it can be used to distinguish those with a septal thickness within normal range. These results are similar to that of Baggish et al[85] who found that adding ECG to personal and family history and physical examination increased the sensitivity of screening from 45.5% to 90.9% but it also decreased PPV from 15.0% to 10.4% with an increase in false positive results.

6.6. Relationship between Hypertension and Left Ventricular Hypertrophy

The theory of 'athlete's heart' suggests that physical training is associated with both LVH and hypertension. This relationship was previously thought to be due to pressure overload on the heart but it is not clear whether LVH is responsible for increased BP or whether increased BP causes LVH. In our study, the majority of those with hypertension also have LVH which would support the pressure overload theory. The intensity and frequency of training may also have an effect on this relationship but this information was not collected.

Diastolic BP has been shown to be more closely related to LVPWd which reflects the pressure overload theory[122]. The correlation between the two in this study was r= 0.051 (p=0.034) which although statistically significant is weak. Studies have shown that athletes with stage II hypertension are likely to go on to develop hypertension in later life and so should be continually monitored[60]. Blood pressure recording is therefore an important component of the screening process and should be annually checked. A letter was sent to a subjects GP and/or club doctor if a high reading was recorded requesting them to arrange a follow up recording but we did not ensure this was done.

6.7. Summary

The aim of our cardiovascular assessment programme (CAYA) was not to screen for SCD, but to provide reassurance that these young people are able to participate in sport and exercise without risk. No subjects were disqualified from sport following screening, but the introduction of the echocardiogram did identify a number of cardiac abnormalities which require follow up.

The main clinical finding identified in this cohort was hypertension (n-318, 18.6%), but a follow up pilot study has suggested this may largely be 'white coat' hypertension. According to the Seattle Criteria[82], only 250 ECG's would be identified as 'abnormal' with one 3 subjects

found to have WPW syndrome and 1 with LQTS. Nearly 41% of subjects demonstrated voltage criteria for LVH on ECG (V1+V5 >35mm) weak correlations were found between this and LVPWd and IVSd ($r=0.137$ and $r=0.141$, $p<0.01$).

The inclusion of echocardiogram for all subjects allowed for calculations of sensitivity and specificity of the ECG which suggested that with a high NPV, the ECG is a useful tool to identify those without pathology, but the additional diagnosis found on echocardiogram provided a more comprehensive cardiovascular health assessment.

Chapter 7 - Conclusions

Part one of this research identified that most deaths in the young in Scotland were due to accidents (27%), self-harm (16%) and cancers (12%). Cardiac causes were responsible for 6.4% of deaths in those aged 1-35 years. Of these cardiac deaths, a third were attributable to coronary heart disease with most of them occurring outside of hospital. This is of concern in such a young age group and suggests that cardiovascular screening with ECG and echocardiogram may not be useful in reducing the number of cardiac deaths in Scotland although due to the inability of these tools to identify CHD. Instead, results suggest that better education regarding lifestyle choices to reduce weight, decrease cholesterol, reduce alcohol intake, help smoking cessation and increase physical activity could help to decrease the prevalence of CHD.

Screening or cardiovascular assessment may still be useful to identify persons at risk of cardiac events such as cardiomyopathy or familial arrhythmias and it may also identify other health related problems such as hypertension which if not treated could become a health problem in the future. From the current study, we cannot comment on whether lives have been saved as this would require a longitudinal investigation to follow up our subjects over time.

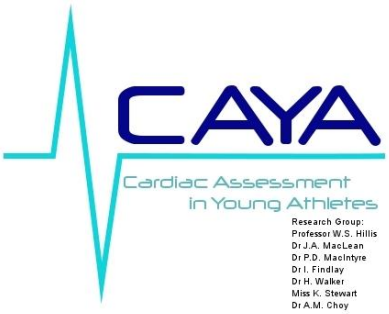
In order for us to be able to accurately calculate the true incidence of SCD in both the general population and deaths related to sport, Scotland and the whole of the UK needs a Register of all sudden deaths to be established with information regarding the origin of the initial collapse and cause of death. In addition to this, the circumstances surrounding each death need to be considered when assigning a cause of death with pathologists made more aware of SADS.

Results of the CAYA programme show the ECG to have a high negative predictive value suggesting it to be a useful tool to identify subjects without underlying cardiac pathology. Routine echocardiography led to a number of conditions being identified in our population, some of which require treatment. Results suggest that any future screening programme should include personal and family history, PE and ECG and should be confined to those who are symptomatic, have a family history of heart problems or are undertaking exercise on a regular basis.

Scotland traditionally is a nation with high levels of deprivation, smoking and inactivity and obesity and associated high blood pressure which are all risk factors for CHD. This study did not set out to examine this disease in the young and would require exercise testing and angiography to investigate this fully which would not be cost effective.

We believe that a screening programme should be available in Scotland but that this should not be mandatory. Based on the results of Part One of the study which show the highest number of deaths due to structural disease such as cardiomyopathy to occur aged 15-19 years, we believe this programme should target 15-16 year olds. We would also wish to highlight and educate young people in the 4 main symptoms of heart disease that people should have further investigation of: chest pain, dyspnoea, syncope and palpitations. In addition to cardiovascular screening, we suggest that automatic external defibrillators (AED) should be more readily available at sports grounds with coaches and officials trained properly in first aid to increase survival rates in the event of a cardiac arrest.

Appendix A - Questionnaire



PERSONAL HISTORY	**YES**	**NO**
Have you ever been told that you have a heart condition?		
Have you ever had chest tightness at rest/exertion?		
Have you ever fainted during exercise?		
Have you ever been told you have asthma?		
Have you ever been told you have raised/high blood pressure?		
Have you ever been told to give up sports because of a health problem?		
Have you ever been diagnosed with a heart murmur?		
Have you ever experienced irregular heart beat (palpitations)?		
Do you become breathless/tired far more quickly than your team mates?		
Have you ever felt dizzy/faint after exercise/exertion?		
Have you ever had a seizure or been diagnosed with epilepsy?		
Have you routinely taken medication in the past two years? If yes, what?		

Has anyone in your family:	**YES**	**NO**
Died suddenly or unexpectedly?		
Been treated for recurrent fainting?		
Had unexplained seizure problems?		
Had an unexplained drowning whilst swimming?		
Had an unexplained car accident?		
Had heart surgery?		
Had a pacemaker implanted?		
Had a defibrillator implanted?		
Been treated for an irregular heartbeat?		
Has anyone in your family been told they have vascular disease?		
Has anyone in your family been told they have Marfan Syndrome?		

Appendix B – Ethical Approval

Dear Miss Stewart

Medical Faculty Ethics Committee

Project Title: Cardiac Assessment of Young Athletes (CAYA)

Project No.: FM04109

The Faculty Ethics Committee has reviewed your application and has agreed that there is no objection on ethical grounds to the proposed study now that the requested revisions have been incorporated. They are happy therefore to approve the project, subject to the following conditions:

- The research should be carried out only on the sites, and/or with the groups defined in the application.
- Any proposed changes in the protocol should be submitted for reassessment, except when it is necessary to change the protocol to eliminate hazard to the subjects or where the change involves only the administrative aspects of the project. The Ethics Committee should be informed of any such changes.
- If the study does not start within three years of the date of this letter, the project should be resubmitted.
- You should submit a short end of study report to the Ethics Committee within 3 months of completion.

Yours sincerely

Dr Una MacLeod
Faculty Ethics Officer

Dr U MacLeod
Clinical Senior Lecturer

General Practice & Primary Care, Division of Community
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Appendix C - Info Sheet

The Cardiac Assessment in Young Athletes (CAYA) screening programme is supported by the Scottish Government to perform a series of tests in the young athletes to exclude conditions which may reduce sporting performance or lead to serious health risks.

Exercise and sporting activities have been shown to give major improvements to health in general, and to promote a healthy heart and circulation. In a few individuals however, exercise can cause problems even to the extent of sudden death, if there is an underlying cardiac abnormality. Cardiac screening has been shown in Italy to confirm normal cardiac function in most sports participants but it can also to be effective in reducing the risks associated with heart disease.

The conditions which should be excluded are heart muscle disease (Cardiomyopathy), structural problems of the heart affecting the valves or blood vessels and abnormalities of the electrical system of the heart.

The screening consists of:

- A health questionnaire regarding your health and your family's medical history including symptoms such as chest pain, undue breathlessness and an abnormal awareness of your heart beat or fainting on exercise which may suggest a problem.
- A medical examination including blood pressure measurements and audible assessment of the heart.
- An electrocardiogram (ECG); this records the electrical signal of your heart from the surface which gives information concerning the rate, rhythm and electrical function.
- An echocardiogram (ECHO); this gives a 2D picture of the heart which shows the structure and shape of the heart muscle and also assesses the valves.

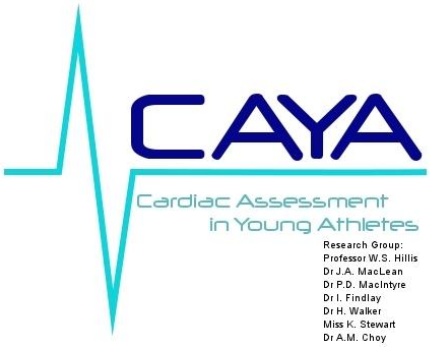
It is important to emphasise that although screening is used to confirm normal cardiac function, occasionally cardiac abnormalities may be identified and may lead to advice being given concerning future exercise activity, and to recommend further investigations and treatment if advisable.

A report of your test results will be sent to your doctor in confidence. If further tests are indicated, contact with you permission, will be made with a local specialist.

In rare cases there may be implications regarding employment and insurance issues.

It is important that you read this background document and understand all the potential outcomes and implications before you undergo screening.

Appendix D – Consent Form



Thank you for volunteering to take part in the CAYA programme. Please read the attached information sheet in order that you will be aware of the potential outcomes if any of the tests show an abnormality of your heart. Screening programmes, such as these, have been shown to reduce the incidence of cardiac complications including the risk of sudden death during activity. Please remember these conditions are rare but like any screening programme, these tests are designed to pick up conditions before symptoms occur. The screening programme is of course voluntary and we will pass the information gained to your GP only with your permission.

I, ... (name) of ..... (address) give informed consent to have heart screening carried out and that I have read and understood the cardiac screening fact sheet. I also give my consent for the information to be passed to my GP and/or Club Doctor in medical confidence.

Signed .....

Appendix E –BP Sub-Study

Thank you for volunteering to take part in the CAYA programme. You have previously been provided with an information sheet regarding the potential outcomes if any of the tests show an abnormality of your heart. Screening programmes such as these, have been shown to reduce the incidence of cardiac complications including the risk of sudden death during activity. Please remember these conditions are rare but like any screening programme, these tests are designed to pick up conditions before symptoms occur.

As part of the CAYA programme you will recall your blood pressure was checked. Analysis of the footballers screened has shown many players have slightly elevated blood pressure. For research purposes a number of these players have been identified to be re-tested. A similar number who had normal blood pressure will also be re-tested for comparison.

Please read the attached information sheet regarding what further testing will be undertaken and sign below if you agree to take part.

I, ... (name) of

.....(address)

give informed consent to have blood pressure screening carried out and that I have read and understood the information sheet. I also give my consent for the information to be passed to my GP in medical confidence if necessary.

Signed ..... (Parent/guardian if under 16 years).

Information Sheet

The CAYA (Cardiac Assessment of Young Athletes) programme has been screening professional footballers in Scotland for cardiac abnormalities since 2008. This is a joint venture between the Scottish Government, the Scottish Football Association and the University of Glasgow. At your initial screening you will have been provided with an information sheet regarding the potential outcomes if any of the tests show an abnormality of your heart. Screening programmes such as these, have been shown to reduce the incidence of cardiac complications including the risk of sudden death during activity. Please remember these conditions are rare but like any screening programme, these tests are designed to pick up conditions before symptoms occur.

As part of the CAYA programme you will recall your blood pressure was checked. Analysis of the footballers screened has shown many players have slightly elevated blood pressure. For research purposes a number of these players have been identified to be re-tested. A similar number who had normal blood pressure will also be re-tested for comparison.

Taking part in this research is voluntary and the CAYA team thank you for your support. Previous research has shown that blood pressure is often artificially high when taken by a doctor or at a screening facility. As a result it has been arranged for each player identified to be given an electrical blood pressure monitor to take home for **4 days each**.

In keeping with recent guidance from the National Institute of Clinical Excellence (NICE):

- Each player should take a blood pressure **twice in the morning and twice in the evening.**
- This should be taken from the **right arm while sitting, relaxed at rest.**
- Please **record all of the measurements on the diary provided** and hand this back with the monitor to your club physio.

References

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