Evidence Summary

Screening to reduce sudden cardiac death in people aged 12-39 years: an appraisal against UKNSC criteria

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What is known about the effects of screening in reducing the incidence of sudden cardiac death in people aged 12-39 years?

The objective of this report is to summarise the peer reviewed literature on screening to reduce sudden cardiac death in young people.

This report follows the review of population screening for hypertrophic cardiomyopathy (HCM) carried out for the UKNSC by Peninsular University in 2008. The focus of that review was the commonest cause of sudden cardiac death. This review widens that question to screening all young people aged 12-39 using questionnaire and ECG. This testing strategy has been proposed because that is the predominant model run within UK charitable and sporting organisations.

Key messages

SCD is an important health problem. However there is little peer reviewed evidence to enable an accurate assessment of the number of people suffering from SCD. There is no assessment of the test accuracy (sensitivity or specificity) in the literature so it is not possible to recommend its use in a national programme.

The conditions that lead to sudden cardiac death are poorly understood and there is no evidence to guide clinicians regarding treatment or lifestyle advice when such a problem is found in a family member or when detected at a screening examination. Guidelines for the management of patients identified as being at risk are consensus based due to a lack of quality evidence (ACC/AHA/ESC 2006[1]). Screening is carried out in a variety of venues and countries. The organisation and outcomes from these programmes are discussed. This literature largely addresses screening in young people participating in sporting activity, is predominantly not peer reviewed and the published outcomes are subject to questions in peer reviewed literature.

There is no direct evidence in a US population that an ECG or any other cardiovascular screening programme will reduce the incidence of SCD in any of the patient populations thought to be at increased risk (USA Institutes of medicine) report

Background

This report was commissioned by the UK National Screening Committee to answer the question: What is the impact of screening in reducing the incidence of sudden cardiac death in young people aged 12 to 39 years? Subsidiary questions were:

- What screening tests are available and are they reliable?
- What is the sensitivity and specificity of these tests?
- What screening practices are currently undertaken nationally (e.g. in Italy), or by national (e.g. Football Association) or by international (e.g. IOC) organisations?
- Where they exist, are current screening practices available to all sport-active young people or only to those who pursue a professional career?
- What evidence is there about population level screening or targeted screening of subgroups, such as sport-active people?

Sudden cardiac death (SCD) is usually defined as death occurring within one hour of the onset of symptoms in a young person without a previously recognised cardiovascular abnormality (Montagnana 2008[2]). Others define SCD as a non-traumatic and unexpected sudden cardiac arrest that occurs within 6 hours of a previously normal state of health (Maron 1996[3]). It is usually precipitated by physical activity. SCD is considered a rare but catastrophic event (Fishbein 2009[4]) with often a great impact on both lay and medical communities (Maron 1996[3]) and attracting media attention. The collapse of Fabrice Muamba in 2012 while playing in a football match for Bolton Wanderers is an example of this.

Causes of SCD. Causes of SCD can be divided into three types: structural, electrical abnormalities and external causes.

Structural causes are due to a variety of problems, most common are hypertrophic cardiomyopathy (HCD) or arrhymogenic right ventricular cardiomyopathy. Electrical abnormalities include long QT syndrome and external causes are due to blunt trauma leading mainly to commotio cordis (the trauma seems to alter the electrical stability of the myocardium, resulting in ventricular fibrillation). Diagnosis is made more complex by the occurrence of the so called 'athletes heart' described by Huston[5] in 1985. The heart responds to large amounts of exercise (chronic demand) by increasing septal and free wall thickness to normalise the stress. Over a period of training, an athlete can develop a thickened ventricular wall and an associated large stroke volume and a low heart rate. Prior 2012[6] states 'it is an important physiological adaptation which helps athletes perform better.. and may make a good athlete great'. This leads to electrical remodelling and distinct changes in ECG. A study by Riding[7] in 836 asymptomatic athletes found a correlation between body surface area and left ventricular wall thickness, but no athlete had a maximal wall thickness of greater than 13mm and no LV internal diameter in diastole of greater than 65mm. A guide for emergency physicians, giving an overview of the various conditions, was published by Germann et al[8] in 2005.

This report will also include Sudden Arrhythmic Death Syndrome (SADS) which is closely related to SCD. SADS is understood to be sudden death due to cardiac arrest brought on by an arrhythmia in the absence of any structural heart disease. At times, the literature uses the terms interchangeably.

It needs to be borne in mind that the cardiovascular benefits of regular exercise are well established. Individuals exercising regularly have an average life expectancy of 7 years longer than their less active counterparts. So, the risk of life years lost due to inactivity has to be considered alongside the risk of SCD (Sarna[9]).

Screening programmes. A mandatory screening programme was initiated in Italy (Corrado 2003[10]) in 1971 and further defined in 1982. This has led to other screening programmes being developed in other settings, some of which are mandatory (e.g. Israel). The utility of screening programmes that use athlete and related family history and examination continues to be the subject of much debate. The addition of ECG screening in Italy and other countries also remains controversial.

The debate over screening for SCD has passionate and well intentioned supporters on both sides, but there appears to be a lack of compelling evidence.

In addition, there is a perversity that has evolved over the last 30 years in that there is a continual increase in obesity and cardiac morbidity due to lack of habitual exercise, alongside a simultaneous rise in the number of individuals participating in ultra-endurance events. For example, probably more than one million people participate in marathons each year (Sharma 2012[11]).

Methods

A comprehensive search was undertaken of the two main bibliographic databases for health-related research, MEDLINE and EMBASE. The nature of the question for this evidence summary required a sensitive search strategy, which lacked specificity, where the emphasis was on retrieving as much as possible of the relevant literature even if this meant that a large amount of irrelevant material had to be checked through. No filters were used to identify particular study types. The search strategy is available as appendix 1. All records were downloaded into an EndNote X5 database and articles that were clearly not relevant were removed. Many of these were concerning exercise testing for cardiac problems in older people. For the remaining records, the title and abstract were carefully checked and for those considered relevant, the full text of the study was sought. Rapid review methodology was used to appraise the evidence[12]. For this evaluation, a hierarchy of study types were sought based on accepted levels of evidence (SIGN –sign.ac.uk)

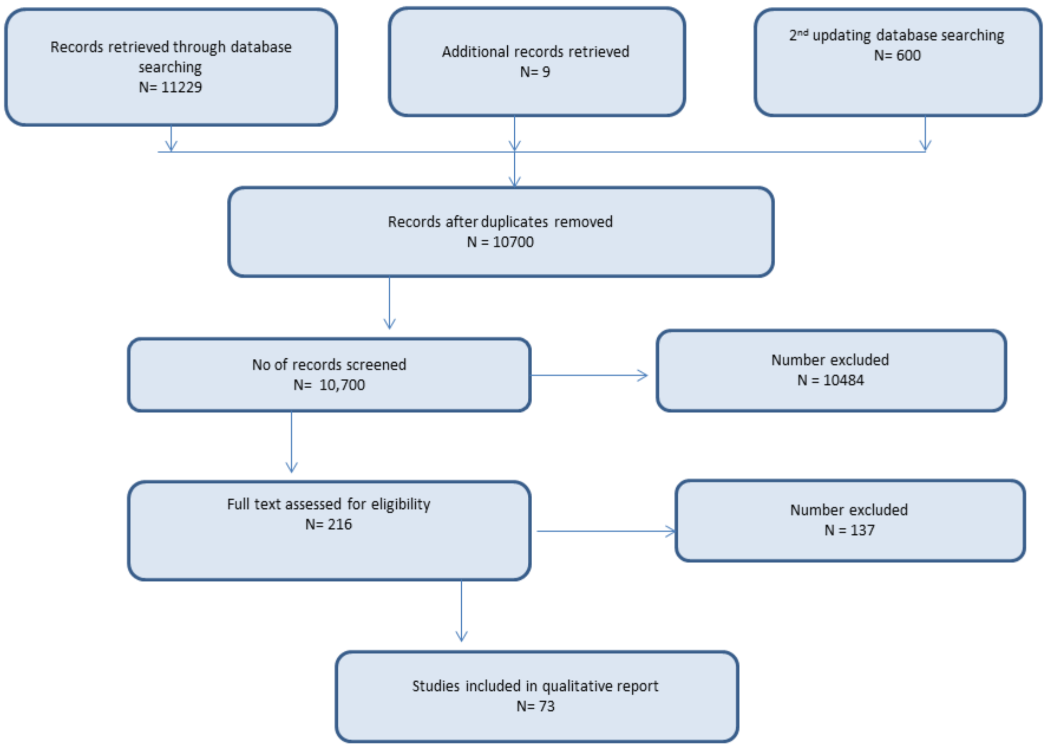
In addition, a number of national sports websites were searched and these organisations were contacted by email requesting policies on screening for SCD. The International guideline library of the Guideline International Network was also searched.

Results of search strategy

The search was completed on March 31st 2013. After duplicates were removed 11,229 records were identified which were imported into the EndNote X5 database. The earliest reports were from 1971. Only reports from 1982 onwards were considered, which covers the most recent 30 years of publication. By removing those which were clearly not relevant based on their title and abstract, a final database of 196 reports was achieved which specifically described an aspect of sudden cardiac death in otherwise healthy young people or athletes. The reports were then examined more closely and single case reports or small case series were eliminated from consideration. Full papers were obtained for 70 studies. The reference lists for these articles were checked and a further 8 studies were identified. Seven review articles were identified (Bille 2006[13], Corrado 2011[14], Drezner 2008[15], Finn 2011[16], Montagnana 2008[2], Pugh 2012[17], Wike 2005[18]) but all were methodologically poor and none fulfilled the basic requirements for a systematic review.

In order to keep the literature search up to date, a second search was conducted in the first week of January 2014. This search yielded a further 605 records after de-duplication; most of which were not relevant. One additional report was identified by the search of the International guideline library. This gave a total of 216 papers that were checked in full, of which 73 papers were selected for inclusion in this report. The flow of records through the search process is presented in the PRISMA flow chart, below.

PRISMA Flow Chart



1. The condition should be an important health problem

2. The epidemiology and natural history of the condition, including development from latent to declared disease, should be adequately understood and there should be a detectable risk factor, disease marker, latent period or early symptomatic stage.

How many deaths occur from sudden cardiac deaths in young people?

Incidence Rates

Sudden cardiac death is stated to be more common in athletes and during or immediately after exercise (ref). Incidence rates for SCD are difficult to define because the number of deaths is small and the total number of young people participating in exercise cannot be estimated precisely. This leads to incidence figures which have wide uncertainty, as shown by wide confidence intervals (CI). In addition, some groups have estimated incidence as events per 100,000 athletes, whereas others use data such as events per 10,000 exercise hours or per 100,000 person years.

It is clear that SCD affects males more than females, with a ratio of approximately 10 male cases to 1 female (Corrado 2011[19]). Although older data gives a ratio of 4 males to 1 female (Guzzo 1996[20]). The baseline incidence of SCD is estimated at 1 in 1000 across the general population but for adolescents and adults younger than 30 years the figure is a hundred fold (i.e. 1 in 100,000) (ACC 2006 [1])

Reported incidence by Country

Reports from 17 countries were identified and used as a basis for identifying incidence or screening policies (de Noronha[21], Elston[22] (UK), Corrado[23] (Italy), ,Marijon[24, 25] (France), Drezner[15], Maron[26] Thompson[27] (USA), Hernelahti[28] (Nordic), Ma[29] (China), Mesihovic -Dinarevic[30] (Bosnia), Pilmer[31] (Canada), Quigley[32] (Ireland), Schmied[33] (Switzerland), Suarez-Mier[34] (Spain) Tester[35] (Singapore), Winkel[36] (Denmark), Yanai[37] (Israel))

- **European Countries.**

Denmark

An incidence for sports-related SCD is estimated at 1.21 (95% CI 0.68-2.00) per 100,000 athlete person years in Denmark by Holst 2010[38]. This team reported a general population (athletes and non athletes) incidence to be 3.76 per 100,000 person years. The authors argue that athletes are not placed at a higher risk by participating in sports

France

A prospective study was performed in France (for those aged 15-75) between 2005 and 2010 (Marijon 2011 [24], Marijon 2013[25]). There were 775 sudden death cases from any cause occurring during moderate to vigorous exercise in the general population i.e sports related. The overall mean incidence was 0.051/100,000 participants (95% CI 0.034-0.068) in women and 1.01/100,000 (95% CI 0.93-1.08) in men. The estimate for the 15-34 year age group is lower with a mean incidence of 0.043/100,000 female participants and 0.5/100,000 male participants. Only 19% of these sudden deaths were related to coronary heart disease

Italy

A 21 year cohort study from the Veneto region of Italy (Corrado 2003[10]) estimated an overall cohort incidence for sudden death of 1 in 100,000 persons per year. The rate among athletes (55 deaths) was 2.3 per 100,000 person years and it was 0.9 per 100,000 person years for non-athletes. The Italian data have been criticised because the number of deaths is far higher than that seen in other geographical areas. There is an argument that the participants in Italy are older and the exercise more intense (Thompson 2007[27]), and others have suggested that the difference is in part due to differences in ethnic and genetic factors (Corrado 2005[39]).

Spain

A study of sudden death during sports was undertaken by Suarez-Mier 2013[34]. This related to some 8862 deaths studied at the Institutio Naciaonal de Toxicology c Ciencias Forenses in Madrid. It was carried out for the period from 1995 to 2012, when there were 168 deaths related to sports, of which 81 were in the 9-35 year age group. Only 3 were competitive athletes.

United Kingdom

In the UK National Audit of Sudden Arrhythmic Death Syndrome[40], the latest report for 2012 states that 47 new cases were added to the database for the 12 month period from February 2012 to January 2013. This brought the total numbers in the database to 364, from a start in July 2008. In the 10-39 year age range, there are 94 males and 71 females (total 165).

An estimate by Elston 2011[22] puts the incidence of SCD in the UK at 1.05 per 100,000 person years, in persons aged 12-35 years and at 4.9 per 100,000 person years for athletes. The authors suggest that the rate is higher due to a larger proportion of males in the athlete group

A UK study by Wilson et al of 1074 national and international junior athletes and 1646 physically active schoolchildren found 9 participants (7 male) with evidence of underlying cardiac disease using a 12 lead ECG (Wilson 2008[41]). The prevalence in junior athletes was 0.5% and it was 0.2% in schoolchildren. None of these cases were symptomatic or had any family history of note.

North America

Canada

A retrospective population-based cohort study was undertaken in Ontario (Pilmer 2013[31]). The study looked at sudden cardiac deaths in those aged 2-40 years, using the 2008 Coroner database. There were 174 cases in a population of 6.6 million. More than 70% of these deaths occurred in the home. Incidence of death increased with age. It was 0.7/100,000 in the 2-18 years range, 2.4/100,000 in the 19-29 years range, and 5.3/100,000 in the 30-40 years range. These data are for all sudden cardiac deaths, and when moderate or vigorous exercise is considered, 33% of the events occurred during exercise in children or adolescents (2-18 years) and 9% during exercise in adults. There were no paediatric deaths during competitive sports.

USA

A USA study (Thompson 2007 [42]) using data from 1995 estimates by Van Camp 1995[43], quotes a rate of one SCD per 133,000 men (0.75 per 100,000) and one SCD per 769,000 women (0.13 per 100,000).

A study by Maron[26] of 1049 sudden deaths due to cardiovascular causes among athletes (out of 1866 sudden cardiac death events) in the USA between 1980 and 2006 was published in 2009. The median age of death was 17 years (range 12-20). Other findings are given in Table 1.

Table 1. Deaths due to SCD for 1049 athletes in USA from 1980-2006

	Number	%
Male	937	89%
White	581	55%
Black	377	36%

Basketball and football	92	68%
Age up to 17 years	677	65%
Age 18-25 years	300	29%
Age 26 years and over	72	7%

SCD occurred most commonly (80% of the deaths) during or just after physical exertion while involved in practice sessions, competition or other sports activities (Maron 2009[26]). There is useful additional data in this study revealing that 416 deaths occurred due to blunt trauma. 65 deaths were due to blunt precordial blows without structural injury leading to commotion cordis. A subsequent update (Maron 2013[44]) estimates a rate of SCD as 0.66/100,000 participants per year, and reports that only a third of SCD were due to diseases that could be reliably detected by the pre-participation programme.

A separate study also based in Minnesota USA (Roberts 2013[45]) reports a much lower incidence: 0.24 per 100,000 athlete years. The authors argue that such an incidence does not warrant ECG screening. It is not clear why these data are so much lower than other reports.

Harmon[46] and colleagues examined the incidence of SCD in National Collegiate Athletic Association athletes from January 2004 to December 2008. During this period, they identified 273 deaths in a total of 1,969,663 athlete participant years. Of these deaths, 187 were due to non-medical or traumatic causes. The incidence of SCD was reported as 1 per 43,770 participants per year. The authors recognise that the incidence is higher than frequently cited estimates and argue that this is due to the range of methodologies used to calculate SCD rates

Accurately assessing the incidence of SCD

Currently, there is a lack of agreed identifiers including reliable identification of the number of deaths, an exact denominator (such as number of athletes), common definitions of the events included and universal definitions of athlete and the population studied (Harmon 2013[46]). The different methodologies currently in use further confuse the picture, make it difficult to compare incidence in different countries or in different populations (for example athletes and non-athletes).

Sheppard 2012[47] argues that the role of the histopathologist is vital in providing a definitive cause of each SCD and to guide the screening management of living relatives. Choi et al[48] argue that active prospective surveillance of the internet provides a means of identifying occurrences of SCD and linking these with coroner reports. This is based on the observation that SCD events in athletes are highly publicised.

Whatever methods are used to assess the incidence, they need to be robust and reliable in order both to determine the size of the problem, the population to which screening should be offered and also to assess accurately the costs of any pre-participation or other type of screening programme.

The literature to guide the advice, guidance, diagnosis or management of an individual picked up at screening is poor. Guidelines for the management of patients with ventricular arrhythmias (not just athletes) are available but are consensus based due to a lack of quality evidence

(ACC/AHA/ESC 2006[1]).Recommendation also exist for athletes with cardiovascular abnormalities covering a wide range of conditions[49]The test

5. There should be a simple, safe, precise and validated screening test.

6. The distribution of test values in the target population should be known and a suitable cut-off level defined and agreed.

8. There should be an agreed policy on the further diagnostic investigation of individuals with a positive test result and on the choices available to those individuals.

What screening tests are available and are they reliable?

Different pre-participation screening strategies for young athletes have been suggested that combine personal history, family history, medical examination and other non-invasive tests including ECG (Shirley 2005[50]).

Two different but strongly held views are promoted, typified by the USA and Italy. The USA approach is a non-mandatory cardiovascular history and medical examination every 4 years during high school and college. Even this level of screening is not standard practice in all States in the USA. ECG is perceived to lead to a high number of false positive results[51]. In Italy, a pre-participation 12 lead ECG is legally mandatory for all athletes in addition to history and examination. Israel has a national policy which is a variation of the Italian policy. These policies are described below. In screening for hypertrophic cardiomyopathy, a series of 9 simple questions was proposed by deWeber 2009[52]:

1. Have you ever passed out or nearly passed out during exercise?

2. Have you ever passed out or nearly passed out after exercise?

3. Have you ever had discomfort, pain, or pressure in your chest during exercise?

4. Does your heart race or skip beats during exercise?

5. Has a doctor ever told you that you have a heart murmur?

6. Has a doctor ever ordered a test for your heart (for example, EKG, echocardiogram)?

7. Has anyone in your family died for no apparent reason?

8. Does anyone in your family have a heart problem?

9. Has any family member or relative died of heart problems or of sudden death before age 50?

What is the sensitivity and specificity of these tests?

Only one study was identified which estimated sensitivity and specificity based on the test as used in Italy. Using a decision tree model, Elston and Stein estimate sensitivity at 88.7% (95% CI 86.6%-90.5%). They estimated specificity at 92.6% (95% CI 92.3%-92.9%). The positive predicted value was 22.5% (95% CI 21.2%-23.8%)[22].

A number of other papers comment on specificity or sensitivity in general or comparative terms[3, 51, 53-55]. Of these only Baggish 2010[51], Maron 1996[3] based their comments on studies which they had conducted; the other comments were based on opinion.

The standardised history and physical exam developed by the American Heart Association (AHA) is considered to have a low sensitivity and specificity in detecting hypertrophic cardiomyopathy and other asymptomatic cardiac diseseases[51, 53, 56]. ECG has low specificity (in the athlete population)as a test because of the physiological changes that intense exercise causes in athletes' hearts[54], however it has been shown to be more sensitive than history and exam alone [53]. An American Heart Association (AHA) group reporting in 2007 (Maron 2007[53]) recognise that their screening programme does not have sufficient sensitivity to detect all cardiovascular abnormalities in young athletes that may lead to death.

The publication of the AHA group report prompted a response from the Italian group. An opinion paper from Pelliccia 2007[57], quoted the Corrado 2006[58] paper. The authors argue that further testing would only be required in 4.8% of the screened population, not 15% as claimed by the AHA group. Finally, Pelliccia et al argue that elite athletes 'are worth it' due to their world visibility and outstanding performances.

There have been no assessments of the accuracy of these tests. This is in part due to the fact that the gold standard would be to analyse the results in people who have died from SCD.

These numbers are very small indeed and would require a huge study population. This is compounded by the fact that SCD is caused by a large number of problems. The test's performance is very unlikely to be the same for each condition.

In fact what is happening is that the tests are being used to pick up people with conditions that *might* lead to SCD. This raises the numbers of screen positive people very significantly indeed: around 1 in 300 are screen positive. (personal communication from CRY). The following table shows the difference between the actual numbers of sudden deaths and the numbers of people identified as being at risk using ECG and health questionnaire. It uses a hypothetical population of 100,000 young people screened per year

Actual deaths from literature in 100,000 young people per year.	**Screen positive (personal communication from CRY)**
2.4[31] (Canada)	330
2-7 per 100,000 (USA)	
3.6 per 100,000 per year[58] (early Italian data)	
4.2 per 100,000 per year[22] (UK)	

The Treatment

10. 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.

Joint guidelines from the American College of Cardiology, the American Heart Association and the European Society of cardiology were published in 2006[1]. These recommend 'that athletes receiving cardiovascular drugs and devices such as pacemakers are generally not allowed to participate in high grade completion. Athletes presenting with syncope or pre-syncope should also not participate until the cause is determined to be both benign and treatable. Athletes with rhythm disorders, cardiac anomalies or syncope should be treated as any other patients.' Recommendations for competitive sports participation in athletes with cardiovascular disease were published by a working group of the European Society of Cardiology in 2005[60]. The recommendations are consensus based providing a comment on whether sports activities should be undertaken or not lis6ted by cardiac condition.

The Screening Programme

13. There should be evidence from high quality Randomised Controlled Trials that the screening programme is effective in reducing mortality or morbidity.

There are no RCTs of screening for SCD but an examination of the literature has shown a variety of programmes underway across sporting organisations and countries.

The United States

Two papers present the USA view. Maron 2007[53] published a scientific statement from the AHA council on nutrition, physical activity and metabolism, a group with 15 members. A later view from the USA National Institutes of Health in young people is presented by Kaltman 2011[61].

Maron and colleagues[53] revisit the 1996 AHA scientific statement and reach the following conclusions:

1. There is no 'zero risk' circumstance in competitive sports.
2. The 1996 AHA recommendations remained virtually unchanged and are presented as Table 2 below, comprising 12 items.

Table 2.
The 12-Element AHA Recommendations for Pre-participation Cardiovascular Screening of Competitive Athletes
Medical history*
Personal history
1. Exertional chest pain/discomfort
2. Unexplained syncope/near-syncope†
3. Excessive exertional and unexplained dyspnea/fatigue, associated with exercise
4. Prior recognition of a heart murmur
5. Elevated systemic blood pressure
Family history

6. Premature death (sudden and unexpected, or otherwise) before age 50 years due to heart disease, in a relative
7. Disability from heart disease in a close relative of 50 years of age or more
8. Specific knowledge of certain cardiac conditions in family members: hypertrophic or dilated cardiomyopathy, long-QT syndrome or other ion channelopathies, Marfan syndrome, or clinically important arrhythmias

Physical examination
9. Heart murmur‡
10. Femoral pulses to exclude aortic coarctation
11. Physical stigmata of Marfan syndrome
12. Brachial artery blood pressure (sitting position)

*Parental verification is recommended for high school and middle school athletes.
†Judged not to be neurocardiogenic (vasovagal); of particular concern when related to exertion.
‡Auscultation should be performed in both supine and standing positions (or with Valsalva manoeuvre), specifically to identify murmurs of dynamic left ventricular outflow tract obstruction.
§Preferably taken in both arms.

From Maron 2007[53]

3. A positive result in one or more of the 12 items may be judged to be sufficient to lead to a referral for a cardiovascular examination. Screening is not mandated by USA law nor has any state mandated the IOC or ESC guidelines. The AHA view is that it neither adopts nor condones the ESC screening recommendations for a routine ECG. In fact, the document recognises that most practitioners would be unable to comply with such a recommendation leading to the potential withdrawal of physicians from the current USA screening programme.
4. Further investigations are only indicated if abnormal findings (as above) are identified.

This group state that there is sufficient evidence to justify a staged implementation with evaluation to assess the values of these tests in a variety of sporting populations. They further note that the impact on mortality seen from the screening in Italy needs to be replicated elsewhere.

A recent study published in 2013 shows that compliance with these USA guidelines is low (Madsen 2013[62]). The team surveyed paediatricians, family physicians and high school athletic directors in Washington USA. Almost 1500 responses were received. Only 6% of all providers and no schools were in compliance with AHA guidelines. Only 6% of the athletic directors who participated reported awareness of the guidelines.

Italian pre-participation screening programme

In 1971, the Italian government announced legislation aimed at providing some medical protection for those citizens who participate in official competitive events, regardless of age (Pelliccia 1995[63], Italian Statutes). It seems that this programme emerged from the 1960 Olympic Games in Rome, leading to a targeted medical programme for elite athletes. The programme was refined by legislation in 1982 (Pelliccia 2006[64], Pelliccia 1995[63]). Under the scheme, all citizens who participate in competitive sports are required to undergo periodic evaluations which involve a general medical and cardiovascular examination with a detailed history of the athlete and their family. In addition, a

12 lead ECG is required. The evaluations are undertaken by licensed physicians in sports medicine who have undertaken a full time post-graduate programme for 4 years. The evaluations take place in both sports clinics and private offices, which can usually be found in any community with a population of 10,000 or more. Those athletes judged to be fit for sports are provided with a certificate of eligibility to participate in competitive sports. Those with a suspicion of cardiovascular disease are referred to a major clinical centre for further evaluation. Some 3 million athletes undergo these examinations each year.

In spite of the legislation, in 1995, Pelliccia and Maron[63] estimated that less than 50% of athletes who were eligible were screened, due to the size of the enterprise and inadequate financial support for the programme.

For elite athletes who may become members of the Italian national team, there is a further level of examination. Approximately 500 athletes per year are referred to the Institute of Sports Medicine and Science in Rome for medical and psychological evaluations before participation in international or national competition. This examination also includes echocardiography. This second level of screening has been funded by lottery monies.

Italian law sets out the scope of cardiovascular screening and if a physician improperly clears an athlete with an abnormality that leads to death, they are deemed to be criminally negligent.

Israel national policy

In 1997, a mandatory pre-participation screening programme for athletes was implemented in Israel (Israel Sports Regulations on Athletes Medical Testing). This law defines athletes as 'individuals who engage in sportive activity at any level of physical endurance'. The screening can only be conducted by certified physicians who have a specialised accreditation. The screening process includes a medical questionnaire, physical exam, resting ECG and 'Bruce-protocol' exercise testing. Medical assessment and ECG is repeated annually. Athletes aged 17-35 years repeat the exercise test every 4 years. Those above this age do so annually. Athletes competing at a national level also have annual exercise tests. Those with abnormal test results are referred to experts. Steinvil et al[65] conducted a systematic search of the two main newspapers in Israel to identify SCD in competitive athletes. There were 24 documented deaths reported from 1985-2009. Most of these were footballers. The authors argue that the drop in deaths seen in the Italian data was also seen in Israel before the initiation of a screening programme. The current SCD rates for Israel are within the range of those reported in other countries. The authors conclude that mandatory ECG screening of athletes in Israel has had no apparent effect on their risk for SCD.

What screening practices are undertaken by national (e.g. Football Association) or by international (e.g. IOC) organisations?

UK Football Association

The following information was provided from the FA in April 2014 by Dr Beasley (Head of Medical Services): ''Through the PFA/FA screening programme we screen approximately 1,200 new scholars (16 year olds) every season. These are usually done in the closed season (May to July) so that the players are all cleared to play for pre-season, but it is not exclusive to just that time, it is an ongoing programme. We also screen any Professional players under the same scheme who have come into the league from non-league clubs, or overseas and have not been offered the opportunity to have a screen whilst they were representing a club at youth level. This is usually around 1,000 mark. On top of this we screen any player who represents England at any level across all of our teams to ensure that we are offering our International players the same level of service that all professional players receive. These numbers are probably around 1,000 (this is a rough guess) per season again. We may well screen more than this over the course of a year, and we are constantly in touch with clubs to ensure a consistent level of service to all players is provided to all Premier League and Football League clubs. All the screen go through an Audit process once we receive copies here to ensure quality control.''

Football Association(FA)

The screening programme been running for 20 years. Screening is carried out by a panel of 8-10 cardiologists. The FA fund the programme which is delivered through the private sector. FA Centre of excellence is St George's Park in Burton which coordinates the process

Size of the programme

1000-1200 screens/year. Twenty-four male and female teams - National teams – England teams

Every participant is screened every 2 years (before national tournaments.) All new 16 years olds are screened but if an abnormal results is reported, a club can take them on anyway. The FA also screens premiership referees

How the screening tests are done

A session of screening would be for 10-12 individuals in one session – often with portable equipment. The sportsperson gets a questionnaire and fills it out before attending screening sessions, the person is then given an ECG and echo.
There are guidelines for reporting normal or abnormal findings and a protocol of what needs further investigation
Occasionally the screening can lead to a borderline result and then panel can discuss. Panel decision to exclude if necessary. The club and players can ignore a positive test (or be excluded) and take their own view

The FA was contacted for screening numbers but do not collect or maintain data on results or exclusions.

Rugby Football Union.

This organisation was contacted but no response was received.

Lawn Tennis Association

The LTA responded as follows: “a cardiac awareness programme has been in place at the LTA since 1994 and currently involves a number of separate but interlinking initiatives, as outlined below.

a. All players joining Team AEGON are offered cardiac screening on a regular basis and CRY come to the NTC to carry screening three or four times a year. The cardiac screening is entirely voluntary but players will be offered repeat screening every two years throughout the time that they are on the elite programme.

b. Key LTA Staff hold First Aid qualifications and this includes some of the premises management team who are on duty at nights and weekends. These individuals are trained in CPR and the use of an AED and 2 AEDS are easily accessible at all times on site (one in main reception and the other in the medical department). The LTA organises CPR and AED retraining sessions annually for their staff

c. All the Tournament Directors of LTA staged competitions have undertaken CPR and AED training and undergo regular retraining. An AED is provided by the LTA at every tournament where an LTA Tournament Director is on duty.”

FIFA World cup referees.

FIFA have developed a pre-competition medical assessment. (FIFA[66],[67]). The assessment covers:

Present and past medical complaints, family history, routine medication, a general physical exam, a detailed cardiovascular exam, 12 lead resting ECG, echocardiography, range of blood tests, detailed musculoskeletal examination covering spinal column, hip groin and thigh, lower leg ankle and foot.

There a short summary assessment with a single overall assessment: Eligibility for competitive football YES/NO.

A pre-competition medical assessment as described above (FIFA) was carried out by experienced physicians for all referees (n= 30) and all assistant referees (n=60) participating in the 2010 FIFA World Cup. Their average age was 39 (range 27-44). A number had underlying pathologies including type 1 diabetes, hypertension and some cardiac issues. Twelve showed suspicious findings on 12 lead resting ECG, but these all proved to be negative on follow up.

A similar exercise was carried out for the 51 female referees and assistants selected for the 2011 FIFA women’s World Cup. No referee was identified as being at risk of SCD during the screening (Keller 2013[68]).

Pre-competition medical assessment is also mandatory for female youth players in all FIFA competitions (Dvorak 2012[69]).

International Olympic Committee (IOC) Consensus statement on periodic health evaluation (PHE) of elite athletes

An IOC expert group convened in 2009 (Ljungqvist 2009[70]) listed nine considerations for designing and implementing periodic health evaluations (PHEs). This group was not required to decide if PHEs should be mandatory. The considerations are précised as follows

1. Must be based on sound evidence.
2. Must be in the primary interest of the athlete.
3. Should be performed by a physician trained in sports medicine ideally the team physician.
4. The nature and scope of the PHE should be appropriate to the nature of the completion and the nature of athlete including age and gender.
5. The PHE should be conducted in an environment that optimises accuracy and ensures privacy.
6. The athlete must give their free and informed consent.
7. If the athlete is deemed to be at serious medical risk they must be discouraged from further training or competition until the necessary measures have been taken.
8. The athlete themselves is responsible for deciding whether to continue training or competition.
9. Any medical certificate should only be issued if the athlete understands both the reason for and the outcome of the PHE. It should only indicate the athlete's fitness or unfitness to participate in further activity.

In its proposal for PHEs, the IOC group recommend that the PHE include:

1. Family history: to determine any cardiovascular problems in one or more relatives.
2. Personal history: to include syncope or near syncope, chest pain, palpitations, shortness of breath, heart sounds and raised blood pressure.
3. Twelve lead ECG: recorded on a non-training day, during rest and following best clinical practice. Any abnormalities to be classified as either most common ECG abnormalities in athletes or less common abnormalities.

Current status of screening in Europe

Table 3 outlines the status of screening in Europe, as identified by Corrado 2011.

Table 3 Pre-participation athletic screening of young competitive athletes in European countries (adapted from Corrado 2008[23] and Corrado 2011[14])

Country	**Medical/Sports Associations**	**Target Athletic Population**	**Screening Protocol**
Belgium	National Sports Federations	Athletes of cycling and motocross sports	History, physical examination, ECG (required)
England	British Lawn Tennis and Football Associations	Competitive athletes	History, physical examination, ECG (required)*

France	National Sports Ministry French Society of Cardiology	Professional athletes of all sports Competitive athletes of all sports	History, physical examination, ECG, echocardiography, exercise testing (required) History, physical examination, ECG (recommended)
Germany	German Association of Sports Medicine, National Sports Federations	Professional athletes of all sports	History, physical examination, ECG, echocardiography, exercise testing (required)
Greece	Hellenic College of Sports Medicine, National Sports Federations	Competitive athletes of all sports	History, physical examination, ECG (recommended)
Italy	National Health System	Competitive athletes	History, physical examination, ECG (required)
Luxembourg	National Sports Ministry, Olympic Medical Committee, National Association of Sports Physicians	Competitive athletes of all sports	History, physical examination, ECG (required)
Netherlands	Working group of Cardiovascular Prevention and Rehabilitation, National Olympic Committee, National Sports Federations, Netherlands Society of Cardiology	Competitive athletes of all sports (age < 35 years) Elite athletes of cycling, motor and flying sports, and diving	History, physical examination, ECG (required) History, physical examination, ECG (required)
Norway	Norwegian Football Association Medical Committee	Professional football athletes	History, physical examination, ECG, echocardiography (required)
Poland	Ministry of Sports and Tourism, Ministry of Health, Polish Cardiac Society, Sports Federations	Competitive athletes (age >23 years) of all sports and national team members	History, physical examination, ECG (required)
Scotland	Government Department of Health	Competitive football athletes (age 16 years)	History, physical examination, ECG (required)
Spain	High Sports Government Council	Competitive athletes of all sports	History, physical examination, ECG (recommended)
Sweden	National Board of Health and Welfare, National Federations of Sports	Elite athletes of all sports	History, physical examination, ECG (recommended)

UK			NSF [71] Quality requirement three: Sudden Cardiac Death. When sudden cardiac death occurs, NHS services have systems in place to identify family members at risk and provide personally tailored, sensitive and expert support, diagnosis, treatment, information and advice to close relatives. (required)
ECG: electrocardiography; competitive athletes: athletes engaged in a regular fashion in exercise training and participating in official athletic competitions as an organized team or individual sport event; elite athletes: athletes of I and II leagues; professional athletes: elite athletes engaged in athletic activities with a labour contract. *Stated to be required but the LTA screening is optional			

The opportunity cost of the screening 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 (ie. value for money). Assessment against this criteria should have regard to evidence from cost benefit and/or cost effectiveness analyses and have regard to the effective use of available resource.

Seven papers report modelling or actual evaluation of costs and or impact and benefits for pre-participation screening to prevent SCD (Elston 2011[22], Halkin 2012[72], Leslie 2012[73], Malhotra 2011[74], Maron 2007[53], Schoenbaum 2012[75], Wheeler 2010[76]). All except one were published in the last three years. Results are presented as costs per life year gained or QALYs (Quality Adjusted Life Years) where available. A sixth paper by Fuller 2000[77] was not included in this section, because the analysis was based on data from 1981.

One study (Elston[22]) is based on UK data. The others are from the USA. All use slightly different assumptions for the economic modelling. They used the standard model of family and personal history with physical exam used in the USA with an added ECG.

Halkin 2012[46] undertook a cost projection study applying the data from the Italian work to the size of the eligible screening population from athletic and high schools in the USA. The authors estimated the cost per life saved to be between US$10.6 million and US$14.4 million. These are the estimated costs per life saved, not costs per year of life saved and such an approach was criticised by Lampert [78] who saw this as a major methodological limitation. One of the main Italian proponents of SCD screening, Pelliccia[79], also responded with a criticism of the costs used by Halkin[46], arguing that these were based on Medicare costs and not on actual screening costs, which may be lower.

Leslie 2012[73] undertook a simulation recording costs (screening, diagnosis, management and treatment) and life years lost caused by mortality from the age of <10 to 75 years. The early age group were schoolchildren on stimulant medications for ADHD and are not reported here. Estimates were made based on three conditions (hypertrophic cardiomyopathy, Wolff-Parkinson White syndrome and Long QT syndrome), so there is no overall estimate of the death rate for SCD. Results are collated in Table 4, below. The authors state that for paediatric screening, the cost effectiveness ratio is unfavourable and that there are opportunities to invest limited health resources in other ways to produce greater population health benefits.

Malhotra 2011[74] determined the cost of a 5-year screening programme at a USA division one college (within National Collegiate Athletics). A screening programme with ECG was conducted over 5 years in 1473 athletes. History and physical exam revealed five significant cardiac abnormalities. ECG with follow up identified a further eight abnormalities. The total cost of the programme was just below US$900,000. Adding ECG increased costs by US$550,000 or US$69,000 for each additional finding. The authors argue that the cost per significant cardiac abnormality did not rise because the ECG programme added cost but identified more abnormalities.

In considering cost effectiveness, the AHA group (Maron 2007[53]) comment that data on this are very limited and express the view that the absolute cost would be enormous. Assuming 10 million high school and middle school athletes and a cost of US$25 for each history and physical plus US$50 for each ECG, the total cost would be US$750 million. Then, assuming that 15% of the athletes require further investigations, estimated at US$500 per case, then a further US$750 million will be required. They add in the costs of administering the programme and the end result is an estimated figure of US$3.4 million for each theoretical death prevented.

Schoenbaum et al[75], based at the USA National Institutes of Health used a Markov model to evaluate the cost effectiveness of three strategies:

1 History and physical exam with an ECG (by cardiologist) only if there were concerns

2. History and physical exam with an ECG routinely (read by specialist) for all. Where concerns were raised during the history and physical, these were referred to a cardiologist

3. History and physical exam with an ECG routinely (read by specialist) for all. When the ECG was positive for a cardiac condition, these were referred to a cardiologist. The modelling covered ages from 14 to 100 years. The authors state that based on a society willingness to pay US$50,000 per QALY, then current screening programmes are not cost effective. Screening based on ECGs (strategy 3) was more favourable but research is needed to improve the quality of the data.

Wheeler 2010[76] looked at the cost effectiveness of a clinical history and physical with or without an ECG. They used a decision model approach and used the rates of SCD reported by Corrado 2006 (Italian data). This group also used a Markov model. The results are presented in the table below. In this case even though the results are above a figure of US$50,000, the authors argue that the cost of history, physical and ECG is reasonable and compares with the cost of dialysis for kidney patients or the provision of public access to defibrillation.

Elston et al[22] 2011 employed a simple decision tree model to evaluate the screening programme used in Italy (history and physical with ECG) and applied this to UK populations of athletes and non-athletes. The population age range was 12-35 years. The authors estimate that without screening, 196 SCDs (95% CI 144-264) would occur in the UK, with 64 of these in athletes. Screening might reduce this by 40 (95% CI 6-74). To achieve this, 1.5 million athletes would need to be screened with 140,000 being referred for further testing and, of these, 31,500 would be disqualified from sport. This relates to 800 athletes prevented from competing to prevent one SCD. The authors further estimate that the number needed to screen (NNS) is 38,000 (95% CI 20,500-267,000) to prevent one SCD. The wide confidence interval reflects the uncertainties in these data. This group did not estimate cost effectiveness.

Table 4 Summary of finding from recent economic estimations

Reference	**Cost per life year gained by addition of ECG**	**Cost per QALY**	**Cost for one averted SCD**
Halkin 2012[72]	Not reported	Not reported	US$10.6 million to US$14.4 million
Leslie 2012[73]	US$91,000 at age 14 years	Not reported	Not reported
Malhotra 2011 [74]	Not reported	Not reported	US$69,000 to find one cardiac abnormality
Maron 2007[53]	Not reported	Not reported	Estimated at $3.4 million for one death prevented
Schoenbaum [75] Strategy 1 (physical exam only)	Not reported	Strategy 1 used as baseline	
Schoenbaum Strategy 2		US$68,800 over strategy 1	131 SCDs averted at a cost of US$900,000 per SCD averted
Schoenbaum Strategy 3		37,700 over strategy 1	127 SCDs averted at a cost of US$600,000 per SCD averted
Wheeler 2010[76]. Cost of history and physical vs no screening	US$199,000	US$301,000	
Wheeler 2010[76]. Addition of ECG to History and physical	US$42,900 at age 16-24	US$61,600	

The research gap

A USA National Institutes of Health report from a National Heart Lung and Blood institute working party have published findings on the research gap for SCD screening. A group of 22 experts largely from the USA with representation from Italy met in April 2010[35]. The expertise was drawn from cardiology and electrophysiology, epidemiology, biostatistics, sports medicine, ethics and screening. They were asked to determine what type of evidence was required and the best methodology to achieve this. They were required to develop a research agenda and identify resources to determine whether screening for SCD would effectively reduce the incidence and add value to health care. Value was defined as 'an improvement in clinical outcomes with an acceptable cost-benefit ratio'.

This group conclude 'there is no direct evidence in a US population that an ECG or any other cardiovascular screening programme will reduce the incidence of SCD in any of the patient populations thought to be at increased risk'.

They recognised the knowledge gaps and suggested the following research proposals:

1. A lack of an accurate estimation of incidence is a major deficiency. They recommended the development of a prospective, population based SCD in the young registry. Details of what should be recorded are given with a statement that it is critical to rule out non cardiac causes of death
2. Due to the lack of knowledge in the epidemiology and aetiology of SCD, they recommended a case control study to facilitate comparisons of epidemiology, anatomical issues and genetic variables.
3. The performance of ECG as a screening tool has not been evaluated in the USA. They recommended pilot ECG screening studies and mention 'an adequately sized cohort' but without giving numbers. They also recommend a centralised ECG interpretation together with a representative sample from across the USA.
4. Recommended development of evidence based guidelines for the management of asymptomatic disease given that early detection does not always lead to improved outcomes
5. They recognised the need for research to assess the impact of screening programmes on individuals and families especially the impact of false positive results.
6. In addition, the group would like to see research that could demonstrate a link between screening and improved outcomes. Ideally, this would be a randomised trial, but given the relative rarity of SCD, it was estimated that a study of 3 million participants would be needed. This is unlikely to be feasible so a form of decision tree analysis was recommended to evaluate the effectiveness and cost of any screening programme.

Finally, the group addressed some of the ethical considerations that will arise from the research proposals. These include the need to contact bereaved family members for a registry scheme and consent from parents of children who died from non-cardiac causes such as a road traffic accident for the case control study.

Other related issues of note

Do athletes report symptoms honestly?

A study of just over 2000 young athletes in Portugal (Providencia[80]) showed that professional athletes reported less cardiac complaints than amateur athletes. The authors argue that this is due to a fear of disqualification. In contrast, amateur athletes with symptoms automatically exclude themselves from sports practice. The authors argue that this scenario reinforces the need for the use of objective tests such as ECG.

Dealing with emergencies

Chandra et al 2013[81] comment that the creation of emergency response plans at sports and athletic venues may improve the outcome of SCD events. They cite Drezner 2006[82], which states that of 36 cases of cardiac arrest with on-site automatic external defibrillators (AEDs), 23 survived to hospital discharge demonstrating the benefit of early defibrillation. However, the Drezner paper states that only one of the five young athletes who suffered a cardiac arrest while playing sport was successfully resuscitated. These numbers are too small to draw reliable conclusions. There is an increased interest in positioning of automatic external defibrillators in public places and at sports facilities. While they can be readily seen in public places on mainland Europe, widespread adoption in the UK has been slow.

Conclusions

It is always regrettable that young people die whatever the circumstances. Sudden cardiac death in the young is a tragic if rare event and the impulse to act to reduce these events is understandable. However there are serious limitations in the literature on quite fundamental issues relating to the condition, the test, the intervention and the cost effectiveness of screening.

This evidence summary highlights the disparity across publications on these topics, with different denominators for young athletes without clear definitions of the term athlete. However some general conclusions can be drawn.

Incidence and economic data

In Europe, where data are available, the reported rate is approximately one death per 100,000 participants per year, except for Italy which has reported rates of 2.3 per 100,000. The USA reports rates of 0.24-1.0 per 100,000. All these data are for males. The rate in females is lower (e.g. 0.13 per 100,000 in the USA). The incidence is difficult to assess due to a variety of definitions. Some figures come from studies in competing athletes, while others are for elite athletes. Some of the data comes from mortality surveys and other data is drawn from screening. Surveys are conducted over different time periods using a variety of metrics to report data. In addition, rates seem to vary from country to country and it is not clear if this is due to genetic variations or, more likely, methods of acquiring the data. It appears from some country data that the incidence of SCD for those participating in sports is lower than that in a general population of the same age range and gender.

All this makes a reliable estimate of the rate of SCD and the impact of screening with or without ECG difficult to estimate. The likelihood is that this will range between the lowest estimates for the cost per life saved of £350,000 (US$600,000) and the highest estimate of £8,500,000 (US$14,400,000). There were little data estimating QALYs (Quality Adjusted Life Years) and what does exist is considerably higher than the generally accepted level of £20,000 per QALY for interventions. As a comparator, UK screening for bowel cancer is estimated to cost approximately £15,000 per QALY (Whyte 2012[83]).

A fundamental difference is between the North American approach of a screening questionnaire, family history and a physical exam and the Italian approach which is to add in an ECG. Until a reliable evidence base is gathered this dichotomy is likely to remain and the issue of cost and benefit will remain unresolved..

References

1. Zipes DP, Camm AJ, Borggrefe M, Buxton AE, Chaitman B, Fromer M, et al. ACC/AHA/ESC 2006 guidelines for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: a report of the American College of Cardiology/American Heart Association Task Force and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Develop guidelines for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death) developed in collaboration with the European Heart Rhythm Association and the Heart Rhythm Society. Europace. 2006;8(9):746-837.
2. Montagnana M, Lippi G, Franchini M, Banfi G, Guidi GC. Sudden cardiac death in young athletes. Internal Medicine. 2008;47(15):1373-8.
3. Maron BJ, Shirani J, Poliac LC, Mathenge R, Roberts WC, Mueller FO. Sudden death in young competitive athletes. Clinical, demographic, and pathological profiles. Jama. 1996;276(3):199-204.
4. Fishbein MC. Cardiac disease and risk of sudden death in the young: the burden of the phenomenon. Cardiovasc Pathol. 2010;19(6):326-8.
5. Huston TP, Puffer JC, Rodney WM. The athletic heart syndrome. N Engl J Med. 1985;313(1):24-32.
6. Prior DL, La Gerche A. The athlete's heart. Heart. 2012;98(12):947-55. Epub 2012/05/26.
7. Riding NR, Salah O, Sharma S, Carre F, O'Hanlon R, George KP, et al. Do big athletes have big hearts? Impact of extreme anthropometry upon cardiac hypertrophy in professional male athletes. BJSM online. 2012;46 Suppl 1:i90-7.
8. Germann CA, Perron AD. Sudden cardiac death in athletes: a guide for emergency physicians. American Journal of Emergency Medicine. 2005;23(4):504-9.
9. Sarna S, Sahi T, Koskenvuo M, Kaprio J. Increased life expectancy of world class male athletes. Med Sci Sports Exerc. 1993;25(2):237-44. Epub 1993/02/01.
10. Corrado D, Basso C, Rizzoli G, Schiavon M, Thiene G. Does sports activity enhance the risk of sudden death in adolescents and young adults? Journal of the American College of Cardiology. 2003;42(11):1959-63. Epub 2003/12/10.
11. Sharma S, Zaidi A. Exercise-induced arrhythmogenic right ventricular cardiomyopathy: fact or fallacy? European Heart Journal. 2012;33(8):938-40. Epub 2011/12/14.
12. Khangura S, Konnyu K, Cushman R, Grimshaw J, Moher D. Evidence summaries: the evolution of a rapid review approach. Systematic reviews. 2012;1:10. Epub 2012/05/17.
13. Bille K, Figueiras D, Schamasch P, Kappenberger L, Brenner JI, Meijboom FJ, et al. Sudden cardiac death in athletes: the Lausanne Recommendations. Eur J Cardiovasc Prev Rehabil. 2006;13(6):859-75.
14. Corrado D, Drezner J, Basso C, Pelliccia A, Thiene G. Strategies for the prevention of sudden cardiac death during sports. Eur J Cardiovasc Prev Rehabil. 2011;18(2):197-208.
15. Drezner JA, Chun JSDY, Harmon KG, Derminer L. Survival trends in the United States following exercise-related sudden cardiac arrest in the youth: 2000-2006. Heart Rhythm. 2008;5(6):794-9.
16. Finn SE, Coviello J. Myocardial infarction & sudden death in recreational master marathon runners. Nurse Pract. 2011;36(2):48-53.
17. Pugh A, Bourke JP, Kunadian V. Sudden cardiac death among competitive adult athletes: a review. Postgrad Med J. 2012;88(1041):382-90.
18. Wike J, Kernan M. Sudden cardiac death in the active adult: causes, screening, and preventive strategies. Curr Sports Med Rep. 2005;4(2):76-82.

19. Corrado D, Schmied C, Basso C, Borjesson M, Schiavon M, Pelliccia A, et al. Risk of sports: do we need a pre-participation screening for competitive and leisure athletes? Eur Heart J. 2011;32(8):934-44.
20. Guzzo J, Nanda K. Sudden cardiac Death. Primary care Update. 1996;3(4):130-4.
21. de Noronha SV, Sharma S, Papadakis M, Desai S, Whyte G, Sheppard MN. Aetiology of sudden cardiac death in athletes in the United Kingdom: a pathological study. Heart. 2009;95(17):1409-14.
22. Elston J, Stein K. Public health implications of establishing a national programme to screen young athletes in the UK. BJSM online. 2011;45(7):576-82.
23. Corrado D, Basso C, Schiavon M, Pelliccia A, Thiene G. Pre-participation screening of young competitive athletes for prevention of sudden cardiac death. Journal of the American College of Cardiology. 2008;52(24):1981-9.
24. Marijon E, Tafflet M, Celermajer DS, Dumas F, Perier M-C, Mustafic H, et al. Sports-related sudden death in the general population. Circulation. 2011;124(6):672-81.
25. Marijon E, Bougouin W, Perier M-C, Celermajer DS, Jouven X. Incidence of sports-related sudden death in France by specific sports and sex. Jama. 2013;310(6):642-3.
26. Maron BJ, Doerer JJ, Haas TS, Tierney DM, Mueller FO. Sudden deaths in young competitive athletes: analysis of 1866 deaths in the United States, 1980-2006. Circulation. 2009;119(8):1085-92.
27. Thompson PD, Levine BD. Protecting athletes from sudden cardiac death. Jama. 2006;296(13):1648-50.
28. Hernelahti M, Heinonen OJ, Karjalainen J, Nylander E, Borjesson M. Sudden cardiac death in young athletes: time for a Nordic approach in screening? Scand J Med Sci Sports. 2008;18(2):132-9.
29. Ma JZ, Dai J, Sun B, Ji P, Yang D, Zhang JN. Cardiovascular pre-participation screening of young competitive athletes for prevention of sudden death in China. J Sci Med Sport. 2007;10(4):227-33.
30. Mesihovic-Dinarevic S, Kulic M, Kreso A. Cardiovascular screening in young athletes in Sarajevo Canton. Bosn. 2010;10(3):227-33.
31. Pilmer CM, Porter B, Kirsh JA, Hicks AL, Gledhill N, Jamnik V, et al. Scope and nature of sudden cardiac death before age 40 in Ontario: a report from the cardiac death advisory committee of the office of the chief coroner. Heart Rhythm. 2013;10(4):517-23.
32. Quigley F. A survey of the causes of sudden death in sport in the Republic of Ireland. British Journal of Sports Medicine. 2000;34(4):258-61.
33. Schmied C, Notz S, Cribari M, Gahwiler R, Keller DI, Luscher TF. Cardiac pre-competiton screening in Swiss athletes. Current situation in competitive athletes and short-time assessment of an exemplary local screening program. Swiss Med Wkly. 2012;142:w13575.
34. Suarez-Mier MP, Aguilera B, Mosquera RM, Sanchez-de-Leon MS. Pathology of sudden death during recreational sports in Spain. Forensic Science International. 2013;226(1-3):188-96.
35. Tester GJ, Watkins GG, Rouse I. The Sports Challenge international programme for identified 'at risk' children and adolescents: a Singapore study. Asia-Pacific journal of public health / Asia-Pacific Academic Consortium for Public Health. 1999;11(1):34-8.
36. Winkel BG. Sudden cardiac death in young Danes. Dan Med J. 2012;59(2):B4403.
37. Yanai O, Phillips ED, Hiss J. Sudden cardiac death during sport and recreational activities in Israel. Journal of Clinical Forensic Medicine. 2000;7(2):88-91.
38. Holst AG, Winkel BG, Theilade J, Kristensen IB, Thomsen JL, Ottesen GL, et al. Incidence and etiology of sports-related sudden cardiac death in Denmark--implications for preparticipation screening. Heart Rhythm. 2010;7(10):1365-71.
39. Corrado D, Pelliccia A, Bjornstad HH, Vanhees L, Biffi A, Borjesson M, et al. Cardiovascular pre-participation screening of young competitive athletes for prevention of sudden death: proposal for a common European protocol. Consensus Statement of the Study Group of Sport Cardiology of the Working Group of Cardiac Rehabilitation and Exercise Physiology and the Working Group of

Myocardial and Pericardial Diseases of the European Society of Cardiology. European Heart Journal. 2005;26(5):516-24. Epub 2005/02/04.
40. HSCIC. National Audit of Sudden Arrthythmic Death Syndrome 2012. Leeds UK: 2013.
41. Wilson MG, Basavarajaiah S, Whyte GP, Cox S, Loosemore M, Sharma S. Efficacy of personal symptom and family history questionnaires when screening for inherited cardiac pathologies: the role of electrocardiography. British Journal of Sports Medicine. 2008;42(3):207-11. Epub 2007/08/25.
42. Thompson PD, Franklin BA, Balady GJ, Blair SN, Corrado D, Estes NA, 3rd, et al. Exercise and acute cardiovascular events placing the risks into perspective: a scientific statement from the American Heart Association Council on Nutrition, Physical Activity, and Metabolism and the Council on Clinical Cardiology. Circulation. 2007;115(17):2358-68.
43. Van Camp SP, Bloor CM, Mueller FO, Cantu RC, Olson HG. Nontraumatic sports death in high school and college athletes. Med Sci Sports Exerc. 1995;27(5):641-7. Epub 1995/05/01.
44. Maron BJ, Haas TS, Ahluwalia A, Rutten-Ramos SC. Incidence of cardiovascular sudden deaths in Minnesota high school athletes. Heart Rhythm. 2013;10(3):374-7.
45. Roberts WO, Stovitz SD. Incidence of sudden cardiac death in Minnesota high school athletes 1993-2012 screened with a standardized pre-participation evaluation. Journal of the American College of Cardiology. 2013;62(14):1298-301.
46. Harmon KG, Asif IM, Klossner D, Drezner JA. Incidence of sudden cardiac death in national collegiate athletic association athletes. Circulation. 2011;123(15):1594-600.
47. Sheppard MN. Aetiology of sudden cardiac death in sport: a histopathologist's perspective. BJSM online. 2012;46 Suppl 1:i15-21.
48. Choi K, Pan YP, Pock M, Chang RKR. Active surveillance of sudden cardiac death in young athletes by periodic internet searches. Pediatric Cardiology. 2013;34(8):1816-22.
49. Anon. 36th Bethesda Conference. Eligibility Recommendations for Competitive Athletes with Cardiovascular Disorders. J Am Coll Cardiol. 2005;45(8):1313-75.
50. Shirley KW, Adirim TA. Sudden cardiac death in young athletes. Clinical Pediatric Emergency Medicine. 2005;6(4):194-9.
51. Baggish AL, Hutter AM, Jr., Wang F, Yared K, Weiner RB, Kupperman E, et al. Cardiovascular screening in college athletes with and without electrocardiography: A cross-sectional study. Ann Intern Med. 2010;152(5):269-75.
52. deWeber K, Beutler A. Hypertrophic cardiomyopathy: ask athletes these 9 questions. J Fam Pract. 2009;58(11):576-84. Epub 2009/11/07.
53. Maron BJ, Thompson PD, Ackerman MJ, Balady G, Berger S, Cohen D, et al. Recommendations and considerations related to preparticipation screening for cardiovascular abnormalities in competitive athletes: 2007 update: a scientific statement from the American Heart Association Council on Nutrition, Physical Activity, and Metabolism: endorsed by the American College of Cardiology Foundation. Circulation. 2007;115(12):1643-455.
54. Mahmood S, Lim L, Akram Y, Alford-Morales S, Sherin K, Committee APP. Screening for sudden cardiac death before participation in high school and collegiate sports: American College of Preventive Medicine position statement on preventive practice. Am J Prev Med. 2013;45(1):130-3.
55. Papadakis M, Sharma S. Electrocardiographic screening in athletes: the time is now for universal screening. Br J Sports Med. 2009;43(9):663-8.
56. Corrado D, Basso C, Schiavon M, Pelliccia A, Thiene G. Pre-participation screening of young competitive athletes for prevention of sudden cardiac death. J Am Coll Cardiol. 2008;52(24):1981-9.
57. Pelliccia A. The preparticipation cardiovascular screening of competitive athletes: is it time to change the customary clinical practice? Eur Heart J. 2007;28(22):2703-5. Epub 2007/10/30.
58. Corrado D, Basso C, Pavei A, Michieli P, Schiavon M, Thiene G. Trends in sudden cardiovascular death in young competitive athletes after implementation of a preparticipation screening program. JAMA. 2006;296(13):1593-601.
59. Maron BJ. Sudden death in young athletes. N Engl J Med. 2003;349(11):1064-75.

60. Pelliccia A, Fagard R, Bjornstad HH, Anastassakis A, Arbustini E, Assanelli D, et al. Recommendations for competitive sports participation in athletes with cardiovascular disease: a consensus document from the Study Group of Sports Cardiology of the Working Group of Cardiac Rehabilitation and Exercise Physiology and the Working Group of Myocardial and Pericardial Diseases of the European Society of Cardiology. Eur Heart J. 2005;26(14):1422-45.
61. Kaltman JR, Thompson PD, Lantos J, Berul CI, Botkin J, Cohen JT, et al. Screening for sudden cardiac death in the young: report from a national heart, lung, and blood institute working group. Circulation. 2011;123(17):1911-8. Epub 2011/05/04.
62. Madsen NL, Drezner JA, Salerno JC. Sudden cardiac death screening in adolescent athletes: an evaluation of compliance with national guidelines. BJSM online. 2013;47(3):172-7.
63. Pelliccia A, Maron BJ. Preparticipation cardiovascular evaluation of the competitive athlete: perspectives from the 30-year Italian experience. American Journal of Cardiology. 1995;75(12):827-9. Epub 1995/04/15.
64. Pelliccia A, Di Paolo FM, Corrado D, Buccolieri C, Quattrini FM, Pisicchio C, et al. Evidence for efficacy of the Italian national pre-participation screening programme for identification of hypertrophic cardiomyopathy in competitive athletes. Eur Heart J. 2006;27(18):2196-200. Epub 2006/07/13.
65. Steinvil A, Chundadze T, Zeltser D, Rogowski O, Halkin A, Galily Y, et al. Mandatory electrocardiographic screening of athletes to reduce their risk for sudden death proven fact or wishful thinking? Journal of the American College of Cardiology. 2011;57(11):1291-6. Epub 2011/03/12.
66. Bizzini M, Schmied C, Junge A, Dvorak J. Precompetition medical assessment of referees and assistant referees selected for the 2010 FIFA World Cup. BJSM online. 2012;46(5):374-6.
67. Thunenkotter T, Schmied C, Grimm K, Dvorak J, Kindermann W. Precompetition cardiac assessment of football players participating in the 2006 FIFA World Cup Germany. Clinical Journal of Sport Medicine. 2009;19(4):322-5.
68. Keller DI, Bizzini M, Feddermann N, Junge A, Dvorak J. FIFA Women's World Cup 2011: pre-competition medical assessment of female referees and assistant referees. BJSM online. 2013;47(3):179-81.
69. Dvorak J, Grimm K, Schmied C, Junge A. Feasibility of precompetition medical assessment at FIFA World Cups for female youth players. BJSM online. 2012;46(16):1132-3.
70. Ljungqvist A, Jenoure P, Engebretsen L, Alonso JM, Bahr R, Clough A, et al. The International Olympic Committee (IOC) Consensus Statement on periodic health evaluation of elite athletes March 2009. British Journal of Sports Medicine. 2009;43(9):631-43. Epub 2009/09/08.
71. DH. NSF for Coronary Heart Disease. Chapter 8 Arrhythmias and Sudden Cardiac Death. 2005.
72. Halkin A, Steinvil A, Rosso R, Adler A, Rozovski U, Viskin S. Preventing sudden death of athletes with electrocardiographic screening: what is the absolute benefit and how much will it cost? J Am Coll Cardiol. 2012;60(22):2271-6.
73. Leslie LK, Cohen JT, Newburger JW, Alexander ME, Wong JB, Sherwin ED, et al. Costs and benefits of targeted screening for causes of sudden cardiac death in children and adolescents. Circulation. 2012;125(21):2621-9.
74. Malhotra R, West JJ, Dent J, Luna M, Kramer CM, Mounsey JP, et al. Cost and yield of adding electrocardiography to history and physical in screening Division I intercollegiate athletes: a 5-year experience. Heart Rhythm. 2011;8(5):721-7.
75. Schoenbaum M, Denchev P, Vitiello B, Kaltman JR. Economic evaluation of strategies to reduce sudden cardiac death in young athletes. Pediatrics. 2012;130(2):e380-9.
76. Wheeler MT, Heidenreich PA, Froelicher VF, Hlatky MA, Ashley EA. Cost-effectiveness of preparticipation screening for prevention of sudden cardiac death in young athletes. Annals of Internal Medicine. 2010;152(5):276-86.

77. Fuller CM. Cost effectiveness analysis of screening of high school athletes for risk of sudden cardiac death. Med Sci Sports Exerc. 2000;32(5):887-90.
78. Lampert R, Myerburg RJ. The true incremental cost of ECG screening: the price is not right, but the cost appears effective. J Am Coll Cardiol. 2013;61(14):1553-4.
79. Pelliccia A. Is the cost the reason for missing the ECG advantages? J Am Coll Cardiol. 2012;60(22):2277-9.
80. Rui Providencia RA, Silva J, Barra S, Gomes PL, Seca L, Costa M, et al. Cardiac assessment of athletes: Can we trust the results of pre-participation questionnaires? European Journal of Cardiovascular Prevention and Rehabilitation. 2011;1):S30.
81. Chandra N, Bastiaenen R, Papadakis M, Sharma S. Sudden cardiac death in young athletes: practical challenges and diagnostic dilemmas. J Am Coll Cardiol. 2013;61(10):1027-40.
82. Drezner JA, Rogers KJ. Sudden cardiac arrest in intercollegiate athletes: detailed analysis and outcomes of resuscitation in nine cases. Heart Rhythm. 2006;3(7):755-9.
83. Whyte S, Chilcott J, Halloran S. Reappraisal of the options for colorectal cancer screening in England. Colorectal disease : the official journal of the Association of Coloproctology of Great Britain and Ireland. 2012;14(9):e547-61. Epub 2012/03/07.

Appendix 1: Search strategy

1st search

Sudden cardiac death search results. March 31st 2013

Database searched	Date searched	Number of results
MEDLINE (OVID) 1950 to 22/03/13	29/03/13	5017
EMBASE (OVID) 1974 to 2013 week 2013 week 12	29/03/13	8515
Total		**13532**
After de-duplication		**11229**

2nd search

Sudden cardiac death search results – Updated search (December 2013)

Database searched	Date searched	Number of results
MEDLINE (OVID) March 2013 to 27/12/13	30/12/13	202
EMBASE (OVID) March 2013 to 2013 week 52	30/12/13	521
Total		**723**
After de-duplication		**605**

MEDLINE (OVID)

1 Mass Screening/ (76695)
2 screen*.tw. (391119)
3 Diagnosis/ (16316)
4 "Diagnostic Techniques and Procedures"/ (2075)
5 diagnos*.tw. (1435958)
6 identif*.tw. (1603770)
7 test*.tw. (1870885)
8 prevalence.tw. (318581)
9 incidence*.tw. (453307)
10 ((systemat* or opportunist* or target* or population or mass) adj2 assess*).tw. (7721)
11 Electrocardiography/ (158164)
12 Electrocardiography, Ambulatory/ (8511)
13 electrocardiogram*.tw. (30810)
14 electrocardiograph*.tw. (34907)
15 ecg.tw. (42441)
16 ekg.tw. (2159)

17 holter.tw. (7603)
18 event monitor*.tw. (656)
19 or/1-8 (4594979)
20 exp Death, Sudden/ (27194)
21 exp Heart Arrest/ (31333)
22 exp Cardiopulmonary Resuscitation/ (10479)
23 exp Tachycardia, Ventricular/ (11627)
24 exp Heart Failure/ (80285)
25 exp Myocardial Infarction/ (139435)
26 exp Ventricular Fibrillation/ or exp cardiomyopathy hypertrophic/ (25370)
27 exp Mortality/ (259685)
28 resuscitUS$.tw. (38159)
29 asystolUS$.tw. (2873)
30 ((cardiac or heart or cardiopulmUS$ or ventricUS$) adj5 (tachycardUS$ or arrest or fibrillatUS$ or fluttUS$ or arrhythmUS$)).tw. (75448)
31 exp death/ (109833)
32 death.tw. (400597)
33 mortality.tw. (392230)
34 or/20-33 (1194745)
35 19 and 34 (374859)
36 limit 35 to ("adolescent (13 to 18 years)" or "young adult (19 to 24 years)" or "adult (19 to 44 years)") (135800)
37 exp Exercise Movement Techniques/ or Exercise/ (65499)
38 exp Sports/ (102774)
39 (sport* or exercise*).tw. (200117)
40 or/37-39 (287812)
41 36 and 40 (5600)
42 surgery.tw. (668919)
43 cancer*.tw. (921225)
44 41 not (42 or 43) (5017)

EMBASE (OVID)

1 Mass Screening/ (49266)
2 screen*.tw. (538543)
3 Diagnosis/ (911063)
4 "Diagnostic Techniques and Procedures"/ (67152)
5 diagnos*.tw. (2036270)
6 identif*.tw. (2113610)
7 test*.tw. (2510922)
8 prevalence.tw. (437977)
9 incidence*.tw. (625936)
10 ((systemat* or opportunist* or target* or population or mass) adj2 assess*).tw. (10771)
11 Electrocardiography/ (130617)
12 Electrocardiography, Ambulatory/ (130617)
13 electrocardiogram*.tw. (39996)
14 electrocardiograph*.tw. (43603)
15 ecg.tw. (65039)
16 ekg.tw. (4016)
17 holter.tw. (11219)
18 event monitor*.tw. (977)
19 or/1-8 (6655152)
20 exp Death, Sudden/ (35653)
21 exp Heart Arrest/ (42503)
22 exp Cardiopulmonary Resuscitation/ (62574)
23 exp Tachycardia, Ventricular/ (25445)
24 exp Heart Failure/ (266130)

25 exp Myocardial Infarction/ (254574)
26 exp Ventricular Fibrillation/ or exp hypertrophic cardiomyopathy/ (39112)
27 exp Mortality/ (592125)
28 resuscitUS$.tw. (52134)
29 asystolUS$.tw. (4154)
30 ((cardiac or heart or cardiopulmUS$ or ventricUS$) adj5 (tachycardUS$ or arrest or fibrillatUS$ or fluttUS$ or arrhythmUS$)).tw. (105179)
31 exp death/ (411960)
32 death.tw. (542468)
33 mortality.tw. (549098)
34 or/20-33 (1865537)
35 19 and 34 (618463)
36 limit 35 to ("adolescent (13 to 18 years)" or "young adult (19 to 24 years)" or "adult (19 to 44 years)") [Limit not valid in Embase; records were retained] (618463)
37 exp Exercise Movement Techniques/ or Exercise/ (207348)
38 exp Sports/ (89385)
39 (sport* or exercise*).tw. (275605)
40 or/37-39 (404692)
41 36 and 40 (23078)
42 surgery.tw. (935423)
43 cancer*.tw. (1286117)
44 41 not (42 or 43) (20523)
45 limit 44 to (adolescent <13 to 17 years> or adult <18 to 64 years>) (8515)

Appendix 2: Support Groups

Cardiac Risk in the Young (CRY) (http://www.c-r-y.org.uk/index.htm)

Cardiac Risk in the Young (CRY) was established in 1995 in the UK to raise awareness of the conditions that can lead to sudden cardiac death. It does this by raising awareness of these conditions and promoting screening for those aged 14-35 years. It runs regular clinics around the UK providing an ECG with interpretation by a cardiologist. The screening is generally free of charge being funded by external groups. CRY also lobby for the introduction of medical screening for the young. They have produced a detailed booklet on SCD which is available on the website (CRY booklet). In addition, there is a linked website providing support to relatives of SCD or SADS (http://www.sads.org.uk/about_sads.htm).

Parent Heart Watch Group (http://www.parentheartwatch.org/Home.aspx)

Parent Heart Watch, inaugurated in the USA in 2005, is a national network of parents, families and partners dedicated to reducing Sudden Cardiac Arrest (SCA) in youth. Its aims are to inform, educate, advocate, and implement nationwide programs related to its mission. It was established by parents who had lost a child to SCD.