

## Assessment of the 12-Lead ECG as a Screening Test for Detection of Cardiovascular Disease in Healthy General Populations of Young People (12–25 Years of Age)

### A Scientific Statement From the American Heart Association and the American College of Cardiology

*Endorsed by the Pediatric and Congenital Electrophysiology Society and American College of Sports Medicine*

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Sudden death (SD) of young people because of a variety of complex, predominantly genetic/congenital cardiovascular diseases is a riveting, devastating event and a public health and policy issue of increasing concern.<sup>1–6</sup> The reliable identification of such individuals at risk for SD has become a major focus of the cardiovascular community for a number of reasons, including the opportunity to reduce SD events through selective disqualification from sports<sup>7</sup> and the primary prevention of SD with the implantable cardioverter-defibrillator for some high-risk patients with genetic

heart diseases.<sup>8–14</sup> In addition, those SDs caused by underlying and unsuspected genetic or congenital cardiovascular diseases that occur in young trained athletes are a highly visible issue and have become a concern in both the public arena and the physician community.<sup>15–17</sup>

Consequently, the desire to screen populations theoretically at risk for cardiovascular disease to reduce morbidity and mortality is understandable in principle, and few would empirically argue against the potential benefit of this practice for some individuals. However, a debate has

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emerged regarding whether the conditions responsible for these tragic events can be detected effectively in populations of various sizes by the available testing and examination techniques, and specifically, there is debate concerning which strategies are potentially the most reliable to separate those individuals with disease from those who are probably unaffected.<sup>15–29</sup>

Most of this dialogue concerning SD prevention has been limited to the screening of young populations of competitive athletes, and the available data specifically related to cardiovascular screening efficacy (on which we largely and unavoidably rely) overwhelmingly come from such populations exclusively composed of trained athletes. Periodically, this has become a polarized controversy and public health debate, triggering a large and growing body of literature, including clinical studies... but notably also an array of recent editorials, opinion pieces, proclamations, and reviews on both sides of the question, often without the advantage of new primary data.<sup>15–86</sup> Most of these come from Italian investigators (n=19) and others (n=14), who suggest that the ECG is a reliable and economically feasible diagnostic test, some prematurely pronouncing a paradigm shift,<sup>49,78</sup> whereas others appear contradictory<sup>49,85</sup>; other statements have come from an American Heart Association (AHA) science advisory<sup>87</sup> and a report from the National Institutes of Health.<sup>23</sup> Indeed, the issue of preparticipation athlete screening for cardiovascular disease has become the subject of discussion in a number of countries, including the United States,\* Italy,<sup>4,18,31</sup> Israel,<sup>28,29,31,92,93</sup> Germany,<sup>94</sup> Sweden,<sup>95</sup> the United Kingdom,<sup>60,96</sup> China,<sup>97</sup> the Netherlands,<sup>98</sup> France,<sup>99</sup> Norway,<sup>58</sup> Denmark,<sup>5,100</sup> Japan,<sup>101,102</sup> Switzerland,<sup>103</sup> and Spain.<sup>104</sup>

The present discussion defines cardiovascular screening as an initiative intended to prospectively identify or raise suspicion of previously unrecognized and largely genetic or congenital cardiovascular diseases known to cause sudden cardiac arrest and SD in young people.<sup>3,105</sup> This has become a highly visible and vigorously debated topic, because the SD risk associated with intense physical activity (in the setting of potentially life-threatening but occult cardiovascular disease) potentially could be modified by withdrawal from a competitive athletic lifestyle<sup>18</sup> and could even be preventable in high-risk patients by prophylactic treatment interventions (eg, implantable cardioverter-defibrillators).<sup>8–14</sup> The writing group believes that it has achieved a comprehensive and balanced portrayal of the highly visible but complex topic of population screening for cardiovascular disease in young people.

### New Scope of the Document

Although reports on cardiovascular screening efficacy have predominantly involved populations of adolescents and young adults participating in competitive athletics, the context of the present discussion is intentionally (and necessarily) much more expansive. Therefore, it is underscored that the present report is not limited in scope to universal mass screening for athlete populations but importantly includes considerations for screening large, young, and truly general populations

(school-aged, 12–25 years old, of both sexes) with respect to relevant logistical, ethical, legal, and societal issues (eg, in the United States or other countries or communities of various sizes, in schools, or in regional or military populations). In the United States, this potential screening population would comprise ≈60 million young people nationally, including as many as an estimated 10 million competitive athletes (7.5 million interscholastic athletes and 500 000 intercollegiate athletes).<sup>2,3,25,55,106</sup>

The theoretical aspiration to screen the entire 12- to 25-year-old population of the United States for cardiovascular disease with ECGs would be an undertaking of enormous magnitude, with massive resource demands, in a population that may be at lower risk than one confined to athletes.<sup>107</sup>

Indeed, systematic cardiovascular screening (beyond periodic preventive health evaluation<sup>5</sup> in recreational athletes and the general adolescent and young adult populations) has not been recommended or pursued previously, and such evaluations typically have been reserved for patients with symptoms suspected to be of cardiovascular origin. On the other hand, the fact that screening has been limited to competitive athletes in the past does not in principle itself justify the future exclusion of youthful nonathletes from screening for lethal cardiovascular disease. Therefore, it appears only logical and fair that when relatively small athlete populations are targeted for screening, at least some consideration should be given to extending this screening to nonathletes in the same jurisdiction and venue.

Finally, this discussion does not specifically address the care provided to healthy individual subjects in an office practice. This represents a much different screening alternative within the US healthcare system, which is restricted by the cost of such examinations generally not reimbursed by insurance carriers (in the absence of suspected disease).

### Screening With the ECG

The 12-lead ECG has been a widely used test to diagnose cardiovascular disease, particularly acute myocardial infarction, in clinic- and hospital-based practice for ≈70 years. Recently, the ECG has been promoted vigorously as a screening test to detect or raise suspicion of predominantly genetic/congenital cardiac disease specifically in large populations of young trained athletes, including consideration for programs in entire countries.†

The present AHA statement represents a detailed critique of the available evidence both for and against the ECG as a screening test to systematically detect cardiovascular disease in large general populations of young people (including national initiatives), as well as in more limited screening venues. The document also evaluates the relative merits of the ECG compared with standard history-taking and physical examination for cardiovascular screening.

This question of screening ECGs in the young has become increasingly relevant, largely by virtue of the reduced mortality rates in competitive athletes reported specifically from the Veneto region of northeastern Italy, which the Italian investigators have attributed to routine screening ECGs.<sup>4,15</sup>

\*References 3, 15, 20, 22, 24–26, 59, 62, 64, 88–91.

†References 4, 5, 16, 18, 19, 21, 28, 31, 32, 36, 45, 49, 57, 62, 78.

Furthermore, in 2005, the European Society of Cardiology (ESC) formally recommended and has strongly promoted national screening initiatives with ECGs (limited to athletes) to other countries in Europe and the United States.<sup>5</sup> Notably, the discussion of such mass screening initiatives and models has come to be regarded as complex by virtue of (1) the low prevalence of cardiovascular diseases responsible for SD in the young population, (2) the low risk of SD among those with these diseases, (3) the large sizes of the populations proposed for screening, and (4) the imperfection of the 12-lead ECG as a diagnostic test in this venue.

Echocardiography, although not a primary subject of the present discussion, does harbor advantages for clinical diagnosis of certain conditions, such as hypertrophic cardiomyopathy (HCM).<sup>108</sup> However, neither echocardiography nor cardiovascular magnetic resonance has been considered seriously as a primary cardiac imaging strategy or modality for large-scale universal preparticipation screening because of impracticality, cost, and interobserver variability.<sup>109</sup> Echocardiograms, nevertheless, are an important part of second-tier examinations that frequently occur when screening ECGs or other clinical findings are judged abnormal.<sup>2,3,17,55,109</sup>

Both AHA<sup>3</sup> and ESC<sup>5</sup> consensus panels have agreed previously that screening to detect cardiovascular abnormalities in asymptomatic young competitive athletes is justifiable in principle on ethical, legal, and medical grounds. Reliable exclusion of cardiovascular disease by such screening may provide a large measure of reassurance to this specific population of young people and their families. However, the US and AHA position against national mandatory screening ECGs of athletes in the United States has periodically been the source of strong reaction and criticism from some investigators.<sup>16,27,39,43,62,77,110</sup> In addition, the question has arisen of whether such a mass screening program with ECGs is ethically defensible if confined to only 1 segment of the population when others may also be at risk.

### Background of US Screening Programs

Although rare, SDs in young people are nonetheless tragic, devastating events. Consequently, the detection of silent predominantly genetic/congenital cardiovascular conditions responsible for SD is an objective consistent with a benevolent and compassionate society. In the past, participants in competitive sports have been preferentially targeted for such screening programs, apparently because of their unique, physically active lifestyle.<sup>4-7,107</sup> Indeed, in the United States, there is a long-standing (>50 years) customary practice of systematic preparticipation screening required for participation in most organized youth and sanctioned high school, college, and professional sports, principally by use of history-taking and physical examination.<sup>20,22,111</sup> Of note, similar mass examination initiatives have not been advocated for the much larger general population of children, adolescents, and young adults who may not participate in organized sports activities, and therefore, there are virtually no data from such cohorts regarding the detection of cardiovascular disease.

In 1996 and again in 2007, the AHA provided consensus recommendations for such evaluations specifically in competitive athletes,<sup>3,105,112</sup> defined as those who participate in an

organized team or individual sport that requires regular competition against others as a central component, places a high premium on excellence and achievement, and requires some form of systematic (and usually intense) training.<sup>7,113</sup> Twelve elements (now 14) of the personal and family history and physical examination were recommended as part of a comprehensive medical questionnaire to be used as a guide to examiners conducting preparticipation examinations (Table 1), although the precise penetrance of these guidelines into various levels of clinical practice is uncertain.<sup>114</sup> Other societies have also formulated useful guidelines for the preparticipation history and physical examination.<sup>115</sup>

In the United States, the preparticipation screening process has lacked a measure of standardization, including in the selection of examiners, who have traditionally included professionals from a variety of disciplines with different levels of training and expertise (eg, physicians, nurse practitioners, physician assistants, and chiropractors in a minority of the states), often participating as volunteers.<sup>3,20,22</sup> Physicians

**Table 1. The 14-Element AHA Recommendations for Preparticipation Cardiovascular Screening of Competitive Athletes**

Medical history*	
Personal history	
1.	Chest pain/discomfort/tightness/pressure related to exertion
2.	Unexplained syncope/near-syncope†
3.	Excessive and unexplained dyspnea/fatigue or palpitations, associated with exercise
4.	Prior recognition of a heart murmur
5.	Elevated systemic blood pressure
6.	Prior restriction from participation in sports
7.	Prior testing for the heart, ordered by a physician
Family history	
8.	Premature death (sudden and unexpected, or otherwise) before 50 y of age attributable to heart disease in ≥1 relative
9.	Disability from heart disease in close relative <50 y of age
10.	Hypertrophic or dilated cardiomyopathy, long-QT syndrome, or other ion channelopathies, Marfan syndrome, or clinically significant arrhythmias; specific knowledge of genetic cardiac conditions in family members
Physical examination	
11.	Heart murmur‡
12.	Femoral pulses to exclude aortic coarctation
13.	Physical stigmata of Marfan syndrome
14.	Brachial artery blood pressure (sitting position)§

AHA indicates American Heart Association.

\*Parental verification is recommended for high school and middle school athletes.

†Judged not to be of neurocardiogenic (vasovagal) origin; of particular concern when occurring during or after physical exertion.

‡Refers to heart murmurs judged likely to be organic and unlikely to be innocent; auscultation should be performed with the patient in both the supine and standing positions (or with Valsalva maneuver), specifically to identify murmurs of dynamic left ventricular outflow tract obstruction.

§Preferably taken in both arms.

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responsible for screening are most often from the primary care and sports medicine disciplines but may also include a variety of other medical or surgical specialists (but rarely with specific cardiovascular training).

However, more recently, cardiologists have become more involved with the care of athletes, mostly at the elite level. This practice contrasts sharply with the Italian model,<sup>116</sup> in which screening is performed by a cadre of specially trained primary care–sports medicine physicians dedicated to examining all athletes in the national program, as well as being responsible for disqualification decisions.<sup>4,5,18</sup>

### Cardiovascular Causes and Epidemiology of SD in the Young

The causes of SD in the age group addressed here have been well documented, although based primarily on studies in the competitive athlete population, often in the form of large registries and forensic databases.<sup>1,2,4–6,117–122</sup> There is no evidence at present that the specific causes of SD differ significantly in nonathletes.

The causes of SD in trained US athletes 12 to 35 years of age have been reported in a consistent fashion since 1980.<sup>1,2,6,117,120–123</sup> A heterogeneous variety of mostly congenital/genetic diseases ( $\approx 20$ ) are responsible for these events, with HCM<sup>1–3,6,7,117,122,124–125a</sup> being the single most common cause of SD, constituting approximately one third of cases.<sup>1,2,6,117,119,125</sup> Congenital coronary anomalies (most commonly those of wrong sinus origin) are responsible for 15% to 20%, with several other diseases each being responsible for  $\approx 5\%$  or less, including myocarditis, valvular heart disease (eg, mitral valve prolapse, aortic stenosis), dilated cardiomyopathy, ruptured aortic aneurysm, premature atherosclerotic coronary artery disease, and arrhythmogenic right ventricular cardiomyopathy/dysplasia (ARVC/D), as well as a variety of other congenital heart malformations. A small proportion of these deaths (2%–3%) are not associated with structural cardiac abnormalities at autopsy, including Wolff-Parkinson-White preexcitation, ion channelopathies, and sickle cell trait. Other causes not directly related to preexisting cardiovascular disease include bronchial asthma, ruptured cerebral aneurysm, use of performance-enhancing or other drugs and substances, heat stroke, and pulmonary embolus.

The mechanism of death in the vast majority of these events is a ventricular tachyarrhythmia, with the major exception being Marfan syndrome and related disorders associated with aortic dilatation, in which SD usually occurs because of aortic dissection/rupture.

SDs occur in a wide variety of sports, most commonly football and basketball in the United States and soccer in European countries. There is considerable gender bias in these events, with a male to female ratio of  $\approx 9:1$  at all levels of competition,<sup>1,2,7,37,117,125–129</sup> and with occurrence reported in a number of racial/ethnic groups, including whites, blacks, Asians and Hispanics.<sup>1,2,6,117,120–122,125–127</sup> Similarly, SD risk was 30-fold less in females than males during recreational sports in a national study from France.<sup>128</sup>

Notably, the pathology of SD reported in trained athletes from the Veneto region of Italy<sup>4,18</sup> differs substantially from the experience elsewhere.<sup>1,2,6,117,119,125</sup> Paradoxically, ARVC/D

(very uncommon in the US data) is uniquely positioned as the most frequent and important single cause of these SDs in Veneto, possibly because of a unique genetic substrate.<sup>4,14,31,130,131</sup> Atherosclerotic coronary artery disease is also relatively common in Veneto, whereas HCM (the most common cause of SD in US registries)<sup>1,2,6,117,122</sup> is a rare cause of these deaths in the Italian (Veneto) experience.

Long-standing screening efforts in athletes in the United States, Italy, and Israel have been predicated on the rationale that individuals engaged in competitive sports represent a special subset of the general population who are at significantly higher risk for SD than individuals of similar age who are not involved in such athletic activities and lifestyle.<sup>6,26,31,107,117</sup> Such an assertion has been used to justify screening initiatives that target only competitive athletes. However, although the premise that SD caused by underlying (and unsuspected) cardiovascular disease is more common with engagement in intense physical exertion is intuitive and supported by some data,<sup>6,107</sup> this issue remains incompletely resolved.

Comparative data and evidence supporting this presumption that athletes are at greater risk than nonathletes comes largely from Veneto, where competitive athletes had a relative risk for SD of 2.5- to 4.5-fold compared with noncompetitive recreational sports participants or nonathletes of similar age.<sup>4,107</sup> Also, the National Collegiate Athletic Association (NCAA) study by Harmon et al<sup>126</sup> inferred greater risk for college athletes in particular sports but did not include a direct comparison to nonathletes and was devoid of forensic data to confirm the true cardiovascular cause of death.

Therefore, we wish to underscore that SDs attributable to unsuspected genetic/congenital cardiovascular diseases are not limited or largely confined to trained athletes. Rather, it is likely that the absolute number of these SD events is higher in the larger population of young people who have not elected to engage in organized sports and may not have a particularly vigorous athletic lifestyle. Indeed, an estimated 10% to 15% of 12- to 25-year-olds participate in organized sports competition, and it is very likely that the majority of those who die suddenly of HCM or other cardiovascular diseases do so unassociated with competitive athletic lifestyles.<sup>106</sup>

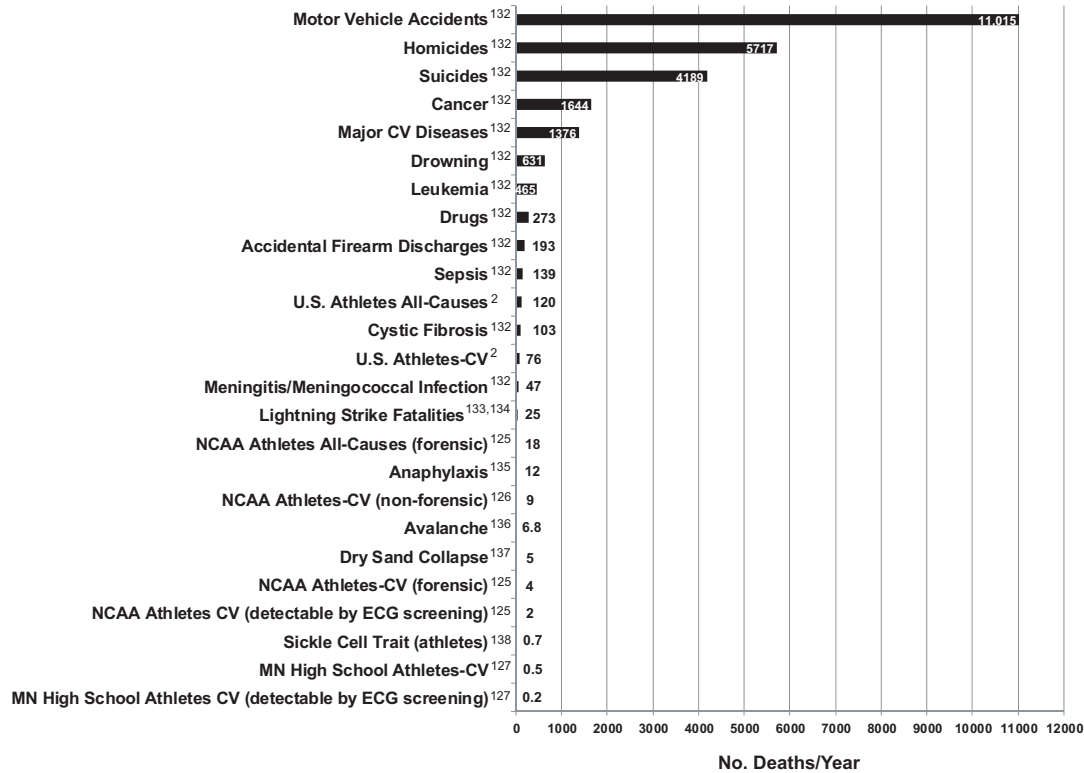
SDs in nonathletes do not receive the same intense media exposure and scrutiny as athletes, which probably accounts for the misperception that such events are less common among them. Indeed, a large prospective, epidemiological, general population study from France showed SDs in young noncompetitive or recreational athletes were  $>15$ -fold more frequent than in competitive athletes; only 6% of sports-related cardiac arrests occurred in competitive situations (10 SDs per million per year), whereas  $>90\%$  took place in recreational settings.<sup>99</sup>

## Magnitude of the Problem

### Young Competitive Athletes

Most data describing the magnitude of cardiovascular SDs in young people come from healthy competitive athlete populations characterized by different levels of training and achievement, as well as various ethnic origins. Based on the preponderance of available evidence from both absolute death rates and incidence figures, assembled largely in high school





**Figure.** Comparative frequencies of death attributable to all causes in young individuals aged <25 years. CV indicates cardiovascular; MN, Minnesota; and NCAA, National Collegiate Athletic Association.

and college-aged competitive athletes, SD events attributable to underlying cardiovascular disease can be considered a relatively low event rate phenomenon.‡

Although incidence rates are important in assessing relative risk in a given population, absolute death rates are also useful in quantifying the overall magnitude of a public health problem. For example, absolute annual death rates have been accessed from the long-standing US National Registry of Sudden Death in Athletes,<sup>2,6,117</sup> which has tabulated >2500 events in young people 8 to 39 years of age over a 33-year period, recording about 75 cardiovascular deaths in a given year. All-cause mortality in athletes, including from blunt trauma, commotio cordis, drugs, and heat stroke, has averaged ≈115 deaths per year.<sup>2</sup> These data are consistent with estimates from other countries. For example, in Denmark, with a population of 5.6 million, ≈2 such cardiovascular deaths are reported annually, equivalent to 110 deaths per year if extrapolated to the US population.<sup>100</sup>

It is important to place into proper perspective these absolute numbers of SDs, because the frequency of these events is a very important variable in the screening debate. Cardiovascular deaths in young athletes in the United States each year are much less frequent than virtually all other causes of death in the same age group<sup>25,125</sup> (Figure). Motor vehicle accidents are the leading cause of death in the young, ≈2500-fold more common than events during sports, and many are linked to alcohol consumption or cellular phone distraction and therefore are largely preventable.<sup>139</sup> For example, in an analysis of NCAA athletes, 3-fold more deaths were caused by accidents than by cardiovascular disease over the same

time period.<sup>126</sup> Furthermore, SDs attributable to cardiovascular disease in young athletes in the United States occur at an annual rate similar to lightning strike fatalities (Figure). In another study,<sup>125</sup> confirmed cardiovascular SDs occurred with a frequency similar to those largely preventable deaths that were attributable to suicide or drug use in NCAA athletes.

Mortality incidence data (expressed as athlete-participation years or person-years) is a crucial element in the dialogue over ECGs and screening, supporting the assertion that cardiovascular deaths related to competitive athletic activities are essentially rare events. A recent 26-year survey (1986–2011) of Minnesota high school athletes reported an incidence of cardiovascular-related deaths of 1 in 150000 per academic year (0.7/100000 person-years).<sup>127</sup> These figures are consistent with data from US high school and collegiate athletes (1:200000, 0.53/100000 person-years),<sup>120</sup> the US National Registry of Sudden Death in Athletes (1:100000, 0.61/100000 person-years),<sup>2</sup> a 12-year survey of Minnesota high school athletes based on obligatory insurance claims (1:200000, 0.5/100000 person-years),<sup>129</sup> young competitive athletes in Minnesota from 1993 to 2004 (1:110000, 0.93/100000 person-years),<sup>130</sup> NCAA athletes with forensic data (1:83000, 1.2/100000 person-years),<sup>125</sup> and athletes in Veneto (1:110000, 0.87/100000 person-years; 1993–2004),<sup>130</sup> as well as young (not necessarily athletic) residents of Olmsted County, Minnesota (1.3/100000 person-years)<sup>140</sup> or Ontario, Canada (1.0/100000 person years),<sup>140a</sup> and young Danish athletes (1.2/100000 person-years).<sup>100</sup>

Mortality rates in college (NCAA) athletes appear to exceed somewhat those in high school student-athletes, possibly because of longer exposure to training. However, mortality rates in college student-athletes are significantly lower

‡References 2, 25, 54, 99, 100, 120, 125, 127, 129, 130.

when studies include postmortem data that establish cardiovascular diagnoses<sup>125</sup> than when the precise cause of SD is unknown (1.1/100 000 versus 2.3/100 000 person-years).<sup>126</sup> Finally, there is no evidence that SDs due to genetic/congenital heart disease in young populations (athletes or nonathletes) have increased in frequency over time.

The reported incidence of 4.3 per 100 000 person-years in Veneto at the time screening ECGs were initiated in 1982 (and presumably largely attributable to ARVC/D) is by far the highest reported from any population.<sup>4</sup> This incidence is almost 2-fold greater than the rate of athlete deaths in Israel (2.6/100 000 person-years), evident both before and after enactment of mandatory screening ECGs legislation.<sup>28</sup> A rate comparable to that in Israel has only been reported in US college (NCAA) athletes by Harmon et al<sup>126</sup> based on 9 deaths per year among 400 000 participants but without autopsy confirmation of the causes of cardiovascular death.<sup>141</sup>

A more recent study in NCAA student-athletes with a more expansive time window and forensic (postmortem) confirmation of the causes of death reported a much lower cardiovascular SD rate of 4 deaths per year, which suggests that the cardiovascular SD rate in NCAA athletes had been overestimated previously by >100%.<sup>125</sup> The 2 studies in the literature that reported the highest cardiovascular SD rate in athletes (>2/100 000 person-years; ie, from Israel<sup>28</sup> and from Harmon et al<sup>126</sup> in NCAA athletes) failed to document the diseases or precise causes of SDs (because of the absence of autopsy data),<sup>141</sup> and therefore, it is not possible to know precisely which (or how many) deaths were actually attributable to cardiovascular diseases or potentially identifiable by screening ECGs.

### Limitations

Because mandatory reporting systems for SDs in young people (including athletes) do not exist in the United States or most other countries, analyses of event frequency (the numerator) are usually highly dependent on accounts in the public record, from the Internet, or from personal communications for the identification of events that provide important epidemiological and clinical information,<sup>§</sup> and this could result in an underestimation of the true mortality rate. In addition, in retrospective population surveys, it is difficult to establish precisely the size of the at-risk populations (the denominator). Therefore, the prevalence and incidence figures relied on in these heterogeneous populations can only be considered reasonable estimates of SD frequency.

Each of the population studies that calculates mortality rates and incidence is imperfect; such studies are encumbered by certain not unexpected limitations and design flaws for determining the absolute number of events (numerator) and the at-risk population (denominator), not the least of which are the different methodologies used for data acquisition in various countries. All of this justifies the scrutiny provided here. Therefore, the writing group recognizes the potential value, but difficult task, of establishing additional registries that reliably document the numerator (SD events) and the denominator (at-risk population) in young people (athletes and nonathletes alike).

The writing group also acknowledges that the public health issue of SD in young people cannot be viewed solely from the perspective of its relatively low incidence. By emphasizing the low SD incidence, we do not wish to suppress interest in secondary prevention treatment strategies that could further reduce the occurrence of these tragic events, ie, enhanced early resuscitation/defibrillation programs and wider dissemination of automated external defibrillators proven to be effective in the management of sudden cardiac arrest on the athletic field.<sup>24,64,142–145</sup>

The unexpected and counterintuitive deaths of young and apparently healthy people, potentially with decades of productive life ahead of them, deserve our full attention. The infrequency of these events in no way mitigates their importance or impact on families and the community. However, it should also be underscored that the unexpected nature of these tragedies on the athletic field magnifies the public perception of their incidence, particularly when a highly visible athlete is involved.

Notably, the visibility and intense media focus on SDs specifically in athletes may have created the erroneous impression that these tragic events are far more common than their actual frequency, or even the misconception that such deaths are virtually confined to athletes. Such misperceptions have legitimized screening initiatives limited to athletes, in turn perhaps diverting resources from the many other important public health issues for this age group, including but not confined to preventable accidents or other causes such as drug abuse, childhood obesity, and suicide intervention (Figure). Indeed, in a 10-year study of US college athletes, Maron et al<sup>125</sup> found suicide and drugs to be as frequently responsible for SD as cardiovascular disease. Although SD caused by cardiovascular disease in young people engaged in competitive sports is a significant public health concern, its relatively low incidence could limit the overall priority for universal primary prevention screening (Figure).

### Public Access Competitive Sports

There have been multiple studies tabulating SD event rates in long-distance running (including the marathon), as well as the triathlon.<sup>144–147</sup> Unlike those in sanctioned high school and college sports, these athletes are usually older adults who participate of their own volition and are most likely to have unsuspected coronary artery disease as the cause of SD, although occasionally HCM or congenital coronary anomalies are responsible.<sup>144–147</sup> Mandatory or mass screening in this athlete population is impractical given the thousands of participants annually, with disqualification for detected cardiovascular disease an unenforceable policy. By convention, participation in such sports has been the prerogative and responsibility of the adult athlete, who accepts the inherent risks of serious injury or death during athletic competition.

SD/cardiac arrest event rates are reported to be  $\approx$ 0.5 per 100 000 marathon competitors, with fatalities in recent events less common because of the greater availability of automated external defibrillators on the race course.<sup>145</sup> In triathlon competition (which includes distance running up to the marathon distance), 1 study reported a higher SD rate of 1.5 per 100 000 participants, with 90% of the events occurring during the swimming segment.<sup>144</sup>

§References 1, 2, 6, 117, 122, 123, 125, 127, 129.

### Professional Athletes

The relatively small number of participants in professional sports (probably ≈5000 in the United States, including major and minor league competition) are unique competitive athletes in several respects. Professional athletes are primarily of adult age (>21 years of age), well compensated for their services with employment contracts, and part of organizations with financial resources for screening beyond those of high schools and college athletic departments.<sup>111</sup> Predraft diagnostic testing with ECGs occurs in ≈90% of the 122 major professional sports teams operating in North America, but routine echocardiography is uncommon (only 15% of teams).<sup>111</sup> The most extensive routine screening is conducted by the National Basketball Association, including history-taking and physical examination and the performance of an ECG, echocardiography, and stress testing.<sup>111</sup> To the best of our knowledge, there are no data documenting the frequency with which potentially lethal cardiovascular abnormalities are identified in professional athletes through systematic screening. However, a cluster of 3 highly visible SD events caused by HCM occurred in professional football, basketball, and hockey during a brief 4-month period (in 2005) in the United States.<sup>148</sup>

Olympic athletes are essentially professionals in many countries. We are unaware of any athlete who has died suddenly of cardiovascular disease during Olympic or world championship competition, and the prevalence of potentially lethal cardiovascular disease at this elite level of competition is undoubtedly low. Nevertheless, the International Olympic Committee and those of several European countries have recommended or adopted testing with ECGs for Olympic candidates,<sup>98,103,149</sup> as has FIFA (Fédération Internationale de Football Association), the international governing body of soccer.<sup>150</sup> Routine screening with ECGs is not required for US Olympic team members.

### Screening Experiences in General Populations of Nonathletes

The few available data estimating the incidence or prevalence of SD in young people in large general populations (not confined to athletes) suggest that mortality rates generally exceed those reported for competitive athletes. Specifically, out-of-hospital cardiac arrest incidence has been reported variously as 6.4 per 100 000 person-years<sup>151</sup> and 3.2 per 100 000 person-years<sup>152</sup> in the pediatric population and 2.3 per 100 000 person-years in a pediatric and young adult population,<sup>153</sup> and the SD rate in the general youthful population of Denmark is 3.76 per 100 000 person-years.<sup>100</sup> The prospective Oregon Sudden Unexpected Death Study<sup>154</sup> reported an incidence of 1.7 per 100 000 person-years among children and adolescents aged 10 to 17 years over 3 years, when extrapolated to the overall US population is equivalent to ≈500 deaths per year, a number significantly higher than that reported from the US National Registry of Sudden Death in Athletes.<sup>2</sup>

Notably, the nonathletes reported from Veneto had the lowest cardiovascular mortality rate reported in a general population (0.79 per 100 000 person-years<sup>4</sup>), but similar to rates in trained athletes in US high schools and colleges,<sup>120</sup> the US National Registry of Sudden Death in Athletes,<sup>2</sup> and data from both Minnesota and Veneto during the 11-year time-frame from 1993 to 2004,<sup>130</sup> as

well as data from Olmsted County, MN, residents.<sup>140</sup> In Denmark there was no difference in the incidence of sudden death between noncompetitive and competitive athletes, both of which were significantly lower than in the general population.<sup>154a</sup>

### Military Personnel

Because engagement in the military is a highly physical enterprise, SD rates attributable to unsuspected cardiovascular disease are often compared with those in trained athletes.<sup>155,156</sup> Sudden nontraumatic cardiac death among active duty military generally occurs at higher rates than in trained athletes, probably because intensive, prolonged exertion is performed under extreme environmental conditions, often by previously untrained individuals; rates are 6.7 per 100 000 person-years in men (1.4/100 000 person-years in women), with 40% of these events temporally related to exertion according to data from a comprehensive US Department of Defense registry.<sup>156</sup> The most common cause of SD among active duty military personnel <35 years of age is premature atherosclerotic coronary artery disease (23% of cases), followed by HCM (12% of cases), but SD is unexplained in a large proportion of cases (40%).

Screening for cardiovascular disease (and other conditions) is usually mandatory for military recruits. For example, each applicant to the US military completes a screening questionnaire and undergoes a physical examination. ECGs are performed only selectively as guided by history, symptoms, or physical findings.<sup>157</sup> However, ECGs are a routine part of medical screening in candidates for aviation duty and in soldiers >40 years old.<sup>158</sup> From Italy, Nistri et al<sup>159</sup> reported on a military screening program from 1992 to 1996 that included history-taking, physical examination, and routine performance of a 12-lead ECG. Among 34 910 conscripts >17 years old, 8% had abnormalities that prompted further evaluation. Of those studied with echocardiography because of an abnormal ECG, 0.7% (n=19) had a new diagnosis of HCM.

### Sudden Infant Death Syndrome

The relation between sudden infant death syndrome (SIDS) and long-QT syndrome (LQTS) was first proposed by Maron et al.<sup>160</sup> Schwartz et al instituted ambitious screening studies with 12-lead ECGs of >30 000 healthy neonates in the first week of life, who were followed up for 1 year,<sup>161</sup> and subsequently a study of almost 45 000 neonates at 15 to 25 days of life.<sup>162</sup> A prolonged QT interval was strongly associated with SIDS, and LQTS mutations in the sodium channel<sup>163–165</sup> were found most commonly in those SIDS infants with longer corrected QT interval values.<sup>166</sup> Therefore, neonatal screening ECGs have been suggested as a means of identifying some cases of LQTS as a cause of SIDS, but this strategy has been controversial.<sup>167</sup> It appears likely that only a small minority of SIDS cases can be linked to LQTS.<sup>164,165</sup> Although the available data suggest that neonatal LQTS can be detected by screening,<sup>162</sup> these studies have failed to demonstrate that lives are saved by this strategy.

### School-Aged Children

Relatively few screening programs have focused on the 1- to 12-year-old age group. The 1973 Japanese School Health Law mandated cardiovascular screening with modified ECG



and history/physical examination for thousands of children in the first, seventh, and tenth grades.<sup>101,102,168</sup> However, few relevant disease-related data have emerged from this initiative given that a variety of generally minor cardiovascular abnormalities or arrhythmias without underlying organic heart disease were identified in only 2% to 3% of children.

### Other Screening Initiatives

Sickle cell trait (HbS) is present in 8% of blacks (and 0.08% of nonblacks), occasionally in association with exercise-related cardiovascular collapse and SD, and often in association with rhabdomyolysis in military recruits and competitive athletes (predominantly college football players).<sup>138</sup> Unlike SD attributable to underlying cardiovascular disease and ventricular tachyarrhythmia, sickle cell trait–related collapse probably results from a more gradual deterioration and cascade of events, with intravascular sickling leading to vascular occlusion, endothelial damage, and impaired blood flow to muscles, which can promote ischemic rhabdomyolysis and disseminated intravascular coagulation.<sup>138,169</sup>

In 2010, the NCAA mandated sickle cell trait screening (with solubility testing) for all student-athletes in Division I sports.<sup>170</sup> This program was created as part of a legal settlement with Rice University and the NCAA filed by the family of a college football player who died of exertional sickling with rhabdomyolysis at age 19 years.<sup>170</sup> Also, all blacks and others are tested routinely for sickle cell trait at birth since 1987, following a recommendation from the National Institutes of Health.<sup>171</sup>

Concerns have been raised regarding the NCAA screening program, including potential infringement on individual privacy and liberty and the effects of such testing on self-image and employability in professional sports.<sup>170</sup> As yet, there are no data that support sickle cell trait testing as lifesaving, although awareness has been raised regarding this potential problem in sports. Although affected athletes are not disqualified from sports, modified conditioning methods have been widely used by college athletic programs to prevent sickle cell trait events. In selected cases, athletes with sickle cell trait have decided not to participate in competition at high-altitude locations.<sup>138</sup>

### Screening Medical History and Physical Examination

There is general agreement that conducting a comprehensive screening personal and family history and physical examination is useful; however, data supporting the efficacy of such a screening strategy alone are limited. Available evidence shows that the personal/family history, as part of the preparticipation examination, is relatively insensitive in identifying (or raising suspicion of) cardiovascular abnormalities, including many of the diseases responsible for SD in competitive athletes (ie, false-negatives).<sup>82,173</sup> In 1 retrospective study of competitive athletes who died suddenly after screening with standard history and physical examination, <5% had a confirmed cardiovascular diagnosis during life.<sup>174</sup>

The relative weakness of the history and physical examination for screening can also be traced to other factors. For example, with ion channelopathies and Wolff-Parkinson-White syndrome, only the ECG potentially defines the clinical phenotype, and the physical examination is unremarkable. For many of the structural cardiac diseases responsible for SD, symptoms, family history of heart disease, and loud pathological heart murmurs are infrequent findings. One potential exception is HCM, in which a systolic heart murmur (indicative of left ventricular outflow obstruction) should be audible at rest in 25% of individuals and in an additional 50% with performance of the Valsalva maneuver or in the standing position.<sup>3,175</sup> Also, at-risk individuals may fail to disclose potentially important symptoms such as syncope or chest pain.<sup>173</sup>

Nevertheless, it should be underscored that an important proportion of adolescents and young adults at risk for SD with primary structural or electrophysiological cardiac abnormalities may have warning signs and symptoms (eg, syncope) or a positive history of heart disease potentially detectable by careful evaluation, although nonetheless misinterpreted or disregarded by medical providers.<sup>72,95,173</sup> Furthermore, all examiners, particularly those in primary care, are often faced with difficult decisions of whether potentially important findings from the history and physical examination such as heart murmurs (which are often functional in nature) or symptoms such as chest pain (common in adolescents and often difficult to interpret) should receive sufficient weight to warrant an expensive cardiovascular referral and evaluation.<sup>173</sup> This often becomes a dilemma for examiners, given that the vast majority of such individuals are likely to be unaffected, and the finding will be benign. Although the 12-lead ECG can be regarded as more sensitive than the history and physical,<sup>91,98,104,172</sup> it is nevertheless associated with reduced specificity because of false-positive results.<sup>17,24,25,55,64,65,88,91</sup> However, the acknowledged insensitivity of the history and physical examination screening cannot be considered a major justification for mass screening of general populations with ECGs.

Unfortunately, there is apparently a considerable lack of awareness (and compliance) regarding the use of history and physical examination questionnaires to guide the preparticipation screening examination.<sup>3,20,22,114,176,177</sup> Indeed, certain standardized and comprehensive questionnaire forms developed specifically to assist primary healthcare providers in performing these examinations have been grossly underused, specifically the AHA recommendations<sup>3,105,112,114</sup> and the Preparticipation Physical Evaluation monograph/form, which is the work of several different societies.<sup>115,176</sup>

It has been an important aspiration to enhance the quality of the history-taking and physical examination process (including the expertise of examiners) in accordance with the specific 14-point recommendations of the AHA<sup>3,105</sup> (Table 1), given that many states have examination questionnaires judged inadequate to reliably raise suspicion of cardiovascular disease in high school student-athletes.<sup>20,22</sup> In 1998, Glover and Maron<sup>22</sup> critiqued the completeness of the screening questionnaire process in each state for high school student-athletes, measuring compliance with the recommended AHA items that serve as a guide to examiners. Nine years later in 2007, reanalysis showed the questionnaires to be more comprehensive by a

References 1–3, 5, 72, 84, 85, 87, 95, 172, 173.



factor of 43%, which suggests that the 1998 data probably triggered revision in several states.<sup>20</sup> Whether this improvement in the questionnaires resulted in greater numbers of affected individuals being identified is unknown, although likely. An analysis of questionnaires used by 879 NCAA member institutions<sup>177</sup> proved similar to the data for US high schools in 1998<sup>20</sup> with respect to the number of AHA items used.<sup>20,22</sup>

In addition, in the United States, a minority of states allow nonphysician examiners with little cardiovascular training to perform preparticipation examination on high school athletes.<sup>20,22</sup> Therefore, future efforts should focus at a minimum on improved dissemination and enhanced practitioner awareness, compliance with (and implementation of) the AHA screening recommendations in the practicing community, and systematic recruitment of physician examiners, as well as the possible creation of an accreditation process.

Consideration should also be given to the standardization of preparticipation examinations and questionnaire forms (as guides to examiners) within each state or possibly nationally in collaboration with organizations such as the National Federation of State High School Associations and the NCAA. In this regard, contrary to the myth that the customary history and physical examinations are of no value or merit, HCM investigators have reported that a number of new HCM diagnoses and referrals do in fact come directly from preparticipation history and physical examinations in athletes.<sup>178</sup>

## Assessment of the 12-Lead ECG as a Population Screening Test

### General Considerations

Although screening ECGs in young people have been used for the purpose of promoting cardiovascular safety, including but not limited to participation in competitive athletics, the value and limitations of screening populations with the 12-lead ECG remain controversial.<sup>¶</sup>

Notably, mass screening with ECGs as discussed here represents the interfacing of complex cardiovascular diseases with an imperfect screening test, and the recognition that no screening strategy or program can be expected to reliably detect all affected individuals or eliminate SD.

The ECG has the capability of raising suspicion for or identifying certain genetic cardiovascular diseases as true-positive results, including ion channelopathies<sup>184</sup> and HCM.<sup>18,185</sup> However, screening ECGs for genetic or congenital cardiovascular disorders in young people has important potential and inherent scientific limitations,<sup>#</sup> particularly in the relationship between pattern analysis of the 12-lead ECG and the heterogeneous structural forms of heart disease that are known to cause SD in the young. The usefulness and consequences of routine screening ECGs depend on the purpose of acquisition of the ECGs, technical quality of the recording, selection of the study population, distinguishing factors within population subgroups (such as age, sex, race, and level of physical activity), inherent performance characteristics of the ECG for the identification of prognostically important abnormalities, quality of

interpretative analysis, and balances among benefits, risks, and the costs of derived information.

The usefulness of the ECG for detection of disorders such as inherited channelopathies and cardiomyopathies is strongly dependent on test sensitivity, specificity, and positive and negative predictive values. However, even effective screening ECGs for the identification of diseases with low prevalence in the general population is not equivalent to identifying individuals who will actually experience clinically adverse outcomes, because the incidence of SD will be substantially lower than the prevalence of disease. The posttest predictive value of the ECG for disorders of low prevalence will necessarily be low, as a simple function of Bayesian analysis.<sup>187,188</sup> However, a low positive predictive value of a test is alone not sufficient to invalidate its screening value if clinically useful and cost-effective methods can reliably separate true-positive from false-positive test results, if interventions can reduce risk, and if society places a high enough value on the process to accept the associated costs in terms of the life-years saved. In terms of HCM, the single most common cause of athletic field deaths,<sup>1,2,6,117,122,125a,127</sup> there is particular concern about relying on a single screening ECG obtained at a single point in time to exclude this disease, given the distinct possibility of left ventricular remodeling and changes in pattern in the ECGs in young patients.<sup>108,119</sup> This is a potential source for false-negative diagnoses.<sup>15,93,185,189,190</sup>

### Technical Factors

Similar to many tests, the ECG is subject to issues related to consistency, reproducibility, and interobserver variability in interpretation. Indeed, performance of the ECG in a real-world mass screening setting will vary when readers and technicians with vastly different expertise and efficiency are confronted with large numbers of studies to perform and interpret rapidly. Computerized electrocardiography can aid in the standardization of measurements by analyses obtained simultaneously with superimposed 12-lead complexes. Central databases of high-quality ECGs with directly comparable methodology will ultimately promote improved separation of normal from abnormal ECGs in relevant populations.

Interpretation of the ECG is based on measurements and the integrative examination of waveform shapes. The usefulness of established criteria for interpretation depends on the accuracy of the recorded signal; however, there are technical sources of potential nonbiological variability that limit the reliability of measurements, distort waveforms, reduce reproducibility, and blur the distinction of normal from abnormal tracings.<sup>191,192</sup> Among the most important of these is operator selection of inadequate bandwidth for the ECG.<sup>193–195</sup> In children and adolescents, inappropriate low-pass filtering (high-frequency cutoff <250 Hz) limits noise in the recorded signal but reduces the amplitude of R waves used to estimate ventricular mass,<sup>195–197</sup> whereas inappropriate high-pass filtering (low-frequency cutoff >0.05 Hz or its digital equivalent) limits baseline wandering but can introduce artifactual deviation of the J point and ST segment.<sup>198,199</sup>

A major source of potential technical error is misplacement of the limb or precordial electrodes, not uncommonly including inadvertent lead reversals,<sup>200–206</sup> in which the V<sub>1</sub> and V<sub>2</sub> leads are placed in the second (rather than the fourth) intercostal space and the left precordial V<sub>5</sub> and V<sub>6</sub> leads are placed

¶References 3, 5, 28, 55, 64, 79, 98, 100, 103, 179–184.

#References 3, 15, 17, 23–25, 28, 29, 59, 64, 74, 88, 89, 184, 186.

below the horizontal extensions of  $V_4$  in the fifth intercostal space.<sup>205,207</sup> Precordial lead misplacement results in distorted precordial R-wave progression, thereby simulating anteroseptal infarction; magnifies otherwise small terminal R' deflections and elevates the ST segments in  $V_1$  and  $V_2$ ; and confuses standard criteria for diagnosis of ventricular hypertrophy.<sup>208–210</sup> Because day-to-day lead misplacement itself often varies, reproducibility of the precordial ECG is poor, and this variability can limit the ability to separate normal from abnormal tracings.<sup>192,208</sup>

Another source of variability in assessment of the ECG involves standardization of interval durations, which have changed with newer technology.<sup>192,211</sup> Evolution of these measurements in the era of digital electrocardiography has altered observed QT intervals (and QRS durations) from the established normal limits that were derived from single-channel (lead) recordings. Difficulty in measuring the QT interval with precision has obvious relevance to the reliable identification of LQTS as part of mass population screening ECGs.<sup>184,211–213</sup>

It is also difficult to establish generally accepted and sex-adjusted upper limits of normal for QT duration suitable for LQTS screening in general populations. For example, even though risk of SD increases with the duration of the QT interval, there is important overlap in QT ranges for healthy normal subjects and genetically affected individuals. There are also technical issues that explain variations in QT partition values, and reliance on computer-generated diagnostic interpretation of ECGs alone will fail to identify many family members at risk for LQTS.<sup>212–214</sup>

QT and other intervals were originally measured from single leads, often limb lead II or  $V_5$ , from the onset of the QRS to the point at which the T wave joined the baseline or at which a tangent from the descending limb of the T wave met the baseline. By definition, single-lead measurements tend to underestimate the true QT interval, because the onset or offset of waveforms may be isoelectric in any given lead,<sup>215</sup> whereas the lead with the earliest QRS onset may be different from that with the latest T-wave end.<sup>212</sup> Measurement of the true duration of an interval on the ECG requires examination of all leads at once to detect the earliest and latest fiducial points. This type of global interval measurement of QT will be systematically longer than QT intervals of individual leads, perhaps by as much as 30 to 40 ms.<sup>215</sup>

In addition, a variety of QT-interval rate-correction formulas have been proposed, and these produce different results, so that Bazett-corrected values cannot be intermixed with Fridericia-corrected measurements.<sup>216–218</sup> Because automated algorithms for determining ECG waveform fiducial points on the ECG vary,<sup>191</sup> measurements used in mass screening for cardiovascular disease must be interpreted in the context of evolving changes in duration standards. In this context, it is essential that population studies with ECGs provide explicit description of the methodology used to determine normal limits and harmonize measurements and limits with the referent populations.

### Reliability of ECG Diagnostic Criteria

A major obstacle in screening is the overlap in measurements with the ECG between healthy subjects and those with prognostically important cardiac disorders, which may involve measurements of amplitudes, interval durations, and waveform shape. Furthermore, the spectrum of alterations in the

ECG in healthy young athletes and nonathletes can overlap and in some cases (5% of elite athletes)<sup>190,219</sup> are indistinguishable from those in patients with cardiovascular diseases that cause SD (particularly HCM).<sup>219</sup> The sensitivity of screening ECGs for the various channelopathies, preexcitation syndromes, and cardiomyopathies can be difficult to establish with precision, because disease severity within populations affects the prevalence and extent of abnormalities on the ECG and because phenotypic expression of these disorders is heterogeneous.

Therefore, screening is complicated by the potentially pathological or nonspecific patterns in the ECGs that occur in general populations, particularly in trained athletes.<sup>179,180,182,183,219–227</sup> In this regard, in 2010 the ESC offered revised recommendations for defining abnormalities in ECGs in trained athletes,<sup>183</sup> with the intent to create a mechanism for reducing expected false-positive results (and increasing specificity) in preparticipation screening ECGs, that is, from unacceptably high rates of up to 15% to 20% to rates of  $\leq 5\%$ .<sup>\*\*</sup> This strategy has been based in part on the assumed premise that in young athletes and other young people, isolated increases in QRS voltages (in the absence of other pattern alterations) have limited specificity and are unlikely to be indicative of pathological hypertrophy (eg, as encountered in HCM).<sup>125a,183</sup>

There have been several efforts to reduce the possibility of false-positive interpretations of ECGs and increase specificity by redefining standards in the ECGs. These have been largely through non-peer-reviewed panel proposals, which are essentially declarations largely unsubstantiated by specific data. The Seattle Criteria,<sup>82,230</sup> which are very similar to the 2010 ESC guidelines,<sup>183</sup> have been promoted in this regard. However, such panels have significant potential limitations, given that their recommendations are not based on independent cohort studies in sizable general populations interrogated systematically with both electrocardiography and echocardiography.<sup>80,81,224</sup> Notably, in the largest sampling reported to date, a population from the United Kingdom (n=7764) that consisted of individuals who were sedentary or participating in recreational physical activity, fully 22% had patterns in the ECGs considered pathological by ESC 2010 criteria.<sup>183,231</sup> These data clearly argue against, and essentially preclude, the feasibility of screening a general population with ECGs for cardiovascular abnormalities.

By reclassifying patterns in the ECGs in 508 college athletes based on the revised 2010 ESC criteria for ECGs, Weiner et al<sup>180</sup> showed that the number of false-positive results in the ECGs could theoretically be reduced from 16% to 10%. However, validation of the 2010 ESC standards will require prospective testing in young populations <35 years of age (with and without cardiac disease and including athletes) to establish the true sensitivity and specificity of the revised criteria.

Finally, the recent recognition that early-repolarization (J wave) syndrome may be relevant to young people as a cause of SD potentially adds considerable complexity to the application of the ECG to mass screening of athletes for a number of reasons, particularly the reliability and reproducibility of pattern interpretation.<sup>229,232–234</sup> The potential significance of this alteration in ECGs to population-based preparticipation screening is unresolved at present.<sup>232–234</sup>

<sup>\*\*</sup>References 33, 52, 57, 71, 88, 91, 172, 179, 180, 219, 223–231.

### Sensitivity and Specificity (False-Positives and False-Negatives)

The sensitivity and specificity of the ECG for detection of cardiovascular disease will vary with the severity of phenotypic expression. In HCM, for example, specificity is reduced (and false-positive results increased) with only modestly increased voltages in the ECGs and repolarization abnormalities, which are not uncommon in this age group, particularly among trained athletes and black males.<sup>††</sup> Furthering the sensitivity and specificity of fully expressed preexcitation in large, healthy screened populations will be reduced by the changing day-to-day fusion of normal and accessory pathway conduction, which commonly results in an entirely normal tracing, and the questionably slurred waveform upstrokes that occasionally are evident in the mid precordial leads of healthy normal subjects.

It is well recognized that physiological (training-related) alterations in the ECGs often overlap with pathological patterns frequently in physically active children and adolescents.<sup>‡‡</sup> Specifically, a myriad of potentially important pattern alterations in the ECGs occur in a significant minority (10%–20%) of athletic individuals, with the proportion dependent on the precise definition of “abnormal” used.<sup>§§</sup> In >1000 elite athletes without echocardiographic evidence of cardiovascular disease, Pelliccia et al<sup>219</sup> found 14% had distinctly abnormal patterns in the ECGs that were highly suggestive of pathological conditions (including HCM)<sup>119,185</sup> and thus were false-positive test results. In a large population of trained athletes from the United Kingdom (n=4081),<sup>231</sup> fully one third of the ECGs were judged to be pathological on the basis of 2010 ESC criteria.<sup>183</sup>

Indeed, most of these patterns will, by Bayesian necessity, be false-positive results, because the prevalence of prognostically important channelopathies, cardiomyopathies, and other conditions is much lower than the prevalence of pathological ECGs.<sup>33,187,188,235</sup> Notably, repolarization abnormalities in the ECGs that involve T-wave inversion and are identified during screening in apparently normal athletes have been shown to occasionally predict future development of HCM or ARVC/D phenotypes, which underscores the potential value of long-term surveillance.<sup>236</sup> These observations, although rare, support consideration for repetitive screening examinations.

It is necessary to place the debate about false-positive results on ECGs into perspective,<sup>|||</sup> particularly in the context of large-population screening programs. At a high enough rate, false-positive ECGs can create excessive and costly second-tier testing (eg, with echocardiograms and magnetic resonance imaging), within the system, and in the process greatly exceeding true-positive results.<sup>3,28,93,97</sup> *However, even if ECGs with false-positive results could be reduced to only 5% in the course of screening 10 million individuals (the estimated number of US competitive athletes), screening ECGs would nevertheless identify a formidable obstacle of 500 000 people who required further testing to exclude underlying heart disease and resolve eligibility for sports participants.* Very few

of these individuals would ultimately prove to have important disease with a risk for SD that required disqualification.<sup>113,237</sup>

Often ignored in this discussion is the importance of false-negative test results in the ECGs, which reflect low sensitivity.<sup>93,97,125,127,189,190</sup> In the current environment, false-negative results can be expected in  $\geq 10\%$  of patients with HCM (the most common cause of SD in young people), with a significant proportion of these showing completely normal patterns.<sup>189</sup> In addition,  $\geq 90\%$  of those with congenital coronary anomalies (the second most common cause of SD in young athletes) will have a normal ECG.<sup>118</sup> Even in the case of LQTS, for which the 12-lead ECG is the only clinical test that reliably detects the disease phenotype,  $\approx 25\%$  to  $30\%$  of genetically affected individuals will have a normal or borderline corrected QT interval, although this percentage is highly dependent on the upper limit of QT duration selected. As in any systematic screening context, the overall benefits of screening ECGs for detection of cardiovascular disease are limited by false-negative test results.

It is evident and commonly accepted that no screening strategy can be considered absolute (ie, 100%) in its ability to detect those cardiovascular diseases responsible for SD in young people. Indeed, a 26-year study of Minnesota athletes (with autopsy examinations)<sup>127,129</sup> showed that only 40% of SDs were attributable to diseases that could be detectable reliably by preparticipation screening even with 12-lead ECGs, which translates to only 2 athletes detected per 1 000 000 participants per year.

There have been several recent efforts, largely from the primary care community in the United States, to improve test specificity of the ECGs and recognition of true abnormalities.<sup>¶¶¶</sup> These initiatives, which attempt to reduce high false-positive rates that can encumber the principle of large-population screening ECGs, have been successful in improving the separation of normal from abnormal ECGs by reducing false-positives to a range of <5% to 10% in some analyses. However, improving the specificity of interpretation of the ECGs in this way may result in a decrease in sensitivity of the test (ie, greater numbers of false-negative results), which in fact represent athletes with potentially lethal cardiovascular diseases such as LQTS and HCM that the screening initiative is designed to recognize and protect.<sup>71,125,179,180,189,223</sup> Therefore, this strategy to reduce false-positive results could be regarded as an unfavorable tradeoff in screening.

### Positive and Negative Predictive Values

The positive predictive value of a test is the proportion of true positive outcomes among all positive tests in a study population. The negative predictive value is the proportion of true negative outcomes among all negative tests.<sup>188</sup> Predictive value depends to a great extent on the incidence of the disease in the population, which is assessed by the test.

For screening tests such as the ECG, the positive predictive value for disease is less dependent on test sensitivity than on its specificity. The positive predictive value of a test (such as the ECG) with imperfect specificity is poor when the population prevalence of the disorder being tested is low, as is the case for all cardiovascular abnormalities associated with SD

<sup>††</sup>References 180, 185, 219, 225, 227, 235, 236.

<sup>‡‡</sup>References 33, 182–184, 219, 221, 224, 236–242.

<sup>§§</sup>References 3, 5, 23, 24, 29, 33, 48, 64, 76, 180, 183, 219, 223.

<sup>|||</sup>References 91, 97, 98, 109, 189, 225–229.

<sup>¶¶¶</sup>References 30, 33, 52, 80–82, 180, 183, 230.



in young people. Even a test with nearly perfect specificity will have more false-positive than true-positive responses when prevalence of disease in the population is <10%.<sup>187</sup>

With a prevalence of disease <1%, and perhaps <0.1% for even the most common channelopathies and inherited forms of cardiomyopathy (ie, HCM), the positive predictive value of the ECG is small or trivial. When the prevalence of rare causes of adverse outcome in young people is as low as 0.1%, the negative predictive value of the ECG nevertheless remains high irrespective of test sensitivity. Indeed, the negative predictive value for extremely low-prevalence events is a questionable statistical concept, because nearly all subjects in the normal screening population will almost certainly remain free of adverse outcomes.

### Impact of Age and Growth

Defining an abnormal ECG is particularly difficult in growing children and adolescents because of changes in heart rate, QRS axis, ventricular predominance, intraventricular conduction, and repolarization morphology. By ≈16 years of age, patterns in the ECGs become similar to those of adults; therefore, normal versus abnormal distinctions in adolescence are often challenging for pediatricians, working at one end of the age spectrum, and for general practitioners and internists working at the other end of the age range. Certainly, in any hypothetical large-population or national screening program, interpreters of ECGs would be required to be familiar with ECGs in adolescents.

Finally, real-world difficulties in test interpretation can be expected in mass screening if the 12-lead ECG is used to detect (or raise suspicion) of those diseases that cause SD in young people and athletes.<sup>184,213</sup> In 1 study, expert pediatric cardiologists blindly interpreted ECGs from young, nonathlete patients with HCM, LQTS, and other conditions.<sup>184</sup> False-positive rates in the range of ≈30% were reported and were lowest for LQTS, Wolff-Parkinson-White, and HCM; 40% of the HCM patients were missed (ie, false-negatives) in the process. Indeed, in another study, correct classification of QT intervals from patients with or without LQTS was achieved by 96% of QT experts and 62% of arrhythmia experts but by <25% of general cardiologists and noncardiologists.<sup>213</sup>

### Race and Sex

It is becoming apparent that sex, race, and ethnicity are important determinants of pattern in the ECG.<sup>6,117,225–227,238–242</sup> Notably, ethnic and racial differences are underscored by Magalski et al,<sup>225</sup> who found potentially pathological patterns in ECGs in 30% of black professional football players compared with only 13% of whites, a difference that was independently associated with race. T-wave inversions in anterior leads V<sub>1</sub> through V<sub>4</sub> have been cited as unique ethnic variants in the ECGs that occur in male athletes of African/Afro-Caribbean origin.<sup>239–241</sup> Similar findings have been reported by Choo et al<sup>226</sup> in 1282 National Football League players. Recently, ECGs were abnormal in 40% of >1200 young black athletes in the United Kingdom, according to 2010 ESC criteria,<sup>183</sup> raising suspicion of cardiac disease.<sup>241</sup>

Therefore, screening ECGs can be influenced by racial distribution, which can potentially inflate false-positive

rates<sup>89,225,227,238–242</sup>; this resonates for African and other black athletes, in whom left ventricular wall thickness can exceed that of white athletes.<sup>238,240</sup> These factors could potentially trigger a cascade of unfortunate events that would generate an overdiagnosis of HCM, as well as unfair and unnecessary disqualification from competitive sports. However, an undercurrent of mistrust regarding broad-based screening initiatives for competitive athletes may exist in certain minority communities. Because ECGs in female athletes are overwhelmingly normal or near normal, their risk of false-positive test results on the ECGs is likely to be decreased compared with males.<sup>219,223</sup>

### Screening ECGs and Clinical Outcome/Mortality Rates

A distinctive body of literature has emerged from several countries describing preparticipation screening strategies, specifically assessing the impact of screening ECGs on mortality in athlete populations.## However, at present and importantly, there is no consensus from these data to support the principle that the addition of 12-lead ECGs to history and physical screening actually reduces mortality.

### The Italian (Veneto) Experience

The sole evidence that a mandatory screening strategy with a resting 12-lead ECG reduces SD mortality in young people comes from the study of competitive athletes in the Veneto region of Italy conducted by Corrado et al.<sup>4,18,31</sup> It is this publication, with its descending mortality curve, that has driven the debate over the screening strategy of ECGs and triggered (if not created) the substantial interest in this area. Since 1982, Italian law has mandated an ambitious national program with clinical screening evaluations for cardiovascular disease in all individuals aged 12 to 35 years engaged in organized competitive sports.<sup>4,18,244</sup> This screening process is subsidized in part by the national health system and performed by accredited sports medicine physician specialists working in dedicated sports medicine centers. The standard evaluation includes personal and family history, physical examination, and resting 12-lead ECG (and step stress test). Eligibility for competitive sporting activity is dependent on a normal screening evaluation that excludes cardiovascular disease, although additional specialized noninvasive testing (eg, echocardiography) is required when abnormal findings are identified on the primary evaluation. Disqualification from participation in competitive sports is governed by restrictive Italian guidelines if evidence of heart disease is identified.<sup>237</sup>

In 2006, Italian investigators reported the impact of their mandatory screening program with ECGs on the mortality of young competitive athletes, (12–35 years old).<sup>4</sup> Although the Italian model is a truly national initiative,<sup>4,18,31,116</sup> the highly visible published data come only from a relatively small region of this country (Veneto), which in fact constitutes a small proportion of the overall Italian population (9%). Therefore, it is unknown to what extent the Veneto data<sup>4</sup> are representative of Italy overall.

##References 4, 18, 28, 88, 109, 130, 190, 243.

Corrado et al<sup>4</sup> compared mortality rates in athletes before the introduction of mandatory screening ECGs versus mortality evident after implementation of the program. The prescreening period was only 2 years in duration (1979–1981), whereas the postscreening period was much longer (22 years; 1982–2004). The authors reported an impressive 90% decline in SD rate, from 4.3 per 100 000 person-years in the prescreening period to 0.87 per 100 000 person-years with screening ECGs. This striking mortality reduction was attributed by the authors entirely to routine inclusion of the ECG into the screening process. However, these retrospective, nonrandomized data are based on a low event rate, with 55 cardiovascular deaths in 26 years (only 2 per year) as the numerator. The estimated denominator of at-risk individuals was extrapolated and interpolated from census data obtained only every 8 years, and without prospectively established interpretation criteria for the ECGs. Therefore, the striking downward linear curve is seemingly not primarily a function of a decrease in events, but rather in part the change in estimated participation rates of at-risk athletes.

These data are potentially very important and justify further study but to date have not been replicated. Indeed, a subsequent study comparing preparticipation screening in competitive athletes from Veneto (ECG) and Minnesota (history and physical examination over the 11-year period of 1993–2004) showed low SD event rates and no differences in mortality (0.93 in Minnesota versus 0.87 in Veneto) despite the different strategies used.<sup>130</sup>

The SD incidence in Veneto of >4 per 100 000 person-years at the onset of mandatory screening<sup>4</sup> is considerably higher than any other reported mortality rate in young athletes in the literature. Given that the brief prescreening phase occurred fully 2 decades before Corrado et al<sup>4</sup> retrospectively evaluated their population, methodology could potentially have contributed to underestimation of the denominator, an exaggeration of the mortality rate at that time, and ultimately, the marked downward trend in survival otherwise attributed to screening ECGs. It is also possible that athletes who were potential candidates for inclusion in the cohort but who had more advanced disease could have died before screening was performed, whereas those who survived and were available for screening constituted a lower-risk subset.<sup>245</sup> Finally, these data are based largely on SDs from arrhythmogenic right ventricular cardiomyopathy, the most common cause of these events reported from Italy.<sup>131</sup> This represents a very different epidemiology of SD than in the United States, where HCM predominates,<sup>1,2,6,117,122,125,127</sup> which underscores the difficulty in making direct comparisons of screening strategies and mortality data between Italy and the United States or other countries.

The studies by Corrado et al<sup>4,18,31</sup> prompted ESC recommendations advocating mandatory screening ECGs for athletes in other countries and in fact has launched an entire impetus for preparticipation mass screening of athletes.<sup>5</sup> However, other independent reports have shed a different light on the potential efficacy of mass screening ECGs to reduce mortality and questioned the advisability of such a strategy.

### The Israeli Experience

Participants in organized sports activities in Israel are required to undergo medical screening that includes a

12-lead ECG.<sup>28,93</sup> The Israeli Sport Law, enacted in 1997, defines athletes requiring screening as those “individuals engaged in sport activities at any level of physical endurance,” from amateur sportsmen to professional athletes.<sup>246</sup> The law also dictates that only physicians certified by a specialized accreditation course can perform screening examinations. Athletes with abnormal screening tests are referred to expert cardiologists or electrophysiologists at the discretion of screening physicians. Similar to Italy, there is no centralized national registry or collection of data in Israel, and consequently, information is lacking regarding the percentage of athletes who are referred for additional testing, or are eventually disqualified.

As in the Italian study, the impact of screening ECGs on SD risk has been estimated in Israel by comparing the incidence of events before and after implementation of the law that mandated screening.<sup>28</sup> However, in contrast to the Italian data, which compared a 2-year prescreening period with a 22-year postscreening period, the Israeli study had the advantage of comparing prescreening and postscreening periods of similar duration (12 years each). Limitations of the Israeli study include estimation of the number of cardiac arrest events (the numerator) from accounts in only 2 newspapers (which could invite underreporting) and derivation of the number of people at risk (the denominator) from surrogate participation rates, as well as the absence of forensic-based diagnoses.

The average annual mortality incidence before and after implementation of mandatory screening ECGs was essentially the same: 2.54 and 2.66 per 100 000 person-years, respectively ( $P=0.88$ ), consistent with screening having no apparent effect on the mortality rate of athletes. Notably, if the Israeli cardiac arrest event rates during the 12 years after screening had been compared arbitrarily with a limited 2-year period immediately before screening (when there was a substantial increase in mortality), the conclusion would have been the same as in the Veneto study, that is, that mandatory screening ECGs significantly reduced SD incidence among athletes. This is because the event rate just before the start of screening was substantially higher than at any other time during the 24-year study period.

This increase in SD rate that occurred in both Italy and Israel just before implementation of the legislation that mandated screening ECGs was likely caused by random fluctuations in this rare phenomenon, with clusters of SDs that happened to occur in 1980 to 1982 in Italy and in 1994 to 1995 in Israel. Such peak occurrence may have captured public attention through the media, in turn promoting legislation mandating screening ECGs. A subsequent “regression to the mean” statistical phenomenon would then produce a reduction in event frequency toward the long-term average that instead might be attributed to the screening program ECGs.<sup>247</sup>

### The US Experience

There have been no national screening programs in the United States similar to those in Italy and Israel. Early screening efforts in relatively small college athlete or school-aged populations with ECGs or echocardiography generally reported low yields of important cardiovascular diseases.<sup>88,89,91,225–227,243</sup>

However, cardiovascular mortality in Minnesota state high school athletes proved to be particularly uncommon (<1/year on average).

### The Danish Experience

Danish law dictates that forensic examination must be performed for all sudden and unexpected deaths and that death certificates must provide detailed information concerning the circumstances and causes of death. Holst et al<sup>100</sup> took advantage of these data to estimate SD risk for the athlete and non-athlete populations of Denmark, a country where screening of athletes is not performed. The incidence of sports-related SD in Denmark is 1.21 per 100 000 person-years,<sup>100</sup> similar to the rate reported for Italy after many years of screening ECGs (0.87/100 000 person-years)<sup>4,130</sup> and in Minnesota with screening performed only by history and physical examination (0.93/100 000 person-years),<sup>130</sup> and lower than the SD rate in the Danish general population of the same age (3.76/100 000 person-years).<sup>100</sup>

### United States Versus Italy: Global Considerations and Comparison of Prior Athlete Screening Demographics

Given the controversy generated over current screening strategies in Italy (as a proposed model) and in the United States, it is worth underscoring certain distinct differences between the 2 countries. First, the population of the United States is 5-fold larger than that of Italy (313 million versus 61 million) and 40 times that of Israel. Furthermore, the United States is 30 times larger in land mass than Italy, which presents an obstacle that impacts the practicality and durability of large-scale screening. Second, the US population is substantially more diverse ethnically and racially than that in Italy, a crucial variable when one interprets patterns in ECGs in athletes or other young people for a variety of cardiovascular diseases, given the known differences in ECG "normality" based on ethnicity, race, age, and sex.<sup>219,225,227,238–241</sup> This is notable with regard to the substantial population of blacks, for whom there is evidence of significant differences in patterns in the ECGs and left ventricular wall thickness compared with whites. Third, the US healthcare system does not include (and realistically cannot create) specialized practitioners dedicated to mass screening, such as those employed in Italian athlete screening since 1982.<sup>4,18,31,116</sup> Indeed, the global economic climate, heightened sensitivity to discriminatory practices, and numerous competing healthcare priorities represent major obstacles to a national mass screening program for the United States, and probably would also for Italy (and other European countries) if such an initiative were proposed today for the first time.

To the best of our knowledge, despite the study about 8 years ago by Corrado et al<sup>4,18</sup> and the ESC recommendations,<sup>5</sup> the Italian model of systematic national cardiovascular screening with ECGs for athletes at all levels of competition presently exists elsewhere only in Israel, and has not been adopted in any of the other 51 European countries; also it has been rejected by Denmark.<sup>100</sup> To date, no national organization in the United States, including the National Institutes of Health, has endorsed such a screening program with ECGs.<sup>23</sup>

However, in the United States, it is customary practice (although not required by law) to routinely screen all high school and college-aged athletes for cardiovascular disease (albeit without ECGs).<sup>20,22,177</sup> Indeed, there are only 3 countries (Italy, Israel, and the United States) in which the practice is to systematically screen all young athletes regardless of their level of competition, achievement, or expertise.

On the other hand, there have been recent initiatives, largely confined to the minority of athletes with elite or professional status, to screen for cardiovascular disease (often with ECGs), with uncertain levels of compliance, ie, in several European countries: France, Spain, Portugal, Greece, Germany, Sweden, the United Kingdom, Belgium, and the Netherlands. The situation is much different in Denmark, where screening of athletes (and nonathletes) is not performed with either history and physical examination or ECGs because of the low incidence of SD in this population.<sup>100</sup>

### Universal Screening and Resource Allocation

In addition to the aforementioned scientific limitations, there are a number of practical issues that together represent serious impediments to all large-scale, general population screening initiatives with ECGs. For example, the resources necessary to create de novo and maintain a mandatory mass screening program effort throughout an entire country would represent a problem of feasibility and quality control. For example, it is likely that an independent infrastructure would be required with designated testing centers and dedicated professional personnel (as in Italy). The use of preexisting but already busy facilities and personnel dedicated to patients with other medical problems in order to perform thousands of additional screening examinations would likely constitute a burden to an already overworked system. The establishment of new screening centers within a geographic area as large as the United States, in which ≈20% of the population resides outside of large metropolitan areas, would be daunting.

Mandated screening programs would also have resource costs, including purchase and maintenance of equipment; selection and training of professional personnel to perform and interpret the tests; availability of administrative staff for scheduling and generating test reports, as well as correspondence regarding test interpretation; follow-up referrals to cardiologists for second-tier subspecialty evaluation with noninvasive testing; establishment and maintenance of electronic data storage; and negotiations with insurance carriers to resolve coverage issues and legal fees.

In such a program, physicians responsible for interpretation of ECGs would need to have expertise in reading pediatric ECGs, according to standardized criteria (which in turn would have to be developed). In past feasibility screening studies, physician interpreters of ECGs (and other personnel) have participated largely on a volunteer basis; however, a formally mandated mass screening program would require contractual arrangements that addressed compensation and malpractice coverage, thereby adding significantly to the cost. The professional and economic burden imposed on the healthcare system by mass screening may be illustrated as follows: Pediatric cardiologists would be the most qualified to perform these examinations and interpretation of the ECGs, but there are



only 1500 of these practitioners in the United States, who, if commissioned, would be required to interpret several thousand ECGs in a given year, even if the program was somehow limited to competitive athletes in the United States.

Secondary (or second-tier) subspecialty evaluations with echocardiography and other testing (eg, cardiovascular magnetic resonance imaging) necessary to assess a diverse array of potential diseases represent the Achilles heel of mandatory mass screening by adding considerably to the complexity and cost of any broad-based screening program, given the anticipated not inconsequential false-positive rate. This “downstream effect” of primary screening could lead to unnecessary and unwarranted restrictions and disqualifications from sports, anxiety and potentially adverse psychosocial consequences, and impediments to insurability or employment opportunities.<sup>3</sup> It is this expensive “downstream” testing mostly in false positives that is potentially the major contributor to cost inefficiency in any large screening program.

Even after such systematic additional testing, cardiovascular disease cannot be excluded reliably in all cases, and some uncertainty in the risk assessment would always remain. Also, in a theoretical government-sponsored screening program, the responsibility for enforcement of disqualification from competitive sports would fall largely to the individual screening physicians, as would the risk of litigation.

### Cost, Charges, and Cost-Effectiveness

Although it is not possible to place a specific monetary value on a young life terminated suddenly and prematurely by underlying (and unsuspected) heart disease, cost is nevertheless an unavoidable concern when one deliberates the merits of large-scale screening programs. Cost-efficacy data have potential value in healthcare policy decisions. All such cost-effectiveness studies must be regarded as highly theoretical estimates, because they are unavoidably based on numerous contestable assumptions.

Furthermore, 2 principal limitations arise in the application of cost-effectiveness analysis to screening ECGs in youthful populations<sup>92</sup>: (1) incomplete registry data to define the incidence of SD in this age group, and (2) absence of large randomized trials that test the hypothesis that screening reduces the frequency of SD events. By definition, a screening strategy cannot be cost-effective if not first demonstrated to be clinically effective.

A commonly accepted benchmark for cost-effectiveness in the United States is <\$75 000 per year of life saved, whereas a cost of >\$75 000 per year is regarded as ineffective.<sup>247a</sup> However, these analyses must be viewed as specific to the healthcare system and disease; for example, screening is generally less cost-effective in the United States because the tests are more expensive.<sup>247a,248</sup>

There are conflicting data estimating the cost per year of life saved in screening models with ECGs that justify closer scrutiny.<sup>92,101,228,248–251</sup> Wheeler et al<sup>248</sup> calculated this measure for US competitive athletes. Although this assessment is useful, it potentially underestimates costs by using the data from Veneto to estimate risk (given that it is modeled largely on mortality attributable to ARVC/D and not HCM). Very conservative estimates of costs for diagnostic testing were offered in a population of 3.7 million athletes (approximately one third the number

in the United States), with infrastructure and administrative costs absent from the model. Nevertheless, the addition of an ECG to a cardiovascular-focused history and physical examination was projected to save 2.06 life-years per 1000 athletes at a cost of \$42 000 per life-year saved. This calculation suggests that the cost-effectiveness of testing ECGs could exceed that of history and physical examination alone and fall within the traditional and socially acceptable norm. History and physical examination screening alone was not cost-effective, and notably, in this model, annual screening ECGs of large cohorts or general populations of young people (not restricted narrowly to athletes) was not considered to be cost-effective.<sup>248</sup>

One study of 1473 NCAA Division I college athletes over 5 years measured the cost of adding ECGs to the screening history and physical examination.<sup>228</sup> Using the criteria of the ESC pertaining to ECGs, the cost per abnormal finding (\$68 836) did not differ significantly between the strategies of history and physical examination alone versus the addition of ECGs. The ECG was more sensitive, identifying 8 more cardiac abnormalities than the 5 detected by examination; however, only 1 of these abnormalities could be considered clinically significant (LQTS); the false-positive rate was high (19%), and 2 athletes were disqualified. The total cost of the 5-year university-based program, including all follow-up testing, was ≈\$900 000. A previous study by Fuller<sup>251</sup> did not provide effectiveness data but estimated the cost per life-year saved of different screening modalities to be as follows: history and physical examination, \$84 000; 12-lead ECG, \$44 000; and 2-dimensional echocardiography, \$200 000.

In contrast, a recent theoretical model judged the addition of ECGs to the preparticipation history and physical examination for athletes as not cost-effective, with excessive costs driven by false-positive findings<sup>250</sup> and with a calculated cost of \$900 000 for a single averted SD. A rigorous simulation model that estimated cost versus benefit for screening ECGs to detect causes of SD in children and adolescents concluded that the anticipated cost would be high relative to the potential health benefits, with an unfavorable cost-effectiveness ratio.<sup>250</sup> Finally, a recent cost-projection model from Israeli investigators found that replicating the Italian strategy for screening ECGs in the United States would result in enormous costs per life saved (up to \$14 million per athlete), with total costs of many billions of dollars per year.<sup>92</sup>

Given limited healthcare resources and an aging population that requires increasing amounts of medical care, it is of importance to consider the absolute cost of a nationwide mass screening program. The substantial cost of outpatient screening within the US healthcare system must be borne by the individual patient or private or public sources, because most insurance carriers will not cover expenses related directly to such routine examinations. This situation differs measurably from that in Italy, other European countries, and Canada, where the healthcare systems are largely socialized.

In 2007, an AHA panel addressed the absolute cost for the screening of athletes.<sup>3</sup> If one assumes there are ≈10 million US high school and college athletes to be screened with ECGs, using estimates based on data from the Centers for Medicare & Medicaid Services for examinations and testing (as well as substantial start-up, infrastructure, and administrative costs),

the conservative overall cost for such a program would be at least \$2 billion per year to start and somewhat less annually thereafter. The precise amount depends on the frequency of examinations in a given program and whether it would be necessary to screen each athlete every year. Based on a recent screening experiment in Texas, working with a grant award of \$1 million, a state-funded pilot project<sup>252</sup> was able to screen only a total of 2350 school children aged 11 to 17 years and found just 1 new patient with HCM and 9 with mitral valve prolapse.<sup>252</sup> If these costs are extrapolated, \$40 million would be required to screen 100 000 students.

To place absolute cost into perspective, the \$2 billion per year exceeds the annual budget of most major US medical centers and is similar to that for the National Heart, Lung, and Blood Institute. Therefore, public health efforts targeting other prevalent problems in this age group that account for many more deaths annually, eg, driving while intoxicated or distracted, drug use, or suicide, would likely be far more cost-effective. This discussion of cost and resource limitations is focused on the United States but in principle may also be relevant to other countries considering mass screening ECGs at this time.

### Insights From Prior Screening Studies with ECGs

A literature search identified 17 published studies including 89 697 healthy subjects that reported the results of large screening initiatives with ECG, echocardiography, or both (as well as history and physical examination\*\*\*; Table 2). Each of these studies was designed to detect a variety of largely genetic/congenital cardiovascular diseases, targeting predominantly adolescent and young adult participants in organized competitive sports ranging from high school to the professional level. These athletes were most commonly in basketball, football, and soccer. The majority of reports were from the United States (60%), but others came from Italy, the United Kingdom, Spain, Germany, and China; several were biracial. The athletes reported in these studies represent a heterogeneous group in terms of duration and intensity of training and level of performance, as well as age, sex, race, and other variables, but appear to generally be in accord with the 36th Bethesda Conference definition of a competitive athlete.<sup>7,113</sup>

The percentage of athletes reported with abnormal findings on ECGs during screening initiatives varies widely from 2.5% in 1 study of high school athletes<sup>229</sup> to 35% in professional athletes,<sup>225</sup> with the average being  $\approx 12\%$ , greatly dependent on the precise criteria used to define abnormal patterns in the ECGs (Table 2). Notably, the vast majority (probably  $>90\%$ ) of abnormal ECGs in these populations represent false-positive test results. The frequency of cardiac abnormalities was on average  $\approx 5\%$  for those detectable by history alone and  $\approx 2.5\%$  for those suspected on the basis of physical examination.

These screening studies reported a relatively low yield of highest-risk cardiac diseases. For example, among the nearly 90 000 athletes screened, there were only 6 definitive diagnoses of HCM,<sup>91,94,104,255</sup> although 38 other athletes with increased septal thickness  $>13$  mm were noted (Table 2). Explanations

for the low frequency of HCM diagnoses are elusive, given that a number of independent surveys worldwide have identified HCM to occur in at least 1 in 500 of the general population (0.2%).<sup>257,258</sup> Nevertheless, it would appear that this discrepancy is very likely attributable to the not insignificant false-negative diagnostic testing rate for HCM using ECG, or history/physical examination. The Italian data from Veneto reported new cases of HCM detected by ECG and history/physical examination screening in 0.07% of 33 735 athletes over a 17-year period.<sup>18</sup>

Overall, the most commonly detected clinically relevant diseases reported in these studies were bicuspid aortic valve, mitral valve prolapse, and Wolff-Parkinson-White syndrome, with LQTS less common. Few studies have described management strategies for those athletes with detected abnormalities, and the reported disqualification rate is low (0.2%–4%).<sup>66,225,254</sup> No data are available regarding the effect that such disqualifications have on mortality rate.

### Community-Based Initiatives With Noninvasive Testing in the United States

For many years in the United States, cardiovascular screening of young people aspiring to engage in competitive sports has occurred in office practices or in relatively small populations such as individual colleges/universities and high schools. Indeed, a number of educational institutions have screened, or are currently systematically screening, prospective athletes for heart disease with a variety of research and nonresearch protocols that include echocardiograms or ECGs<sup>259</sup>: Harvard University, University of Wisconsin, Howard University, University of Virginia, Georgetown University, Stanford University, University of Washington, and other institutions with programs in selected sports. Such screening efforts have benefited some young individuals through identification of potentially life-threatening cardiovascular disorders. Such initiatives have been supported consistently by the 1996 and 2007 AHA Scientific Statements,<sup>3,105</sup> as well as the present document.

In addition, over the past decade, and stimulated by the increasing recognition of SDs occurring in young athletes, a multitude of public and community-based preparticipation screening programs have emerged in the United States for the purpose of identifying cardiovascular disease in athletes. These initiatives are often promoted by fee-for-service vendors, and many advertise solely on the Internet, with direct marketing to consumers (ie, parents, high schools, and athletic programs). Several such companies have started with great enthusiasm and then ultimately dissolved after the considerable logistical and technical challenges became apparent (eg, Heart Screen America [Massachusetts], Ultrasound Services [Pennsylvania]); another fee-for-service screening company in Illinois was closed by the Attorney General when a technician was found to be practicing medicine without a license by promoting screening services to schools (Table 3). These real-world programs also operate with a large measure of volunteerism and with funding derived from private non-profit foundations and government grants, fundraising donations, school budgets, for-profit companies, hospitals, medical

\*\*\*References 66, 88, 89, 91, 94, 96, 97, 104, 223, 225, 228, 229, 253–256.

**Table 2. Studies Examining Cardiovascular Screening of Trained Athletes\***

Author/ Reference	No. of Year Athletes	Age, Mean (Range), y	% Male	Race, %	Level	Elite	Country	% Abnormal					Other Testing, %	% DQ	Diseases Detected	
								Hx	PE	ECG	Echo	Sport				
Linder et al <sup>66</sup>	1981	1268	15 (12–19)	N/A	W: 65; B: 35	HS	No	US	1.7	7.4	N/A	N/A	BB; FB	4.8	0.2	N/A
Maron et al <sup>88</sup>	1987	501	19 (17–30)	71	W: 76; B: 23	C	No	US	1.9	3.2	11.3	19	FB; T&F	20	0	1 HBP; 14 MVP; 3 >IVS
LaCorte et al <sup>253</sup>	1989	1424	13–18	N/A	N/A	HS	No	US	6.5	N/A	5	0	N/A	N/A	0	6 WPW
Lewis et al <sup>89</sup>	1989	265	19 (18–28)	93	B: 99	C	No	US	N/A	N/A	N/A	24	FB; BB; T&F	N/A	N/A	1 ASD; 30 MVP; 4 HBP; 29 >IVS
Fuller et al <sup>254</sup>	1997	5615	13–19	60	N/A	HS	No	US	2	3.5	2.5	N/A	N/A	10	0.4	1 AR; 5 HBP; 6 WPW; 1 SVT
Ma et al <sup>97</sup>	2007	351	23 (13–33)	48	A: 100	N/A	Yes	China	N/A	N/A	4.5	4	N/A	0	0	3 >IVS; 13 MR
Stefani et al <sup>256</sup>	2008	2273	8–60	65	N/A	N/A	No	Italy	N/A	1.1	N/A	2.5	BB; S; T; Cy; SW	N/A	0.7	58 BAV
Pelliccia et al <sup>223</sup>	2007	32652	8–78	80	N/A	N/A	No	Italy	N/A	N/A	12 (5% markedly abnormal)	N/A	BB; S; T; Cy; SW	N/A	N/A	N/A
Basavarajiah et al <sup>96</sup>	2008	3500	13 (13–16)	75	N/A	HS	Yes	UK	N/A	N/A	N/A	4%	S; T; RB; SW	N/A	N/A	6 WPW; 9 LQT
Magalski et al <sup>225</sup>	2008	1959	23 (20–29)	100	W: 31; B: 67	Pro	Yes	US	N/A	N/A	25	3	FB; R	N/A	0	6 >IVS
Hevia et al <sup>104</sup>	2011	1220	23	96	N/A	N/A	No	Spain	1	0.1	6	0.7	S	7.4	N/A	2 HCM
Baggish et al <sup>91</sup>	2010	510	19	61	W: 68; B: 10; A: 12	C	No	US	3.8	2.3	17	2	N/A	6	0.6	1 PS; 1 HCM; 1 myocarditis
Malhotra et al <sup>228</sup>	2011	1473	19	49	W: 71; B: 13; A: 2	C	No	US	6	6	19	N/A	N/A	24	2	1 BAV; 4 WPW; 1 LQT; 1 CM; 5 EPS/ ablation
Magalski et al <sup>227</sup>	2011	964	N/A	48	W: 74 B: 20 A: 1	C	No	US	23	3	35 (10% distinctly abnormal)	1	FB; R; T&F	N/A	0.9	1 LQT; 1 AOE; 7 WPW
Marek et al <sup>229</sup>	2011	32,561	16 (14–19)	N/A	W: 66; B: 7; A: 8	HS	No	US	N/A	N/A	2.5	N/A	N/A	2.5	N/A	N/A
Rizzo et al <sup>255</sup>	2012	3100	11 (6–17)	N/A	N/A	HS	No	Italy	N/A	N/A	N/A	2	S	N/A	N/A	2 HCM; 23 BAV; 1 AOE; 10 MVP; 20 ASD
Thünenkötter et al <sup>94</sup>	2010	605	27	100	N/A	Pro (World Cup)	Yes	Germany	1.5	3	4.8	1	S	N/A	0	1 HCM

A indicates Asian; AOE, aortic enlargement; AR, aortic regurgitation; ASD, atrial septal defect; B, black; BAV, bicuspid aortic valve; BB, basketball; C, college; CM, cardiomyopathy; Cy, cycling; DQ, disqualified; Echo, echocardiography; EPS, electrophysiological study; FB, football; HBP, high blood pressure; HCM, hypertrophic cardiomyopathy; HS, high school; Hx, history; >IVS, increased septal thickness; LQT, long-QT interval pattern; MR, mitral regurgitation; MVP, mitral valve prolapse; N/A, not available; PE, physical examination; Pro, professional; PS, pulmonic stenosis; R, rowing; RB, rugby; S, soccer; SVT, supraventricular tachycardia; SW, swimming; T, tennis; T&F, track and field; W, white; and WPW, Wolff-Parkinson-White syndrome.

\*Data accessed as of May 2013.

schools, private practice physician groups, and other sources often organized by parents of children with SD. Notably, however, such initiatives are largely unregulated, independent, self-promoted medical enterprises, and many have been short-lived, with very few outcome data reported.

Community-based screening initiatives are conducted in a variety of venues, including gymnasiums, community centers, schools, and even houses of worship. Quality control is a concern because of the variable expertise of volunteer technicians and the inconsistent availability and commitment of

supervising physicians. In addition, most of these programs operate without resources to ensure follow-up after testing. The failure to obtain close oversight from cardiovascular specialists can create a situation in which the screening company is practicing medicine without proper licensure, as well as the risk that HIPAA (US Health Insurance Portability and Accountability Act of 1996) privacy protection is not ensured. Screening sessions are usually announced through high schools, and attendance is voluntary, with compliance highly dependent on the interest of the students and their parents.



**Table 3. Community-Based Cardiovascular Screening Programs for Athletes and Nonathletes\***

Organization	Year Begun	Subjects	Location	ECG	Echo	H & P	No. Screened to Date	Funding	Fee	Testing		Referral Rate, %	Notification of Results†	Formal Database
										Perform	Interpret			
Midwest Heart Foundation	2006	HS	Chicago, IL	+	0	0	51 000	Donations; grants; industry; school system	Free	Trained laypeople/medical volunteers	Single volunteer cardiologist	2	C	+
Anthony Bates Foundation	2002	HS; college	AZ; KS; CA	+	+	0	7000	Industry; fundraising; donations	Donations accepted	MPV	Volunteer cardiologists	10	A	+
Team of Physicians for Students	2000	HS	Phoenix, AZ	+	Selective; limited	+	18 000	Donations; fundraising; grants	Free	Medical professional/student volunteers	Volunteer ER and cardiologists (on-site)	2–9	A	+
Chad Foundation	2000	6 mo–30 y	Los Angeles, CA; NY	+	Limited	+	5100	Donations; fundraising; grants	\$25	MPV	Volunteer cardiologists	15–20	A	0
Heartfelt Project	2007	5–24 y	CA	+	Limited	+	10 000	Foundation	Donations accepted <\$100	MPV	Volunteer cardiologists (off-site)	1–2 (to cardiologists)	B	0
Heart for Sports	1999–2007 (now inactive)	HS	CA; FL; NY; MA; SC	0	+	+	10 000	Donations; grants	Free	MPV	Volunteer cardiologists (on-site)	1–2 (to cardiologists)	A	0
Championship Hearts Foundation	2000	HS	Austin, TX	0	Limited	0/+	11 200	Donations	Free	MPV	Cardiologists (on-site and off-site)	N/A	D	+
State of Texas	2008	HS	TX	+	Limited	0/+	4500	Grant: Texas legislature (\$1 million); donations; grants	Free	MPV	Cardiologists (on-site and off-site)	8	D	+
Sparkling Angels	2002	HS/ Junior college	Orange County, CA	+	0	0	10 000	Donation; fundraising	Free	MPV	2 Cardiologists	3–5	B	+
Heart Hype	2008	HS (track and field)	Baltimore, MD	+	Limited	+	900	Industry donations	Free	MPV	Pediatric and adult cardiologists (on-site)	1	A	+
Stanford University	2000	College	Palo Alto, CA	+	Selective; limited	+	4000	Athletic department; funds; time donated from medical staff	Free	Medical professionals (volunteer and paid staff)	Medical professionals (on-site); off-site cardiologists	N/A	A	+
Beaumont Hospital	2007	13–18 y	Detroit, MI area	+	Selective	+	8000	Internal	\$25	MPV	Cardiologists	10	D	+
Cypress ECG Project	2009/2011	HS (athletes)	TX/WA	+	Referred	0	20 000	Fee for service/ 501c3	\$10–\$15	Nonmedical staff	Cardiologist (off-site)	4	E	+

+ Indicates present; 0, absent; AZ, Arizona; CA, California; Echo, echocardiography; ER, emergency room physicians; FL, Florida; H&P, history and physical examination; HS, high school; IL, Illinois; KS, Kansas; MA, Massachusetts; MD, Maryland; MI, Michigan; MPV, medical professional volunteers; N/A, not available; NY, New York; SC, South Carolina; TX, Texas; and WA, Washington.

\*Data accessed as of May 2013; minimum of 5000 ECGs performed and reported.

†For notification of results, A indicates on-site documentation provided to participant or parent; B, notification mailed to parent/guardian; C, online system with pass key for participants to retrieve reports; and D, combination of A and B.

Some programs promote broad-based screening for heart disease, whereas others have limited their scope to HCM. Screening has been conducted with standard 2-dimensional

echocardiography, although portable instruments (which may not incorporate recording capability) are commonly used, and sometimes with protocols that by design limit

scanning time. Typically, these programs underestimate those organizational and administrative tasks that extend beyond the performance of echocardiograms or ECGs, including reliable parental notification of testing results; the securing of resources necessary for enrollment, recruiting, and effective marketing; and electronic data entry and storage. Also, some subjects may choose not to seek second-tier evaluations when recommended or may not have medical insurance that permits access to cardiologist consultation to resolve diagnoses suspected by primary screening. There is also potential liability when such screening programs fail to diagnose lethal cardiac conditions and thereby provide false assurance in the process.

There are currently several companies (eg, CompuMed, Inc [California]; Prevention Health Network, LLC [Kansas]; and Sportlink, advertised as “We heart you”) and medical clinics (eg, Saint Luke’s Athletic Heart Clinic, Kansas City, MO) that market screening ECGs to high schools, often citing sudden cardiac arrest risks and aspiring to identify HCM or other diseases and prevent SD. Many of these initiatives are limited to screening ECGs, although others include echocardiograms. Some programs partner with charitable organizations, and individual fees vary between \$35 and \$125. ECGs are sent out for interpretation (sometimes overseas) or on contract to area cardiologists. Now, after a decade, numerous community screening efforts in trained athletes have provided insights into the implementation and feasibility of such programs and systems; however, relatively little is known regarding the effectiveness of disease detection or SD prevention, and few published data have emerged.

### Practical and Logistical Considerations

There are multiple logistical and societal considerations involved in evaluating a general population screening protocol. Although proponents of mandatory screening ECGs are well intentioned, several broad considerations unavoidably impact these programs conceptually. First is the ethical and fairness issue of confining mass screening ECGs to any one particular segment of society (eg, competitive athletes, or college students who are athletes), which can be regarded as narrow in scope and in effect exclusionary (if not discriminatory and elitist), and therefore ethically unjustifiable. For example, it would not be sustainable to limit preparticipation screening to male athletes just because SD rates are much lower in female participants (1:9),<sup>1,2,6,7,37,128</sup> or to athletes in sports such as basketball and football because those sports are associated with higher risk than others.

In purely theoretical terms, fairness on this issue would require national screening ECGs to be available to all 60 million individuals in the United States aged 12 to 25 years; however, that is obviously an impractical initiative (if not virtually impossible logistically) that would undoubtedly be encumbered by enormous numbers of false-positive and false-negative results<sup>231,241</sup>; and consequently, it is not recommended by the present writing group. A mandatory national and federally funded initiative, whether it was confined to athletes or was extended to the general population, would undoubtedly be confronted with significant societal obstacles.

The argument advanced by some that a large, expensive program for millions of citizens is justifiable as long as it results in even a single life saved is an emotional (albeit understandable) perspective that ignores a multitude of scientific practical, ethical, and economic considerations. Concerns about equity and fairness apply to any screening program, ie, in national or other large populations, and to community, college/university, or high school–based screening initiatives that traditionally target athletes and essentially exclude other students from access to the same testing capable of detecting potentially lethal diseases, even when public funds or resources are used.

Notably, there is no reason to believe that the largely genetic heart diseases responsible for sudden and unexpected death in young people occur any more frequently in athletes than nonathletes, and therefore, the absolute number of such SDs must necessarily be higher in the larger group of nonathletes. Indeed, by design, cardiovascular screening has been confined to a highly selected segment of the potential at-risk population. For example, in the context of young students, only approximately one third participate in organized high school competitive sports, and just 1% are engaged in intercollegiate athletics.

In addition, societal and cultural considerations may create resistance and limit public acceptance of mandatory screening, including the inevitable perception by some that disqualification from sports and lost eligibility represents an infringement on individual liberty and the freedom to assume personal risks (even for SD). This may explain the experience of several investigators, including Marek et al,<sup>229</sup> who found that even when screening ECGs were offered at no cost to high school students in the Chicago, IL, metropolitan area, only ≈50% of those eligible ultimately elected to participate in the program. Furthermore, the current debate concerning screening ECGs is taking place at a time when the effectiveness and also the prudence of mass screening tests for cancer (ie, breast [mammography],<sup>260,261</sup> prostate [prostate-specific antigen test],<sup>262–266</sup> colorectal [colonoscopy],<sup>263–266</sup> ovarian,<sup>266</sup> and lung<sup>266,267</sup>) are being questioned. Relevant to this discussion is the current environment in which a substantial proportion of Americans are opposed to mandates within the healthcare system.

### World Health Organization Criteria for Mass Screening

Designing the optimal and most practical strategy to screen young people for underlying cardiovascular disease is complex, with a simple and definitive solution seemingly elusive. The World Health Organization has consistently advocated that such screening in asymptomatic populations can be justified, provided that all stipulated World Health Organization criteria are met.<sup>268</sup> However, it is apparent that the screening of large general populations (or specifically athletes) for cardiovascular disease with ECGs does not appear to comply in principle with such criteria for the following reasons:

- The 12-lead ECG does not qualify as a precise, validated, and suitable screening test known to reliably distinguish the affected from the nonaffected.

- General agreement is lacking on the criteria for defining an abnormal ECG in screening such populations.
- Evidence is lacking from randomized or prospective controlled trials showing that screening ECGs are effective in reducing morbidity and mortality.
- Projected absolute costs of screening ECGs are not balanced with respect to other medical care expenditures in society.
- It is uncertain what proportion of the potential population to be screened, when fully informed with regard to the consequences of testing, would consent to participate.

In other respects, however, mass screening ECGs are consistent with World Health Organization principles.<sup>263,268</sup> For example, to be considered an important public health problem, the diseases for which screening is intended to detect are not required to be common (which they are not, in the populations under consideration here). Rather, the importance of a public health problem is considered from the standpoint of both the individual and the community. Thus, even rare conditions with serious consequences to the individual and family may justify screening measures, as long as detection will likely lead to effective treatment interventions.

### Summary of Prior Consensus Recommendations Concerning Screening ECGs in Populations

1. AHA: Screening to detect cardiovascular disease in athletes is supported in principle by the AHA. Accordingly, a complete and targeted 12-point history and physical examination performed by qualified examiners was recommended in both 1996 and 2007.<sup>3,105,112</sup> The AHA does not support national mandatory screening ECGs of athletes, because the logistics, manpower, financial, and resource considerations make such a substantial program inapplicable to the US healthcare system. Individual quality-controlled local, community, or student-related initiatives were, however, supported by AHA if conducted properly and with adequate resources.
2. The AHA recommended screening ECGs (as Class IIa) for all children before administration of stimulant medications used to treat attention deficit/hyperactivity disorders to avoid heart rhythm disturbances that may occur with such drugs in children with structural heart disease.<sup>269</sup> An opposing viewpoint was subsequently published by the American Academy of Pediatrics.<sup>270</sup>
3. ESC: The Sport Cardiology Study Group of the ESC recommends systematic preparticipation screening for young competitive athletes, including a family and personal history, physical examination, and 12-lead ECG (as in the Italian model).<sup>5</sup> This strategy has not been translated on a national basis to other countries (with the exception of Israel).
4. International Olympic Committee: The International Olympic Committee recommends a targeted personal and family history, physical examination, and 12-lead ECG for all sports participants at the beginning of competitive activity, and to be repeated every 2 years thereafter.<sup>98,103,271</sup> The commitment of national Olympic teams

to such programs throughout the world is unclear, but to date this recommendation has not been adopted in the United States.

5. A recent National Institutes of Health (National Heart, Lung, and Blood Institute) position paper did not support mass screening of young athletes (aged <40 years) with ECGs, concluding that insufficient data were currently available to resolve this controversy.<sup>23</sup> The working group recommended pilot screening study ECGs in target populations to test the sensitivity and specificity of the ECG for cardiac diagnosis but did not offer funding or resources for such ambitious projects.

### Ethical Considerations

If one presumes a case could be made for the allocation of resources for a mass screening program to detect potentially life-threatening disorders of the heart in generally healthy populations of young people, 3 key ethical challenges would need to be addressed to implement such an initiative.<sup>272</sup> First, who should give consent to screening? Second, who will receive the results of screening tests? And, third who will make a determination concerning what degree of risk is consistent with participation in physical activities once test results are obtained?

When children and adolescents are tested, it is almost always an ethical requirement that parents or a guardian be notified about the testing and that their consent be a prerequisite for testing. Although there is some dispute about whether both parents must give written consent for minor children, generally parents have the right and expect to be involved in the provision of any routine medical diagnostic testing to their children, with the possible exception of interventions pertaining to reproductive and substance abuse matters.<sup>273</sup>

Certain programs or states may approach parental consent in a way similar to that which exists for many vaccinations; that is, parental permission is presumed prospectively, but there is an opportunity for a parent to opt out of testing. On a presumption model of consent, a child would automatically receive testing before participation in school-based or publicly sponsored sports activities. The burden would fall on those sponsoring the testing to inform parents of their right to opt their child out of the testing program and then on parents to decide whether to act on that decision.

The ability to opt out or decline can be made relatively simple; for instance, parents can sign a standard form brought to them by the student before testing, and the student can return it to the testing location. Alternatively, a declination form can be sent by the testing agent directly to the parent before testing. Some commentators have suggested that to discourage people from opting out, the process can be made more difficult by including requirements for the parent or guardian to sign a declination of testing in person at the testing site, or in front of a notary public, after receiving and understanding valid information about the risk of sudden cardiac death in young people from an appropriate healthcare provider.<sup>274</sup>

Children themselves have the right to assent to or decline testing if they are mature enough to understand the nature of the testing and the risks involved to their privacy and ability to play sports. Many states recognize that as children mature,



they should become the guardians of their own personal health information and partners in medical decision-making, supplementing the responsibility ordinarily held by their parents.<sup>274a</sup> This means that screening programs must have policies in place to deal with refusals by mature children, requests for testing by adolescents despite parental refusal, and requests by children not to inform their parents of either the testing or its results.

Test results should be disclosed to parents and to those children old enough to understand them as allowed by law. It is part of the informed consent process to disclose the fact that other parties will have access to test results. Physicians undertaking screening may do so as “gatekeepers,” also controlling the right to allow participation in certain sports or physical activities. But even if authorized to control and limit participation, they may also wish to share negative or concerning test results with a child’s primary care provider or a specialist or other third parties. There must be clear rules governing disclosure of test results to anyone beyond the child and parents or guardian. It is also important to design a policy in advance that dictates how to process important information that may be disclosed during testing (eg, pregnancy, abuse, suicidal thoughts) that is not being sought but nevertheless may be offered by the child.

Anyone not in direct care of the child cannot obtain access to medical information about the child without the express written consent of a parent.<sup>275</sup> This includes school authorities, coaches, team physicians, school nurses, trainers, the media, or any other party not providing direct clinical care.<sup>276</sup> Diagnostic test results concerning risk factors for SD will not sustain an argument for disclosure that overrides the presumption of confidentiality with respect to parents and their children. Moreover, if disclosure results in adverse consequences for the child in terms of social stigma, psychological harm, or difficulty in finding insurance or employment or in any other way, then liability may fall on anyone who discloses test results to those not involved in the provision of clinical care to the child.

Lastly, it should not be assumed that an abnormal test result will always be accepted by either a child or parent as a sufficient basis for exclusion from a particular type of activity. Although medical screening for diseases and disorders such as epilepsy or infectious and communicable diseases may be grounds for exclusion from certain types of activities or settings, the determination of risk is not the same as a diagnosis of disease. There may well be disputes about how to best manage risk, particularly with children who are skilled athletes or parents who wish to zealously promote the athletic careers of their child. Even in the face of catastrophic outcome, risk information is not beyond challenge with respect to exclusionary policies or requests for special accommodation. Although not the opinion or expressed policy of the AHA, the writing group believe that it may take legislation to mandate exclusion from sports activity with an adverse test result over parental or child objections.

### Medical-Legal Considerations

Mass screening of people 12 to 25 years of age (a population of ≈60 million males and females in the United States) for cardiovascular abnormalities is not legislatively mandated

by the US Congress or any state legislature. Even though a significant percentage of this population participates in compulsory physical education classes or voluntary recreational or competitive athletics involving strenuous exercise, which may increase the risk of SD caused by a latent cardiovascular abnormality, no major US national medical organization or society has recommended that a 12-lead ECG be required as part of mass screening for cardiovascular abnormalities. Moreover, based on a thorough analysis of the relevant medical and economic factors (as well as practical considerations), the 1996 and 2007 AHA recommendations<sup>3,105</sup> developed by an experienced group of US medical experts did not recommend use of a 12-lead ECG as part of mass screening for a subset of the population, that is, competitive athletes (who number ≈10 million), despite documented but rare instances of SD during athletic competition, conditioning, or training.

The United States has not enacted any legislation similar to the national laws of countries such as Italy<sup>4,18,116,244</sup> and Israel,<sup>28,29,92,93,246</sup> both of which require use of a 12-lead ECG as part of mandatory preparticipation screening to identify cardiovascular disease in all people desiring to participate in organized competitive athletics. The laws of these 2 countries, even when combined with several European countries’ voluntary adoption of the International Olympic Committee recommendation that an ECG be part of cardiovascular screening for Olympic athletes, do not conclusively establish an international standard or custom to require use of a 12-lead ECG in mass screening of large populations of young people for cardiovascular abnormalities. Even if it were sufficient to establish an international (or European) standard, current law (which is sparse) suggests that US courts would apply a national or state standard of care determined by the US medical profession in any litigation alleging that the failure to use a 12-lead ECG as part of routine mass screening to detect cardiovascular abnormalities constitutes medical malpractice.<sup>276,277</sup>

Medicine and the law have the same objectives of ensuring that reliable, scientifically based, and cost-effective clinical procedures are used in medical screening of large general populations. US law recognizes that the medical profession is in the best position to determine the appropriate nature and scope of recommended screening for pathological abnormalities in any large domestic population, including the attendant costs and benefits of the screening examination as a whole, as well as each of its individual components.<sup>90,278,279</sup> US law permits the US medical profession to use the best available scientific research and its members’ collective medical judgment to develop consistent, reliable, cost-effective guidelines and protocols to identify latent genetic or congenital cardiovascular abnormalities within certain segments of the population. Therefore, the present 2014 AHA guidelines should be based on the best available objective evidence and the underlying premise that cardiovascular screening programs (independent of size, scope, or design) should be driven by sound scientific principles and policy rather than by relatively rare catastrophic events, emotion, or subjective political pressure from advocacy groups that is not medically or scientifically based.

The law requires that individual physicians use reasonable care when conducting medical examinations for the purpose

of detecting foreseeable medical abnormalities that may cause SD or serious injury.<sup>277</sup> This legal standard, which is established by the applicable state tort law, historically requires a physician to follow customary medical practice (ie, what is usually done) in his or her specialty. However, accepted (ie, what is appropriate to do) or reasonable conduct under the circumstances (ie, what a reasonable physician would have done) is now the standard of care in many states.<sup>280</sup>

A physician is not per se legally liable for an athlete's injury or death caused by an undiscovered cardiovascular condition or abnormality. Depending on the particular jurisdiction, malpractice liability for failure to discover a latent, asymptomatic cardiovascular disease requires proof that the examining physician deviated from customary, accepted, or reasonable medical practice in his or her specialty while performing screening, and that proper use of appropriate diagnostic criteria would likely have disclosed the underlying medical condition before injury or death occurred.

Even if some US cardiologists and other physicians believe that use of a 12-lead ECG as a part of mass screening of young athletes for cardiovascular abnormalities constitutes "best practice," and some educational institutions use it in screening their student-athletes, failing to do so does not necessarily constitute medical malpractice.

Currently, there is no definitive judicial precedent (ie, judge-made case law) concerning the legal effect of compliance or noncompliance with the 1996 or 2007 AHA screening recommendations in medical malpractice litigation.<sup>90,279</sup> Thus, it is important to understand that as with those recommendations, the legal effect of the present 2014 screening guidelines is uncertain and will likely vary by jurisdiction. In some states, these guidelines may constitute some evidence of the medical standard of care for mass screening of large populations of young people. In other states, compliance with these guidelines may establish a rebuttable presumption that a physician has in fact met the appropriate legal standard of care, or this may not even be admissible evidence concerning the issue. In most states, however, the legal consequences of failure to comply with AHA screening guidelines cannot be determined definitively at this time.<sup>281</sup>

Despite the lack of any specific legal precedent to minimize potential legal liability for medical malpractice, it is prudent for physicians to provide the minimum level of screening recommended by the present AHA guidelines (eg, 14-point medical history and physical examination) when conducting mass screening of large, generally healthy populations of young people.<sup>281</sup> Courts have recognized that it is appropriate for physicians to follow current consensus screening guidelines in determining an athlete's cardiovascular fitness to participate in competitive sports, thereby suggesting that this is evidence of good medical practice.<sup>282,283</sup> There is a strong argument that compliance with the minimum requirements of the guidelines constitutes at least some evidence of physician conformity to the medical standard of care and may provide the basis for a successful defense against alleged malpractice. On the other hand, failure to provide the minimum level of screening recommended by these guidelines may give rise to litigation that could result in medical malpractice liability for death or injury caused by a cardiovascular abnormality that probably would have been discovered by following the guidelines.<sup>278</sup>

Although the present 2014 AHA guidelines do not require testing with 12-lead ECGs as part of mass screening for cardiovascular abnormalities, it is advisable to inform young athletes and their parents of the potential benefits and limitations of testing with 12-lead ECGs in detecting cardiovascular disease, to answer their questions, and to suggest they contact their personal physician if its use as an additional screening tool in individual cases is desired.

## Recommendations

The committee affirms that cardiovascular screening programs (independent of size, scope, or design) should be driven by sound scientific principles and policy and not by reaction to catastrophic events or political pressure from advocacy groups. In light of this acknowledgment and the data reviewed in the present document, the following recommendations for cardiovascular screening in young people aged 12 to 25 years are presented:

- 1. It is recommended that the AHA 14-point screening guidelines (Table 1) and those of other societies, such as the Preparticipation Physical Evaluation monograph,<sup>115</sup> be used by examiners as part of a comprehensive history-taking and physical examination to detect or raise suspicion of genetic/congenital and other cardiovascular abnormalities (Class I; Level of Evidence C).**
- 2. It is recommended that standardization of the questionnaire forms used as guides for examiners of high school and college athletes in the United States be pursued (Class I; Level of Evidence C).**
- 3. Screening with 12-lead ECGs (or echocardiograms) in association with comprehensive history-taking and physical examination to identify or raise suspicion of genetic/congenital and other cardiovascular abnormalities may be considered in relatively small cohorts of young healthy people 12 to 25 years of age, not necessarily limited to athletes (eg, in high schools, colleges/universities, or local communities), provided that close physician involvement and sufficient quality control can be achieved. If undertaken, such initiatives should recognize the known and anticipated limitations of the 12-lead ECG as a population screening test, including the expected frequency of false-positive and false-negative test results, as well as the cost required to support these initiatives over time (Class IIb; Level of Evidence C).**
- 4. Mandatory and universal mass screening with 12-lead ECGs in large general populations of young healthy people 12 to 25 years of age (including on a national basis in the United States) to identify genetic/congenital and other cardiovascular abnormalities is not recommended for athletes and nonathletes alike (Class III, no evidence of benefit; Level of Evidence C).**
- 5. Consideration for large-scale, general population, and universal cardiovascular screening in the age group 12 to 25 years with history-taking and physical examination alone is not recommended (including on a national basis in the United States) (Class III, no evidence of benefit; Level of Evidence C).**

### Final Insights

The preponderance of evidence indicates that SD in young athletes (and probably nonathletes) in the age range of 12 to 25 years should be regarded as a low event rate occurrence. The writing group understands that additional data regarding the cost efficacy of screening initiatives and testing performance in large populations, as well as the prevalence/incidence of SD events, would be potentially helpful. However, to achieve a precise incidence of SD in youthful populations would require a national mandatory reporting process with a centralized database and dedicated resources, a program that will be difficult to establish and maintain. Furthermore, a randomized trial of sufficient scale comparing mortality in populations tested with ECGs versus populations not tested with ECGs is impractical.

Therefore, currently, there is insufficient information available to support the view that universal screening ECGs in asymptomatic young people for cardiovascular disease is appropriate or possible on a national basis for the United States, in competitive athletes or in the general youthful population, and practical issues essentially exclude either strategy from any realistic consideration. The future evolution of mass screening programs with ECGs in other countries ultimately depends on the particular socioeconomic and cultural background and available resources within these particular healthcare systems.

At present, there is no mechanism available in the United States to effectively create national programs of such magnitude, whether limited to athletes or including the wider

population of all young people. Furthermore, there is insufficient evidence that particularly large-scale/mass screening initiatives are feasible or cost-effective within the current US healthcare infrastructure, or that routine 12-lead ECGs (supplemental to history and physical examination) provide added mortality benefit for prevention of sudden cardiovascular death. The ECG can promote detection of specific cardiovascular diseases and thereby benefit some individuals in a screening environment, but cannot be regarded as an ideal or effective test when applied to large healthy populations.

An additional, but unresolved, ethical issue concerns whether students who voluntarily engage in competitive athletic programs should have the advantage of cardiovascular screening, while others who choose not to be involved in such activities (but may be at the same or similar risk), are in effect excluded from the same opportunity. Therefore, in principal, it is prudent that screening of relatively small populations of students should not be restricted to competitive athletes, but strong consideration should be given to making this process available to all students.

The writing group acknowledges the tragic nature of SDs in the young, but does not believe the available data support a significant public health benefit from using the 12-lead ECG as a universal screening tool. The writing group, however, does endorse more widespread dissemination of automated external defibrillators, which are effective in saving young lives on the athletic field and elsewhere.<sup>125</sup>



## Disclosures

## Writing Group Disclosures

Writing Group Member	Employment	Research Grant	Other Research Support	Speakers' Bureau/Honoraria	Expert Witness	Ownership Interest	Consultant/Advisory Board	Other
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This table represents the relationships of writing group members that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all members of the writing group are required to complete and submit. A relationship is considered to be "significant" if (a) the person receives \$10 000 or more during any 12-month period, or 5% or more of the person's gross income; or (b) the person owns 5% or more of the voting stock or share of the entity, or owns \$10 000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

\*Modest.

†Significant.

**Reviewer Disclosures**

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(Continued)

Reviewer Disclosures, *Continued*

Reviewer	Employment	Research Grant	Other Research Support	Speakers' Bureau/Honoraria	Expert Witness	Ownership Interest	Consultant/Advisory Board	Other
Luciana T. Young	Ann and Robert H. Lurie Children's Hospital of Chicago	PI: Pediatric echocardiography Z-score and electrocardiogram database project (IRB#2013-15302), funded by the Pediatric Heart Network (PHN) and the NHLBI, NIH/DHHS*; PI: The Marfan trial (IRB# 2008-13423), Funded by the Pediatric Heart Network (PHN) and the National Heart, Lung, and Blood Institute, NIH/DHHS*; PI: Marfan Trial genetic ancillary study (IRB#2008-13423), Funded by the Pediatric Heart Network and the National Heart, Lung, and Blood Institute, NIH/DHHS*; PI: Marfan Quality of Life Study (IRB#2011-14386), Funded by the Pediatric Heart Network (PHN) and the NHLBI, NIH/DHHS*; PI: Circulating TGF- $\beta$ levels in Marfan syndrome (IRB#2011-14507), Funded by the Pediatric Heart Network (PHN) and the NHLBI, NIH/DHHS*; Co-investigator: Fetal cardiovascular overgrowth and maternal diabetes (ENH IRB#11-241), Funded by the University of Chicago CTSA grant number CTSA IL1 TR000430*; Co-investigator: A phase 3/4, prospective, multinational, open-label, noninferiority study of alglucosidase alfa manufactured at the 160L and 4000L scales in treatment of naïve patients with infantile-onset Pompe disease (IRB#2012-15003), Funded by Genzyme*	None	Invited lecturer, 10th Annual American Society of Echocardiography 2013 Sonographer Update: The Transpositions*	None	None	Board of Directors, American Registry of Diagnostic Medical Sonography*; Medical Advisory Board Member, University of Wisconsin Milwaukee (UWM)-sponsored Diagnostic Medical Sonography (DMS) Program*; National Advisory Board to establish a consensus statement on the cardiopulmonary management of MPS/Morquio syndrome*	None

This table represents the relationships of reviewers that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all reviewers are required to complete and submit. A relationship is considered to be "significant" if (a) the person receives \$10 000 or more during any 12-month period, or 5% or more of the person's gross income; or (b) the person owns 5% or more of the voting stock or share of the entity, or owns \$10 000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

\*Modest.

†Significant.

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KEY WORDS: AHA Scientific Statements ■ cardiomyopathy ■ electrocardiogram ■ genetics ■ screening ■ sudden death



## Assessment of the 12-Lead ECG as a Screening Test for Detection of Cardiovascular Disease in Healthy General Populations of Young People (12–25 Years of Age): A Scientific Statement From the American Heart Association and the American College of Cardiology

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