Cost-Effectiveness of Preparticipation Screening for Prevention of Sudden Cardiac Death in Young Athletes

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**Background:** Inclusion of 12-lead electrocardiography (ECG) in preparticipation screening of young athletes is controversial because of concerns about cost-effectiveness.

**Objective:** To evaluate the cost-effectiveness of ECG plus cardiovascular-focused history and physical examination compared with cardiovascular-focused history and physical examination alone for preparticipation screening.

**Design:** Decision-analysis, cost-effectiveness model.

**Data Sources:** Published epidemiologic and preparticipation screening data, vital statistics, and other publicly available data.

**Target Population:** Competitive athletes in high school and college aged 14 to 22 years.

**Time Horizon:** Lifetime.

**Perspective:** Societal.

**Intervention:** Nonparticipation in competitive athletic activity and disease-specific treatment for identified athletes with heart disease.

**Outcome Measure:** Incremental health care cost per life-year gained.

**Results of Base-Case Analysis:** Addition of ECG to preparticipation screening saves 2.06 life-years per 1000 athletes at an incremental total cost of $89 per athlete and yields a cost-effectiveness ratio of $42.900 per life-year saved (95% CI, $21200 to $71300 per life-year saved) compared with cardiovascular-focused history and physical examination alone. Compared with no screening, ECG plus cardiovascular-focused history and physical examination saves 2.6 life-years per 1000 athletes screened and costs $199 per athlete, yielding a cost-effectiveness ratio of $76100 per life-year saved ($52400 to $130000).

**Results of Sensitivity Analysis:** Results are sensitive to the relative risk reduction associated with nonparticipation and the cost of initial screening.

**Limitations:** Effectiveness data are derived from 1 major European study. Patterns of causes of sudden death may vary among countries.

**Conclusion:** Screening young athletes with 12-lead ECG plus cardiovascular-focused history and physical examination may be cost-effective.

**Primary Funding Source:** Stanford Cardiovascular Institute and the Breedwor Foundation.


For author affiliations, see end of text.

Young athletes are the healthiest members of society, yet more than 90 competitive young athletes die suddenly and unexpectedly in the United States each year (1). Most of these deaths are attributed to underlying structural heart disease, including hypertrophic cardiomyopathy, anomalous coronary artery anatomy, arrhythmogenic right ventricular cardiomyopathy, and aortic aneurysm (1). Athletes with intrinsic arrhythmic diseases, including the long QT, Brugada, and Wolf–Parkinson–White syndromes, also have an increased risk for sudden death.

Although the risk for sudden cardiac death for the young competitive-athlete population as a whole is low (2 per 100 000 persons per year) (1, 2), it is at least 2.5-fold higher than that of the age-matched nonathlete population (3). The risk for sudden cardiac death increases with increasing peak intensity of exercise and increasing level of competition (4, 5). The underlying autopsy-proven cardiac abnormality has been appropriately diagnosed during life in only a small minority of young athletes who have sudden cardiac death (6, 7). In athletes with underlying but undiscovered heart disease, the risk for sudden cardiac death may be more than 100-fold higher than that of unaffected peers. Identification and appropriate treatment for these high-risk persons may substantially reduce their likelihood of dying suddenly (8, 9).

Ongoing debate (10, 11) surrounds the optimal approach to screening young competitive athletes for occult cardiovascular disease to minimize sudden cardiac death. Current strategies for screening U.S. high school and college student-athletes before competitive exercise follow the recommendations of the 36th Bethesda Conference (12, 13), which refines previous suggestions for screening before competitive exercise (14, 15). The Bethesda Conference recommended screening with focused personal history, family history, and physical examination tailored toward
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Detection of cardiac abnormalities but did not explicitly recommend routine use of 12-lead electrocardiography (ECG). In Italy, preparticipation screening is governed by decree of the Italian Ministry of Health, which requires physician-led screening with history, physical examination, and ECG (16). In the 30 years since ECG screening was introduced in Italy, longitudinal evidence from the Veneto region of Italy has suggested an 89% absolute risk reduction in risk for sudden cardiac death in competitive athletes, such that the total risk for sudden cardiac death in screened athletes is now similar to that in contemporary, age-matched nonathletes (9). The success of the Italian approach has led the European Society of Cardiology to adopt a common European protocol, including ECG as the centerpiece of cardiovascular screening (17), and the International Olympic Committee to recommend ECG screening for Olympic athletes (18).

The cost of adding ECG to the screening program has been a central argument against its routine use (13). Expert commentators have identified a formal cost-effectiveness analysis as an urgent need (10, 11, 19). By contrast, the cost of ECG screening was not discussed in a recent American Heart Association scientific statement (20) recommending ECG screening for young patients with attention deficit hyperactivity disorder who were prescribed stimulants (21). Previous cost analyses of screening athletes with ECG have not fully accounted for the costs and benefits of screening (6, 22, 23). We sought to model the cost-effectiveness of including 12-lead ECG as part of preparticipation cardiovascular screening for young athletes.

Methods

Design

We used a decision model (Figure 1) to project the costs and survival rates for U.S. male and female athletes participating in high school and college interscholastic athletics who had a single cardiovascular preparticipation screening evaluation to identify underlying cardiac diseases predisposing to sudden cardiac death. The model evaluated 3 screening options: no screening; cardiovascular-focused history and physical examination alone, as recommended by the American Heart Association consensus panel (13); and cardiovascular-focused history and physical examination plus 12-lead ECG with interpretation, as recommended by the European Society of Cardiology Consensus Panel (17). We adhered to recommendations for conduct of cost-effectiveness analyses (24) by using a societal perspective on health care costs and benefits, following lifetime effects of interventions, and applying a 3% annual discount rate. We did not include costs and benefits unrelated to cardiovascular health of the athletes screened in the analysis.

Context

Estimates suggest that about 1 in 220,000 young athletes have sudden cardiac death each year. The European Society of Cardiology and the International Olympic Committee recommend that preparticipation screening for sports include electrocardiography; however, screening in the United States typically does not include electrocardiography.

Contribution

This analysis estimated that adding electrocardiography to history and physical examination to screen athletes aged 14 to 22 years saves 2.06 life-years per 1000 athletes screened at a cost of $42,000 per life-year saved compared with screening with history and physical alone. The addition of electrocardiography seemed to remain cost-effective in a range of sensitivity analyses.

Caution

Analysis was based largely on 1 European study, and patterns of cardiac disease differ geographically.

—The Editors

Decision Model

We assigned a cohort of patients to 1 of 4 branches on the basis of results of preparticipation testing and actual presence or absence of underlying cardiac disease. We modeled preparticipation testing as an initial primary screening test followed by a secondary testing step. We modeled persons who we did not find to be at risk or who, despite having a positive test result, did not continue on to secondary testing, in the negative primary-testing group. We divided persons in the negative-testing branch into those without disease (true negative) and those with underlying (occult) cardiac disease, which put them at increased risk for sudden cardiac death (false negative). Persons in the positive-testing branch were subjected to secondary testing, which was modeled to have comparatively high sensitivity and specificity versus initial screening. If we found that these persons had disease, we modeled them to receive treatment (as necessary) and restricted them from athletic activity, as appropriate (true positive). We assigned persons who had a negative result on secondary testing to either the true-negative (Figure 1, group C) or the false-negative (Figure 1, group B) branch on the basis of underlying cardiac disease status. Each branch then used a Markov process to model, on a yearly basis, the incidence of death, including incident sudden cardiac death and incident baseline risk for death (minus the baseline risk for sudden cardiac death for nonathletes without heart disease) by age (25); the cost of medical care; and the utility-adjusted quality of life. In each subsequent year, a 0.1% or 1% annual rate of being reclassified to have disease during the course of routine care occurred in the secondary testing false-negative and screening false-negative groups, respec-
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Figure 1. Decision analysis model.

Prevalence and Rates of Sudden Cardiac Death

We calculated rates of sudden cardiac death in athletes and nonathletes (Table 1) by using data from a study by Corrado and colleagues (9) and applied them to the U.S. population on the basis of the best available epidemiologic data (Appendix Figures 1 and 2 and Appendix Table 1, available at www.annals.org). These rates were similar to the rates derived from the study by Corrado and colleagues (9). We derived high and low estimates of sudden cardiac death incidence from alternative data sources suggesting variations in prevalence of predisposing disease or incidence of sudden cardiac death in athletes (Appendix Table 1). We derived background annual mortality rates from U.S. vital statistics data from 2004 (25).

Costs

We obtained baseline yearly medical costs from National Center for Health Statistics data from 2004 (35). We obtained clinical history and physical, ECG tracing and interpretation, and secondary testing costs (Table 1) from Medicare reimbursement schedules and the Consumer Price Index, adjusted when appropriate to 2004 U.S. dollars (33, 34). Initial screening costs included estimated indirect time and travel costs for screening. We modeled best-case costs by assuming efficiencies of mass screening (cost for ECG $5) in secondary analyses. Secondary testing costs were based on a second clinic visit, echocardiography, and exercise test or Holter monitor as average secondary testing guided by expected prevalence of underlying diseases (Appendix Table 1). A disease-specific
approach to determining secondary testing methods, including cardiac magnetic resonance imaging or commercially available genetic testing, when appropriate in a minority of athletes undergoing secondary screening, generated a similar mean value. We estimated initial treatment and follow-up above yearly baseline costs on the basis of expected rates of utilization for athletes who had a positive screening result on initial or secondary testing, and we used wide estimates for high and low ranges because of the uncertainty inherent in these estimates. This estimate includes expected initial-year societal costs for cardiac surgery ($48,000 per person) (36) for 1%, electrophysiology study and ablation ($18,000 per person) (37) for 2%, and implantable cardioverter-defibrillator implantation ($28,000 per person) (38) for 2% of the true-positive population.

**Effectiveness of Treatment and Nonparticipation**

We estimated baseline effectiveness of correct identification and treatment of athletes with occult heart disease from a large published longitudinal study evaluating effectiveness of preparticipation screening in Italy (9). The effect of treatment or nonparticipation, expressed as the ratio of the risk for sudden cardiac death for a competitive athlete with occult heart disease versus the risk for sudden cardiac death for athletes identified with heart disease and treated appropriately, varied widely. We calculated the baseline risk reduction directly from the findings of Corrado and colleagues (9) and modified the risk reduction to account for expected differences in baseline prevalence of predisposing underlying disease in U.S. versus Italian athletes, including a lower expected prevalence of arrhythmogenic right ventricular cardiomyopathy and an increased frequency of premature coronary artery disease (1). This ratio was varied from 1, reflecting no effect of screening-based discovery of disease, to 23, calculated as the maximum literature-derived rate of sudden cardiac death in athletes divided by the minimum estimate of sudden cardiac death in nonathletes after identification.

**Table 1. Costs, Effectiveness Assumptions, and Test Characteristics**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Base Case</th>
<th>Low Estimate</th>
<th>Low CI for Simulation</th>
<th>High CI for Simulation</th>
<th>High Estimate (Reference)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SCD risk per 100,000 person-years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Athlete with heart disease</td>
<td>174 (9)</td>
<td>35 (5)</td>
<td>150</td>
<td>200</td>
<td>335 (1)</td>
</tr>
<tr>
<td>Athlete with no heart disease</td>
<td>0.4 (9)</td>
<td>0.11 (5)</td>
<td>0.3</td>
<td>0.5</td>
<td>0.1 (1)</td>
</tr>
<tr>
<td>Athlete disqualified with heart disease</td>
<td>28 (9)</td>
<td>9.1</td>
<td>16</td>
<td>50</td>
<td>174 (1)</td>
</tr>
<tr>
<td>Nonathlete with no heart disease</td>
<td>0.2 (9)</td>
<td>0.11</td>
<td>0.18</td>
<td>0.22</td>
<td>0.1 (1)</td>
</tr>
<tr>
<td>Heart disease prevalence</td>
<td>1.2 (9)</td>
<td>0.3 (2)</td>
<td>1</td>
<td>1.4</td>
<td>2.5 (1)</td>
</tr>
<tr>
<td>Test characteristics</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensitivity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>H &amp; P</td>
<td>15 (26)</td>
<td>3 (7, 27)</td>
<td>8</td>
<td>25</td>
<td>30 (28)</td>
</tr>
<tr>
<td>ECG + H &amp; P</td>
<td>68 (9, 26)</td>
<td>37 (29)</td>
<td>50</td>
<td>73</td>
<td>75 (8)</td>
</tr>
<tr>
<td>Specificity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>H &amp; P</td>
<td>97 (9, 28)</td>
<td>73 (30)</td>
<td>92</td>
<td>96</td>
<td>96 (23, 26, 31)</td>
</tr>
<tr>
<td>ECG + H &amp; P</td>
<td>95 (9, 32)</td>
<td>84 (29)</td>
<td>93</td>
<td>97</td>
<td>98 (26)</td>
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<tr>
<td>Costs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Screening</td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>H &amp; P</td>
<td>73 (33)</td>
<td>0</td>
<td>55</td>
<td>84</td>
<td>2315</td>
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<tr>
<td>ECG</td>
<td>34 (33)</td>
<td>5</td>
<td>30</td>
<td>58</td>
<td>3045</td>
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<tr>
<td>Evaluation</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Cardiology visit</td>
<td>128 (33)</td>
<td>98</td>
<td>-</td>
<td>-</td>
<td>2756</td>
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<tr>
<td>Echocardiography</td>
<td>253 (33)</td>
<td>171</td>
<td>-</td>
<td>-</td>
<td>18258</td>
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<tr>
<td>Stress test</td>
<td>135 (33)</td>
<td>85</td>
<td>-</td>
<td>-</td>
<td>560</td>
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<tr>
<td>Cardiac MRI</td>
<td>1160 (33)</td>
<td>670</td>
<td>-</td>
<td>-</td>
<td>2200</td>
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<tr>
<td>Holter monitor</td>
<td>380 (33)</td>
<td>110</td>
<td>-</td>
<td>-</td>
<td>740</td>
</tr>
<tr>
<td>Cardiac CT</td>
<td>560 (33)</td>
<td>360</td>
<td>-</td>
<td>-</td>
<td>1800</td>
</tr>
<tr>
<td>Total cost</td>
<td>580 (33)</td>
<td>330</td>
<td>400</td>
<td>780</td>
<td>3006</td>
</tr>
<tr>
<td>Treatment for discovered heart disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cost (1st year)</td>
<td>50000 (9)</td>
<td>10000</td>
<td>4000</td>
<td>6000</td>
<td>15000</td>
</tr>
<tr>
<td>Cost per year (annual)</td>
<td>3500 (9)</td>
<td>50</td>
<td>250</td>
<td>450</td>
<td>1200</td>
</tr>
</tbody>
</table>

* = computed tomography; ECG = 12-lead electrocardiography; H & P = cardiovascular-focused history and physical examination; MRI = magnetic resonance imaging; SCD = sudden cardiac death.

Numbers in parentheses are references.

* Author consensus estimates.

$ Medicare reimbursement cost of $61 - $12 indirect cost for H & P and Medicare reimbursement cost of $27 + $7 indirect cost for ECG.

Maximum estimates for costs of ECG, echocardiography, exercise testing, Holter monitor, and clinical facility use charges obtained by averaging charges from a random sampling of 20 California hospitals' chargemasters from 2007 (34).

Averaged over a population who underwent secondary testing and was found to have positive results, above baseline medical costs; each identified individual is modeled to have 2 additional clinic visits, additional echocardiography, stress testing, and Holter monitor and either MRI or CT (average $2500 per individual); electrophysiology study and ablation, cardiac surgery, or implantable cardioverter-defibrillator implantation (total 5% of identified individuals distributed average $1500 per individual); and medications, counseling, other clinic visits, and second opinions ($1500 per individual).
Table 2. Base-Case Analysis Comparing Methods of Cardiovascular Screening to Prevent SCD in Student-Athletes

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Athletes Recommended for Secondary Testing, n</th>
<th>Identified Athletes at Increased Risk for SCD, n</th>
<th>Cases of SCD in Athletes, n*</th>
<th>LYS Saved, undiscounted</th>
<th>LYS Saved, discounted LYS</th>
<th>LYS Saved per 1000 Athletes, discounted LYS</th>
<th>Total Incremental Cost vs. Baseline, million $</th>
</tr>
</thead>
<tbody>
<tr>
<td>No screening</td>
<td>0</td>
<td>0</td>
<td>1100</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>H &amp; P</td>
<td>117 000</td>
<td>6700</td>
<td>1010</td>
<td>5100</td>
<td>2060</td>
<td>0.56</td>
<td>410</td>
</tr>
<tr>
<td>ECG + H &amp; P</td>
<td>213 000</td>
<td>30 200</td>
<td>670</td>
<td>24 200</td>
<td>9700</td>
<td>2.62</td>
<td>736</td>
</tr>
<tr>
<td>ECG + H &amp; P**</td>
<td>96 000</td>
<td>23 500</td>
<td>670</td>
<td>19 200</td>
<td>7630</td>
<td>2.06</td>
<td>327</td>
</tr>
</tbody>
</table>

*ECG = 12-lead electrocardiography; H & P = cardiovascular-focused history and physical examination; ICER = incremental cost-effectiveness ratio; LY = life-year; SCD = sudden cardiac death.

† Cumulative cases of SCD in athletes from age of screening to 35 years. Additional LYS are saved by treatment of discovered underlying heart disease.

‡ Probabilistic sensitivity analysis—based 95% CI.

§ Average remaining life expectancy is 61.89 years; the average remaining discounted life expectancy is 27.73 years, and the total discounted lifetime medical cost for the screened population is $388 billion.

¶ Weak dominance occurs when a strategy is less costly and less effective and has a higher ICER than a more expensive strategy.

** Assuming that H & P—based screening is included in baseline medical care.

Test Characteristics

We used the findings from 2 studies (9, 26) to derive the test characteristics of cardiovascular-focused history and physical examination (Table 1). History and physical examination characteristics may be substantially more or less sensitive (3% to 30%) and specific (73% to 98%) on the basis of the thresholds used to determine a positive test result (27, 28, 30, 39). We modeled ECG test characteristics on the basis of findings from longitudinal studies of competitive athletes in Italy (8, 9, 40). Baseline test characteristics are similar to those found in screening of secondary school-aged student-athletes in Nevada or England (26, 27) but have higher specifcity than when ECG testing is applied to elite athletes or African-American athletes (41–46). Interpretation of ECG was assumed to follow European consensus document guidance with modifications, which recommends secondary testing only with distinctly abnormal ECG findings, including prolonged QT, bundle-branch block, deep ST-segment depression and T-wave inversion, and arrhythmias and excluding voltage criteria for left ventricular hypertrophy and prolonged PR interval (44, 47, 48). We evaluated a range of assumptions for the test characteristics of history and physical and ECG to account for substantial variability in the reported sensitivity and specificity of screening tests for undiagnosed cardiac disease in athletes.

Utilities

We used Health Utilities Index-Mark 3 scores (Appendix Table 1) derived from a cross-sectional population sample (49) for adolescents of normal health (0.94) in whom heart disease was discovered (0.89) in secondary analyses. We assumed that utility scores for athletes who were disqualified from competition were equivalent to those for adolescents with heart disease in the first year. We discounted the decrement in utility linearly over 4 years from diagnosis; all patients had equivalent utility scores from 5 years onward after receiving a diagnosis. Regardless of secondary testing results, we ascribed athletes with a positive initial screening result a 5% decrement in quality of life lasting 1 week versus adolescents with normal health.

Sensitivity Analyses

We did sensitivity analyses to account for uncertainty in model assumptions and to address variability in published clinical data. We did univariate sensitivity analyses over low and high absolute estimates and low and high estimates of the expected population median (Table 1 and Appendix Table 1). We varied risk ratios and test characteristics over the ranges derived from the screening literature. We did Monte Carlo simulations, varying each input over a distribution with the base case as the median and the low and high estimates of the median representing the 95% CI limits of two 1-sided normal distributions, with values limited to positive numbers (or values from 0 to 1 for utilities or test characteristics) to evaluate the overall CIs of the model. We chose a random value from within this distribution for each variable, and we chose variables that were interdependent together.

Role of the Funding Source

The Breitwur Foundation and the Stanford Cardiovascular Institute funded this study. Dr. Wheeler was supported by a U.S. Public Health Service training grant from the National Heart, Lung, and Blood Institute, National Institutes of Health. The funding sources had no role in the design and conduct of the study; in the collection, analysis, and interpretation of the data; in the reporting, preparation, or review of the manuscript; or in the decision to submit the manuscript for publication.

www.annals.org
Table 2—Continued

<table>
<thead>
<tr>
<th>Incremental Cost per Athlete Screened, discounted $</th>
<th>ICER, 95% CI, discounted $/LY saved</th>
<th>ICER, discounted $/LY saved</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>111</td>
<td>153 000–412 000</td>
<td>Weakly dominated</td>
</tr>
<tr>
<td>199</td>
<td>62 400–130 000</td>
<td>76 100</td>
</tr>
<tr>
<td>89</td>
<td>21 200–71 300</td>
<td>42 100</td>
</tr>
</tbody>
</table>

**RESULTS**

**Validation of the Model**

The base-case model compared outcomes for all U.S. student-athletes undergoing 3 cardiovascular screening options from age 16 years. Not screening athletes led to an average remaining life expectancy of 61.9 years in those without underlying cardiac disease and 60.8 years in those with underlying heart disease (27.3 years and 26.9 years on a discounted basis, respectively). In addition, because athletes with underlying heart disease have a risk for subsequent discovery of their condition through routine medical care, development of symptoms, or aborted sudden cardiac arrest, they have higher medical costs ($329 000 vs. $310 000 per person or $114 000 vs. $105 000 per person in current costs on a discounted basis). The total number of sudden deaths in young athletes in the model over 8 years of increased risk due to athletic activity averages 89 per year, with a risk for sudden death for 2.4 per 100 000 athletes per year. These numbers closely approximate the average of 90 nontraumatic sudden cardiac deaths in young, competitive athletes per year in the United States (1).

**Evaluation of Screening Methods Versus No Screening**

Screening with cardiovascular-focused history and physical saved 0.56 life-year per 1000 athletes compared with no screening (Table 2). The per-athlete incremental cost of history and physical versus no screening was $133 or $111 on a discounted basis. We screened 3.7 million competitive athletes in high-risk activity (Appendix Table 1); we recommended an additional 117 000 athletes for secondary testing and identified 6000 athletes at increased risk for sudden cardiac death. The total incremental cost was $410 million, assuming an optimized, cardiovascular-focused history and physical. The cost-effectiveness ratio for history and physical versus no screening was $199 000 per life-year saved on a discounted basis ($301 000 per quality-adjusted life-year [QALY] saved).

Screening with ECG and cardiovascular-focused history and physical saved an average of 2.6 life-years per 1000 athletes screened compared with no screening (Table 2). We recommended an additional 213 000 athletes for secondary testing, and we identified 30 200 athletes at increased risk at a total incremental cost of $736 million. The incremental cost of screening with ECG plus history and physical compared with no screening was $199 per athlete, including all secondary testing and treatment costs. The cost-effectiveness ratio of ECG plus history and physical versus no screening was $76 100 per life-year saved. With utility adjustments, this increased to $111 000 per QALY saved.

**Addition of ECG to History and Physical Examination**

From a health economics standpoint, our analyses indicate that the strategy of using history and physical examination to screen for sudden death should fall out of consideration by weak dominance (50). However, performance of a routine history and physical examination that includes components of cardiovascular history and physical examination may be considered part of the standard of care, independent of cardiovascular screening effects in young athletes. In this case, the history and physical examination and associated subsequent costs may be considered part of the baseline medical costs of the health care system. To assess this approach, we evaluated the incremental addition of 12-lead ECG to history and physical alone. Comparison of ECG plus history and physical examination to cardiovascular-focused history and physical examination alone saves $2.1 life-years per 1000 athletes screened at an incremental cost of $88 per athlete. At a cost of $327 million, 96 000 additional athletes had secondary testing, and we identified 23 500 athletes potentially at risk. The incremental cost-effectiveness ratio of adding ECG plus history and physical examination versus history and physical examination alone was $42 900 per life-year saved ($61 600 per QALY saved).

**One-Way Sensitivity Analyses**

The cost-effectiveness of screening was generally robust to changes of the input variables within ranges estimated for the population mean (Figure 2). For each of the cost and effectiveness inputs, variation within the ranges used for probabilistic sensitivity analyses resulted in ECG plus history and physical examination having an incremental cost-effectiveness ratio of $50 000 to $100 000 per life-year saved compared with no screening and of $25 000 to $60 000 per life-year saved compared with cardiovascular-focused history and physical examination alone. In comparison with history and physical examination alone, ECG plus history and physical examination exceeded a cost-effectiveness ratio of $100 000 per life-year saved with low rates of sudden cardiac death in athletes, low population prevalence of disease, or low efficacy of screening. Varying the age at screening from 12 to 22 years had minimal effect on the cost-effectiveness of screening, although age may materially affect the sensitivity and specificity of testing by ECG or history and physical examination. Changes in the estimated sensitivity and specificity of
The incremental cost-effectiveness ratios (ICERs) of ECG + H & P versus no screening (top) and versus H & P alone (bottom) are shown as changed by varying critical measurements through possible ranges. The base-case estimates (top [976 100 per life-year saved] and bottom [842 900 per life-year saved]) are shown (vertical lines). The horizontal solid boxes represent the ICER resulting from inputting the described variable over the expected range of the mean value (also used in probabilistic sensitivity analysis); the horizontal lines represent the ICER found using expected minimum and maximum inputs, which may be applicable to certain specific subgroups or particular payers. The table shows the low-value input, the low-value input used for probabilistic sensitivity analysis, the high-value input used for probabilistic sensitivity analysis, and the high-value input for each variable or combination of variables. In the bottom panel, the ICER between ECG + H & P and H & P alone is dependent not on H & P cost but on the interpretation of H & P results before ECG interpretation. "Risk ratio: athlete versus DQ" is the mortality risk reduction associated with disqualification and treatment of athletes with underlying occult heart disease versus continued participation without diagnostic. "EGC cost" is cost of ECG greater than H & P cost. All costs are all screening cost variables, including primary and secondary screening tests and initial and recurring screening-related treatment costs, input into the model concurrently. DQ = disqualified; EGC = 12-lead electrocardiography; H & P = cardiovascular-focused history and physical examination; SCD = sudden cardiac death; sens/spec = sensitivity/specificity.

* Per 100 000 life-years.
† x-fold risk reduction.
‡ Base-case assumption.
§ ECG + H & P found to be both cost- and life-saving versus comparator.

The incremental cost-effectiveness ratios (ICERs) of ECG + H & P versus no screening (top) and versus H & P alone (bottom) are shown as changed by varying critical measurements through possible ranges. The base-case estimates (top [976 100 per life-year saved] and bottom [842 900 per life-year saved]) are shown (vertical lines). The horizontal solid boxes represent the ICER resulting from inputting the described variable over the expected range of the mean value (also used in probabilistic sensitivity analysis); the horizontal lines represent the ICER found using expected minimum and maximum inputs, which may be applicable to certain specific subgroups or particular payers. The table shows the low-value input, the low-value input used for probabilistic sensitivity analysis, the high-value input used for probabilistic sensitivity analysis, and the high-value input for each variable or combination of variables. In the bottom panel, the ICER between ECG + H & P and H & P alone is dependent not on H & P cost but on the interpretation of H & P results before ECG interpretation. "Risk ratio: athlete versus DQ" is the mortality risk reduction associated with disqualification and treatment of athletes with underlying occult heart disease versus continued participation without diagnostic. "EGC cost" is cost of ECG greater than H & P cost. All costs are all screening cost variables, including primary and secondary screening tests and initial and recurring screening-related treatment costs, input into the model concurrently. DQ = disqualified; EGC = 12-lead electrocardiography; H & P = cardiovascular-focused history and physical examination; SCD = sudden cardiac death; sens/spec = sensitivity/specificity.

* Per 100 000 life-years.
† x-fold risk reduction.
‡ Base-case assumption.
§ ECG + H & P found to be both cost- and life-saving versus comparator.
the combination of ECG plus history and physical examination resulted in comparatively small changes in the incremental cost-effectiveness ratio.

Lower effectiveness of disqualification resulting from identification of athletes with underlying cardiac disease (risk reduction, 33% vs. 84%) increased the incremental cost-effectiveness ratio to more than $188 000 per life-year saved for ECG plus history and physical examination versus no screening. An intermediate but more modest 50% sudden cardiac death risk reduction with treatment and disqualification led to an incremental cost-effectiveness ratio for ECG plus history and physical examination of $119 000 versus no screening and $63 600 per life-year saved versus history and physical examination alone. In the base-case analysis, we used conservative estimates for the change in sudden death risk in athletes with underlying heart disease. In a sensitivity analysis (Appendix Table 2, available at www.annals.org), we assumed a more substantial increase in risk for death with time. This reduced the incremental cost-effectiveness ratio of screening for ECG plus history and physical examination to $28 000 per life-year saved versus history and physical examination alone and $46 000 per life-year saved versus no screening.

Some investigators have expressed concern about the potentially prohibitive costs of initial and secondary testing. Varying the incremental cost of ECG from $5 to $304 per athlete corresponds to an incremental cost-effectiveness ratio of $28 900 to $174 000 per life-year saved for ECG versus history and physical examination alone. An incremental cost-effectiveness threshold for ECG screening of $100 000 per life-year saved for history and physical examination alone corresponds to an incremental ECG cost over history and physical examination of $151. Varying the cost of secondary testing from $330 to $3000 per athlete who had a positive test result on initial screening changes the cost per life-year saved from $59 700 to $73 500 for ECG plus history and physical examination versus history and physical examination alone.

### Probabilistic Analysis

A probabilistic analysis evaluating 10 000 iterations of the model shows that addition of ECG was incrementally life-saving in more than 99.8% of simulations versus history and physical examination alone (Figure 3 and Appendix Table 3, available at www.annals.org). In 99.9% of simulations, ECG plus cardiovascular-focused history and physical examination was less than the $100 000 per life-year saved cost-effectiveness threshold compared with cardiovascular-focused history and physical examination alone. Compared with no screening, ECG plus history and physical examination costs less than $100 000 per life-year saved in 79.9% of simulations. In contrast, history and physical examination alone cost more than $100 000 per life-year saved in all 10 000 simulations.

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**Figure 3. Probabilistic sensitivity analysis.**

![Probabilistic sensitivity analysis](https://www.annals.org)

ECG = 12-lead electrocardiography; H & P = cardiovascular-focused history and physical examination; ICER = incremental cost-effectiveness ratio.

**Top.** Scatterplot of simulation done for each of 3 base-case comparisons, varying each input variable over the expected range of the population median. In nearly all simulations, H & P is weakly dominated by ECG + H & P because it is less costly, is less effective, and has a higher ICER. The ICERs can be measured by dividing the discounted life-years saved by the incremental discounted cost. Reference lines for ICERs of $50 000 per life-year saved and $100 000 per life-year saved are shown. Dots below each of these lines represent simulations, with ICERs shown below these willingness-to-pay thresholds. **Bottom.** Willingness-to-pay curves for comparisons between ECG + H & P and H & P, ECG + H & P and no screening, and H & P and no screening. Proportion of simulations plotted versus ICER for each of 3 base-case comparisons are shown. Simulations that were not life-saving are included in the proportion of simulations greater than $300 000 per life-year saved. The probability of preferring ECG + H & P over H & P alone is 68% at a willingness-to-pay threshold of $50 000 per life-year saved and 99.9% at $100 000 per life-year. ECG + H & P is cost-effective and life-saving in 0.2% of simulations versus H & P alone. The probability of preferring ECG + H & P over no screening is 0% at a willingness-to-pay threshold of $50 000 per life-year and 79.9% at $100 000 per life-year. The probability of preferring H & P over no screening is 0% at $100 000 per life-year.
Cost-Effectiveness of Other Screening Methods

In exploratory analyses, we evaluated the cost-effectiveness of screening by using assumptions for screening methods in several recent published sources (9, 13, 27, 44, 51, 52). We estimated screening test characteristics for each method and estimated a screening cost for each method (Appendix Table 4 and Appendix Figure 3, available at www.annals.org). These data confirm that the specificity of screening has a substantial effect on cost-effectiveness. Comparing these data with base cases shows that on the basis of cost per life-year saved, screening athletes with ECG alone to detect cardiovascular disease may be the preferred strategy, may cost less, and may detect more at-risk individuals than history and physical examination alone. Univariate and probabilistic sensitivity analyses (Appendix Figures 4 and 5, available at www.annals .org) suggest that screening with highly specific ECG alone may be less than societal willingness-to-pay thresholds in nearly all cases.

DISCUSSION

Preparticipation screening of student-athletes for cardiovascular disease using a single, appropriately interpreted ECG and cardiovascular-focused history and physical examination reduces sudden cardiac death and has an acceptable cost-effectiveness ratio of $76 000 per life-year saved, compared with a strategy of no screening. The addition of ECG to the current recommended standard of history and physical examination also reduces sudden death, with an incremental cost-effectiveness ratio of $42 900 per life-year. Screening athletes with cardiovascular-focused history and physical examination alone is unlikely to save money (> $199 000 per life-year added) compared with a strategy of no screening, mainly because of the strategy’s relatively poor sensitivity and specificity in young athletes (7, 26, 27, 30, 31, 53). Despite concerns about total cost, the incremental life-years saved by including ECG are significant. Of note, these results assume the use of a high threshold for ECG positivity, which is critical to cost-effective implementation of ECG plus screening with cardiovascular-focused history and physical examination. Organized mass screenings of young athletes may improve the efficiency of cardiovascular screening and improve its cost-effectiveness.

The epidemiology of sudden cardiac death in athletes differs between the United States and Italy, with U.S. athletes having hypertrophic cardiomyopathy more often and arrhythmogenic right ventricular cardiomyopathy occurring more in Italian athletes (1, 7–9, 40). Although these differences may lead to lower efficacy of screening in the U.S. context, no studies have definitively addressed this question (8, 9, 32, 40). Data from our study, including those modeling the effects of lower efficacy, should inform the appropriateness of undertaking a trial of sufficient magnitude to determine the efficacy of screening U.S. student-athletes.

Of importance, our data are based on a single screening per student-athlete engaged in interscholastic or inter-collegiate high-risk sports rather than annual screening, which is currently recommended by consensus documents (13, 17). Exploratory analyses (Appendix Figures 6 and 7 and Appendix Table 5, available at www.annals.org) suggest that annual screening of any kind, or extending screening to all middle school and high school students, is highly unlikely to be cost-effective in reduction of sudden cardiac death. In the case of extending screening to a wider population of young people, a mixture of the strategies of no screening and ECG with history and physical examination will be the most economically optimal, given any system-wide budget constraint. As with all screening strategies, limiting screening to a higher-risk subgroup will lead to difficult policy choices, and ethical concerns about inequality and preferential treatment will arise. Student-athletes participating in interscholastic sports have been identified as a high-risk subgroup (1–6). Male sex; African-American ethnicity; and participation in football, basketball, or elite-level or professional sports seem to be additional risk factors for athlete-associated sudden death (5, 44–46).

Screening has potentially substantial effects that extend beyond clearance for sports participation. Preparticipation history and physical examination may have additional benefits on injury reduction, general health awareness, updating vaccination status, or modeling positive lifelong health care interactions in young persons. These potential effects are not accounted for in the model. In addition, the long-term effects of early diagnosis and treatment of high-risk diseases, as well as common diseases, such as hypertension and hyperlipidemia, are not well described or easily evaluated. Risk factor reduction or early treatment of such conditions as hypertension that do not warrant exclusion from sports in the United States should be weighed against the potential for harm associated with disqualifying athletes at intermediate risk for sudden cardiac death. In addition, the benefit of college athletic participation in promoting lifelong physical activity is unmistakable (54).

The validity of utility measurements in young adults is debated, as adolescent and parental preferences and risk tolerance are often at odds (55, 56). Although we included quality-of-life measures in our secondary analyses, studies that inform personal, family, and community perspectives on utility, with respect to participation, disqualification, and sudden cardiac death in young athletes, are needed. The effects of substantial decrements in utility caused by positive primary screening or exclusion from athletic activity and treatment of underlying cardiac disease could easily offset any life-saving benefits with quality-of-life decrements.

Consensus panels developed current ECG criteria and have been repeatedly shown to restrict secondary testing from 2% to 9% of the screened population (17, 27, 40, 44,
45). Although this is acceptable in cost-effectiveness terms, improvements in specificity, as refinement of criteria over time has shown (17, 27, 40, 44, 45), may be expected from the application of digital processing techniques to large databases of athlete ECG results to redefine the “normal” athlete ECG. Use of less stringent criteria to determine positive screening by ECG or history and physical examination or screening of selected populations (for example, elite cyclists or professional basketball players) may result in substantially more referrals for secondary testing (30, 31, 53).

In conclusion, we show that preparticipation screening of young athletes with ECG plus cardiovascular-focused history and physical examination is reasonable in cost and is effective at saving lives. Screening with ECG can be cost-effective compared with common benchmarks, such as dialysis for patients with chronic kidney disease ($20 000 to $80 000 per QALY saved), or interventions, such as public access to defibrillation ($55 000 to $162 000 per QALY saved) or implantable cardioverter-defibrillator implantation ($34 000 to $70 000 per QALY saved), for prevention of sudden cardiac death (37, 57–59). Dedicated cardiovascular screening with history and physical examination is substantially more costly and marginally more effective than no screening. Sensitivity analyses show that in nearly all cases, screening with ECG plus cardiovascular-focused history and physical examination is the preferred strategy.

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Reproducible Research Statement: Study protocol, statistical code, and data set: Available from Dr. Ashley (e-mail, euan@stanford.edu).

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