“‘A billion here, a billion there and pretty soon you’re talking real money’ is a quote attributed to the late Senator Everett Dirksen. Whether or not he actually spoke those words, it is believed that, if he did not, he would have heartily approved having been quoted as such. At this time in American history, this quote as it relates to medical spending is appropriate to the debate. No doubt, this is a complex issue at face value. We have philosophical, ethical, and moral issues surrounding this debate and the 2 types of EBM—evidence-based medicine and emotional-based medicine—as well. Biases and heuristics flavor the decision making and cloud the public policy issues that are central to how we decide what to do and for whom. The role of this column is to present the reader with the information that would allow a prudent practitioner to make an informed decision about whether to advocate for universal screening of children and adolescents with an ECG to prevent sudden cardiac death (SCD).

Response by Vetter p 702

Philosophy, Ethics, and Moral Values

Two opposing schools of thought—utilitarianism and deontology—are central to this debate. Utilitarianism was favored by Jeremy Bentham (1748–1832) and John Stuart Mill (1806–1873) who were consequentialists who believed that whether or not an act is morally right depends on its consequences with respect to utility, thus the term utilitarianism. The essence of their belief system was the Greatest Happiness Principle or, more plainly speaking, the greatest good for the greatest number of people. Deontology, on the other hand, is based on the Greek word todeon meaning duty. The central theme here is explained by 2 imperatives—hypothetical and categorical. The hypothetical imperative belies the concept of finding a means to an end, and the categorical says imperative that you act from a sense of duty, a self-given law that is binding for all rational agents. So, in Kant’s world, ethical rules bind one to their duty, and, thus, there is an unconditional requirement over all circumstances and the end justifies the means. For those readers who are Star Trek fans, this is the argument between Spock and Kirk where Spock sacrifices himself, explaining that “the needs of the many outweigh the needs of the few,” and Kirk retorts later, “sometimes the needs of the few outweigh the needs of the many.”

When we come to the end of the day, after all the scientific evidence is presented and analyzed, after all the biases and heuristics are explained, the debate between these 2 concepts, utilitarianism versus deontology, is what people vote on when asked, “Do you favor using ECGs to screen the young to prevent SCD?” Nevertheless, I will attempt to persuade...
you, the reader, that the use of the 12-lead surface ECG is not an acceptable tool to answer this question. Moreover, I will attempt to demonstrate that implementing such a policy would be a detriment to our society.

Scope of the Problem
It is commonly stated that sudden death in the population of patients between 1 to 19 or 21 years of age is uncommon.1 Exactly how uncommon it is varies but is mostly unknown.2 The most recent study of this group was published in 2014 by Pilmer et al.1 They looked at the death investigation system in Ontario, Canada that included coroners who must investigate all deaths that are “sudden, unexpected or from unnatural causes.” A centralized database on these investigations is kept for review. This is an important study, because nothing like this exists in the United States, which has been a frequent complaint of those who say we underestimate the number of sudden deaths in the United States. The authors looked at the time period of 2005 to 2009. Excluding cases with known infectious issues, significant comorbidities, drug overdoses and drowning, or automobile accidents, they found 116 cases. An autopsy was performed in 113 of these cases. The 3 patients excluded already had established clinical diagnoses that would explain their deaths. Physical activity at the time of death was also recorded. The crude rate of death was 0.78 per 100000 person-years, and the median interquartile age was 12.7 years, with males accounting for 66% of the cohort. Children >10 years of age were more likely to have structural heart disease. The breakdown of causes for the entire group were as follows: myocarditis, 25%; arrhythmogenic right ventricular dysplasia, 16%, and another 9% listed as possible; hypertrophic cardiomyopathy (HCM), 14%; other myocardial disease, 16%; aortic dissection, 5%; and anomalous right coronary artery, 4%. Several other diagnoses were all ≈2% to complete the group. As for activity, the most common activity was sleep 41% and normal activities of daily living 41%. Moderate or vigorous activity was seen in only 16%. The results of this important study were that >80% of the deaths occurred at rest or during nonexertional activities of daily living, and most occurred at home. In addition, the incidence of a cardiac prodrome was distinctly low before a sudden death occurred. The authors point out that ECGs may be abnormal in patients with definite HCM or arrhythmogenic right ventricular dysplasia, but they do not necessarily lend themselves to identifying the other diseases found in this group. Meyer et al2 published a study in 2012 that included all SCDs in King County (Washington State) over a 30-year period (1980–2009). Looking only at patients 3 to 13 years of age (30 cases) and then at patients 14 to 24 years of age (60 cases), they found an average of 3 cases per year. Age-stratified incidence rates were as follows: 0 to 2 years of age, 2.28 per 100000 person-years; 3 to 13 years of age, 0.61 per 100000 person-years; and 14 to 24 years of age, 1.44 per 100000 person-years. The risk of SCD in patients 14 to 24 years of age, a group pertinent to the discussion here, was 1:69000 person-years. The diseases in that group broke down to: primary arrhythmia, 23%; congenital heart disease, 23%, dilated cardiomyopathy, 14%; HCM, 2%; other, 26%; myocarditis, 4%; and long QT syndrome, 8%. The authors noted that the incidence of SCD in this nonathlete population was ≈3 times lower (24.5% versus 71.7%) than in athletes, noting, however, that in a study by Harmon et al,3 they found a significantly higher incidence. Another study from Denmark over a 7-year period found an incidence of SCD in patients 1 to 18 years to be 1.1 per 100000 person-years.4 Atkins et al5 reported the incidence of SCD in children (1–11 years of age) to be 4/100000 person-years and adolescents (12–19 years of age) to be 6/100000 person-years. Finally, a second study by Pilmer et al6 using an identical model to that described above, reported an incidence of SCD of 0.7/100000 patient-years in children 2 to 18 years of age. Only 9% of the sudden deaths occurred during moderate or vigorous exercise. No pediatric SCDs were reported during organized sports. Of the 18 patients in that age group, 10 had structural heart disease, 2 had myocarditis, 2 had HCM, 1 had dilated cardiomyopathy, and 3 had arrhythmogenic right ventricular dysplasia. The bottom line from all of these studies is that SCD in the population aged 1 year to the 19- to 21-year age group is quite low.

Having roughly defined the incidence of SCD in this group of patients, the next question we must answer is: What is the incidence of ECG abnormalities in that same group of patients? There is no large-scale study of children in that age group looking at ECG abnormalities and linking them to a gold standard for structural heart disease like echocardiography. However, a recent study by Chandra et al7 looked at individuals 14 to 35 years of age who underwent subsidized ECG screening in the United Kingdom. These 11845 individuals, “irrespective of athletic status, symptoms or family history of premature cardiac disease” had ECGs performed and analyzed by the authors with an agreement of 97% between the 2 authors, who had been blinded to any clinical information, for what they called the group 2 patients. The ECG findings in group 2 included T-wave inversion, findings suggestive of underlying cardiomyopathy or structural heart disease including ST depression, pathological Q waves, and complete bundle-branch block. They found that white athletes and nonathletes had about the same percentage of abnormalities on their ECGs as black athletes, who had twice as many abnormalities as black nonathletes. There were 7764 nonathletes and 4081 athletes in the group 2 pattern cohort. Echocardiograms were performed on all 784 nonathletes with group 2 findings on their ECGs.

The echocardiograms were performed and evaluated by an investigator who was blinded to the ECG findings, and to whether or not the individual was an athlete, as well. A normal heart was seen in 84% of individuals. In nonathletes, an abnormal ECG was found in 10.1% of individuals, but the echocardiograms only demonstrated abnormalities in 2%. Most of these abnormalities were T-wave inversions in adolescents, which is a common normal finding. With the use of European Society of Cardiology guidelines for QT intervals, 52.3% were found to have long QT or short QT intervals resulting in a high
number of false positives. Overall, 20% of the cohort would have abnormalities in their ECGs that would prompt further testing. Marek et al did a retrospective study of >32,000 non-athlete high school students from 38 ECG screening events between 2006 and 2009. These studies were interpreted by 6 cardiologists who had “knowledge of the ECG changes that occur in conditions associated with SCD.” They found abnormalities in 2.5% (817 students) requiring further evaluation. Not surprisingly, the most common abnormalities were left ventricular hypertrophy and ST-T wave abnormalities, both 17%; left-axis deviation, 13.5%; and prolonged QTc, 12.2%. There is no mention of the sensitivity or specificity because we do not have definitive follow-up, so we are unable to evaluate the issue of false positives or negatives.

Looking at these data retrospectively at 1 time period without the use of serial ECGs is problematic. We know that HCM is a progressive disease and so a normal ECG now does not mean that, 2 to 3 years from now, especially in this age group, that the ECG will not evolve into a more typical HCM pattern with left ventricular hypertrophy. It is also well known among experienced ECG readers that patients who have long QT syndrome may have 1 or several ECGs that demonstrate a normal QTc only to have a grossly abnormal ECG at another time more diagnostic of prolonged QT syndrome. Thus, the issue then becomes: does 1 normal ECG reading in a large population create a false sense of security among the community that the child does not have an underlying condition capable of resulting in SCD (ie, false-negative)? Moreover, what are the liability issues for the physician who read the ECG as normal if the individual subsequently experiences a SCD. At the end of the day, all we know from this study is that, if we screen a large sample of adolescents nationally, we will have to follow up more. 2.5% of them. There are between 70 and 74 million individuals between the ages of 1 and 19 years living in the United States. Thus, every year, we would have to re-evaluate between 1.75 and 2 million children and adolescents.

A Quick Look at the Statistical Issues

I will not attempt to belabor the basic statistical analyses involved here. The reader has a myriad of resources to review basic statistical issues. The basics of sensitivity and specificity are well known to most readers of scientific literature. However, I pause to reinforce the concepts of negative and positive predictive values. The positive predictive value of a screening test is influenced by the sensitivity and specificity but, more importantly, by the prevalence of the disease. Quite simply put, as a disease becomes more prevalent in a population, more individuals are diseased, so the probability among those with a positive test will have to be higher.

Let us take the information we currently have and derive a scenario for mass ECG screening. If we take an incidence rate for SCD in the population discussed here at the commonly cited numbers of 0.8 to 6.2 per 100,000, and we use 70 million as the number of children and adolescents in the population, then we have somewhere between 560 (using 0.8) and 4200 (using 6.2) children/adolescents dying of SCD in the United States each year. We know from the 2 Canadian studies cited earlier that the incidence was on the lower range of this estimate, so, for argument’s sake, let us assume an incidence of 2 per 100,000 population. The prevalence of the actual diseases is likely to be much higher, because only a small percentage of patients with the most common diseases we are focused on actually die during their childhood or adolescence. Now, let us assume the prevalence is 50 times higher than the incidence or 1000 per 100,000 people (that results in a prevalence estimate of 0.01). In addition, let us make the sensitivity of the ECG in determining the presence of disease 100% and the specificity (the probability that the test will determine all the negatives in a population) 99%. Given that idealized scenario (in favor of mass screening), the result would be a positive predictive value of only 0.09. Because we know intuitively that the prevalence is not going to be within an order of magnitude of 500 times higher than the reported incidence, one can easily see that, from a statistical perspective, the use of the ECG to screen this population becomes nonsensical. Finally, as pointed out by Richardson, one must calculate a number needed to be screened to account for those individuals who refuse to undergo the screening program for 1 reason or another. Benefits of screening are only available to those who are actually screened, and this will affect mortality rate reduction when more individuals participate. However, if individuals understand that there is a certain false-positive rate associated with screening that will adversely affect them in some way (job, activity, etc), then the participation rate drops and the eventual number of patients that need to be treated for a condition may not reach a power sufficient to show a positive effect of therapy on the reduction of mortality. This will ultimately skew the utility of the screening program downward.

Should Middle and High School Athletes Be Considered a Separate Category?

Although this is not a debate on the utility of screening athletes as opposed to nonathletes with ECGs before participation, I will briefly address the issue here. We know from several of the cited studies that most SCDs (≈75%) do not take place during or around the time of athletic events. However, more athletic SCDs are witnessed because there are audiences watching these events. The availability heuristic or bias popularized by Tversky and Kahneman biases those who most ardently advocate screening for these individuals. These events are found on the evening news, YouTube, and other sources of social media. It is difficult for physicians to separate their personal emotions as the result of seeing a sudden death from the desire to something about it by ordering a simple test like an ECG. Realistically, in the United States, an abnormal ECG triggers a pediatric cardiac evaluation and, with that, more and expensive testing to try and corroborate the abnormal ECG finding with an underlying disease. This, in turn, triggers social, emotional, and economic costs. These range from removing a child from participation for an undetermined period of time until the
evaluation is complete, to feelings of anger on the part of both child and parent, and the additional costs of echocardiograms, MRIs, and genetic testing, as well.

However, this is not the major issue here. The issue is a moral one invoking the concept of equanimity in our society. If we agree to screen all athletes with ECGs as some suggest, then visualize this scenario: Parents of a student athlete are able to get ECG screening for their child playing lacrosse, but another child, who is a mathlete for the same school and works under stress to keep an A average, gets none. How many parents, mistakenly understanding that ECG screening works under stress to keep an A average, gets none. How does this artificial and unscientifically based decision make any sense?

Cost Efficacy
There is nobody involved with health care in the United States who is not aware of the issue of the economic burden that the this segment of our economy has on the national consciousness. We simply cannot afford to use healthcare resources inefficiently as we move forward. Estimates that range in the billions of dollars per year for mass screening are not illusory. Detractors of these estimates claim ridiculously low estimates of the cost of an ECG and a follow-up echocardiogram quoting dollar costs and reimbursement that only serve their point of view. Two important studies should be mentioned here that deal with cost-effectiveness. Leslie et al used simulation models that took into account the prevalence, sensitivity, and treatment algorithms for 3 of the common conditions associated with SCD: HCM, Wolff-Parkinson-White syndrome, and long QT syndrome (anomalous right coronary artery would not be picked up on an ECG until an infarction had occurred or there was the presence of significant injury/ischemia). The incremental cost-effectiveness of ECG screening under the best-case scenario (most favorable outcome for screening) resulted in an incremental cost-effectiveness of between $91,000 and $204,000 per life-year saved. Dencev et al used a model to evaluate alternative strategies (history and physical, history and physical plus ECG if history and physical was abnormal, or history and physical and ECG with referral to a pediatric cardiologist if either the history and physical or the ECG was abnormal). The goal was the reduction in SCD in children treated with stimulant medications for attention deficit disorder. Their results showed a borderline incremental cost-effectiveness of $39,000 per quality-adjusted life-year; however, there was only a 55% chance of it being <$30,000 (the usual standard for evaluating cost-effectiveness of a quality-adjusted life-year) after the data were submitted for sensitivity analysis. The opportunity costs of having physicians performing and reading ECGs and echocardiograms and diagnostic imaging using cardiac MRI, as well, are ignored. This is also true for the overhead costs of using technicians with benefits (more will be needed) and providing malpractice insurance coverage for the interpreters of the studies. Moreover, the use of valuable physician time and resources to evaluate children who ultimately have false-positive testing and that takes the physician away from caring for children already identified to have heart disease must be addressed. We must ask ourselves if we want to add this kind of program to the debate on healthcare spending now going on in the United States.

Conclusion
In summarizing the argument against universal ECG screening in the young, I believe that I have shown that SCD in the young is a very rare occurrence and that, statistically, there is no support for the inexactness of a test like the ECG even if there is 100% sensitivity and 99% specificity. This is a result of the prevalence of the underlying disease process also being rare and that the cost is prohibitive in our current healthcare environment. The concept of utilitarianism—the most good for the most people—is what is required in this circumstance, rather than singling out small groups of individuals because the cost-effectiveness is not justified. Moreover, I hope that I have dispelled the notion that the athlete should be treated differently based on the scientific evidence presented. I fervently believe we owe our patients, and the nation as a whole, medical decision making founded in evidence-based medicine rather than emotional-based medicine.

Disclosures
None.

References
Response to Friedman

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Dr Friedman argues that sudden cardiac death is rare, that the ECG has poor test characteristics and is costly, and that screening decisions should be based on evidence and unemotional criteria, founded on 19th century philosophy and ethics, to derive the “most good for the most people.” He suggests that supporting ECG screening to identify those children at risk for sudden cardiac death is based on emotion. He does not address the current screening, the history and physical examination, mandated in most states, that cannot be supported by evidence-based medicine.

I suggest that the ECG screening decision be made by ascertaining scientific data. Current evidence, including cost-effectiveness, and knowledge gaps, as well, has been stated in the accompanying article and speaks for itself.

A basic tenet of medicine is to treat those with uncommon diseases, which may lead to unexpected discoveries with public health impact. Evidence should be developed from prospective studies to determine whether there is a screening modality that identifies individual and family risk to determine an effective treatment to prevent sudden cardiac death. Without such data, any argument against screening is subject to the same emotional bias that confounds both sides of this issue.

Health policy needs a forward-looking evidence-based foundation to achieve the best practice for those affected by the uncommon, yet significant and unnecessary consequence of sudden cardiac death. I submit that much more is gained by working toward a solution for this issue than by denying that it exists or that it costs society too much to address.

Electrocardiographic Screening Should Not Be Implemented for Children and Adolescents Between Ages 1 and 19 in the United States
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