Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION



# Key Concepts in the Evaluation of Screening Approaches for Heart Disease in Children and Adolescents : A Science Advisory From the American Heart Association

William T. Mahle, Craig A. Sable, Paul G. Matherne, J. William Gaynor and Michael H. Gewitz

*Circulation* published online April 30, 2012
Circulation is published by the American Heart Association. 7272 Greenville Avenue, Dallas, TX 72514
 Print ISSN: 0009-7322. Online ISSN: 1524-4539

# Key Concepts in the Evaluation of Screening Approaches for Heart Disease in Children and Adolescents

## A Science Advisory From the American Heart Association

William T. Mahle, MD, FAHA; Craig A. Sable, MD, FAHA; Paul G. Matherne, MD, FAHA; J. William Gaynor, MD; Michael H. Gewitz, MD, FAHA; on behalf of the American Heart Association Congenital Heart Defects Committee of the Council on Cardiovascular Disease in the Young

The consequences of undiagnosed heart conditions in children and adolescents can be catastrophic. A number of conditions such as hypertrophic cardiomyopathy, coronary artery anomalies, long-QT syndrome, and critical congenital heart disease may have sudden cardiac death as an initial presentation. These tragic cases very often gain media attention. Understandably, the community has been seeking better ways of screening for such conditions. These initiatives may be local or even driven at the level of the state legislature. However, despite the best intentions, many of these screening programs may not fully consider the needed infrastructure and staffing, the costs of widespread implementation, or the impact of false-positive or false-negative results.

The American Heart Association (AHA) is very often asked to support these extended screening strategies. In accordance with its mission statement, "Building healthier lives, free of cardiovascular diseases and stroke," the AHA is strongly committed to programs that improve the early detection of life-threatening cardiac conditions in children. The goal of this advisory, therefore, is to review some of the potential screening approaches, to provide a framework for evaluating these strategies, and to understand the elements that would be required for endorsement and broad adoption.

### Screening of the School-Age Child

There is now awareness that children and adolescents who are otherwise asymptomatic can suffer catastrophic events resulting from previously unrecognized cardiovascular disease. This is most evident in children and teenagers who participate in competitive sports. Sadly, there continue to be reports of school-age children dying suddenly of such conditions as hypertrophic cardiomyopathy and anomalies of the coronary artery.[1,2] Because of these devastating events, many in the community and within the health profession are looking for strategies to prevent or at least to reduce the frequency of such events. The AHA has previously considered screening paradigms for young athletes. These strategies were outlined in "Recommendations and Considerations Related to Preparticipation Screening for Cardiovascular Abnormalities in Competitive Athletes: 2007 Update: A Scientific Statement From the American Heart Association Council on Nutrition, Physical Activity, and Metabolism."[3] That panel emphasized the importance of risk assessment with questionnaires and physical examination but did "not believe it to be either prudent or practical to recommend the routine use of tests such as 12-lead ECG or echocardiography in the context of mass, universal screening."

More recently a National Institutes of Health, National Heart, Lung, and Blood Institute Working Group addressed several of the key outstanding issues in screening for sudden cardiac death.[4] This comprehensive analysis provided specific recommendations for how research could help inform the decision-making process concerning what, if any, role screening modalities such as ECG should play as a supplement to physical examination and history in efforts to reduce sudden cardiac death in the young. These recommendations focused on the epidemiology and cause of sudden cardiac death, the performance of screening strategies, the management of asymptomatic heart disease, and the impact of a screening program.



This statement was approved by the American Heart Association Science Advisory and Coordinating Committee on March 8, 2012. A copy of the document is available at http://my.americanheart.org/statements by selecting either the "By Topic" link or the "By Publication Date" link. To purchase additional reprints, call 843-216-2533 or e-mail kelle.ramsay@wolterskluwer.com.

The American Heart Association requests that this document be cited as follows: Mahle WT, Sable CA, Matherne PG, Gaynor JW, Gewitz MH; on behalf of the American Heart Association Congenital Heart Defects Committee of the Council on Cardiovascular Disease in the Young. Key concepts in the evaluation of screening approaches for heart disease in children and adolescents: a science advisory from the American Heart Association. *Circulation.* 2012;125:●●●–●●●.

Expert peer review of AHA Scientific Statements is conducted by the AHA Office of Science Operations. For more on AHA statements and guidelines development, visit http://my.americanheart.org/statements and select the "Policies and Development" link.



**(*Circulation*. 2012;125:00-00.)**



***Circulation* is available at http://circ.ahajournals.org** **DOI: 10.1161/CIR.0b013e3182579f25**

The aforementioned document provided a clear roadmap to assess and develop enhanced screening strategies. In the interim, however, many communities in the United States continue to explore the role of supplementary screening techniques. These enhanced screening programs are often modeled on previous strategies carried out at the regional or national level in other countries. A seminal study offered some evidence for ECG screening to prevent sudden death in young athletes in the Veneto region of Italy.[5,6] This mandatory program is limited to athletes. Thus, it is not clear that communities in the United States would see the same benefit. The postscreen sudden death rate in Veneto region is similar to the sudden death rate in a similar-sized population in Minnesota in whom screening was performed with history and physical examination but without routine ECG acquisition.[7] Another national screening protocol was instituted in Israel that included not only ECGs but also exercise stress tests. A recent review of this program suggested that the sudden death rate has not been affected.[8] An additional concern is that focusing only on competitive athletes is discriminatory. Children and adolescents often engage in vigorous physical activity outside structured athletic programs. Moreover, sudden cardiac death is not limited to physical exertion.[9] Hence, screening programs focused only on athletic participation have too narrow a scope.

## Local or Regional Strategies Used in United States for Screening School-Age Children

Currently, there are no standardized strategies in the United States for screening the school-age child, and there are few published studies assessing the performance of pilot screening protocols. A 1997 study from Nevada screened 5615 high school athletes with ECGs at 30 schools. That study reported a sensitivity of 70% for detecting cardiac disease with ECG compared with 6% for history and physical examination alone.[10] However, most of the positives from this study were minor rhythm abnormalities with no cases of either cardiomyopathy or anomalous coronary detected. Another study among university students demonstrated enhanced detection of silent cardiac disease with the addition of the ECG, but the false-positive rate reached 17%.[11] Vetter and colleagues[12] reported that office-based screening of a general pediatric population (aged 5–19 years), which included ECG and echocardiography, was feasible. Previously undetected heart defects were found in 23 of 400 children (5.8%), 10 of which were considered to be serious. The largest study in the United States screened >32 000 high school students; however, comprehensive follow-up data were not available, so false-positive and false-negative rates are not known.[13]

In addition to the small number of peer-reviewed reports, numerous groups have conducted local screening of student-athletes for heart defects using a combination of ECG and echocardiography. Often, these programs are in response to a recent sudden death in the community or in a family member. The screening programs may be sponsored by local physicians, sometimes in collaboration with vendors or nonprofit organizations. These efforts are often praised by local parent groups and media but generally have not been used to generate data that can be used to support more rigorous screening protocols.

Some for-profit agencies offer reduced-cost echocardiograms or ECGs that are marketed directly to athletic programs or individuals. These entities have used social media and direct advertising to reach target audiences. Not uncommonly, these programs include references to recent sudden death events to promote the need for enhanced screening. It is entirely possible that for-profit entities may prove to provide a flexible cost-effective means to screen the pediatric population at risk for sudden death. However, for the most part, these for-profit agencies have not reported the findings of their screening programs. Therefore, it is difficult to evaluate the efficacy of such initiatives.

Because of these limitations, the 2007 AHA statement on athletic preparticipation did not endorse mandatory screening with ECG or other noninvasive tests.[3] This recommendation is sound and remains relevant to the current approach to the school-age child.

## Approaches to Screening the Infant or Young Child for Sudden Cardiac Death

Long-QT syndrome or variant channelopathies are cardiac conditions that may be asymptomatic yet lead to sudden death in the very young.[14] Accordingly, there has been interest in exploring strategies to identify children with the long-QT syndrome in the general population. Early identification of the long-QT syndrome is particularly attractive because medications, use of automatic implantable defibrillators, and modifications of activities have been associated with significant reduction in risk of sudden death.[15,16] Because sudden death events may occur even in infancy, investigators have focused screening strategies in early childhood, especially the neonatal period. A standard 12-lead ECG has been proposed as the most practical screening tool. Many of the data to support this methodology derive from a broad screening program in Italy that focused primarily on reducing the incidence of sudden infant death syndrome.[17] Similar screening strategies have been used elsewhere,[18] and the concept has been endorsed by a European Cardiology Society task force.[19]

Despite the promising results from the Italian experience, this strategy has not been widely adopted more than a decade after this approach was first proposed. A number of concerns have been raised about this screening strategy.[20] First, interpretation of the neonatal ECG can be challenging, and the overlap of normal variants and the long-QT pattern is significant.[21] Even in adults, interpretation of the ECG among observers is varied, and many clinicians, including board-certified cardiologists, may fail to identify critical features of the long-QT syndrome.[22] In the United States, most newborn screening strategies are designed to be performed at the time of the delivery hospitalization. Because sensitivity and specificity are very poor for ECG screening in the first few days of life,[23] an optimal ECG screening program would require evaluation beyond the first week of life. This would require an extensive screening infrastructure in primary care practices, which may be a considerable challenge in less centralized healthcare systems such as that which exists in the United States. To the best of our knowledge, there are no active clinical ECG-based screening

**Table. Overview of Screening for Cardiac Disease in Children and Adolescents**

| Populations | Diseases | Screening Methods |
|---|---|---|
| General pediatric population | Critical congenital heart defects | History<br>Physical examination<br>Blood pressure<br>ECG<br>Echocardiography<br>Genetic testing |
| Newborns | Hypertrophic cardiomyopathy | |
| School-age children | Coronary anomalies | |
| Sports preparticipation | Arrhythmogenic right ventricular dysplasia | |
| | Channelopathies | |
| | Marfan syndrome | |

programs of newborns for the long-QT syndrome in North America. Hence, there is too little evidence to support a strategy of routine ECG screening in the infant.

## Pulse Oximetry for Timely Diagnosis of Critical Congenital Heart Disease

It is also now well known that late detection or failure to detect critical congenital heart disease in young infants may lead to death.[24,25] This important topic was addressed in detail in the 2009 statement entitled "Role of Pulse Oximetry in Examining Newborns for Congenital Heart Disease: A Scientific Statement From the American Heart Association and American Academy of Pediatrics."[26] Since that publication, a number of additional European studies have provided insights into the strengths and weaknesses of this approach and have proposed strategies such as repeated measurements and upper- and lower-extremity saturations to enhance detection and to reduce false-positive results.[27–29] On the basis of these studies, there has been ongoing effort and collaborative discussion among advocacy groups and state and federal agencies to evaluate and promote pulse oximetry as an enhanced methodology for screening for critical congenital heart disease in newborns.[30] Recently, the Secretary of Health and Human Services endorsed the concept of screening newborns for critical congenital heart disease with pulse oximetry. The AHA formally supports these recommendations.[31] As with any new initiative, it will be critically important to assess how this screening initiative performs throughout various healthcare models and across the population.

## Paradigm for Advancing Cardiovascular Screening Programs

The Council for Cardiovascular Disease in the Young of the AHA recognizes the importance of improving the detection of silent cardiovascular disease in children and the possible incorporation of such strategies into routine practice (Table). The AHA closely monitors the outcomes of local testing screening strategies and advocates for research to support data collection and rigorous assessment of these approaches. The following underlying principles should guide these screening strategies:

1. New screening programs should be based on sound principles and should not be simply reactive to recent catastrophic events. A successful screening program will require extensive planning and will not be able to eliminate sudden cardiac deaths completely. Estimates of the prevalence of silent cardiac diseases of interest are needed to anticipate what benefit might be realized through enhanced screening.
2. Any broad screening strategy should be widely supported and available to all children. The AHA does not support screening strategies that are focused only on children who have the financial means to pay for such screening, leaving socioeconomically disadvantaged youths out of the process. This is especially true because studies suggest that certain racial groups may be at a higher risk of sudden death.[32]
3. Pilot screening programs must track their performance. At the very least, screening initiatives should record the proportion of positive screens and what follow-up was recommended. When possible, the collection of data on the follow-up of positive screens such as the false-positive rate and need for additional diagnostic studies is strongly encouraged.
4. Pediatric cardiovascular specialists need to be included in strategies that look to identify cardiac disease so that any enhanced screening strategies are practical in terms of manpower and integrate well into the current practice of identifying children thought to be at increased risk for arrhythmia, ischemia, or sudden death events.
5. Secondary prevention of sudden death with training of cardiopulmonary resuscitation and deployment of automatic external defibrillators must be emphasized and supported by local entities such as school boards or state legislatures.[33]

## Role of Local Government to Fund, Initiate, and Mandate Changes

Governmental authorities have often been involved in the development and implementation of population-based health screening programs. Most evident of these, for example, is the very successful newborn blood-spot screening program for heritable metabolic disorders. This program was initiated decades ago at the state level and is maintained primarily by state budgetary and regulatory authorities. Typically, as with the blood-spot program, governmental involvement has been confined to presymptomatic screening for select inherited and congenital conditions. These programs consider the screening process to be a part of an essential public health commitment and require consumer (patient) education, systematic follow-up to definitive diagnosis, and reliable linkage to long-term treatment and management to be inherent to any supported screening program. In this format, the state governments have been productive in terms of population-based screening.

On the other hand, expansion of screening programs in response to new medical knowledge, to new technologies, or to political pressure from specific illness advocacy groups is often challenged by state funding constraints and by push-back from a financially stressed provider community. States have not always been successful in meeting these particular challenges. In an attempt to affect these issues for the health of the population at large, the federal government, through the Newborn Screening Saves Lives Act of 2008, has recently become involved by providing funding support and by helping states improve program performance.

The newborn screening programs (blood-spot, hearing assessment, and others) represent an effective professional community, state government, and federal government trilateral relationship that has addressed controversies about both cost and evidence of efficacy. Nevertheless, the role of government in mandatory resource-consuming programs in which costs may not be shared equally among the beneficiaries remains controversial. Recently affected patients, their families, and supporters have taken a more active role in advocating for screening by directly approaching policymakers and legislators. This wave of advocacy at the level of state legislatures for expansion of screening programs of all types involving a widening range of diseases children and young adults will continue to challenge both the professional community and governmental systems. It is imperative that the success of the trilateral paradigm developed as part of the newborn screening programs be preserved and that hastily conceived, politically expedient programmatic changes not be implemented in the absence of comprehensive, science-based preliminary testing of screening hypotheses and methodologies. The very recent decision to expand the newborn screening program with the addition of pulse oximetry screening for critical congenital heart disease fulfills these criteria and thus has appropriately won endorsement at the federal government level after an extended deliberative and evidence-based process.

## Parents and Patients as Advocates

The development of screening techniques depends on new medical technologies or, in some cases, applications of existing tools to address important public health concerns. However, in all cases, advocacy groups, driven in large part by patients and their families, play an important role in advancing new screening strategies. Advocacy groups draw attention to the public health importance of the condition, fund preliminary research, and support legislative initiatives. The AHA has relied on patients and their families to support many key initiatives, including cardiovascular screening programs.

Advocates of cardiac screening in children will no doubt play a critical role in shepherding some of the screening strategies described above from concept to practice. It is important for these groups to reach out to the AHA for support. The AHA can provide extensive data on the public health and economic implications of silent cardiac disease in childhood. The AHA can promote well-structured pilot programs or provide scientific statements to inform policymakers. If there are sufficient data, the AHA may provide an endorsement of broad adoption of screening policies, as was the case in newborn pulse oximetry screening. However, if there is insufficient evidence to support screening programs, the AHA may simply advocate for more resources to study the problem.

One must recognize that recommendations that are appropriate in terms of screening in the US pediatric population may or may not apply in other countries. In some cases, data gathered outside the United States can help guide policy decisions in the United States and vice versa. For example, research in Europe on pulse oximetry screening was invaluable in shaping US recommendations. Conversely, health delivery systems vary considerably among countries. Thus, such endorsement of screening strategies will appropriately differ. The AHA seeks to complement the efforts of organizations such as the European Society of Cardiology vis-à-vis screening programs.

## Conclusions

Screening for cardiovascular disease that may lead to sudden death in children is of great importance to public health; assessment of screening methodologies for cardiovascular disease in other pediatric populations is critical to the mission of the AHA and the Council for Cardiovascular Disease in the Young. The AHA will strongly support novel approaches to screening in accordance with the principles outlined above. Funding studies to evaluate these strategies is essential to address this problem effectively. However, before the AHA endorses universal screening programs, assembling sound data and the support of other key stakeholders such as governmental agencies and the healthcare community will be necessary.



## Disclosures

**Writing Group Disclosures**

| Writing Group Member | Employment | Research Grant | Other Research Support | Speakers' Bureau/Honoraria | Expert Witness | Ownership Interest | Consultant/ Advisory Board | Other |
|---|---|---|---|---|---|---|---|---|
| William T. Mahle | Children's Healthcare of Atlanta | None | None | None | None | None | None | None |
| J. William Gaynor | Children's Hospital of Philadelphia | None | None | None | None | None | None | None |
| Michael H. Gewitz | New York Medical College | Food and Drug Administration Orphan Drug Program* | None | None | None | None | None | None |
| Paul G. Matherne | University of Virginia | None | None | None | None | None | None | None |
| Craig A. Sable | Children's National Medical Center | None | None | None | None | None | None | None |

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.

**Reviewer Disclosures**

| Reviewer | Employment | Research Grant | Other Research Support | Speakers' Bureau/Honoraria | Expert Witness | Ownership Interest | Consultant/ Advisory Board | Other |
|---|---|---|---|---|---|---|---|---|
| Stuart Berger | Medical College of Wisconsin | None | None | None | None | None | None | None |
| Welton Gersony | Children's Hospital of New York | None | None | None | None | None | None | None |
| Barry J. Maron | Minneapolis Heart Institute Foundation | None | None | None | None | None | None | 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.

## References


1. Basso C, Maron BJ, Corrado D, Thiene G. Clinical profile of congenital coronary artery anomalies with origin from the wrong aortic sinus leading to sudden death in young competitive athletes. *J Am Coll Cardiol*. 2000; 35:1493–1501.
2. Decker JA, Rossano JW, Smith EO, Cannon B, Clunie SK, Gates C, Jefferies JL, Kim JJ, Price JF, Dreyer WJ, Towbin JA, Denfield SW. Risk factors and mode of death in isolated hypertrophic cardiomyopathy in children. *J Am Coll Cardiol*. 2009;54:250–254.
3. Maron BJ, Thompson PD, Ackerman MJ, Balady G, Berger S, Cohen D, Dimeff R, Douglas PS, Glover DW, Hutter AM Jr, Krauss MD, Maron MS, Mitten MJ, Roberts WO, Puffer JC. Recommendations and considerations related to preparticipation screening for cardiovascular abnormalities in competitive athletes: 2007 update: a scientific statement from the American Heart Association Council on Nutrition, Physical Activity, and Metabolism. *Circulation*. 2007;115:1643–1655.
4. Kaltman JR, Thompson PD, Lantos J, Berul CI, Botkin J, Cohen JT, Cook NR, Corrado D, Drezner J, Frick KD, Goldman S, Hlatky M, Kannankeril PJ, Leslie L, Priori S, Saul JP, Shapiro-Mendoza CK, Siscovick D, Vetter VL, Boineau R, Burns KM, Friedman RA. Screening for sudden cardiac death in the young: report from a National Heart, Lung, and Blood Institute Working Group. *Circulation*. 2011;123:1911–1918.
5. Corrado D, Basso C, Pavei A, Michieli P, Schiavon M, Thiene G. Trends in sudden cardiovascular death in young competitive athletes after implementation of a preparticipation screening program. *JAMA*. 2006;296: 1593–1601.
6. Maron BJ, Haas TS, Doerer JJ, Thompson PD, Hodges JS. Comparison of U.S. and Italian experiences with sudden cardiac deaths in young competitive athletes and implications for preparticipation screening strategies. *Am J Cardiol*. 2009;104:276–280.
7. Maron BJ, Gohman TE, Aeppli D. Prevalence of sudden cardiac death during competitive sports activities in Minnesota high school athletes. *J Am Coll Cardiol*. 1998;32:1881–1884.
8. Steinvil A, Chundadze T, Zeltser D, Rogowski O, Halkin A, Galily Y, Perluk H, Viskin S. Mandatory electrocardiographic screening of athletes to reduce their risk for sudden death proven fact or wishful thinking? *J Am Coll Cardiol*. 2011;57:1291–1296.
9. Berger S, Dhala A, Friedberg DZ. Sudden cardiac death in infants, children, and adolescents. *Pediatr Clin North Am*. 1999;46:221–234.
10. Fuller CM, McNulty CM, Spring DA, Arger KM, Bruce SS, Chryssos BE, Drummer EM, Kelley FP, Newmark MJ, Whipple GH. Prospective screening of 5,615 high school athletes for risk of sudden cardiac death. *Med Sci Sports Exerc*. 1997;29:1131–1138.
11. Baggish AL, Hutter AM Jr, Wang F, Yared K, Weiner RB, Kupperman E, Picard MH, Wood MJ. Cardiovascular screening in college athletes with and without electrocardiography: a cross-sectional study. *Ann Intern Med*. 2010;152:269–275.
12. Vetter VL, Dugan N, Guo R, Mercer-Rosa L, Gleason M, Cohen M, Vogel RL, Iyer R. A pilot study of the feasibility of heart screening for sudden cardiac arrest in healthy children. *Am Heart J*. 2011;161: 1000.e3–1006.e3.
13. Marek JC, Bufalino V, Davis J, Marek K, Gami A, Stephan W, Zimmerman F. Feasibility and findings of large-scale electrocardiographic screening in young adults: data from 32,561 subjects. *Heart Rhythm*. 2011;8:1555–1559.
14. Tester DJ, Ackerman MJ. Cardiomyopathic and channelopathic causes of sudden unexplained death in infants and children. *Annu Rev Med*. 2009; 60:69–84.
15. Goldenberg I, Bradley J, Moss A, McNitt S, Polonsky S, Robinson JL, Andrews M, Zareba W; International LQTS Registry Investigators. Beta-blocker efficacy in high-risk patients with the congenital long-QT syndrome types 1 and 2: implications for patient management. *J Cardiovasc Electrophysiol*. 2010;21:893–901.
16. Horner JM, Kinoshita M, Webster TL, Haglund CM, Friedman PA, Ackerman MJ. Implantable cardioverter defibrillator therapy for congenital long QT syndrome: a single-center experience. *Heart Rhythm*. 2010;7:1616–1622.
17. Schwartz PJ, Stramba-Badiale M, Segantini A, Austoni P, Bosi G, Giorgetti R, Grancini F, Marni ED, Perticone F, Rosti D, Salice P. Prolongation of the QT interval and the sudden infant death syndrome. *N Engl J Med*. 1998;338:1709–1714.
18. Cruz Ca˜]nete M, Rus Mansilla C, Gómez Lara A, Gavilán Expósito ML, Calleja Cabezas P, Gavilán Pérez M. Usefulness of electrocardiographic screening in a neonatal population [in Spanish]. *An Pediatr (Barc)* 2011; 74:303–308.
19. Schwartz PJ, Garson A Jr, Paul T, Stramba-Badiale M, Vetter VL, Wren C; European Society of Cardiology. Guidelines for the interpretation of the neonatal electrocardiogram: a task force of the European Society of Cardiology. *Eur Heart J*. 2002;23:1329–1344.
20. Chang RK, Rodriguez S, Gurvitz MZ. Electrocardiogram screening of infants for long QT syndrome: survey of pediatric cardiologists in North America. *J Electrocardiol*. 2010;43:4–7.
21. Hancock EW, Deal BJ, Mirvis DM, Okin P, Kligfield P, Gettes LS. AHA/ACCF/HRS recommendations for the standardization and interpretation of the electrocardiogram: part V: electrocardiogram changes associated with cardiac chamber hypertrophy: a scientific statement from the American Heart Association Electrocardiography and Arrhythmias Committee, Council on Clinical Cardiology; the American College of Cardiology Foundation; and the Heart Rhythm Society. *Circulation*. 2009; 119:e251–e261.
22. Viskin S, Rosovski U, Sands AJ, Chen E, Kistler PM, Kalman JM, Rodriguez Chavez L, Iturralde Torres P, Cruz F FE, Centurión OA, Fujiki A, Maury P, Chen X, Krahn AD, Roithinger F, Zhang L, Vincent GM, Zeltser D. Inaccurate electrocardiographic interpretation of long QT: the majority of physicians cannot recognize a long QT when they see one. *Heart Rhythm*. 2005;2:569–574.
23. De Groote K, Suys B, Deleeck A, De Wolf D, Matthys D, Van Overmeire B. How accurately can QT interval be measured in newborn infants? *Eur J Pediatr*. 2003;162:875–879.
24. Chang RK, Gurvitz M, Rodriguez S. Missed diagnosis of critical congenital heart disease. *Arch Pediatr Adolesc Med*. 2008;162: 969–974.
25. Abu-Harb M, Hey E, Wren C. Death in infancy from unrecognised congenital heart disease. *Arch Dis Child*. 1994;71:3–7.
26. Mahle WT, Newburger JW, Matherne GP, Smith FC, Hoke TR, Koppel R, Gidding SS, Beekman RH 3rd, Grosse SD; on behalf of the American Heart Association Congenital Heart Defects Committee of the Council on Cardiovascular Disease in the Young, Council on Cardiovascular Nursing, and Interdisciplinary Council on Quality of Care and Outcomes Research; and the American Academy of Pediatrics Section on Cardiology and Cardiac Surgery, and Committee on Fetus and Newborn. Role of pulse oximetry in examining newborns for congenital heart disease: a scientific statement from the American Heart Association

and American Academy of Pediatrics. *Circulation*. 2009;120:447–458.
27. de-Wahl Granelli A, Wennergren M, Sandberg K, Mellander M, Bejlum C, Inganas L, Eriksson M, Segerdahl N, Agren A, Ekman-Joelsson BM, Sunnegårdh J, Verdicchio M, Ostman-Smith I. Impact of pulse oximetry screening on the detection of duct dependent congenital heart disease:a Swedish prospective screening study in 39,821 newborns. *BMJ*. 2009;338:a3037.
28. Riede FT, Wörner C, Dähnert I, Möckel A, Kostelka M, Schneider P. Effectiveness of neonatal pulse oximetry screening for detection of critical congenital heart disease in daily clinical routine: results from a prospective multicenter study. *Eur J Pediatr*. 2010;169:975–981.
29. Ewer AK, Middleton LJ, Furmston AT, Bhoyar A, Daniels JP, Thangaratinam S, Deeks JJ, Khan KS; PulseOx Study Group. Pulse oximetry screening for congenital heart defects in newborn infants (PulseOx): a test accuracy study. *Lancet*. 2011;378:785–794.
30. http://www.hrsa.gov/advisorycommittees/mchbadvisory/heritabledisorders/recommendations/correspondence/cyanoticheartsecre09212011.pdf. Accessed August 30, 2011.
31. Kemper AR, Mahle WT, Martin GR, Cooley WC, Kumar P, Morrow WR, Kelm K, Pearson GD, Glidewell J, Grosse SD, Howell RR. Strategies for implementing screening for critical congenital heart disease. *Pediatrics*. 2011;128:e1259–e1267.
32. Maron BJ, Carney KP, Lever HM, Lewis JF, Barac I, Casey SA, Sherrid MV. Relationship of race to sudden cardiac death in competitive athletes with hypertrophic cardiomyopathy. *J Am Coll Cardiol*. 2003;41:974–980.
33. Hazinski MF, Markenson D, Neish S, Gerardi M, Hootman J, Nichol G, Taras H, Hickey R, O'Connor R, Potts J, van der Jagt E, Berger S, Schexnayder S, Garson A Jr, Doherty A, Smith S. Response to cardiac arrest and selected life-threatening medical emergencies: the medical emergency response plan for schools: a statement for healthcare providers, policymakers, school administrators, and community leaders. *Circulation*. 2004;109:278–291.

KEY WORDS: AHA Scientific Statements ■ children screening