

Re: Cardiovascular Monitoring of Children and Adolescents With Heart Disease Receiving Stimulant Drugs. Vetter VI, et al. Circulation. 2008;117:2407-2423.

To the editors:

The recent Scientific Statement from the American Heart Association (AHA) concerning cardiovascular monitoring of pediatric patients receiving stimulant medications for attention deficit disorder has been met with a large amount of media attention, and a vigorous, mostly negative, response from partner pediatric organizations. Some of this response was likely due to two issues. First, there was a major error in Table 3 of the paper, in which the ECG was listed as having a Class I indication, whereas it is listed in the text as having a Class II indication. Second, an AHA press release on April 21, 2008 (still available on the AHA website) is entitled “Children with ADHD should get heart tests before treatment with stimulant drugs” and misleadingly suggests that this was an AHA recommendation. As officers of the Pediatric and Congenital Electrophysiology Society (PACES), we would like to address several concerns on behalf of our membership, which consists of nearly all pediatric arrhythmia specialists in the U.S.

First, we appreciate the effort that the Council on Cardiovascular Disease in the Young has devoted to correcting these errors, as well as those by the AHA in publishing a clarifying news release jointly with the American Academy of Pediatrics, emphasizing a Class II indication for ECGs in children with no other suspicion of heart disease. We are distressed, however, that the original journal article has not been corrected; instead, a separate list of corrections was published. We are also concerned that the original, misleading, press release is still accessible on the website of the AHA.

Second, the authors point out that there are no scientific studies to show that screening ECGs will decrease the incidence of sudden death, or even that there is an increased risk of sudden death in children taking these medications. Thus, the classification was a “level of evidence C” and depended on “only consensus opinion of experts, case studies, or standard of care.” However, the paper was not supported by a policy conference or consensus building procedure such as the Bethesda Conference. To address this deficit, our society performed a survey of our membership to determine their view of the appropriate indication class and level of evidence for obtaining a screening ECG prior to initiation of stimulant medication in asymptomatic children without a suspicion of heart disease. A total of 101 pediatric electrophysiologists (roughly 2/3 of our membership) responded. The results are summarized here:

Classification	Number (percentage)	Level of	Number (percentage)
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		evidence	
I	3 (3.0%)	A	2 (66.7%)
		B	0
		C	1 (33.3%)
II a	13 (12.9%)	A	1 (7.7%)
		B	1 (7.7%)
		C	11 (84.6%)
II b	70 (69.3%)	A	1 (1.4%)
		B	4 (5.7%)
		C	65 (92.9%)
III	15 (14.8%)	A	0
		B	2 (13.3%)
		C	13 (86.7%)

Our members strongly support a Class II indication for ECG screening, but differ from the authors of the article in classifying it as a class IIb indication, for which “usefulness/efficacy is less well established by evidence/opinion” rather than class IIa, for which “weight of evidence/opinion is in favor of usefulness/efficacy.” It is important to note that in a case of “level of evidence C”, the correct indication Class is in fact determined primarily by the type of consensus established in this survey rather than the opinions of a few authors.

The value of an ECG as a screening tool for cardiovascular disease in the pediatric population is an area of active debate. However, at this time, the AHA itself is on record as not recommending routine ECG screening for children and adolescents because of problems with both the sensitivity and specificity of the ECG as a general screening test¹.

Further, there is no evidence of an increased risk of sudden death in those receiving ADHD drugs over the general population, and no evidence for the efficacy of ECG screening to prevent sudden death in this population. Consequently, in agreement with our broad membership of pediatric arrhythmia specialists, we believe that at this time universal ECG screening of this select population is not supported by the available data. Clearly, further studies to determine the best way to identify cardiovascular risks in all children are warranted.

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Reference List

- (1) Maron BJ, Thompson PD, Ackerman MJ et al. Recommendations and considerations related to preparticipation screening for cardiovascular abnormalities in competitive athletes: 2007 update: a scientific statement from the American Heart Association Council on Nutrition, Physical Activity, and Metabolism: endorsed by the American College of Cardiology Foundation. *Circulation* 2007 March 27;115(12):1643-455.

Response:

The Writing Group would like to thank the Officers of PACES for their comments. Given that the role of science is to seek new knowledge and understanding, the questioning of any statement is to be desired. The principles of reasonable and respectful interchange should be the goal and constructive criticism should have its basis in logic and correct information. We recognize the concerns of these Officers but would like to indicate some of our concerns regarding their response.

We would like to apologize for the errors in our manuscript which the PACES Officers have pointed out and assure them that corrections have been made. Similarly, the press release that troubled them had been removed from the website by the time we received their letter. The web version of the article has been corrected. Unfortunately, the printed version was already “out” before the errors were noted.

The PACES Officers correctly point out that the Level of Evidence used for this statement was “C” which indicates only diverging expert opinion, case studies, or standard-of-care. They point out that our consensus was not obtained through a conference or consensus building procedure such as the Bethesda Conferences which is true, but this is not the standard format of AHA scientific statements. They state that they have addressed this deficit by conducting a survey of their membership to determine their view of the appropriate indication class and level of evidence for obtaining a screening ECG prior to initiation of stimulant medication.

In an informal survey such as this, the information may or may not be representative of how a fully informed participant would respond. Thus, the data

presented by the PACES Officers may fully represent the pediatric cardiology community or it may indicate a misunderstanding of the intent of the scientific statement based on the early errors in presentation in the media and print.

For clarification purposes, the intent and motivation behind the scientific statement was to respond to the FDA concerns that led to Medication Guides that state that those with heart conditions should not be treated with stimulant medications. The AAP in its testimony to the FDA on March 22, 2006 made the following statement, "Until studies have answered the questions about cardiac side effects, the AAP agrees it would be prudent to revise the labeling of stimulants in such a way as to alert clinicians to possible cardiac side effects, particularly in people with known structural heart defects." If one chooses not to ignore the FDA and AAP statements, then one must try to determine the best way to identify heart conditions in children. Our goal was to aid the pediatricians, developmental and ADHD specialists, and psychiatrists in following FDA concerns and identifying patients with heart disease, either known or undiagnosed. Once a child is diagnosed with a heart condition, our recommendation was that the pediatric cardiologist would be the best resource to determine the safety of the medication in any specific patient with a heart condition. We were motivated, as well, by concerns that patients with congenital heart defects or other cardiac conditions would not receive appropriate treatment of their ADHD with stimulant medications. Our goal was to enhance appropriate and safe use of these medications in the appropriate patients.

We would like to emphasize that our statement regarding ECG consideration was a Class IIa recommendation. We understand that there is considerable controversy regarding whether it should be Class IIa or IIb, Level of Evidence C. We are encouraged that the majority of the pediatric electrophysiology community agreed with a Class II recommendation for the consideration of ECGs in this setting. We wonder if all of those who responded recognized this difference between Class I and II and the differences between the designations *a* and *b*? It would appear that the membership of PACES represent around 10% of the pediatric cardiology community, a group who responded somewhat differently to a similar survey. These differences would seem to reflect the lack of data in this area, the methodological difficulties with such surveys and support the collection of Registry and prospective data from studies.

As a point of clarification, we are not recommending ECG screening but rather, consideration of the addition of an ECG when it can help in the evaluation of a patient. We are sorry that we failed to clarify our position and that the PACES Officers misunderstood our position and thought we were recommending universal ECG screening which was not the case. The PACES Officers state that the AHA is on record as not recommending routine ECG screening for children and adolescent "because of problems with both the sensitivity and specificity of the ECG as a general screening test." There appear to be many other reasons

that ECGs were not recommended that relate more to manpower, infrastructure, and costs rather than ECG sensitivity and specificity.¹ The problem with the ECG is not the sensitivity and specificity per se which are in the 70 to 95% and 95-99% range respectively,²⁻⁴ but the low prevalence of conditions that cause SCD and the problems of predictive value related to that fact. On the other hand, one needs to consider the value of years of life saved for children, the high human cost of missing a diagnosis and the multiplier effect of diagnosing genetic conditions. All of these issues make the calculation of cost effectiveness or cost utility challenging.

We agree with the PACES Officers that further studies to determine the best way to identify cardiovascular risks in all children are warranted and look forward to working with them to achieve this goal.

Reference List

- (1) Maron BJ, Thompson PD, Ackerman MJ et al. Recommendations and considerations related to preparticipation screening for cardiovascular abnormalities in competitive athletes: 2007 update: a scientific statement from the American Heart Association Council on Nutrition, Physical Activity, and Metabolism: endorsed by the American College of Cardiology Foundation. *Circulation* 2007 March 27;115(12):1643-455.
- (2) Pelliccia A, Di Paolo FM, Corrado D et al. Evidence for efficacy of the Italian national pre-participation screening programme for identification of hypertrophic cardiomyopathy in competitive athletes. *Eur Heart J* 2006 September;27(18):2196-200.
- (3) Fuller CM, McNulty CM, Spring DA et al. Prospective screening of 5,615 high school athletes for risk of sudden cardiac death. *Med Sci Sports Exerc* 1997 September;29(9):1131-8.
- (4) Fuller CM. Cost effectiveness analysis of screening of high school athletes for risk of sudden cardiac death. *Med Sci Sports Exerc* 2000 May;32(5):887-90.