Reexamining the Emperor’s New Clothes
Ambiguities in Current Cardiac Screening Recommendations for Youth With Attention Deficit Hyperactivity Disorder

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On April 21, 2008, the American Heart Association (AHA) released a policy statement that was widely interpreted as recommending routine ECGs as part of the evaluation of children for whom stimulant medications were being considered for treatment of attention deficit hyperactivity disorder (ADHD). The rationale was to improve the identification of rare but clinically important cardiac conditions that might predispose children and adolescents with ADHD who are taking stimulant medications to sudden cardiac death (SCD). This recommendation contradicted existing ADHD treatment guidelines published by the American Academy of Pediatrics (AAP) and the American Academy of Child and Adolescent Psychiatry, as well as the conclusions of the Food and Drug Administration’s Pediatric Advisory Committee, none of which had recommended routine ECGs before instituting stimulant medication treatment. On May 16, 2008, the AHA and AAP, cosponsored by the American Academy of Child and Adolescent Psychiatry, jointly issued a news release clarifying that obtaining an ECG before starting medication was “reasonable” but not mandatory. An erratum to the AHA’s statement was next published, downgrading the classification and level of evidence regarding the cardiac effects of medications used to treat ADHD. On May 28, 2008, the AAP published its own policy statement contending that medications used to treat ADHD have not been shown to cause SCD, sufficient evidence for routine ECG before starting stimulant medications is not available, and that “until these questions are answered, a recommendation to obtain routine ECGs for children receiving ADHD medications is not warranted.”

These conflicting statements and their interpretations by the media and public catapulted primary care clinicians, cardiologists, mental health professionals, school personnel, health plans, insurance companies, and families into a maelstrom of uncertainty concerning the appropriate cardiac screening of children and adolescents with ADHD. An estimated 4.4 million children and adolescents in the United States have ADHD and are at an elevated risk for academic failure, strained peer and family relations, poor self-image, delinquency, substance use, low occupational performance, and automobile infractions. Substantial evidence exists for the role of multimodal treatment, including stimulant medication and home and school behavioral interventions, in the reduction of ADHD symptoms in youth with ADHD. Approximately 2.5 million youth fill ≥1 prescription for stimulant medication each year.

Proponents of ECG screening emphasized that stimulants increase the work of the cardiovascular system through elevated heart rate and blood pressure and theoretically may precipitate SCD in individuals with undetected cardiac arrhythmias or cardiomyopathies. Others cautioned that screening such a large population may have multiple unintended negative consequences. For example, fewer families may choose to pursue medication as part of an evidence-based ADHD treatment. Pediatric and adult cardiologists may be inundated with routine pediatric ECG reading and interpretation. Moreover, the pursuit of nonspecific ECG findings with further testing, such as echocardiography, may strain already-limited pediatric medical care delivery resources.

In the classic fable of the emperor’s new clothes, the young boy’s announcement not only exposed the emperor’s lack of clothing but also highlighted flaws in the underlying system. The controversy during the past 6 months underscores the profound deficiencies in data with which to tailor broad-sweeping or population-wide recommendations. Like the emperor’s new clothes, the debate also brings into focus some specific challenges related to policy statement or guidelines development in pediatrics, where most disorders are rare and adverse events as related to treatment even rarer. These system challenges are described below.

Data Implications: Defining and Finding the Data Needed
The events of the last 6 months demonstrate that additional data are urgently needed to clarify (1) the risk of SCD among youth taking stimulant medications compared with youth in other populations, (2) the effect of medication type on risk of SCD, (3) the role of comorbid conditions, and (4) the role of other interventions in the reduction of SCD in children with ADHD.
the general population; (2) the impact of ADHD therapy on the incremental risk of SCD associated with the most common cardiac conditions placing youth at risk for SCD, specifically Wolff-Parkinson-White Syndrome, long-QT syndrome, and hypertrophic cardiomyopathy; (3) the sensitivity and specificity of protocols to identify youth at risk for SCD across the age span; (4) the economic costs associated with these strategies; and (5) the health benefits and risks associated with pursuing or forgoing stimulant treatment for ADHD. The authors of the original AHA statement acknowledged the real need for a concerted effort to collect these data and called for the establishment of a registry for gathering data on a larger, more organized scale.

Efforts to promote collaborative research networks and integrated databases across the country, led by the National Association of Children’s Hospitals and Related Institutions, the National Institutes of Health through its Clinical and Translational Sciences Awards, and other groups, should continue to be endorsed and fiscally supported. However, the numbers needed to propagate such a registry remain a challenge for drawing conclusions about many of the critical questions delineated above and unveiled in the different versions of the guidelines published this summer. For example, a registry to examine the trade-offs related to whether to conduct ECG screenings would need to be sufficiently large to stratify by age and different underlying cardiac disorders, given the variability across the major causes of pediatric SCD.21,22 It may be that different screening and management protocols will be necessary for youth at different ages and with different underlying cardiac problems.

Research Implications: Using Data to Develop Policy

The debate over the last summer has also demonstrated the challenges inherent in finding and interpreting data with the goal to develop policy when a condition or an adverse treatment event may be extremely rare. In developing policy in adult disorders, policy makers often rely on multiple, randomized clinical trials and use techniques such as meta-analysis to identify consensus across studies. Despite the higher prevalence rates of most adult disorders and the vastly increased numbers of studies available, Jeremy Grimshaw of the Cochrane Collaboration’s Effective Practice and Organization of Care Group in 2004 commented on the ongoing lack of generalizable evidence-based data to inform policy making.23 These methodological limitations are amplified in rare pediatric conditions.

SCD is uncommon in children; population-based mortality rates range from 0.5 to 3.0 per 100,000 patient-years.24–27 Adverse cardiac events in response to stimulant medications among youth with ADHD are even more unusual. Consequently, the amount of directly applicable empirical data on which to base screening and management recommendations is limited. That limitation is not just the lack of comprehensive data collection (although that has certainly been true). Conducting even a single clinical trial to directly evaluate the benefits of screening children with ADHD for SCD risk factors would be complicated by logistical and ethical considerations. Also, because ADHD patients are currently undergoing treatment, and new ADHD patients are continuously diagnosed, there is a need to identify practices that are (provisionally) optimal given the currently available information. Cohen and Neumann28 recently proposed the application of decision analysis to evaluate clinical practice guidelines in rare pediatric disorders and delineate its distinct advantages over more traditional guideline development criteria. Novel research methodological approaches like this must be encouraged in developing the basis for guidelines addressing rare phenomena like those highlighted in the controversy that occurred this past summer.

Policy Implications: Focusing on Context

The AHA document offers a valuable, systematic review of the available evidence, following traditional systematic evidence syntheses and rating the evidentiary basis for the recommendations; the AAP statement responded with a different interpretation of the available data. Evidence synthesis has always called for attention to context (eg, sample characteristics, setting generalizability, robustness of findings) in the review of individual studies. However, newer approaches to evidence synthesis call for more transparency regarding the context within which policy statements are developed (eg, explicit specification of targeted outcomes of interest; process for identifying reviewed studies; eligibility criteria used with respect to populations of interest, interventions, comparators, outcomes, and study designs; and quantitative characterization of the uncertainty associated with recommended screening and management strategies).

As Greenhalgh and Russell29 eloquently argue, we need to be aware that policy making is not simply the “harvesting of objective facts to be fed into a logical decision-making sequence.” From the choice of the questions we ask, the data we collect, and the weighting of the evidence to the presentation of the data within the policy statement, the process remains value-laden. Schon30 has called for “frame reflective awareness” as an openly acknowledged secondary process in policy development, where the values and premises on which individuals are basing their decisions and the processes used are constantly iterated and reiterated. This type of approach is particularly relevant when the available data are limited and policies may have far-reaching effects on clinical practice and patient outcomes. The fact that traditional policy statements do not always address these contextual issues explicitly can lead to discrepant interpretations of risk and benefit trade-offs between different organizations, depending on their priorities, perspectives, and values. The AHA and AAP statements could be strengthened by communicating the reference frames within which different trade-offs were evaluated. The statements would also benefit from deliberate quantification and documentation of the impact of uncertainty accompanying the available data that may affect different organizations’ estimates of the trade-offs between different screening and management strategies.

Practice Implications: Workforce Preparation and Monitoring

The AAP statement recommended that the primary care pediatrician determine the need for an ECG based on a
targeted cardiac history and physical examination. However, primary pediatricians may be uncomfortable with this suggestion because of limited exposure to outpatient cardiology during their residency training. The need for better training in a number of subspecialty disorders presenting in the outpatient setting was reaffirmed through the survey by Freed et al, of recently trained pediatric generalists, 59% of whom endorsed the desire to have participated in additional outpatient subspecialty training during residency had it been available to them. Although cardiology remains an elective during pediatric residency training, the Accreditation Council on Graduate Medical Education’s most recent pediatric requirements affirm the importance of training in outpatient settings for all subspecialty rotations.

The controversy and responses over the past summer also demonstrate the broad impact of these recommendations on primary care clinicians, subspecialists, health plans, healthcare resources, and families. Published statements have the power to shape clinical decision making and healthcare resource use. This power carries responsibility to quantify the impact of screening and follow-up on finite medical resources, as well as to address the means by which the pediatric workforce should be prepared for proposed changes. The AAP acknowledged the need to couple policy recommendations with workforce preparation when they published their ADHD diagnostic and treatment guidelines, they concurrently launched a tool kit for pediatric clinicians to use to implement the ADHD guidelines in practice, an online interactive educational training program for conducting a quality-improvement activity related to ADHD in their practice (www.eqipp.org), and a series of continuing medical education workshops on ADHD across the country. The controversy from this past summer indicates that we need to quickly but deliberately determine whether additional investment in training primary care clinicians is warranted, taking into account the opportunity costs (ie, what other practice changes or disorders will not be focused on) and comparing those costs to the potential benefits. We must also consider the impact on pediatric and adult cardiology services and what, if any, support is needed. In the interim, pediatric primary care clinicians and cardiac specialists need to develop collaborative approaches to identifying youth with possible risk for SCD.

Summary

The recent controversy over ECG screening for children with ADHD raised more questions than it answered. It exposed the paucity of data currently available to address the issue of ECG screening in youth before starting treatment with stimulants. The debate also raised broader questions about the role of the history, physical examination, and ECG in identifying causes of SCD in youth with ADHD and the management of youth once they are determined to have a cardiac disorder. It highlighted the challenges of using traditional methodologies to develop evidence-based policies in rare conditions where high-caliber population-based data may be limited, and it called attention to context in the development of policy. Finally, the controversy shed light on the need to consider the impact of policy statements on practice settings, to consider what practice changes we most want to prioritize, to prepare those settings for any necessary changes, and to monitor the impact on youth outcomes. The debate has also been a clarion call for researchers, policy makers, and professional organizations to examine how we currently sew together information to develop policies. It remains to be seen whether we will heed the call, recognize the limited material with which we are currently working, and jointly tailor creative, innovative approaches for researching, developing, and implementing guidelines for rare, but potentially lethal, pediatric conditions.

References

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