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Re: Childhood Lipid Screening: Evidence and Conflicts

McCrindle et al titled their response to our commentary, “Bringing Evidence to the Debate.” However, they primarily reiterated the rationale already in the guidelines, rather than bringing new evidence to address our concerns.

One concern was that the guideline did not address the cost-efficacy of its recommendations. McCrindle et al cited studies of the cost-efficacy of screening for the rare (1 in 500) genetic condition familial hypercholesterolemia (FH). However, such a narrowly focused screening program was not recommended in the guideline. The $8700 per year gained that they quote is irrelevant because it refers to a program to screen family members of known FH cases, not to the population-wide screening program they recommend, which would be far less cost-effective.

McCrindle et al are right in that our commentary contained opinions. So did theirs. It may help to highlight areas where we agree and disagree.

We agree that:

1. Childhood lipid levels can identify children at increased risk of atherosclerosis decades later.
2. Clinical trials have shown that treating the 1 child in 500 who has FH can lead to improvements in intermediate outcomes such as coronary atherosclerosis.
3. Trials of whether treating the much larger number of children with high lipid levels as recommended by the proposed guidelines reduces future coronary events have not been done and are unlikely ever to be feasible.

Our areas of disagreement relate both to the aggressive nature of the National Heart, Lung, and Blood Institute guidelines and to the process by which they were produced.

1. We disagree that it is acceptable to make screening recommendations without estimating the health benefits, harms, and costs that might result. Because such estimates are essential for informed decision-making, we disagree that the “guidelines provide clinicians with the necessary evidence … to make their own informed judgment as to the utility and role for these recommendations.”
2. In the absence of randomized trial evidence of clinical event benefits, we disagree with making a “strong recommendation,” requiring a “compelling rationale for an alternative approach” (quoted from Tables 1–3, Evidence Grading System, Strength of Recommendations).2
3. Most important, we disagree that it is appropriate for panel members with extensive conflicts of interest to have leading roles in creating practice guidelines.

Conflicts of interest among authors of guidelines were discussed in a recent report3 from the Institute of Medicine (IOM). With the exception of disclosing conflicts, none of the panel’s recommendations were followed (Table). The panel members, however well-meaning, are only human, and it is unreasonable to believe that the large body of research on conflicts of interest that led to the IOM recommendations does not apply to them. A flawed process led to overly aggressive guidelines in which the strength of the evidence was misrepresented and key evidence needed to evaluate the guidelines was lacking. We can and should do better. Let’s start by following this key IOM recommendation: scientists with extensive conflicts of interest should not be permitted to have leadership or voting roles on guideline panels.

Table IOM
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Recommendations for Managing Potential Conflicts of Interest Among Panels Writing Clinical Practice Guidelines

Recommendation 7.1: Groups that develop clinical practice guidelines should generally exclude as panel members individuals with conflicts of interest.... In the exceptional situation in which avoidance of panel members with conflicts of interest is impossible,... groups should:
*Publicly document that they made a good-faith effort to find experts without conflicts of interest by issuing a public call for members and other recruitment measures
*Examine the possibility of excluding the conflicted expert
*Examine the possibility of excluding the entire conflicted panel

*Exclude panel members with conflicting interests from deliberating, drafting, or voting on specific recommendations, and
*Publicly disclose the relevant conflicts of interest of panel members

Table

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Universal Lipid Screening: Response Regarding Implications for Primary Care Practice

The Expert Panel guidelines for cardiovascular health and risk reduction in childhood, commissioned by the National Heart, Lung, and Blood Institute, are a valuable resource for pediatric care providers, addressing the major risk factors associated with development of atherosclerosis. Endorsed by the American Academy of Pediatrics, the recommendations correspond with the age and developmental stages in Bright Futures, so they can be incorporated into routine health maintenance. The recommendations are presented with a summary of the evidence, allowing clinicians to apply their own knowledge and experience in deciding what is necessary for each child and family. The Expert Panel was selected to include representatives from pediatrics, family medicine, cardiology, nutrition, and nursing. Each brought their expertise to evaluation of the evidence and recommendations that can be readily integrated into practice. For example, there are specific recommendations for safely transitioning to lower intake of energy-dense foods, such as fat-free milk. Recommended daily calories by age, gender, and activity level are provided, as well as age-specific diet recommendations that practitioners can use to promote cardiovascular health. Practical and specific recommendations like this are provided for each of the major risk factors.

Universal lipid screening is the most discussed issue in the guidelines. It was also widely debated within the subgroup reviewing the evidence, risks, and benefits, as well as by the entire panel. The consensus recommendation is to assess all children between 9 and 11 years of age with a nonfasting non–high-density lipoprotein cholesterol (non–HDL-C) = total cholesterol – HDL-C) level. The primary purpose of screening is to identify the ~1 in 500 children who are heterozygous for familial hypercholesterolemia (FH), realizing that other forms of important dyslipidemia would be identified as well. Children with FH have elevated total and low-density lipoprotein cholesterol levels from birth and are at risk for early cardiovascular disease. 5% of individuals with this condition will have a coronary artery event before 30 years of age. Previous guidelines have relied on family history to initiate screening, but the evidence shows this approach to be insufficient.3,4 The panel concluded that universal screening was necessary to detect this important, common family condition. The nonfasting non–HDL-C level is an accurate screen for dyslipidemia, and elimination of the need to be fasting should make testing easier. Age 9 to 11 years was selected because most children entering fifth or sixth grade are required to have a health maintenance examination and because low-density lipoprotein cholesterol levels fall with puberty before rising to prepuberty levels. An additional benefit to screening of children is the identification of parents who are unaware that they have FH. Knowing a child’s cholesterol level can initiate family screening and a targeted lifestyle intervention.

Providers of children’s health care are familiar with screening to identify disease states that do not present on physical examination. As the medical home for children and families, we use behavioral screening to identify conditions such as maternal depression, developmental delay, and autism. We assess for disease states and behaviors throughout childhood, although their sequelae may not be manifest until adulthood. An example is screening for tobacco use. Pediatric care providers are therefore well positioned to identify children with dyslipidemia who need early intervention to prevent development of premature cardiovascular disease.

The guidelines have only been available for 1 year, and it will take more time to become familiar and comfortable with the recommendations. Following the risk factor algorithms makes it clear that the guidelines only rarely recommend specialist referral. Rather, the approach is risk identification and management by the primary care practitioner. Just as those of us who care for children have
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