5. Popkin BM, Duffey K, Gordon-Larsen P. Environmental influences on food choice, physical activity and energy balance. *Physiol Behav*. 2005;86(5):603-613.

6. Dietz WH. Overweight in childhood and adolescence. *N Engl J Med*. 2004;350(9):855-857.

7. El-Sayed Moustafa JS, Froguel P. From obesity genetics to the future of personalized obesity therapy. *Nat Rev Endocrinol*. 2013;9(7):402-413.

8. Belsky DW, Moffitt TE, Houts R, et al. Polygenic risk, rapid childhood growth, and the development of obesity. *Arch Pediatr Adolesc Med*. 2012;166(6):515-521.

9. van Jaarsveld CHM, Boniface D, Llewellyn CH, Wardle J. Appetite and growth: a longitudinal sibling analysis [published online February 17, 2014]. *JAMA Pediatr*. doi:10.1001/jamapediatrics.2013.4951.

10. Llewellyn CH, Trzaskowski M, van Jaarsveld CHM, Plomin R, Wardle J. Satiety mechanisms in genetic risk of obesity [published online February 17, 2014]. *JAMA Pediatr*. doi:10.1001/jamapediatrics.2013.4944.

11. Kilpeläinen TO, Qi L, Brage S, et al. Physical activity attenuates the influence of FTO variants on obesity risk. *PLoS Med*. 2011;8(11):e1001116.

12. Elks CE, Loos RJF, Sharp SJ, et al. Genetic markers of adult obesity risk are associated with greater early infancy weight gain and growth. *PLoS Med*. 2010;7(5):e1000284.

13. Wardle J, Carnell S, Haworth CMA, Farooqi IS, O'Rahilly S, Plomin R. Obesity associated genetic variation in FTO is associated with diminished satiety. *J Clin Endocrinol Metab*. 2008;93(9):3640-3643.

14. Plomin R, Haworth CM, Davis OS. Common disorders are quantitative traits. *Nat Rev Genet*. 2009;10(12):872-878.

15. Belsky DW, Moffitt TE, Caspi A. Genetics in population health science. *Am J Public Health*. 2013;103(suppl 1):S73-S83.

16. Qi Q, Chu AY, Kang JH, et al. Sugar-sweetened beverages and genetic risk of obesity. *N Engl J Med*. 2012;367(15):1387-1396.

17. Li S, Zhao JH, Luan J, et al. Physical activity attenuates the genetic predisposition to obesity in 20,000 men and women from EPIC-Norfolk prospective population study. *PLoS Med*. 2010;7(8):1-9.

Potential—and Potential Pitfalls—of Screening Newborns for Critical Congenital Heart Disease

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Before discharge from a newborn nursery, most US infants undergo screening for a diverse list of medical conditions. In addition to the newborn metabolic screen, recommended screening in each newborn includes testing for hearing loss,[1] a serum or transcutaneous measurement of bilirubin level for jaundice,[2] and, for infants born at less than 37 weeks' gestation, a 90-minute "car seat challenge" to evaluate for possible hypoxia.[3] The most recent addition to this menu is the recommendation that newborns undergo screening with pulse oximetry for critical congenital heart disease (CCHD) by assessing preductal and postductal oxygen saturation levels before discharge.[4] That's a lot of screening to be completed during a birth hospitalization averaging less than 48 hours for term infants born vaginally.[5] In addition, this screening is expected to be accomplished in an atmosphere supportive of maternal-infant bonding and the initiation of successful breastfeeding.

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Given this crowded agenda, critical assessment of the utility of the various recommended screening tests is appropriate. In this issue, Peterson et al[6] provide useful data on the potential benefit of pulse oximetry screening. The goal of these investigators was to more precisely quantify the proportion of US infants with late detection of CCHD (defined as detection >3 days after birth) who would theoretically benefit from pulse oximetry screening. For their analysis, the authors used data from the National Birth Defects Prevention Study.[7] This database has several advantages compared with administrative databases, including multistate population-based ascertainment of infants with birth defects. Cases were actively identified and verified using multiple medical records as sources. Demographic information was compiled by telephone interview. Most important, the investigators excluded infants with syndromic features, rightfully assuming that these newborns would be more likely to undergo evaluation for cardiac disease than would normal-appearing and seemingly healthy neonates. Infants identified with late detection of nonsyndromic CCHD at autopsy or through diagnostic echocardiography were reasonably labeled as those who might benefit from screening, that is, 29.5% of all children with CCHD in their final analysis.

Because congenital heart disease is the most common birth defect and because a significant proportion of affected children have life-threatening cardiac lesions,[7-9] the suggestion by Peterson et al[6] that late diagnosis might be avoided in as many as 29.5% of those with CCHD with the use of pulse oximetry screening is potentially quite significant. However, before concluding that this finding provides definitive evidence of the benefit of screening, we should put the results in context by objectively evaluating how well the tenets of a good screening test are fulfilled.

A fundamental problem of the analysis by Peterson et al[6] is the lack of a denominator; the reader is left wondering, 29.5% of what? Estimates of the incidence of CCHD are in the range of 1 to 3 cases per 1000 births,[9-11] but these incidence rates include newborns with syndromic and nonsyndromic disease, which biases extrapolation of the results from the present study. The underlying assumption that early diagnosis via screening leads to better outcomes than late diagnosis (ie, after children develop CCHD symptoms) presents an additional problem. Peterson et al[6] describe 6 infants included in their analysis who were found at autopsy to have CCHD potentially amenable to treatment that could have been detected by early oxygen saturation screening. We can reasonably assume that these children would have benefited from CCHD screening during their newborn nursery stay. However, whether early diagnosis would have been beneficial to most newborns with CCHD detected late remains unclear. As ac-

knowledged by the authors, 44.9% of the infants identified with late-detected CCHD had a coarctation of the aorta. Although a portion of such children may have a catastrophic outcome if a ductal-dependent lesion goes undetected in the first few days of life, outcomes in many, if not most, children with coarctation of the aorta are not dependent on diagnosis during the newborn nursery stay.

Before the widespread implementation of pulse oximetry screening in the United States, many clinicians were concerned that screening would result in a high number of false-positive test results, leading to expensive, unnecessary, and anxiety-inducing workups of infants without CCHD. Anecdotal evidence suggests that these concerns are largely unfounded. This impression was confirmed in a report on the statewide screening program in New Jersey.[12] In this report, only 27 asymptomatic newborns without CCHD had false-positive pulse oximetry results of more than 70 000 infants undergoing screening, yielding a false-positive rate of approximately 0.04%. False-negative screening results may be more problematic. In a recent meta-analysis,[13] the overall sensitivity of pulse oximetry screening was estimated at 76.5%. Barriers to and problems with large-scale implementation have recently been identified, notably, the need to consider simplification of the currently recommended algorithm.[14] Single-foot oximetry, with sensitivity and specificity statistically similar to those of combined preductal and postductal testing, may prove to be the preferred method of screening for its sheer simplicity.

Pulse oximetry screening for CCHD is *probably* the right thing to do. The data from the study by Peterson et al[6] provide a high-end estimate of the potential benefit of screening. However, whether the actual benefits outweigh the downsides (overall costs of screening, delayed diagnoses because of false-negative screen results, the costs of evaluation and the heightened anxiety ensuing for families of children with false-positive screen results, and identification of children with CCHD for whom early diagnosis offers no added benefit over later detection) remains an unanswered question. Unfortunately, because pulse oximetry screening has become the recommended and/or mandated standard of care, this dilemma will be difficult to resolve.

ARTICLE INFORMATION

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REFERENCES

1. Hearing JCOI; American Academy of Pediatrics, Joint Committee on Infant Hearing. Year 2007 position statement: principles and guidelines for early hearing detection and intervention programs. *Pediatrics*. 2007;120(4):898-921.

2. Maisels MJ, Bhutani VK, Bogen D, Newman TB, Stark AR, Watchko JF. Hyperbilirubinemia in the newborn infant ≥35 weeks' gestation: an update with clarifications. *Pediatrics*. 2009;124(4):1193-1198.

3. Bull MJ, Engle WA; Committee on Injury, Violence, and Poison Prevention and Committee on Fetus and Newborn; American Academy of Pediatrics. Safe transportation of preterm and low birth weight infants at hospital discharge. *Pediatrics*. 2009;123(5):1424-1429.

4. Mahle WT, Newburger JW, Matherne GP, et al; 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; 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(5):447-458.

5. Young PC, Korgenski K, Buchi KF. Early readmission of newborns in a large health care system. *Pediatrics*. 2013;131(5):e1538-e1544. doi:10.1542/peds.2012-2634.

6. Peterson C, Ailes E, Riehle-Colarusso T, et al. Late detection of critical congenital heart disease among US infants: estimation of the potential impact of proposed universal screening using pulse oximetry [published online February 3, 2014]. *JAMA Pediatr*. doi:10.1001/jamapediatrics.2013.4779.

7. Yoon PW, Rasmussen SA, Lynberg MC, et al. The National Birth Defects Prevention Study. *Public Health Rep*. 2001;116(suppl 1):32-40.

8. Parker SE, Mai CT, Canfield MA, et al; National Birth Defects Prevention Network. Updated National Birth Prevalence estimates for selected birth defects in the United States, 2004-2006. *Birth Defects Res A Clin Mol Teratol*. 2010;88(12):1008-1016.

9. Botto LD, Correa A, Erickson JD. Racial and temporal variations in the prevalence of heart defects. *Pediatrics*. 2001;107(3):32. doi:10.1542/peds.107.3.e32.

10. Wren C, Reinhardt Z, Khawaja K. Twenty-year trends in diagnosis of life-threatening neonatal cardiovascular malformations. *Arch Dis Child Fetal Neonatal Ed*. 2008;93(1):F33-F35.

11. Talner CN. Report of the New England Regional Infant Cardiac Program, by Donald C. Fyler, MD, *Pediatrics*, 1980;65(suppl):375-461. *Pediatrics*. 1998;102(1, pt 2):258-259.

12. Garg LF, Van Naarden Braun K, Knapp MM, et al. Results from the New Jersey statewide critical congenital heart defects screening program. *Pediatrics*. 2013;132(2):e314-e323. doi:10.1542/peds.2013-0269.

13. Thangaratinam S, Brown K, Zamora J, Khan KS, Ewer AK. Pulse oximetry screening for critical congenital heart defects in asymptomatic newborn babies: a systematic review and meta-analysis. *Lancet*. 2012;379(9835):2459-2464.

14. Kochilas LK, Lohr JL, Bruhn E, et al. Implementation of critical congenital heart disease screening in Minnesota. *Pediatrics*. 2013;132(3):e587-e594. doi:10.1542/peds.2013-0803.