Translating Best Evidence into Best Care

EDITOR'S NOTE: Studies for this column are identified using the Clinical Queries feature of PubMed, "hand" searching *JAMA*, *JAMA Pediatrics*, *Pediatrics*, *The Journal of Pediatrics*, and *The New England Journal of Medicine*, and from customized EvidenceUpdates alerts.

EBM PEARL: SCREENING: Screening is a population-based tool to identify asymptomatic or unrecognized symptomatic individuals with a treatable disease (at least somewhat treatable). Screening is, fundamentally, a diagnostic test. The diagnostic test characteristics in screening are adjusted to balance sensitivity and specificity in favor of sensitivity—few false negatives. Enhancing sensitivity typically leads to worsening specificity by increasing false positives. The balance attempts to minimize harms: (1) not identifying patients with disease, and (2) treating, further testing, or both in patients who do not have disease but test positive. While diagnostic testing is the key issue in screening, there are a number of other notably important issues that require attention in a screening program. In 2008, the World Health Organization (WHO) modified an earlier version of screening criteria.[1] What follows are a few of the salient points of that revision. "The objectives of the screening should be defined at the outset. There should be a defined target population. There should be scientific evidence of screening program effectiveness. The program should integrate education, testing, clinical services, and program management. The overall benefits of screening should outweigh the harms." Please see the WHO bulletin for additional details. Three articles in this volume's Current Best Evidence discuss screening (celiac disease, congenital heart disease, and autism).

APPLICATION/TRANSLATION PEARL: INTRODUCTION AND DEFINITION: With this edition of Current Best Evidence, we begin a series of "Pearls" discussing the fairly weighty issue of how to bring the evidence back to the bedside. Let us start at the beginning: the EBM definition, upon which we base EBM practice. "EBM is a systematic approach to clinical problem solving which allows the integration of the best available research evidence with clinical expertise and patient values."[2] From the definition, we see the goal and the promise of EBM. The "research evidence" part of the definition has notably improved over the past 30 years. This is the part of the EBM definition that clinicians and others typically associate with EBM. It is also the most easily quantifiable in terms of research methodology, medical treatment effects, and diagnostic test characteristics. The clinical expertise (weighing diagnostic test and therapy benefits and harms) within the context of patient values (broadly considered as the patient's environmental and personal frame of reference) part of the definition is currently less quantified and often highly complex. However, without this aspect of the definition, EBM practice is impossible. In the coming issues of Current Best Evidence, we will discuss these application and translation details as they emerge from the EBM definition.

—Jordan Hupert, MD

References

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Perfusion index, in addition to pulse oximetry may enhance detection of neonatal severe congenital heart disease

Schena F, Picciolli I, Agosti M, Zuppa AA, Zuccotti G, Parola L, et al. Perfusion Index and Pulse Oximetry Screening for Congenital Heart Defects. *J Pediatr* 2017;183:74-9.

Question Among asymptomatic newborns, what is the diagnostic accuracy of combined pulse oximetry (POX) and perfusion index (PI) screening, in diagnosing severe congenital heart disease (sCHD)?

Design Multicenter, prospective cohort study.

Setting 10 tertiary and 6 nontertiary maternity hospitals in Italy.

Participants 42 169 asymptomatic neonates.

Intervention Combined pre- and postductal POX and PI screening.

Outcomes Detection of sCHD.

Main Results 3 babies with sCHD were detected, post-test probability for a positive test 0.42% (95%CI, 0.14%-1.22%). Four babies with sCHD were missed, post-test probability for a negative test 0.0096% (95% CI, 0.0002%, 0.0191%).

Conclusions PI may have a role in enhancing sCHD screening.

Commentary We recently demonstrated that PI is significantly correlated with left ventricular output in healthy term infants.[1] Schena et al now demonstrate that a combination of POX and PI may be used for sCHD screening. The study methods were well thought out and were clearly detailed. The chosen PI cut-off value <0.90 may affect the results, as Granelli et al reported that values of PI <0.70 may indicate illness and a value <0.50 indicates definite underperfusion.[2] The authors explained that their PI cutoff choice was based on previously unreported data suggesting that the PI is slightly higher after 48 hour of life. Data by Granelli et al come from infants 1 to 120 hours of age.[2] It is noteworthy that the POX and PI combination seemed to provide most benefit in nontertiary hospitals, where sCHD detection resources may have been less available than in tertiary hospitals. The hope is that this study will encourage future trials confirming a role for PI in neonatal sCHD-screening.

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Response to name may enhance autism spectrum disorder screening

Miller M, Iosif AM, Hill M, Young GS, Schwichtenberg AJ, Ozonoff S. Response to name in infants developing autism spectrum disorder: a prospective study. *J Pediatr* 2017;183:141-6.

Question Among infants, what is the diagnostic accuracy of response to name, compared with more extensive testing, in diagnosing autism spectrum disorder (ASD)?

Design Prospective study of siblings of children with ASD (high risk [HR]) and controls (low risk [LR]).

Setting University-based outpatient setting in California.

Participants HR and LR infants with first assessment between 6 and 9 months of age.

Intervention Response to name compared with definitive testing.

Outcomes Development of ASD.

Main Results Both overall sensitivity and specificity for at least 1 failure between 12-24 months were 70% with wide 95% CIs: 50%-90% and 62%-78%, respectively.

Conclusions Response to name may enhance ASD screening detection.

Commentary Despite the excitement of recent advances in biomarker research that might lead to pre-symptomatic detection, the development of simple early detection strategies for ASD that can be administered in primary care remains a major priority. Miller et al report that failing to respond to name on 1 or more visits between 12 and 24 months was associated with 70% sensitivity and 70% specificity for ASD at age 36 months, although the classification accuracy at individual time points was less favorable. Nevertheless, failure to respond to name is one of the most consistently reported early concerns of parents,[1] and the ease of incorporating the task into a brief office visit suggests that this could be a valuable addition. There are a few caveats. First, the findings were mainly derived from HR infants and in the controlled context of a university-based research study. Replication will be needed in a primary care context, with the task administered by the child's clinician, in the usual office environment. Second, although one of the study's unique strengths is the interactive nature of the task, one should be cautious in assuming that a clinician's observation during a brief interaction would be more accurate than parental report. Indeed, in a recent study[2] of the parent-report analog of the observational scale from which the task used in the current study was derived, classification accuracy of the corresponding "response to name" item at 12 months was similar. Finally, the relative merits focusing on a single vs a larger set of markers warrants further consideration. That said, because of its brevity and ease of use, uptake of a briefer test might be greater in community practice. It is important that we continue to consider how surveillance for early signs of ASD may benefit from a multi-pronged approach over time, and how brief, low-cost methods might complement and augment more time- and/or resource-intensive approaches.

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The Quick-Wee infant urine collection method

Faster clean catch urine collection (Quick-Wee method) from infants: randomised controlled trial. *BMJ* 2017;357:j1341.

Question Among infants requiring a clean urine sample, what is the efficacy of the Quick-Wee method, compared with a standard clean-catch technique, in obtaining a urine sample?

Design Randomized controlled trial.

Setting Pediatric emergency department, Royal Children's Hospital, Melbourne, Australia.