Current Best Evidence: Translating Best Evidence into Best Care

EDITOR'S NOTE: Studies for this issue were identified using alerts from *Archives of Disease in Childhood-Education and Practice, Archives of Disease in Childhood-Fetal and Neonatal, Archives of Disease in Childhood, British Medical Journal, Journal of the American Medical Association, JAMA Pediatrics, New England Journal of Medicine, Pediatric Infectious Disease Journal, Pediatrics, The Journal of Pediatrics,* and *The Lancet*. Search terms were "paediatrics" [All Fields] OR "pediatrics" [All Fields] OR "pediatrics" [MeSH Terms]. In addition, studies were identified using the Clinical Queries feature of PubMed. Cleo Pappas, MLIS, retired, Library of the Health Sciences, University of Illinois at Chicago, contributed to the review and selection of this month's abstracts.

EVIDENCE-BASED MEDICINE PEARL: ZERO IN THE NUMERATOR AND THE "RULE OF 3": If a study mentions that "no adverse events were observed," is the procedure or therapy safe to use? One may feel differentially confident if no adverse events were observed among 10 research subjects versus 1000. A quick way to estimate the upper limit of the 95% CI for no events (with 0 at the lower limit) is based on the total sample size (the denominator); the "rule of 3" (*JAMA* 1983;164:1171-4) 3/n, where n is the total sample size, and is a close estimate of the 95% CI upper limit. For example, if no events were observed in a sample of 10 patients, the 95% CI upper limit is 3/10 = 30%; for 1000 patients, the 95% CI is 0.3%. An example of a study with no events may be noted in Chalmers et al (see piece by Snodgrass on page 1069 regarding article Chalmers et al; *J Pediatr* 2014;164:1171-4).

—Jordan Hupert, MD

LITERATURE SEARCH PEARL: STAYING UP-TO-DATE—MCMASTER PLUS RESOURCES AND EVIDENCEUPDATES: Keeping up-to-date in one's clinical field is a core activity of any clinician. Brian Haynes, MD, and his colleagues have developed an international physician, nurse, and therapist network, all trained in evidence-based medicine skills, who are continuously searching a set of 120 core, methodologically high-quality journals (including *The Journal of Pediatrics*) for valid, clinically useful studies. This network, McMaster PLUS (Mc+), is part of the McMaster University Health Information Research unit (http://hiru.mcmaster.ca/hiru/HIRU_McMaster_PLUS_projects.aspx). One of the Mc+ projects, EvidenceUpdates (http://plus.mcmaster.ca/EvidenceUpdates/Default.aspx; free registration), in partnership with *BMJ* (http://www.bmj.com), electronically delivers current, methodologically and clinically-relevant articles to clinicians, based on each clinician's specific clinical interest. One may also search for articles at Evidence Updates.

—Jordan Hupert, MD

Substantial lifelong cost of autism spectrum disorder

Buescher AV, Cidav Z, Knapp M, Mandell DS. Costs of Autism Spectrum Disorders in the United Kingdom and the United States. *JAMA Pediatr* 2014;168:721-8.

Question Among children with autism spectrum disorder (ASD), what is the lifetime societal direct and indirect costs of this disorder (including individual and parental productivity costs)?

Design Literature review.

Setting US and United Kingdom (UK).

Participants Children with ASD.

Intervention Presence of ASD.

Outcomes Mean annual medical, nonmedical, and indirect economic costs and lifetime costs.

Main Results The lifelong cost of supporting an individual with ASD and intellectual disability was $2.4 million in the US and £1.5 million (US $2.2 million) in the UK. During adulthood, residential care or supportive living accommodation and individual productivity loss contributed the highest costs. Medical costs were higher in adults than children.

Conclusions The substantial direct and indirect economic effect of ASD emphasizes the need to continue the search for effective interventions that make best use of scarce societal resources.

Commentary Estimates of the cost of autism are not uncommon. This study is unique in that it brings together and updates the latest information from the US and the UK. In cost of illness studies, the usefulness and relevance of the findings are dependent on the inputs to the model, and this study has made use of a range of data sources. However, there are places where expert opinion was used, or information from one side of the Atlantic Ocean was applied on the other. Given these limitations, the paper could have included some further sensitivity analyses in which these assumptions are varied in order to capture the impact they have on the totals presented. By their own admission, the authors note that

an estimate of the cost of ASD cannot form the basis of how to prevent or meet the needs of those with the diagnosis. Now that policy and practice discussion can be informed by the latest estimates of the cost of the disorder, it is time for economists to focus on undertaking cost-effectiveness analyses in areas of high cost, so that the resources used maximize the quality of life for people with ASD[1].

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Vaccine promotion messages may not encourage vaccination

Nyhan B, Reifler J, Richey S, Freed GL. Effective messages in vaccine promotion: a randomized trial. *Pediatrics* 2014;133:e835-42.

Question Among parents with young children, what is the efficacy of vaccine-promotion-type messages, compared with controls, in enhancing intention to vaccinate?

Design Web-based randomized controlled trial.

Setting US.

Participants Nationally-based Knowledge Networks panel.

Intervention One of 4 measles, mumps, and rubella (MMR) related, vaccine-promotion messages (based on public health communications information): (1) lack of evidence that MMR causes autism; (2) dangers of the diseases prevented by the MMR; (3) images of children who have diseases prevented by the MMR vaccine; and (4) a dramatic narrative about an infant who almost died of measles. Additionally, there was one non-vaccine–related control message.

Outcomes Misperceptions, side-effect beliefs, and intent to vaccinate with MMR.

Main Results None of the interventions increased parental intent to vaccinate a future child, and, among some parents, there was increased misperceptions or reduced vaccination intention.

Conclusions Current public health communications about vaccines may not be effective.

Commentary Vaccination resistance and distrust emerged early and have coexisted ever since. Parents may be selective about, defer, or immunize despite having concerns.[1] There is no clear evidence of increasing immunization hesitancy, however. In the United Kingdom, for example, vaccination is at its highest level, including MMR coverage. Setting aside practical barriers to vaccination, no distinct division exists between those choosing or declining vaccines.[1] Multiple factors influence this decision and evidence for interventions reducing vaccine refusal or hesitancy is limited.[2] In the study by Nyhan et al, none of the four MMR-related messages increased parental intent to vaccinate, although details of their children's age (and thus MMR relevance) were missing. The study suggested that some interventions, although better informing, may increase safety concerns and reduce intent to vaccinate. In reality, multilayered (as opposed to single fact) information provision is more typical, with individual access determined by personal need. Health professionals are key,[3] and the resultant interactive process can better direct to appropriate resources and allows tailored discussion. What is clearly needed, however, is adequate premarket testing with outcome measures that capture impact on knowledge and on intended behavior.

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Completion of circumcision when distal hypospadias is discovered intra-procedurally and its effect on subsequent hypospadias repair

Chalmers D, Wiedel CA, Siparsky GL, Campbell JB, Wilcox DT. Discovery of hypospadias during newborn circumcision should not preclude completion of the procedure. *J Pediatr* 2014;164:1171-74.

Question Among infants with an intact prepuce undergoing circumcision, what is the association of circumcision completion when hypospadias is discovered intra-procedurally, compared with aborting the procedure and compared with no circumcision attempt, on adverse affects of hypospadias repair?

Design Prospective cohort.

Setting Pediatric urology clinic in Colorado, US.