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: PREVALENCE RATIO (PR): The PR is the ratio of disease prevalence in the exposed versus the non-exposed groups. The PR makes far fewer appearances in the medical literature than the odds ratio (OR) when measuring the association of an exposure to an outcome. One notable reason is that the OR has statistical properties that work well with logistic analysis, a popular statistical method (and the PR does not work as well). When the prevalence is rare, the OR will serve as a good approximation of the PR. When prevalence is common, the OR will overestimate the true PR. There are statistical methods that may be used with the PR. An example of the PR used in the medical literature can been found in the study by Iannotti et al (abstracted with a commentary by Dr Marion Roche), discussed in this edition of Current Best Evidence.

APPLICATION/TRANSLATION PEARL: QUALITY AND MAGNITUDE OF THE EVIDENCE: "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."[1] This is the classic David Sackett EBM definition, noting the 3 legs supporting EBM practice, the first of which is ". . .integration of the best available research evidence." This "leg" presumes identifying a knowledge gap, developing a specific question (the answer to which will fill the gap), and the expertise, or access to expertise, to search for and critically appraise medical research studies. This last point, critical appraisal, is composed of 3 aspects: assessing the scientific validity of the study, interpretation of the results, and the level of evidence (eg, primary study, systematic review, synthesis, summary). While much focus has been placed in educational settings on understanding the basic EBM statistics (for interpretation of results), validity assessment is the primary force behind one's confidence in the overall value of study. Each type of study (therapy, diagnosis, etc) has its own set of validity measures, satisfactory fulfillment of which fosters appropriate confidence to proceed with discerning the magnitude of the results. Critical appraisal is step one in applying/translating research. The more confidence one has in the basic scientific validity and in the magnitude of the results, the more confidence one has in bringing research study results to the bedside.

—Jordan Hupert, MD

Reference

1. Sackett DL, Strauss SE, Richardson WS, Rosenberg W, Haynes RB. Evidence-based medicine: how to practice and teach EBM. London: Churchill-Livingstone; 2000.

An egg a day enhances growth in resource-poor communities

Iannotti LL, Lutter CK, Stewart CP, Gallegos Riofrío CA, Malo C, Reinhart G, et al. Eggs in Early Complementary Feeding and Child Growth: A Randomized Controlled Trial. *Pediatrics* 2017;140. pii: e20163459.

Question Among children in resource-poor communities, what is the therapeutic efficacy of a daily supplemental egg, compared with usual diet, on enhancing growth?

Design Randomized controlled trial.

Setting Five rural parishes of the Cotopaxi Province in Ecuador.

Participants Mother (caregiver)-infant pairs. Infants, 6-9 months, in good health.

Intervention One egg a day for 6 months versus control (no supplemental eggs provided).

Outcomes Linear and mass growth.

Main Results There was a reduced prevalence of stunting by 47% (adjusted prevalence ratio [aPR], 0.53; 95% CI, 0.37-0.77) and underweight by 74% (aPR, 0.26; 95% CI, 0.10-0.70).

Conclusions Daily egg ingestion in resource poor areas enhances growth.

Commentary Global efforts toward the World Health Assembly target to reduce stunting by 40% are currently off track, due to limited investment in implementation of effective public health interventions.[1,2] This randomized controlled trial of an intervention in which 1 egg was provided daily for

6 months to households of children 6-9 months of age, reported increased linear growth, reduced stunting and underweight prevalence, and no observed allergic reactions to eggs. This is a welcome approach to improve growth with local food, and the magnitude of stunting reductions and the increase in linear growth in this study are noteworthy and beyond the magnitude seen in other infant and young child feeding interventions.[2] These results, at a time where there is a shift from avoidance of potential food allergens to encourage earlier introduction of eggs and other common allergenic foods in complementary feeding,[3] may enable public health programs to normalize and encourage including eggs in complementary feeding for infants as young as 6 months, through social marketing and guidance for caregivers and health professionals. In many food insecure contexts where stunting is of public health concern, interventions would be needed to enable access to eggs for daily consumption. We need to understand the feasibility and cost effectiveness of implementing programs to increase egg consumption with and without the provision of eggs at a larger scale, while monitoring and confirming safety in contexts with different allergy profiles. The mechanisms for eggs to improve growth warrant additional study; there are likely additional benefits from vitamin and fatty acid consumption.

Marion L. Roche, PhD, MSc, MIPH
Nutrition International
Ottawa, Ontario, Canada

References

1. International Food Policy Research Institute (IFPRI). Global nutrition report 2016: from promise to impact: ending malnutrition by 2030. Washington (DC): IFPRI; 2016.
2. Bhutta ZA, Das JK, Rizvi A, Gaffey MF, Walker N, Horton S, et al. Evidence-based interventions for improvement of maternal and child nutrition: what can be done and at what cost? Lancet 2013;382:452-77.
3. Ierodiakonou D, Garcia-Larsen V, Logan A, Groome A, Cunha S, Chivinge J, et al. Timing of allergenic food introduction to the infant diet and risk of allergic or autoimmune disease a systematic review and meta-analysis. JAMA 2016;316:1181-92.

Clostridium difficile infection and commonly used pediatric medications

Adams DJ, Eberly MD, Rajnik M, Nylund CM. Risk Factors for Community-Associated Clostridium difficile Infection in Children. *J Pediatr* 2017;186:105-9.

Question Among children with community-associated *Clostridium difficile* infection (CA-CDI), what is the association with medication or outpatient healthcare exposure?

Design Matched case control.

Setting US Military Health System.

Participants Children aged 1-18 years.

Intervention Medication or healthcare exposure versus no exposure.

Outcomes CA-CDI.

Main Results Recent exposures to the following were associated with CA-CDI: clindamycin, OR 73.0 (95% CI 13.9-384.7), third-generation cephalosporins, OR 16.3 (95% CI 9.1-29.3), and proton pump inhibitors, OR 8.2 (95% CI 2.4-28.4). Other classes of antibiotics, proton-pump inhibitors, and outpatient health clinics were also associated.

Conclusions CA-CDI is associated with medications commonly used in pediatric practice, as well as with outpatient healthcare setting exposure.

Commentary CA-CDI accounts for the vast majority of pediatric CDIs.[1] Adams et al provide an extensive understanding of CA-CDI risk factors by studying a large demographically and geographically diverse pediatric cohort over a 12-year period. This study reinforces mindful prescribing of antibiotics and acid-suppression medications. However, a significant minority of patients with CA-CDI did not have identifiable risk factors, suggesting that our understanding of pediatric CDI pathophysiology remains incomplete. We cannot yet conclude that transmission of *C. difficile* occurs commonly in the outpatient setting. Rigorous molecular epidemiologic assessment (eg, whole genome sequencing) of strains causing CA-CDI, along with environmental sampling, will be needed to make this conclusion. Inpatient transmission was surprisingly infrequent in adults with hospital-onset CDI.[2] The *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) code used for case identification reliably identifies children who tested positive for *C. difficile* but not necessarily those whose test reliably differentiated infection and colonization. Nucleic acid amplification tests (NAATs), such as PCR, though highly sensitive, do not differentiate infection and colonization.[3] As *C. difficile* NAATs were not FDA-approved until 2009 and not widely used until years later, most of the study period preceded the NAAT era, thus supporting their case validation. Nonetheless, pediatricians should understand the limitations of NAATs when evaluating for CDI in outpatients, particularly among those who have a more likely cause of diarrhea.

Larry K. Kociolek, MD, MSCI
Northwestern University
Chicago, Illinois

References

1. Wendt JM, Cohen JA, Mu Y, Dumyati GK, Dunn JR, Holzbauer SM, et al. *Clostridium difficile* infection among children across diverse US geographic locations. Pediatrics 2014;133:651-8.
2. Eyre DW, Cule ML, Wilson DJ, Griffiths D, Vaughan A, O'Connor L, et al. Diverse sources of *C. difficile* infection identified on whole-genome sequencing. N Engl J Med 2013;369:1195-205.
3. Kociolek LK. Strategies for optimizing the diagnostic predictive value of *Clostridium difficile* molecular diagnostics. J Clin Microbiol 2017;55:1244-8.