



#### Author Disclosure

Dr Bair-Merritt has disclosed no financial relationships relevant to this article. This commentary does not contain a discussion of an unapproved/investigative use of a commercial product/device.

## Systematic Reviews and Meta-Analyses

Megan H. Bair-Merritt, MD, MSCE\*

### Case Studies

- *You are seeing an 11-month-old infant who has bronchiolitis. A medical student rotating through your practice asks you if the empiric evidence supports prescribing albuterol. In between patients, you search the medical literature and find hundreds of articles written on this topic. You would like one article that summarizes the existing evidence regarding the effectiveness of beta<sub>2</sub>-agonists for treating bronchiolitis.*
- *You are seeing an otherwise healthy 3-year-old boy who has had 4 days of infectious diarrhea. His mother would like to give him Lactobacillus and asks your opinion. You do not have time to find and read multiple papers on this topic but would like to provide a sound, evidence-based answer to the child's mother.*

### Introduction

Pediatric medical research continues to grow exponentially, and because of the vast quantity of articles, keeping abreast of current literature may be overwhelming. In addition, individual studies often are constrained by small sample sizes, which limits the ability to detect significant relationships, and by recruitment from a single site, which limits generalizability. Rigorous literature reviews, therefore, are needed to synthesize available information and to guide practice.

Systematic reviews and meta-analyses identify, in an organized and objective manner, existing studies

about a particular clinical question and answer the question by synthesizing the relevant data in each included study. Such synthesis of multiple studies provides clinicians with a robust means by which to make informed clinical decisions. Systematic reviews summarize existing studies descriptively; meta-analyses use statistics to combine the results from each included study and generate a single summary statistic. Using one systematic review/meta-analysis about the efficacy of beta<sub>2</sub>-agonists (1) and one meta-analysis about *Lactobacillus* therapy, (2) this article discusses the uses and limitations of these research tools.

### Systematic Review

A systematic review uses a well-defined approach to locate and summarize articles related to a clinical question. Rigorously conducted systematic reviews should include the following:

1) A focus on a specific clinical question such as “Are beta<sub>2</sub>-agonists effective in decreasing respiratory distress in infants who have bronchiolitis?”

2) A thorough and objective search of the scientific literature guided by a formal and prescribed protocol that is well-documented and reproducible. This search should use multiple databases (such as MEDLINE®, PsycINFO®, and CINAHL®) and employ additional sources of information (such as manual search of bibliographies and consultation with content experts). Use of an explicit search strategy minimizes biases in finding and including relevant studies. The goal is to find all potentially relevant articles.

\*Assistant Professor of Pediatrics, Division of General Pediatrics & Adolescent Medicine, Johns Hopkins University, Baltimore, Md.

3) A clear explanation of which studies were included and which were excluded. For example, the article about beta<sub>2</sub>-agonists included only randomized control trials. (1)

4) A descriptive results section summarizing the findings from the included studies and addressing the quality of included studies.

### Meta-analysis

A meta-analysis pools the statistical information from a systematically collected group of articles and reports an overall summary statistic that incorporates all of the data in all of the included articles. For example, in the *Lactobacillus* meta-analysis, the authors combined the statistical data from nine studies and found that, on average, *Lactobacillus* decreased the duration of infectious diarrhea by 0.7 days. (2)

A meta-analysis should meet all of the requirements listed for a systematic review. In addition, a meta-analysis should:

1) Present a summary statistic using data from all of the included studies. For this pooled estimate, studies that include more subjects should be given greater weight.

2) Test the homogeneity versus heterogeneity of the included studies (sample, intervention, outcome) to determine whether combining the statistics from the studies is possible. For example, it may be inappropriate to combine the results of one study of beta<sub>2</sub>-agonists whose reported

outcome was parental report of infants' symptoms with another study whose reported outcome was reduction in days of hospital admission.

3) Assess for publication bias. Often, positive studies are more likely to be published than are negative studies. Certain statistical tests and diagrams help researchers determine whether smaller studies that have negative findings are potentially missing from the review.

### Advantages and Limitations

Because both systematic reviews and meta-analyses pool results from multiple studies, their findings offer a compilation of evidence that potentially has greater power to inform clinical decisions than would an individual study.

Researchers may conduct a systematic review rather than a meta-analysis because the existing research on the given clinical question is too limited to perform a meta-analysis or the individual studies related to the study question are so different that averaging their results is not meaningful. For example, in the beta-agonist article, the authors concluded that the outcomes of the inpatient studies were too diverse to combine the statistics. (1)

The most significant limitation of both systematic reviews and meta-analyses is commonly described as "garbage in, garbage out." In other words, if the quality of the studies included in the systematic review or

meta-analysis is poor, the summary conclusions are similarly inadequate.

### The Cochrane Library

The Cochrane Library is an international, nonprofit organization of independent researchers who compile systematic reviews on a wide range of medical topics. The topics include a range of pediatric health issues such as "drugs for preventing migraine headaches in children" and "feed thickener for infants who have gastroesophageal reflux." The Cochrane Library can be accessed at the following website: <http://www3.interscience.wiley.com/cgi-bin/mrwhome/106568753/HOME>. Depending on individual affiliation, a fee may be charged to access the reviews.

### References

1. Flores G, Horwitz RI. Efficacy of beta<sub>2</sub>-agonists in bronchiolitis: a reappraisal and meta-analysis. *Pediatrics*. 1997;100:233-239
2. Van Niel CW, Feudtner C, Garrison MM, Christakis DA. *Lactobacillus* therapy for acute infectious diarrhea in children: a meta-analysis. *Pediatrics*. 2002;109:678-684

### Suggested Reading

- Hudley S, Cummings SR, Browner WS, et al. *Designing Clinical Research*. Philadelphia, Pa: Lippincott Williams & Wilkins; 2001
- Woodward M. *Epidemiology: Study Design and Data Analysis*. Boca Raton, Fla: Chapman & Hall; 2005