

geographic variation in receipt of therapy, despite adjustment for clinical characteristics, may be explained not only by psychologist supply but also by parent, child, or pediatrician preferences for or comfort with nonpharmacologic care.

We acknowledge limitations common to analyses of claims data, including no information on services that were not billed to commercial insurance and a limited ability to determine severity of illness or clinical appropriateness for therapy. We cannot comment on therapy receipt in those smaller and more rural counties that we excluded. Nonetheless, our study is the first, to our knowledge, to document the substantial variation in receipt of therapy services among US children treated with ADHD medications and is directly relevant to the ongoing public discourse about how this common condition should be treated.

Walid F. Gellad, MD, MPH  
Bradley D. Stein, MD, PhD  
Teague Ruder, MA  
Rochelle Henderson, PhD  
Sharon G. Frazee, PhD, MPH  
Ateev Mehrotra, MD, MPH  
Julie M. Donohue, PhD

**Author Affiliations:** Center for Health Equity Research and Promotion, VA Pittsburgh Healthcare System, Pittsburgh, Pennsylvania (Gellad); RAND Corporation, Pittsburgh, Pennsylvania (Gellad, Stein, Ruder, Mehrotra); Division of General Medicine and Center for Pharmaceutical Policy and Prescribing, University of Pittsburgh, Pittsburgh, Pennsylvania (Gellad); Department of Psychiatry, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania (Stein); Express Scripts, St Louis, Missouri (Henderson, Frazee); Harvard Medical School, Department of Health Care Policy, Boston, Massachusetts (Mehrotra); Department of Health Policy and Management, University of Pittsburgh Graduate School of Public Health, Pittsburgh, Pennsylvania (Donohue).

**Corresponding Author:** Walid F. Gellad, MD, MPH, RAND Corporation, 4570 Fifth Ave, Ste 600, Pittsburgh, PA 15213 ([wgellad@rand.org](mailto:wgellad@rand.org)).

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**Study concept and design:** Gellad, Henderson, Frazee, Mehrotra, Donohue.

**Acquisition, analysis, or interpretation of data:** Gellad, Stein, Ruder, Henderson, Frazee, Donohue.

**Drafting of the manuscript:** Gellad, Stein, Frazee.

**Critical revision of the manuscript for important intellectual content:** Stein, Ruder, Henderson, Frazee, Mehrotra, Donohue.

**Statistical analysis:** Ruder.

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**Study supervision:** Gellad, Frazee.

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## COMMENT & RESPONSE

### Undertreated and Untreated Pain Should Be Considered an Adverse Event of Neonatal Circumcision

**To the Editor** We read with great interest the article by El Bcheraoui et al<sup>1</sup> recently published in *JAMA Pediatrics*. We believe that the rates of adverse events of male circumcision may have been underestimated. As a matter of fact, the authors did not mention intraoperative and postoperative pain as an adverse effect, especially in neonates. Nonetheless, authors in other studies consider undertreating or untreating procedural pain to be an actual adverse event.<sup>2</sup>

An adverse event is defined as an injury related to medical management, including failure to diagnose and treat. Undertreated male circumcision pain has been shown to determine long-lasting negative effects on future infant behavior.<sup>3</sup> In addition, current guidelines recommend analgesia for neonatal male circumcision.<sup>4</sup> Analgesia is now considered an integral part of routine care whatever the invasive procedure is, particularly in neonates and children.

Unfortunately, it has been evidenced that analgesia for procedural pain in children is not routine in neonatal male circumcision.<sup>5</sup> Relief from pain is a human right that should never be violated, even if a neonate's parents give consent. We hope that future studies similar to that by El Bcheraoui et al<sup>1</sup> will include intraoperative and postoperative pain when estimating the risk of adverse effects for neonatal male circumcision.

Sofia Bisogni, RN, BSN, MSN  
Nicole Olivini, MD  
Filippo Festini, RN, BSN

**Author Affiliations:** Department of Health Sciences, University of Florence, Meyer Children Hospital, Florence, Italy.

**Corresponding Author:** Filippo Festini, RN, BSN, Department of Health Sciences, University of Florence, Meyer Children Hospital, Viale Pieraccini 24, Florence, Italy 50139 ([filippo.festini@unifi.it](mailto:filippo.festini@unifi.it)).

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**In Reply** We thank Bisogni et al for their comments recently published in *JAMA Pediatrics* about intraoperative and postoperative pain as an adverse event (AE) to male circumcision (MC). Use of appropriate analgesia for pain management is a good practice that should be the standard of care during and after any surgical procedure because it can substantially control pain.<sup>1</sup> In a prospective study of 583 neonatal circumcisions performed between December 1, 2005, and December 1, 2008, when appropriate analgesia was applied, 93.5% of neonates circumcised in the first week of life showed no indication of pain on an objective standardized neonatal pain rating system used by the authors.<sup>2</sup>

The recently published article,<sup>3</sup> which found a low incidence of AEs (less than 0.5%) associated with MC in US medical settings during 2001 to 2010, is based on data from a health care reimbursement claims database. This database captures only diagnoses and procedures billed to third parties. The analysis studied the association between 41 AEs, not including pain and MC. A search of the same health care reimbursement claims database for the *International Classification of Diseases, Ninth Revision* codes 338.18 (other acute postoperative pain) and 338.19 (other acute pain) detected 1 patient with pain associated with the MC procedure among 1 400 920 circumcised males. Taking into consideration the possibility that pain may be an underreported AE in the health care reimbursement claims' database used for this analysis, a more thorough analysis of the association of pain and MC would require additional data sources, including information related to use of and type of pain control methods. As previously recommended,<sup>3</sup> future researchers studying the association between AEs and MC should consider using additional data sources to ascertain AEs that are not captured in data from reimbursement claims.

**Charbel El Bcheraoui, PhD**  
**Kenneth L. Dominguez, MD**  
**Peter H. Kilmarx, MD**

**Author Affiliations:** Epidemic Intelligence Service, Division of Applied Sciences, Scientific Education, and Professional Development Program, Office of Surveillance, Epidemiology, and Laboratory Services, Centers for Disease Control and Prevention, Atlanta, Georgia (El Bcheraoui); Division of HIV/AIDS Prevention, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, Centers for Disease Control and Prevention, Atlanta, Georgia (El Bcheraoui, Dominguez, Kilmarx); Institute for Health Metrics and Evaluation, University of Washington, Seattle (El Bcheraoui).

**Corresponding Author:** Charbel El Bcheraoui, PhD, Institute for Health Metrics and Evaluation, University of Washington, 2301 Fifth Ave, Ste 600, Seattle, WA 98121 (charbel@uw.edu).

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## Nebulized Hypertonic Saline for Bronchiolitis

**To the Editor** We read with interest the study by Wu et al<sup>1</sup> recently published in *JAMA Pediatrics*, examining the effect of nebulized hypertonic saline vs normal saline administration in infants with bronchiolitis. We commend the authors for undertaking a large randomized clinical trial to complement existing evidence of the decreasing length of stay with hypertonic saline use.<sup>2-5</sup> However, we have concerns regarding the study analysis and interpretation and believe cautious interpretation of the findings is warranted.

While 3447 patients were diagnosed with bronchiolitis during the study period, only 1254 patients were assessed for eligibility. There was no explanation why a large number of patients was not assessed; this may have affected the population studied, potentially skewing the data toward a more mild to moderate spectrum of illness (indicated by the reported pretreatment Respiratory Distress Assessment Instrument scores). The large number of children discharged from the emergency department may also reflect milder disease. Unfortunately, the lack of minimum or maximum severity criteria for study entry and lack of stratification of severity confounds the efficacy of hypertonic saline use in a disease with a known spectrum of severity.

We question the clinical significance of length-of-stay data when measured in days because this is a blunt measure for short admissions. Given that the study was underpowered for this outcome, we suggest using hours instead of days, with a survival analysis to investigate time from emergency department presentation to discharge. The advantage would be the use of data from all randomized patients in the analysis, not only admitted patients, presenting a richer data set with more clinical relevance. Additionally, as the length-of-stay data are not normally distributed, it would have been more informative to report the median and interquartile range rather than mean and standard deviation. We are also concerned that the Respiratory Distress Assessment Instrument score during admission was assessed at daily points only and was not reflective of pretreatment severity or posttreatment outcome. In the relevant analyses, the authors only appear to consider the pre- and postmeasurements of the first treatment.

To conclude, while hypertonic saline use in children with bronchiolitis in the emergency department appears to decrease admission to the hospital, it remains unclear whether this applies to all cases of bronchiolitis, irrespective of severity, given the lack of stratification. As  $\beta$ -agonist and nebulized saline administration are not universal for bronchiolitis in all settings, this would be important information to allow generalizability of findings.

**Victoria Louise Heaton, MBBS**  
**Natalie Boon Lin Tan, MBBS, BSci, LLB**  
**Laura Marco, MBBS**