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REPLY

The thoughtful comments of Drs Hallman, Personen, and Teramo regarding our recently published metaanalysis are appreciated.[1] We are aware of the ongoing interest of these researchers on the adverse effects of antenatal exposure to indomethacin, including an elevated risk for bronchopulmonary dysplasia (BPD).[2]

While attempting to replicate their subgroup analysis of our data, excluding comparison groups not receiving tocolytics, we noted an abstraction error that resulted in an incorrect pooled effect estimate for the BPD outcome. In our report, the data as reported by Van Overmeire et al[3] were transposed inadvertently, resulting in an incorrect pooled relative risk of BPD of 1.12 (95% confidence interval, 0.79−1.59).

We have revised our metaanalysis overall and, in particular, for the BPD outcome, and we conclude that the use of indomethacin as a tocolytic agent is associated not only with an increased risk for severe intraventricular hemorrhage, necrotizing enterocolitis, and periventricular leukomalacia but also for BPD (relative risk, 1.37; 95% confidence interval, 1.19−1.60; Table).

Based on our previous metaanalysis of published randomized trials[4] and our current metaanalysis of observation studies,[1] we fully agree that the use of indomethacin antenatally to prevent preterm birth causes important neonatal adverse effects that, in fact, include an elevated risk of bronchopulmonary dysplasia. ■

TABLE

Risk for bronchopulmonary dysplasia associated with the antenatal maternal exposure to indomethacin (corrected data)

Study	Group (n/N)		Relative risk (95% confidence interval)
	Exposed	Not exposed	
Van Overmeire	18/38	9/38	2.00 (1.03-3.88)
Ojala	3/82	2/94	1.72 (0.29-10.04)
Gerson	3/24	4/33	1.03 (0.25-4.19)
Al-Alaiyan	2/15	4/15	0.50 (0.11-2.33)
Soraisham	61/75	75/148	1.35 (1.16−1.57)
Sood	22/63	106/565	1.86 (1.27−2.72)
Vermillion	19/75	39/150	0.97 (0.61−1.56)
M-H pooled RR			1.37 (1.19−1.59)

Heterogeneity $X^2 = 7.66$ (degrees of freedom = 6; P = 0.264).

RR, relative risk; *CI*, confidence interval; *M-H*, Mantel-Haenszel.

Hammers. Reply. Am J Obstet Gynecol 2015.

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Prenatal aneuploidy screening using cell-free DNA

TO THE EDITORS: We sincerely thank the Society for Maternal-Fetal Medicine Publication Committee for its recent article that addressed noninvasive prenatal testing (NIPT).[1] The document provides invaluable information and guidance for practitioners. A concept that was not addressed was test accuracy, which is itself a discrete measure of screening

test validity. Accuracy is particularly important with regard to NIPT because commercial laboratories that offer these tests often advertise them as ">99% accurate"[2] but provide no further explanation of how this figure is derived or what it means. Test accuracy simply is the fraction of all test results that correctly categorize patients regarding the condition of interest. This measure is expressed as the total of true-positive and true-negative test results divided by the total number of tests performed. For several reasons, accuracy is of limited value in assessing test performance.[3]

In our experience, patients and clinicians commonly and mistakenly interpret the advertised accuracy as representative of the test's positive predictive value. As the committee and we note, the positive predictive value of NIPT results rarely approaches the >99% value advertised for accuracy.[1,4] The positive predictive value, which is calculated as the number of true-positive test results divided by the sum of true-positive and false-positive test results, is quite different from accuracy, although both vary with condition prevalence.[3,4] We therefore suggest that pretest patient counseling directly address the issue of advertised accuracy vs actual positive predictive value. Such proactive discussions hopefully will dispel any misconceptions regarding accuracy and NIPT performance. ■

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REPLY

Thank you for your letter and interest regarding the recent Society for Maternal-Fetal Medicine (SMFM) Consult #36: prenatal aneuploidy screening using cell-free DNA (cfDNA).[1] We wholeheartedly agree that clear and comprehensive information and education are needed regarding the implementation of these tests into clinical practice.

We further agree that test accuracy is a metric of limited clinical value and that positive predictive value is the key to interpretation of post-test risk after cfDNA aneuploidy screening.

To assist providers in counseling their patients, the Perinatal Quality Foundation and the National Society for Genetic Counselors now provide access to an on-line positive predictive value calculator that is available for general use (https://www.perinatalquality.org/Vendors/NSGC/NIPT/).

We hope that such tools will help facilitate improved quality of care with enhanced patient and provider understanding of cfDNA aneuploidy screening performance. ■

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A cautionary note about Monsel's solution

TO THE EDITORS: I read with interest the Expert Review by Miller et al entitled, "Use of Monsel's solution to treat obstetrical hemorrhage: a review and comparison to other topical hemostatic agents."[1] Although the authors cautioned against exposure of the peritoneal cavity to Monsel's solution, I do not feel that they adequately represented the danger. Their reference number 30 (Shuhaiber J et al[2]) is a case report of vaginal packing after cervical cone biopsy with pads soaked with Monsel's solution. In that report, Monsel's solution actually caused a full-thickness necrosis of the uterus and