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Editorial Note: The corresponding author of the original article was not approached for a reply to this letter.

1. Mitchell LE. Folic acid for the prevention of neural tube defects: the US Preventive Services Task Force Statement on Folic Acid Supplementation in the Era of Mandatory Folic Acid Fortification. *JAMA Pediatr.* 2017;171(3):217-218.
2. Heseker HB, Mason JB, Selhub J, Rosenberg IH, Jacques PF. Not all cases of neural-tube defect can be prevented by increasing the intake of folic acid. *Br J Nutr.* 2009;102(2):173-180.
3. U.S. Preventive Services Task Force. Folic acid for the prevention of neural tube defects: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med.* 2009;150(9):626-631.
4. Parr CL, Magnus MC, Karlstad Ø, et al. Maternal folate intake during pregnancy and childhood asthma in a population-based cohort. *Am J Respir Crit Care Med.* 2017;195(2):221-228

Proposed Definition of Necrotizing Enterocolitis May Be of Limited Value

To the Editor Battersby et al¹ report on the development and diagnostic performance of a new gestational age-specific case definition for necrotizing enterocolitis (NEC) and claim to compare its diagnostic performance with that of the Vermont Oxford Network (VON) definition. Unfortunately, they did not use the complete VON definition, leading to incorrect estimates of its performance.

The VON definition provides 3 options for identifying infants with NEC: (1) inspection during surgery, (2) inspection at post mortem, or (3) using standardized clinical and radiographic criteria (VON Manual of Operations, <http://www.vtoxford.org>). The authors based their assessment only on the third component of the VON definition, ignoring that cases could also be identified at surgery or post mortem, thus substantially underestimating the sensitivity, specificity, positive predictive value, and area under the receiver operating curve and overestimating the misclassification rate of the VON definition.

However, even had the authors used the correct VON definition, we have concerns about their methods that call into question the estimates of diagnostic test performance from their study population.

First, large proportions of infants are excluded: 67.5% of infants admitted to participating units (8019 of 11885) and 41.4% of infants with abdominal radiographs (2728 of 6594). These high proportions raise serious questions about the generalizability of the study findings. Among the exclusions were infants with probable NEC, missing diagnoses, and inconsistencies during cross validation. These exclusions may have resulted in cases with specific clinical or radiographic findings required for the diagnosis of NEC being preferentially omitted, and the reported estimates of sensitivity and specificity may thus not apply beyond the study

population. Furthermore, in the study population, the prevalence of NEC was 23%, which is nearly 5 times higher than in other populations.² Because positive predictive value depends on disease prevalence, the reported positive predictive value will not apply to populations with lower NEC rates.

Second, the gold standard used for the diagnosis of NEC is poorly defined. For the 3435 infants who did not have surgery, NEC was determined when the clinician considered the diagnosis as “unequivocally yes or no.” The criteria for an “unequivocal” diagnosis are not stated, and data on interrater reliability are not provided. Without a reliable gold standard, the estimates of diagnostic performance presented are of limited value.

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1. Battersby C, Longford N, Costeloe K, Modi N; UK Neonatal Collaborative Necrotising Enterocolitis Study Group. Development of a gestational age-specific case definition for neonatal necrotizing enterocolitis. *JAMA Pediatr.* 2017;171(3):256-263.
2. Horbar JD, Edwards EM, Greenberg LT, et al. Variation in performance of neonatal intensive care units in the United States. *JAMA Pediatr.* 2017;171(3):e164396.

In Reply We thank Horbar and colleagues for their interest in our article¹ and appreciate this opportunity to clarify the points raised. We based our assessment on the Vermont Oxford Network criterion 3 alone (standardized clinical and radiographic findings)² because our aim was to develop a case definition for necrotizing enterocolitis suitable for population surveillance using clinical and radiological findings likely to be available across a range of clinical settings. Thus, VON criteria 1 (findings at surgery) and 2 (findings at post mortem) are outcomes in our study.

We excluded infants if their radiographs were not performed for abdominal concerns but for other unrelated reasons (eg, for central catheter positioning); this made up most exclusions, with only a few additionally excluded because a final diagnosis was not available. These exclusions are appropriate because we were deliberately selecting a population of infants in whom there was some clinical concern around the possibility of necrotizing enterocolitis. This does not introduce a bias in the comparison of

our case definition with that of VON because the assessment was made on the same set of infants.

The prevalence figure of 23% in the study population relates to the infants in whom there was clinical suspicion of necrotizing enterocolitis; therefore, this rate cannot be compared with that in other unselected general populations where it will be much lower.

We acknowledged and discussed the limitation imposed by using clinical judgement as the “gold standard.” However, we pointed out that this is a reasonable, valid approach in the absence of a reliable diagnostic biomarker.

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1. Battersby C, Longford N, Costeloe K, Modi N; UK Neonatal Collaborative Necrotising Enterocolitis Study Group. Development of a gestational age-specific case definition for neonatal necrotizing enterocolitis. *JAMA Pediatr.* 2017;171(3):256-263.
2. VON Manual of Operations. <http://www.vtoxford.org>. Accessed March 23, 2017.

CORRECTION

Error in Sensitivity and Specificity Estimates: In the Original Investigation titled “Development of a Gestational Age-Specific Case Definition for Neonatal Necrotizing Enterocolitis,”¹ published online January 3, 2017, and in the March 2017 issue of *JAMA Pediatrics*, there was an error in the sensitivity and specificity estimates in the Results section of the Abstract, the Results section of the text, and the Supplement. In the Abstract, the sentence should read, “The case definition has a sensitivity of 63.9% (95% CI, 60.6-67.0), a specificity of 96.8% (95% CI, 96.1-97.4)...” In the text, the sentence should read, “Applying this to the entire data set yielded a sensitivity of 63.9% (95% CI, 60.6-67.0), a specificity of 96.8% (95% CI, 96.1-97.4)...” In the Supplement, the third row of the eTable should read “63.9 (60.6-67.0)” and “96.8 (96.1-97.4)” under the Sensitivity and Specificity columns, respectively. Importantly, this error did not affect the conclusions of the study.² This article was corrected online.

1. Battersby C, Longford N, Costeloe K, Modi N; UK Neonatal Collaborative Necrotising Enterocolitis Study Group. Development of a gestational age-specific case definition for neonatal necrotizing enterocolitis. *JAMA Pediatr.* 2017;171(3):256-263.
2. Horbar JD, Soll RF, Edwards EM. Proposed definition of necrotizing enterocolitis may be of limited value [published online May 1, 2017]. *JAMA Pediatr.* doi:[10.1001/jamapediatrics.2017.0974](https://doi.org/10.1001/jamapediatrics.2017.0974)

Error in Abstract: In the Special Communication titled “Implementation of an Integrated Approach to the National HIV/AIDS Strategy for Improving Human Immunodeficiency Virus Care for Youths,”¹ published online May 22, 2017, there was an error in the Abstract. The Main Outcomes and Measures portion of the Abstract should read “Cross-agency collaboration, youth-friendly linkage to care services, community mobilization to address structural barriers to care, cooperation among services, proportion of all men who have sex with men who tested, and rates of linkage to prevention services.” This article was corrected online.

1. Fortenberry JD, Koenig LJ, Kapogiannis BG, Jeffries CL, Ellen JM, Wilson CM. Implementation of an integrated approach to the national HIV/AIDS strategy for improving human immunodeficiency virus care for youths [published online May 22, 2017]. *JAMA Pediatr.* doi:[10.1001/jamapediatrics.2017.0454](https://doi.org/10.1001/jamapediatrics.2017.0454)