respiratory failure and parenchymal lung disease. Few clinicians would question the fact that an infant who requires 50% oxygen has worse lung function than one who is receiving 25% oxygen to maintain normal arterial oxygenation. Before concluding that the need for oxygen at 36 weeks postmenstrual age is not informative about the severity of lung disease or long-term morbidities, we need to thoroughly evaluate the association between different fractions of inspired oxygen and long-term respiratory or neurologic outcomes while adjusting for other confounding factors.

Another limitation of the proposed definition is that it is based on a one-time assessment. In this situation, a preterm infant who exhibits acute respiratory deterioration at approximately 36 weeks and needs mechanical ventilation would be labeled as having severe BPD even if his or her lungs were normal. This limitation can be easily avoided by including an indicator of the chronicity of the parenchymal lung disease. Although the proposed definition may work in a large population base and predict long-term outcomes, it will not always reflect the severity of lung disease and therefore will not be appropriate for research or benchmarking focused on pulmonary outcomes.

Although most clinicians would agree that more contemporary definitions of BPD are necessary, these definitions must be based on the premise that BPD is secondary to chronic parenchymal lung disease. Therefore, any definition of BPD, whether based on diagnostic or therapeutic criteria, should reflect the severity of lung disease and exclude nonpulmonary indications for respiratory support. The proposed definition, though marginally better at predicting outcomes, will not consistently meet the challenge of defining BPD. ■

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Need for an International Consensus on the Definition of Bronchopulmonary Dysplasia

To the Editor:

The definition and diagnosis of bronchopulmonary dysplasia (BPD) are widely debated topics in neonatology (1). The half-century-long history of different definitions highlights the changing paradigm for managing pulmonary immaturity (2). Jensen and colleagues compared 18 BPD definitions based on levels of supplemental oxygen and respiratory support provided at 36 weeks postmenstrual age (PMA) (3). They reported categorizations of BPD severity that predicted serious respiratory morbidities or mortality at 18–26 months corrected age. This study is a useful addition to the literature; however, it inherently accepts a fundamental misconception that 36 weeks PMA is somehow a "magic" postnatal age when preterm infants are mature enough to be off respiratory support. There is no physiological or clinical basis for using 36 weeks PMA as a cutoff.

The authors assessed various categorizations of BPD severity only at 36 weeks PMA and did not consider other PMA timings because of data limitations. It is well known that BPD at 36 weeks PMA is not a robust marker for predicting long-term outcomes (1). Physiological and developmental considerations have led investigators to suggest using a PMA closer to the expected due date, because even late-preterm and early-term infants of 34–38 weeks gestation have a higher risk of developing respiratory issues than infants of 39–41 weeks gestation (4). Although using a later PMA may increase missed assessments due to transfer of infants to step-down units or discharge home before assessment, obtaining such information from step-down units or families is not impossible. Shennan and colleagues chose 36 weeks PMA as a cutoff for BPD based on a compromise between sensitivity and specificity; however, in the 30 years since their work was published, there have been marked changes in the relevant population (with gestational ages as low as 22 wk), approaches, and technology available to provide respiratory support (both invasive and noninvasive) (5). Thus, applying a cutoff without any physiological basis seems to represent a halt in progress. Moreover, the first 12 BPD definitions assessed by Jensen and colleagues had similar predictive abilities, with a difference in area-under-the-curve values of 0.01. A recent study reported that the ability to predict long-term respiratory morbidities improved as the timing to define or diagnose BPD increased from 36 to 40 weeks PMA, indicating that 40 weeks PMA is the best time for

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predicting respiratory outcomes (1, 6). Evaluation of the data from Jensen and colleagues may provide supporting or refuting evidence for this maturational cutoff for defining BPD.

We agree that our goal should be to adopt an evidence-informed or data-driven approach to identify neonates of extremely low gestational age with a future risk of developing pulmonary and neurodevelopmental issues. The critical task for members of the neonatal community is to decide what we aim to achieve in defining BPD. Do we want to identify nearly all children who may develop adverse outcomes (minimum false negatives), do we want to rule out all who may not develop adverse outcomes (minimum false positives), or do we want to settle for a compromise and accept a middle ground? The answer may require careful thinking. We may want to use criteria with minimum false negatives when identifying children for closer surveillance during childhood, to predict and manage respiratory adverse outcomes; use criteria with minimum false positives when testing experimental therapies, to rationalize exposure for many children; and use "compromise" criteria (with acceptable sensitivity and specificity cutoffs) for quality improvement initiatives, benchmarking, and assessing trends. Discussions about these issues need to happen through an international forum and consensus process, as is currently underway via the International Neonatal Consortium (1). Purpose-defined BPD criteria derived from an international consensus process and supported by data are essential for avoiding ongoing confusion and inconsistency. ■

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Reply to Bancalari *et al*. and to Isayama and Shah

From the Authors:

Much of the recent debate on how to define bronchopulmonary dysplasia (BPD) has focused on identifying diagnostic criteria that adequately predict meaningful childhood outcomes (1). The goal of our study group was to help inform this debate by providing an evidence-based definition of BPD that was chosen according to the ability to predict respiratory and neurodevelopmental outcomes at 18–26 months corrected age (2). In a contemporary, multicenter cohort of very preterm infants, we found that stratification of disease severity based on the mode of respiratory support administered at 36 weeks postmenstrual age (PMA), irrespective of current or prior exposure to supplemental oxygen, discriminated best between infants with and without adverse early childhood outcomes (2).

In separate letters, Bancalari and colleagues and Isayama and Shah stress that choosing contemporary diagnostic criteria for BPD will require compromise. We agree that a single definition of BPD is unlikely to serve all purposes. For example, the clinical and diagnostic information required to establish the underlying respiratory pathophysiology may differ from that used to predict the presence or absence of future respiratory morbidity. Nevertheless, we believe that our study provides valuable information on how best to define BPD in the current era.

To our knowledge, there are no widely available, uniformly applied, validated diagnostic tests that can precisely characterize the etiology of respiratory failure in preterm infants. Therefore, all commonly used definitions of BPD invoke clinical respiratory support—treatment with supplemental oxygen and, in some cases, the mode of respiratory support—as proxy measures of the underlying respiratory illness (3). Bancalari and colleagues write that "inspired oxygen is the simplest and most sensitive indicator of the severity of respiratory failure and parenchymal lung disease." However, heterogeneity in oxygen administration is a noted limitation of the existing diagnostic criteria for BPD (1). Moreover, supplemental oxygen is used to treat multiple cardiopulmonary diseases in preterm infants, including apnea, pneumonia, pulmonary hypoplasia, and pulmonary arterial hypertension.

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