Do We Need Another Set of Growth Charts for Premature Infants?

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Growth charts are an essential part of neonatal care. Plotting infant data on growth charts at birth and postnatally over time allows us to assess the quantity and quality of growth compared with a reference we want to call "normal."[1,2] Assessing the degree to which weight, length, head circumference, and BMI are abnormal at birth and monitoring how an infant is growing compared with normal allows clinicians to assess health and risk for future morbidity.[1–9] Growth charts are used to inform nutritional support and medical care. Clinicians often do not rigorously consider how these curves were created, smoothed, and/or validated.[2] Every reported "standard/reference" growth curve has been challenged.[2,8,10–13] In this issue of *Pediatrics*, new weight and head circumference growth charts for infants born between 22 and 29 weeks' gestational age (GA) from Boghossian et al[14] aim to provide us with better standards.

Premature infants are not normal. Factors that lead to premature delivery affect fetal growth (maternal smoking, hypertension, preeclampsia, diabetes, and repeated courses of antenatal steroids).[15,16] Percentile graphs on any set of growth curves are influenced by how thoroughly infants with abnormal growth due to maternal illness/practices are excluded.[17,18] Meaningful assignment of poor and excessive growth requires the following: accurate knowledge of GA; accurate measurement of weight, length, and head circumference; and cutoff values based on reference data from a relevant population.[19] Measurement of these factors is challenging. Estimation of GA is often not precise. Although weights according to electronic balances are accurate, individual head and length measurements are less reliable. Growth charts differ in many ways, including sample selection, how GA is defined (eg, completed or midweeks), combined or sex-specific charts,[12,20] and combined or race/ethnicity-specific charts.[21] The chart we choose as a reference thus affects our assessment.[2]

Anthropometric measurements are not categorical; they are numeric. Assignment of "small for GA," "appropriate for GA," and "large for GA" change continuous variables (weight, length, and head circumference) into categorical variables. Assigning a percentile to an anthropometric measurement allows clinicians to consider the rarity of the individual assessment; it does not quantify how different the individual is from the relevant population norm. For infants born before 25 weeks, each additional day of gestation[22] and each increase in birth weight by 100 g increases the likelihood of survival.[23] Quantitating the degree of abnormal growth (too much or too little) by using a *z* score provides more information than assigning a percentile (or category).[2]

The question remains: should we adopt and add a new set of growth charts to the expanding number of charts being used? The absolute differences between the new charts[14] and the charts of Olsen et al[20] are small: median of 43 g in weight (5% absolute error rate) and 0.5 cm in head circumference (2% absolute error rate) for sex- and GA-specific

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TABLE 1 GA-Specific Percent of African American Infants

Source	GA										
	22	23	24	25	26	27	28	29	30	31	32
Centers for Disease Control and Prevention	38%	37%	36%	34%	33%	31%	29%	29%	26%	24%	23%
Pediatrix Clinical Data Warehouse	36%	34%	31%	30%	28%	26%	25%	24%	21%	20%	19%

GA based on obstetric/clinical estimate (http://wonder.cdc.gov/natality.html, accessed September 5, 2016).

differences. The uniformity of the differences across all GAs would suggest that the data of Boghossian et al[14] include smaller infants and that there is a systematic difference in how the 2 sets of charts were created. Boghossian et al defined GA as number of days, not as completed weeks of gestation. Rochow et al[19] showed that plotting weekly birth weight percentiles at the start of the completed week of gestation (the approach of Olsen et al) resulted in a leftward shift of percentile charts similar to what is presented. The data of Boghossian et al[14] are more contemporary, and mortality in premature infants has decreased.[24] This scenario would favor a selection of smaller infants into the data used to produce the charts.

Selection bias in the most immature infants is a problem for all charts derived from NICU admissions. The proportion of infants offered care increases from 22% to 99% for infants born at 22 versus 26 weeks' GA.[22] Mortality in infants born at 22 to 24 weeks' GA is high.[25] Growth charts based on a selected population (admitted to the NICU and survived)[14,20] are biased. The sample sizes at 22 and 23 weeks' GA are relatively small compared with more mature infants. The impact of this selection bias on mathematical modeling is hard to determine without comparison with an unselected cohort of infants that includes all births.

The concept of relevant population is important. African American infants are overrepresented at lower GAs (Table 1). As Boghossian et al[14] suggest, until we better define relevant population samples, we will misassign risk based on *z* scores and percentiles for African American infants.[14,26] Birth weight distributions specific for GA, sex, race/ethnicity, and region are better at identifying the infants at higher risk for neonatal morbidity.[11,21,27–29]

We applaud the important observations made by Boghossian et al[14] and agree with the authors that clinicians tasked with assessing the nutrition, growth, and well-being of a fetus, a newly born infant, or the growth of a premature infant in the NICU need tools that correct for differences in sex, race/ethnicity, heritage, and genetics. We fear we still lack the perfect set of tools.

ABBREVIATION

GA: gestational age

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