Monitoring the Postnatal Growth of Preterm Infants: A Paradigm Change

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There is no consensus regarding how the growth of preterm infants should be monitored or what constitutes their ideal pattern of growth, especially after term-corrected age. The concept that the growth of preterm infants should match that of healthy fetuses is not substantiated by data and, in practice, is seldom attained, particularly for very preterm infants. Hence, by hospital discharge, many preterm infants are classified as postnatal growth–restricted. In a recent systematic review, 61 longitudinal reference charts were identified, most with considerable limitations in the quality of gestational age estimation, anthropometric measures, feeding regimens, and how morbidities were described. We suggest that the correct comparator for assessing the growth of preterm infants, especially those who are moderately or late preterm, is a cohort of preterm newborns (not fetuses or term infants) with an uncomplicated intrauterine life and low neonatal and infant morbidity. Such growth monitoring should be comprehensive, as recommended for term infants, and should include assessments of postnatal length, head circumference, weight/length ratio, and, if possible, fat and fat-free mass. Preterm postnatal growth standards meeting these criteria are now available and may be used to assess preterm infants until 64 weeks' postmenstrual age (6 months' corrected age), the time at which they overlap, without the need for any adjustment, with the World Health Organization Child Growth Standards for term newborns. Despite remaining nutritional gaps, 90% of preterm newborns (ie, moderate to late preterm infants) can be monitored by using the International Fetal and Newborn Growth Consortium for the 21st Century Preterm Postnatal Growth Standards from birth until life at home.

abstract

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The nutritional care for preterm newborns remains a challenge in clinical practice. Despite international feeding guidelines in which it is recognized that human milk is the best source of nutrition for preterm infants,[1] their implementation varies widely even for those born at 33 to <37 weeks' gestation,[2] who constitute 8% to 9% of all births, represent the vast majority of preterm infants,[3] and remain at higher risk than their term counterparts.

In addition, there is no international consensus regarding how the growth of preterm infants should be monitored or what constitutes the ideal pattern of growth, including the period after they have reached term. This situation is even more unclear for those born very preterm (ie, <32 weeks' gestation),[4,5] who are at the highest risk but only represent 10% of all preterm births.[3]

Given the complexity of the subject and its clinical, sociocultural, and economic

importance, we would like to present a new approach for monitoring the postnatal growth of preterm infants. This is based on the use of international growth standards, specific for preterm infants[6] and is constructed on the basis of the following:

1. the World Health Organization (WHO) prescriptive approach to monitoring human growth so as to match the WHO Child Growth Standards for term infants[7,8];
2. the data derived from preterm infants in a longitudinal study from early pregnancy to 2 years of age, who were selected because they were at low risk of adverse clinical outcomes and had no evidence of intrauterine growth restriction, as assessed by serial ultrasound scans; and
3. well-accepted recommendations for feeding preterm infants by using human milk.

Here we present the evidence supporting our proposition.

SHOULD PRETERM INFANTS GROW LIKE FETUSES?

The idea that the growth of preterm infants should match the growth of healthy fetuses is not substantiated by data and, even more relevant, in practice is seldom attained, especially for very preterm infants.[9] This strategy, largely accepted,[4,10] is based on the American Academy of Pediatrics' (AAP) 1977 general statement that the growth of preterm infants should follow that of the normal human fetus,[11] although weight gain is typically measured rather than overall growth anthropometric measures in clinical practice. With comparisons of the postnatal growth of very preterm infants with size-at-birth reference charts by gestational age, the neonatal community was alerted years ago that most of these infants will not reach the median weight of the reference fetus by hospital discharge and that many will be classified as extrauterine growth–restricted infants.[12]

The AAP statement is focused only on the early postnatal period up to term-corrected age (ie, 40 postmenstrual weeks), which is a major limitation and does not relate to subsequent postnatal growth, a crucial period for the health and nutritional status of preterm infants. It has been suggested that the AAP recommendation is indirectly supported by studies revealing an association for very preterm infants between rapid growth during the first postnatal weeks and neurocognitive benefits later in life. The authors of these reports, however, do not equate such rapid growth with "growing like a fetus" because these infants never reach the same growth patterns as fetuses.

Of concern is the limited high-quality data for recommending the optimal macronutrient intake for preterm infants. The authors of a systematic review demonstrated that most of the evidence in favor of "enhanced nutrition" for preterm infants is derived from observational studies,[13] with only 1 intervention trial showing an association between increased feeding and improved cognition, albeit solely in boys.[14] The qualitative heterogeneity of these results requires further analysis, but it is possible that the differences could be caused by residual confounding effects from variables independently affecting both infant growth and cognition that were not fully adjusted for in the analyses of observational studies.[15]

Hence, confirmation of a link between faster postnatal growth and childhood outcomes is still required. Interestingly, recent observational data suggest that very preterm infants, despite having lower weight gain when fully breastfed, experience a reduced risk of severe neonatal complications after adjusting for potential confounding factors.[16]

There are other aspects to consider when attempting to force preterm infants to gain weight as if they were still in utero. Firstly, most are unable to follow the weight recommendation; the authors of a study of the growth of infants <1500 g in US NICUs from the Vermont Network concluded that, despite receiving high-quality care, half were classified with "postnatal growth failure" or "severe growth failure," defined, respectively, as weights on hospital discharge below the 10th or third centile of a birth weight chart.[4]

Second, very preterm infants fed on human milk have accelerated head circumference growth from birth until discharge, even during periods of poor postnatal weight gain.[17] A third important consideration is that infants who experience accelerated growth early in life may have increased fat accretion and be at higher risk of metabolic and cardiovascular problems later in life. However, as is the case with the neurocognitive data, most of the evidence for increased risk is derived from observational studies, in which there is rarely adjustment for adult body size at the time of the evaluation.[13]

Therefore, the available evidence does not indicate that the postnatal growth of preterm infants should match that of fetuses up to 40 postmenstrual weeks.[18] The nutrition recommendations and growth monitoring strategies for preterm infants are even less clear because the focus in the literature has mainly been on the nutrition of very preterm infants. However, a preterm infant is not, in any nutritional, metabolic, or physiologic sense, a fetus and should not be managed as such in clinical practice.

REFERENCES VERSUS STANDARDS: 2 DIFFERENT TOOLS TO MONITOR GROWTH OF PRETERM INFANTS

References and standards are different entities and have different objectives, applications, and interpretations.[10] References, often based on data routinely collected decades earlier with limited or no standardization and quality control of the measures, are descriptive tools; they are used to describe how subjects have grown at a particular time and place. Conversely, prescriptive standards, with rigorous anthropometric measures collected prospectively, are used to define how subjects should grow under optimal conditions, according to, in the case of preterm infants, their clinical status and degree of maturation.[19,20] This prescriptive strategy for monitoring human growth has been recommended by WHO since 1995 and was used to guide the construction of the WHO Child Growth Standards that are now used globally.[7] Interestingly, by recommending that "the growth of preterm infants should follow that of the normal human fetus,"[11] the AAP is implicitly recognizing the need for a standard and not a reference. We fully agree with this concept, but the appropriate subjects are not fetuses.

Throughout the literature, it is stated that standards cannot be produced for preterm infants because infants born preterm are neither normal nor healthy. However, we believe it is possible to produce standards based on a subpopulation of preterm infants who have accurate gestational ages at birth, are born to healthy mothers with uncomplicated pregnancies (ie, no obvious maternal, placental, or fetal cause for the preterm birth), and have no congenital abnormalities or evidence of fetal growth restriction on ultrasound.

These infants are immature, with clinical complications arising from their prematurity, but they are as normal or healthy as they can be for their postmenstrual age–specific level of organ and physiologic maturation.[20] They have more in common physiologically and metabolically with the total preterm population than fetuses who remained in utero, and with advancing postmenstrual age, the frequency and severity of the associated complications fall. This preterm newborn subpopulation, which we estimate represents close to 30% of all preterm newborns with a neonatal mortality as low as 5 per 1000 at hospital discharge,[3] is precisely the prescriptive population used to construct the international postnatal growth standards, specific to preterm infants. They represent the best available approximation to the prescriptive growth of preterm infants, although their limitations, especially for very preterm infants, are acknowledged.[6,20]

Standards are universal and independent of time and place. Thus, they are not intended to be representative of a given population or region and can be used to assess all fetuses and newborns, irrespective of their ancestral background, socioeconomic status, and level of health care provision. These characteristics are crucial in the 21st century, considering the extent of ancestral admixture, migration, refugee crises, and global economic growth. Hence, standards are ideal tools for harmonizing research protocols, systematic reviews and meta-analyses, and international comparisons of nutritional status.

A graphic demonstration of the universality of prescriptive standards is the exact convergence at term (the point of overlap) of the International Fetal and Newborn Growth Consortium for the 21st Century (INTERGROWTH-21st) Newborn Size at Birth Standards[21] and WHO Child Growth Standards (Fig 1).[22] Specifically, for term infants (ie, the gestational age at which both studies overlapped), the mean (SD) birth weight of newborns >37 weeks' gestation was 3.3 (0.5) kg in the INTERGROWTH-21st study population and 3.3 (0.5) kg in the WHO Multicentre Growth Reference Study. The mean (SD) length and head circumference at birth were 49.3 (1.8) cm and 33.9 (1.3) cm in the INTERGROWTH-21st study population and 49.5 (1.9) cm and 34.2 (1.3) cm in the Multicentre Growth Reference Study population. In these 2 projects, data were collected a decade apart in different countries,[23] but the authors of both studies used a population-based design, recruited healthy populations, and used the same entry criteria at both the population and individual levels, as well as using the same equipment, data collection methods, and standardization procedures.

The biological relevance of the exact agreement between the newborn and infant standards shown in Fig 1 should not be underestimated. A similar previous exercise did not yield such results because the populations included were not selected by using the WHO criteria for producing prescriptive standards.[24] In fact, the agreement was poor in the meta-analysis of 5 published weight-for-gestational-age reference charts at 40 weeks' gestation, when compared with the WHO Child Growth Standards; the resulting centiles for weight at term-corrected age were considerably higher than the WHO estimates. To harmonize the charts, the investigators were forced to "interpolate smooth values," and "extra points were manually selected at 40, 43 and 46 weeks," assuming that the growth of preterm infants followed "approximately a straight line." The slope of the centiles was then determined by fitting the WHO values at 50 weeks' postmenstrual age (ie, the gap between 36 and 50 weeks is an extrapolation).[24] Acknowledging these limitations,

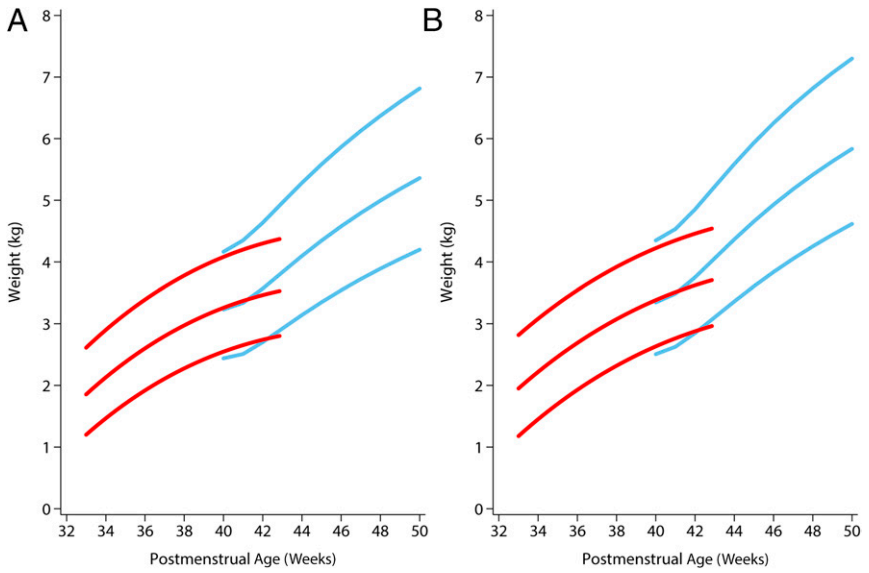

FIGURE 1

Third, 50th, and 97th centiles for birth weight by gestational age from the INTERGROWTH-21st Newborn Size Standards (red lines), followed by the corresponding third, 50th, and 97th centiles from the WHO Child Growth Standards (light blue lines) for term newborn infants (40 weeks' gestation). A, Girls. B, Boys. Modified from Villar et al.[23]

the authors stated that "the INTERGROWTH-21st study, currently underway, will rectify this problem, because their purpose is to develop prescriptive standards for fetal and preterm growth."[24]

LIMITATIONS OF CURRENT STRATEGIES

We have recently published the first systematic review of the methodological quality of such tools. We identified 61 longitudinal references (no standards were available), most of which had considerable limitations in terms of the quality of gestational age estimation, standardization of anthropometric measures, feeding regimens, and how morbidities were described. Some study authors concentrated only on subpopulations of very preterm infants or limited the follow-up to term, and only 1 of the 61 publications had a score >66% in the quality evaluation.[25]

There is also confusion between the assessment of size at birth and the postnatal growth of preterm infants. Whether standards or references are used, the former is a measure at a single time point, taken immediately after birth, which reflects the infant's growth before birth; it is a summary measure of the fetus' attained size. Conversely, the latter involves repeated measures taken prospectively to evaluate the health and nutritional status of the infant at various times after birth: infant growth. The 2 are distinct biological entities, that is, a static evaluation at the end of intrauterine growth versus an evaluation over time of postnatal growth, with different aims, timings, and assessment methods. Clearly, therefore, different clinical tools should be used for each of these entities.

One approach could be to monitor the postnatal growth of preterm infants up to term, by using ultrasound-derived fetal growth standards, again based on the unproven concept that preterm infants should grow as fetuses. Such standards are now available for head and abdominal circumference, as well as for estimated fetal weight.[26,27] To illustrate the problems with this strategy, in Fig 2 we present the comparison, at the same postmenstrual age, between the INTERGROWTH-21st Estimated Fetal Weight Standards[27] and the INTERGROWTH-21st Preterm Postnatal Growth Standards (for weight, with both sexes combined), both based on the same cohort of pregnant women.[6] It should be recognized, however, that ultrasound examination of the fetus does not provide length measures, an important component of postnatal growth assessment.

The patterns of growth are clearly different, because how weight is acquired in and ex utero is based on different biological processes and influenced by separate environmental and nutritional constraints. Importantly, the largest difference between the curves is seen at <34 weeks' gestation and is even more evident at <30 weeks' gestation, which are the gestational age windows of greatest concern to neonatologists. This is also to be expected because most preterm newborns at <30 weeks' gestation cannot be compared with the large number of fetuses remaining in utero under healthy conditions. Thus, it is highly unlikely that very preterm newborns, even if overfed, will on average ever reach the weight attained by the growing fetus (Fig 2).

Another option is the use of cross-sectional, size-at-birth-by-gestational-age charts, as a proxy for fetal growth.[19] This strategy has 2 principal problems: (1) the inappropriate use of cross-sectional data at birth to monitor growth after birth as discussed above and (2) the assumption that healthy fetal size is the goal for preterm postnatal growth. Consequently, the INTERGROWTH-21st Newborn Size at Birth Standards[21] and the Very Preterm Size at Birth References,[28] as well as any single site reference or meta-analysis of size at birth,[29] are all unsuitable for measuring the postnatal growth of preterm infants.

In Fig 3, we demonstrate that the patterns of size at birth across the range of gestational ages are different and that centiles are always higher (with larger differences at lower gestational ages) than the postnatal growth of preterm infants taken from the same underlying population. To reach such postnatal weights in a few weeks after birth requires considerable nutritional effort for preterm infants adapting metabolically to a new environment.

Similarly, comparing the meta-analysis of size-at-birth charts[24] with the INTERGROWTH-21st Preterm Postnatal Growth Standards[6] reveals the nutritional effort involved in pushing very preterm infants to gain weight as fetuses until 40 postmenstrual weeks. As a result, many will become either overweight for their length or will be incorrectly classified as extrauterine growth–restricted (Fig 4).

It was recently recognized that fetal growth as the recommended target "is not met by the majority of preterm babies."[10] Furthermore, large improvements in the survival of very preterm infants have been made in the past decades without these infants attaining the postnatal fetal growth rates proposed.[20] Why then is a nutritional goal recommended that is neither evidence-based nor achieved by most preterm infants?

The issues being discussed here have major clinical implications. The use of size-at-birth charts inevitably leads to an overdiagnosis of extrauterine growth restriction affecting a large proportion of all preterm infants and almost all of the very preterm ones[4] when they reach term-corrected age, even if they have experienced some catch-up growth. This means that, in addition to the morbidities associated with their immaturity, preterm infants may acquire an iatrogenic health problem for which treatment, that is, nutritional support, is needed. Interestingly, when such extrauterine growth restriction is treated, preterm infants reaching term-corrected age remain underweight but with proportionally more fat than fat-free mass compared with term newborns.[30,31] This disproportionate tissue distribution could be in the

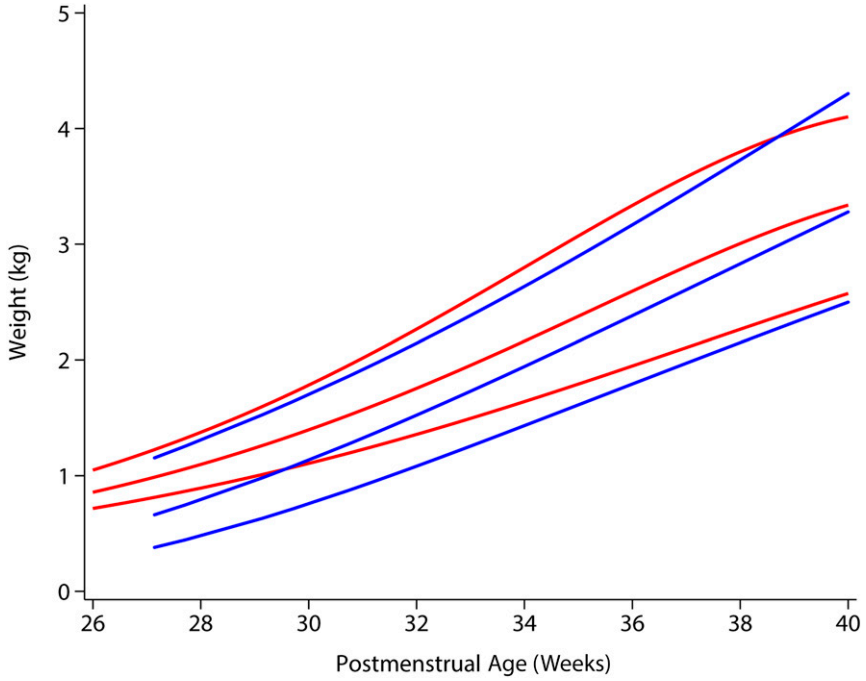

FIGURE 2
Comparison of third, 50th, and 97th centiles of the INTERGROWTH-21st Preterm Postnatal Weight Standards for both sexes combined (blue lines) with the INTERGROWTH-21st Estimated Fetal Weight by Ultrasound Standards for both sexes combined (red lines).

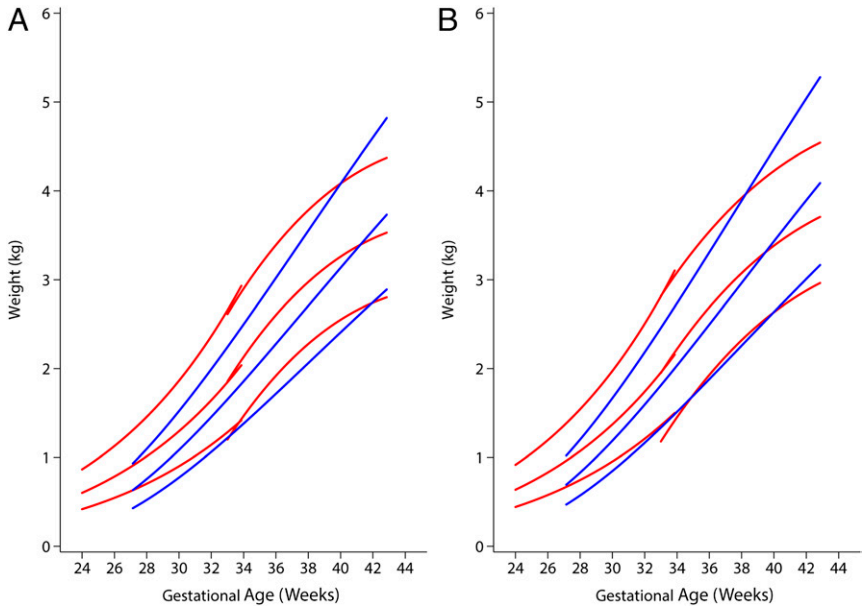

FIGURE 3
Comparison of third, 50th, and 97th centiles of the INTERGROWTH-21st Preterm Postnatal Weight Standards (blue lines) with birth weight by gestational age from the INTERGROWTH-21st Very Preterm Size at Birth Reference charts (24–32 weeks' gestation) (red lines), followed by birth weight by gestational age from the INTERGROWTH-21st Newborn Size Standards (33–43 weeks' gestation) (red lines). A, Girls. B, Boys.

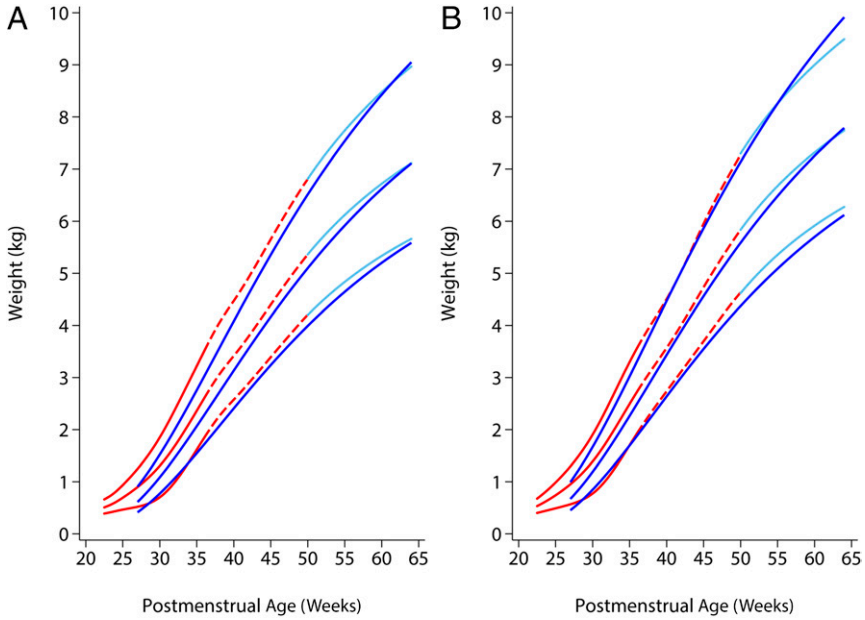

FIGURE 4

Comparison of third, 50th, and 97th centiles of the INTERGROWTH-21st Preterm Postnatal Weight Standards (solid blue lines) with Fenton and Kim's[24] 2013 meta-analysis of 6 published charts (solid red lines), followed by the extrapolated lines (dashed red lines) and the WHO Child Growth Standards (solid light blue lines) after 50 weeks' postmenstrual age. A, Girls. B, Boys. The dashed red lines in the Fenton charts correspond to the gestational ages at which the charts were extrapolated, from 36 weeks' gestation to join the WHO values at 50 weeks' postmenstrual age.

pathway of the relationship between preterm birth and the greater risk of chronic disease.[32]

PRETERM POSTNATAL GROWTH STANDARDS

Recognizing the limitations described above, INTERGROWTH-21st has produced prospective, longitudinal, prescriptive, postnatal growth standards specifically for preterm infants from 27 weeks' gestation. Infants included in these standards were born to healthy mothers with well-dated pregnancies (rather than based on birth weight) and no evidence of intrauterine growth restriction assessed by serial ultrasound scans from <14 weeks' gestation.[6]

This unique cohort of preterm infants, who received up-to-date medical and feeding counseling, were followed up by using rigorous, standardized methodology for anthropometric measurement and assessment of health, food patterns, motor development, and neurodevelopment until 2 years of age. The results of this follow-up study reveal that, at the critical 2-year milestone, the growth of the infants that contributed to the INTERGROWTH-21st Preterm Postnatal Growth Standards was similar to that of the WHO Child Growth Standards. The median for length and head circumference was at the 47th centile of the WHO Child Growth Standards; for weight, the median was at the 53rd centile. The corrected postnatal ages at which the WHO milestones for gross motor development were achieved by these preterm infants overlapped well with the third, 50th, and 97th centiles of the WHO range for healthy term infants.[33]

Hence, we suggest that the correct comparator for assessing the growth of preterm infants is a cohort of preterm newborns who experienced an uncomplicated intrauterine life and infancy. The INTERGROWTH-21st Preterm Postnatal Growth Standards, which meet these criteria, have been recommended by WHO[34] and the Centers for Disease Control and Prevention[35] in the context of the recent Zika virus outbreak. These standards can be used to assess preterm infants until 64 weeks' postmenstrual age (6 months' corrected age), the time at which they overlap, without the need for any adjustment, with the WHO Child Growth Standards for term newborns.[6]

The INTERGROWTH-21st Preterm Postnatal Growth Standards are the first available standards specifically constructed for monitoring the postnatal growth of preterm infants with data to evaluate outcomes at 2 years of age. Centiles for weight, length, and head circumference, with corresponding *z* scores, are available in paper, Web-based, and smartphone formats for the follow-up of preterm infants from hospital care to outpatient clinics and family care.[36] These standards are, as expected, different from the UK-WHO, Fenton meta-analysis of size-at-birth charts and the INTERGROWTH-21st Newborn Size at Birth Standards but complement the WHO Child Growth Standards for term infants, which are their natural counterpart.

The INTERGROWTH-21st Preterm Postnatal Growth Standards comply with the Standardized Reporting of Neonatal Nutrition and Growth checklist[19]: (1) well-monitored pregnancies without ultrasound evidence of fetal growth restriction; (2) reliable estimation of gestational age; (3) preterm infants (<37 weeks' gestation) without using the proxy of low or very low birth weight; (4) "agreed international" character of the study; (5) standardized measures taken from birth; (6) the ability to calculate *z* scores correctly and report growth as *z* scores and *z* score changes; and (7) charts available as centiles and *z* scores.[36]

In addition to standardized anthropometric measures, all INTERGROWTH-21st sites adopted an evidence-based, nutritional protocol derived from presently recommended guidelines mostly for stable infants who can have enteral feeding. The protocol was relatively easy to implement and well accepted by clinical staff and mothers.[8] Thus, we find it puzzling that these 2 major items, namely standardization of the main outcome (infant size) and the feeding protocol (the main independent variable), are usually not included as criteria to evaluate or compare the methodologies of growth studies for preterm infants.

A potential limitation of the standards is the relatively small sample size of very preterm infants. This was unavoidable because the standards were based on a prescriptive approach and were, therefore, derived from low-risk women (N = 4607), who (1) had conceived naturally, (2) were recruited in the first trimester of pregnancy with accurate pregnancy dating, and (3) received regular, evidence-based antenatal care. Among these women, the preterm birth rate was 5%; hence, the preterm newborns, from whom the standards were produced, were not a convenient sample recruited at birth. Among this preterm group, which represented 0.1% of all births in the cohort, only 2% were live births at ≤30 weeks' gestation.[6]

There are additional issues to consider when judging the "small" sample size of this study:

1. WHO recommends, as a general rule, a total sample of 200 subjects of each sex for studies of human growth from a longitudinal design[37];
2. longitudinal studies are more precise than cross-sectional ones and, in fact, it has been estimated that a longitudinal study of fetal growth requires half the sample size of a cross-sectional study to estimate a given centile with the same precision[38] (ie, our 201 preterm newborns, who contributed 1750 measures during the follow-up, have power equivalent to a sample of 3500 in a cross-sectional study);
3. the strict standardized protocols, identical equipment, training of staff, and quality control procedures reduced measurement error and the likelihood of biased estimates;
4. the resulting curves do not display unexpected behavior at any gestational age that can be related to the small amount of data available; and
5. plots of individual measurements with overlapping centile curves and comparisons of empirical and fitted centiles showed good agreement.

Although it is likely that a larger sample would have improved the precision of the extreme centiles at low gestational ages, those that are close to the median would not be expected to change much.

Hence, the INTERGROWTH-21st Preterm Postnatal Growth Standards are a robust tool for monitoring the growth of more than 90% of preterm infants who are born at ≥32 weeks' gestation. This is presently relevant because these preterm infants are now recognized to be at high risk of short- and long-term complications and because the increasing rate of preterm births observed in many countries (associated with infertility treatments) is mostly caused by an increase in moderate and late preterm births.[39]

The diagnosis of extrauterine growth restriction for preterm infants when they reach term-corrected age should, therefore, be reserved for those who fail to follow the growth patterns (ie, below 2 SDs or a given centile) of their preterm counterparts in these standards, rather than the growth patterns of fetuses who remain in utero.

The INTERGROWTH-21st standards may be used from the time of the first postnatal assessment (ie, after the evaluation of size at birth) to special care and postnatal clinics, by neonatologists and pediatricians alike, up to 6 months' postterm. These standards allow for a comprehensive evaluation of weight, length, and head circumference and the early detection, specific for each anthropometric measure, of true growth disturbances.

The evaluation of head circumference as routine practice is important given its differential fetal growth pattern vis à vis weight. For example, by 33 weeks' gestation, 90% of the head circumference at term has been attained[26] (ie, preterm infants reaching 40 weeks' postmenstrual age appear to have recouped more head circumference than weight).

The construction of charts for very preterm infants (<32 weeks' gestation) is problematic: few arise from low-risk pregnancies, the nutritional guidelines available for infants this premature have considerable limitations, and clinical practice varies widely mostly because the evidence base is not strong, as highlighted in a recent review.[2] Hence, it is not surprising that there is little consensus regarding how best to monitor their growth.

It is time, therefore, to modify the unproven general concept that preterm newborns should grow like fetuses until term-corrected age because their nutritional requirements are modulated by different environmental conditions and they experience considerable nutritional and health challenges far beyond 40 weeks' postmenstrual age. Their growth is not similar to that of a fetus even under the best scenario (ie, the low-risk, preterm cohort without evidence of fetal

growth restriction studied in the INTERGROWTH-21st Project).

We feel it is not logical to recommend that most preterm newborns should mimic fetuses just because of the nutritional uncertainties surrounding the initial few postnatal weeks of very preterm infants. Until these gaps in scientific knowledge are filled and the extreme centiles on growth charts are better estimated, the 90% of preterm newborns (those born at 33 to <37 weeks' gestation) can start benefiting by matching the WHO Child Growth Standards with the INTERGROWTH-21st Preterm Postnatal Growth Standards, thereby providing continuity of care from the first postnatal day to life at home.

In terms of clinical practice, for the very preterm infants, it could be argued that, during the first postnatal weeks, monitoring growth should be performed only to follow a growth trajectory rather than as a screening tool to detect growth disturbance. Hence, the INTERGROWTH-21st standards, even with their small sample size at these gestational ages, are still valuable because they facilitate continuity of care for future clinical assessments. Furthermore, we have suggested that this could be viewed as a therapeutic dilemma that needs to be tested by comparing different feeding regimens in large, multicenter, randomized controlled trials with long-term growth and development as outcomes.[6]

The weight loss that occurs during the first days of postnatal life is an important clinical feature, but we believe it does not have to be incorporated in the postnatal growth standards because it is not a genuine growth alteration. Rather, it is a short-term adaptive process, partially attributed to the contraction of the extracellular body fluid, occurring mostly independently of hydroelectrolytic and nutrient supply and only affecting weight. The ensuing weight gain, which starts soon afterward, does reflect actual growth.

The early neonatal weight loss should, of course, be monitored like any other parameter in the clinical evolution of a preterm newborn, such as an acute episode of weight loss related to a nonnutritional condition (eg, an episode of infection, for which infant growth standards are routinely used). In addition, excessive weight loss or the failure to regain birth weight should be investigated and addressed accordingly.[40]

For moderate and late preterm infants, who represent the majority of the preterm population, robust preterm postnatal growth standards are available for monitoring weight, length, and head circumference up to 6 months' postterm-corrected age.[36,41]

The conceptual basis of international prescriptive standards is that they can be used regardless of the pregnancy, delivery, and newborn experience of the underlying population. Local selection of cutoff points (eg, less than the third or 10th centiles) may be required according to the availability of resources. Of course, a minimum number of primary health care units are required to cover the area and allow a minimum number of follow-up visits to take place, as is the case for infant monitoring with any growth chart.

Interestingly, recent evidence has demonstrated that the use of the INTERGROWTH-21st Preterm Postnatal Growth Standards reduced the diagnosis of extrauterine growth retardation when compared with charts that mimic fetal growth.[42] This is of clinical relevance to all settings, but perhaps more so to resource limited regions, because resources can then be focused on the high-risk subpopulation of preterm infants.

In the future, we envisage body composition patterns among preterm infants being included into the monitoring strategy to prevent overfeeding these infants to complement the recently published body composition at birth standards.[43]

ABBREVIATIONS

AAP: American Academy of Pediatrics
INTERGROWTH-21st: International Fetal and Newborn Growth Consortium for the 21st Century
WHO: World Health Organization

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