Chapter 15
Growth Monitoring of Preterm Infants During Stay in the Neonatal Unit and into Early Childhood

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Abstract Monitoring growth is important in preterm infants as they are at a high risk for postnatal growth restriction which can lead to impaired long term growth and neurodevelopment. In the absence of better charts, intrauterine growth charts are recommended by leading professional paediatric organisations for monitoring the growth of preterm infants. The aim when caring for preterm infants is to at least match the growth velocity from published best postnatal growth charts and strive towards reaching ideal growth velocities from intrauterine growth charts. The Fenton chart appears to be suitable for monitoring growth of preterm infants during their stay in the neonatal intensive care unit (NICU). Recently, Fenton charts have been updated using the WHO 2006 charts for the 40–50 weeks' post conception age group. Once a post-conception age of 40 weeks is reached, the WHO 2006 growth charts can be used for monitoring ongoing growth. The ongoing "Intergrowth-21st study" has the potential to overcome the deficiencies of all current growth charts. It will enable the establishment of prescriptive growth charts for monitoring the growth of preterm infants during and beyond their NICU stay into early childhood. Care should be taken to avoid excessive catch up growth which is associated with increased risk of diabetes, hypertension, and obesity in later life.

Key points

1. Growth charts are essential for defining health and nutritional status and early detection and management of growth disorders in infants and children.
2. Growth monitoring is especially important in preterm infants as they are at a high risk for postnatal growth restriction which can lead to impaired long term growth and neurodevelopment.

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3. A ‘standard’ chart that represents the ideal healthy growth of a population is prescriptive whereas a ‘reference’ chart that describes the population without making claims about the health of its sample is descriptive in nature.
4. In the absence of ideal growth charts, intrauterine growth charts are considered suitable for monitoring the growth of preterm infants until they reach term.
5. In the absence of ideal charts, the WHO 2006 growth charts may be used for monitoring the growth of ex-preterm infants.
6. The International Fetal and Newborn Growth Consortium study is designed to produce a set of international standards (normative charts for fetal growth, birth weight for gestational age and postnatal growth of preterm infants) for clinical applications and monitoring trends in populations.

Disturbances in health and nutrition, regardless of their aetiology, almost always affect growth [1]. Hence, growth assessment using growth charts is a useful tool for defining health and nutritional status in children [2]. Growth monitoring helps to improve nutrition, educate the care givers, and enables early detection and referral for conditions manifested by growth disorders [3]. The most common measurements for evaluating growth are weight, length/height, head circumference and body mass index. Growth monitoring of preterm infants is even more important because, as described below, many studies have shown that (a) preterm infants suffer from postnatal growth restriction and (b) postnatal growth restriction is associated with long term adverse neurodevelopmental outcomes.

1 Preterm Infants Suffer from Postnatal Growth Restriction

1.1 In a retrospective longitudinal cohort study, Horemuzova et al. (Sweden) evaluated the physical growth of all infants born before 26^{+0} weeks of gestation and surviving to full-term age ($n = 162$), admitted to the NICU of Karolinska Hospital between January 1990 and December 2002 [4]. Body weight was recorded daily, head circumference (HC) weekly and length twice a month. The majority of the infants showed a pronounced postnatal growth restriction for all growth variables with increasing deviation from the reference with age. At discharge from NICU, 75 % of those initially appropriate for gestational age (AGA) infants were below − 2 standard deviation scores for at least one of the body size variables [4].

1.2 In a retrospective cohort study [5], 101 children with a BW ≤ 750 g, born between 1996 and 2005 in the University Hospital Utrecht, The Netherlands, were followed until 5.5 years. Height, weight, occipital-frontal circumference at birth, 15 months and 2 years corrected age and 3.5 and 5.5 years were measured. Between birth and 5.5 years catch-up growth in height, weight for height, weight and OFC was seen in 72.2, 55.2, 28.6 and 68.9 % respectively of the small for gestational age (SGA) infants. For AGA infants they found substantial catch-down growth in height (15.4 %) and weight (33.8 %).

2 Physical Growth and Neurodevelopmental Outcomes in Preterm Infants

2.1 Association Between Postnatal Growth During NICU Stay and Neurodevelopmental Outcomes

1. Ehrenkranz et al. [6] assessed the predictive value of in-hospital growth velocity on neurodevelopmental and growth outcomes at 18–22 months post-conceptional age among extremely low birth weight (ELBW) infants (501–1,000 g). Of the 600 discharged infants, 495 (83 %) were evaluated at a corrected age (CA) of 18–22 months. As the rate of weight gain increased from 12.0 to 21.2 g/kg per day, there was decrease in the incidence of cerebral palsy, Mental Developmental Index (MDI) < 70 and Psychomotor Developmental Index (PDI) < 70 on Bayley Scale of Infant Development (BSID), abnormal neurologic examination, neurodevelopmental impairment, and need for rehospitalisation. Similar findings were observed in relation to the rate of head circumference growth. They concluded that the growth velocity during an ELBW infant's NICU hospitalisation exerts a significant and possibly independent effect on neurodevelopmental and growth outcomes at 18–22 months of CA.

2. Franz et al. [7] evaluated the neurological outcomes of a total of 219 of 263 (83 %) long-term survivors at a median corrected age of 5.4 years. Increasing SD scores for weight and head circumference from birth to discharge were associated with a reduced risk for an abnormal neurologic examination.

3. Shah et al. [8] aimed to identify measure of postnatal growth failure associated with long-term outcome in preterm infants born at < 28 weeks' gestation. Four measures of defining postnatal growth failure at 36 weeks corrected gestational age: (1) weight < 10th centile, (2) weight < 3rd centile, (3) z score difference from birth > 1 and, (4) z score difference from birth > 2; were compared for their predictive values and strength of association with adverse neurodevelopmental outcomes at 18–24 months.

Postnatal growth failure defined as a decrease in z score of > 2 between birth and 36 weeks corrected gestational age had the best predictive values compared to other postnatal growth failure measures. However, it was significantly associated with PDI ($p = 0.006$) but not with MDI ($p = 0.379$). Postnatal growth failure defined by z score change influenced psychomotor but not mental tasks in this cohort.

2.2 Association Between Post-Discharge Growth and Neurodevelopmental Outcomes in Preterm Infants

1) Ramel et al. [9] reported that pre- and post-discharge linear growth suppression in very low birth weight (VLBW: Birth weight $< 1{,}500$ g) infants was negatively associated with developmental outcomes at 24 months CA. In their retrospective study,

weight, recumbent length and head circumference were recorded at birth, hospital discharge and at 4, 12 and 24 months CA in 62 VLBW infants. Standardized Z-scores for weight (WZ), length (LZ) and head circumference (HCZ) were calculated. Twenty-four-month neurodevelopmental function was analysed as a function of growth status. Controlling for WZ and HCZ at each age, lower LZ at 4 and 12 months CA was associated with lower cognitive function scores at 24 months CA ($p \leq 0.03$).

2) Ghods et al. [10] conducted a retrospective cohort study to determine whether head circumference (HC) catch-up is associated with improved neurocognitive development. 179 preterm very low birth weight (VLBW) (Birth weight ≤ 1,500 g) infants were followed to the age of 5.5 years. The association between HC catch-up and neurodevelopmental outcome was assessed and perinatal risk factors, infant characteristics and nutritional practices associated with HC catch-up were determined. HC catch-up occurred in 59 (34 %) infants and was positively correlated with neurodevelopmental outcome. They concluded that among preterm VLBW infants, there is a close relation between HC growth and neurodevelopmental outcome.

3) Powers et al. [11] assessed the post-discharge growth and developmental progress of 135 VLBW preterm infants in a predominantly Hispanic population and reported that failure to thrive and microcephaly increased neurodevelopmental impairment risk at 3 years of age regardless of gestational age.

4) Kan et al. [12] aimed to determine the associations between weight and head circumference, at birth and postnatally, with cognitive, academic and motor outcomes at age 8 years for very preterm children free of neurosensory impairment. 179 very preterm infants (gestational age < 28 weeks) born in 1991 and 1992 who were free of neurosensory impairment were included in the study. At 8 years of age children had cognitive, academic and motor assessments. Weight and head circumference data were collected at birth, at the time of discharge (weight only), at 2 years of age and at 8 years of age, and growth restriction was calculated using Z-scores (standard deviation scores) relative to the expected mean for age using the British 1990 growth reference charts [13]. Weight at any age was mostly unrelated to any outcomes. While head circumference at birth was not related to school-aged outcomes, smaller head circumferences at ages 2 and 8 years were associated with poorer performance in most outcome measures. Catch-up growth in weight in early childhood was not associated with 8-year outcomes.

5) Latal-Hajnal [14] studied the significance of growth status at birth and postnatal growth on neurodevelopmental outcome in VLBW infants. Growth and neurodevelopment were examined in 219 VLBW (< 1,250 g) children, 94 small for gestational age (SGA) (< 10th percentile) and 125 appropriate for gestational age (AGA) (> 10th percentile). Outcome at age 2 was assessed with the Bayley Scales of Infant Development MDI, PDI and a standardized neurologic examination. After adjustment for co variables including cerebral palsy (CP), SGA children with weight < 10th percentile at age 2 had lower mean PDI than SGA children with catch-up growth to weight > 10th percentile (mean [SD], 89.9 [17.4] versus 101.8 [14.5]; $p < .001$). AGA children with catch-down growth (weight < 10th percentile at age 2) were, independent of CP, more likely to have lower mean MDI (94.9 vs. 101.7, $p = .05$) and PDI (81.9

vs. 95.1; $p < .001$) than AGA children remaining > 10th percentile at age 2. They also more frequently had severe CP (22.9 % vs. 1.2 %; $p = .008$). They concluded that in VLBW children, the course of postnatal growth rather than the appropriateness of weight for gestational age at birth determines later neurodevelopmental outcome.

6) Casey et al. [15] assessed the 8-year growth, cognitive, behavioural status, health status, and academic achievement in low birth weight preterm infants who had failure to thrive only, were SGA only, had failure to thrive plus were SGA, or had normal growth. A total of 985 infants received standardized evaluations to age 8; 180 infants met the criteria for failure to thrive between 4 and 36 months' gestational corrected age. The following outcome variables were collected at age 8: growth, cognitive, behavioural status, health status, and academic achievement. Multivariate analyses were performed among the 4 growth groups on all 8-year outcome variables. Children who both were SGA and had failure to thrive were the smallest in all growth variables at age 8, and they also demonstrated the lowest cognitive and academic achievement scores. The children with failure to thrive only were significantly smaller than the children with normal growth in all growth variables and had significantly lower IQ scores. Those who were SGA only did not differ from those with normal growth in any cognitive or academic achievement measures. There were no differences among the 4 groups in behavioural status or general health status. They concluded that low birth weight preterm infants who develop postnatal growth problems, particularly when associated with prenatal growth problems, demonstrate lower physical size, cognitive scores, and academic achievement at age 8 years.

3 Types of Growth Charts

A 'standard' chart represents the ideal healthy growth of a population and hence is of prescriptive nature. To derive such ideal healthy growth charts, the study population should be from a cohort of infants born to healthy mothers with uncomplicated pregnancy and delivery. In addition, the study infants should be raised under optimal environmental conditions including breastfeeding, immunisations and follow recommended dietary practices. The study infants should be free from any disease that could hinder growth. Longitudinal follow up and measurement of anthropometry of such infants will help derive the 'standard' growth charts which will be of prescriptive nature. The WHO 2006 growth charts (term infants) are standard growth charts.

In contrast, a 'reference' chart describes the population without making claims about the health of its sample and hence is descriptive in nature [16–18] (Table 15.1). The 'reference' charts are derived by measuring the anthropometry of a sample of infants and children at various ages and plotting them on graph. The sample is thus cross-sectional rather than longitudinal. In addition, health of the children in the study population is not taken into consideration. Majority of the currently available growth charts in full term infants and children are 'reference' charts.

Table 15.1 Differences between reference and standard charts

Reference charts	Standard charts
Simply describe the growth of a population without taking into consideration the health of the population	Provide guidance on how a child should grow; not just how a child is growing
Based on cross sectional data; relatively easy to acquire large sample size	Based on prospective and longitudinal monitoring of healthy growth; difficult to acquire large sample size
Increase in incidence of childhood obesity means future descriptive charts will enable more children to be classified as normal even though overweight/obese	Have the potential to identify overweight and obesity early, which can help bring in early interventions
Have the potential to over diagnose under nutrition, which in turn can lead to unnecessary overfeeding	Have the potential to avoid over diagnosis of under nutrition

4 Types of Growth Charts Currently Available for Preterm Infants During Stay in the Neonatal Unit

4.1 Standard Charts

At present, there are no prescriptive standard growth charts available for preterm infants. Theoretically speaking, infants born prematurely should continue to grow at intrauterine rates until they reach term. The American Academy of Pediatrics [17] and Canadian Pediatric society [18] recommend intra uterine growth rates as the ideal growth of preterm infants.

4.1.1 Considered Being, But Not Really “Intra Uterine Growth” Charts (Table 15.2)

There are more than 25 studies reporting on ‘intrauterine growth charts’. These have been best summarized by Karna et al. [19].

Until recently, Lubchenko [20] and Babson und Benda [21] charts were commonly used in many neonatal units around the world. Fenton et al. [22] updated the Babson and Benda growth charts to develop contemporary ‘intrauterine growth charts’. Using preset criteria, three recent large population based surveys of birth weight for gestational age were identified. The Canadian study by Kramer [23] which had a sample size of 676,605 infants delivered between 22–43 weeks was used for updating the intrauterine weight section. Two large studies from Sweden [24] and Australia [25] were used to update the intrauterine head circumference and length section. The data were averaged together using a weighted average based on total sample size to derive the 3rd, 10th, 50th, 95th and 97th percentiles and create one growth chart. CDC 2000 growth charts were used to generate the growth charts from corrected gestation of 40 weeks onwards. The Fenton chart appears to be useful in monitoring the growth of preterm infants during their NICU stay. It is used by many North

American, European and Australian centres. Recently Olsen et al. have published growth charts for New intrauterine growth charts based on United States data [26] and it will be useful if Fenton charts are updated incorporating this new information from USA. The latest updated Fenton charts have used WHO 2006 growth charts instead of CDC 2000 charts to generate growth charts from post-conceptional age of 40 weeks until 10 weeks post term (BMC Pediatrics, 2013, 13:59).

Inherent issues with intrauterine growth charts Even though they are called "intrauterine" charts, they are in fact cross sectional data derived from anthropometry measured at birth on preterm infants delivered at various gestations. It is well known that fetuses delivered prematurely may not have reached full growth potential due various maternal/fetal morbidities and hence do not reflect the "ideal" growth. Also, these charts do not take into consideration, the normal 5–8 % weight loss that occurs in healthy preterm infants in the first week of life.

4.1.2 'Fetal Growth Charts' (Table 15.2)

Strictly speaking, only charts derived from longitudinal studies should be called growth charts, growth being a process extended over time [27]. Hence it may appear logical that ideal 'intrauterine growth charts' should be derived from serial and longitudinal assessment of physical parameters of weight, length and head circumference using fetal ultrasound technique [28]. However, the drawback of this method is that fetal ultrasound is not very accurate in predicting the fetal weight. A systematic review which analysed data from 58 articles over 28 years found wide variability in diagnostic accuracy of ultrasound examination in predicting the fetal weight. Overall only 62 % (8,895/14,384) of the sonographic predictions were within 10 % of the actual weight. The accuracy was affected significantly by the time interval between examination and delivery, person doing the sonography (registered diagnostic medical sonographers had better accuracy than physicians or residents), and the gestation at assessment (assessment closer to term were more accurate compared to preterm patients) [29].

Another systematic review came to similar conclusions. The reviewers searched four important databases (MEDLINE, EMBASE, ZETOC, and The Cochrane Library). Studies including the estimation of fetal weight by 11 different research groups using different formulas were included in the review. No preferred method for the ultrasound estimation of fetal weight emerged from their review. They found that the size of the random errors was quite wide, with 95 % confidence intervals exceeding 14 % of birth weight in all studies. They concluded that the accuracy of EFW using fetal ultrasound is compromised by large intra- and inter-observer variability and efforts must be made to minimise this variability if EFW is to be clinically useful [30]. In addition, maternal morbidities can result in fetal growth restriction, which in turn can result in non- ideal growth charts.

In view of such limitations, fetal weight charts derived from the currently available ultrasound technology may not be appropriate for use as ideal postnatal growth of preterm infants. However, recent advances in technology have resulted in more frequent use of 3-D ultrasound for fetal biometry measurements. Chan et al. [31] in a prospective study compared the inter- and intra-observer variation of fetal biometric measurements utilising two-dimensional (2D) and three-dimensional (3D) ultrasound imaging. Three pairs of doctors trained in sonography evaluated singleton pregnancies in the mid-trimester. Measurements of the biparietal diameter (BPD), head circumference (HC), abdominal circumference (AC), and femur length (FL) were taken in duplicate by each doctor using 2D imaging and then again using 3D volume data sets. Each set of paired doctors evaluated 12 patients. Inter- and intra-observer variations were calculated as the SD of the difference between paired measurements performed by the doctor pairs and by the individual doctors, respectively. Bland–Altman plots were used to visually compare measurement bias and agreement by 2D and 3D methods. The intra-observer variation of HC, AC, and FL was significantly lower for 3D compared with 2D ultrasound. Inter-observer variation was not significantly different when measured with 2D and 3D ultrasound, with the exception of FL, which was lower when measured with 3D ultrasound. They concluded that the use of 3D ultrasound significantly reduces intra-observer variation for HC, AC, and FL and reduces inter-observer variation for FL [31]. Schild et al. [32] in a prospective cohort study, obtained biometric data of 150 singleton fetuses weighing $\leq$ 1,600 g at birth by sonographic examination within 1 week before delivery. Exclusion criteria were multiple pregnancy, intrauterine death as well as major structural or chromosomal anomalies. Their new formula was compared with currently available equations for estimating weight in the preterm fetuses. They concluded that in fetuses weighing $\leq$ 1,600 g at birth, the new formula using 3D ultrasound is superior to weight estimation by traditional formulae using 2D measurements [32]. These data indicate that 3D ultrasonography may have the potential to be a more accurate measure of fetal anthropometry than the traditional 2D ultrasounds. If these preliminary promising findings are proven correct in multiple large studies, intrauterine growth curves derived from such method may have the potential to be used as ideal growth curves for monitoring preterm infants after birth.

4.2 Postnatal 'Reference' Growth Charts (Table 15.2)

Many reference charts that describe the actual longitudinal growth of preterm infants during the course of their stay in the NICU have been published [33, 34]. If these reference charts are used to monitor the ongoing growth of preterm infants, extra-uterine growth retardation would be considered as normal. Hence they are not ideal for monitoring the growth of preterm infants. However, these charts give an idea of what can be achieved with the available resources and limits set by the morbidities of prematurity and can be used to compare the growth of preterm infants between different units.

Table 15.2 Growth charts for monitoring preterm infant growth until term

Intrauterine growth charts	Fetal growth charts	Postnatal growth charts
Not really intrauterine. Based on cross sectional data derived from anthropometry measured at birth on preterm infants delivered at various gestations.	Based on longitudinal assessment of healthy fetal growth; truly intrauterine	Describe the growth of preterm infants, without taking into consideration morbidities of prematurity; descriptive and not prescriptive
Recommended by American Academy of Pediatrics and Canadian Pediatric society; Commonly used charts	Ultrasound measurement of fetal anthropometry is subject to wide interpersonal variability; Fetal ultrasound is not very accurate in estimating fetal weight	Useful for comparing different units

5 A Note of Caution While Aiming to Achieve the Perfect Intrauterine Growth Rates

Even though the intra uterine growth charts may appear idealistic goals, one needs to decide if it is really feasible and safe to attain those parameters. Any attempts to promote physical growth by aggressive enteral and parenteral nutrition may potentially harm the sick preterm infant. Rapid increases in enteral feeding are known risk factor for necrotising enterocolitis (NEC) [35]. In ELBW infants, higher fluid intake and less weight loss during the first 10 days of life are associated with an increased risk of death and BPD [36, 37]. In addition excessive catch up growth in early neonatal period for may result in adverse cardiovascular outcomes later in life. Finken et al. [38] and Euser et al. [39] found that in subjects born very preterm, rapid infancy weight gain until 3 months was associated with trend towards higher insulin levels at 19 years. They also concluded that rapid weight gain in both infancy and early childhood is a risk factor for adult adiposity and obesity. Similar concerns have been raised by other investigators [40, 41].

6 Growth Charts to Monitor Preterm Infants from Post-Conception Age of 40 Weeks into Early Childhood

Until recently, many countries used the growth charts released by Centers for Disease Control and Prevention (CDC 2000) for monitoring the growth of term infants and children. The same charts are usually used for ongoing growth monitoring of preterm infants after reaching post conceptional age of 40 weeks. The inherent problem with the CDC 2000 and similar charts is that they are ‘reference’ charts, which simply describe the sample population without making any claims about the health of the sample. Because of various environmental and lifestyle influences, the prevalence of overweight in children and adolescents has increased markedly over the past few decades. Hence, any new reference charts, which are derived from such population of overweight children, would accept these abnormally high weights-for-age as normal [42, 43]. Use of such charts would also result in more children being wrongly and frequently diagnosed as underweight resulting in unnecessary nutritional supplementation and may contribute to obesity and associated morbidities.

To some extent, the CDC 2000 growth charts addressed this by excluding the data derived from the National Health and Nutrition Examination Survey (NHANES) III for children 6 years of age for weight-for-age and body mass index (BMI)- for-age charts. This was carried out because they had identified that compared with the NHANES II (1976–1980), the NHANES III (1988–1994) children were of higher weight-for-age [44]. Despite this adjustment, the 97th and the 99.9th percentile charts (+ 2 and + 3 z-scores) are located very high on the CDC weight-for-age and BMI-for-age charts, meaning that fewer overweight and obese children and adolescents are identified as such because the norms have been raised. The lower centiles have also been shifted upwards, leading to overestimation of under nutrition, and thus advice leading to overfeeding [45]; also, precautions that were taken by the CDC cannot be confidently expected from innumerable number of ‘reference’ charts which are being published regularly from different countries all over the world.

To overcome the problems inherent with ‘reference’ charts, with a complete change in philosophy, the World Health Organization (WHO) conducted the Multi-centre Growth Reference Study (MGRS) in order to establish the ‘standard’ growth charts for children between 0 and 6 years [46]. The MGRS was conducted between 1997 and 2003 in 6 countries from diverse geographical regions: Brazil, Ghana, India, Norway, Oman and the United States. The study combined a longitudinal follow-up of 882 infants from birth to 24 months with a cross-sectional component of 6,669 children aged 18–71 months. The study populations lived in socioeconomic conditions favourable to growth. The individual inclusion criteria for the longitudinal component were: no known health or environmental constraints to growth, mothers willing to follow MGRS feeding recommendations (i.e., exclusive or predominant breastfeeding for at least 4 months, introduction of complementary foods by 6 months of age and continued breastfeeding to at least 12 months of age), no maternal smoking before and after delivery, single-term birth and absence of significant morbidity. The eligibility criteria for the cross-sectional component were the same as those for the longitudinal component with the exception of infant feeding practices. A minimum of 3 months of any breastfeeding was required for participants in the study’s cross-sectional component. Weight-for-age, length/height-for-age, weight-for-length/height and body mass index-for-age percentile and Z-score values were generated for boys and girls aged 0–60 months. The pooled sample from the 6 participating countries allowed the development of a truly international reference. The standards explicitly identify breastfeeding as the biological norm and establish the breastfed child as the normative model for growth and development. They also demonstrate that healthy children from around the world who are raised in healthy environments and follow recommended feeding practices have strikingly

Table 15.3 Rationale for advocating WHO 2006 (0–2 years) growth charts for post discharge monitoring of preterm infants

1	Based on exclusively or predominantly breastfed babies
2	Study population (both mother and baby) were in optimal health enabling optimal growth
3	Study population quite recent: 1996–2003
4	Study population was from multiple countries and multiple ethnicities
5	Sophisticated statistical analyses
6	Multiple and longitudinal measurements of the infants growth parameters
7	Conceptually, better than the other currently available charts

similar patterns of growth. In addition, to establish 'standard' prescriptive charts for older children and adolescents, the WHO reconstructed the 1977 National Center for Health Statistics (NCHS)/WHO growth reference using state-of-the-art statistical methods. The 1977 growth references were used because they were from a population prior to the occurrence of the current epidemic of childhood obesity. These new charts were released by the WHO in 2007 for general use [47]. These charts are recommendations for how children should grow. More than 125 countries including UK, USA, Canada and New Zealand have started using the WHO growth charts for full term infants [48] (Table 15.3).

The full set of tables and charts are available on the WHO website (www.who.int/childgrowth/en) together with tools such as software and training materials.

Since their publication, many studies have shown the usefulness of WHO growth charts in predicting obesity and other cardiovascular morbidities.

De Onis et al. [49] examined the association between cardiovascular risk and childhood overweight and obesity using the BMI cut-offs recommended by the WHO. Children were classified as normal weight, overweight and obese according to the WHO BMI-for-age reference. Blood pressure, lipids, glucose, insulin, homeostasis model assessment-insulin resistance (HOMA-IR) and uric acid levels were compared across BMI groups. The subjects were children (*n* 149) aged 8–18 years. About 37, 22 and 41 % of children were classified respectively as normal weight, overweight and obese. Obese children were 10·6 times more likely than normal-weight children to have hypertension; OR for other associations were 60·2 (high insulin), 39·5 (HOMA-IR), 27·9 (TAG), 16·0 (low HDL-cholesterol), 4·3 (LDL-cholesterol) and 3·6 (uric acid). Overweight children were more likely than normal-weight children to have hypertension (OR = 3·5), high insulin (OR = 28·2), high HOMA-IR (OR = 23·3) and high TAG (OR = 16·1). Nearly 92 and 57 % of the obese and overweight children, respectively, had one or more risk factor. They concluded that obesity and overweight defined using the WHO BMI-for-age cut-offs identified children with higher metabolic and vascular risk.

Shields et al. [50] compared prevalence estimates of excess weight among Canadian children and youth according to three sets of body mass index (BMI) reference cut-points. The cut-points were based on growth curves generated by the WHO, the International Obesity Task Force (IOTF), and the CDC (USA). Prevalence estimates of overweight and obesity were produced for 2- to 17-year-olds using the three sets of BMI cut-points. Estimates were based on data from 8,661 respondents from the 2004 Canadian Community Health Survey and 1,840 respondents from the 1978/1979 Canada Health Survey. In both surveys, the height and weight of children were measured. They found that 2004 prevalence estimate for the combined overweight/obese category was higher (35 %) when based on the WHO cut-points compared with the IOTF (26 %) or CDC (28 %) cut-points. Estimates of the prevalence of obesity were similar based on WHO and CDC cut-points (13 %), but lower when based on IOTF cut-points (8 %).

In the absence of other ideal growth charts, it is appropriate to use the WHO growth charts to monitor the ongoing growth of preterm infants after reaching post-conceptional age of 40 weeks.

6.1 Evidence Supporting the Use of WHO 2006 Growth Charts for Monitoring Preterm Infants After Discharge

Nash et al. [51] aimed to determine whether the pattern of growth of very low birth weight (VLBW) infants during the first 2 years, assessed using the WHO-GS or the traditional Centers for Disease Control and Prevention reference growth charts (CDC-RGC), is associated with neurodevelopment [51]. Pattern of weight, length, and head circumference gain of appropriate-for-gestation VLBW preterm infants ($n = 289$) from birth to 18–24 months corrected age was classified, using the WHO-GS and CDC-RGC, as sustained (change in Z-score ≤ 1 SD), decelerated (decline > 1 SD), or accelerated (incline > 1 SD). Development was assessed using the Bayley Scales of Infant and Toddler Development (BSID)-III at 18–24 months corrected age. Using the WHO-GS, children with a decelerated pattern of weight gain had lower cognitive (10 points), language (6 points), and motor (4 points) scores than infants with sustained weight gain ($p < 0.05$), even after adjustment for morbidities. No association was found using the CDC-RGC. They concluded that a decelerated pattern of weight gain, determined with the WHO-GS, but not the CDC-GRC, is associated with poorer neurodevelopment scores on the BSID-III than a pattern of sustained growth [51].

Belfort et al. [52] aimed to identify sensitive periods of postnatal growth for preterm infants relative to neurodevelopment at 18 months' corrected age. They studied 613 infants born at < 33 weeks' gestation who participated in the DHA for Improvement of Neurodevelopmental Outcome (DINO) trial. They calculated linear slopes of growth in weight, length, BMI, and head circumference from 1 week of age to term (40 weeks' postmenstrual age), term to 4 months, and 4–12 months using the WHO growth charts, and estimated their associations with Bayley Scales of Infant Development, 2nd Edition, MDI and PDI in linear regression. The median gestational age was 30 weeks. Mean $\pm$ SD MDI was 94 ± 16, and PDI was 93 ± 16. From 1 week to term, greater weight gain (2.4 MDI points per z score [95 % confidence interval (CI): 0.8–3.9]; 2.7 PDI points [95 % CI: 1.2–0.2]), BMI gain (1.7 MDI points [95 % CI: 0.4–3.1]; 2.5 PDI points [95 % CI: 1.2–3.9]), and head growth (1.4 MDI points [95 % CI: – 0.0–2.8]; 2.5 PDI points [95 % CI: 1.2–3.9]) were associated with higher scores. From term to 4 months, greater weight gain (1.7 points [95 % CI: 0.2–3.1]) and linear growth (2.0 points [95 % CI: 0.7–3.2]) were associated with higher PDI. From 4 to 12 months, none of the growth measures was associated with MDI or PDI score. They concluded that in preterm infants, greater weight and BMI gain to term were associated with better neurodevelopmental outcomes. After term, greater weight gain was also associated with better outcomes, but increasing weight out of proportion to length did not confer additional benefit.

7 Future Research

As discussed above, neither "intrauterine growth charts" nor "fetal growth charts" nor "postnatal growth charts" are suitable for monitoring the growth of preterm infants till they become term. Similarly, CDC 2000 and WHO 2006 growth charts are also not ideal for monitoring the growth of ex-preterm infants.

In order to establish normative growth charts, the Inter Growth 21st study has been commenced by the International Fetal and Newborn Growth Consortium [53, 54]. The goal is to develop new "prescriptive" standards describing normal fetal and preterm neonatal growth over time and newborn nutritional status, and to relate these to neonatal health risk.

The primary objective is to produce a set of international Fetal and Newborn Growth Standards (fetal growth, birth weight for gestational age and postnatal growth of preterm infants) for practical applications in clinical use and for monitoring trends in populations.

The study aims to recruit 4,500 healthy women aged 18–35, who had regular menstrual cycles and conceived spontaneously and do not have major health issues and practice healthy lifestyles. Study participant women are being recruited from 9 countries across five continents. They undergo 6 scans in addition to the initial dating scans. They are scheduled at 5 weekly intervals: 14–18 weeks, 19–23 weeks, 24–28 weeks, 29–33 weeks, 34–38 weeks and 39–42 weeks. Apart from the additional scans, they receive the standardized antenatal care. Based on expected 9 % rate of prematurity, it is expected that around 360 infants would be born to these mothers (26–37 weeks gestation). Their longitudinal growth will be monitored for 8 months. This would include measuring weight, length and head circumference every 2 weeks for the first 8 weeks and then monthly until 8 months after birth. Those suffering from death or serious morbidities of prematurity such as NEC will be excluded. This study will enable the derivation of prescriptive intrauterine growth charts as well as postnatal growth charts from a diverse population across five continents.

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