Postnatal Growth of Preterm Infants During The First Two Years of Life: Catch-Up Growth Accompanied by Risk of Overweight

Junyan Han
Children's Hospital of Fudan University

Yuan Jiang
Children's Hospital of Fudan University

Jun Huang
Shanghai Minhang District Maternal and Child Health Care Hospital

Yue Zhang
Shanghai Minhang District Maternal and Child Health Care Hospital

Ying Zhang
Shanghai Minhang District Maternal and Child Health Care Hospital

Yi Zhang
Children's Hospital of Fudan University

Xiaotian Chen
Children's Hospital of Fudan University

Yun Li
Shanghai Minhang District Maternal and Child Health Care Hospital

Weili Yan (yanwl@fudan.edu.cn)
Children's Hospital of Fudan University

Research

Keywords: Preterm, Growth, Catch-up growth, Overweight

DOI: https://doi.org/10.21203/rs.3.rs-41373/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License
Abstract

Background: Early postanal growth of preterm infants has many effects on early and late health. However, evidence on growth pattern in Chinese preterm infant population during early life is insufficient. This study aims to describe the growth trajectory, catch-up growth, and risk of overweight of preterm infants during the first two years of life in a Chinese community population.

Methods: All preterm infants (n=10624) received routine childcare in one primary maternal and child healthcare network in eight years were included. Body weight and length/height at corrected age (CA) 40 weeks, CA 3 months, 6 months, 9 months, 12 months, 18 months, and 24 months were extracted and converted to z-scores based on the World Health Organization (WHO) standards. According to the intrauterine growth status, infants were divided into small for gestational age (SGA), appropriate for gestational age (AGA), and large for gestational age (LGA) infants. Changes of z-score were used to describe the growth velocity. Generalized estimating equation (GEE) model was used to analyze growth trajectory trends over time.

Results: Body weight and length/height were overall above the WHO standards during the first two years of life. Z-score increased significantly by 0.08 (95%CI: 0.06-0.10) in weight and 0.07 (95%CI: 0.04-0.09) in length/height from CA 40 weeks to 3 months, and then levels off until CA 24 months after adjustment. Over 90% AGA/LGA preterm infants achieved catch-up growth before CA 24 months, with the majority did before CA 3 months. It took more time for SGA infants to achieve catch-up growth than AGA/LGA infants. However, risk of overweight appeared along with catch-up growth, the proportion of infants with risk of overweight being at the peak (25.6% of all preterm infants and 39.4% of LGA infants) at CA 3 months. Growth trajectories of SGA showed declining trends, but those of LGA showed increasing trends during the first two years.

Conclusions: Body weight and length/height of preterm infants are above the WHO standards in the Chinese community population during the first two years of life. Catch-up growth is accompanied by the risk of overweight as early as CA 3 months.

Background

More than one in 10 of the world’s babies born in 2014 were preterm infants, resulting in an estimated 14.8 million preterm births (1). Because of the vast population base, the number of preterm infants in China ranked second in the world (1, 2). Although the survival rate of preterm has increased over past decades along with the development of perinatal and neonatal medicine, they are still more susceptible to growth restriction, delayed motor, and language development in later life (3, 4).

Growth trajectory monitoring is an essential part of children's healthcare, especially for preterm infants. Previous studies on growth trajectory have shown that preterm and/ or low birth weight infants were shorter and lighter than term infants of the same postmenstrual age (PMA). Meanwhile, they often have a rapid growth or catch-up growth period after post-discharge (5, 6). Early catch-up growth is beneficial for
neurodevelopment (7). Belfort et al.’s study in 945 preterm infants showed rapid growth from term age to four months was associated with better intelligence quotient at 18 years old (8). However, associations between excessive growth in infancy and overweight/obesity, insulin resistance, and elevated blood pressure in childhood or adulthood have been reported in recent studies (9, 10). A study in Korean population reported a phenomenon of early accelerated growth or “early catch-up growth” in preterm infants, which might be associated with Asian cultural values and childrearing practices (11). Nevertheless, evidence on growth pattern, especially on catch-up growth, in Chinese preterm infants is still limited.

This study aims to describe the growth trajectory, catch-up growth, and risk of overweight of preterm infants during the first two years of life in a community-based Chinese population, and to compare the growth differences between small for gestational age (SGA) infants, appropriate for gestational age (AGA) infants, and large for gestational age (LGA) infants.

**Methods**

**Data source and subjects**

Study data were extracted from the routine database of the Maternal and Child Healthcare Network of Minhang district in Shanghai, China. It was a population-based database launched by the government, which recorded all infants’ routine healthcare information living in this district constituted of 13 communities for 2.53 million permanent residents. This study included all preterm infants (born before 37 weeks of gestation) who received routine healthcare during the period from January 1, 2010, to December 31, 2017. Infants with a missed or ambiguous birth date, birth weight, or without growth parameter data (body weight and length/height) were excluded. Corrected age (CA) was used in all analyses, defined as the additional age from 40 weeks of PMA. Follow-up data were grouped into CA 40 weeks (40 weeks of PMA), 3 months, 6 months, 9 months, 12 months, 18 months, and 24 months based on their original date of visit. The institutional scientific research department approved the analysis protocol. Personal identification information was removed from the extracted dataset for analyses.

**Measurements and definitions**

Body weight and length/height were measured and recorded by trained pediatricians and nurses in community healthcare centers at each routine visit. An electronic scale with 0.01kg accuracy was used to measure body weight. Length/height was measured using a length board in a supine position, or a measurement system in standing position reading to the nearest 0.1cm. For each infant, z-score of measurements were computed using the Lambda-Mu-Sigma (LMS) parameters based on the international standards (12, 13). The Fenton preterm growth standard (from 22 to 50 weeks of gestation) (12) was used to calculated z-scores at birth, and the World Health Organization (WHO) standards for children 0-5 years old (13) were used to calculated z-scores from CA 40 weeks to 24 months. According to the intrauterine growth status, all preterm infants were classified as SGA, AGA, and LGA infants, defined...
as birth weight <10\textsuperscript{th} percentile, 10\textsuperscript{th}-90\textsuperscript{th} percentile, and >90\textsuperscript{th} percentile on the Fenton Growth Chart, respectively (12).

According to WHO standards, catch-up growth was defined as weight or length/height for age $\geq$ 25\textsuperscript{th} percentile for AGA and LGA infants and $\geq$ 10\textsuperscript{th} percentile for age for SGA infants (13, 14). Infants whose weight for length $>$ 90\textsuperscript{th} percentile of the WHO standard were defined as at risk of overweight (13, 14).

**Statistical analyses**

Measurement values were included in analyses only if the original date of visits were within two weeks around the specific follow-up points. Those measurement values beyond mean $\pm$ 3 standard deviation (SD) were removed as outliers. Demographics and clinical characteristics were described as mean and SD for continuous variables and absolute numbers with percentages for categorical variables. Growth measurements of our population and the WHO standards were compared using $t$-test for each follow-up time point. Generalized estimating equation (GEE) model was used to regression trajectory trends of these growth measurements over time, and growth velocity defined as the z-score change over the periods (15, 16) using the lincom function. Gestational age, gender, birth weight z-score, and intrauterine growth status was adjusted as covariates. Stata 16.0 software (Stata Corp, College Station, TX, USA) was used for all the statistical analyses, and the significance level was set at 5% (two-tailed). Figures were drawn using GraphPad Prism 8.0 for Windows (GraphPad Software, La Jolla California, USA).

**Results**

**Clinical characteristics**

A total of 10705 preterm infants met the inclusion criteria. Among them, 80 infants without any follow-up measurement and one infant missing the birth information were excluded. Finally, 10624 infants were included in the study, with gestational age 35.0$\pm$1.8 weeks (rang 24$^{+5}$ -36$^{+6}$ weeks) and birth weight 2463$\pm$520g. Basic characteristics were shown in Table 1. Among all preterm infants, the majority were late preterm infants (>34 weeks of gestation, 82.7%) and AGA infants (86.0%). Over 75% of infants had highly educated parents (one of the parents received an education in college or above). The body weight z-score was 0.04$\pm$0.91 at birth.

**Growth of preterm infants from CA 40 weeks to CA 24 months**

As shown in Figure 1 and Additional file 1, body weight increased 7.90 kg in males and 7.72 kg in females from CA 40 weeks to CA 24 months. The mean increment in length/height was 33.2 cm and 33.4 cm for males and females, respectively. All growth parameters in our study population were significantly above the WHO standards, especially in weight (all P-values $<$0.001). Growth appears to be faster in male preterm infants than female during the first two years of life.
Table 2 showed an estimated change of z-scores (growth velocities) during the six time periods after adjustment. From CA 40 weeks to 3 months, z-score of body weight and length/height increased significantly by 0.08 \([95\% \text{ confidence interval (CI)}: 0.06-0.10]\) and 0.07 \([95\% \text{ CI: 0.04-0.09}]\), respectively (all \(P\)-values <0.001). After that, z-score of body weight declined significantly among periods from CA 3 to 18 months (all \(P\)-values <0.001), while with an exception for the change from CA 18 to 24 months \((P=0.071)\). For length/height, the growth velocity also showed a declining trend from CA 6 to 18 months (all \(P\)-values <0.001), while remaining stable from CA 3 to 6 months and from CA 18 to 24 months \((P>0.05)\). Some covariates, including gestational age, birth weight, gender, and intrauterine growth status, showed significant contributions in growth. (Additional file 2).

**Catch-up growth and risk of overweight**

Figure 2A showed the catch-up growth of preterm infants. We found that 92.7% and 90.0% of AGA/LGA infants achieved catch-up growth in weight and length/height before two years old. Most catch-up growth (94.6% in weight and 90.1% in length/height) occurred before CA 3 months. Regarding SGA infants, the proportion achieved catch-up growth (>10th percentile of the WHO standards) reached 90.3% in weight and 87.3% in length/height before CA 24 months. The proportion of catch-up growth in SGA infants kept increasing but much lower than that in AGA/LGA infants, especially before CA 12 months.

The risk of overweight appeared accompanied by catch-up growth (Figure 2B). At CA 40 weeks, 20.6% of infants were at risk of overweight. This proportion increased to the peak (25.6%) at CA 3 months, and then gradually decreased to 14.5% at CA 24 months. Risk of overweight even occurred in SGA infants, and the proportion ranged from 5.0% to 15.1% during the first two years of life. The proportion of infants with risk of overweight was significantly higher in LGA infants than that in AGA and SGA infants. Especially at CA 3 months, up to 39.4% of LGA infants were at risk of overweight.

**Growth of SGA, AGA, and LGA preterm infants**

Figure 3 showed z-scores of body weight and length/height in SGA, AGA, and LGA infants. Differences between these subgroups gradually decreased during the first two years of life.

For SGA infants, body weight and length/height z-scores were significantly lower than the WHO standards by 0.83±1.23 and 1.06±1.27 at CA 40 weeks. From CA 40 weeks to CA 24 months, these z-scores showed overall increasing trends, with the mean of z-score increasing by 0.78 in weight and 1.04 in length/height. When CA 24 months, these measurements (body weight z-score=-0.05 and length/height z-score=-0.02, Additional file 3) were closed to the mean level of WHO standard (z-score=0). The period with the fastest growth velocity was from CA 40 weeks to 3 months, weight z-score increased by 0.37 \([95\% \text{ CI: 0.28-0.45, \(P\)-value<0.001}]\) and length/height z-score increased by 0.37 \([95\% \text{ CI: 0.16-0.49, \(P\)-value <0.001}]\) (Table 3).

For AGA infants, the means of body weight and length were overall above the WHO standards from CA 40 weeks to 24 months (Figure 3 and Additional file 3). Z-score increased significantly by 0.08 \([95\% \text{ CI: 0.07-0.10}]\).
0.11) and 0.07 (95%CI 0.05-0.10) from CA 40 weeks to 3 months in body weight and length/height, respectively (all $P$-values<0.001). After that, z-scores of measurements showed overall declining trends until CA 24 months (Table 3).

For LGA infants, z-score of these measurements showed overall declining trends during the first two years (Table 3). From CA 40 weeks to 24 months, the mean of z-scores declined by 0.96 in weight and 0.87 in length/height, respectively (Additional file 3). Z-score of body weight declined significantly from CA 40 weeks to 9 months (all $P$-values <0.001) and from CA 12 to 18 months (decline by 0.24, 95%CI=-0.33- -0.15, $P$-value <0.001). Length/height z-scores also showed declining trends from CA 40 weeks to 3 months (decline by 0.29, 95%CI=-0.38- -0.20, $P$-value <0.001) and from CA 6 to 18 months (all $P$-values <0.001) (Table 3).

**Discussion**

This study provides evidence on the growth trajectory during the first two years of life in a large Chinese preterm population, showing that the body weight and length/height were overall higher than the WHO standards. Over 90% of AGA/LGA infants and over 85% of SGA infants achieved catch-up growth before CA 24 months. It demonstrated a trend of “catch-up” growth in SGA infants and a trend of “catch-down” growth in LGA infants. However, over a quarter of infants had been at risk of overweight as early as CA 3 months, and this proportion reached 39.4% in LGA infants. To date, we are the first reporting early overweight risk accompanying catch-up growth in the Chinese preterm infant population.

Our study noticed that growth trajectories of preterm infants were consistent over the WHO standards from CA 40 weeks to CA 24 months, especially for weight. Recent studies in Chinese population also found that growth rate in preterm infants was higher than that in term infants during the first year of life (17, 18). Several possible reasons might explain this phenomenon. Firstly, we believed that rapid growth is directly related to the childrearing practice of their parents, giving their preterm babies more care and feeding to make up the low birth weight. Besides, the “One Child” policy in China before 2016 might be another explanation. Parents and caregivers devote more effort to their only child among these people. A point that the heavier the baby is, the healthier he/she will be is widely accepted (18).

Catch-up growth was important for preterm infants to reduce the risk of stunning and achieve a better neurodevelopment outcome in later life (19–21), especially to SGA infants who had a higher risk of growth retardation and delayed development during infancy and childhood (22, 23). Olbertz et al.’s study showed that few SGA infants could achieve catch-up growth after age two (24). Currently, no consensus has reached on which catch-up growth pattern is optimal for preterm infants (25–27). In our study, most AGA/LGA infants achieved catch-up growth before the first three months. Nevertheless, it occurred lately in other studies, at 6 months or 11–12 months (28, 29). The difference in later outcomes between early and later achieving catch-up growth is unclear. Further study is needed to answer this question. In addition, we found that it took more time for SGA preterm infants to achieve catch-up growth than AGA/LGA infants. Early aggressive nutrition strategy might be necessary for SGA infants to timely
achieve the optimal catch-up growth and healthy development, which is in line with a similar point in previous studies (23, 30).

One of our main findings was that the risk of overweight accompanying catch-up growth in this Chinese preterm infant population, and over a quarter of preterm infants were at risk of overweight as early as CA 3 months. Furthermore, the risk of overweight in LGA infants was even higher and up to 40% at CA 3 months. Previous studies showed that excessive weight gain during early life was associated with increased overweight or obesity in childhood (31), and weight gain too fast in infancy was linked with a higher prevalence of type 2 diabetes and cardiovascular disease in adulthood (32–35). Therefore, controlling the risk of overweight in preterm infants at the same time of promoting optimal catch-up growth is becoming an issue and a challenge in primary child healthcare practice, especially for SGA and LGA infants. The optimal pattern of infant growth is likely to depend on different risk–balance considerations in different populations and one size might not fit all (36).

This study has some strengths. Firstly, this study has the largest sample size of Chinese preterm infant population compared with published reports. Additionally, the study population was from a community-based childcare network. These features make our findings generalizable for other developing metropolises. Secondly, the WHO standards were used to evaluate the growths makes this study more comparable with studies in other populations.

The present study also has some limitations. Firstly, missing data were inevitable, especially in a routine childcare database. For example, only 2824 (26.4%) preterm infants complete the follow-up at CA 24 months, and most of them (2562/2824, 90.7%) were late preterm infants (gestational age > 34 weeks). Thus, overestimate may exist. Secondly, since the feeding information was not available, we had no chance to explore the effects of different feeding strategies on the growth pattern of preterm infants. Further prospective studies were still needed.

Conclusions

Body weight and length/height of preterm infants in the Chinese community population are above the WHO standards during the first two years of life. Although over 85% of preterm infants achieved catch-up growth before two years old, the risk of overweight has existed as early as CA 3 month. More attention is needed to promote proper catch-up growth in preterm infants for better long-term health.

List Of Abbreviations

AGA, appropriate for gestational age; CA, corrected age; CI, confidence interval; GEE, generalized estimating equation; LGA, large for gestational age; LMS, Lambda-Mu-Sigma; NICU, neonatal intensive care unit; PMA, postmenstrual age; SD, standard deviation; SGA, small for gestational age infants; WHO, World Health Organization.
Declarations

Ethics approval and consent to participate

The institutional scientific research department approved the analysis protocol.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

This work was financially supported by the National Natural Science Foundation of China (Grant No. 81273168).

Authors’ contributions

WY and YL conceived the study and guide the data analysis. JH and YJ drafted the manuscript and analyzed the data. YiZ and XC contributed to analyzing data and making charts. JuH, YuZ, and YingZ collected and controlled the quality of data. All authors were involved in writing the paper, interpreting the results, and had final approval of the submitted and published versions.

Acknowledgements

The authors thank all the nurses and technicians of Maternal and Child Health Care Network in Minhang District for collecting data who were not included in the author list.

References

1. Chawanpaiboon S, Vogel JP, Moller AB, Lumbiganon P, Petzold M, Hogan D, et al. Global, regional, and national estimates of levels of preterm birth in 2014: a systematic review and modelling analysis. Lancet Glob Health. 2019;7(1):e37-e46.

2. Howson CP, Kinney MV, McDougall L, Lawn JE. Born too soon: preterm birth matters. Reprod Health. 2013;10 Suppl 1:S1.
3. Streimish IG, Ehrenkranz RA, Allred EN, O'Shea TM, Kuban KC, Paneth N, et al. Birth weight- and fetal weight-growth restriction: impact on neurodevelopment. Early Hum Dev. 2012;88(9):765-71.

4. Dusick AM, Poindexter BB, Ehrenkranz RA, Lemons JA. Growth failure in the preterm infant: can we catch up? Semin Perinatol. 2003;27(4):302-10.

5. Roberts G, Cheong J, Opie G, Carse E, Davis N, Duff J, et al. Growth of extremely preterm survivors from birth to 18 years of age compared with term controls. Pediatrics. 2013;131(2):e439-45.

6. Bocca-Tjeertes IF, van Buuren S, Bos AF, Kerstjens JM, Ten Vergert EM, Reijneveld SA. Growth of preterm and full-term children aged 0-4 years: integrating median growth and variability in growth charts. J Pediatr. 2012;161(3):460-5 e1.

7. Bocca-Tjeertes IF, Kerstjens JM, Reijneveld SA, de Winter AF, Bos AF. Growth and predictors of growth restraint in moderately preterm children aged 0 to 4 years. Pediatrics. 2011;128(5):e1187-94.

8. Belfort MB, Gillman MW, Buka SL, Casey PH, McCormick MC. Preterm infant linear growth and adiposity gain: trade-offs for later weight status and intelligence quotient. J Pediatr. 2013;163(6):1564-9 e2.

9. Singhal A. Should We Promote Catch-Up Growth or Growth Acceleration in Low-Birthweight Infants? Nestle Nutr Inst Workshop Ser. 2015;81:51-60.

10. Ekelund U, Ong KK, Linne Y, Neovius M, Brage S, Dunger DB, et al. Association of weight gain in infancy and early childhood with metabolic risk in young adults. J Clin Endocrinol Metab. 2007;92(1):98-103.

11. Ahn Y, Sohn M, Jun Y, Lee S. Growth patterns and their implications for preterm infants in a culture of rapid modernization. J Child Health Care. 2013;17(3):242-52.

12. Fenton TR, Nasser R, Eliasziw M, Kim JH, Bilan D, Sauve R. Validating the weight gain of preterm infants between the reference growth curve of the fetus and the term infant. BMC Pediatr. 2013;13:92.

13. The WHO Child Growth Standards. www.who.int/childgrowth/standards/en/.

14. Editorial board of the Chinese journal of pediatrics, The Subspecialty Groups of Child Health Care, The Society of Pediatrics, Chinese Medical Association Neonatology group, The Society of Pediatrics, Chinese Medical Association. Post-discharge feeding recommendations for preterm or low-birth-weight infants. Chinese Journal of Pediatrics 2016;54(1):6-12.

15. Fenton TR, Chan HT, Madhu A, Griffin IJ, Hoyos A, Ziegler EE, et al. Preterm Infant Growth Velocity Calculations: A Systematic Review. Pediatrics. 2017;139(3).

16. Simon L, Hanf M, Frondas-Chauty A, Darmaun D, Rouger V, Gascoin G, et al. Neonatal growth velocity of preterm infants: The weight Z-score change versus Patel exponential model. PLoS One. 2019;14(6):e0218746.

17. Zhang L, Li Y, Liang S, Liu XJ, Kang FL, Li GM. Postnatal length and weight growth velocities according to Fenton reference and their associated perinatal factors in healthy late preterm infants during birth to term-corrected age: an observational study. Ital J Pediatr. 2019;45(1):1.
18. Kang L, Wang H, He C, Wang K, Miao L, Li Q, et al. Postnatal growth in preterm infants during the first year of life: A population-based cohort study in China. PLoS One. 2019;14(4):e0213762.

19. Cooke RJ. Postnatal growth and development in the preterm and small for gestational age infant. Nestle Nutr Workshop Ser Pediatr Program. 2010;65:85-95; discussion 6-8.

20. Raaijmakers A, Allegaert K. Catch-Up Growth in Former Preterm Neonates: No Time to Waste. Nutrients. 2016;8(12).

21. Victora CG, Barros FC, Horta BL, Martorell R. Short-term benefits of catch-up growth for small-for-gestational-age infants. Int J Epidemiol. 2001;30(6):1325-30.

22. Clayton PE, Cianfarani S, Czernichow P, Johannsson G, Rapaport R, Rogol A. Management of the child born small for gestational age through to adulthood: a consensus statement of the International Societies of Pediatric Endocrinology and the Growth Hormone Research Society. J Clin Endocrinol Metab. 2007;92(3):804-10.

23. Kesavan K, Devaskar SU. Intrauterine Growth Restriction: Postnatal Monitoring and Outcomes. Pediatr Clin North Am. 2019;66(2):403-23.

24. Olbertz DM, Mumm R, Wittwer-Backofen U, Fricke-Otto S, Pyper A, Otte J, et al. Identification of growth patterns of preterm and small-for-gestational age children from birth to 4 years - do they catch up? J Perinat Med. 2019;47(4):448-54.

25. Villar J, Giuliani F, Barros F, Roggero P, Coronado Zarco IA, Rego MAS, et al. Monitoring the Postnatal Growth of Preterm Infants: A Paradigm Change. Pediatrics. 2018;141(2).

26. Singhal A, Fewtrell M, Cole TJ, Lucas A. Low nutrient intake and early growth for later insulin resistance in adolescents born preterm. Lancet. 2003;361(9363):1089-97.

27. Fanaro S. Which is the ideal target for preterm growth? Minerva Pediatr. 2010;62(3 Suppl 1):77-82.

28. Zhao R, Xu L, Wu ML, Huang SH, Cao XJ. Maternal pre-pregnancy body mass index, gestational weight gain influence birth weight. Women Birth. 2018;31(1):e20-e5.

29. Gong YH, Ji CY, Shan JP. A longitudinal study on the catch-up growth of preterm and term infants of low, appropriate, and high birth weight. Asia Pac J Public Health. 2015;27(2):NP1421-31.

30. Morag I, Stern Levkovitz O, Siman-Tov M, Frisch M, Pinhas-Hamiel O, Strauss T. Postnatal Growth Disadvantage of the Small for Gestational Age Preterm Twins. Nutrients. 2018;10(4).

31. Vohr BR, Heyne R, Bann CM, Das A, Higgins RD, Hintz SR. Extreme Preterm Infant Rates of Overweight and Obesity at School Age in the SUPPORT Neuroimaging and Neurodevelopmental Outcomes Cohort. J Pediatr. 2018;200:132-9 e3.

32. Stettler N, Zemel BS, Kumanyika S, Stallings VA. Infant weight gain and childhood overweight status in a multicenter, cohort study. Pediatrics. 2002;109(2):194-9.

33. Stettler N, Kumanyika SK, Katz SH, Zemel BS, Stallings VA. Rapid weight gain during infancy and obesity in young adulthood in a cohort of African Americans. Am J Clin Nutr. 2003;77(6):1374-8.

34. Embleton ND, Korada M, Wood CL, Pearce MS, Swamy R, Cheetham TD. Catch-up growth and metabolic outcomes in adolescents born preterm. Arch Dis Child. 2016;101(11):1026-31.
35. Cameron N, Pettifor J, De Wet T, Norris S. The relationship of rapid weight gain in infancy to obesity and skeletal maturity in childhood. Obes Res. 2003;11(3):457-60.

36. Singhal A. Long-Term Adverse Effects of Early Growth Acceleration or Catch-Up Growth. Ann Nutr Metab. 2017;70(3):236-40.

Tables
# Table 1
Characteristics of all preterm infants [mean ± SD or n(%)]

| Characteristics                              | Total (n = 10624) |
|----------------------------------------------|-------------------|
| Male, n (%)                                  | 5895 (55.5)       |
| Primiparity, n (%)                           | 5955 (56.1)       |
| Gestational age, weeks                       | 35.0 ± 1.8        |
| Birth weight, g                              | 2463 ± 520        |
| Birth weight z-score\(^a\)                   | 0.04 ± 0.91       |
| Caesarean section, n (%)                     | 6376 (60.0)       |
| Maternal age, years                          | 29.7 ± 4.9        |
| Paternal age, years                          | 31.7 ± 5.9        |
| ≥ college (maternal education)               | 6945 (76.6)       |
| ≥ college (paternal education)               | 7102 (78.3)       |
| Subgroup by gestational age                  |                   |
| <28 weeks, n (%)                             | 40 (0.4)          |
| 28 ~ 31\(^+6\) weeks, n (%)                 | 642 (6.0)         |
| 32 ~ 33\(^+6\) weeks, n (%)                 | 1161 (10.9)       |
| 34 ~ 36\(^+6\) weeks, n (%)                 | 8781 (82.7)       |
| Subgroup by birth weight                     |                   |
| <1000 g, n (%)                               | 35 (0.3)          |
| 1000~1499 g, n (%)                           | 437 (4.1)         |
| 1500~2499 g, n (%)                           | 4810 (45.3)       |
| >2500 g, n (%)                               | 5342 (50.3)       |
| Intrauterine growth status                   |                   |
| SGA, n (%)                                   | 681 (6.4)         |
| AGA, n (%)                                   | 9141 (86.0)       |

\(^a\) Z-scores were computed according to the Fenton Preterm Infants Growth Charts;

SD, standard deviation; SGA, small for gestational age; AGA, appropriate for gestational age; LGA, large for gestational age.
| Characteristics                  | Total (n = 10624) |
|--------------------------------|------------------|
| LGA, n (%)                     | 802 (7.6)        |

\(^a\) Z-scores were computed according to the Fenton Preterm Infants Growth Charts;
SD, standard deviation; SGA, small for gestational age; AGA, appropriate for gestational age; LGA, large for gestational age.

Table 2
Change of z-scores in preterm infants from CA 40 weeks to 24 months

| Corrected age       | Z-score change of weight | Z-score change of length/height |
|---------------------|---------------------------|---------------------------------|
|                     | Difference (95%CI)\(^a\) | \(P\)-value | Difference (95%CI)\(^a\) | \(P\)-value |
| Overall             | -                         | < 0.001   | -                         | < 0.001 |
| CA 40 weeks-3 months| 0.08 (0.06–0.10)          | < 0.001   | 0.07 (0.04–0.09)          | < 0.001 |
| CA 3–6 months       | -0.07 (-0.09– -0.05)      | < 0.001   | 0.01 (-0.01-0.04)         | 0.310   |
| CA 6–9 months       | -0.10 (-0.12– -0.08)      | < 0.001   | -0.07 (-0.10- -0.05)      | < 0.001 |
| CA 9–12 months      | -0.08 (-0.10- -0.06)      | < 0.001   | -0.09 (-0.12- -0.07)      | < 0.001 |
| CA 12–18 months     | -0.17 (-0.20- -0.15)      | < 0.001   | -0.11 (-0.14- -0.08)      | < 0.001 |
| CA 18–24 months     | -0.02 (-0.06-0.00)        | 0.071     | 0.00 (-0.03-0.04)         | 0.918   |

\(^a\) Gestational age, gender, birth weight z-score, and intrauterine growth status were adjusted;
CA, corrected age; CI, confidence interval.
Table 3
Growth velocities of SGA, AGA, and LGA preterm infants from CA 40 weeks to 24 months

| Subgroup | Corrected age | Weight |   | Length/height |   |
|----------|---------------|--------|---|----------------|---|
|          |               |        |   | Difference (95%CI)<sup>a</sup> | P-value | Difference (95%CI) | P-value |
|          |               |        |   |                |        |                |        |
| SGA      | Overall       | -      |   |                | < 0.001 |                | < 0.001 |
|          | CA 40 weeks- 3 months | 0.37 (0.28–0.45) | < 0.001 | 0.37 (0.16–0.49) | < 0.001 |
|          | CA 3–6 months | 0.14 (0.06–0.23) | 0.001 | 0.27 (0.15–0.38) | < 0.001 |
|          | CA 6–9 months | 0.05 (-0.03-0.15) | 0.243 | 0.07 (-0.06-0.19) | 0.278 |
|          | CA 9–12 months | 0.04 (-0.06-0.13) | 0.433 | -0.00 (-0.13-0.13) | 0.992 |
|          | CA 12–18 months | -0.10 (-0.20-0.00) | 0.057 | 0.03 (-0.10-0.17) | 0.640 |
|          | CA 18–24 months | 0.15 (0.01–0.29) | 0.035 | 0.25 (0.07–0.44) | 0.008 |
| AGA      | Overall       | -      |   |                | < 0.001 |                | < 0.001 |
|          | CA 40 weeks- 3 months | 0.08 (0.07–0.11) | < 0.001 | 0.07 (0.05–0.10) | < 0.001 |
|          | CA 3–6 months | -0.07 (-0.09-0.05) | < 0.001 | 0.00 (-0.02-0.03) | 0.751 |
|          | CA 6–9 months | -0.10 (-0.12-0.08) | < 0.001 | -0.07 (-0.10-0.05) | < 0.001 |
|          | CA 9–12 months | -0.09(-0.11-0.07) | < 0.001 | -0.10 (-0.12-0.07) | < 0.001 |
|          | CA 12–18 months | -0.17 (-0.20-0.15) | < 0.001 | -0.12 (-0.14-0.09) | < 0.001 |
|          | CA 18–24 months | -0.03 (-0.06-0.00) | 0.032 | -0.00 (-0.04-0.04) | 0.999 |
| LGA      | Overall       | -      |   |                | < 0.001 |                | < 0.001 |
|          | CA 40 weeks- 3 months | -0.22(-0.29-0.14) | < 0.001 | -0.29 (-0.38-0.20) | < 0.001 |

<sup>a</sup> Gestational age, gender, birth weight z-score, and intrauterine growth status were adjusted;

SGA, small for gestational age; AGA, appropriate for gestational age; LGA, large for gestational age; CA, corrected age; CI, confidence interval.
| Gestational Age | Mean Difference (95% CI) | p Value | Lower 95% CI of Difference |
|-----------------|-------------------------|---------|---------------------------|
| CA 3–6 months   | -0.21 (-0.29-0.14)      | < 0.001 | -0.08 (-0.17-0.01)        |
| CA 6–9 months   | -0.20 (-0.29-0.12)      | < 0.001 | -0.18 (-0.27-0.08)        | < 0.001 |
| CA 9–12 months  | -0.07 (-0.16-0.02)      | 0.129   | -0.13 (-0.23-0.03)        | 0.009   |
| CA 12–18 months | -0.24 (-0.33-0.15)      | < 0.001 | -0.13 (-0.24-0.03)        | 0.012   |
| CA 18–24 months | -0.03 (-0.15-0.09)      | 0.667   | -0.08 (-0.22-0.05)        | 0.218   |

*Gestational age, gender, birth weight z-score, and intrauterine growth status were adjusted; SGA, small for gestational age; AGA, appropriate for gestational age; LGA, large for gestational age; CA, corrected age; CI, confidence interval.*
Figure 1

Growth trajectories of preterm infants from CA 40 weeks to 24 months (A) Growth trajectory of body weight in preterm infants and the mean level of the WHO standard. (B) Growth trajectory of length/height in preterm infants and the mean level of the WHO standards. The mean of body weight increased 7.90 kg in males and 7.72 kg in females from CA 40 weeks to 24 months. The mean increment in length/height was 33.2 cm in males and 33.4 cm in females, respectively. Compared with the WHO standards, growth trajectories in this study were much higher for both males and females, especially in weight. Growth in males was faster than that in females. CA, corrected age; WHO, World Health Organization.
A. Catch-up growth

- **Weight-AGA/LGA**
- **Length/height-AGA/LGA**
- **Weight-SGA**
- **Length/height-SGA**

- **CA**: 40w, 3m, 6m, 9m, 12m, 15m, 18m, 21m, 24m

B. Risk of overweight

- **All**
- **SGA**
- **AGA**
- **LGA**

- **CA**: 40w, 3m, 6m, 9m, 12m, 15m, 18m, 21m, 24m
Catch-up growth and risk of overweight in preterm infants (A) Catch-up growth of preterm infants. Most AGA/LGA infants (92.7% in weight, 90.0% in length/height) achieved catch-up growth at CA 24 months. The proportion increased significantly from CA 40 weeks to CA 3 months (from 90.2% to 94.6% in weight and from 85.7% to 90.1% in length/height). For SGA infants, the proportion of catch-up growth kept increasing but was much lower than that in AGA/LGA infants, especially before CA 12 months. At CA 24 months, 90.3% and 87.3% of SGA infants achieved catch-up growth in weight and length/height, respectively. (B) Risk of overweight in preterm infants. At CA 40 weeks, 20.6% of infants were at risk of overweight. This proportion increased to the peak (25.6%) at CA 3 months, and then gradually decreased to 14.5% at CA 24 months. The risk of overweight also occurred in SGA infants, and the proportion ranged from 5.0% to 15.1% during the first two years of life. The incidence of risk of overweight in LGA infants was higher than that in AGA and SGA. CA, corrected age; SGA, small for gestational age; AGA, appropriate for gestational age; LGA, large for gestational age.
Figure 3

A

Weight

Z-score

CA

40w 3m 6m 9m 12m 15m 18m 21m 24m

SGA
AGA
LGA

B

Length/height

Z-score

CA

40w 3m 6m 9m 12m 15m 18m 21m 24m

SGA
AGA
LGA

Figure 3
Growth trajectories of LGA, AGA, and SGA preterm infants from CA 40 weeks to 24 months (A) Growth of body weight in LGA, AGA, and SGA infants during the first two years. (B) Growth of length/height in LGA, AGA, and SGA infants during the first two years. All SGA infants showed catch-up growth trend in the first two years of life. From CA 40 weeks to CA 24 months, the mean z-score of SGA infants increased 0.78 in weight, 1.04 in length/height. For AGA infants, z-scores declined slightly by 0.29 in weight, and 0.13 in length/height. LGA infants showed trends of decline, with the mean z-scores declined by 0.96 in weight and 0.87 in length/height. CA, corrected age; SGA, small for gestational age; AGA, appropriate for gestational age; LGA, large for gestational age.

** Supplementary Files **

This is a list of supplementary files associated with this preprint. Click to download.

- Additionalfiles.pdf