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Growth Trajectory at 24 Months of Preterm Infants after Discharge: A Longitudinal Study in Indonesia

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ABSTRACT

Maintaining optimal growth of preterm infants after hospital discharge remains a challenge. There has been no data on the long-term growth trajectory of preterm infants in Indonesia. We aimed to describe the growth trajectory of preterm infants up to 24 months of corrected age and its variation among gestational age groups. A longitudinal study was conducted in Cipto Mangunkusumo Hospital, Jakarta from 2018 to 2020. All preterm infants who were discharged during the study period were included. Growth trajectory analysis used weight-for-age (WAZ), length-for-age (LAZ), and weight-for-length (WFL) z-score of 3-month time intervals across gestational age groups using repeated measure ANOVA and generalized estimating equation regression. Length trajectory was specifically reported as a stunted proportion. Among 306 preterm infants included, most were moderate preterm (49.67%) and low birth weight (69.93%). Overall WAZ at 0 month were in the median of the curve, then decreased at 3 months, but consistently increased slowly until 24 months. The WAZ trends were unique across gestational age groups, but statistically similar ($p = 0.263$). The proportion of stunted gradually decreases to 13.40% at 24 months, mostly among the moderate preterm group in the first 6 months ($p<0.001$) but then becomes similar at 24 months. All subjects were in the normal range for WFL but had variations in trends across gestational age groups ($p<0.001$). Growth trajectory differed between weight, length, and weight-for-length in the first 24 months and varied among gestational age groups. Close follow-up is crucial to ensure optimal growth after NICU discharge.

Abbreviation:

AGA = appropriate for gestational age

ANOVA = analysis of variance

CI = confidence interval

LAZ = length-for-age

NICU = neonatal intensive care unit

WAZ = weight-for-age

WFL = weight-for-length

WHO = World Health Organization

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Introduction

Preterm birth has become the leading cause of death and contributes significantly to long-term morbidities worldwide.[1] Indonesia is estimated as the top five countries with the highest preterm birth rate, about 10.4 per 100 live births or nearly 550,000 preterm births each year, contributing 3.5% of global preterm births.[2, 3] Maternal nutrition-related factors are still major risk factors for preterm birth in Indonesia.[4-7]

Advances in neonatal care management in Indonesia have improved the survival rate of preterm infants as seen in other countries.[8-10] However, concern about suboptimal postnatal growth and development among this high-risk population remains, especially after discharge from the hospital, where growth monitoring is often either neglected or forgotten; thus, close follow-up is a necessary strategy.[11, 12] Previous cohorts in Asian developing countries reported a significant delay in weight, length, and head circumference of preterm infants after discharge from the Neonatal Intensive Care Unit (NICU).[13-15] Growth after discharge in this population may be influenced by baseline complexity of comorbidities during NICU stay, nutritional status at discharge, post-discharge nutrition, and also socioeconomic condition.

Continuous adequate nutrition and stimulation after discharge are essential not only for preterm infants' survival but also for physical growth, cognitive and mental development, and later productivity across the entire life span.[16, 17] Poor postnatal weight gain in preterm infants has been shown to harm neurodevelopment as physical growth during the first 1000 days of life is an important proxy for organ development, especially the brain's maturation, myelinization, and synaptogenesis. Therefore, NICU graduates need to catch up with growth by 24 months of corrected age. However, nutrition therapy had to be handled delicately because rapid postnatal growth crossing weight centiles might lead to insulin resistance and metabolic syndromes.[18, 19]

There has been no data on the long-term growth trajectory of preterm infants in Indonesia. This study is the first longitudinal study in Indonesia that follows preterm infant growth after discharge. This study aimed to describe the growth trajectory of preterm infants discharged from NICU until 24 months of corrected age and its variation among gestational age groups. This work also aims to give insights and guide clinicians in the growth of preterm infants to prevent long-term consequences related to preterm birth in Indonesia.

Methods

Study design and setting

This is a longitudinal study that repeatedly measure infants growth parameters from NICU discharge until 24 months of corrected age. This study was conducted from January 2018 to December 2020 in the Cipto Mangunkusumo Hospital, Jakarta, a tertiary-level referral hospital. Cipto Mangunkusumo Hospital provide the most advance neonatal care and also a center for neonatologist training center in Indonesia. This observational study was conducted according to the guidelines laid down in the Declaration of Helsinki. This study was approved by the Research Ethic Committee of Faculty of Medicine, Universitas Indonesia, Jakarta.

Study population

Eligibility criteria were preterm infants (gestational age <37 weeks) discharged from NICU during the study period. Exclusion criteria were infants with severe congenital anomalies or syndromes, conditions that interfere with anthropometric parameters (e.g., hydrops and hydrocephalus), large-for-gestational age (birth weight > 90th percentile), small-for-gestational age (birth weight < 10th percentile), intrauterine growth restriction (as reported by obstetrician), or having anomalies related to feeding difficulty (such as cleft lip or laryngomalacia) and living outside Jakarta. At the time of subject recruitment, almost 30% infants were classified as small-for-gestational age or having intrauterine growth restriction.

Assessment and follow-up

The gestational age was determined by obstetric ultrasound examination. We classified preterm infants based on WHO subcategories: late preterm (34 to <37 weeks), moderate preterm (32 to <34 weeks), very preterm (28 to <32 weeks), and extreme preterm (<28 weeks). Baseline characteristic data, including neonatal sepsis, hemodynamically significant persistent ductus arteriosus, intraventricular hemorrhage, and necrotizing enterocolitis, were taken to describe the conditions and treatment of infants during intensive care in the NICU.

Patients were discharged if at least 36 weeks of corrected age and had appropriate weight gain. After discharge, parents were asked to visit pediatric outpatient clinic either in our hospital or nearest hospital. We contacted parents by phone or text message regularly to remind them to visit outpatient clinic. According to Indonesian guidelines, regular visits are recommended each month in the first six months, then every three months until 24 months of corrected age. Subjects might come earlier if asked by the pediatrician. We specifically obtained data at 0, 3, 6, 9, 12, 15, 18, 21, and 24 months of corrected age with a tolerance of ±2 weeks for each time point. Any anthropometric examination done outside our hospital were recorded according to data in the medical record as reported by parents or pediatricians.

Anthropometric examination (weight and height) was carried out by a specially-trained nurse under the supervision of a physician using calibrated tools. The measurement was then plotted on the WHO Child Growth Standard weight-for-age curve (WAZ), height-for-age curve (HAZ), and weight-for-length curve (WFL). Data regarding anthropometric measurements were collected by research assistants from patient medical records.

We also provide the type of nutrition at discharge and during follow-up. The type of enteral nutrition consists of breastmilk, human milk fortifier, and formula (preterm formula (0.81 kcal/ml), standard formula (0.67 kcal/ml), high-density formula (1 kcal/ml), or hydrolyzed or amino acid-based formula).

Outcomes

The main outcome of interest in this study are trends of WAZ and WFL and also the proportion of stunted infants (defined as HAZ below -2 z-score according to the WHO Child Growth Standard). We also analyzed the differences of trends and proportion across gestational age groups.

Data analysis

Data were extracted from an integrated online database and rearranged based on the time of clinic visit to construct a longitudinal data presentation. For standardization, weight measurement was converted from grams and centimeter to z-score of WAZ, HAZ, and WFL using ‘zanthro’ command in STATA. Outlier data (>99th or <1st centile on the growth chart) were imputed to the average values based on gestational age groups. A growth trajectory was constructed by connecting the median z-score value of each time interval with a linear line. We also provide the 95% confidence interval (CI) data of each timepoints. The proportion of infants who were stunted were presented as number and percentage. To optimize analysis, a

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subgroup merge will be conducted if a gestational age group were having lower than 30 participants.

Adjustment for potential confounders (calorie intake and parental stimulation) was not necessary as nutrition and stimulation recommendations were personalized for each subject during an outpatient visit. A brief 24-hours food recall is a standard procedure to evaluate the adequacy of caloric intake. Any intervention for faltering growth might include nutrient intake by using high-dense caloric formula, parental education of feeding rules, and any investigation for acute illness. An individual incomplete specific time interval data will be imputed according to gender and gestational age rather than excluded in order to minimize the risk of selection bias.

The difference in weight or length during the time interval was analyzed using repeated measure ANOVA, the difference between two time interval was analyzed using paired t-test or Wilcoxon test, while the difference in proportions was assessed using Chi-square or Fisher exact test. Analysis of trajectory trends between gestational age groups were conducted using generalized estimating equation regression. Based on the sample size calculation to estimate the prevalence of underweight, stunted, and malnutrition, a minimum of 300 subjects were required to achieve a power study of 80%. A p-value < 0.05 was considered statistically significant. Data analysis was done by using STATA v15.

Results

During the study period, 336 preterm infants were discharged from the neonatal unit, and 306 of them were eligible to participate in this study (**Figure 1**). The reason for exclusion was due to living outside Java Island. Almost two third were females, and the overall mean birth weight was 1804 (±415) g. Most of the infants were moderate preterm and had low birth weight. Causes of preterm birth were mostly due to preeclampsia and intrauterine infection.

The highest prevalence of comorbidities was neonatal sepsis, which accounted for 21.25%. Necrotizing enterocolitis was found in 11.25% of infants. At discharge, female had slightly higher weight, length, and weight-for-length z-score. **Table 1** shows the baseline characteristics of included subjects.

At the first six months of corrected age or before the introduction of solid foods, 70.4% of infants receive breastmilk (25.2% exclusive breastmilk while the rest is in combination with) and 32.8% among them had an additional human milk fortification. About 53% of infants received formula, mostly high-density calorie formula (1 kcal/ml) to support growth. The type of formula varied based on the pediatrician's nutritional assessment.

An observation of the weight trend was presented in three months interval, as seen in **Figure 2**. Overall WAZ at 0 month were in the median of the curve. A drop in z-score at 2-3 months (from z-score -0.16 to -1.22, $p<0.001$) was followed by a gradual increase to -0.87 at 9 months and finally to 0.38 at 24 months, higher than weight at 0 months ($p<0.001$).

We then analyzed the WAZ based on gestational age groups (**Figure 3**). Due to low number of extreme preterm, we merge very to extreme preterm into one group. All groups had a normal range of Z-score at 0 months and were found to have growth decrement in the first 3 months after birth, with the biggest decrease seen in the very to extreme preterm groups (decrease 2.44±0.14 z-score, $p<0.001$). After that, they all had an improvement in WAZ gain significantly from 3 months to 24 months. Interestingly, there were a second period of WAZ drop among very to extreme preterm at 6 to 9 months and among late preterm at 11-13 months. The late preterm and moderate preterm groups showed an earlier start of WAZ gain compared to the extreme to very preterm group. At 24 months, the WAZ of all groups were above the median of the curve: 0.28, 0.38, and 0.67 for late, moderate, and very to extreme preterm infants, respectively, ($p<0.001$). The overall different weight trajectory trends between gestational age groups were statistically not significant ($p = 0.263$).

In general, almost half (49.4%) of included infants were stunted at 3 months of corrected age. The percentage declined along with the growth of the infants, as shown in **Table 2**. The percentage of stunted infants (**Supplementary Figure 1**) was then decreased to 44.4%, 23.5%, 31.4%, 18.9%, and 13.4% at 6, 9, 12, 18, and 24 months, respectively ($p<0,001$).

Moderate preterm had the highest proportion of stunted at the first 6 months but then declined due to catch-up growth. At 12 months, the very to extreme preterm group had the highest proportion of stunted. The proportion differed over time ($p<0.001$) but at an equal proportion in 24 months ($p = 0.205$).

Using both weight and height information, we construct a graph of weight-for-length z-score for 24 months, displayed in **Figure 4.** During the follow-up period, regardless of the WAZ and stunted status, all infants were in the normal range of weight-for-length (between -2 and

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2 z-score) although we found a decrement during the 6 to 12 months period. The trends between gestational age groups were visually similar but statistically differ over time (p = <0.001) as seen in **Supplementary Figure 2**.

Discussion

This is the first longitudinal study in Indonesia to describe the growth trajectory of preterm infants after discharge until 24 months of corrected age. In sum, preterm infants had a decrement of WAZ during the first three months of corrected age and gained WAZ gradually until 24 months to meet the median of the curve. Almost half of them were categorized as stunted at discharge but gradually decreased at 24 months. All infants in this study had good growth trajectories as they were always in the normal range for weight-for-length z-score. We believe this result is an important finding in neonatal care, especially for developing countries. These results also suggested that close follow-up of preterm infants after NICU discharge is crucial as growth faltering might occur anytime during the first 24 months.

Some important note is that the survival rate of very and extreme preterm in Indonesia during the study period (2018-2020) is low. Our unpublished data reported 24.9% and 47.4% 1-month survival rates for extreme and very preterm, respectively. Survived infants tend to have fewer comorbidities, while procedures- and environment-related stressors during the critical phase strongly affect long-term outcomes.[20, 21] This might explain the higher WAZ and WFL of very to extreme preterm infants at 0 months of corrected age. However, they were all regressed into the mean at 24 months along with other gestational age groups.

The major challenge in conducting a longitudinal study in developing countries after discharge was encouraging parents to make regular visits, especially after 6 months of corrected age. Good communication should be made to inform parents regarding the importance of close follow-up, even in healthy ex-preterm infants as it could bring advantages to growth and development.[22] An optimal recommendation is a monthly visit during the first 24 months, but some reported a decreasing trend after 12 months.[23, 24] On the other hand, a multicentre study in Europe reported that parents' dissatisfaction with post-discharge healthcare delivery was high.[25] Otherwise, an over-visit might be a sign of parental anxiety.[26]

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In our hospital, enteral nutrition was started from the first day of life and advanced based on feeding tolerance. Aggressive total parenteral nutrition was given to infants born under 32 weeks of gestational age. Full feed target should be reached in 1 week, 1-2 weeks, or 2-3 weeks in late, moderate, and very to extreme preterm infants, respectively. Measurable factors related to malnutrition were hospital malnutrition (postnatal growth failure) that can occur before discharge; thus, nutrition during NICU stay is as important as post-discharge feeding practice.(27, 28) Complementary foods were commonly given at 6 months but can be started as early as 4 months, according to the growth and readiness of the infants. The WHO had recommended that infants should be exclusively breastfed for the first 6 months in order to achieve optimum growth and development.(29) The Indonesian Pediatric Society does not recommend starting complementary feeding before 4 months.

The weight trajectory was nearly a U-shaped with nadir point at 3 months and gradually increasing to 24 months. Similar to the result of this study, previous research in Minneapolis reported that weight was at the lowest point in 3-4 months corrected age (between z-score -1.0 and -1.5) and gradually increased until 24 months.(16) A cohort in India also showed a similar growth trajectory to our study.(14) Among infants <34 weeks and <1500 g, weight decreased from -2.3 at 0 months to -2.5 at 3 months, gradually increasing to -1.7 at 12 months. Weight z-score at 3 months was found to be an independent predictor of being underweight at 12 months (OR 4.34 95%CI 2.38-7.69).(14) On the other hand, a population-based study in China revealed the fastest period of catch-up growth was at the first 3 months of corrected age before the z-score fell.(30) Another study by Han et al reported an increase in weight at the first 3 months (+0.08 z-score) but then decreased until 24 months among AGA preterm infants.(31) During this period, a close follow-up is needed to ensure nutritional adequacy by adjusting calorie intake from breast milk or formula and also infant feeding practice by the caregiver. Half of preterm infants receive full formula feeding after 1 month of corrected age, but mostly below recommended energy intake.(32)

The growth trajectory after 3 months, according to the change in WAZ, was a follow-the-curve growth pattern (change in z-score between -0.67 and 0.67), which is an indicator of appropriate trends.(32, 33) Weight gain is still useful to evaluate growth in preterm infants.(34) However, rapid catch-up (change > 0.67 z-score) causes an early adiposity rebound and is related to obesity at 5 years.(33) Compared to term infants, preterm infants tend to have more body fat at term corrected age but lessened at 3 months.(35) It is debatable whether other parameters such as weight-for-length or body mass index will accurately present body composition in preterm infants.[36, 37] In this study, all infants were in a normal range for weight-for-length during the entire 24-month follow-up period.

Failure to regain weight in the first 3 months possibly caused the failure of length gain; as also reported previously.[38] Stunted cases in the first months of life were higher than in 24 months of corrected age. An increase in body length is quite constant during the first 24 months.[30] According to the WHO framework, stunting is a stunted case caused by impaired growth that is influenced by poor nutrition, repeated infection, and inadequate psychosocial stimulation, all of which can highly occur among preterm infants.[39] Data on stunted vary between studies. Gonzales-Garcia et al reported 15% of stunted at 24 months [40] while Mukhopadhyay et al reported 32% stunted at 12 months among very low birth weight infants.[14] Extremely low birth weight infants had a significant catch of height at 3 to 12 months and possibly had higher height at 24 months (z-score -0.8 compared to -1.7 for very preterm).[14] An interesting finding in this study was that the very-to-extreme preterm group had an increased proportion of stunted at 12 months, while the other preterm group had a declining trend. Further investigation is needed to evaluate any factors that contribute to the growth trends, such as timing of complementary feeding, total duration of receiving breastmilk, caregiver feeding practice, total daily caloric intake measurement, and parental stimulation. A possible explanation might be a transition to full solid foods without adequate caloric intake. An individualized evaluation should be made and account for parental/caregiver feeding behaviour, thus it would be difficult to conclude a single cause of this phenomenon.

The proportion of infants receiving breastmilk in our study was quite satisfactory as it became a common problem after discharge. Exclusive breastmilk was received in 25% of infants, higher than a previous cohort in China (10.4 to 19%)[41] and similar to a study in South Carolina (27.3%).[42] A Danish cohort reported that exclusive breastfeeding can reach as high as 58 to 68% among preterm infants.[43, 44] In our observation, the success of catch-up growth depends on total caloric intake rather than the type of milk. Up to 62% of preterm infants had insufficient calorie intake (<120 kcal/kg) after discharge.[32] It implies that pediatricians or nutritionists had a crucial role in providing nutritional care to preterm infants after discharge. Calorie intake analysis should be made upon follow-up clinic and early intervention should be made to optimize infant growth.

Long-term outcomes of catch-up growth in preterm infants are developmental status. How large the impact of nutrition on later neurodevelopment among preterm infants is debatable. Nutrition adequacy, represented as growth, is strongly related to neurodevelopmental outcomes.[45] However, a recent study concluded that brain injury and low maternal education are stronger predictors of cognitive impairment instead of weight, height, and head circumference at 36 weeks postmenstrual age.[46] Compared to full-term infants, preterm infants had lower cognitive performance in later years.[13] The younger the infants were born, the higher the risk for developmental delay.[47] A possible explanation is that prematurity-related morbidity (intraventricular hemorrhage, infection, necrotizing enterocolitis, and other comorbidities) causes brain injury, specifically among white matter areas.[48]

Limitation

We only include a small number of extreme preterm due to low survival at that time, thus any information acquired from extreme preterm should be interpreted carefully. Insufficient data for head circumference limited the researcher to assess the prevalence of microcephaly which can reflect growth restriction due to malnutrition and also potential neurodevelopmental problems, however, any intracranial abnormalities should be evaluated as confounding factors. Deep exploration of qualitative aspects of preterm baby care at home, such as stimulation and feeding practice, should be investigated as well.

We did not specifically analyze parental sociodemographic factors, patient family size, and in-hospital factors (duration of hospitalization, neonatal comorbidities) as a contributing factor to long-term growth. A further exploration of this aspect is important.

We also noted that maternal nutritional factors are among the risk factors of preterm birth, however, our data is incomplete. We cannot rely on maternal body mass index or mid-upper arm circumference to reflect the nutritional status. A routine laboratory examination for anemia, infection, fatty acid profile, and micronutrients such as zinc and vitamin D level is more appropriate to represent maternal nutritional status other than weight at pregnancy. Further research should be conducted to evaluate the relationship of these maternal nutritional parameters.

Further research

Future research to determine risk factors of growth and developmental delay and also sex-dependent growth trajectory and neonatal nutritional requirements in Indonesia should be done. Hence, researchers should note that anthropometric measurements should be plotted on the growth chart and health workers should pay more attention to any deviation on the growth curve, especially in the first 3 months of corrected age. Finally, a long-term follow-up study is mandatory to evaluate the outcome of Indonesian preterm infants. Information gathered from this data analysis was then used by the authors to design a prospective cohort study (CIPTO Study) of which the protocol had been published.[49]

Conclusion

Growth trajectory trends differed between weight, length, and weight-for-length in the first 24 months. Weight reached its nadir point at 3 months, then gradually increased above the median curve at 24 months. There also was a reduction of stunted proportion at 24 months of corrected age. Otherwise, there was a normal weight-for-length trend from discharge to 24 months. The growth trajectories were varied between different gestational age groups. Close follow-up with an individualized approach is crucial for optimal growth of preterm infants after NICU discharge.

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Ethical statement

This studies had been approved by the Ethical Committee, Faculty of Medicine, Universitas Indonesia with protocol number 19-03-0228. Written informed consent to participate in this study was provided by the participants' legal guardian.

Data availability statement: Data are available upon request. Further inquiries can be directed to the corresponding author.

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Conflict of interest: The authors declare that the study was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Author contributions: RR and HGH are the primary investigators that design the study. RR, HGH, DUN, and AAS carrying out the study, collect the data, and conduct the data analysis. Findings are interpreted by all authors (RR, HGH, DUN, ATPI, PMTM, DS, MARS, AK, AAV, RDR). HGH wrote the first draft and then finalized by all authors.

References

1. Walani SR. Global burden of preterm birth. Int J Gynaecol Obstet. 2020;150:31-3.
2. Blencowe H, Cousens S, Oestergaard MZ, et al. National, regional, and worldwide estimates of preterm birth rates in the year 2010 with time trends since 1990 for selected countries: A systematic analysis and implications. Lancet. 2012;379:2162-72.
3. Chawanpaiboon S, Vogel JP, Moller A-B, 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:e37-e46.
4. Haksari EL. Historical perspectives: Low birthweight and preterm infants in Indonesia. Neoreviews. 2019;20:e548-e60.
5. Sungkar A, Fattah ANA, Surya R, et al. High preterm birth at Cipto Mangunkusumo Hospital as a national referral hospital in Indonesia. Med J Indones. 2017;26:198.
6. Hidayat ZZ, Ajiz EA, Achadiyani NBSP, et al. Risk factors associated with preterm birth at Hasan Sadikin General Hospital in 2015. Open J Obstet Gynecol. 2016;13:9.
7. Sebayang SK, Dibley MJ, Kelly PJ, et al. Determinants of low birthweight, small-for-gestational-age and preterm birth in Lombok, Indonesia: Analyses of the birthweight cohort of The SUMMIT Trial. Trop Med Int Health. 2012;17:938-50.
8. Owen LS, Manley BJ, Davis PG, et al. The evolution of modern respiratory care for preterm infants. Lancet. 2017;389:1649-59.
9. Harding JE, Cormack BE, Alexander T, et al. Advances in nutrition of the newborn infant. Lancet. 2017;389:1660-8.
10. The Lancet. Prospects for neonatal intensive care. Lancet. 2017;389:1582.
11. Saigal S, Doyle LW. An overview of mortality and sequelae of preterm birth from infancy to adulthood. Lancet. 2008;371:261-9.

12. Saigal S. Functional outcomes of very premature infants into adulthood. Semin Fetal Neonatal Med. 2014;19:125-30.
13. Wang PW, Fang LJ, Tsou KI. The growth of very-low-birth-weight infants at 5 years old in Taiwan. Pediatr Neonatol. 2014;55:114-9.
14. Mukhopadhyay K, Mahajan R, Louis D, et al. Longitudinal growth of very low birth weight neonates during first year of life and risk factors for malnutrition in a developing country. Acta Paediatr. 2013;102:278-81.
15. Japakasetr S, Sirikulchayanonta C, Suthutvoravut U, et al. Implementation of a nutrition program reduced post-discharge growth restriction in thai very low birth weight preterm infants. Nutrients. 2016;8:820.
16. Ramel SE, Demerath EW, Gray HL, et al. The relationship of poor linear growth velocity with neonatal illness and two-year neurodevelopment in preterm infants. Neonatology. 2012;102:19-24.
17. Lucas A, Morley R, Cole TJ. Randomised trial of early diet in preterm babies and later intelligence quotient. BMJ. 1998;317:1481-7.
18. Parkinson JRC, Hyde MJ, Gale C, et al. Preterm birth and the metabolic syndrome in adult life: A systematic review and meta-analysis. Pediatrics. 2013;131:e1240-e63.
19. Toftlund LH, Halken S, Agertoft L, et al. Early nutrition and signs of metabolic syndrome at 6 y of age in children born very preterm. Am J Clin Nutr. 2018;107:717-24.
20. Smith GC, Gutovich J, Smyser C, et al. Neonatal intensive care unit stress is associated with brain development in preterm infants. Ann Neurol. 2011;70:541-9.
21. Grunau RE, Whitfield MF, Petrie-Thomas J, et al. Neonatal pain, parenting stress and interaction, in relation to cognitive and motor development at 8 and 18months in preterm infants. Pain. 2009;143:138-46.
22. Ballantyne M, Benzies K, Rosenbaum P, et al. Mothers' and health care providers' perspectives of the barriers and facilitators to attendance at Canadian neonatal follow-up programs. Child Care Health Dev. 2015;41:722-33.
23. Wade KC, Lorch SA, Bakewell-Sachs S, et al. Pediatric care for preterm infants after nicu discharge: High number of office visits and prescription medications. J Perinatol. 2008;28:696-701.

24. Taslimi Taleghani N, Fallahi M, Soltanttooyeh Z, et al. Post-discharge follow-up of preterm infants at high-risk neonatal follow-up clinic of a maternity hospital. J Compr Ped. 2019;11:e93379.

25. Seppänen A-V, Sauvegrain P, Draper ES, et al. Parents' ratings of post-discharge healthcare for their children born very preterm and their suggestions for improvement: A European cohort study. Pediatr Res. 2021;89:1004-12.

26. Allen EC, Manuel JC, Legault C, et al. Perception of child vulnerability among mothers of former premature infants. Pediatrics. 2004;113:267-73.

27. Liao WL, Lin MC, Wang TM, et al. Risk factors for postdischarge growth retardation among very-low-birth-weight infants: A nationwide registry study in Taiwan. Pediatr Neonatol. 2019;60:641-7.

28. Rohsiswatmo R, Kaban RK, Sjahrulla MAR, et al. Defining postnatal growth failure among preterm infants in Indonesia. Front Nutr. 2023;10:1101048.

29. World Health Organization & United Nations Children's Fund (UNICEF). Global strategy for infant and young child feeding. Geneva: World Health Organization; 2003.

30. Kang L, Wang H, He C, et al. Postnatal growth in preterm infants during the first year of life: A population-based cohort study in China. PLoS One. 2019;14:e0213762.

31. Han J, Jiang Y, Huang J, et al. Postnatal growth of preterm infants during the first two years of life: Catch-up growth accompanied by risk of overweight. Ital J Pediatr. 2021;47:66.

32. Ribas SA, Cunha DB, Paravidino VB, et al. Protein and energy intake and nutritional evolution of preterm infants after hospital discharge: A longitudinal study. Early Hum Dev. 2020;149:105136.

33. Chandra S, Spitzer AR. Association between postnatal catch-up growth and obesity in childhood: Prospective cohort study. Clin Pediatr (Phila). 2000;39:731-2.

34. Greer FR, Norlin S, Olsen IE. How should the preterm infant grow? Current Pediatrics Reports. 2020;8:202-8.

35. Ramel SE, Gray HL, Ode KL, et al. Body composition changes in preterm infants following hospital discharge: Comparison with term infants. J Pediatr Gastroenterol Nutr. 2011;53:333-8.

36. Nagel E, Desjardins C, Earthman C, et al. Weight for length measures may not accurately reflect adiposity in preterm infants born appropriate for gestational age

https://doi.org/10.1017/S0007114524002538 Published online by Cambridge University Press

during hospitalisation or after discharge from the neonatal intensive care unit. Pediatr Obes. 2021;16:e12744

37. Ferguson AN, Grabich SC, Olsen IE, et al. BMI is a better body proportionality measure than the ponderal index and weight-for-length for preterm infants. Neonatology. 2017;113:108-16.
38. Figueras-Aloy J, Palet-Trujols C, Matas-Barceló I, et al. Extrauterine growth restriction in very preterm infant: Etiology, diagnosis, and 2-year follow-up. Eur J Pediatr. 2020;179:1469-79.
39. Wamani H, Åstrøm AN, Peterson S, et al. Boys are more stunted than girls in sub-saharan africa: A meta-analysis of 16 demographic and health surveys. BMC Pediatr. 2007;7:17.
40. González-García L, Mantecón-Fernández L, Suárez-Rodríguez M, et al. Postnatal growth faltering: Growth and height improvement at two years in children with very low birth weight between 2002-2017. Children (Basel). 2022;9:1800.
41. Jiang X, Jiang H. Factors associated with post NICU discharge exclusive breastfeeding rate and duration amongst first time mothers of preterm infants in Shanghai: a longitudinal cohort study. Int Breastfeed J. 2022;17:34-9.
42. Zhang X, Donnelly B, Thomas J, et al. Growth in the high-risk newborn infant post-discharge: results from a neonatal intensive care unit nutrition follow-up clinic. Nutr Clin Pract. 2020;35:738-44.
43. Maastrup R, Hansen BM, Kronborg H, et al. Factors associated with exclusive breastfeeding of preterm infants: results from a prospective national cohort study. PLoS One. 2014;9:e89077.
44. Maastrup R, Rom AL, Walloee S, Sandfeld HB, Kronborg H. Improved exclusive breastfeeding rates in preterm infants after a neonatal nurse training program focusing on six breastfeeding-supportive clinical practices. PLoS One. 2021;16:e0245273.
45. Cordova EG, Cherkerzian S, Bell K, et al. Association of poor postnatal growth with neurodevelopmental impairment in infancy and childhood: Comparing the fetus and the healthy preterm infant references. The J Pediatr. 2020;225:37-43.
46. Fenton TR, Nasser R, Creighton D, et al. Weight, length, and head circumference at 36 weeks are not predictive of later cognitive impairment in very preterm infants. J Perinatol. 2021;41:606-14.

47. Schonhaut L, Armijo I, Pérez M. Gestational age and developmental risk in moderately and late preterm and early term infants. Pediatrics. 2015;135:e835-41.

48. Rogers EE, Hintz SR. Early neurodevelopmental outcomes of extremely preterm infants. Semin Perinatol. 2016;40:497-509.

49. Rohsiswatmo R, Hikmahrachim HG, Sjahrulla MAR, et al. The cohort of indonesian preterm infants for long-term outcomes (CIPTO) study: A protocol. BMC Pediatr. 2023;23:518.

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Table 1. Baseline characteristics of preterm infants during NICU admission

Characteristics	n	%
Sex		
Male	122	39.87
Female	184	60.13
Gestational age, weeks		
Mean (SD)	32.8 (±2.5)	
Median (min-max)	33 (25-36)	
Late preterm	86	28.10
Moderate preterm	152	49.67
Very preterm	41	13.40
Extreme preterm	27	8.82
Birth weight, gram		
Mean (SD)	1804 (±415)	
Median (min-max)	1836 (493-2073)	
Low birth weight (1500 - <2500 g)	214	69.93
Very low birth weight (1000 - <1500 g)	68	22.22
Extremely low birth weight (<1000 g)	24	7.84
Mode of delivery		
Caesarean section	187	61.11
Vaginal delivery	119	38.89
Cause of preterm birth		
Preeclampsia	135	44.12
Intrauterine infection	91	29.74
Others	80	26.14
Comorbidities		
Neonatal sepsis	23	21.25
Intraventricular haemorrhage	4	3.75
Hyaline membrane disease	2	1.88
Necrotizing enterocolitis	42	11.25

Characteristics	n	%
Weight at discharge, z-score*		
Overall	-0.16 (-0.61 to 0.42)	
Male	-0.30 (-0.81 to 0.19)	
Female	-0.01 (-0.49 to 0.61)	
Length at discharge, z-score*		
Overall	-0.80 (-1.41 to -0.25)	
Male	-1.07 (-1.55 to -0.54)	
Female	-0.65 (-1.26 to -0.15)	
Weight-for-length at discharge, z-score*		
Overall	0.39 (-0.53 to 1.85)	
Male	0.40 (-0.49 to 1.36)	
Female	0.36 (-0.56 to 1.86)	

*presented as median (IQR)

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Table 2. The proportion of stunted at 3, 6, 9, 12, 18, and 24 months based on gestational age groups

	Age at observation											
	3 months		6 months		9 months		12 months		18 months		24 months	
	n	%	n	%	n	%	n	%	n	%	n	%
All (N = 306)	151	49.35	136	44.44	72	23.53	96	31.37	58	18.95	41	13.40
Late preterm (N = 86)	39	45.35	38	44.19	22	25.58	18	20.93	12	13.95	12	13.95
Moderate preterm (N = 152)	84	55.26	71	46.71	28	18.42	36	23.68	17	11.18	22	14.47
Very to extreme preterm (N = 68)	28	41.18	27	39.71	22	32.35	42	61.76	29	42.65	7	10.29

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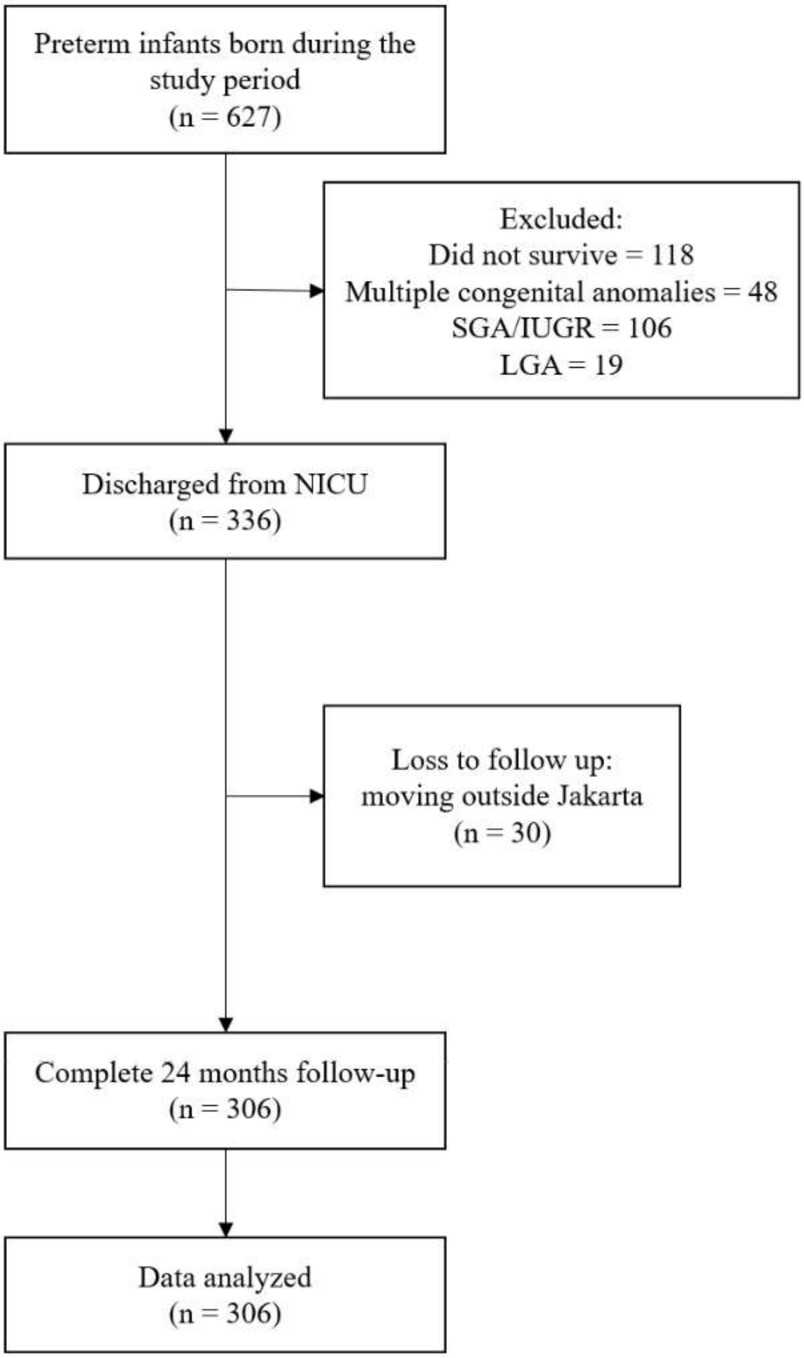

Figure 1. Subject recruitment flow diagram

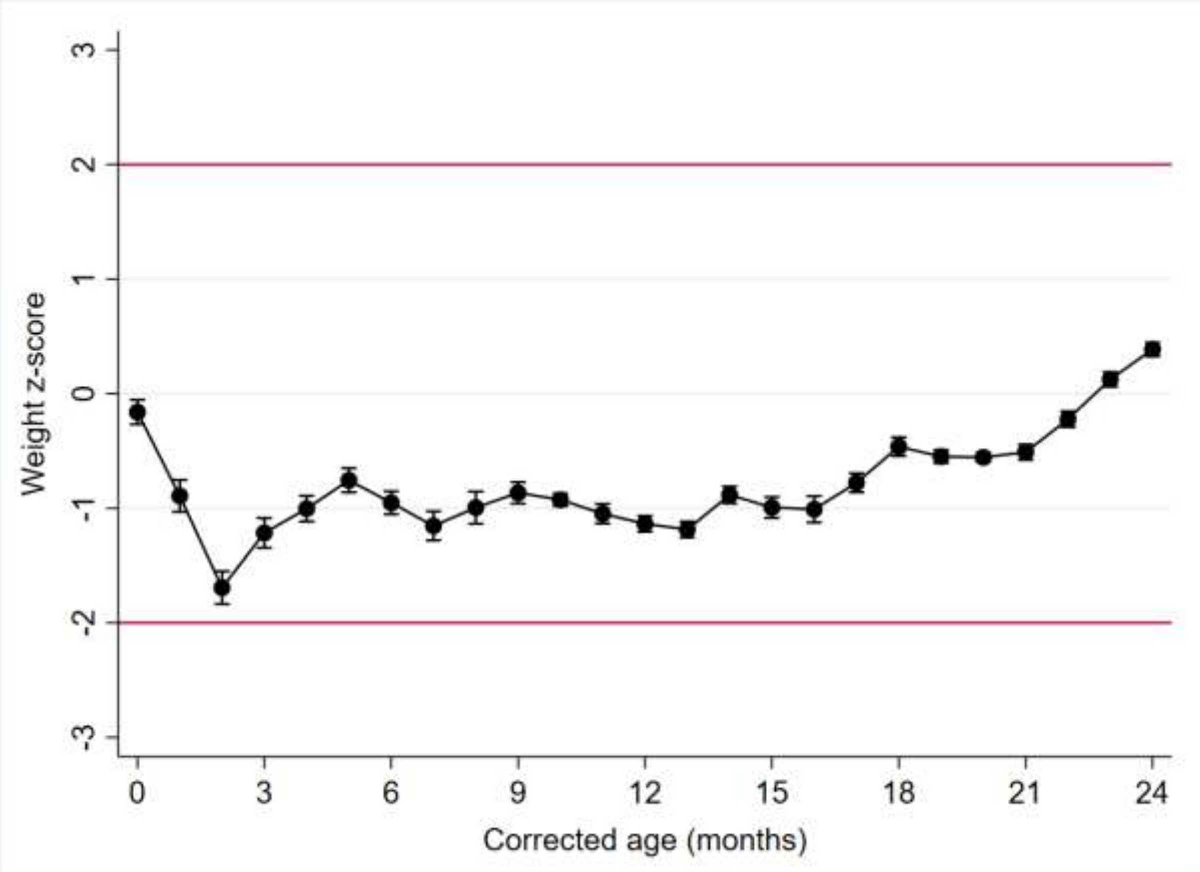

Figure 2. Overall median and 95%CI weight trajectory in WAZ from 0 to 24 months corrected age. Red line refers to reference for normal WAZ value.

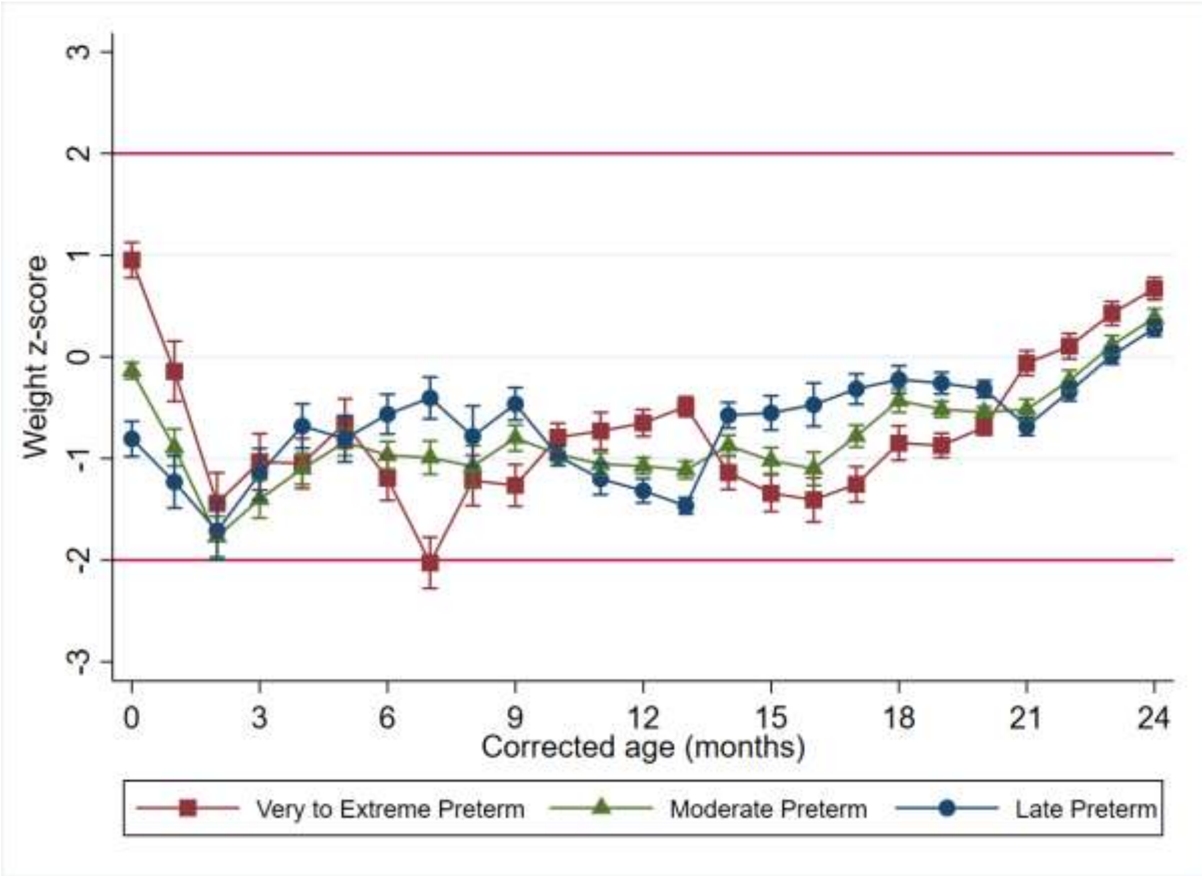

Figure 3. Median and 95%CI weight trajectory in WAZ from 0 to 24 months corrected age for late (blue line, circle dot), moderate (green line, triangle dot) and very to extreme (red line, square dot) preterm infants. Red line refers to reference for normal WAZ value.

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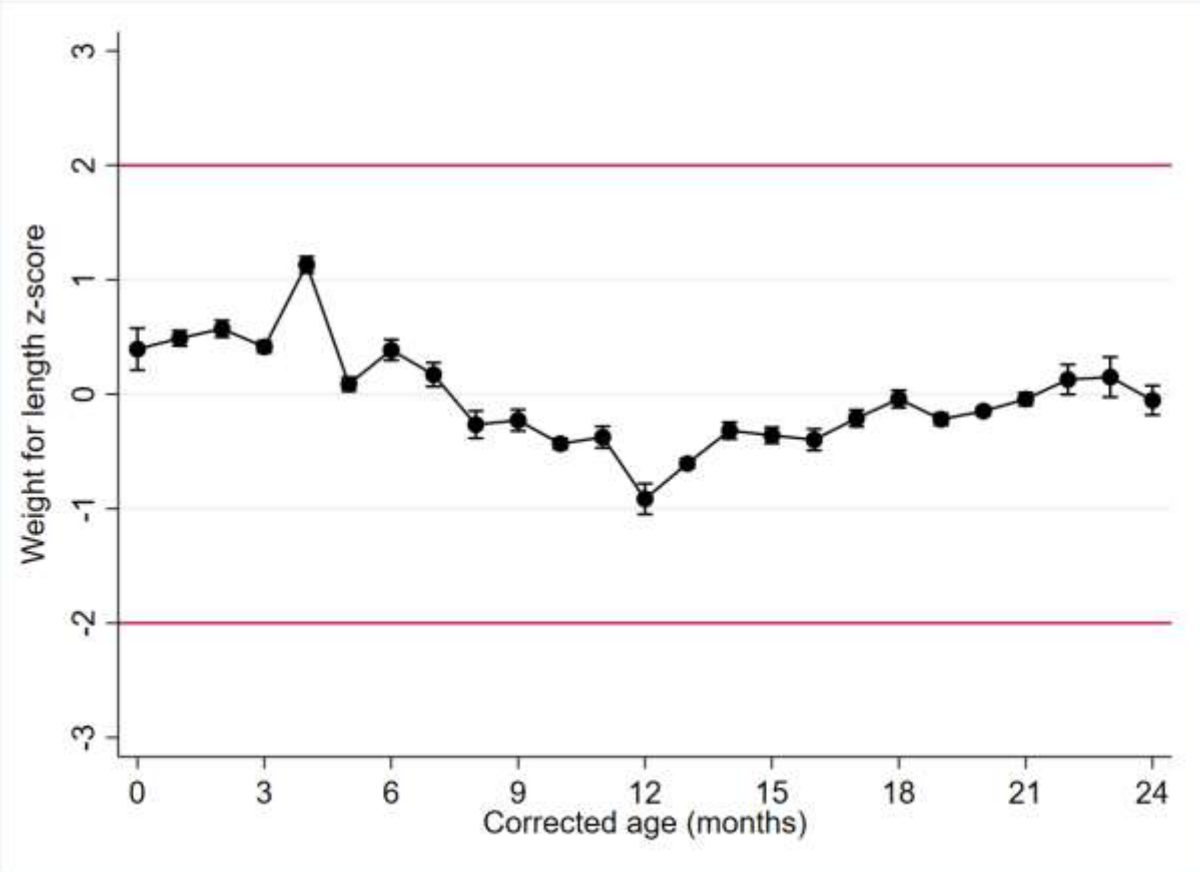

Figure 4. Overall median and 95%CI weight-for-length trajectory from 0 to 24 months corrected age. Red line refers to reference for normal WFL value.

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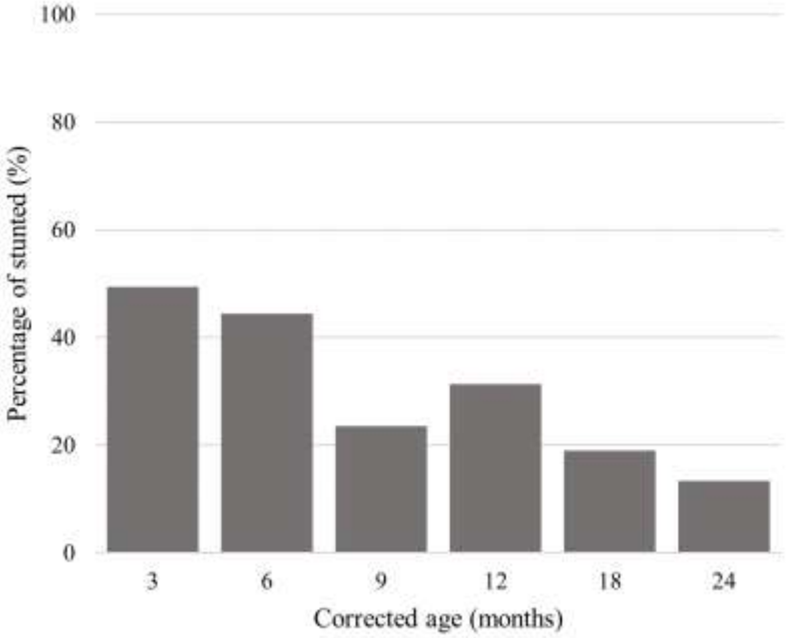
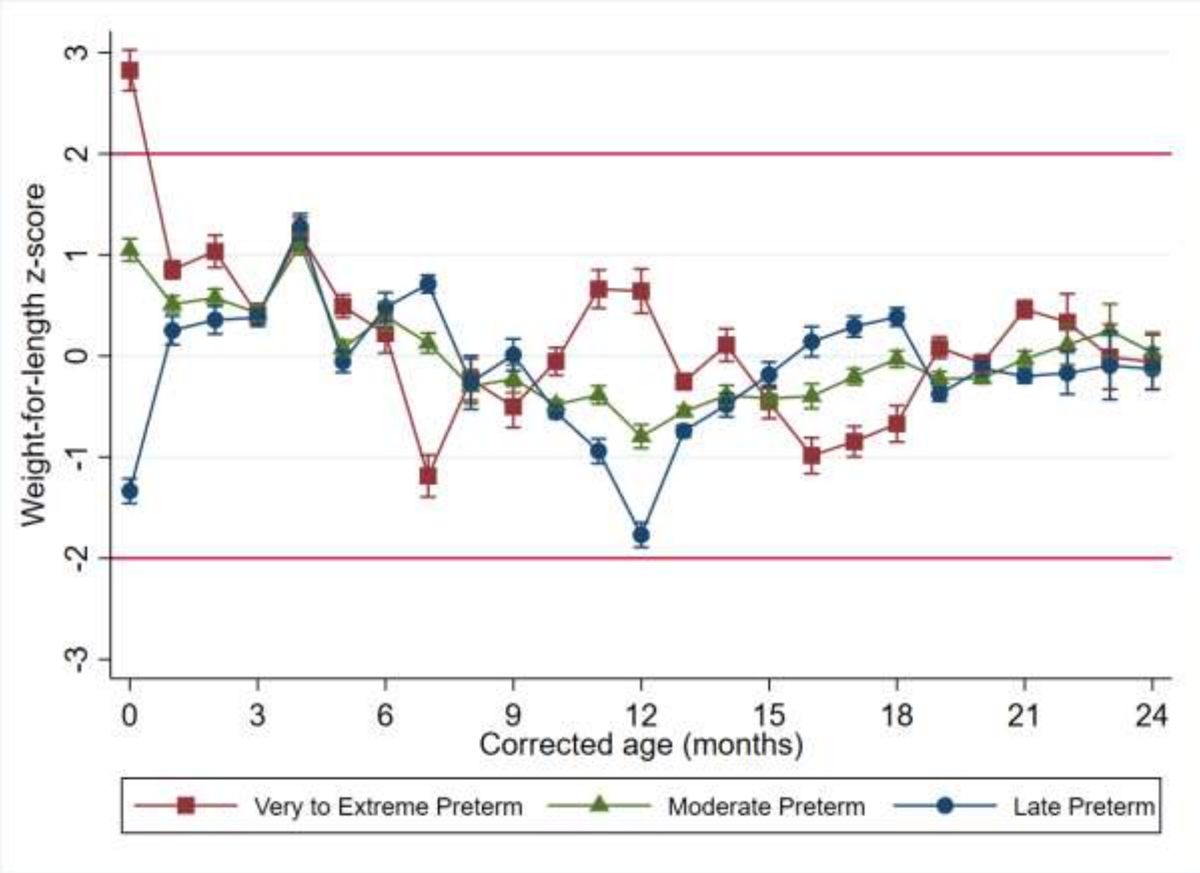


Supplementary Figure 1. Overall prevalence of stunted in the first 24 months corrected age



Supplementary Figure 2. Median and 95%CI weight-for-length trajectory from 0 to 24 months corrected age for late (blue line, circle dot), moderate (green line, triangle dot) and very to extreme (red line, square dot) preterm infants. Red line refers to reference for normal WFL value.

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