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Low length/weight growth trajectories of early-term infants during the first year: evidence from a longitudinal study in China

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ABSTRACT

Objective To identify common length, weight and body mass index (BMI) growth trajectories of term infants during infancy, and to determine their association with early-infancy.

Design Prospective longitudinal study.

Setting Wuhan, China.

Patients A total of 4308 term infants (born at 37–41 weeks of gestation) were included. All term infants were single live birth with no defects and birth weight ≥2500 g, and their mothers were permanent residents of Wuhan for more than 2 years. After excluding 887 infants, a total of 3421 term infants (1028 early-term infants born at 37–38 weeks of gestation and 2393 full-term infants born at 39–41 weeks of gestation) entered the statistical analysis stage.

Main outcome measures Patterns of length, weight and BMI growth trajectories by using group-based trajectory modelling.

Results Three distinct physical growth trajectories were identified as follows: length: low stable (1056, 30.9%), moderate stable (1887, 55.2%) and high increasing (475, 13.9%); weight: low stable (1031, 30.1%), moderate stable (1887, 55.2%) and high increasing (475, 13.9%); BMI: low stable (689, 20.1%), moderate stable (2167, 63.4%) and high increasing (564, 16.5%). Compared with the full-term infants, early-term infants were more likely to remain at low-stable trajectory in length (OR: 1.40; 95% CI: 1.29 to 1.53). These associations were still helpful.

Conclusion Our results suggested the heterogeneity of term infants existed in length, weight and BMI growth trajectories of early childhood. Compared with full-term birth, early-term birth was related to low length and weight trajectories rather than BMI trajectory. Further research is needed to evaluate the duration of these low trajectories and their possible long-term health effects.

INTRODUCTION

Early-term infants (born at 37–38 weeks of gestation) have been considered to be a heterogeneous group compared with full-term infants (born at 39–41 weeks of gestation). More and more evidence has suggested that early-term infants are more likely to have a host of adverse health outcomes compared with full-term infants. Early-term births, compared with full-term births, are not only associated with the increased risk of neonatal mortality, morbidity and admissions, but also associated with the long-term adverse outcomes, such as developmental delay, wheezing and asthma in childhood, cognitive deficit, poor school performance and psychiatric problem. The high number of early-term births creates a health burden and has long been considered a public health problem.

Few studies have explored the physical growth of early-term infants. Evidence from the UK Millennium Cohort Study suggested that height at 3 years was negatively associated with gestational age. However, the association...
was no longer statistically significant among the early-term infants after adjusting the child’s age at interview and potential confounders. It is necessary to clarify how long the gestational age affects children’s height (also known as the length in infancy) and weight. A cohort study of small-for-gestational age (SGA) children conducted in Japan showed that childhood poor height trajectory was related to early-term infants. However, height or weight growth may be heterogeneous during early childhood and these two above-mentioned studies assumed homogeneity of the study population. It is necessary to conduct a research on early-term infants that aims to identify physical growth trajectories with an analytical approach that can recognise the heterogeneity of the study population.

Group-based trajectory modelling (GBTM) is one of the latent mixture modelling, in which trajectory groups are used as a statistical device for approximating possible trajectories across population members. GBTM assumes heterogeneity between subgroups and matches each individual to the appropriate subgroup trajectory. Several studies have used the GBTM to identify distinct body mass index (BMI) trajectories. A study of (mostly) Caucasian population in the USA identified four distinct BMI trajectory patterns (consistently low, increase in the first year, increase in the second year and consistently high) among children younger than 2 years old. An Australia birth cohort study identified four distinct BMI trajectory patterns (low, intermediate, high or accelerating growth) from birth to 3.5 years old, and found that maternal obesity in early pregnancy increased the risk of being in the accelerating trajectory patterns. However, there is a lack of study on the impact of early-term birth on physical growth trajectories.

The purposes of our study were to identify distinct length, weight and BMI growth trajectories of term infants during the first year of life (the fastest physical growth period after birth) by using GBTM, and to explore the association between early-term birth and physical growth trajectories in China.

**METHODS**

**Study population**

This study contains a total of 4308 term infants selected from a previous case–control study. The cases were every pregnant woman who had a preterm birth between 10 June 2011 and 9 June 2013, and controls (matching with cases on the place of residence) were randomly selected from all women with term births (37 weeks of gestation and beyond). All term infants were a single live birth, with no birth defects and birth weight ≥2500g and their mothers had lived in the inner-city districts of Wuhan for more than 2 years and gave birth here. More details can be found in the previous study. In this study, we continued to investigate the physical growth of these 4308 term infants. Briefly, their mothers were required to complete the face-to-face interview using a structured questionnaire including characteristics of parents and infants. The data of this study contain six measurements of the length and weight within the first year of life (months 0, 1, 3, 6, 8 and 12). The first measurement was taken at birth in the delivery hospital, while the rest five measurements were taken by trained doctors in the community health service centres using standard techniques. The questionnaire information and anthropometric data were uploaded and stored in a uniform database.

In the statistical analysis stage, we excluded 887 infants because of post-term birth (42 weeks of gestation and beyond), SGA, logically incorrect (for example, the length of 8 months is lower than the length of 6 months), biologically implausible (length-for-age z-score (LAZ) <−6 or >6, weight-for-age z-score (WAZ) <−6 or >5) anthropometric data and <2 visits. Finally, 3421 term infants were eligible and included in the analysis.

**Gestational age and growth trajectory**

Gestational age at birth was calculated based on the last menstrual period (LMP) and/or ultrasound scans. The results of ultrasound scans offered to all pregnant women would be adopted when they could not provide the exact date of their LMP. We divided infants into early-term (37–38 weeks of gestation) groups and full-term (39–41 weeks of gestation) groups.

Due to the large number of infants, it was difficult to ensure that all participants take anthropometric measurements at completely accurate follow-up time points. For example, an infant with an actual age (the date when the anthropometric measurements were taken minus the date of birth) of 96 days would be treated as 3 months old for management. As shown in online supplemental table S1, there was no significant difference between the actual age of early-term infants at every follow-up time point with that of full-term infants, which also improved the reliability of our results. The BMI was calculated as weight in kilograms divided by length in metres squared (kg/m²). According to the WHO Child Growth Standards at different ages, length, weight, and BMI were converted to LAZ, WAZ, and BMI-for-age z-score (BMIZ), respectively. The infants whose length was measured and analysed at these six time points were 3418 (99.9%), 3245 (94.9%), 3037 (88.8%), 2899 (84.7%), 2844 (83.1%) and 2734 (79.9%), respectively. The infants whose weight was measured and analysed at these six time points were 3417 (99.9%), 3245 (94.9%), 3037 (88.8%), 2899 (84.1%), 2800 (81.8%) and 2679 (78.3%), respectively. Then LAZ, WAZ and BMIZ were used to model physical growth trajectories by GBTM. Finally, the length, weight and BMI growth trajectories included 3420 out of 3421 infants, respectively.

**Covariates**

Information on parental height and weight (measured by skilled doctors or nurses), maternal weight before pregnancy, smoking and drinking in pregnancy was obtained from the questionnaire survey. Information on maternal age at delivery, parity, delivery mode, pregnancy...
complications, infant sex, birth length, birth weight and neonatal complications was abstracted from the medical records. In our study, gestational hypertension or pre-eclampsia, placental abruption or placenta previa and premature rupture of membranes were classified as pregnancy complications. Meanwhile, respiratory distress syndrome, neonatal pneumonia, pathological jaundice and neonatal diarrhoea were classified as neonatal complications. Maternal pre-pregnancy BMI \( (\text{kg/m}^2) \) was calculated as maternal weight before pregnancy (kg) divided by maternal height squared \( (\text{m}^2) \) and \( \geq 24.0 \) was considered maternal pre-pregnancy overweight/obesity. Maternal weight gain during pregnancy was obtained by subtracting maternal weight before pregnancy from the weight at delivery.

### Statistical analysis

Physical growth trajectories were identified by GBTM conducted in SAS version 9.4 Proc Traj.\(^{24, 25}\) According to professional interpretations and the Bayesian information criterion, the optimal model in the matter of the number of subgroups and the best polynomial order of each subgroup trajectory are selected. The posterior probability of each subgroup that we selected in this study was \( \geq 0.70 \). It meant all the subgroups fit well.

Analysis of covariance was used to compare differences in body growth at every follow-up. Polytomous logistic regression model was used to estimate the association of gestational age categories (early-term and full-term) and patterns of physical growth trajectories. Variables relating to childhood growth were included in the adjusted model,\(^{10, 26-28}\) such as maternal age at delivery, parental height, parental weight, smoking or drinking in pregnancy. Just like the method of screening covariates in some high-quality studies,\(^{29, 30}\) some variables that changed the matched OR more than 10% were included in our adjusted model, such as pregnancy and neonatal complications, parity, delivery mode and infant sex.

### Patient and public involvement

No patients or the public were involved in the study design, setting the research questions, interpretation or writing up of results, or reporting of the research.

#### RESULTS

Among 3421 participants, there were 1028 (30.0%) early-term infants and 2393 (70.0%) full-term infants. Descriptive characteristics of infants stratified by gestational age categories were presented in table 1. Early-term infants were more likely to be boys, born by caesarean section and have neonatal complications, while their mothers were older and more likely to have complications during pregnancy. As for the comparison of growth status at the single time point (table 2), early-term infants were lower at months 0, 1, 3 and 6 in length, and were lower at

### Table 1 Descriptive characteristics of term infants

| Maternal and paternal characteristics | Total (n=3421) | Early-term (n=1028) | Full-term (n=2393) | P value |
|--------------------------------------|---------------|---------------------|-------------------|---------|
| Maternal age at delivery, mean (SD)  | 28.4 (3.9)    | 28.8 (4.1)          | 28.3 (3.9)        | <0.001  |
| Maternal height, mean (SD), cm       | 161.3 (4.4)   | 161.1 (4.5)         | 161.4 (4.4)       | 0.057   |
| Maternal weight before pregnancy, mean (SD), kg | 53.5 (6.6) | 53.8 (6.6) | 53.4 (6.7) | 0.146   |
| Maternal pre-pregnancy overweight/obesity, no(%) | 316 (9.2) | 103 (10.0) | 213 (8.9) | 0.300   |
| Maternal weight gain during pregnancy, mean (SD), kg/m² | 14.6 (4.0) | 14.4 (3.8) | 14.7 (4.1) | 0.089   |
| Paternal height, mean (SD), cm       | 173.5 (4.7)   | 173.6 (4.8)         | 173.4 (4.6)       | 0.368   |
| Paternal weight, mean (SD), kg       | 71.0 (9.7)    | 71.1 (10.1)         | 70.9 (9.6)        | 0.521   |
| Smoking in pregnancy, no (%)         | 22 (0.6)      | 9 (0.9)             | 13 (0.5)          | 0.265   |
| Drinking in pregnancy, no (%)        | 171 (5.0)     | 57 (5.5)            | 171 (5.0)         | 0.337   |
| Pregnancy complications, no (%)      | 318 (9.3)     | 154 (15.0)          | 164 (6.9)         | <0.001  |
| Caesarean section, no (%)            | 2422 (70.8)   | 762 (74.1)          | 1660 (69.4)       | 0.005   |

**Infant characteristics**

| Boys, no (%)          | 1866 (54.5) | 612 (59.5) | 1254 (52.4) | <0.001   |
| Firstborn, no (%)     | 2876 (84.1) | 824 (80.2) | 2052 (85.8) | 0.001    |
| Birth length, mean (SD), cm | 50.2 (1.2) | 49.9 (1.3) | 50.3 (1.1) | <0.001   |
| Birth weight, mean (SD), kg | 3.38 (0.37) | 3.25 (0.38) | 3.44 (0.35) | <0.001   |
| Neonatal complications, no (%) | 351 (10.3) | 122 (11.9) | 229 (9.6) | 0.042    |
months 0 and 1 in weight than full-term infants. Different from the length and weight, early-term infants’ BMI status were lower at birth but higher at months 6 and 8.

Three distinct length trajectories from birth to 1 year old were identified among 3420 term infants by GBTM. Model fit results when the LAZ, WAZ and BMIZ trajectories were in the best fit according to GBTM were shown in the online supplemental table S2. The fitted value of the trajectory at each follow-up time point was shown in the online supplemental table S3. As shown in figure 1, LAZ in 1056 infants (30.9%) decreased slightly at 1 month old and remained at a low level (low-stable subgroup); LAZ in 1887 (55.2%) infants maintained moderate levels throughout the follow-up period (moderate-stable subgroup); and LAZ in 477 (13.9%) infants started with relatively high level, increased rapidly before 8 months old and slightly decreased at 12 months old (high-increasing subgroup). The proportion of early-term infants in the three subgroups (low stable, moderate stable and high increasing) was 37.4%, 52.0% and 10.6%, respectively, while the proportion of full-term infants was 28.1%, 56.5% and 15.4%, respectively. The distributions of LAZ trajectory patterns were statistically different (p<0.001) between early-term infants and full-term infants.

Three distinct weight and BMI trajectories (also characterised as low-stable, moderate-stable and high-increasing subgroups) were displayed in figures 2 and 3, respectively. The distributions of WAZ trajectory patterns were also statistically different (p=0.001) between early-term infants (34.6%, 52.0% and 13.4%, respectively) and full-term infants (28.2%, 56.4% and 15.4%, respectively). Different from LAZ and WAZ trajectories, the distributions of BMIZ trajectory patterns were not statistically different (p=0.779) between early-term infants (20.8%, 62.5% and 16.6%, respectively) and full-term infants (19.9%, 63.7% and 16.4%, respectively).

Table 3 showed the results of polytomous logistic regression analyses. Early-term infants had greater odds of being in low-stable growth patterns both in length (OR: 1.45; 95% CI: 1.23 to 1.70) and weight (OR: 1.33; 95% CI: 1.13 to 1.57). Early-term birth infants had fewer odds of being in the high-increasing growth pattern only in length (OR: 0.65; 95% CI: 0.50 to 0.85).
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0.75; 95% CI, 0.60 to 0.95). The associations were slightly decreased but still significant after adjusting potential confounding factors. There was no statistical association between BMI trajectory patterns and gestational age categories. Results of association stratified by infant sex were presented in table 4. These mentioned associations were more evident among girls, but the association between high-increasing growth pattern and early-term birth among boys was no longer statistically significant.

DISCUSSION

In this study, we revealed heterogeneous trajectories in the physical growth of term-birth infants during the first year after birth by using GBTM. We identified three distinct length, weight and BMI trajectories with characterised features as low-stable, moderate-stable and high-increasing growth. Early-term birth was related to low length/weight growth trajectory.

In our study, early-term infants were more likely to maintain ‘low-stable’ growth trajectories in length and weight, but less likely to have ‘high-increasing’ growth trajectories in length. This finding is worth noting even if the physical status of early-term infants was not statistically different from those of the full-term infants at some follow-up time point (≥8 months old in length and ≥3 months old in weight, respectively). For some later follow-up time point, there were no statistical differences in length or weight between early-term and full-term infants. The WHO Multicentre Growth Reference Study had confirmed that many living environment factors will affect the physical growth of children.31 So it might be that other factors unobserved in this study such as illness, sleep and outdoor activities covered up the influence of gestational age on physical growth at a single time point. We also found that except for its BMI at birth, early-term infants were no longer lower than full-term infants, and even higher at some time points like months 6 and 8 (table 2). We thought this was because early-term infants’ weight gain rate was higher than its length growth rate.

Few studies focused on early-term infants at length or weight trajectory. A study of SGA infants showed that early-term SGA infants’ height trajectory SD scores and the catch-up rate for height maintained lower level up to...
18 months old in comparison with full-term SGA infants; a finding that was similar with our results.19 More studies focused on children’s BMI trajectory. A study to identify BMI trajectories from birth to 10 years old reported that gestational age was lower in the lower percentile BMI trajectories.32 However, the generalisation of these studies was limited by the assumption that the study population was homogeneous. Other studies using GBTM (followed up to 8 and 12 years old, respectively) suggested no difference in gestational age among BMI trajectories.33 34 These findings were possibly due to that the longer follow-up years had concealed the impact produced by different gestational ages, which reminds us to explore the duration of the low trajectories in childhood. As for this study, we examined the influence of gestational age on BMI trajectory during infancy and observed no statistical association between them.

Furthermore, the low weight growth trajectories or low weight gain in infancy had been reported to be associated with adverse health outcomes. A birth cohort study reported that poor bone mineralisation at 7 years old was related to lower weight trajectory.35 Another study that included 5390 term infants found that lower weight gain in infancy was associated with poor adult (31 years old) lung function.36 Moreover, early-term infants included in this study showed a high risk of neonatal complications

**Table 3** OR (95% CI) of the association of different term infants with LAZ, WAZ and BMIZ trajectories

| Types of gestational age | Low stable | High increasing |
|--------------------------|------------|-----------------|
|                          | Crude | Adjusted | Crude | Adjusted |
| LAZ*                    |       |          |       |          |
| Early-term              | 1.45 (1.23 to 1.70) | 1.40 (1.19 to 1.66) | 0.75 (0.60 to 0.95) | 0.72 (0.56 to 0.92) |
| Full-term               | 1.00 (reference) | 1.00 (reference) | 1.00 (reference) | 1.00 (reference) |
| WAZ*                    |       |          |       |          |
| Early-term              | 1.33 (1.13 to 1.57) | 1.29 (1.09 to 1.53) | 0.94 (0.75 to 1.17) | 0.88 (0.70 to 1.11) |
| Full-term               | 1.00 (reference) | 1.00 (reference) | 1.00 (reference) | 1.00 (reference) |
| BMIZ†                   |       |          |       |          |
| Early-term              | 1.07 (0.89 to 1.29) | 0.91 (0.48 to 1.73) | 1.03 (0.84 to 1.26) | 1.02 (0.53 to 1.97) |
| Full-term               | 1.00 (reference) | 1.00 (reference) | 1.00 (reference) | 1.00 (reference) |

*Adjusted for maternal age at delivery, maternal height, maternal weight before pregnancy, paternal height, paternal weight, maternal smoking, drinking, complications during pregnancy, infant sex, whether infant was mother’s firstborn, caesarean section, and neonatal complications.
†Adjusted for maternal age at delivery, maternal pre-pregnancy overweight/obesity, weight gain during pregnancy, maternal smoking, drinking, complications during pregnancy, infant sex, whether infant was mother’s firstborn, caesarean section, and neonatal complications.
BMI, body mass index; BMIZ, BMI-for-age z-score; LAZ, length-for-age z-score; WAZ, weight-for-age z-score.

**Table 4** Adjusted ORs for different growth trajectories stratifying by infant sex

| Types of gestational age | Low stable | High increasing |
|--------------------------|------------|-----------------|
|                          | Boys | Girls | P value for interaction | Boys | Girls | P value for interaction |
| LAZ*                    |       |       |                   |       |       |                   |
| Early-term              | 1.31 (1.06 to 1.63) | 1.59 (1.22 to 2.09) | 0.323 | 0.82 (0.59 to 1.13) | 0.62 (0.43 to 0.90) | 0.192 |
| Full-term               | 1.00 | 1.00 |                   | 1.00 | 1.00 |                   |
| WAZ*                    |       |       |                   |       |       |                   |
| Early-term              | 1.25 (1.01 to 1.55) | 1.38 (1.06 to 1.81) | 0.669 | 0.78 (0.58 to 1.05) | 1.06 (0.75 to 1.50) | 0.245 |
| Full-term               | 1.00 | 1.00 |                   | 1.00 | 1.00 |                   |
| BMIZ†                   |       |       |                   |       |       |                   |
| Early-term              | 1.05 (0.82 to 1.35) | 1.08 (0.80 to 1.45) | 0.930 | 0.82 (0.62 to 1.07) | 1.35 (0.97 to 1.88) | 0.037 |
| Full-term               | 1.00 | 1.00 |                   | 1.00 | 1.00 |                   |

*Adjusted for maternal age at delivery, maternal height, maternal weight before pregnancy, paternal height, paternal weight, maternal smoking, drinking, complications during pregnancy, whether infant was mother’s firstborn, caesarean section, and neonatal complications.
†Adjusted for maternal age at delivery, maternal pre-pregnancy overweight/obesity, weight gain during pregnancy, maternal smoking, drinking, complications during pregnancy, whether infant was mother’s firstborn, caesarean section, and neonatal complications.
BMI, body mass index; BMIZ, BMI-for-age z-score; LAZ, length-for-age z-score; WAZ, weight-for-age z-score.
like in previous studies.3–6 37 38 Further research is necessary to discuss whether early-term infants’ early childhood length/weight trajectory plays an intermediary role between neonatal complications and childhood adverse health outcomes.

There were several notable limitations in our study. First, there may be selection bias because of the non-population-based study. Second, although our results were robust but controlling extenive potential confounders, residual confounding could not be eliminated completely for some variables not covered in this study, such as different growth environment factors, feeding and lifestyle of individuals. Third, our study only obtained follow-up data during infancy. We would need further research to explore how long the different growth trajectories in early childhood persist and determine whether the differences would affect health in later childhood and even adulthood.

Conclusion
In this study, we identified three distinct trajectories characterised as low stable, moderate stable, and high increasing in length, weight, and BMI by using GBTM. Our study found the association of early-term birth and low length/weight rather than BMI trajectory during infancy, which provided evidence for avoiding non-medically indicated early-term deliveries. Further studies are needed to demonstrate the duration of the trends and their possible long-term health effect.

Correction notice
This article has been corrected since it first published. Author ‘Rong Yang’ affiliation has been updated.

Contributors
KC conceptualised and designed the study, carried out the initial analyses, drafted the initial manuscript, and reviewed and revised the manuscript. LS, BL, YL and MW carried out the initial analyses and reviewed and revised the manuscript. LW, JB and QL collected data and reviewed and revised the manuscript. LS, BL, YL and MW carried out the initial analyses and reviewed and revised the manuscript. LW, JB and QL collected data and reviewed and revised the manuscript. YZ and ZT coordinated and supervised data collection, YW conceptualised and designed the study and critically reviewed the manuscript for important intellectual content. Ry conceptualised and designed the study, coordinated and supervised data collection, and critically reviewed the manuscript for important intellectual content. Ry was responsible for the overall content as the guarantor.

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None declared.

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Not required.

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Data are available upon reasonable request. Data are available on reasonable request by contacting corresponding author (Rong Yang, 442748767@qq.com).

Supplemental material
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