

The associations of preterm birth and low birth weight with childhood growth curves between birth and 12 years: a SITAR-based longitudinal analysis

Ruta Morkuniene, Tim J. Cole, Ruta Levuliene, Andrej Suchomlinov & Janina Tutkuvienė

To cite this article: Ruta Morkuniene, Tim J. Cole, Ruta Levuliene, Andrej Suchomlinov & Janina Tutkuvienė (2025) The associations of preterm birth and low birth weight with childhood growth curves between birth and 12 years: a SITAR-based longitudinal analysis, *Annals of Human Biology*, 52:1, 2472757, DOI: [10.1080/03014460.2025.2472757](https://doi.org/10.1080/03014460.2025.2472757)

To link to this article: <https://doi.org/10.1080/03014460.2025.2472757>



© 2025 The Author(s). Published by Informa UK Limited, trading as Taylor & Francis Group



[View supplementary material](#)



Published online: 17 Mar 2025.



[Submit your article to this journal](#)



Article views: 858



[View related articles](#)



[View Crossmark data](#)

RESEARCH PAPER

OPEN ACCESS



The associations of preterm birth and low birth weight with childhood growth curves between birth and 12 years: a SITAR-based longitudinal analysis

Ruta Morkuniene^a, Tim J. Cole^b, Ruta Levuliene^c, Andrej Suchomlinov^a and Janina Tutkuvienė^a

^aDepartment of Anatomy, Histology and Anthropology, Institute of Biomedical Sciences, Faculty of Medicine, Vilnius University, Vilnius, Lithuania;

^bUCL Great Ormond Street Institute of Child Health, London, UK; ^cInstitute of Applied Mathematics, Vilnius University, Vilnius, Lithuania

ABSTRACT

Background: Children born preterm grow differently from those born at term.

Aim: To compare growth in length/height, weight, and BMI of preterm- and term-born children, grouped by birth weight (BW) and gestational age (GA).

Subjects and Methods: Longitudinal data of 950 children (birth to 12 years) were collected retrospectively. Growth trajectories were modelled using SITAR (Superimposition by Translation and Rotation) by sex, with three groups each for GA and BW.

Results: SITAR summarised growth patterns from birth to 12 years and explained 76–79% of height variance, 90–92% for weight, and 72–75% for BMI. Early preterm and low BW groups were shorter, lighter and thinner on average than their term or normal BW peers, with late preterm and low-normal BW groups intermediate. Effects were larger for BW than GA, e.g. early preterm girls/boys were 0.3/0.8 kg lighter, 0.9/0.9 cm shorter and 0.8/0.8 kg/m² thinner, while low BW girls/boys were 0.5/1.0 kg lighter, 1.5/1.4 cm shorter and 0.8/0.9 kg/m² thinner. Moreover, faster growth rates were associated with lower BW.

Conclusion: Both BW and GA significantly impacted growth, but low BW more so than early preterm birth. This underscores the need for targeted interventions for low BW children to address potential long-term growth challenges.

ARTICLE HISTORY

Received 9 December

2024

Revised 11 February 2025

Accepted 21 February
2025

KEYWORDS

Preterm infants; growth;
longitudinal study; SITAR

Introduction

Preterm infants, particularly those born very preterm (before 32 weeks) or with very low birth weight (VLBW), are at high risk for medical and developmental challenges, including growth restriction with long-lasting effects into adulthood. Numerous studies have established clear links between birth parameters, postnatal growth restriction, and subsequent growth failure, with significant short- and long-term health consequences (Curtis and Rigo 2004; Casey 2008; Euser et al. 2008). Specifically, preterm infants often experience substantial growth failure early in the postnatal period, typically followed by incomplete catch-up growth over the first 2–3 years, leading to lower average adult height than term-born peers (Euser et al. 2008). Moreover, the smaller the birth weight, the longer the compensatory growth period (Casey 2008). This is particularly true for small for gestational age (SGA) infants born before 32 weeks, who demonstrate slower catch-up growth during early childhood and face poorer neurodevelopmental outcomes if they fail to catch up (Itabashi et al. 2007; Ruys et al. 2019).

In addition to these challenges, VLBW infants, especially those who are SGA, are also at considerable risk for later growth failure and adverse health outcomes in adulthood, including obesity, type 2 diabetes, cardiovascular diseases, and stroke (Curtis and Rigo 2004; Embleton and Wood 2019; Heidemann et al. 2019; Casirati et al. 2022). Notably, extremely preterm survivors (born before 26 weeks) tend to remain shorter and lighter into adulthood, however, often having elevated BMI (Ni et al. 2020). Furthermore, shorter final height is associated with decreasing gestational age, a particularly pronounced trend in women born very preterm (Derraik et al. 2017).

This pattern of growth challenges is also evident among moderately preterm-born children, who consistently remain shorter and weigh less than their term-born peers during the early years of life (Santos et al. 2009; Bocca-Tjeertes et al. 2011). This disparity often persists into adolescence; moderately preterm-born children also face growth challenges, consistently being shorter and weighing less than their term-born peers during the early years of life (Wood et al. 2003; Svedenkrans et al. 2013). However, findings vary significantly

CONTACT Janina Tutkuvienė ✉ janina.tutkuvienė@mf.vu.lt Department of Anatomy, Histology and Anthropology, Institute of Biomedical Sciences, Faculty of Medicine, Vilnius University, Ciurlionio str. 21, LT-03101 Vilnius, Lithuania

Supplemental data for this article can be accessed online at <https://doi.org/10.1080/03014460.2025.2472757>.

© 2025 The Author(s). Published by Informa UK Limited, trading as Taylor & Francis Group

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. The terms on which this article has been published allow the posting of the Accepted Manuscript in a repository by the author(s) or with their consent.

across studies regarding the age at which preterm-born children catch up with their peers, the pace and rate of their growth, the onset of puberty, or differences observed between sexes (Itabashi et al. 2007; Euser et al. 2008; Ruys et al. 2019). Additionally, by adulthood, some studies suggest that very, moderately, and late preterm-born men and women may achieve similar adult size, age at peak height velocity, and pubertal timing as term-born peers (Suikkanen et al. 2022; Vinther et al. 2023). Different classification methods (e.g. gestational age vs. birth weight) and study parameters may influence these varying findings, significantly impacting observed growth patterns (Hollanders et al. 2017).

Moreover, while traditional classifications such as small for gestational age (SGA), appropriate for gestational age (AGA), and large for gestational age (LGA) offer valuable clinical insights, they integrate birth weight (BW) and gestational age (GA) into a single measure. This integration, while clinically useful, may obscure the independent influences of BW and GA on later health outcomes. As highlighted by VanderWeele et al. (2012), directly adjusting for an intermediate variable (such as BW) when assessing the impact of an exposure can lead to biased results. Therefore, in this study, we adopt a stratification approach, examining BW and GA as separate variables to disentangle their respective impacts on long-term growth and health outcomes.

This allows us to investigate the effects of different GA strata and BW strata independently, offering new perspectives on the interplay between prenatal growth and developmental trajectories. Specifically, BW reflects cumulative energy reserves and trade-offs during foetal development (Singer et al. 2021), while GA captures the timing of developmental processes and the duration of exposure to the intrauterine environment. By analysing these factors independently, we aim to provide a nuanced understanding of prematurity-related health challenges, framed within the contexts of developmental biology (Bateson et al. 2004) and evolutionary medicine (Gluckman and Hanson 2004). Analysing these factors separately is essential for aetiological research, as including both in the same model can lead to multicollinearity and paradoxical interpretations. This approach allows for a clearer understanding of the distinct roles of GA and BW in shaping growth trajectories while avoiding confounding in causal analyses. The aforementioned inconsistent findings on growth, influenced by classification methods, study duration, and ongoing debates about the optimal growth rate for preterm infants (Greer and Olsen 2013; Fenton et al. 2018), underscore the need for further research into the growth characteristics of different sub-groups of preterm infants. Until now, the growth of such infants has predominantly been examined through cross-sectional studies, leaving a gap in longitudinal research (Van de Pol and Allegaert 2020). Furthermore, analysing largely variable human growth (Cameron 2022) requires expertise in longitudinal statistical methods, which can be analytically challenging (Cole 2006; Johnson 2015; Cole 2019). This large variability, especially in growth outcomes among preterm infants, calls for robust growth models to accurately capture and understand these patterns over time. Growth models (Beath 2007; Cole et al.

2010; Johnson et al. 2013; Elhakeem et al. 2022) are essential for analysing longitudinal data, as they capture overall growth patterns in the population while including and accounting for individual characteristics of growth trajectories. However, traditional growth models, such as linear or nonlinear regression, often struggle to accommodate the unique growth trajectories observed in preterm infants. In contrast, the SITAR (SuperImposition by Translation And Rotation) model has proven to be a valuable tool in this context (Cole et al. 2010). By aligning individual growth curves with a population-average curve and adjusting for differences in growth timing and intensity, SITAR provides a more nuanced understanding of growth dynamics. This makes it particularly effective for studying preterm infants, whose growth patterns can significantly deviate from the norm.

Considering all the above the aim of this study is to examine growth outcomes in preterm infants, focusing on both GA and BW, using SITAR-based longitudinal analysis. To achieve this, the study has the following objectives: (1) evaluate children's growth patterns (height, weight, BMI) in relation to BW groups using SITAR modelling; (2) assess growth trajectories across GA groups for the same measures; and (3) perform a comparative analysis of the resulting growth curves and derive practical insights for clinical or developmental applications.

Materials and methods

Study design and cohort selection

The retrospective longitudinal study analysed medical records from two primary health care centres and their affiliates in Vilnius, Lithuania, involving 950 children (469 boys, 481 girls). It included preterm infants (GA 22–36 weeks) born between 2000–2015 and term infants (GA 37–42 weeks) born in 1996. Although the preterm cohort (2000–2015) and the term cohort (1996) were born several years apart, both grew into adolescence during a similar timeframe, experiencing comparable environmental, socioeconomic, and nutritional conditions (Gyventojai ir socialinė statistika. - Oficialiosios statistikos portalas 2024). All growth data were collected within the same geographical region and healthcare system, minimising variability from systemic differences. The birth variables were sex, birth weight (BW), and gestational age (GA). Height (or length up to age 2) and weight were subsequently measured longitudinally, with BMI calculated from these measurements. The three birth weight (BW) groups (Low, Low-normal, Normal) and three gestational age (GA) groups (Early preterm, Late preterm, Term) were considered (see Table 1). The distributions of birth-related variables, expressed in frequencies, are given in Table 1.

All individuals with at least one measurement were included in the analysis. Height (length up to 2 years) and weight were collected from birth to 12 years, monthly for the first year, three times for the second and third years, and twice a year after that. There were 16,159 measurements. The median numbers of measurements per child was 17, inter-quartile range was 13–21.

SITAR model

The SITAR model (SuperImposition by Translation And Rotation) (Cole et al. 2010) was applied to obtain mean curves for the period from birth to 12 years for height, weight, and BMI in GA and BW groups of boys and girls. SITAR is a mixed effects model featuring a cubic spline mean curve and three subject-specific random effects (size, timing, intensity) that adjust the mean curve to best match the subjects' data (Cole et al. 2010; Pizzi et al. 2014; Cole 2020). It is a shape-invariant model such that individuals are assumed to have the same shape of the growth curve, subject to three transformations: (1) shift the curve up/down (size parameter), (2) shift it left/right (timing or tempo), (3) stretch/shrink the age scale (intensity or velocity). The effect of covariates can be included in the SITAR model as fixed effects, i.e. the model can include separate fixed effects for each SITAR parameter (Johnson et al. 2014; Pizzi et al. 2014).

The corrected postnatal age was used in the analysis: Corrected postnatal age = chronological age (years) + (gestation weeks – 40) * 7/365.25. The correction was applied to children of all gestations, including term, and at all ages. This avoided a disjunction between term and preterm, and at 1 and 2 years of age. To avoid negative ages, nine months (i.e. 3/4 years) were added to corrected postnatal age giving postconceptual age, also known as postmenstrual age, which

is equivalent to gestational age at birth plus chronological age.

The number of degrees of freedom (d.f.), which controls the smoothness of the natural cubic spline, was chosen to minimise the Bayesian Information Criterion (BIC). Models without and with logarithmic transformation were considered. The analysis showed that log transforming age improved model fit. Outliers with standardised residuals exceeding 4 in absolute value were excluded. If the model failed to converge, we fitted reduced models, omitting some fixed and/or random effects, and models omitting the timing random effect fitted best. There were sex differences in the mean growth curve approaching early adolescence, so separate models were fitted for boys and girls. Initially, we explored models that included both GA group and BW group as covariates; however, to avoid collinearity and to independently assess their aetiological effects, we analysed these variables separately. So separate models for BW group and GA group were fitted, by sex. The timing of AR was derived as the age at the lowest BMI point on the modelled mean BMI curves.

The analysis was done in R version 4.4.1 using the SITAR package version 1.4.0 (Cole 2023). The ggplot2 package version 3.5.1 was employed to visualise the results.

Ethics approval

The study was approved by the Lithuanian Bioethics Committee (Permission No. 57, last updated 2017-02-06) and was performed according to the relevant ethical guidelines and regulations.

Results

SITAR models were fitted to height, weight, and BMI from birth to 12 years (Table 2), each adjusted separately for GA group and BW group in boys and girls. Models with log-transformed age fitted better, with degrees of freedom ranging from 6 to 8. The variance explained ranged from 72% to 92%, with the best fit for weight (92% for girls, 90% for boys).

Table 3 shows significant mean differences for the period from birth to 12 years between the GA and BW groups in the SITAR height models by sex. Girls and boys in the early preterm GA group were on average 0.9 cm shorter than those

Table 1. Number of children in the gestational and birth weight groups by sex.

Sex	Birth weight Gestational age	Low (<2500 g)	Low-normal (2500– <3000 g)	Normal (3000– <4000 g)	Total
Boy	Early preterm (<34 weeks)	67	1	0	68
	Late preterm (34–<37 weeks)	67	70	24	161
	Term (37–<42 weeks)	2	12	226	240
	Total (boys)	136	83	250	469
Girl	Early preterm (<34 weeks)	75	3	0	78
	Late preterm (34–<37 weeks)	71	68	21	160
	Term (37–<42 weeks)	5	33	205	243
	Total (girls)	151	104	226	481
Total	Early preterm (<34 weeks)	142	4	0	146
	Late preterm (34–<37 weeks)	138	138	45	321
	Term (37–<42 weeks)	7	45	431	483
	Total	287	187	476	950

Table 2. Summary of SITAR models fitted to height, weight and BMI by sex, adjusted separately for GA group and BW group.

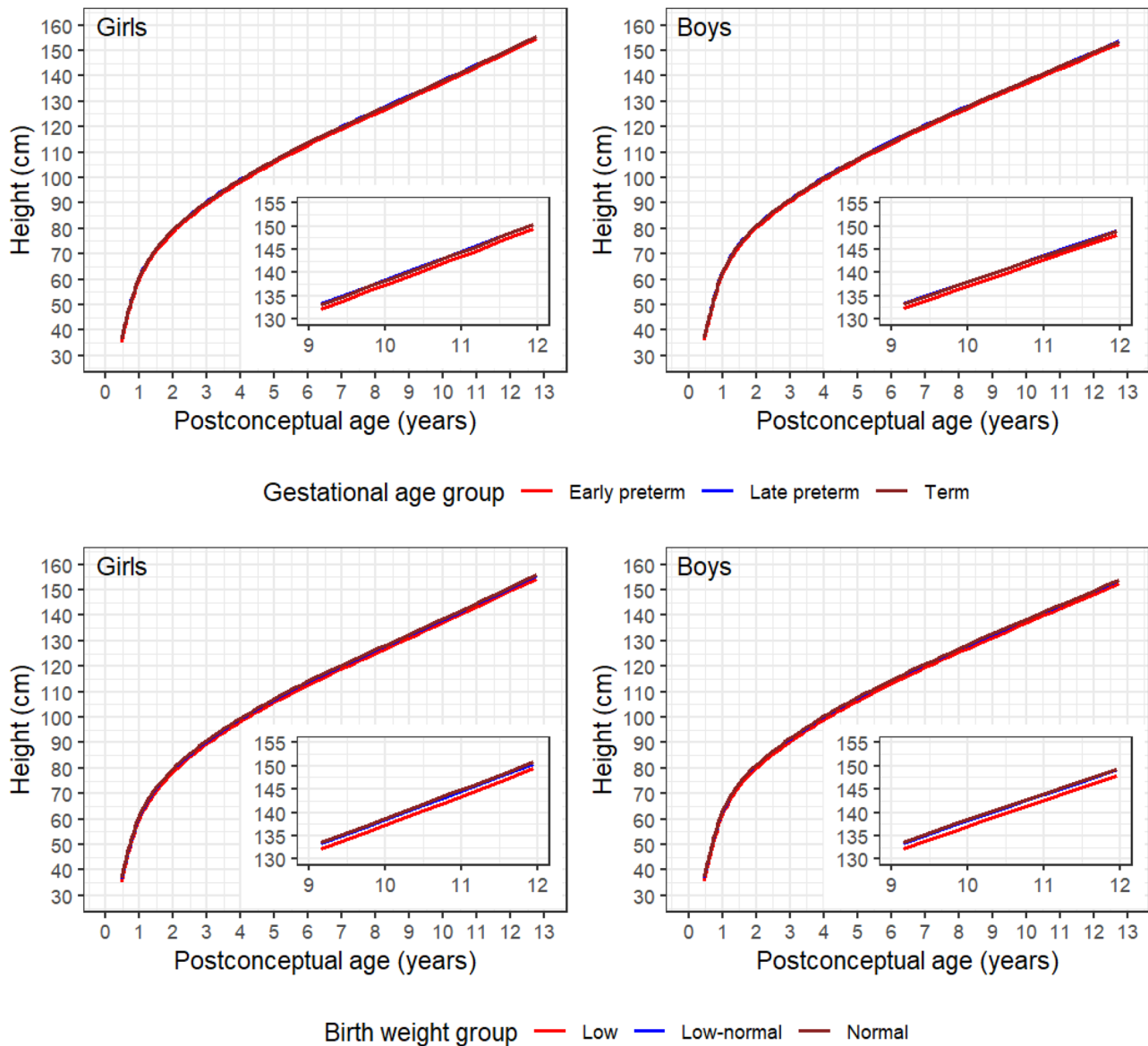
Sex	Fixed effects	Response variable	Points	d.f.	Random effects*	Variance explained (%)	Residual SD
Girls (n = 481)	GA	Height (cm)	7939	7	a c	78.5	2.1
		Weight (kg)	7914	7	a c	91.7	1.2
		BMI (kg/cm ²)	7949	8	a b c	75.2	1.0
	BW	Height (cm)	7939	7	a c	78.5	2.1
		Weight (kg)	7915	6	a c	91.6	1.2
		BMI (kg/cm ²)	7951	8	a b c	75.3	1.0
Boys (n = 469)	GA	Height (cm)	7897	8	a c	76.6	2.1
		Weight (kg)	7869	7	a c	90.4	1.2
		BMI (kg/cm ²)	7894	7	a b c	72.2	1.0
	BW	Height (cm)	7896	6	a c	76.4	2.1
		Weight (kg)	7869	7	a c	90.4	1.2
		BMI (kg/cm ²)	7894	8	a b c	72.3	1.0

*Random effects: a = size, b = timing, c = intensity.

Table 3. Significant GA and BW group mean differences in the SITAR height model for the period from birth to 12 years.

Covariate	Sex	Effect	SITAR parameter	Coefficient (95% CI) (cm)	Standard error (cm)	p-Value
GA	Girls	Early preterm	a (size)	-0.92 (-1.49; -0.34)	0.29	0.002
		Late preterm	a (size)	0.08 (-0.37; 0.53)	0.23	0.7
	Boys	Early preterm	a (size)	-0.89 (-1.48; -0.29)	0.30	0.003
		Late preterm	a (size)	0.09 (-0.34; 0.53)	0.22	0.7
BW	Girls	Low	a (size)	-1.45 (-1.90; -0.99)	0.23	<0.001
		Low-normal	a (size)	-0.35 (-0.86; 0.15)	0.26	0.2
	Boys	Low	a (size)	-1.43 (-1.88; -0.99)	0.23	<0.001
		Low-normal	a (size)	-0.18 (-0.71; 0.34)	0.27	0.5

References: Term GA group; Normal BW group.

**Figure 1.** Mean SITAR height curves for the GA and BW groups.

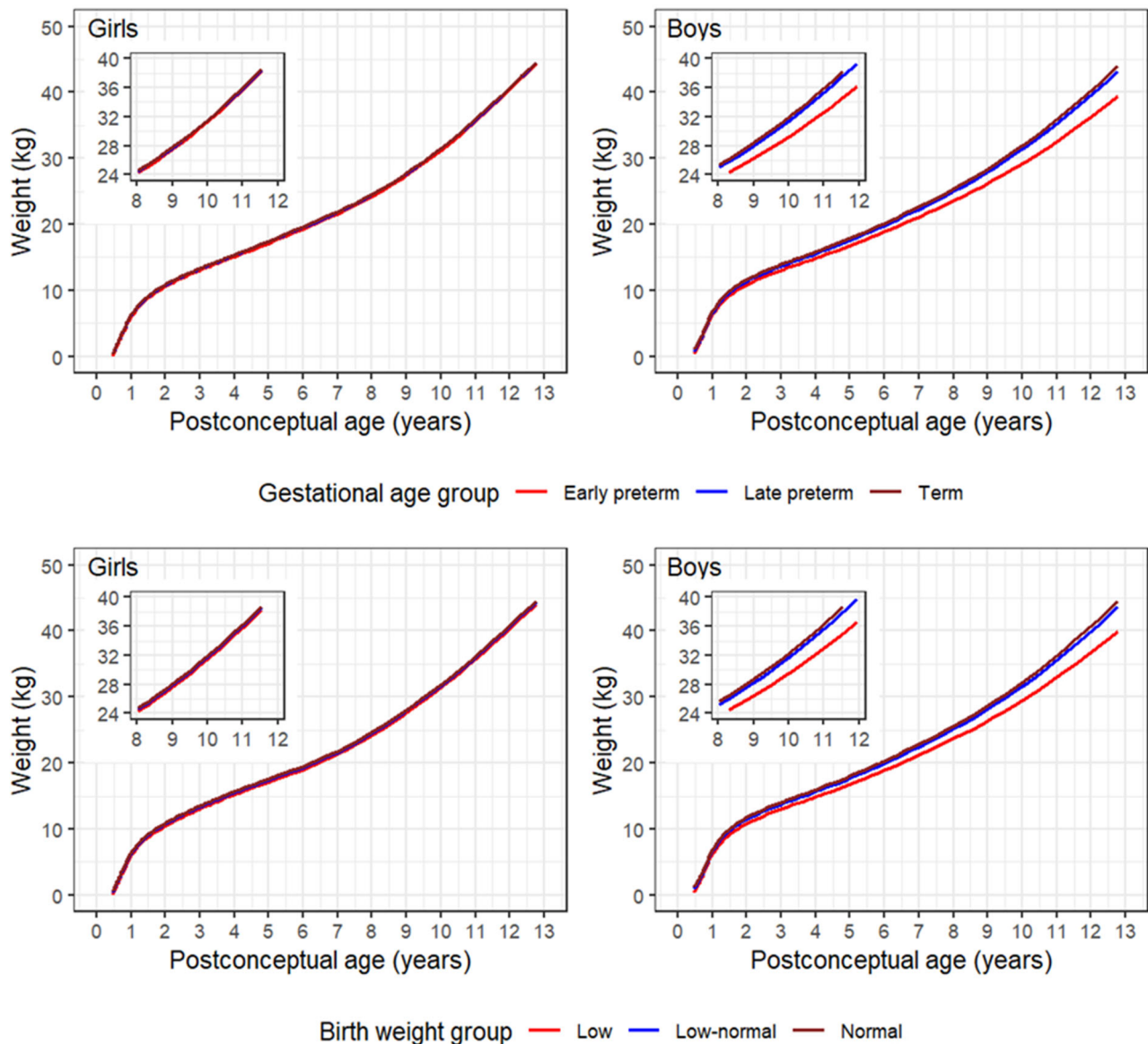
in the term group. Furthermore, low BW girls and boys were 1.4 cm significantly shorter than their normal BW peers. Figure 1 shows mean curves by BW and GA group and sex, where despite the significant ~1 cm differences in size between groups in Table 3 the group curves were closely aligned. The inset graphs focus on ages 9–12, where the group differences were more evident, with a constant offset between groups but no sign of the curves diverging.

Table 4 shows significant effects of GA and BW on weight size and intensity across the entire study period (0–12 years), with these effects being more pronounced in boys than girls. On average, boys in the early preterm group were 0.8 kg lighter than their term peers (95% CI: -1.19 to -0.48), compared to 0.3 kg for girls (95% CI: -0.50 to -0.07). Similarly, in the low BW group, boys were 1.0 kg lighter than their normal BW counterparts (95% CI: -1.26 to -0.73), compared to 0.5 kg

Table 4. Significant GA and BW group mean differences in the SITAR weight model for the period from birth to 12 years.

Covariate	Sex	Effect	SITAR parameter	Coefficient (95% CI)	Standard error	p-Value
GA group	Girls	Early preterm	a (size)	-0.29 (-0.50; -0.07)	0.11	0.009
		Late preterm	a (size)	-0.07 (-0.24; 0.09)	0.09	0.4
	Boys	Early preterm	a (size)	-0.83 (-1.19; -0.48)	0.18	<0.001
		Late preterm	a (size)	-0.26 (-0.53; -0.01)	0.13	0.05
		Early preterm	c (intensity)	-0.040 (-0.068; -0.012)	0.01	0.005
BW group	Girls	Late preterm	c (intensity)	-0.005 (-0.025; 0.015)	0.01	0.6
	Boys	Low	a (size)	-0.46 (-0.62; -0.29)	0.09	<0.001
		Low-normal	a (size)	-0.15 (-0.34; 0.04)	0.10	0.1
		Low	a (size)	-1.00 (-1.26; -0.73)	0.14	<0.001
		Low-normal	a (size)	-0.30 (-0.61; 0.02)	0.160	0.07
		Low	c (intensity)	-0.037 (-0.058; -0.016)	0.011	0.001
		Low-normal	c (intensity)	-0.006 (-0.030; -0.019)	0.013	0.7

References: Term GA group; Normal BW group. Coefficients: size – kg, intensity – fractional.

**Figure 2.** Mean SITAR weight curves for the GA and BW groups.

for girls (95% CI: -0.62 to -0.29), showing a significant sex difference. GA and BW also significantly impacted growth intensity in boys, with the early preterm group showing 4% and the low BW group showing 3.7% less intense growth spurts compared to their term and normal BW counterparts.

Figure 2 shows the mean weight curves for girls and boys, where the differences between the GA and BW groups were more obvious than for height (Figure 1). The girls' curves were closely aligned across groups throughout childhood, indicating a smaller effect of GA and BW on weight development in

Table 5. Significant GA and BW group mean differences in the SITAR BMI model for the period from birth to 12 years.

Covariate	Sex	Effect	SITAR parameter	Coefficient (95% CI)	Standard error	p-Value
GA Group	Girls	Early preterm	a (size)	−0.77 (−1.05; −0.48)	0.14	<0.001
		Late preterm	a (size)	−0.46 (−0.68; −0.24)	0.11	<0.001
		Early preterm	b (timing)	−0.110 (−0.123; −0.089)	0.007	<0.001
		Late preterm	b (timing)	−0.080 (−0.095; −0.070)	0.009	<0.001
	Boys	Early preterm	a (size)	−0.81 (−1.13; −0.49)	0.16	<0.001
		Late preterm	a (size)	−0.60 (−0.83; −0.36)	0.11	<0.001
		Early preterm	b (timing)	−0.120 (−0.136; −0.098)	0.010	<0.001
		Late preterm	b (timing)	−0.078 (−0.091; −0.065)	0.007	<0.001
	Girls	Low	a (size)	−0.81 (−1.03; −0.58)	0.11	<0.001
		Low-normal	a (size)	−0.22 (−0.47; 0.03)	0.13	0.09
		Low	b (timing)	−0.069 (−0.085; −0.054)	0.009	<0.001
		Low-normal	b (timing)	−0.028 (−0.046; −0.011)	0.008	0.001
BW Group	Girls	Low	a (size)	−0.92 (−1.17; −0.68)	0.13	<0.001
		Low-normal	a (size)	−0.48 (−0.77; −0.19)	0.15	0.001
	Boys	Low	b (timing)	−0.078 (−0.094; −0.062)	0.008	<0.001
		Low-normal	b (timing)	−0.054 (−0.073; −0.036)	0.010	<0.001

References: Term GA group; Normal BW group. Coefficients: size – kg, intensity, timing – fractional.

girls. In contrast, for boys, the curves diverged more noticeably across groups, particularly after age 9, with preterm and lower BW boys growing more slowly than their term and normal BW peers. The insets highlight these patterns, showing much larger differences for boys than girls, particularly for early preterm and low BW compared to the other groups.

Table 5 shows the significant effects of GA and BW on BMI size and timing over the entire 12-year period modelled. Mean BMI was smaller for the early/late preterm GA and low/low-normal BW groups, by 0.8/0.3 kg/m² in girls and 0.9/0.6 kg/m² in boys. Similarly, timing was earlier in the two preterm groups, by 0.11/0.08 units in both sexes, and to a lesser extent with the BW groups, by 0.08/0.05 units. A negative timing coefficient indicates an earlier growth spurt, where the fractional coefficient can be multiplied by 100 and viewed as a percentage difference. The larger effect for GA than BW is because the timing effect is a shift on the age scale and hence corresponds directly to GA.

Figure 3 shows the mean BMI curves for the GA and BW groups in girls and boys, highlighting distinct trends in BMI development across the groups. The early preterm children are initially lower than the late preterm and term children and with an earlier adiposity peak and earlier adiposity rebound (AR). But after age 9–10 the GA curves cross and the early preterm becomes relatively higher, which is what the earlier AR predicts. For the BW curves the low BW group is consistently lower than the other two groups until the curves merge at around age 12. However, the age at AR is very similar in all three BW groups, and the low BW curve does not cross the others in the same way as the early preterm group.

AR occurred earlier in the early/late preterm GA groups compared to term, by 10.2/5.3 months in boys and 7.8/7.8 months in girls (Supplementary Table 1). Similarly, AR timing was earlier in the low/low-normal BW groups than normal BW, by 7.6/5.2 months in boys and 5.2/0.0 months in girls (Supplementary Table 1).

Discussion

This study analyses growth in children born preterm using the SITAR model to assess height, weight, and BMI

trajectories up to 12 years of age. Our findings demonstrate significant disparities in growth patterns between children grouped by birth weight (BW) and gestational age (GA). Importantly, low BW emerged as a more robust aetiological determinant of adverse growth outcomes than early preterm birth, as children in the low BW group exhibited notably smaller size effects than in the early preterm group, with growth deficits persisting into later years. Low BW girls/boys showed greater growth deficits, being 1.4 cm shorter and 0.5/1.0 kg lighter than their normal BW peers, compared to early preterm girls/boys, who were 0.9 cm shorter and 0.3/0.8 kg lighter than term peers. Low BW children were 1.4 cm shorter than their normal BW peers, compared to early preterm, who were 0.9 cm shorter, resulting in an additional deficit of 0.5 cm for the low BW group relative to the early preterm group. Similarly, low BW girls/boys were 0.5/1.0 kg lighter than their normal BW peers, compared to early preterm girls/boys, who were 0.3/0.8 kg lighter, reflecting a further deficit of 0.2/0.2 kg for the low BW group relative to the early preterm group.

While our findings suggest the bigger role of BW than GA in determining long-term growth outcomes, this influence is particularly evident in height and weight. Low BW children exhibit significant and persistent deficits in height and weight compared to their peers, with some studies reporting that extremely low BW (ELBW) infants remain smaller and lighter throughout childhood and adolescence (Van de Pol and Allegaert 2020). Even with catch-up growth during adolescence, ELBW children often fail to reach the same height as term-born peers, with deficits persisting into adulthood (Doyle et al. 2004; Saigal et al. 2006; Hack et al. 2014). Although height and weight are critical growth indicators, BMI trajectories also highlight important differences. For example, some research suggests that normalising BMI does not imply a full resolution of growth challenges, as height may continue to lag behind, emphasising the need for targeted interventions in low BW children (Jones-Smith et al. 2007; Van de Pol and Allegaert 2020). This contrasts with findings that GA is a crucial factor, with each additional week of gestation contributing to improved growth outcomes, including height, weight, and BMI, after discharge (Jasper

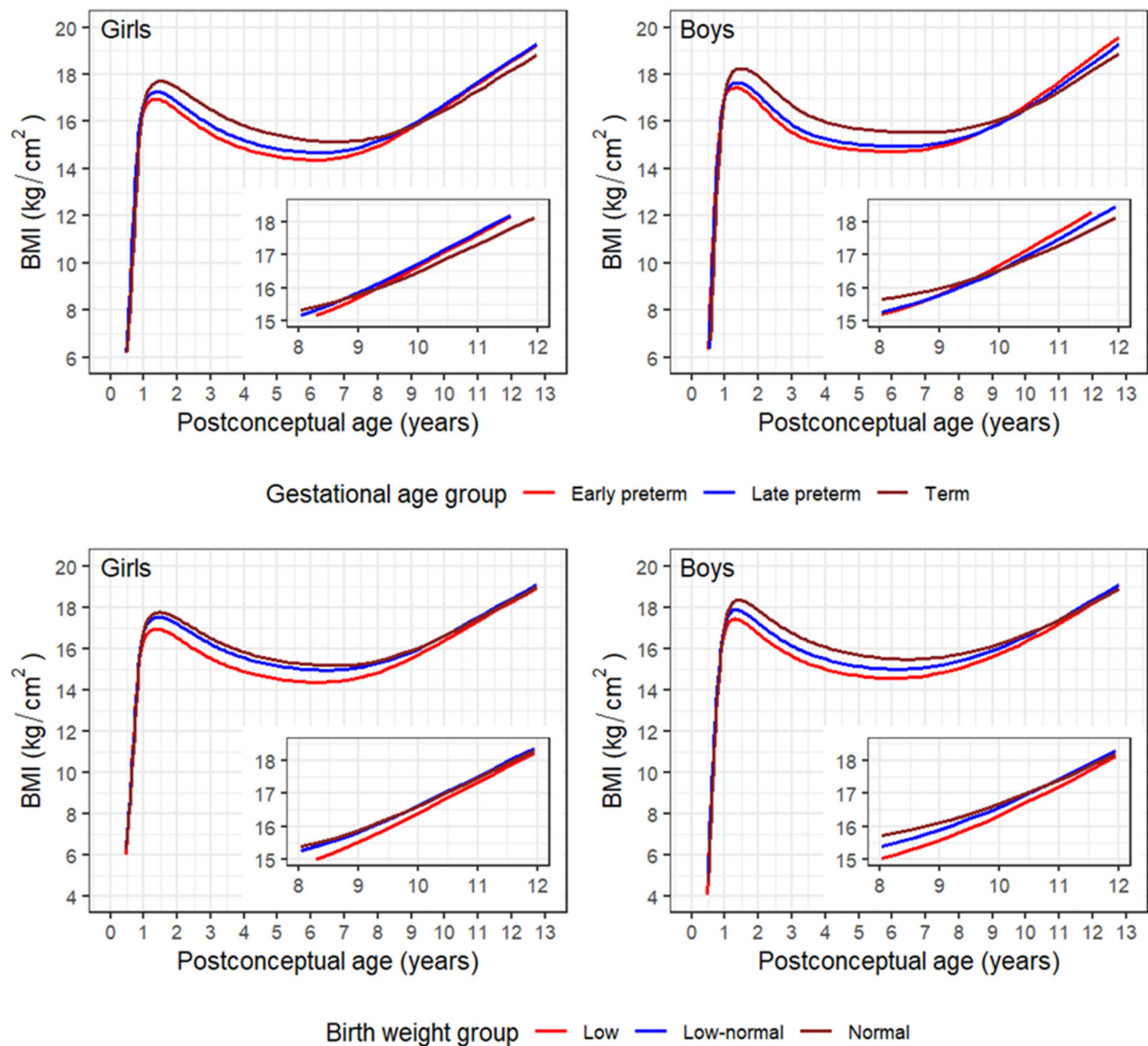


Figure 3. Mean SITAR BMI curves for the GA and BW groups.

et al. 2021). However, in our cohort, extremely preterm (EP) infants remained shorter and lighter compared to term-born controls throughout childhood, with girls and boys being 0.9cm shorter and 0.8kg lighter, respectively. Additionally, EP infants exhibited an elevated BMI by adulthood, consistent with other findings in the literature (Ni et al. 2020).

In general, BMI rapidly increases in the first year, declines to a nadir at around age 6, and then rises again in a phase known as the adiposity rebound (AR) (Kang 2018). Studies have shown that early AR (before age 5) occurs in a significant proportion of preterm infants, with rates as high as 54% in some cohorts (Baldassarre et al. 2020). This earlier timing is associated with increased BMI and a higher risk of developing obesity or worse cardiometabolic health later in life (Rolland-Cachera et al. 2006; Ou-Yang et al. 2020; Fonseca et al. 2021). In our study, AR timing appears later in term-born children compared to preterm groups, indicating that preterm children may experience an earlier AR. Moreover, the magnitude of AR differs significantly between the groups. In the GA

groups, early preterm children experience a stronger AR, with their BMI rising sharply after AR and surpassing term-born children by age 9–9.5, indicating a higher risk of overweight and future obesity (Kang 2018). However, for BW groups, while the timing of AR remains more consistent, the magnitude varies. These groups show a more gradual and stable BMI increase after AR, with no curve crossing, suggesting they may follow a healthier BMI trajectory. According to the literature (Kang 2018; Moon 2020), a later AR (at or after 7 years of age) is associated with a lower risk of overweight, decreased likelihood of developing obesity, and an increased chance of reversing obesity in young children, highlighting its protective role against long-term obesity and metabolic risks. Moreover, within the GA groups, early and late preterm children follow more similar growth trajectories, with the term group being more distinct until the crossing occurs. The BW groups are more evenly spaced in BMI throughout childhood, particularly among boys, indicating a more stable difference between groups. This could imply that BW has a

more linear relationship with BMI, while GA may affect growth more dynamically, especially in the preterm vs. term-born distinction. As BW reflects in-utero energy reserves more directly than gestational age (GA), our findings support the hypothesis of energy trade-offs impacting long-term growth and may contribute to understanding developmental plasticity, emphasising how in-utero nutritional and environmental conditions shape energy allocation for optimal growth (Bateson et al. 2004; Gluckman and Hanson 2004). However, both perspectives (Bateson et al. 2004; Gluckman and Hanson 2004) agree that preterm infants, regardless of GA or BW, are a heterogeneous group with physiological and developmental immaturity, leading to varying growth outcomes.

Moreover, our study identified that boys are more vulnerable to long-term growth deficits than girls. Specifically, low BW boys weighed 1.0 kg less than normal BW boys, whereas low BW girls weighed only 0.5 kg less than normal BW girls. The confidence intervals confirm a statistically significant difference between sexes in the low BW group. This suggests that girls may have greater resilience in terms of weight outcomes, though they still experience significant growth deficits, especially in height. Boys also experience less intense growth spurts (3.7% less intense growth spurt than their normal BW peers), indicating they may have difficulty catching up in growth. This vulnerability in boys was also noted in their more pronounced long-term growth challenges compared to girls (Curtis and Rigo 2004). However, other studies (Suikkanen et al. 2022) reported no increased risk for early puberty in preterm boys or girls, suggesting that while sex-based differences in growth trajectories exist, they may not extend to pubertal timing. These conflicting findings indicate that while boys may be more prone to growth challenges, further research is needed to explore how these vulnerabilities manifest across different stages of development.

Notably, children in the low BW group exhibited faster weight gain but less intense BMI increases during the observed period, indicating a distinct growth trajectory that may contribute to long-term growth challenges. This aligns with findings by Jones-Smith et al. (2007, 2013), who found that accelerated growth during infancy, especially among small or normal-sized infants, is associated with an increased risk of childhood overweight. Their research highlights the complexity of growth patterns, noting that infants born larger do not experience the same risks, suggesting that early life growth velocity plays a role in later overweight risk, particularly in smaller infants. Our findings suggest that faster early growth spurts in early preterm children may predispose them to future health risks, including obesity, underscoring the potential protective role of delayed adiposity rebound (AR) against long-term obesity and metabolic risks, as mentioned previously.

One of the strengths of this study is the application of the SITAR model, which provides a refined understanding of growth trajectories by accounting for individual differences in size, timing, and intensity. Moreover, our large sample size and extended follow-up period enhance the generalisability of our findings. Furthermore, although the preterm cohort (2000–2015) and the term cohort (1996) were born several years apart, they grew into adolescence during a similar

timeframe, ensuring similar environmental, socioeconomic, and nutritional conditions (Gyventojai ir socialinė statistika. - Oficialiosios statistikos portalas 2024). All growth data were collected from the same geographical region and healthcare system, reducing variability due to systemic differences. This overlap minimises the potential influence of secular trends on our findings. Additionally, advances in neonatal care in Lithuania were implemented from 1995 onward, ensuring that the care provided during the study period was relatively consistent for the preterm cohort.

Nonetheless, the study's retrospective nature introduces certain limitations. Although we could not directly account for the pubertal stage in this study, the SITAR model is designed to adjust for pubertal timing and intensity through its random effects. These effects capture individual differences in the age of peak growth velocity (timing) and the magnitude of the growth spurt (intensity), key components of pubertal growth. For example, in our data, girls exhibited smaller timing variance in SITAR compared to boys, suggesting more consistent growth patterns during the observed age range, which could indicate earlier growth dynamics in girls relative to boys below age 13. Demonstrating how these random effects alter the mean growth curve could provide additional insight, particularly as boys may be underrepresented in terms of pubertal growth in this dataset. Since some studies suggest that very, moderately, and late preterm individuals may reach similar adult size, peak height velocity, and pubertal timing as term-born peers (Suikkanen et al. 2022; Vinther et al. 2023), extending the data collection into adolescence could better capture these dynamics and their impact on long-term growth outcomes.

Additionally, this study focused on infant sex, GA, and BW as primary variables for growth modelling due to their well-established relevance in determining growth trajectories. While other potential covariates, such as maternal age and maternal education attainment, may influence growth outcomes, their adjustment would likely have minimal impact in this analysis, as the same infants are being compared for both BW and GA. The study's primary focus on preterm-specific and birth-related variables aligns with its objectives. However, future research could incorporate a broader range of covariates in studies with more heterogeneous populations to provide additional insights into growth determinants. In conclusion, our study highlights the significant role of BW in shaping growth trajectories, with low BW often exerting a stronger influence than GA, but not uniformly affecting all parameters. Specifically, GA appears to be more prominent in shaping BMI trajectories, as evidenced by the sharper velocity in BMI post-adiposity rebound in early preterm children. This divergence suggests that while low BW is linked to sustained growth deficits, GA influences BMI patterns more dynamically, potentially elevating the risk of overweight and obesity in early preterm groups. In our data, boys in the low BW group exhibited larger weight deficits compared to girls in the same group during the growth period studied.

Clinically, these findings underscore the need for targeted growth interventions in children with low BW, as their growth deficits persist longer than those associated with preterm birth alone. These findings suggest that clinical interventions

should prioritise children born with low BW (including their preterm status) to address their unique growth challenges and optimise developmental outcomes. Further research is needed to investigate the growth characteristics of low birth weight and preterm infants, particularly in relation to different metabolic factors and environmental exposures.

Consent statement

All data used in this research were retrospective, anonymised and handled in accordance with relevant data protection regulations. As such, individual consent was not required for this study.

Authors contributions

R.M. collected, analysed, interpreted the data, and took the lead in writing the manuscript with the input from other authors. J.T. raised the main conceptual idea, designed and supervised the study, helped in data interpretation and manuscript writing, and revised the final version. T.J.C. advised on the fitting of the SITAR models, commented on the study design and contributed to revising the manuscript. R.L. performed the statistical analysis, provided suggestions for data interpretation, and contributed to revising the manuscript. A.S. contributed to the interpretation of the results and the final version of the manuscript.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Funding

The author(s) reported there is no funding associated with the work featured in this article.

Data availability statement

The datasets collected and analysed during the current study are available upon reasonable request from the corresponding author.

References

- Baldassarre ME, Di Mauro A, Caroli M, Schettini F, Rizzo V, Panza R, De Giorgi A, Capozza M, Fanelli M, Laforgia N, et al. **2020**. Premature birth is an independent risk factor for early adiposity rebound: longitudinal analysis of BMI data from birth to 7 years. *Nutrients*. 12(12):3654. doi: [10.3390/nu12123654](https://doi.org/10.3390/nu12123654).
- Bateson P, Barker D, Clutton-Brock T, Deb D, D'Udine B, Foley RA, Gluckman P, Godfrey K, Kirkwood T, Lahr MM, et al. **2004**. Developmental plasticity and human health. *Nature*. 430(6998):419–421. doi: [10.1038/nature02725](https://doi.org/10.1038/nature02725).
- Beath KJ. **2007**. Infant growth modelling using a shape invariant model with random effects. *Stat Med*. 26(12):2547–2564. doi: [10.1002/sim.2718](https://doi.org/10.1002/sim.2718).
- Bocca-Tjeertes IFA, Kerstjens JM, Reijneveld SA, de Winter AF, Bos AF. **2011**. Growth and predictors of growth restraint in moderately preterm children aged 0 to 4 years. *Pediatrics*. 128(5):e1187–94–e1194. doi: [10.1542/peds.2010-3781](https://doi.org/10.1542/peds.2010-3781).
- Cameron N. **2022**. Chapter 1. The pattern of human growth. In: Cameron N, Schell LM, editors. *Human growth and development*. 3rd ed. Boston: Academic Press. p. 1–22.
- Casey PH. **2008**. Growth of low birth weight preterm children. *Semin Perinatol*. 32(1):20–27. doi: [10.1053/j.semperi.2007.12.004](https://doi.org/10.1053/j.semperi.2007.12.004).
- Casirati A, Somaschini A, Perrone M, Vandoni G, Sebastiani F, Montagna E, Somaschini M, Caccialanza R. **2022**. Preterm birth and metabolic implications on later life: a narrative review focused on body composition. *Front Nutr*. 9:978271. doi: [10.3389/fnut.2022.978271](https://doi.org/10.3389/fnut.2022.978271).
- Cole T. **2023**. Super imposition by translation and rotation growth curve analysis [Internet]. [accessed 2024 Sep 18]. Available from: <https://cran.r-project.org/web/packages/sitar/index.html>.
- Cole TJ, Donaldson MDC, Ben-Shlomo Y. **2010**. SITAR—a useful instrument for growth curve analysis. *Int J Epidemiol*. 39(6):1558–1566. doi: [10.1093/ije/dyq115](https://doi.org/10.1093/ije/dyq115).
- Cole TJ. **2006**. The international growth standard for preadolescent and adolescent children: statistical considerations. *Food Nutr Bull*. 27(4 Suppl Growth Standard):S237–S243. doi: [10.1177/156482650602745507](https://doi.org/10.1177/156482650602745507).
- Cole TJ. **2019**. Commentary: methods for calculating growth trajectories and constructing growth centiles. *Stat Med*. 38(19):3571–3579. doi: [10.1002/sim.8129](https://doi.org/10.1002/sim.8129).
- Cole TJ. **2020**. Tanner's tempo of growth in adolescence: recent SITAR insights with the Harpenden Growth Study and ALSPAC. *Ann Hum Biol*. 47(2):181–198. doi: [10.1080/03014460.2020.1717615](https://doi.org/10.1080/03014460.2020.1717615).
- Curtis MD, Rigo J. **2004**. Extrauterine growth restriction in very-low-birth-weight infants. *Acta Paediatr*. 93(12):1563–1568. doi: [10.1080/08035250410022198](https://doi.org/10.1080/08035250410022198).
- Derraik JGB, Lundgren M, Cutfield WS, Ahlsson F. **2017**. Association between preterm birth and lower adult height in women. *Am J Epidemiol*. 185(1):48–53. doi: [10.1093/aje/kww116](https://doi.org/10.1093/aje/kww116).
- Doyle LW, Faber B, Callanan C, Ford GW, Davis NM. **2004**. Extremely low birth weight and body size in early adulthood. *Arch Dis Child*. 89(4):347–350. doi: [10.1136/adc.2002.025924](https://doi.org/10.1136/adc.2002.025924).
- Elhakeem A, Hughes RA, Tilling K, Cousminer DL, Jackowski SA, Cole TJ, Kwong ASF, Li Z, Grant SFA, Baxter-Jones ADG, et al. **2022**. Using linear and natural cubic splines, SITAR, and latent trajectory models to characterise nonlinear longitudinal growth trajectories in cohort studies. *BMC Med Res Methodol*. 22(1):68. doi: [10.1186/s12874-022-01542-8](https://doi.org/10.1186/s12874-022-01542-8).
- Embleton ND, Wood C. **2019**. Metabolic outcomes in very low birth-weight and preterm infants in later life. *J Pediatr*. 95(3):260–263. doi: [10.1016/j.jpeds.2018.06.002](https://doi.org/10.1016/j.jpeds.2018.06.002).
- Euser AM, de Wit CC, Finken MJ, Rijken M, Wit JM. **2008**. Growth of preterm born children. *Horm Res*. 70(6):319–328. doi: [10.1159/000161862](https://doi.org/10.1159/000161862).
- Fenton TR, Anderson D, Groh-Wargo S, Hoyos A, Ehrenkranz RA, Senterre T. **2018**. An Attempt to standardize the calculation of growth velocity of preterm infants—evaluation of practical bedside methods. *J Pediatr*. 196:77–83. doi: [10.1016/j.jpeds.2017.10.005](https://doi.org/10.1016/j.jpeds.2017.10.005).
- Fonseca MJ, Moreira C, Santos AC. **2021**. Adiposity rebound and cardiometabolic health in childhood: results from the Generation XXI birth cohort. *Int J Epidemiol*. 50(4):1260–1271. doi: [10.1093/ije/dyab002](https://doi.org/10.1093/ije/dyab002).
- Gluckman PD, Hanson MA. **2004**. Living with the past: evolution, development, and patterns of disease. *Science*. 305(5691):1733–1736. doi: [10.1126/science.1095292](https://doi.org/10.1126/science.1095292).
- Greer FR, Olsen IE. **2013**. How fast should the preterm infant grow? *Curr Pediatr Rep*. 1(4):240–246. doi: [10.1007/s40124-013-0029-1](https://doi.org/10.1007/s40124-013-0029-1).
- Gyventojai ir socialinė statistika. - Oficialiosios statistikos portalas. **2024**. [Internet]. [accessed 2024 Dec 31]. Available from: <https://osp.stat.gov.lt/lietuvos-ekonomikos-raida/gyventojai-ir-socialine-statistika>.
- Hack M, Schluchter M, Margevicius S, Andreias L, Taylor HG, Cuttler L. **2014**. Trajectory and correlates of growth of extremely-low-birth-weight adolescents. *Pediatr Res*. 75(2):358–366. doi: [10.1038/pr.2013.209](https://doi.org/10.1038/pr.2013.209).
- Heidemann LA, Procianny RS, Silveira RC. **2019**. Prevalence of metabolic syndrome-like in the follow-up of very low birth weight preterm infants and associated factors. *J Pediatr*. 95(3):291–297. doi: [10.1016/j.jpeds.2018.02.009](https://doi.org/10.1016/j.jpeds.2018.02.009).
- Hollanders JJ, van der Pal SM, van Dommelen P, Rotteveel J, Finken MJ. **2017**. Growth pattern and final height of very preterm vs. very low

- birth weight infants. *Pediatr Res.* 82(2):317–323. doi: [10.1038/pr.2017.63](https://doi.org/10.1038/pr.2017.63).
- Itabashi K, Mishina J, Tada H, Sakurai M, Nanri Y, Hirohata Y. 2007. Longitudinal follow-up of height up to five years of age in infants born preterm small for gestational age; comparison to full-term small for gestational age infants. *Early Human Dev.* 83(5):327–333. doi: [10.1016/j.earlhumdev.2006.07.002](https://doi.org/10.1016/j.earlhumdev.2006.07.002).
- Jasper EA, Cho H, Breheny PJ, Bao W, Dagle JM, Ryckman KK. 2021. Perinatal determinants of growth trajectories in children born preterm. *PLoS One.* 16(1):e0245387. doi: [10.1371/journal.pone.0245387](https://doi.org/10.1371/journal.pone.0245387).
- Johnson L, van Jaarsveld CHM, Llewellyn CH, Cole TJ, Wardle J. 2014. Associations between infant feeding and the size, tempo and velocity of infant weight gain: SITAR analysis of the Gemini twin birth cohort. *Int J Obes.* 38(7):980–987. doi: [10.1038/ijo.2014.61](https://doi.org/10.1038/ijo.2014.61).
- Johnson W, Balakrishna N, Griffiths PL. 2013. Modeling physical growth using mixed effects models. *Am J Phys Anthropol.* 150(1):58–67. doi: [10.1002/ajpa.22128](https://doi.org/10.1002/ajpa.22128).
- Johnson W. 2015. Analytical strategies in human growth research. *Am J Hum Biol.* 27(1):69–83. doi: [10.1002/ajhb.22589](https://doi.org/10.1002/ajhb.22589).
- Jones-Smith JC, Fernald LCH, Neufeld LM. 2007. Birth size and accelerated growth during infancy are associated with increased odds of childhood overweight in Mexican children. *J Am Diet Assoc.* 107(12):2061–2069. doi: [10.1016/j.jada.2007.09.011](https://doi.org/10.1016/j.jada.2007.09.011).
- Jones-Smith JC, Neufeld LM, Laraia B, Ramakrishnan U, Garcia-Guerra A, Fernald LCH. 2013. Early life growth trajectories and future risk for overweight. *Nutr Diabetes.* 3(2):e60. doi: [10.1038/nutd.2012.32](https://doi.org/10.1038/nutd.2012.32).
- Kang MJ. 2018. The adiposity rebound in the 21st century children: meaning for what? *Korean J Pediatr.* 61(12):375–380. doi: [10.3345/kjp.2018.07227](https://doi.org/10.3345/kjp.2018.07227).
- Moon RC. 2020. Late adiposity rebound and the probability of developing and reversing childhood obesity. *J Pediatr.* 216:128–135.e3. doi: [10.1016/j.jpeds.2019.09.065](https://doi.org/10.1016/j.jpeds.2019.09.065).
- Ni Y, Beckmann J, Gandhi R, Hurst JR, Morris JK, Marlow N. 2020. Growth to early adulthood following extremely preterm birth: the EPICure study. *Arch Dis Child Fetal Neonatal Ed.* 105(5):496–503. doi: [10.1136/archdischild-2019-318192](https://doi.org/10.1136/archdischild-2019-318192).
- Ou-Yang M-C, Sun Y, Liebowitz M, Chen C-C, Fang M-L, Dai W, Chuang T-W, Chen J-L. 2020. Accelerated weight gain, prematurity, and the risk of childhood obesity: a meta-analysis and systematic review. *PLoS One.* 15(5):e0232238. doi: [10.1371/journal.pone.0232238](https://doi.org/10.1371/journal.pone.0232238).
- Pizzi C, Cole TJ, Richiardi L, dos-Santos-Silva I, Corvalan C, De Stavola B. 2014. Prenatal influences on size, velocity and tempo of infant growth: findings from three contemporary cohorts. *PLoS One.* 9(2):e90291. doi: [10.1371/journal.pone.0090291](https://doi.org/10.1371/journal.pone.0090291).
- Rolland-Cachera MF, Deheeger M, Maillot M, Bellisle F. 2006. Early adiposity rebound: causes and consequences for obesity in children and adults. *Int J Obes.* 30 (S4):S11–S17. doi: [10.1038/sj.ijo.0803514](https://doi.org/10.1038/sj.ijo.0803514).
- Ruys CA, Hollanders JJ, Bröring T, van Schie PEM, van der Pal SM, van de Lagemaat M, Lafeber HN, Rotteveel J, Finken MJJ. 2019. Early-life growth of preterm infants and its impact on neurodevelopment. *Pediatr Res.* 85(3):283–292. doi: [10.1038/s41390-018-0139-0](https://doi.org/10.1038/s41390-018-0139-0).
- Saigal S, Stoskopf B, Streiner D, Paneth N, Pinelli J, Boyle M. 2006. Growth trajectories of extremely low birth weight infants from birth to young adulthood: a longitudinal, population-based study. *Pediatr Res.* 60(6):751–758. doi: [10.1203/01.pdr.0000246201.93662.8e](https://doi.org/10.1203/01.pdr.0000246201.93662.8e).
- Santos IS, Matijasevich A, Domingues MR, Barros AJ, Victora CG, Barros FC. 2009. Late preterm birth is a risk factor for growth faltering in early childhood: a cohort study. *BMC Pediatr.* 9(1):71. doi: [10.1186/1471-2431-9-71](https://doi.org/10.1186/1471-2431-9-71).
- Singer D, Thiede LP, Perez A. 2021. Adults born preterm—long-term health risks of former very low birth weight infants. *Dtsch Arztebl Int.* 118(31–32):521–527.
- Suikkanen J, Nurhonen M, Cole TJ, Paalanen M, Matinolli H-M, Tikanmäki M, Väärasmäki M, Järvelin M-R, Hovi P, Kajantie E, et al. 2022. Preterm birth and subsequent timing of pubertal growth, menarche, and voice break. *Pediatr Res.* 92(1):199–205. doi: [10.1038/s41390-021-01690-5](https://doi.org/10.1038/s41390-021-01690-5).
- Svedenkrans J, Henckel E, Kowalski J, Norman M, Bohlin K. 2013. Long-term impact of preterm birth on exercise capacity in healthy young men: a national population-based cohort study. *PLoS One.* 8(12):e80869. doi: [10.1371/journal.pone.0080869](https://doi.org/10.1371/journal.pone.0080869).
- Van de Pol C, Allegaert K. 2020. Growth patterns and body composition in former extremely low birth weight (ELBW) neonates until adulthood: a systematic review. *Eur J Pediatr.* 179(5):757–771. doi: [10.1007/s00431-019-03552-z](https://doi.org/10.1007/s00431-019-03552-z).
- VanderWeele TJ, Mumford SL, Schisterman EF. 2012. Conditioning on intermediates in perinatal epidemiology. *Epidemiology.* 23(1):1–9. doi: [10.1097/EDE.0b013e31823aca5d](https://doi.org/10.1097/EDE.0b013e31823aca5d).
- Vinther JL, Cadman T, Avraam D, Ekstrøm CT, Sørensen TIA, Elhakeem A, Santos AC, Pinot de Moira A, Heude B, Iñiguez C, et al. 2023. Gestational age at birth and body size from infancy through adolescence: an individual participant data meta-analysis on 253,810 singletons in 16 birth cohort studies. *PLoS Med.* 20(1):e1004036. doi: [10.1371/journal.pmed.1004036](https://doi.org/10.1371/journal.pmed.1004036).
- Wood NS, Costeloe K, Gibson AT, Hennessy EM, Marlow N, Wilkinson AR. 2003. The EPICure study: growth and associated problems in children born at 25 weeks of gestational age or less. *Arch Dis Child Fetal Neonatal Ed.* 88(6):F492–F500.