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# Early childhood growth trajectory and later cognitive ability: Evidence from a large prospective birth cohort of healthy term-born children

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**Key Messages**

- Associations of early childhood growth and later cognitive ability have typically been studied based on size at one or two ages and a single measure of cognition.
- We examined individual growth trajectories of height and weight measured multiple times over the first 6.5 years in relation to cognitive ability at age 6.5 and 16 years and its change over time, using two random-effects models with distinct characterization of growth.
- When we modelled the pattern of growth over the first 6.5 years as a whole, the overall height and weight over time and earlier acceleration in growth were positively associated with cognitive scores at both 6.5 and 16 years.
- When we differentiated growth during infancy and post-infancy, birth size and faster post-infancy growth in height and weight were positively associated with later cognitive abilities, while growth during infancy was not.
- We found no associations between growth trajectories and the change in cognitive ability over time.

## Abstract

**Background:** Most studies of associations between child growth and cognitive ability were based on size at one or two ages and a single measure of cognition. Thus, we aimed to characterize different aspects of early growth and their associations with cognitive outcomes in childhood through adolescence.

**Methods:** In a sample of 12,368 Belarusian children born at term, we examined associations between length/height and weight trajectories over the first 6.5-years of life with cognitive ability at 6.5 and 16 years and its change over time. We estimated growth trajectories using two random-effects models—the Super Imposition by Translation and Rotation to model overall patterns of growth and the Jenss-Bayley to distinguish growth in infancy vs post-infancy. Cognitive ability was measured using the Wechsler Abbreviated Scales of Intelligence at 6.5 years and the computerized NeuroTrax test at 16 years.

**Results:** Higher length/height between birth and 6.5 years was associated with higher cognitive scores at 6.5 and 16 years [2.7 points (95% CI: 2.1, 3.2) and 2.5 points (95% CI: 1.9, 3.0), respectively, per standard deviation (SD) increase]. A 1-SD delay in the childhood height growth spurt was negatively associated with cognitive scores [-2.4, 95% CI: (-3.0, -1.8) at age 6.5; -2.2, 95% CI: (-2.7, -1.6) at 16 years]. Birth size and post-infancy growth velocity were positively associated with cognitive scores at both ages. Height trajectories were not associated with the change in cognitive score. Similar results were observed for weight trajectories.

**Conclusion:** Among term infants, overall size, timing of the childhood growth spurt~~,~~ size at birth, and post-infancy growth velocity were all associated with cognitive ability at early school age and adolescence.

**Keywords:**

Growth trajectory; IQ; cognition; SITAR model; Jenss-Bayley model; height

## Background

Early childhood is a crucial period for the development of cognitive ability (1). Growth (increase in body size) is affected by both genetic and environmental factors that may also affect other outcomes, including cognition (2, 3). Evidence on the relationships between growth in early childhood and later cognitive ability is limited. Most previous studies have measured size at a single time point or growth between two time points (4). Few have considered both weight and height, and even fewer have focused on healthy children born at term (5-11).

Studies relating growth during infancy to later cognition among term-born children have reported conflicting results (5-9). We have previously reported that faster weight gain from birth to age of three months was positively associated with cognitive ability at 6.5 years (10), whereas other studies have found growth in weight in the first eight weeks (9) or the first five months (11) of life to be the most important period for cognitive ability at eight years and 56 months, respectively. Differences in age at growth assessment and in methods used to characterize growth may explain the inconsistent findings, suggesting the need to model the overall trajectory of growth over time. Finally, most studies have measured cognitive outcomes at a single pre-school or early school age (5, 7, 9-11). Cognitive ability may not remain static throughout childhood and adolescence (12, 13), and it is unknown whether the association between childhood growth and cognitive ability persists over time.

In the present study, we aimed to examine associations of different *characteristics* of early growth, rather than the amount of growth during a period, with cognitive outcomes in childhood through adolescence in a large cohort of healthy term-born children. We used two complementary random-effects models to characterize individual-specific growth trajectories that parameterize different aspects of physical growth in early life.

## Methods

### Study participants

We used data from the Promotion of Breastfeeding Intervention Trial (PROBIT), a cluster-randomized trial of a breastfeeding promotion intervention in the Republic of Belarus. A detailed description of PROBIT is available elsewhere (14, 15). In brief, 17,046 healthy mother-infant pairs were recruited from 31 hospitals and affiliated polyclinics during their postpartum hospital stay in 1996-1997. The experimental intervention was based on the WHO-UNICEF Baby-Friendly Hospital Initiative. Eligible infants initiated breastfeeding and were born at term (37 weeks of gestation or later) with birth weight $\geq$2,500 grams and 5-minute Apgar score of five or more (14). Research-trained polyclinic pediatricians interviewed and examined the infants and children during scheduled follow-up visits at 1, 2, 3, 6, 9, and 12 months and 6.5, 11.5 and 16 years (14). Most participants completed all first-year assessments (96.7%), and 81.5% and 78.7% completed the 6.5-years and 16-years follow-up assessments, respectively. Our analytical sample included the 12,368 children with valid measures of cognitive ability at both 6.5 and 16 years (see Supplementary Figure S1 for the recruitment and follow-up of the PROBIT cohort to 16 years of age).

The initial PROBIT trial and all subsequent follow-ups were approved by the Belarusian Ministry of Health and received ethical approval from the McGill University Health Centre Research Ethics Board. The Institutional Review Board at Harvard Pilgrim Health Care and the Avon Longitudinal Study of Parents and Children (ALSPAC) Law and Ethics Committee also provided ethical approval for the 11.5- and 16-year follow-up visits. A parent or legal guardian provided written informed consent in Russian at all research visits, and all participants provided written assent for the 11.5- and 16-year visits.

## Growth trajectories

Linear growth and weight represent different aspects of growth and are influenced by distinct genetic and/or environmental determinants. For example, genetic factors strongly affect growth in height, but their influence on weight growth is less pronounced (16, 17). Weight gain is more influenced by acute conditions of illness or malnutrition, whereas linear growth is more strongly influenced by chronic diseases and nutritional deficiencies (18). We therefore examined height and weight trajectories as the two growth metrics relevant to cognitive development. Weight and length were retrieved from obstetric records at birth and measured at the above-mentioned scheduled follow-up visits by study pediatricians. Measures between 1 and 6.5 years were retrieved from polyclinic visit records for each child (median number of measures=11, interquartile range [IQR]: 2.9-13).

Individual-specific growth trajectories using these repeated measures from birth to age 6.5 years were estimated from two random-effects models: the Super Imposition by Translation and Rotation (SITAR) and the Jenss-Bayley (JB) models (19-21). Child growth trajectories were modeled from birth to age 6.5 years because data on height and weight after 6.5 years were available for the scheduled follow-up visits only at 11.5, and 16 years.

The SITAR model is a shape-invariant, non-linear model that identifies the population-average growth curve and estimates individual-specific deviations from the average curve in three distinct growth parameters according to the following equation:

$$y_{it}=\alpha_i+h[\frac{t-\beta_i}{e^{(-\gamma_i)}}] \tag{1}$$

where $y_{it}$ is the height/length or weight for subject *i* at age *t* , *h(t)* is a natural cubic spline curve of height or weight against age, and $\alpha_i$, $\beta_i$, and $\gamma_i$ are individual-specific random effects of size, tempo, and velocity, respectively (19). Size *(α)* represents child-specific variations in overall size (length/height or weight) from the population mean (i.e., up or down shift of the growth curve around the population average curve) from birth to 6.5 years, with positive values corresponding to taller or heavier children than the average over the entire period considered. Tempo (*β*) indicates child-specific differences in the timing of the growth spurt (i.e., left or right shift of the growth curve along the age scale), with positive values corresponding to children with a later growth spurt, which would capture the timing of growth spurt in infancy in our study population. Velocity (*γ)* describes child-specific variations in the duration and the rate of the individual's growth by shrinking or stretching the growth curve against the age scale, with positive values indicating slower growth (i.e., stretching the curve and reducing the slope to make the curve shallower) (19). Graphical representation of SITAR parameters is presented in Supplementary Figure S2 (19: p. 1560).

Exploiting frequently measured length/height and weight during infancy in our data, we also employed the Jenss-Bayley (JB) model, which differentiates the pattern of growth from birth to childhood into two periods: non-linear growth during infancy, characterized by a sharp increase in the first months of life followed by slowly declining (decelerating) growth rate; and linear growth in childhood (20). Growth trajectories from the JB model can be expressed as:

$$y_{it} = e^{a_i} + e^{-b_i} \cdot t_i + e^{c_i} (1 - e^{-e^{-di} . \mathrm{t_i}}) \tag{2}$$

where $y_{it}$ is the length/height or weight of child *i* at age *t* and $a_i$, $b_i$, $c_i$, and $d_i$ are the individual-specific random-effects (20). The four individual-specific parameters are size at birth (*a*), the childhood growth rate after infancy (*b*), the degree of catch-up growth during infancy (*c*), and the deceleration in growth rate during infancy (*d*) (20). Random-effect parameters from both models were internally standardized as sex-specific z-scores (mean=0, SD=1). See Supplementary Figure S3 for illustration of JB parameters (20: p. 159).

## Outcomes: cognitive ability scores

At the 6.5-year follow-up, study pediatricians administered the Wechsler Abbreviated Scales of Intelligence (WASI) (22). The WASI assesses two major domains of cognitive ability, verbal and performance IQ, which can be combined to yield a full-scale IQ score. Cognitive ability at age 16 years was measured using the validated Russian version of the computer-administered NeuroTrax test (previously known as the Mindstreams test), which has shown strong reliability (test re-test reliability coefficients range 0-40-0.84) and construct validity (correlation with traditional neuropsychological tests ranged from 0.40 to 0.67 for different cognitive domains) (NeuroTrax Corp., Modiin, Israel) (23-26). The NeuroTrax test assesses cognitive ability on seven domains (memory, executive function, visual-spatial perception, verbal function, attention, information processing speed, and motor skills) and a global cognitive function as the average of domain scores (23). In this study, the full-scale IQ of WASI and the overall cognitive score of the NeuroTrax test were used to compare the two measures after each was internally standardized ($\mu$=100, SD=15). To examine associations with change in cognitive ability over time, we used the difference between the cognitive scores at the age of 16 and 6.5 years. The full-scale IQ of WASI can be thought of as a mediator of the effect of childhood growth on the overall cognitive score at 16 years, and thus adjusting for it may result in over-adjustment and an underestimation of the association between early childhood growth and IQ at 16 years (27).

## Potential confounders

Potential confounders were identified *a priori* based on the literature (28-32). They included maternal smoking during pregnancy, type of delivery, any delivery or postnatal complications, sex of the child, gestational age at birth, 5-minute Apgar score, parental education and occupation, maternal height, area of residence, birth order, maternal age and marital status at childbirth, and the randomized intervention group (breastfeeding promotion or control) since growth during infancy and cognitive ability scores both differed by intervention group (23, 33, 34).

**Data analysis**

We estimated associations of individual growth parameters with the mean cognitive scores at ages 6.5 and 16 years and with the mean change score using generalized estimating equations (GEE) to account for clustering within polyclinics and robustly estimate standard errors of the regression coefficients. For associations of growth parameters estimated from the SITAR model, we first estimated the crude and confounder-adjusted associations of each parameter. Then, we estimated these associations after mutually adjusting for three SITAR growth parameters (fully-adjusted model), as these parameters represent different aspects of *overall* growth trajectory during the defined study period (birth to age 6.5 years). For the JB parameters, the crude and confounder-adjusted associations were also estimated first. However, the fully-adjusted model (i.e., with other growth parameters in the same model) was built considering the temporal sequence of estimated growth parameters. Thus the fully-adjusted model for parameter *a* (size at birth) did not include any other JB parameters (i.e., all post-birth measures), while the fully-adjusted model for growth parameters of infancy (*c* or *d*) accounted for birth size (parameter *a*) but not for growth rate after infancy (parameter *b*). The fully adjusted model for parameter *b* mutually included parameters *a*, *b*, and *d* (we excluded parameter *c* because of collinearity; see Supplementary Table S1 for collinearity diagnostics).

As a sensitivity analysis, we repeated analyses using the verbal-IQ from WASI and the verbal function score from the NeuroTrax test as cognitive outcomes. We also explored two alternative definitions and methods of analysis of the change score. First, cognitive scores at each age were converted into percentiles scores (i.e., all subjects were ranked from 1 to 100 according to their full-IQ from the WASI scale at the age of 6.5 and according to their Global Cognitive Function score at the age of 16 years), and the change score was calculated as the difference between the percentile scores at age 16 and 6.5 years. Second, cognitive scores were categorized into decile scores (i.e., all subjects were ranked from 1 to 10 according to their cognitive scores at 6.5 and 16 years), and the change score was calculated as the difference between the decile scores of cognitive abilities at the two ages. Because of sex differences in growth and cognitive scores (35), we tested for possible effect modification by sex. All statistical analyses were conducted using Stata version 14.2 (StataCorp, College Station, TX, USA).

## Results

Table 1 shows characteristics of the study children (n=12,368). The IQR for the internally standardized cognitive scores was 89.8-108.5 at 6.5 years and of 92.6 110.6 at 16 years; the two scores were moderately correlated (correlation coefficient=0.31 (95% CI: 0.29-0.33); correlation between the verbal sub-scores was 0.22 (95% CI: 0.20-0.23)). Whereas the mean change score was close to zero (-0.2), children in the sample showed considerable variation in their change score (SD=17.6; IQR: -10.3, 12.1; range: -90.9, 53.2). Characteristics of participants in the sample were generally similar to those children excluded due to a missing cognitive score at either age 6.5 or 16 years (Supplementary Table S2).

(Table 1 here)

Table 2 shows descriptive statistics of the growth parameters from SITAR and JB models before standardization, as well as their correlations. The SITAR size and tempo were positively correlated, indicating that children with bigger size over time tended to have later onset of childhood growth spurt. The SITAR velocity parameter was negatively correlated with size and tempo, suggesting that children with slower growth (shallower growth curve) had smaller size over time and an earlier childhood growth spurt. For the JB parameters, birth size was only weakly correlated with the other JB growth parameters, whereas parameter *b* (growth rate after infancy) was negatively correlated with parameter *c* and positively correlated with parameter *d*. This suggests that children with greater growth deceleration rate and lower catch-up growth in infancy had faster growth post-infancy. Correlations between the SITAR and JB parameters are shown in Supplementary Table S3. Children who were taller and heavier over time (size) had a higher degree of catch-up growth (JB-*c*) and lower deceleration rate in infancy (JB-*d*), whereas children with later onset of the childhood growth spurt (tempo) had higher catch-up growth in infancy, but slower growth post-infancy (JB-*b*) as expected from the negative correlation between the SITAR tempo and velocity.

(Table 2 here)

Figure 1 shows the associations of individual growth parameters from the SITAR and JB models for height with cognitive scores at age 6.5 (Figure 1a) and 16 (Figure 1b) years. In crude and confounder-adjusted models, the size and velocity parameters were positively associated with cognitive ability at both ages, whereas the results for the tempo parameter suggest small negative associations with both cognitive outcomes. Associations for the size and tempo parameters considerably increased in magnitude once we jointly adjusted for the three SITAR parameters in the fully-adjusted model. For example, children who were taller by 1-SD over the 6.5 years than the study population average had a 2.7 and 2.5-point higher full-scale IQ score at age 6.5 and 16 years respectively, compared to those who had an identical age at peak velocity and growth velocity. Similarly, a 1-SD (~0.15 month in boys and 0.19 month in girls) delay in the age at peak height velocity was associated with 2.4-point (95% CI: (-3.0, -1.8)) and 2.2-point (95% CI: (-2.7,

-1.6)) lower cognitive scores at age 6.5 and 16 years, respectively, after adjusting for potential confounders and other SITAR growth parameters. The peak height velocity in the PROBIT sample occurred at 1.1 months in boys and 1.3 months in girls, on average. Associations between length/height velocity and cognitive scores were generally of small magnitude, particularly after mutually adjusting for other SITAR parameters.

For the JB parameters, birth length (*a*) and post-infancy height growth velocity (*b*) were positively associated with cognitive scores at ages 6.5 and 16 years after adjusting for confounders, and associations of parameter *b* became stronger after adjusting for JB parameters for infancy growth (+1.8 and +1.0 for cognitive scores at 6.5 and 16 years, respectively). Associations with parameters of growth in infancy (*c* and *d*) were negligible in the adjusted models.

Associations between SITAR and JB length/height growth parameters with the change in cognitive scores are shown in Figure 2. Associations of SITAR parameters were close to zero except for velocity, which showed a small negative association with the change score (-0.4 points; 95% CI: (-0.8, 0.0) in the fully-adjusted model). Associations between JB parameters with the change score were also close to zero in all models except for parameter *b*, which was associated with a small decrease in the mean cognitive score (-0.7; 95% CI: (-1.5, 0.0)) once we mutually controlled for birth size and growth in infancy, as well as confounders.

Supplementary Table S4 presents the average cognitive score at the mean value of individual growth parameters and at +/- 2 SD from the means estimated from the SITAR and JB models for height. Children whose height over the first 6.5 years of life was 2 SD above the population average growth curve had approximately 10-point higher scores at both early school age and adolescence than those who were 2 SD below the population average curve. Similarly, children whose growth spurt occurred much earlier (2 SD, ~0.30 months in boys and 0.37 months in girls) than average had IQ scores that were, on average, 10 points higher than those of children with 2 SD delay in their childhood growth spurt. As children with earlier childhood growth spurts tend to have higher growth velocity post-infancy, faster growth after infancy (+2 SD above the population average) was associated with much better cognitive scores, particularly at early school age, than being at the lower extreme of growth velocity (-2 SD) during the same period (~7 points lower).

Results based on weight growth parameters are presented in Supplementary Figures S4 and S5. Overall, we observed associations similar to those for length/height trajectories, but of slightly smaller magnitude. Our analyses using verbal ability scores from WASI and the verbal function sub-score from the NeuroTrax test also yielded comparable results to those presented above (Supplementary Figures S6, S7, S8). Results using two alternative methods to analyze the change in cognitive outcomes were similar to those using the change score as calculated in the main analysis (Supplementary Figures S9 and S10). We observed no evidence of effect modification by sex (P-values ranged from 0.36 to 0.93).

## Discussion

In a prospective cohort of 12,368 Belarusian children born at term, we examined associations between multiple but distinct growth characteristics and cognitive abilities in early school age and in adolescence. Findings using growth parameters estimated from SITAR highlight the association of the *overall* pattern of growth from birth to age 6.5 years with cognitive outcomes. Children with greater length/height or weight throughout the first 6.5 years of life had better cognitive outcomes at both early school age and adolescence. Our results also highlight the relative importance of timing of growth spurt in early childhood: a later growth spurt of height or weight was associated with lower cognitive scores at both ages, independent of size and growth velocity. However, growth velocity (the magnitude and duration of the childhood growth spurt) in the first 6.5 years had a negligible association with cognition at either age after controlling for prior size and age at the growth spurt.

When growth trajectories were characterized separately for infancy and post-infancy in the JB model, both larger size at birth and faster growth of weight and length/height after infancy were positively associated with cognitive outcomes, while associations with growth parameters during infancy were close to the null across models and both cognitive outcomes. These findings are somewhat different from our earlier analysis of PROBIT children (10), in which we applied linear spline random-effects model to estimate early childhood growth trajectories and observed that birth weight and weight gain in the first three months of life had a larger positive association with cognitive scores at age 6.5 years than later growth, whereas different periods of growth in length/height over the first five years had similar associations with IQ (10). Growth parameters in that analysis (10) assumed a linear growth within four pre-specified periods (birth, 0-3 months, 3-12 months, and 1-5 years), whereas the JB model assumes non-linear infant growth (sharp increase in the first months of life, followed by a slowly declining growth rate) followed by a linear pattern of growth after infancy.

For the first time, our study documents the persistence of associations between early growth and later cognitive ability over time. Consistent patterns of associations with cognitive scores were observed at early school age and during adolescence. The lack of associations between growth trajectories and the change in cognitive score also supports the persistence of associations over time. Nonetheless, most growth parameters from both models were more strongly associated with cognition at early school age than in adolescence. This may well be related to the proximity in time of measuring early school age IQ score relative to the age of growth trajectory modeling.

Major strengths of our study include its large sample size, high rate of follow-up, prospective cohort design, and multiple anthropometric measurements from birth to 6.5 years. The assessment of cognitive function at two time points is also a strength of our study, given the paucity of research that has examined the association between growth and cognitive outcomes measured more than once. Characterizing individual-specific growth parameters from two established but different growth models is also a unique contribution of our study. SITAR models overall growth trajectories over the entire age period, while JB separately models infant and post-infancy growth. Unlike standard regression-based (36) and conditional body size analyses (37), these random-effects models account for missing data and allow for repeated measurements of weight/height that are not necessarily measured at the same age for all individuals; thus all available individual data can be used.

Nevertheless, our results should be interpreted in light of several limitations. First, our cohort was restricted to children born healthy at term with birth weight ≥2,500 grams, all of whom initiated breastfeeding. Thus, our results may not be generalizable to those born preterm or with other birth complications, or those exclusively formula-fed. Our results may also not be generalizable to other settings, such as populations with a higher prevalence of obesity. Although our multiple socioeconomic indicators may serve as proxy measures for unmeasured confounders, we cannot rule out potential residual confounding. For instance, parental cognitive ability could have affected parenting behaviors such as other (post-weaning) feeding practices, factors affecting the child’s physical activity, and the home environment, all of which may affect both the growth and cognitive development of their children (38, 39). We also lacked information on family income, which is linked to both childhood growth and cognition. Nonetheless, income disparities in Belarus, a former Soviet Republic, are far lower than in most Western countries, and residual confounding by it would not be substantial. Second, the two cognitive scores were derived from different instruments, both susceptible to measurement error. The WASI was administered by the polyclinic pediatrician and thus the mean WASI score showed some clustering by polyclinic (10), whereas the NeuroTrax cognitive testing was computer-assisted and self-administered by study participants and thus susceptible to measurement errors due to lack of supervision and possible fatigue. These differences and the regression to the mean phenomenon (40) may explain the moderate correlations between the two cognitive scores and the close to null associations for the change score as an outcome (23). Nevertheless, all associations observed were very similar for both cognitive outcomes. Missing data may possibly have introduced selection bias, despite the high rate of follow-up of children at both the 6.5-year and 16-year assessments. However, children included in the sample and those excluded due to missing cognitive scores appeared quite similar (Table S2). Finally, our study did not account for pubertal growth, as we had only one additional measure of weight and height between the ages of 6.5 and 16.

In conclusion, findings based on both models indicated that children who were bigger at birth, those with earlier onset of the childhood growth spurt, and those who gained more height and weight after infancy and hence were taller and heavier over time performed better in cognitive testing at later ages. Our results showed positive associations between the overall height and weight over time, and the timing of the childhood growth spurt, and later cognition. These findings highlight the importance of considering children’s growth as a continuum from birth throughout childhood, rather than a ‘sensitive period’ in infancy, when determining associations with later health outcomes, including cognition. Our finding that child growth after infancy, but not growth during infancy, was associated with later cognition, especially at early school age, suggests that genetic and post-infancy environmental factors may have important roles in cognitive development (41, 42). Genetic factors affect both child growth and cognitive abilities, and their contribution to cognitive development has been shown to increase as the child ages (43, 44). Post-infancy environmental influences such as the family social milieu, nutrition, and child's overall health, may also play an important role in both childhood growth and brain development. Healthcare professionals monitoring the growth and development of children should be aware that although rapid gain of weight and height in children has been linked to several negative health outcomes (37, 45-47), our results suggest that faster child growth in both height and weight is associated with better cognitive abilities. Future studies on growth in later childhood or around puberty and later cognition would benefit us to better understand the relationship between child growth and cognitive functioning. Further studies are also needed to investigate whether associations persist into adulthood and to consider important cognition-related life outcomes as academic success, educational attainment, and employment.

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**Table 1.** Characteristics (n (%)) and cognitive scores among 12,368 study participants in the Promotion of Breastfeeding Intervention Trial (PROBIT) cohort

| Category | Percent or mean (SD) |
|---|---|
| **Child's sex** | |
| Female | 49% |
| Male | 51% |
| **Gestational age at birth (weeks)** | |
| 37-38 weeks | 19% |
| 39-41 weeks | 80% |
| >42 weeks | 1% |
| **Type of delivery** | |
| Vaginal | 89% |
| Cesarean | 11% |
| **Apgar score at 5 min** ***[mean (SD)]*** | 8.58 (0.6) |
| **Delivery complication** | |
| No | 92% |
| Yes | 8% |
| **Infant postnatal complication** | |
| No | 94% |
| Yes | 6% |
| **Randomized Group** | |
| Intervention group | 50% |
| Control group | 50% |
| **No. of older siblings** | |
| 0 | 56% |
| 1 | 35% |
| 2+ | 9% |
| **Area of residence** | |
| East/Urban | 31% |
| East/Rural | 16% |
| West/Urban | 24% |
| West/Rural | 29% |
| **Cognitive Scores** ***[mean (SD)]*** | |
| Full-scale cognitive score at age 6.5 years | 100.1 (15.1) |
| Full-scale cognitive score at age 16 years | 99.9 (14.9) |
| Change score [a] | -0.2 (17.6) |
| **Mother's height (cm)** ***[mean (SD)]*** | 164.4 (5.6) |
| **Mother's age (years)** ***[mean (SD)]*** | 24.5 (4.9) |
| **Mother's smoking in pregnancy** | |
| No | 98% |
| Yes | 2% |
| **Mother's marital status at birth** | |
| Married | 90% |
| Cohabitating | 7% |
| Unmarried | 4% |
| **Mother's education** | |
| University degree | 13% |
| Partial university | 52% |
| Secondary education | 32% |
| <Secondary education | 4% |

| | |
|---|---|
| **Father's education** | |
| University degree | 12% |
| Partial university | 46% |
| Secondary education | 36% |
| <Secondary education | 2% |
| Missing | 3% |
| **Mother's occupation** | |
| Manual | 34% |
| Non-manual | 44% |
| Unemployed | 22% |
| **Father's occupation** | |
| Manual | 54% |
| Non-manual | 28% |
| Unemployed /unknown | 17% |
| Missing | 1% |

[a] The change score was calculated as the difference between the cognitive scores at the age of 16 years and 6.5 years.

**Table 2.** Correlations between individual growth parameters from the Super Imposition by Translation and Rotation (SITAR) and Jenss-Bayley (JB) models for weight and height among 12,368 participants in the Promotion of Breastfeeding Intervention Trial (PROBIT) cohort.

| SITAR height growth parameters | | | | | SITAR weight growth parameters | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | SD | Correlations | | | | SD | Correlations | | |
| | | $\alpha$ | $\beta$ | $\gamma$ | | | $\alpha$ | $\beta$ | $\gamma$ |
| $\alpha$ (cm) | .05 | - | - | - | $\alpha$ (kg) | .10 | - | - | - |
| $\beta$ (fractional)[a] | .11 | 0.87 | - | - | $\beta$ (fractional) | .08 | 0.58 | - | - |
| $\gamma$ (fractional)[b] | .04 | -0.19 | -0.33 | - | $\gamma$ (fractional) | .07 | -0.25 | -0.72 | - |

| JB height growth parameters | | | | | | JB weight growth parameters | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | μ | SD | Correlations | | | | μ | SD | Correlations | | |
| | | | $a$ | $b$ | $c$ | | | | $a$ | $b$ | $c$ |
| $a$ (cm) | 51.77 | 1.03 | - | - | - | $a$ (kg) | 3.25 | 1.06 | - | - | - |
| $b$ (cm/day) | .02 | 1.16 | 0.11 | - | - | $b$ (kg/day) | .01 | 1.27 | 0.34 | - | - |
| $c$ (cm) | 23.94 | 1.30 | -0.07 | -0.81 | - | $c$ (kg) | 5.72 | 1.24 | 0.17 | -0.53 | - |
| $d$ (no unit) | .004 | 1.47 | 0.01 | 0.81 | -0.94 | $d$ (no unit) | .01 | 1.28 | 0.27 | 0.51 | -0.88 |

Notes:

From the SITAR model, parameters $\alpha$, $\beta$, and $\gamma$ represent the size, tempo, and velocity respectively. From the JB model, parameters $a$, $b$, $c$, and $d$ represent the size at birth, the growth rate after infancy, the degree of catch-up growth during infancy, and the deceleration in growth rate in infancy respectively.

[a] the SD of tempo is presented as a fractional due to the log age scale. It can be multiplied by 100 and viewed as a percentage.

[b] the SD of velocity is presented as a fractional multiplier and it can be multiplied by 100 and viewed as a percentage.


a. Full-scale IQ at age 6.5 years
b. Global cognitive score at age 16 years
Crude
Confounder-adjusted
Fully-adjusted
SITAR Parameters
Jness-Bayley Parameters
α
β
γ
a
b
c
d
0.9 (0.6, 1.2)
0.4 (0.2, 0.6)
2.7 (2.1, 3.2)
-0.3 (-0.5, 0.0)
-0.3 (-0.6, 0.0)
-2.4 (-3.0, -1.8)
1.3 (0.9, 1.7)
0.8 (0.5, 1.1)
0.6 (0.2, 0.9)
1.4 (1.1, 1.6)
0.9 (0.6, 1.2)
0.7 (0.5, 1.0)
0.5 (0.3, 0.7)
1.8 (1.2, 2.4)
0.6 (0.2, 0.9)
0.2 (0.0, 0.5)
0.3 (0.0, 0.5)
0.4 (0.0, 0.8)
-0.2 (-0.5, 0.1)
-0.2 (-0.4, 0.1)
-3.3
0
3.3
Mean cognitive score with 95% CI
0.8 (0.5, 1.1)
0.5 (0.2, 0.8)
2.5 (1.9, 3.0)
-0.1 (-0.4, 0.2)
-0.1 (-0.4, 0.2)
-2.2 (-2.7, -1.6)
0.7 (0.4, 1.0)
0.3 (0.0, 0.7)
0.2 (-0.1, 0.4)
1.1 (0.9, 1.4)
0.9 (0.7, 1.2)
0.5 (0.2, 0.8)
0.4 (0.1, 0.6)
1.0 (0.4, 1.5)
0.4 (0.1, 0.6)
0.2 (-0.1, 0.4)
0.2 (-0.1, 0.5)
0.2 (-0.2, 0.5)
0.0 (-0.3, 0.4)
0.0 (-0.3, 0.3)
-3.3
0
3.3
Mean cognitive score with 95% CI

**Figure 1**. Mean differences (95% CI) in cognitive score according to SD increases in individual growth parameters from the Super Imposition by Translation and Rotation (SITAR) and the Jenss-Bayley (JB) models for *height*. From the SITAR model, parameters $\alpha$, $\beta$, and $\gamma$ represent the size, tempo, and velocity respectively. From the JB model, parameters $a$, $b$, $c$, and $d$ represent the size at birth, the growth rate after infancy, the degree of catch-up growth during infancy, and the deceleration in growth rate in infancy respectively. The crude model only adjusted for clustering. The confounder-adjusted model included the growth parameters individually, adjusted for confounders. The fully-adjusted model for the SITAR parameters included all three growth parameters, as well as confounders. The fully-adjusted model for the JB parameters was built considering the temporal sequence of estimated growth parameters: only confounders were included for parameter birth size ($a$) as outcome; confounders and birth size for growth parameters of infancy ($c$ and $d$); and confounders and birth size and growth rate in infancy for post-infancy growth ($b$).

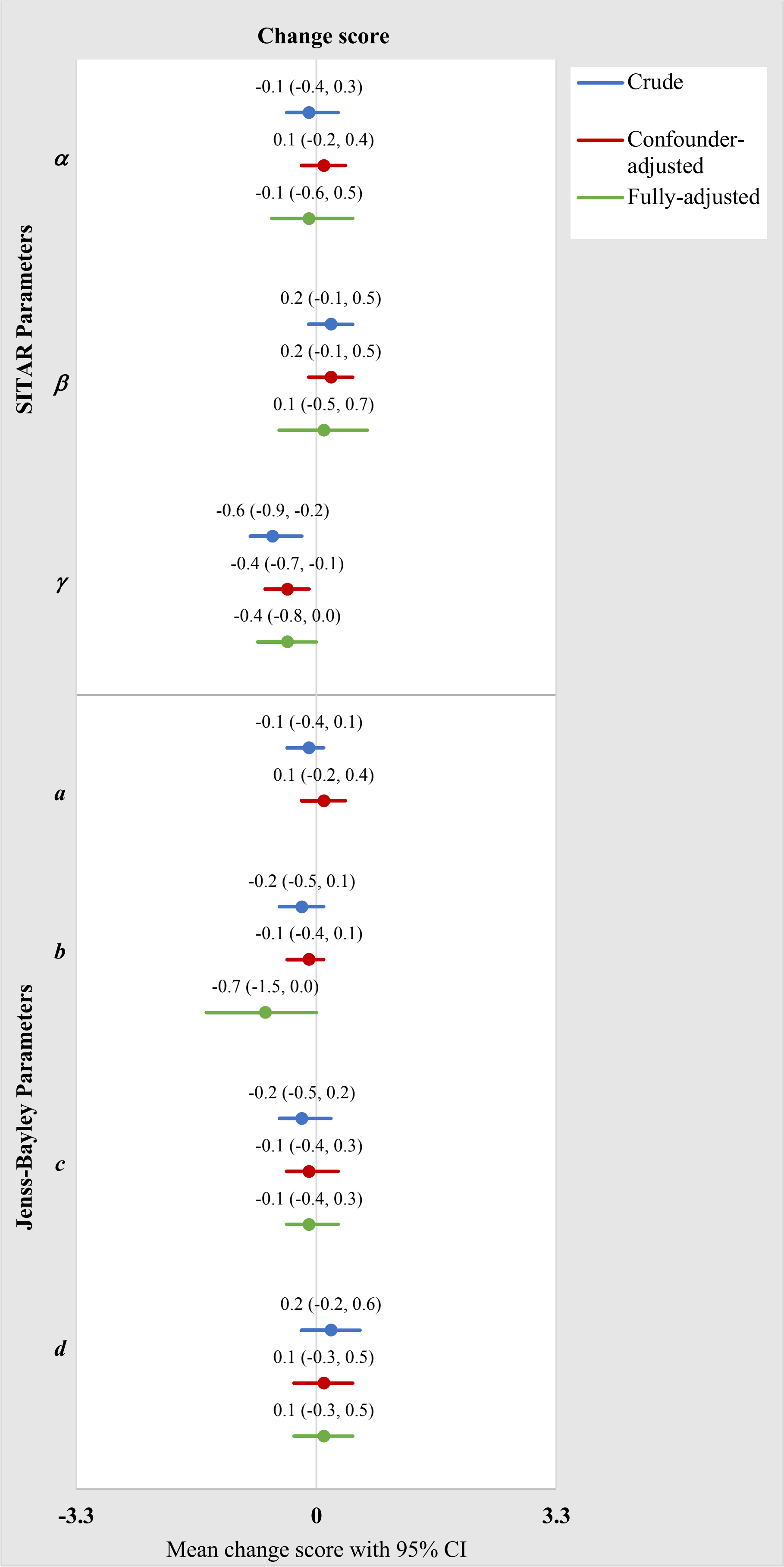
Change score
Crude
Confounder-adjusted
Fully-adjusted
SITAR Parameters
α
-0.1 (-0.4, 0.3)
0.1 (-0.2, 0.4)
-0.1 (-0.6, 0.5)
β
0.2 (-0.1, 0.5)
0.2 (-0.1, 0.5)
0.1 (-0.5, 0.7)
γ
-0.6 (-0.9, -0.2)
-0.4 (-0.7, -0.1)
-0.4 (-0.8, 0.0)
Jenss-Bayley Parameters
a
-0.1 (-0.4, 0.1)
0.1 (-0.2, 0.4)
b
-0.2 (-0.5, 0.1)
-0.1 (-0.4, 0.1)
-0.7 (-1.5, 0.0)
c
-0.2 (-0.5, 0.2)
-0.1 (-0.4, 0.3)
-0.1 (-0.4, 0.3)
d
0.2 (-0.2, 0.6)
0.1 (-0.3, 0.5)
0.1 (-0.3, 0.5)
-3.3
0
3.3
Mean change score with 95% CI

**Figure 2**. Mean differences (95% CI) in change score according to SD increases in individual growth parameters from the Super Imposition by Translation and Rotation (SITAR) and the Jenss-Bayley (JB) models for *height*. From the SITAR model, parameters $\alpha$, $\beta$, and $\gamma$ represent the size, tempo, and velocity respectively. From the JB model, parameters $a$, $b$, $c$, and $d$ represent the size at birth, the growth rate after infancy, the degree of catch-up growth during infancy, and the deceleration in growth rate in infancy respectively. The crude model only adjusted for clustering. The confounder-adjusted model included the growth parameters individually, adjusted for confounders. The fully-adjusted model for the SITAR parameters included all three growth parameters, as well as confounders. The fully-adjusted model for the JB parameters was built considering the temporal sequence of estimated growth parameters: only confounders were included for parameter birth size ($a$) as outcome; confounders and birth size for growth parameters of infancy ($c$ and $d$); and confounders and birth size and growth rate in infancy for post-infancy growth ($b$). The change score was calculated as the difference between the IQ scores at the age of 16 years and 6.5 years.