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Sociodemographic predictors of early postnatal growth: evidence from a Chilean infancy cohort.

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Title: Sociodemographic predictors of early postnatal growth: evidence from a Chilean infancy cohort

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Abstract

Objectives

Infant anthropometric growth varies across socioeconomic factors, including maternal education and income, and may serve as an indicator of environmental influences in early life with long term health consequences. Previous research has identified sociodemographic gradients in growth with a focus on the first year and beyond, but estimates are sparse for growth before six months. Thus, our objective was to examine the relationship between early life environmental factors and infant growth patterns between birth and five months of age.

Design

Prospective cohort study

Settings

Low- to middle-income neighborhoods in Santiago, Chile (1991-1996).

Participants

1,412 participants from a randomized iron deficiency anemia preventive trial in healthy infants.

Main outcome measures

Longitudinal anthropometrics including monthly weight (kg), length (cm) and weight-for-length (WFL) values. For each measure, we estimated three individual-level growth parameters (size, timing, and velocity) from SuperImposition by Translation and Rotation (SITAR) models. Size and timing changes represent vertical and horizontal growth curve shifts, respectively, and velocity change represents growth rate shifts.

Results

We used lasso regression with post-selection inference methods to estimate the linear association between each of the growth parameter outcomes and environmental exposures including gestational age, maternal age, education, and socioeconomic position (SEP). Lower SEP was associated with a slower linear (length) growth as demonstrated through the velocity growth parameter (-0.22, 95% CI=-0.13,-0.31) – outcome units are percent change in velocity from the average growth curve. Lower SEP was also associated with later WFL growth timing as demonstrated through the tempo growth parameter for females (0.25, 95% CI=0.05,0.42) – outcome units are shifts in days from the average growth curve.

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Conclusion

Previous research on growth in older infants and children shows associations between lower SEP with slower length velocity. We found evidence supporting this association in the first five months of life, which may inform age-specific prevention efforts aimed at infant growth.

Strengths and Limitations of this Study

- The sample includes monthly anthropometric measures in first five postnatal months – not available in any study to date and allowing better fitting models of growth.
- We used a detailed measure of socioeconomic position specific to low- to middle-income groups, an understudied population.
- As the sample was low- to middle-income, these results may not generalize to groups with even lower or higher income or SEP.

Introduction

Interest in early life infant growth has grown as evidence accumulates that it is associated with the development of adult disease, sometimes decades later. Some chronic disease outcomes associated with infant growth characteristics include obesity, endothelial dysfunction, and metabolic syndrome (1–3). Explanations for these associations include early infancy as a critical window of time for susceptibility to environmental exposures for chronic disease risk factors (4). Socioeconomic position (SEP) is one such exposure. SEP is associated with child growth patterns, in particular, length (5–12) and weight (13–16). In these studies, lower SEP is generally associated with faster weight gain during childhood, while the inverse holds true for length. These socioeconomic gradients in growth appear to emerge in early life (7) and persist (5).

Gaps remain in our understanding regarding sociodemographic predictors of growth during infancy and childhood. One such gap relates to the earliest period of infant growth. Studies to date include only a few observations before six months, leading to linear specifications between weight or height and time. However, curvilinear models of growth offer better model fit for early infancy growth. Growth during the first six months in the human lifespan is characterized by accelerated growth at the outset and leveling off at around six months (17). Understanding the relationship between early infant growth and sociodemographic factors may yield new information that highlight the potential for earlier interventions to promote optimal health.

Identifying novel associations in this age range can better pinpoint the timing and influence of sociodemographic factors. Given the sparsity of information in the literature focusing on these points, our aim in this study is to examine sociodemographic predictors of infant weight, length and weight-for-length (WFL) growth from zero to five months in an infancy cohort of over 1,400 healthy Chilean children. Based on observations of infants older than

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six months, we expect that SEP will be inversely associated with weight gain and positively associated with length growth.

Methods

Study sample

The data in this study are drawn from the Santiago Longitudinal Study (SLS), a cohort study from low- to middle-income neighborhoods in Santiago, Chile. Between 1991 and 1996, infants were recruited for an infancy iron deficiency anemia preventive trial (18) or neuromaturation study (19). Inclusion criteria for the infancy studies included term infants with birthweight $\geq$ 3.0 kg, vaginal birth, no major health problems for the infant, and, for the preventive trial, no iron deficiency anemia present at five to six months. Those with iron deficiency anemia and the next nonanemic control were invited to participate in the neuromaturation study and are not considered here. Participant eligibility and follow-up information have previously been reported (18). The Santiago Longitudinal Study (SLS) had been approved by Institutional Review Boards from 1) the University of Michigan, Ann Arbor, 2) Institute of Nutrition and Food Technology (INTA), Chile and 3) University of California, San Diego.

We characterized the growth period prior to treatment randomization, which occurred at six months. Anthropometric measures prior to study enrollment were obtained from the medical chart. The total sample size included 1,657 infants who completed the preventive trial. The participants included in this analysis numbered 1,412 individuals from the preventive trial with anthropometric measures for at least two time points before six months.

Outcome and sociodemographic measures

Anthropometric measurements included weight (kg), length (cm), and weight-for-length (WFL) (g/cm). Weight was measured to the nearest 0.01 kg on an electronic scale at local public health clinics. Length was measured on a recumbent board to the nearest 0.1 cm. Gestational age (GA), obtained from the medical chart, was among the set of variables included in the models as a covariate.

Sociodemographic measures were self-reported by the mother, including maternal age (years), total years of education, and the modified Graffar index (20), an index of SEP used in lower-income countries (21). The modified Graffar index represents a sum of 10 measures regarding education, family composition, and housing characteristics, which are summed to create a scale with higher values indicating lower social class (Appendix Table A1). Mothers self-reported breastfeeding characteristics from birth, including date of first bottle and age at weaning if weaned. From this information, we created variables for breastfeeding as the sole source of milk and mixed breast and bottle feeding at five months.

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Statistical analyses

Summary statistics included median and interquartile ranges for continuous variables and percent with counts for categorical variables. All summary statistics were stratified by child sex.

We used two steps to assess the association between infant growth and sociodemographic predictors: 1) SuperImposition by Translation and Rotation (SITAR) approach (22) to estimate infant weight, length and weight-for-length (WFL) growth characteristics from birth to five months followed by 2) linear regression to estimate the relationship between sociodemographic predictors and these growth characteristics. We used a nonlinear mixed effects model (23) to estimate the growth characteristics with the R nlme package (24). Each model produces up to three different SITAR growth parameters per individual, which have been named 'size', 'tempo' and 'velocity' (22) (Figure 1). 'Size' indicates a shift of the growth curve up and down for an individual relative to the average growth curve. 'Tempo' indicates a shift of the growth curve to the left or right on the age scale for an individual relative to the average growth curve. Lastly, 'velocity' indicates a transformation of the age scale in the nonlinear model, shrinking or enlarging the age scale for an individual relative to the average growth curve. These three parameters are noted as having biologically meaningful interpretations, which are difficult to obtain with other growth models (23). Unless otherwise noted, any references to 'size', 'tempo', and 'velocity' refer to these parameters from the SITAR construct applied to early infant growth. We assessed best model fit for each anthropometric measure via the lowest Bayesian Information Criterion (BIC) for growth independent of any covariates. After evaluating all possible combinations of SITAR models from one to three parameters for each of the three anthropometric measures, best fit (Appendix Table A2) models included: 1) all three growth parameters for weight (BIC=-22941), 2) sex-specific growth trajectories with tempo and velocity parameters for length (BIC=-38001), and 3) sex-specific growth trajectories with size and tempo parameters for WFL (BIC=-22809).

Figure 1 about here

The results from the second step analyses are reported. In addition to analyses combining and adjusting for sex of the child, sex-stratified analyses were used for all three anthropometric outcomes, as some estimated associations between the SITAR growth parameters and SEP indicators differed by sex of the child.

The adjusted models in the second step started with four covariates: gestational age, maternal age, maternal total years of education, and Graffar index (20). We removed covariates from the model based on the least absolute shrinkage and selection operator (lasso) approach (25). This approach has better performance than conventional model selection methods with a univariate approach (26) such as stepwise methods (27). The lasso approach assists in selecting predictors with the strongest coefficients (28) while balancing bias and variation in the model. We used the glmnet package in R (29) to estimate shrunken parameters and the selectiveInference package (30) to provide inference via statistical tests and confidence intervals. Each set of comparisons by outcome, i.e. weight, length or weight-for-length were considered separately, controlling multiple

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comparisons with a Bonferroni correction at an alpha level of 0.05. A coefficient for the predictor of a weight size growth parameter outcome in the second step indicates a change in log(kg) for a one-unit change in the predictor; we multiply this coefficient by 100 to make a symmetric percentage difference on a modified percentage scale (31). Similarly, a one-unit change in the predictor corresponds to a symmetric percentage change in the velocity growth parameter. Time (days) is not log transformed and the coefficient for this outcome corresponds to a shift in the time scale in days.

For analyses, we used a complete case data set, i.e., all participants with non-missing covariates. The proportion of missing data was less than one percent for all variables except the Graffar index, which had less than three percent missing. The median number of non-missing outcome (anthropometric) values was six out of six monthly measures (birth to five months). The percent of missing outcome values at each time point ranged from 9% at months 1 and 2 to 0.2% at birth. In a post hoc data analysis we used logistic regression models to estimate associations between SEP (the Graffar Index) as a continuous variable, and binary breastfeeding status outcomes – any or exclusive – at five months.

Patient and public involvement

Participants were mothers and infants recruited for research. The mothers were not involved in setting the study design, research questions or outcome measures for this study.

Results

Participants (n=1,412) were 53% male and 47% female. Median gestational age (Q1, Q3) was 40 weeks (39, 40); preterm infants (< 37 weeks GA) were excluded by design. Mothers were 26 years of age (median (IQR) 26 (22,31) and had a median (IQR) of 10 (8,12) years of education at the time of their infant's birth (Table 1). For the six monthly anthropometric measurements, each infant had at least two observations, and 72% had measures at all six time points.

Put table 1 about here

The following sections show results of the growth trajectory analyses for the three anthropometric outcomes: weight (kg), length (cm) and weight-for-length (WFL) (g/cm). All p-values are adjusted for multiple comparisons.

Weight trajectories: size, tempo and velocity

All three SITAR parameters, i.e. 'size, 'tempo' and 'velocity', best satisfied model fit diagnostic tests for weight trajectories (Appendix Table A2). Maternal age was positively associated with the weight size parameter for female infants (0.21, 95% CI = 0.07, 0.34) in the unadjusted model (Table 2), with a 0.21 percentage difference from the average growth curve for each year increase in maternal age. Maternal age was inversely associated with weight velocity parameter in female infants (-0.41, 95% CI = -0.71, -0.12) in the unadjusted model, indicating that higher maternal age was associated with slower weight growth.

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Gestational age in the pooled sample was significantly associated with the weight tempo parameter (-2.01, 95% CI = -2.98, -1.70) in the adjusted model, indicating a leftward shift of about two days for each additional week in gestational age. This indicates earlier timing of weight gain in infants who were born with higher gestational age (Table 2). There was no substantive difference in this association in the sex-stratified analyses.

put table 2 about here

Length trajectories: tempo and velocity

For length (linear) growth, the 'tempo' and 'velocity' SITAR growth parameters best satisfied model fit diagnostic tests (Appendix Table A2). In the pooled group, the coefficient of association between the Graffar index and the velocity parameter (-0.22, 95% CI = -0.13, -0.31) (Table 3) indicated that for each unit increase in the Graffar index, there was a -0.22 percent difference from the average length velocity. This reflects a positive relationship between the length velocity parameter and SEP. This positive association was not substantively different in the sex-stratified analyses, all of which indicated faster linear (length) growth with higher SEP. In contrast to the sex-stratified analyses, all covariates remained in the pooled adjusted model with less than 6% decline from the unadjusted SEP coefficient (-0.23, 95% CI = -0.31, -0.15).

Gestational (GA) age was inversely associated with the length tempo parameter in the pooled sample (-2.94, 95% CI = -3.51, -2.41), indicating a leftward shift of about three days of the trajectory on the time scale, and a faster start to length growth, for each one week increase in gestational age (Table 3). GA was also associated with the length velocity parameter for the pooled sample (0.61, 95% CI =0.06, 1.15).

put Table 3 about here

Weight-for-length trajectories: size and tempo

For WFL growth, the 'size' and 'tempo' SITAR parameters best satisfied model fit diagnostic tests (Appendix Table A2). Lower SEP was positively associated with the WFL tempo parameter for females (0.25, 95% CI = 0.05, 0.42) in the adjusted model. This estimate approximates a rightward shift in time (days) relative to the average growth curve indicating later growth timing with lower SEP.

Similar to weight and length trajectories, GA was inversely associated with the WFL tempo parameter in the pooled sample (-1.99, 95% CI = -2.83, -1.49) (Table 4) indicating about a two-day shift to the left on the time scale from the average growth curve for every one week increase in gestational age. Similar values were found in the sex-stratified analyses, all indicating earlier timing of WFL growth with higher gestational age.

put Table 4 about here

The post hoc analysis examining the association between odds of exclusive or any breastfeeding at five months and the continuous SEP measure (the Graffar index) did not find a substantive or significant association (data not shown).

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Discussion

In this research, we found that lower SEP, measured by the Graffar index, was inversely associated with length growth characteristics in the first six months. Lower SEP was associated with later timing of WFL growth as reflected by the positive association between the Graffar Index and the WFL tempo parameter. These higher tempo values translate to a rightward shift in growth relative to the average growth curve as well as a later age at peak velocity (32). This delay in growth can be considered an unfavorable outcome associated with lower SEP.

Of three previous studies investigating associations between sociodemographic predictors and infant growth before six months, two found a positive association between length (linear) growth and maternal education (8,10), used as a proxy for SEP. Only one study found an inverse association with length growth (12). Many studies including age ranges exceeding six months of age up to five years of age demonstrated a positive association between maternal education and length/height growth (7,8,10). The majority of these studies support the conclusion that lower SEP is associated with slower length/height (linear) growth in infancy and early childhood.

Several prior studies representing high-income European countries have noted that their findings of either an inverse (12) or no relationship (7) between SEP and length (linear) growth may not generalize to low- to middle-income countries. Deviations from the Western diet and lifestyle were one of the reasons given for this limitation. Chile, the country from which our data were collected, offers an interesting context in this respect. The recruitment period for this study, 1991 to 1996, occurred as Chile was transitioning from a low-income to an upper-middle income country. In 1990, 40% of the Chilean population was below the poverty line (33); by 2012 Chile was classified by WHO as an upper middle-income country (34). There were nutrition and epidemiologic transitions (35,36) beginning in the 1970s and continuing during the 1990s when study infants were enrolled. Specifically, consumption of high-calorie food, accompanied by a sedentary lifestyle, resulted in rising obesity prevalence across all socioeconomic levels. In the context of an emerging Western diet and lifestyle, we found that lower SEP was associated with poorer length (linear) growth in early infancy. Of course, contemporary generations in Chile experience deteriorated SEP in a new context of over-nutrition and higher levels of sedentary behavior. Thus current studies in Chile may find distinct relationships between SEP and early growth when compared with generations born 20 years ago.

Plausible biological mechanisms, linked to modifiable factors, have been proposed for the observed association between lower SEP and length growth in the first five postnatal months. Breastfeeding and maternal smoking are two commonly proposed mechanisms, although evidence is limited. In our sample, breastfeeding was close to universal (37,38) and not associated with infant weight change in the first year. For maternal smoking status, prior studies did not find that either prenatal or postnatal smoking substantially altered the association between SEP and growth (11,12,16).

Maternal age was the only sociodemographic predictor positively associated with the SITAR size growth parameter for weight. This was similarly reported in another cohort

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from the same geographic area of Santiago, Chile, the Growth and Obesity Cohort Study (GOCS) (13), which started a decade later and studied ages between birth and 2 years. Our findings add to this previous work. Through our intense focus on the first five prenatal months, our results demonstrate that the association between SEP and weight growth appears earlier in the postnatal period than previously documented.

Other potential mechanisms operating through SEP could include gestational weight gain and maternal nutrient status. Size at birth, considered a proxy for these two factors and represented in these analyses by the size SITAR parameter, was not associated with any of the sociodemographic measures. Further research will be useful in clarifying the biological mechanisms behind the association between SEP and early infant growth.

Strengths of this study include the combination of an analytic approach to growth that better captures the nonlinear characteristic of growth in the first five months of life with a detailed measure of socioeconomic position appropriate to the context of a lower income setting. Another strength is the monthly anthropometric measures collected in the first five postnatal months. We also note several limitations. The sample size is smaller than other studies with sample sizes in the thousands or tens of thousands (5,13,14). Our study was therefore not powered to detect some effects reported in larger studies. Another limitation is that the Graffar index, developed to assess differences in low- to middle-income populations, limits the generalizability of our findings to higher income groups.

This investigation examined various growth characteristics from birth to five months and their association with sociodemographic factors in a Chilean infancy cohort. We found associations between lower SEP and slower length (linear) growth, which are similar in direction to previous findings for maternal education that span periods of time greater than the first six months and up to five years of age (7,8,10,12). The association between maternal age and weight size, in our study, was similar to findings in other studies of growth between birth and two years of age (13). In sum, our results extend findings from previous research by showing that sociodemographic factors affect infant growth even in the first five months of growth and in relatively homogenous low- to middle-income populations.

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Contributors

AVH designed the study, conducted the data analysis, and wrote the first draft of the paper. KEN and SG supervised and contributed to the study design and interpretation of results. EB helped acquire the data. All authors both contributed to revisions of the draft for intellectual content and approved the final version of the manuscript.

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Competing interests

None declared.

Patient consent

Not required.

Ethics approval

The Santiago Longitudinal Study (SLS) had been approved by Institutional Review Boards from 1) University of Michigan Medical Center, Ann Arbor, 2) Institute of Nutrition and Food Technology (INTA), Chile and 3) University of California, San Diego. The Office of Human Research Ethics at the University of North Carolina, Chapel Hill exempted this current research using existing anonymous data from review under the 45 CFR 46.101(b) regulatory category.

Data sharing agreement

No additional data are available.

Disclaimer

AHA had no role in the study design, data collection, and analysis, decision to publish or preparation of the manuscript.

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Table1. Descriptive statistics of sociodemographic characteristics, median [IQR]

Characteristic	Male	Female	Total
n	747	665	1412
Gestational age (weeks)	40.0 [39.0, 40.0]	40.0 [39.0, 40.0]	40.0 [39.0, 40.0]
Graffar Index	27.0 [23.0, 33.0]	27.0 [23.0, 33.0]	27.0 [23.0, 33.0]
Maternal age (years)	26.0 [21.8, 30.9]	25.5 [21.7, 30.3]	25.8 [21.8, 30.8]
Maternal Education (years)	10.0 [8.0, 12.0]	10.0 [8.0, 12.0]	10.0 [8.0, 12.0]

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Table 2. Sociodemographic predictors and association with weight SITAR growth parameters[a,b], stratified by sex of Longitudinal Study, 1991-1996

	Males						Females							
	Unadjusted			Adjusted[c]			Unadjusted			Adjusted[c]			Unadjust	
Characteristic	**Size**	**Tempo**	**Velocity**	**Size**	**Tempo**	**Velocity**	**Size**	**Tempo**	**Velocity**	**Size**	**Tempo**	**Velocity**	**Size**	**Tempo**
Gest age	0.59 (-0.12, 1.31)	**-2.28 (-3.15, -1.41)**	-0.81 (-2.28, 0.66)	NA	**-1.96 (-3.15, -1.40)**	NA	0.76 (-0.02, 1.54)	**-2.38 (-3.32, -1.45)**	-2.14 (-3.87, -0.42)	0.45 (-0.32, 9.88)	**-2.23 (-3.35, -1.47)**	-1.58 (-3.85, 0.08)	0.64 (0.10, 1.18)	**-2.35 (-2.98, -1.71)**
Maternal age	0.11 (-0.00, 0.23)	-0.06 (-0.20, 0.09)	-0.07 (-0.31, 0.17)	0.07 (-0.11, 0.21)	-0.06 (-0.21, 0.26)	-0.06 (-0.33, 0.82)	**0.21 (0.07, 0.34)**	-0.02 (-0.18, 0.15)	**-0.41 (-0.71, -0.12)**	0.19 (-6.13, 0.22)	0.01 (-2.29, 0.13)	-0.36 (-0.67, -0.04)	**0.16 (0.07, 0.25)**	-0.03 (-0.14, 0.07)
Maternal education	-0.03 (-0.32, 0.26)	0.14 (-0.21, 0.49)	-0.04 (-0.62, 0.55)	NA	NA	NA	-0.01 (-0.31, 0.29)	0.06 (-0.30, 0.43)	-0.03 (-0.69, 0.64)	0.00 (-Inf, -0.41)	0.12 (-0.95, 0.52)	NA	-0.03 (-0.24, 0.19)	0.10 (-0.15, 0.36)
Graffar Index[d]	-0.12 (-0.23, -0.01)	-0.13 (-0.27, 0.01)	-0.15 (-0.39, 0.08)	-0.08 (-0.22, 0.07)	-0.13 (-0.28, 0.03)	-0.13 (-0.41, 0.28)	-0.07 (-0.19, 0.06)	0.12 (-0.03, 0.28)	0.28 (0.00, 0.57)	-0.03 (-5.15, 0.23)	0.13 (-0.24, 0.29)	0.23 (-0.16, 0.52)	-0.09 (-0.18, -0.00)	-0.01 (-0.11, 0.09)

[a] Size units are percentage change in log(weight) from average, tempo units are time (days), velocity units in percent change from average.
[b] Bold values indicate significance with Bonferroni correction at alpha level of 0.05
[c] Adjusted linear regression models only include non-zero coefficients from lasso regression models that include all covariates in full model.
[d] Higher Graffar index values indicate lower socioeconomic status.

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Table 3. Sociodemographic predictors and association with length SITAR growth parameters[a,b] stratified by sex of child in the Santiago Longitudinal Study, 1991-1996

	Males				Females				Both			
	Unadjusted		Adjusted[c]		Unadjusted		Adjusted[c]		Unadjusted		Adjusted[c]	
Characteristic	Tempo	Velocity	Tempo	Velocity	Tempo	Velocity	Tempo	Velocity	Tempo	Velocity	Tempo	Velocity
Gest age	**-3.33 (-4.09, -2.56)**	**0.99 (0.29, 1.68)**	**-3.05 (-4.10, -2.55)**	NA	**-2.57 (-3.36, -1.79)**	0.25 (-0.52, 1.02)	**-2.53 (-3.33, -1.77)**	NA	**-2.97 (-3.52, -2.42)**	**0.64 (0.12, 1.15)**	**-2.94 (-3.51, -2.41)**	**0.61 (0.06, 1.15)**
Maternal age	-0.04 (-0.18, 0.09)	0.09 (-0.03, 0.20)	-0.01 (-0.10, 1.64)	NA	**-0.17 (-0.30, -0.03)**	0.01 (-0.13, 0.14)	-0.15 (-0.29, 0.01)	NA	-0.10 (-0.19, -0.00)	0.05 (-0.04, 0.14)	-0.07 (-0.17, 0.06)	0.02 (-0.35, 0.10)
Maternal education	0.06 (-0.26, 0.38)	0.12 (-0.16, 0.40)	NA	NA	-0.18 (-0.49, 0.13)	0.28 (-0.01, 0.58)	-0.14 (-0.45, 0.52)	0.16 (-0.35, 0.52)	-0.05 (-0.28, 0.17)	0.20 (-0.00, 0.40)	-0.06 (-0.27, 0.73)	0.13 (-0.21, 0.34)
Graffar Index[d]	0.06 (-0.06, 0.19)	**-0.26 (-0.37, -0.15)**	0.05 (-0.25, 0.36)	**-0.21 (-0.37, -0.14)**	**0.16 (0.03, 0.29)**	**-0.19 (-0.32, -0.07)**	0.13 (-0.03, 0.26)	**-0.17 (-0.31, -0.05)**	**0.11 (0.02, 0.20)**	**-0.23 (-0.31, -0.15)**	0.09 (-0.02, 0.18)	**-0.22 (-0.31, -0.13)**

[a] Size units are percentage change in log(length) from average, tempo units are time (days), velocity units in percent change from average.
[b] Bold values indicate significance with Bonferroni correction at alpha level of 0.05
[c] Adjusted linear regression models only include non-zero coefficients from lasso regression models that include all covariates in full model.
[d] Higher Graffar index values indicate lower socioeconomic status.

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Table 4. Sociodemographic predictors and association with weight-for-length (WFL) SITAR growth parameters[a,b] stratified by sex of child in the Santiago Longitudinal Study, 1991-1996

	Males				Females				Both			
	Unadjusted		Adjusted[c]		Unadjusted		Adjusted[c]		Unadjusted		Adjusted[c]	
Characteristic	Size	Tempo	Size	Tempo	Size	Tempo	Size	Tempo	Size	Tempo	Size	Tempo
Gest age	0.09 (-0.55, 0.73)	**-2.03 (-2.91, -1.15)**	NA	**-1.58 (-2.90, -1.11)**	0.05 (-0.58, 0.69)	**-2.34 (-3.35, -1.32)**	NA	**-2.32 (-3.35, -1.33)**	0.07 (-0.38, 0.52)	**-2.17 (-2.84, -1.51)**	NA	**-1.99 (-2.83, -1.49)**
Maternal age	0.07 (-0.03, 0.18)	-0.09 (-0.23, 0.06)	0.04 (-0.23, 0.16)	-0.08 (-0.24, 0.17)	0.02 (-0.09, 0.13)	-0.18 (-0.36, -0.00)	NA	-0.13 (-0.36, 0.14)	0.05 (-0.03, 0.12)	-0.13 (-0.24, -0.02)	0.03 (-0.16, 0.12)	-0.11 (-0.22, 0.03)
Maternal education	-0.09 (-0.35, 0.16)	0.08 (-0.27, 0.44)	NA	NA	-0.10 (-0.35, 0.14)	0.00 (-0.40, 0.40)	NA	0.07 (-2.11, 0.42)	-0.10 (-0.28, 0.08)	0.04 (-0.22, 0.31)	NA	NA
Graffar Index[d]	-0.08 (-0.18, 0.02)	-0.07 (-0.21, 0.07)	-0.05 (-0.17, 0.15)	-0.08 (-0.24, 0.17)	0.08 (-0.02, 0.19)	**0.26 (0.10, 0.43)**	0.04 (-0.21, 0.18)	**0.25 (0.05, 0.42)**	-0.01 (-0.08, 0.07)	0.08 (-0.03, 0.19)	NA	0.06 (-0.14, 0.17)

[a] Size units are percentage change in log(WFL) from average, tempo units are time (days), velocity units in percent change from average.
[b] Bold values indicate significance with Bonferroni correction at alpha level of 0.05
[c] Adjusted linear regression models only include non-zero coefficients from lasso regression models that include all covariates in full model.
[d] Higher Graffar index values indicate lower socioeconomic status.

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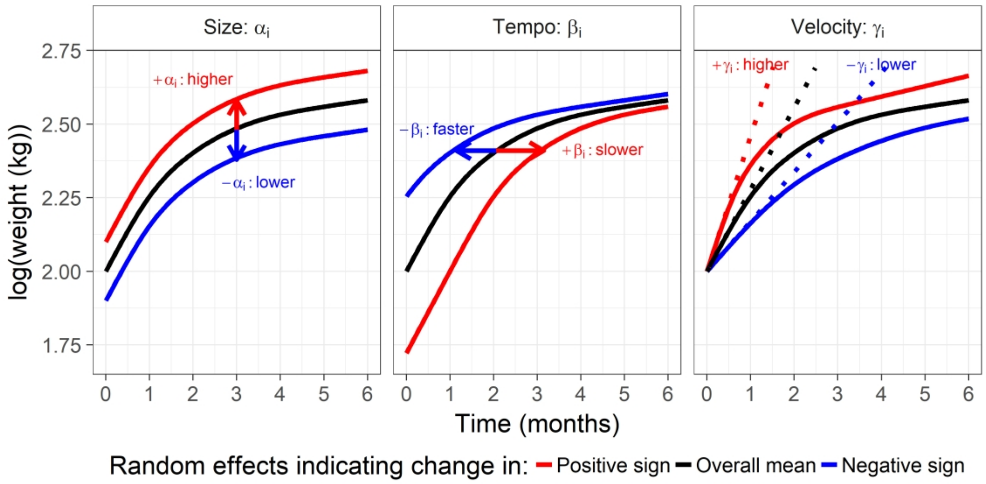

Figure 1. Type of change in random effects relative to the sample mean trajectory in weight growth curve trajectories following a shape invariant model (SIM).

Appendix Table 1. Description of items used for Graffar index

Graffar item	Scale	n(%)
n		1412
No. people in hh 'eating from 1 pot' (%)	1: 1-3	230 (16.3)
	2: 4-6	865 (61.3)
	3: 7-9	254 (18.0)
	4: 10-12	55 (3.9)
	5: 13-15	6 (0.4)
	6: over 16	2 (0.1)
Father's presence in household (%)	1: father is present; not left hh	1197 (84.8)
	3: left hh but sends money	66 (4.7)
	4: partially left hh	38 (2.7)
	6: completely gone	111 (7.9)
Head of household's highest educational level (%)	1: university completed	12 (0.9)
	2: university not completed	9 (0.6)
	3: h.s. or technical studies completed	325 (23.0)
	4: completed 8th grade	664 (47.1)
	5: did not reach 8th grade	382 (27.1)
	6: no schooling	19 (1.3)
Property ownership (%)	1: owned	269 (19.1)
	2: home mortgage	83 (5.9)
	3: rent	243 (17.2)
	4: given to you as a gift	117 (8.3)
	5: squatters w tents or construction	7 (0.5)
	6: lving in back of main house	693 (49.1)
Type of house construction (%)	1: very large house	15 (1.1)
	2: smaller house	181 (12.8)
	3: tiny concrete house	330 (23.4)

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Appendix Table 1. Description of items used for Graffar index

Graffar item	Scale	n(%)
	4: self-constructed home	398 (28.2)
	5: wooden house	94 (6.7)
	6: wooden house w/ less than three rooms	394 (27.9)
Characteristics of the kitchen (%)	1: independent kitchen in one room	931 (65.9)
	6: kitchen in a room with multiple uses	481 (34.1)
Sewage,plumbing (%)	1: inside plumbing	1402 (99.3)
	5: out house	9 (0.6)
	6: just go in woods	1 (0.1)
Water (%)	1: water from inside home faucet	949 (67.2)
	6: water from outside faucet	463 (32.8)
No. times garbage collected per week (%)	1: more than 4x/week	6 (0.4)
	2: 3 times/week	1288 (91.2)
	3: 2 times/week	117 (8.3)
	6: never	1 (0.1)
Total count of previous six goods,possessions (tv, washing machine, stereo, refrig., car) (%)	1: 13-15 (own all six goods)	77 (5.5)
	2: 10-12	311 (22.3)
	3: 7-9	302 (21.6)
	4: 4-6	277 (19.9)
	5: 1-3	374 (26.8)
	6: 0	54 (3.9)

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Appendix Table 2. Nonlinear mixed effects model fit evaluation: BIC for all evaluated models

Trajectory type	Model ID	Model description	BIC[a]
Weight	no random effects	no random effects	NA
	m2	random size (alpha0)	-19546.4
	m3	random tempo (beta0)	-17232
	m4	random velocity (beta1)	-18323
	m5	random tempo and velocity (beta0 and beta1)	-21901.5
	m5.strat	m5 + sex-spec effects	-22123.4
	m5.strat2	m5.strat + sex-spec corr structure	-22107.5
	m6	random size and tempo (alpha0 and beta0)	-21740.4
	m7	random size and velocity (alpha0 and beta1)	-21629.8
	m8	random size, tempo and velocity (alpha0, beta0, and beta1)	
Height	no random effects	no random effects	NA
	m2	random size (alpha0)	-37399.5
	m3	random tempo (beta0)	-36684.1
	m4	random velocity (beta1)	-34985.7
	m5	random tempo and velocity (beta0 and beta1)	-37820
	m5.strat	m5 + sex-spec effects	
	m5.strat2	m5.strat + sex-spec corr structure	-37978.2
	m6	random size and tempo (alpha0 and beta0)	-37381.5
	m7	random size and velocity (alpha0 and beta1)	-37819.9
WFL	no random effects	no random effects	NA
	m2	random size (alpha0)	-21147.2
	m3	random tempo (beta0)	-18852.1
	m4	random velocity (beta1)	-20549.9
	m5	random tempo and velocity (beta0 and beta1)	-22598
	m5.strat	m5 + sex-spec effects	-22761.2
	m5.strat2	m5.strat + sex-spec corr structure	-22751.3
	m6	random size and tempo (alpha0 and beta0)	

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Appendix Table 2. Nonlinear mixed effects model fit evaluation: BIC for all evaluated models

Trajectory type	Model ID	Model description	BIC[a]
	m7	random size and velocity (alpha0 and beta1)	-22484.6

[a]Bold values indicate lowest value within a trajectory evaluation.

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Reporting checklist for cohort study.

Based on the STROBE cohort guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

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		Reporting Item	Page Number
Title and abstract			
Title	#1a	Indicate the study’s design with a commonly used term in the title or the abstract	1

Abstract	#1b	Provide in the abstract an informative and balanced summary of what was done and what was found	3
Introduction			
Background / rationale	#2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	#3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	#4	Present key elements of study design early in the paper	5
Setting	#5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Eligibility criteria	#6a	Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up.	5
Eligibility criteria	#6b	For matched studies, give matching criteria and number of exposed and unexposed	na
Variables	#7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5
Data sources / measurement	#8	For each variable of interest give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than	5

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		one group. Give information separately for for exposed and unexposed groups if applicable.	
Bias	#9	Describe any efforts to address potential sources of bias	6
Study size	#10	Explain how the study size was arrived at	5
Quantitative variables	#11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	6
Statistical methods	#12a	Describe all statistical methods, including those used to control for confounding	6
Statistical methods	#12b	Describe any methods used to examine subgroups and interactions	na
Statistical methods	#12c	Explain how missing data were addressed	7
Statistical methods	#12d	If applicable, explain how loss to follow-up was addressed	na
Statistical methods	#12e	Describe any sensitivity analyses	na
Results			
Participants	#13a	Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-	7

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		up, and analysed. Give information separately for for exposed and unexposed groups if applicable.	
Participants	#13b	Give reasons for non-participation at each stage	7
Participants	#13c	Consider use of a flow diagram	na
Descriptive data	#14a	Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders. Give information separately for exposed and unexposed groups if applicable.	7
Descriptive data	#14b	Indicate number of participants with missing data for each variable of interest	7
Descriptive data	#14c	Summarise follow-up time (eg, average and total amount)	na
Outcome data	#15	Report numbers of outcome events or summary measures over time. Give information separately for exposed and unexposed groups if applicable.	na
Main results	#16a	Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	7-8
Main results	#16b	Report category boundaries when continuous variables were categorized	na
Main results	#16c	If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	na

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Other analyses	#17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	na
Discussion			
Key results	#18	Summarise key results with reference to study objectives	8-9
Limitations	#19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias.	10
Interpretation	#20	Give a cautious overall interpretation considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence.	10
Generalisability	#21	Discuss the generalisability (external validity) of the study results	10
Other Information			
Funding	#22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	10

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Sociodemographic predictors of early postnatal growth: evidence from a Chilean infancy cohort.

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Keywords:	EPIDEMIOLOGY, PUBLIC HEALTH, Community child health < PAEDIATRICS

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Title: Sociodemographic predictors of early postnatal growth: evidence from a Chilean infancy cohort

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Abstract

Objectives

Infant anthropometric growth varies across socioeconomic factors, including maternal education and income, and may serve as an indicator of environmental influences in early life with long term health consequences. Previous research has identified sociodemographic gradients in growth with a focus on the first year and beyond, but estimates are sparse for growth before six months. Thus, our objective was to examine the relationship between sociodemographic factors and infant growth patterns between birth and five months of age.

Design

Prospective cohort study

Settings

Low- to middle-income neighborhoods in Santiago, Chile (1991-1996).

Participants

1,412 participants from a randomized iron deficiency anemia preventive trial in healthy infants.

Main outcome measures

Longitudinal anthropometrics including monthly weight (kg), length (cm) and weight-for-length (WFL) values. For each measure, we estimated three individual-level growth parameters (size, timing, and velocity) from SuperImposition by Translation and Rotation (SITAR) models. Size and timing changes represent vertical and horizontal growth curve shifts, respectively, and velocity change represents growth rate shifts. We estimated the linear association between growth parameters and gestational age, maternal age, education, and socioeconomic position (SEP).

Results

Lower SEP was associated with a slower linear (length) velocity growth parameter (-0.22, 95% CI=-0.31,-0.13) – outcome units are percent change in velocity from the average growth curve. Lower SEP was associated with later WFL growth timing as demonstrated through the tempo growth parameter for females (0.25, 95% CI=0.05,0.42) – outcome units are shifts in days from the average growth curve. We found no evidence of associations between SEP and the weight size, timing, or velocity growth rate parameters.

Conclusion

Previous research on growth in older infants and children shows associations between lower SEP with slower length velocity. We found evidence supporting this association in

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the first five months of life, which may inform age-specific prevention efforts aimed at infant growth.

Strengths and Limitations of this Study

- The sample includes monthly anthropometric measures in the first five postnatal months – not available in any study to date and allowing better fitting growth models.
- We used the Graffar Index, a detailed measure of socioeconomic position (SEP) specific to low- to middle-income groups, an understudied population, which may reduce misclassification of SEP.
- As the sample was low- to middle-income, these results may not generalize to groups with even lower or higher income or SEP.

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Introduction

Interest in early life infant growth has grown as evidence accumulates that it is associated with the development of adult disease, sometimes decades later. Some chronic disease outcomes associated with infant growth characteristics include obesity, endothelial dysfunction, and metabolic syndrome (1–3). Explanations for these associations include early infancy as a critical window of time for susceptibility to environmental exposures for chronic disease risk factors (4). Socioeconomic position (SEP) is one such exposure. SEP is associated with child growth patterns, in particular, length (5–12) and weight (13–16). In these studies, lower SEP is generally associated with faster weight gain during childhood, while the inverse holds true for length. These socioeconomic gradients in growth appear to emerge in early life (7) and persist (5).

Gaps remain in our understanding regarding sociodemographic predictors of growth during infancy and childhood. One such gap relates to the earliest period of infant growth. Studies to date include only a few observations before six months, leading to linear specifications between weight or height and time. However, curvilinear models of growth offer better model fit for early infancy growth. Growth during the first six months in the human lifespan is characterized by accelerated growth at the outset and leveling off at around six months (17). Given these unique features, early infant growth may yield unique associations with predictors not influential during later periods of growth. Understanding the relationship between early infant growth and sociodemographic factors may yield new information that highlight the potential for earlier interventions to promote optimal health.

Identifying novel associations in this age range can better pinpoint the timing and influence of sociodemographic factors. Given the sparsity of information in the literature focusing on these points, our aim in this study is to examine sociodemographic predictors of infant weight, length and weight-for-length (WFL) growth from zero to five months in an infancy cohort of over 1,400 healthy Chilean children. Based on prior research in middle- to high-income countries applied to a wider range of ages in childhood that is described above, we expected that SEP will be inversely associated with weight gain and positively associated with length growth.

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Methods

Study sample

The data in this study are drawn from the Santiago Longitudinal Study (SLS), a cohort study from low- to middle-income neighborhoods in Santiago, Chile. Between 1991 and 1996, infants were recruited for an infancy iron deficiency anemia preventive trial (18) or neuromaturation study (19). Inclusion criteria for the infancy studies included full term infants [greater than or equal to 37 weeks gestational age (GA)] with birthweight $\geq$ 3.0 kg, vaginal birth, no major health problems for the infant, and, for the preventive trial, no iron deficiency anemia present at five to six months. Those with iron deficiency anemia and the next nonanemic control were invited to participate in the neuromaturation study and are not considered here. Participant eligibility and follow-up information have previously been reported (18). The Santiago Longitudinal Study (SLS) had been approved by Institutional Review Boards from 1) the University of Michigan, Ann Arbor, 2) Institute of Nutrition and Food Technology (INTA), Chile and 3) University of California, San Diego.

We characterized the growth period prior to treatment randomization, which occurred at six months. Anthropometric measures prior to study enrollment were obtained from the medical chart. The total sample size included 1,657 infants who completed the preventive trial.

Outcome and sociodemographic measures

Anthropometric measurements included weight (kg), length (cm), and weight-for-length (WFL) (g/cm). Weight was measured to the nearest 0.01 kg on an electronic scale at local public health clinics. Length was measured on a recumbent board to the nearest 0.1 cm. Gestational age (GA), obtained from the medical chart, was among the set of variables included in the models as a covariate.

Sociodemographic measures were self-reported by the mother, including maternal age (years), total years of education, and the modified Graffar index (20), an index of SEP used in lower-income countries (21). The modified Graffar index represents a sum of 10 measures regarding education, family composition, and housing characteristics, which are summed to create a scale with higher values indicating lower social class (Appendix Table A1). Mothers self-reported breastfeeding characteristics from birth, including date of first bottle and age at weaning if weaned. From this information, we created variables for breastfeeding as the sole source of milk and mixed breast and bottle feeding at five months.

Statistical analyses

Summary statistics included median and interquartile ranges for continuous variables and percent with counts for categorical variables. All summary statistics were stratified by child sex.

We used two steps to assess the association between infant growth and sociodemographic predictors: 1) SuperImposition by Translation and Rotation (SITAR) approach (22) to

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estimate infant weight, length and weight-for-length (WFL) growth characteristics from birth to five months followed by 2) linear regression to estimate the relationship between sociodemographic predictors and these growth characteristics. We used a nonlinear mixed effects model (23) to estimate the growth characteristics with the R nlme package (24). Each model produces up to three different SITAR growth parameters per individual, which have been named 'size', 'tempo' and 'velocity' (22) (Figure 1). 'Size' indicates a shift of the growth curve up and down for an individual relative to the average growth curve. 'Tempo' indicates a shift of the growth curve to the left or right on the age scale for an individual relative to the average growth curve. Lastly, 'velocity' indicates a transformation of the age scale in the nonlinear model, shrinking or enlarging the age scale for an individual relative to the average growth curve. These three parameters are noted as having biologically meaningful interpretations, which are difficult to obtain with other growth models (23). Unless otherwise noted, any references to 'size', 'tempo', and 'velocity' refer to these parameters from the SITAR construct applied to early infant growth.

Figure 1 about here

The results from the second step analyses are reported. In addition to including males and females and adjusting for sex of the child (in the pooled analyses), sex-stratified analyses were also used for all three anthropometric outcomes, as some estimated associations between the SITAR growth parameters and SEP indicators differed by sex of the child.

The adjusted models in the second step started with four covariates: gestational age, maternal age, total years of maternal education, and Graffar index (20). We removed covariates from the model based on the least absolute shrinkage and selection operator (lasso) approach (25). This approach has better performance than conventional model selection methods with a univariate approach (26) such as stepwise methods (27). The lasso approach assists in selecting predictors with the strongest coefficients (28) while balancing bias and variation in the model. We used the glmnet package in R (29) to estimate shrunken parameters and the selectiveInference package (30) to provide inference via statistical tests and confidence intervals. Each set of comparisons by outcome, i.e. weight, length or weight-for-length were considered separately. Multiple comparisons increase the possibility of statistically significant study findings by chance alone. Therefore, we controlled for multiple comparisons using a Bonferroni correction at an alpha level of 0.05. A coefficient for the predictor of a weight size growth parameter outcome in the second step indicates a change in log(kg) for a one-unit change in the predictor; we multiply this coefficient by 100 to make a symmetric percentage difference on a modified percentage scale (31). Similarly, a one-unit change in the predictor corresponds to a symmetric percentage change in the velocity growth parameter. Time (days) is not log transformed and the coefficient for this outcome corresponds to a shift in the time scale in days.

For analyses, we used a complete case data set, i.e., all participants with non-missing covariates. The proportion of missing data was less than one percent for all variables except the Graffar index, which had less than three percent missing. The median number of non-missing outcome (anthropometric) values was six out of six monthly measures (birth to five months). The percent of missing outcome values at each time point ranged from 9%

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at months 1 and 2 to 0.2% at birth. In a post hoc data analysis we used logistic regression models to estimate associations between SEP (the Graffar Index) as a continuous variable, and binary breastfeeding status outcomes – any or exclusive – at five months.

Patient and public involvement

Participants were mothers and infants recruited for research. The mothers were not involved in setting the study design, research questions or outcome measures for this study.

Results

Participants (n=1,412) were 53% male and 47% female. Median gestational age (Q1, Q3) was 40 weeks (39, 40). Median maternal age (Q1, Q3) was 26 years (22, 31), and mothers had a median (IQR) of 10 (8, 12) years of education at the time of their infant's birth (Table 1). For the six monthly anthropometric measurements prior to six months, each infant had at least two observations, and 72% had measures at all six time points.

Put table 1 about here

We assessed best model fit for each anthropometric measure via the lowest Bayesian Information Criterion (BIC) for growth independent of any covariates. After evaluating all possible combinations of SITAR models from one to three parameters for each of the three anthropometric measures, best fit (Appendix Table A2) models included: 1) all three growth parameters for weight, i.e. 'size', 'tempo', and 'velocity', 2) sex-specific growth trajectories with tempo and velocity parameters for length, and 3) sex-specific growth trajectories with size and tempo parameters for WFL.

The following sections outline the adjusted results of the growth trajectory analyses for the three anthropometric outcomes: weight (kg), length (cm) and weight-for-length (WFL) (g/cm).

Weight trajectories: size, tempo and velocity

After including all covariates in the model, gestational age was the only characteristic associated with any weight growth parameters. In the pooled sample, gestational age was significantly associated with the weight tempo parameter (-2.01, 95% CI = -2.98, -1.70), indicating a leftward shift of about two days for each additional week in gestational age. This indicates earlier timing of weight gain in infants who were born with higher gestational age (Table 2). There was no substantive difference in this association in the sex-stratified analyses.

put table 2 about here

Length trajectories: tempo and velocity

When evaluating the relationship between deviations from the average length growth characteristics and sociodemographic predictors, we found associations for SEP and

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gestational age. In the pooled group, the coefficient of association between the Graffar index and the velocity parameter (-0.22, 95% CI = -0.31, -0.13) (Table 3) indicated that for each unit increase in the Graffar index, lower values indicating higher SEP, there was a -0.22 percent decline from the average length velocity. Conversely, this association reflects a positive relationship between the length velocity parameter and SEP. This coefficient was not substantively different in the sex-stratified analyses, all of which indicated faster linear (length) growth with higher SEP. In contrast to the sex-stratified analyses, all covariates remained in the pooled adjusted model with less than 5% change from the unadjusted SEP coefficient (-0.23, 95% CI = -0.31, -0.15).

Similar to SEP, GA was also positively associated with the length velocity parameter, demonstrating a 0.61 percent (95% CI =0.06, 1.15) increase from the average length velocity in the pooled sample for every unit increase in GA (weeks). Gestational age was inversely associated with the length tempo parameter in the pooled sample (-2.94, 95% CI = -3.51, -2.41), indicating a leftward shift of about three days of the trajectory on the time scale, and a faster start to length growth, for each one week increase in gestational age (Table 3).

put Table 3 about here

Weight-for-length trajectories: size and tempo

Evaluations of shifts in WFL size and tempo from the average indicated associations with SEP and GA. Increases in the Graffar Index, equivalent to lower SEP, were associated with a positive shift in the WFL tempo parameter for females (0.25, 95% CI = 0.05, 0.42). This estimate approximates a rightward shift in time (days) relative to the average growth curve indicating later growth timing with lower SEP.

Similar to weight and length trajectory analyses, an increase in gestational age was inversely associated with a decline in tempo from the average in the pooled sample (-1.99, 95% CI = -2.83, -1.49) (Table 4) indicating about a two-day shift to the left on the time scale from the average growth curve for every one week increase in gestational age. Similar values were found in the sex-stratified analyses, all indicating earlier timing of WFL growth with higher gestational age.

put Table 4 about here

The post hoc analysis examining the association between odds of exclusive or any breastfeeding at five months and the continuous SEP measure (the Graffar index) did not find a substantive or significant association (data not shown).

Discussion

In this research, we found that lower SEP, measured by the Graffar index, was inversely associated with length growth characteristics -- but not weight -- in the first six months. Lower SEP was associated with later timing of WFL growth as reflected by the positive association between the Graffar Index and the WFL tempo parameter. These higher tempo

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values translate to a rightward shift in growth relative to the average growth curve as well as a later age at peak velocity (32). This delay in growth can be considered an unfavorable outcome associated with lower SEP.

Maternal age was not associated with any of the three adjusted growth parameters for length, weight, or weight-for-length. Gestational age (GA) was inversely associated with the tempo growth parameters for length, weight, and weight-for-length indicating higher GA is associated with earlier timing of these three measures. Gestational age is also positively associated with length velocity in the pooled sample indicating faster length change with increasing GA.

Of three previous studies investigating associations between sociodemographic predictors and infant growth before six months, two found a positive association between length (linear) growth and maternal education (8,10), used as a proxy for SEP. Only one study found an inverse association with length growth (12). Many studies including age ranges exceeding six months of age up to five years of age demonstrated a positive association between maternal education and length/height growth (7,8,10). The majority of these studies support the conclusion that lower SEP is associated with slower length (linear) growth in infancy and early childhood.

Several prior studies representing high-income European countries have noted that their findings of either an inverse (12) or no relationship (7) between SEP and length (linear) growth may not generalize to low- to middle-income countries. Deviations from the Western diet and lifestyle were one of the reasons given for this limitation. Chile, the country from which our data were collected, offers an interesting context in this respect. The recruitment period for this study, 1991 to 1996, occurred as Chile was transitioning from a low-income to an upper-middle income country. In 1990, 40% of the Chilean population was below the poverty line (33); by 2012 WHO classified Chile as an upper middle-income country (34). There were nutrition and epidemiologic transitions (35,36) beginning in the 1970s and continuing during the 1990s when study infants were enrolled. Specifically, consumption of high-calorie food, accompanied by a sedentary lifestyle, resulted in rising obesity prevalence across all socioeconomic levels. In the context of an emerging Western diet and lifestyle, we found that lower SEP was associated with poorer length (linear) growth in early infancy. Of course, contemporary generations in Chile experience lower SEP in a new context of over-nutrition and higher levels of sedentary behavior. Thus, current studies in Chile may find distinct relationships between SEP and early growth when compared with generations born 20 years ago.

Plausible biological mechanisms, linked to modifiable factors, have been proposed for the observed association between lower SEP and length growth in the first five postnatal months. Breastfeeding and maternal smoking are two commonly proposed mechanisms, although evidence is limited. In our sample, breastfeeding was close to universal (37,38) and not associated with infant weight change in the first year. We did not evaluate maternal smoking in this study given the large proportion of missing information. However, prior studies did not find that either prenatal or postnatal maternal smoking substantially altered the association between SEP and growth (11,12,16).

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Maternal age was the only sociodemographic predictor positively associated with the unadjusted SITAR size growth parameter for weight. This was similarly reported in another cohort from the same geographic area of Santiago, Chile, the Growth and Obesity Cohort Study (GOCS) (13), which started a decade later and studied ages between birth and 2 years. Our findings add to this work. Through our intense focus on the first five postnatal months, our results demonstrate that the association between SEP and weight growth appears earlier in the postnatal period than previously documented.

Other potential mechanisms relating to SEP could include gestational weight gain and maternal nutrient status. Size at birth, considered a proxy for these two factors and represented in these analyses by the size SITAR parameter, was not associated with any of the sociodemographic measures. Further research will be useful in clarifying the biological mechanisms behind the association between SEP and early infant growth.

Strengths of this study include the combination of an analytic approach to growth that better captures the nonlinear characteristic of growth in the first five months of life with a detailed measure of socioeconomic position appropriate to the context of a lower income setting. Another strength is the monthly anthropometric measures collected in the first five postnatal months. We also note several limitations. The sample size (n = 1,412) is smaller than other studies with sample sizes in the thousands or tens of thousands (5,13,14). Our study, therefore, may not have been powered to detect some effects reported in larger studies. Another limitation is that the Graffar index, developed to assess differences in low- to middle-income populations, limits the generalizability of our findings to higher income groups.

This investigation examined various growth characteristics from birth to five months and their association with sociodemographic factors in a Chilean infancy cohort. We found associations between lower SEP and slower length (linear) growth, which are similar in direction to previous findings for maternal education that span periods of time greater than the first six months and up to five years of age (7,8,10,12). The association between maternal age and weight size, in our study, was similar to findings in other studies of growth between birth and two years of age (13). In sum, our results extend findings from previous research by showing that sociodemographic factors affect infant growth even in the first five months of growth and in relatively homogenous low- to middle-income populations.

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Contributors

AVH designed the study, conducted the data analysis, and wrote the first draft of the paper. KEN and SG supervised and contributed to the study design, interpretation of results, and draft revisions. EB helped acquire the data. All authors

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(AVH,KEN,SG,RB,EB,BL,AGH,AJ,MG,VSV) both contributed to revisions of the draft for intellectual content and approved the final version of the manuscript.

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Competing interests

None declared.

Patient consent

Not required.

Ethics approval

The Santiago Longitudinal Study (SLS) had been approved by Institutional Review Boards from 1) University of Michigan Medical Center, Ann Arbor, 2) Institute of Nutrition and Food Technology (INTA), Chile and 3) University of California, San Diego. The Office of Human Research Ethics at the University of North Carolina, Chapel Hill exempted this current research using existing anonymous data from review under the 45 CFR 46.101(b) regulatory category.

Data sharing agreement

No additional data are available.

Disclaimer

AHA had no role in the study design, data collection, and analysis, decision to publish or preparation of the manuscript.

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Table1. Descriptive statistics of sociodemographic characteristics, median [IQR]

Characteristic	Male	Female	Total
n	747	665	1412
Gestational age (weeks)	40.0 [39.0, 40.0]	40.0 [39.0, 40.0]	40.0 [39.0, 40.0]
Graffar Index	27.0 [23.0, 33.0]	27.0 [23.0, 33.0]	27.0 [23.0, 33.0]
Maternal age (years)	26.0 [21.8, 30.9]	25.5 [21.7, 30.3]	25.8 [21.8, 30.8]
Maternal Education (years)	10.0 [8.0, 12.0]	10.0 [8.0, 12.0]	10.0 [8.0, 12.0]

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Table 2: Sociodemographic predictors and association with weight SITAR growth parameter[a,b], stratified by sex of child in the Santiago Longitudinal Study, 1991-1996

	Males						Females						Total					
	Unadjusted			Adjusted[c]			Unadjusted			Adjusted[c]			Unadjusted			Adjusted[c]		
Characteristic	Size	Tempo	Velocity	Size	Tempo	Velocity	Size	Tempo	Velocity	Size	Tempo	Velocity	Size	Tempo	Velocity	Size	Tempo	Velocity
Gest age	0.59 (-0.12, 1.31)	**-2.28 (-3.15, -1.41)**	-0.81 (-2.28, 0.66)	NA	**-1.96 (-3.15, -1.40)**	NA	0.76 (-0.02, 1.54)	**-2.38 (-3.32, -1.45)**	-2.14 (-3.87, -0.42)	0.45 (-0.32, 9.88)	**-2.23 (-3.35, -1.47)**	-1.58 (-3.85, 0.08)	0.64 (0.10, 1.18)	**-2.35 (-2.98, -1.71)**	-1.53 (-2.70, -0.37)	0.53 (-0.05, 1.15)	**-2.01 (-2.98, -1.70)**	-1.06 (-2.67, 0.01)
Maternal age	0.11 (-0.00, 0.23)	-0.06 (-0.20, 0.09)	-0.07 (-0.31, 0.17)	0.07 (-0.11, 0.21)	-0.06 (-0.21, 0.26)	-0.06 (-0.33, 0.82)	**0.21 (0.07, 0.34)**	-0.02 (-0.18, 0.15)	**-0.41 (-0.71, -0.12)**	0.19 (-6.13, 0.22)	0.01 (-2.29, 0.13)	-0.36 (-0.67, -0.04)	**0.16 (0.07, 0.25)**	-0.03 (-0.14, 0.07)	-0.20 (-0.39, -0.00)	0.15 (-0.78, 0.22)	-0.01 (-0.16, 0.83)	-0.18 (-0.56, 0.22)
Maternal education	-0.03 (-0.32, 0.26)	0.14 (-0.21, 0.49)	-0.04 (-0.62, 0.55)	NA	NA	NA	-0.01 (-0.31, 0.29)	0.06 (-0.30, 0.43)	-0.03 (-0.69, 0.64)	0.00 (-Inf, -0.41)	0.12 (-0.95, 0.52)	NA	-0.03 (-0.24, 0.19)	0.10 (-0.15, 0.36)	-0.04 (-0.50, 0.41)	0.00 (-10.67, 0.04)	0.04 (-1.59, 1.58)	-0.05 (-0.75, 4.42)
Graffar Index[d]	-0.12 (-0.23, -0.01)	-0.13 (-0.27, 0.01)	-0.15 (-0.39, 0.08)	-0.08 (-0.22, 0.07)	-0.13 (-0.28, 0.03)	-0.13 (-0.41, 0.28)	-0.07 (-0.19, 0.06)	0.12 (-0.03, 0.28)	0.28 (0.00, 0.57)	-0.03 (-5.15, 0.23)	0.13 (-0.24, 0.29)	0.23 (-0.16, 0.52)	-0.09 (-0.18, -0.00)	-0.01 (-0.11, 0.09)	0.06 (-0.12, 0.25)	-0.06 (-0.83, 0.04)	-0.00 (-0.06, 3.49)	0.02 (-1.66, 0.32)

[a] Size units are percentage change in log(weight) from average, tempo units are time (days), velocity units in percent change from average.

[b] Bold values indicate significance with Bonferroni correction at alpha level of 0.05

[c] Adjusted linear regression models only include non-zero coefficients from lasso regression models that include all covariates in full model.

[d] Higher Graffar index values indicate lower socioeconomic status.

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Table 3: Sociodemographic predictors and association with length SITAR growth parameters[a,b], stratified by sex of child in the Santiago Longitudinal Study, 1991-1996

	Males				Females				Both			
	Unadjusted		Adjusted[c]		Unadjusted		Adjusted[c]		Unadjusted		Adjusted[c]	
Characteristic	Tempo	Velocity	Tempo	Velocity	Tempo	Velocity	Tempo	Velocity	Tempo	Velocity	Tempo	Velocity
Gest age	**-3.33 (-4.09, -2.56)**	**0.99 (0.29, 1.68)**	**-3.05 (-4.10, -2.55)**	NA	**-2.57 (-3.36, -1.79)**	0.25 (-0.52, 1.02)	**-2.53 (-3.33, -1.77)**	NA	**-2.97 (-3.52, -2.42)**	**0.64 (0.12, 1.15)**	**-2.94 (-3.51, -2.41)**	**0.61 (0.06, 1.15)**
Maternal age	-0.04 (-0.18, 0.09)	0.09 (-0.03, 0.20)	-0.01 (-0.10, 1.64)	NA	**-0.17 (-0.30, -0.03)**	0.01 (-0.13, 0.14)	-0.15 (-0.29, 0.01)	NA	-0.10 (-0.19, -0.00)	0.05 (-0.04, 0.14)	-0.07 (-0.17, 0.06)	0.02 (-0.35, 0.10)
Maternal education	0.06 (-0.26, 0.38)	0.12 (-0.16, 0.40)	NA	NA	-0.18 (-0.49, 0.13)	0.28 (-0.01, 0.58)	-0.14 (-0.45, 0.52)	0.16 (-0.35, 0.52)	-0.05 (-0.28, 0.17)	0.20 (-0.00, 0.40)	-0.06 (-0.27, 0.73)	0.13 (-0.21, 0.34)
Graffar Index[d]	0.06 (-0.06, 0.19)	**-0.26 (-0.37, -0.15)**	0.05 (-0.25, 0.36)	**-0.21 (-0.37, -0.14)**	**0.16 (0.03, 0.29)**	**-0.19 (-0.32, -0.07)**	0.13 (-0.03, 0.26)	**-0.17 (-0.31, -0.05)**	**0.11 (0.02, 0.20)**	**-0.23 (-0.31, -0.15)**	0.09 (-0.02, 0.18)	**-0.22 (-0.31, -0.13)**

[a] Size units are percentage change in log(length) from average, tempo units are time (days), velocity units in percent change from average

[b] Bold values indicate significance with Bonferroni correction at alpha level of 0.05.

[c] Adjusted linear regression models only include non-zero coefficients from lasso regression models that include all covariates in full model.

[d] Higher Graffar index values indicate lower socioeconomic status.

Table 4: Sociodemographic predictors and association with weight-for-length (WFL) SITAR growth parameters[a,b,c] stratified by sex of child in the Santiago Longitudinal Study, 1991-1996

	Males				Females				Both			
	Unadjusted		Adjusted[e]		Unadjusted		Adjusted[e]		Unadjusted		Adjusted[e]	
Characteristic	Size	Tempo	Size	Tempo	Size	Tempo	Size	Tempo	Size	Tempo	Size	Tempo
Gest age	0.09 (-0.55, 0.73)	**-2.03 (-2.91, -1.15)**	NA	**-1.58 (-2.90, -1.11)**	0.05 (-0.58, 0.69)	**-2.34 (-3.35, -1.32)**	NA	**-2.32 (-3.35, -1.33)**	0.07 (-0.38, 0.52)	**-2.17 (-2.84, -1.51)**	NA	**-1.99 (-2.83, -1.49)**
Maternal age	0.07 (-0.03, 0.18)	-0.09 (-0.23, 0.06)	0.04 (-0.23, 0.16)	-0.08 (-0.24, 0.17)	0.02 (-0.09, 0.13)	-0.18 (-0.36, -0.00)	NA	-0.13 (-0.36, 0.14)	0.05 (-0.03, 0.12)	-0.13 (-0.24, -0.02)	0.03 (-0.16, 0.12)	-0.11 (-0.22, 0.03)
Maternal education	-0.09 (-0.35, 0.16)	0.08 (-0.27, 0.44)	NA	NA	-0.10 (-0.35, 0.14)	0.00 (-0.40, 0.40)	NA	0.07 (-2.11, 0.42)	-0.10 (-0.28, 0.08)	0.04 (-0.22, 0.31)	NA	NA
Graffar Index[d]	-0.08 (-0.18, 0.02)	-0.07 (-0.21, 0.07)	-0.05 (-0.17, 0.15)	-0.08 (-0.24, 0.17)	0.08 (-0.02, 0.19)	**0.26 (0.10, 0.43)**	0.04 (-0.21, 0.18)	**0.25 (0.05, 0.42)**	-0.01 (-0.08, 0.07)	0.08 (-0.03, 0.19)	NA	0.06 (-0.14, 0.17)

[a] Size units are percentage change in log(WFL) from average, tempo units are time (days), velocity units in percent change from average.

[b] Bold values indicate significance with Bonferroni correction at alpha level of 0.05.

[c] Adjusted linear regression models only include non-zero coefficients from lasso

regression models that include all covariates in full model.

[d] Higher Graffar index values indicate lower socioeconomic status

Figure 1 caption: Type of change in random effects relative to the sample mean trajectory in weight growth curve trajectories following a shape invariant model (SIM).

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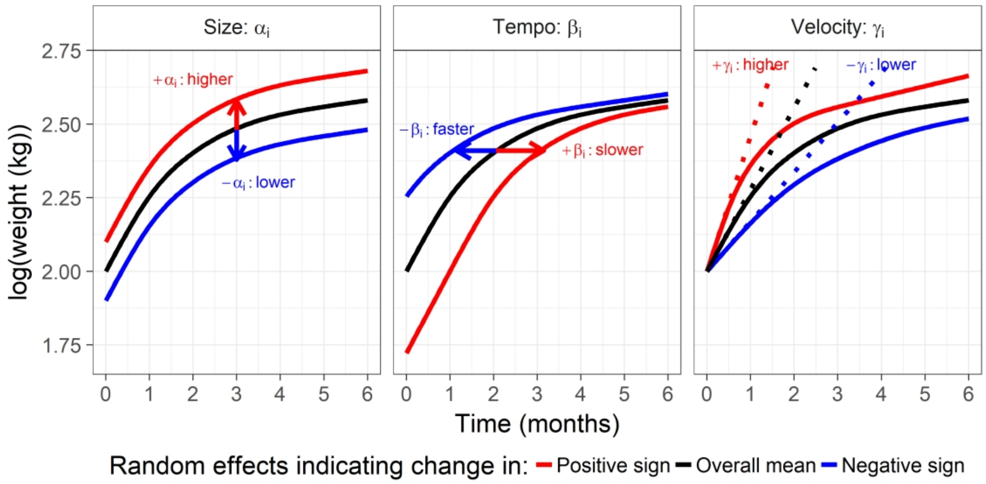

Figure 1. Type of change in random effects relative to the sample mean trajectory in weight growth curve trajectories following a shape invariant model (SIM).

Appendix Table 1. Description of items used for Graffar index

Graffar item	Scale	n(%)
N		1412
No. people in hh ‘eating from 1 pot’ (%)	1: 1-3	230 (16.3)
	2: 4-6	865 (61.3)
	3: 7-9	254 (18.0)
	4: 10-12	55 (3.9)
	5: 13-15	6 (0.4)
	6: over 16	2 (0.1)
Father’s presence in household (%)	1: father is present; not left hh	1197 (84.8)
	3: left hh but sends money	66 (4.7)
	4: partially left hh	38 (2.7)
	6: completely gone	111 (7.9)
Head of household’s highest educational level (%)	1: university completed	12 (0.9)
	2: university not completed	9 (0.6)
	3: h.s. or technical studies completed	325 (23.0)
	4: completed 8th grade	664 (47.1)
	5: did not reach 8th grade	382 (27.1)
	6: no schooling	19 (1.3)
Property ownership (%)	1: owned	269 (19.1)
	2: home mortgage	83 (5.9)
	3: rent	243 (17.2)
	4: given to you as a gift	117 (8.3)
	5: squatters w tents or construction	7 (0.5)
	6: lving in back of main house	693 (49.1)
Type of house construction (%)	1: very large house	15 (1.1)
	2: smaller house	181 (12.8)
	3: tiny concrete house	330 (23.4)

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Appendix Table 1. Description of items used for Graffar index

Graffar item	Scale	n(%)
	4: self-constructed home	398 (28.2)
	5: wooden house	94 (6.7)
	6: wooden house w/ less than three rooms	394 (27.9)
Characteristics of the kitchen (%)	1: independent kitchen in one room	931 (65.9)
	6: kitchen in a room with multiple uses	481 (34.1)
Sewage,plumbing (%)	1: inside plumbing	1402 (99.3)
	5: out house	9 (0.6)
	6: just go in woods	1 (0.1)
Water (%)	1: water from inside home faucet	949 (67.2)
	6: water from outside faucet	463 (32.8)
No. times garbage collected per week (%)	1: more than 4x/week	6 (0.4)
	2: 3 times/week	1288 (91.2)
	3: 2 times/week	117 (8.3)
	6: never	1 (0.1)
Total count of previous six goods,possessions (tv, washing machine, stereo, refrig., car) (%)	1: 13-15 (own all six goods)	77 (5.5)
	2: 10-12	311 (22.3)
	3: 7-9	302 (21.6)
	4: 4-6	277 (19.9)
	5: 1-3	374 (26.8)
	6: 0	54 (3.9)

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Appendix Table 2: Nonlinear mixed effects model fit evaluation: BIC for all evaluated models

Trajectory type	Model ID	Model description	BIC[a]
Weight	no random effects	no random effects	NA
	m2	random size (alpha0)	-19546.4
	m3	random tempo (beta0)	-17232
	m4	random velocity (beta1)	-18323
	m5	random tempo and velocity (beta0 and beta1)	-21901.5
	m5.strat	m5 + sex-spec effects	-22123.4
	m5.strat2	m5.strat + sex-spec corr structure	-22107.5
	m6	random size and tempo (alpha0 and beta0)	-21740.4
	m7	random size and velocity (alpha0 and beta1)	-21629.8
	m8	random size, tempo and velocity (alpha0, beta0, and beta1)	**-22940.66**
Height	no random effects	no random effects	NA
	m2	random size (alpha0)	-37399.5
	m3	random tempo (beta0)	-36684.1
	m4	random velocity (beta1)	-34985.7
	m5	random tempo and velocity (beta0 and beta1)	-37820
	m5.strat	m5 + sex-spec effects	**-38000.74**
	m5.strat2	m5.strat + sex-spec corr structure	-37978.2
	m6	random size and tempo (alpha0 and beta0)	-37381.5
	m7	random size and velocity (alpha0 and beta1)	-37819.9
WFL	no random effects	no random effects	NA
	m2	random size (alpha0)	-21147.2
	m3	random tempo (beta0)	-18852.1
	m4	random velocity (beta1)	-20549.9
	m5	random tempo and velocity (beta0 and beta1)	-22598
	m5.strat	m5 + sex-spec effects	-22761.2
	m5.strat2	m5.strat + sex-spec corr structure	-22751.3
	m6	random size and tempo (alpha0 and beta0)	**-22808.5**
	m7	random size and velocity (alpha0 and beta1)	-22484.6

[a]Bold values indicate lowest value within a trajectory evaluation.

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Reporting checklist for cohort study.

Based on the STROBE cohort guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the STROBE cohortreporting guidelines, and cite them as:

von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies.

		Reporting Item	Page Number
Title and abstract			
Title	#1a	Indicate the study's design with a commonly used term in the title or the abstract	1

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Abstract	#1b	Provide in the abstract an informative and balanced summary of what was done and what was found	3
Introduction			
Background / rationale	#2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	#3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	#4	Present key elements of study design early in the paper	5
Setting	#5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Eligibility criteria	#6a	Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up.	5
Eligibility criteria	#6b	For matched studies, give matching criteria and number of exposed and unexposed	na
Variables	#7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5
Data sources / measurement	#8	For each variable of interest give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than	5

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		one group. Give information separately for for exposed and unexposed groups if applicable.	
Bias	#9	Describe any efforts to address potential sources of bias	6
Study size	#10	Explain how the study size was arrived at	5
Quantitative variables	#11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	6
Statistical methods	#12a	Describe all statistical methods, including those used to control for confounding	6
Statistical methods	#12b	Describe any methods used to examine subgroups and interactions	na
Statistical methods	#12c	Explain how missing data were addressed	7
Statistical methods	#12d	If applicable, explain how loss to follow-up was addressed	na
Statistical methods	#12e	Describe any sensitivity analyses	na
Results			
Participants	#13a	Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-	7

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		up, and analysed. Give information separately for for exposed and unexposed groups if applicable.	
Participants	#13b	Give reasons for non-participation at each stage	7
Participants	#13c	Consider use of a flow diagram	na
Descriptive data	#14a	Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders. Give information separately for exposed and unexposed groups if applicable.	7
Descriptive data	#14b	Indicate number of participants with missing data for each variable of interest	7
Descriptive data	#14c	Summarise follow-up time (eg, average and total amount)	na
Outcome data	#15	Report numbers of outcome events or summary measures over time. Give information separately for exposed and unexposed groups if applicable.	na
Main results	#16a	Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	7-8
Main results	#16b	Report category boundaries when continuous variables were categorized	na
Main results	#16c	If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	na

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Other analyses	#17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	na
Discussion			
Key results	#18	Summarise key results with reference to study objectives	8-9
Limitations	#19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias.	10
Interpretation	#20	Give a cautious overall interpretation considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence.	10
Generalisability	#21	Discuss the generalisability (external validity) of the study results	10
Other Information			
Funding	#22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	10

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BMJ Open

Sociodemographic predictors of early postnatal growth: evidence from a Chilean infancy cohort.

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Title: Sociodemographic predictors of early postnatal growth: evidence from a Chilean infancy cohort

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Abstract

Objectives

Infant anthropometric growth varies across socioeconomic factors, including maternal education and income, and may serve as an indicator of environmental influences in early life with long term health consequences. Previous research has identified sociodemographic gradients in growth with a focus on the first year and beyond, but estimates are sparse for growth before six months. Thus, our objective was to examine the relationship between sociodemographic factors and infant growth patterns between birth and five months of age.

Design

Prospective cohort study

Settings

Low- to middle-income neighborhoods in Santiago, Chile (1991-1996).

Participants

1,412 participants from a randomized iron deficiency anemia preventive trial in healthy infants.

Main outcome measures

Longitudinal anthropometrics including monthly weight (kg), length (cm) and weight-for-length (WFL) values. For each measure, we estimated three individual-level growth parameters (size, timing, and velocity) from SuperImposition by Translation and Rotation (SITAR) models. Size and timing changes represent vertical and horizontal growth curve shifts, respectively, and velocity change represents growth rate shifts. We estimated the linear association between growth parameters and gestational age, maternal age, education, and socioeconomic position (SEP).

Results

Lower SEP was associated with a slower linear (length) velocity growth parameter (-0.22, 95% CI=-0.31,-0.13) – outcome units are percent change in velocity from the average growth curve. Lower SEP was associated with later WFL growth timing as demonstrated through the tempo growth parameter for females (0.25, 95% CI=0.05,0.42) – outcome units are shifts in days from the average growth curve. We found no evidence of associations between SEP and the weight size, timing, or velocity growth rate parameters.

Conclusion

Previous research on growth in older infants and children shows associations between lower SEP with slower length velocity. We found evidence supporting this association in the first five months of life, which may inform age-specific prevention efforts aimed at infant length growth.

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Strengths and Limitations of this Study

- The sample includes monthly anthropometric measures in the first five postnatal months – not available in any study to date and allowing better fitting growth models.
- We used the Graffar Index, a detailed measure of socioeconomic position (SEP) specific to low- to middle-income groups, an understudied population, which may reduce misclassification of SEP.
- As the sample was low- to middle-income, these results may not generalize to groups with even lower or higher income or SEP.

Introduction

Interest in early life infant growth has grown as evidence accumulates that it is associated with the development of adult disease, sometimes decades later. Some chronic disease outcomes associated with infant growth characteristics include obesity, endothelial dysfunction, and metabolic syndrome [1–3]. Explanations for these associations include early infancy as a critical window of time for susceptibility to environmental exposures for chronic disease risk factors [4]. Socioeconomic position (SEP) is one such exposure. SEP is associated with child growth patterns, in particular, length [5–12] and weight [13–16]. In these studies, lower SEP is generally associated with faster weight gain during childhood, while the inverse holds true for length. These socioeconomic gradients in growth appear to emerge in early life [7] and persist [5].

Gaps remain in our understanding regarding sociodemographic predictors of growth during infancy and childhood. One such gap relates to the earliest period of infant growth. Most studies to date include three or fewer observations before six months [5–8,10,11,13,14,16], preventing nonlinear specifications between weight or height spanning this time. However, curvilinear models of growth with more than three observations offer better model fit for early infancy growth. Growth during the first six months in the human lifespan is characterized by accelerated growth at the outset and leveling off at around six months [17]. Given these unique features, early infant growth may yield unique associations with predictors not influential during later periods of growth. Understanding the relationship between early infant growth and sociodemographic factors may yield new information that highlight the potential for earlier interventions to promote optimal health.

Identifying novel associations in this age range can better pinpoint the timing and influence of sociodemographic factors. Given the sparsity of information in the literature focusing on these points, our aim in this study is to examine sociodemographic predictors of infant weight, length and weight-for-length (WFL) growth from zero to five months in an infancy cohort of over 1,400 healthy Chilean children. Based on prior research in middle- to high-income countries applied to a wider range of ages in childhood that is described above, we expected that SEP will be inversely associated with weight gain and positively associated with length growth.

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Methods

Study sample

The data in this study are drawn from the Santiago Longitudinal Study (SLS), a cohort study from low- to middle-income neighborhoods in Santiago, Chile. Between 1991 and 1996, infants were recruited for an infancy iron deficiency anemia preventive trial [18] or neuromaturation study [19]. Inclusion criteria for the infancy studies included full term infants [greater than or equal to 37 weeks gestational age (GA)] with birthweight $\geq$ 3.0 kg, vaginal birth, no major health problems for the infant, and, for the preventive trial, no iron deficiency anemia present at five to six months. Those with iron deficiency anemia and the next nonanemic control were invited to participate in the neuromaturation study and are not considered here. Participant eligibility and follow-up information have previously been reported [18]. The Santiago Longitudinal Study (SLS) had been approved by Institutional Review Boards from 1) the University of Michigan, Ann Arbor, 2) Institute of Nutrition and Food Technology (INTA), Chile and 3) University of California, San Diego.

We characterized the growth period prior to treatment randomization, which occurred at six months. Anthropometric measures prior to study enrollment were obtained from the medical chart. The total sample size included 1,657 infants who completed the preventive trial.

Outcome and sociodemographic measures

Anthropometric measurements included weight (kg), length (cm), and weight-for-length (WFL) (g/cm). Weight was measured to the nearest 0.01 kg on an electronic scale at local public health clinics. Length was measured on a recumbent board to the nearest 0.1 cm. Gestational age (GA), obtained from the medical chart, was among the set of variables included in the models as a covariate.

Sociodemographic measures were self-reported by the mother, including maternal age (years), total years of education, and the modified Graffar index [20], an index of SEP used in lower-income countries [21]. The modified Graffar index represents a sum of 10 measures regarding education, family composition, and housing characteristics, which are summed to create a scale with higher values indicating lower social class (Appendix Table A1). Mothers self-reported breastfeeding characteristics from birth, including date of first bottle and age at weaning if weaned. From this information, we created variables for breastfeeding as the sole source of milk and mixed breast and bottle feeding at five months.

Statistical analyses

Summary statistics included median and interquartile ranges for continuous variables and percent with counts for categorical variables. All summary statistics were stratified by child sex. We used two steps to assess the association between infant growth and sociodemographic predictors: 1) SuperImposition by Translation and Rotation (SITAR) approach [22] to estimate infant weight, length and weight-for-length (WFL) growth characteristics from birth to five months followed by 2) linear regression to estimate the

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relationship between sociodemographic predictors and these growth characteristics. We used a nonlinear mixed effects model [23] to estimate the growth characteristics with the R nlme package [24]. Each model produces up to three different SITAR growth parameters per individual, which have been named 'size', 'tempo' and 'velocity' [22] (Figure 1). 'Size' indicates a shift of the growth curve up and down for an individual relative to the average growth curve. 'Tempo' indicates a shift of the growth curve to the left or right on the age scale for an individual relative to the average growth curve. Lastly, 'velocity' indicates a transformation of the age scale in the nonlinear model, shrinking or enlarging the age scale for an individual relative to the average growth curve. These three parameters are noted as having biologically meaningful interpretations, which are difficult to obtain with other growth models [23]. Unless otherwise noted, any references to 'size', 'tempo', and 'velocity' refer to these parameters from the SITAR construct applied to early infant growth.

Figure 1 about here

The results from the second step analyses are reported. In addition to including males and females and adjusting for sex of the child (in the pooled analyses), sex-stratified analyses were also used for all three anthropometric outcomes, as some estimated associations between the SITAR growth parameters and SEP indicators differed by sex of the child.

The adjusted models in the second step started with four covariates: gestational age, maternal age, total years of maternal education, and Graffar index [20]. We removed covariates from the model based on the least absolute shrinkage and selection operator (lasso) approach [25]. This approach has better performance than conventional model selection methods with a univariate approach [26] such as stepwise methods [27]. The lasso approach assists in selecting predictors with the strongest coefficients [28] while balancing bias and variation in the model. We used the glmnet package in R [29] to estimate shrunken parameters and the selectiveInference package [30] to provide inference via statistical tests and confidence intervals. Each set of comparisons by outcome, i.e. weight, length or weight-for-length were considered separately. Multiple comparisons increase the possibility of statistically significant study findings by chance alone. Therefore, we controlled for multiple comparisons using a Bonferroni correction at an alpha level of 0.05. A coefficient for the predictor of a weight size growth parameter outcome in the second step indicates a change in log(kg) for a one-unit change in the predictor; we multiply this coefficient by 100 to make a symmetric percentage difference on a modified percentage scale [31,32]. Similarly, a one-unit change in the predictor corresponds to a symmetric percentage change in the velocity growth parameter. Time (days) is not log transformed and the coefficient for this outcome corresponds to a shift in the time scale in days.

For analyses, we used a complete case data set, i.e., all participants with non-missing covariates. The proportion of missing data was less than one percent for all variables except the Graffar index, which had less than three percent missing. The median number of non-missing outcome (anthropometric) values was six out of six monthly measures (birth to five months). The percent of missing outcome values at each time point ranged from 9% at months 1 and 2 to 0.2% at birth. In a post hoc data analysis we used logistic regression

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models to estimate associations between SEP (the Graffar Index) as a continuous variable, and binary breastfeeding status outcomes – any or exclusive – at five months.

Patient and public involvement

Participants were mothers and infants recruited for research. The mothers were not involved in setting the study design, research questions or outcome measures for this study.

Results

Participants (n=1,412) were 53% male and 47% female. Median gestational age (Q1, Q3) was 40 weeks (39, 40). Median maternal age (Q1, Q3) was 26 years (22, 31), and mothers had a median (IQR) of 10 (8, 12) years of education at the time of their infant's birth (Table 1). For the six monthly anthropometric measurements prior to six months, each infant had at least two observations, and 72% had measures at all six time points.

Put table 1 about here

We assessed best model fit for each anthropometric measure via the lowest Bayesian Information Criterion (BIC) for growth independent of any covariates. After evaluating all possible combinations of SITAR models from one to three parameters for each of the three anthropometric measures, best fit (Appendix Table A2) models included: 1) all three growth parameters for weight, i.e. 'size', 'tempo', and 'velocity', 2) sex-specific growth trajectories with tempo and velocity parameters for length, and 3) sex-specific growth trajectories with size and tempo parameters for WFL.

The following sections outline the adjusted results of the growth trajectory analyses for the three anthropometric outcomes: weight (kg), length (cm) and weight-for-length (WFL) (g/cm).

Weight trajectories: size, tempo and velocity

After including all covariates in the model, gestational age was the only characteristic associated with any weight growth parameters. In the pooled sample, gestational age was significantly associated with the weight tempo parameter (-2.01, 95% CI = -2.98, -1.70), indicating a leftward shift of about two days for each additional week in gestational age. This indicates earlier timing of weight gain in infants who were born with higher gestational age (Table 2). There was no substantive difference in this association in the sex-stratified analyses.

put table 2 about here

Length trajectories: tempo and velocity

When evaluating the relationship between deviations from the average length growth characteristics and sociodemographic predictors, we found associations for SEP and gestational age. In the pooled group, the coefficient of association between the Graffar

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index and the velocity parameter (-0.22, 95% CI = -0.31, -0.13) (Table 3) indicated that for each unit increase in the Graffar index, lower values indicating higher SEP, there was a -0.22 percent decline from the average length velocity. Conversely, this association reflects a positive relationship between the length velocity parameter and SEP. This coefficient was not substantively different in the sex-stratified analyses, all of which indicated faster linear (length) growth with higher SEP. In contrast to the sex-stratified analyses, all covariates remained in the pooled adjusted model with less than 5% change from the unadjusted SEP coefficient (-0.23, 95% CI = -0.31, -0.15). Similar to SEP, GA was also positively associated with the length velocity parameter, demonstrating a 0.61 percent (95% CI =0.06, 1.15) increase from the average length velocity in the pooled sample for every unit increase in GA (weeks). Gestational age was inversely associated with the length tempo parameter in the pooled sample (-2.94, 95% CI = -3.51, -2.41), indicating a leftward shift of about three days of the trajectory on the time scale, and a faster start to length growth, for each one week increase in gestational age (Table 3).

put Table 3 about here

Weight-for-length trajectories: size and tempo

Evaluations of shifts in WFL size and tempo from the average indicated associations with SEP and GA. Increases in the Graffar Index, equivalent to lower SEP, were associated with a positive shift in the WFL tempo parameter for females (0.25, 95% CI = 0.05, 0.42). This estimate approximates a rightward shift in time (days) relative to the average growth curve indicating later growth timing with lower SEP.

Similar to weight and length trajectory analyses, an increase in gestational age was inversely associated with a decline in tempo from the average in the pooled sample (-1.99, 95% CI = -2.83, -1.49) (Table 4) indicating about a two-day shift to the left on the time scale from the average growth curve for every one week increase in gestational age. Similar values were found in the sex-stratified analyses, all indicating earlier timing of WFL growth with higher gestational age.

put Table 4 about here

The post hoc analysis examining the association between odds of exclusive or any breastfeeding at five months and the continuous SEP measure (the Graffar index) did not find a substantive or significant association (data not shown).

Discussion

In this research, we found that lower SEP, measured by the Graffar index, was inversely associated with length growth characteristics – but not weight – in the first five months. Lower SEP was associated with later timing of WFL growth as reflected by the positive association between the Graffar Index and the WFL tempo parameter. These higher tempo values translate to a rightward shift in growth relative to the average growth curve as well as a later age at peak velocity [33]. This delay in growth can be considered an unfavorable outcome associated with lower SEP.

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Maternal age was not associated with any of the three adjusted growth parameters for length, weight, or weight-for-length. Gestational age (GA) was inversely associated with the tempo growth parameters for length, weight, and weight-for-length indicating higher GA is associated with earlier timing of these three measures. Gestational age is also positively associated with length velocity in the pooled sample indicating faster length change with increasing GA.

Of three previous studies investigating associations between sociodemographic predictors and infant growth before six months, two studies found a significant and fully-adjusted positive association between length (linear) growth and maternal education [8,10], used as a proxy for SEP. Only one study found an inverse association with length growth [12], which was close to null upon adjustment. Many studies including age ranges exceeding six months of age up to five years of age demonstrated a positive association between maternal education and length/height growth [7,8,10]. The majority of these studies support the conclusion that lower SEP is associated with slower length (linear) growth in infancy and early childhood.

Several prior studies representing high-income European countries have noted that their findings of no evidence of a relationship [7,12] between SEP and length (linear) growth prior to six months may not generalize to low- to middle-income countries. Deviations from the Western diet and lifestyle were one of the reasons given for this limitation. Chile, the country from which our data were collected, offers an interesting context in this respect. The recruitment period for this study, 1991 to 1996, occurred as Chile was transitioning from a low-income to an upper-middle income country. In 1990, 40% of the Chilean population was below the poverty line [34]; by 2012 WHO classified Chile as an upper middle-income country [35]. There were nutrition and epidemiologic transitions [36,37] beginning in the 1970s and continuing during the 1990s when study infants were enrolled. Specifically, consumption of high-calorie food, accompanied by a sedentary lifestyle, resulted in rising obesity prevalence across all socioeconomic levels. In the context of an emerging Western diet and lifestyle, we found that lower SEP was associated with poorer length (linear) growth in early infancy. Of course, contemporary generations in Chile experience lower SEP in a new context of over-nutrition and higher levels of sedentary behavior. Thus, current studies in Chile may find distinct relationships between SEP and early growth when compared with generations born 20 years ago.

Plausible biological mechanisms, linked to modifiable factors, have been proposed for the observed association between lower SEP and length growth in the first five postnatal months. Breastfeeding and maternal smoking are two commonly proposed mechanisms, although evidence is limited. In our sample, breastfeeding was close to universal [38,39] and not associated with infant weight change in the first year. We did not evaluate maternal smoking in this study given the large proportion of missing information. However, prior studies did not find that either prenatal or postnatal maternal smoking substantially altered the association between SEP and growth [11,12,16].

Maternal age was the only sociodemographic predictor positively associated with the unadjusted SITAR size growth parameter for weight. This was similarly reported in another cohort from the same geographic area of Santiago, Chile, the Growth and Obesity

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Cohort Study (GOCS) [13], which started a decade later and studied ages between birth and 2 years. Our findings add to this work. Through our intense focus on the first five postnatal months, our results demonstrate that the association between SEP and weight growth appears earlier in the postnatal period than previously documented.

Other potential mechanisms relating to SEP could include gestational weight gain and maternal nutrient status. Size at birth, considered a proxy for these two factors and represented in these analyses by the size SITAR parameter, was not associated with any of the sociodemographic measures. Further research will be useful in clarifying the biological mechanisms behind the association between SEP and early infant growth.

Strengths of this study include the combination of an analytic approach to growth that better captures the nonlinear characteristic of growth in the first five months of life with a detailed measure of socioeconomic position appropriate to the context of a lower income setting. Another strength is the monthly anthropometric measures collected in the first five postnatal months. We also note several limitations. The sample size (n = 1,412) is smaller than other studies with sample sizes in the thousands or tens of thousands [5,13,14]. Our study, therefore, may not have been powered to detect some effects reported in larger studies. Another limitation is that the Graffar index, developed to assess differences in low- to middle-income populations, limits the generalizability of our findings to higher income groups.

This investigation examined various growth characteristics from birth to five months and their association with sociodemographic factors in a Chilean infancy cohort. We found associations between lower SEP and slower length (linear) growth, which are similar in direction to previous findings for maternal education that span periods of time greater than the first six months and up to five years of age [7,8,10,12]. The association between maternal age and weight size, in our study, was similar to findings in other studies of growth between birth and two years of age [13]. In sum, our results extend findings from previous research by showing that sociodemographic factors affect infant growth even in the first five months of growth and in relatively homogenous low- to middle-income populations.

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Contributors

AVH designed the study, conducted the data analysis, and wrote the first draft of the paper. KEN and SG supervised and contributed to the study design, interpretation of results, and draft revisions. EB helped acquire the data. All authors (AVH,KEN,SG,RB,EB,BL,AGH,AJ,MG,VSV) both contributed to revisions of the draft for intellectual content and approved the final version of the manuscript.

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Competing interests

None declared.

Patient consent

Not required.

Ethics approval

The Santiago Longitudinal Study (SLS) had been approved by Institutional Review Boards from 1) University of Michigan Medical Center, Ann Arbor, 2) Institute of Nutrition and Food Technology (INTA), Chile and 3) University of California, San Diego. The Office of Human Research Ethics at the University of North Carolina, Chapel Hill exempted this current research using existing anonymous data from review under the 45 CFR 46.101(b) regulatory category.

Data sharing agreement

No additional data are available.

Disclaimer

AHA had no role in the study design, data collection, and analysis, decision to publish or preparation of the manuscript.

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Table1. Descriptive statistics of sociodemographic characteristics, median [IQR]

Characteristic	Male	Female	Total
n	747	665	1412
Gestational age (weeks)	40.0 [39.0, 40.0]	40.0 [39.0, 40.0]	40.0 [39.0, 40.0]
Graffar Index	27.0 [23.0, 33.0]	27.0 [23.0, 33.0]	27.0 [23.0, 33.0]
Maternal age (years)	26.0 [21.8, 30.9]	25.5 [21.7, 30.3]	25.8 [21.8, 30.8]
Maternal Education (years)	10.0 [8.0, 12.0]	10.0 [8.0, 12.0]	10.0 [8.0, 12.0]

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Table 2: Sociodemographic predictors and association with weight SITAR growth parameter[a,b], stratified by sex of child in the Santiago Longitudinal Study, 1991-1996

	Males						Females						Total					
	Unadjusted			Adjusted[c]			Unadjusted			Adjusted[c]			Unadjusted			Adjusted[c]		
Characteristic	Size	Tempo	Velocity	Size	Tempo	Velocity	Size	Tempo	Velocity	Size	Tempo	Velocity	Size	Tempo	Velocity	Size	Tempo	Velocity
Gest age	0.59 (-0.12, 1.31)	**-2.28 (-3.15, -1.41)**	-0.81 (-2.28, 0.66)	NA	**-1.96 (-3.15, -1.40)**	NA	0.76 (-0.02, 1.54)	**-2.38 (-3.32, -1.45)**	-2.14 (-3.87, -0.42)	0.45 (-0.32, 9.88)	**-2.23 (-3.35, -1.47)**	-1.58 (-3.85, 0.08)	0.64 (0.10, 1.18)	**-2.35 (-2.98, -1.71)**	-1.53 (-2.70, -0.37)	0.53 (-0.05, 1.15)	**-2.01 (-2.98, -1.70)**	-1.06 (-2.67, 0.01)
Maternal age	0.11 (-0.00, 0.23)	-0.06 (-0.20, 0.09)	-0.07 (-0.31, 0.17)	0.07 (-0.11, 0.21)	-0.06 (-0.21, 0.26)	-0.06 (-0.33, 0.82)	**0.21 (0.07, 0.34)**	-0.02 (-0.18, 0.15)	**-0.41 (-0.71, -0.12)**	0.19 (-6.13, 0.22)	0.01 (-2.29, 0.13)	-0.36 (-0.67, -0.04)	**0.16 (0.07, 0.25)**	-0.03 (-0.14, 0.07)	-0.20 (-0.39, -0.00)	0.15 (-0.78, 0.22)	-0.01 (-0.16, 0.83)	-0.18 (-0.56, 0.22)
Maternal education	-0.03 (-0.32, 0.26)	0.14 (-0.21, 0.49)	-0.04 (-0.62, 0.55)	NA	NA	NA	-0.01 (-0.31, 0.29)	0.06 (-0.30, 0.43)	-0.03 (-0.69, 0.64)	0.00 (-Inf, -0.41)	0.12 (-0.95, 0.52)	NA	-0.03 (-0.24, 0.19)	0.10 (-0.15, 0.36)	-0.04 (-0.50, 0.41)	0.00 (-10.67, 0.04)	0.04 (-1.59, 1.58)	-0.05 (-0.75, 4.42)
Graffar Index[d]	-0.12 (-0.23, -0.01)	-0.13 (-0.27, 0.01)	-0.15 (-0.39, 0.08)	-0.08 (-0.22, 0.07)	-0.13 (-0.28, 0.03)	-0.13 (-0.41, 0.28)	-0.07 (-0.19, 0.06)	0.12 (-0.03, 0.28)	0.28 (0.00, 0.57)	-0.03 (-5.15, 0.23)	0.13 (-0.24, 0.29)	0.23 (-0.16, 0.52)	-0.09 (-0.18, -0.00)	-0.01 (-0.11, 0.09)	0.06 (-0.12, 0.25)	-0.06 (-0.83, 0.04)	-0.00 (-0.06, 3.49)	0.02 (-1.66, 0.32)

[a] Size units are percentage change in log(weight) from average, tempo units are time (days), velocity units in percent change from average.

[b] Bold values indicate significance with Bonferroni correction at alpha level of 0.05

[c] Adjusted linear regression models only include non-zero coefficients from lasso regression models that include all covariates in full model.

[d] Higher Graffar index values indicate lower socioeconomic status.

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Table 3: Sociodemographic predictors and association with length SITAR growth parameters[a,b], stratified by sex of child in the Santiago Longitudinal Study, 1991-1996

	Males				Females				Both			
	Unadjusted		Adjusted[c]		Unadjusted		Adjusted[c]		Unadjusted		Adjusted[c]	
Characteristic	Tempo	Velocity	Tempo	Velocity	Tempo	Velocity	Tempo	Velocity	Tempo	Velocity	Tempo	Velocity
Gest age	**-3.33 (-4.09, -2.56)**	**0.99 (0.29, 1.68)**	**-3.05 (-4.10, -2.55)**	NA	**-2.57 (-3.36, -1.79)**	0.25 (-0.52, 1.02)	**-2.53 (-3.33, -1.77)**	NA	**-2.97 (-3.52, -2.42)**	**0.64 (0.12, 1.15)**	**-2.94 (-3.51, -2.41)**	**0.61 (0.06, 1.15)**
Maternal age	-0.04 (-0.18, 0.09)	0.09 (-0.03, 0.20)	-0.01 (-0.10, 1.64)	NA	**-0.17 (-0.30, -0.03)**	0.01 (-0.13, 0.14)	-0.15 (-0.29, 0.01)	NA	-0.10 (-0.19, -0.00)	0.05 (-0.04, 0.14)	-0.07 (-0.17, 0.06)	0.02 (-0.35, 0.10)
Maternal education	0.06 (-0.26, 0.38)	0.12 (-0.16, 0.40)	NA	NA	-0.18 (-0.49, 0.13)	0.28 (-0.01, 0.58)	-0.14 (-0.45, 0.52)	0.16 (-0.35, 0.52)	-0.05 (-0.28, 0.17)	0.20 (-0.00, 0.40)	-0.06 (-0.27, 0.73)	0.13 (-0.21, 0.34)
Graffar Index[d]	0.06 (-0.06, 0.19)	**-0.26 (-0.37, -0.15)**	0.05 (-0.25, 0.36)	**-0.21 (-0.37, -0.14)**	**0.16 (0.03, 0.29)**	**-0.19 (-0.32, -0.07)**	0.13 (-0.03, 0.26)	**-0.17 (-0.31, -0.05)**	**0.11 (0.02, 0.20)**	**-0.23 (-0.31, -0.15)**	0.09 (-0.02, 0.18)	**-0.22 (-0.31, -0.13)**

[a] Size units are percentage change in log(length) from average, tempo units are time (days), velocity units in percent change from average

[b] Bold values indicate significance with Bonferroni correction at alpha level of 0.05.

[c] Adjusted linear regression models only include non-zero coefficients from lasso regression models that include all covariates in full model.

[d] Higher Graffar index values indicate lower socioeconomic status.

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Table 4: Sociodemographic predictors and association with weight-for-length (WFL) SITAR growth parameters[a,b,c] stratified by sex of child in the Santiago Longitudinal Study, 1991-1996

	Males				Females				Both			
	Unadjusted		Adjusted[c]		Unadjusted		Adjusted[c]		Unadjusted		Adjusted[c]	
Characteristic	Size	Tempo	Size	Tempo	Size	Tempo	Size	Tempo	Size	Tempo	Size	Tempo
Gest age	0.09 (-0.55, 0.73)	**-2.03 (-2.91, -1.15)**	NA	**-1.58 (-2.90, -1.11)**	0.05 (-0.58, 0.69)	**-2.34 (-3.35, -1.32)**	NA	**-2.32 (-3.35, -1.33)**	0.07 (-0.38, 0.52)	**-2.17 (-2.84, -1.51)**	NA	**-1.99 (-2.83, -1.49)**
Maternal age	0.07 (-0.03, 0.18)	-0.09 (-0.23, 0.06)	0.04 (-0.23, 0.16)	-0.08 (-0.24, 0.17)	0.02 (-0.09, 0.13)	-0.18 (-0.36, -0.00)	NA	-0.13 (-0.36, 0.14)	0.05 (-0.03, 0.12)	-0.13 (-0.24, -0.02)	0.03 (-0.16, 0.12)	-0.11 (-0.22, 0.03)
Maternal education	-0.09 (-0.35, 0.16)	0.08 (-0.27, 0.44)	NA	NA	-0.10 (-0.35, 0.14)	0.00 (-0.40, 0.40)	NA	0.07 (-2.11, 0.42)	-0.10 (-0.28, 0.08)	0.04 (-0.22, 0.31)	NA	NA
Graffar Index[d]	-0.08 (-0.18, 0.02)	-0.07 (-0.21, 0.07)	-0.05 (-0.17, 0.15)	-0.08 (-0.24, 0.17)	0.08 (-0.02, 0.19)	**0.26 (0.10, 0.43)**	0.04 (-0.21, 0.18)	**0.25 (0.05, 0.42)**	-0.01 (-0.08, 0.07)	0.08 (-0.03, 0.19)	NA	0.06 (-0.14, 0.17)

[a] Size units are percentage change in log(WFL) from average, tempo units are time (days), velocity units in percent change from average.

[b] Bold values indicate significance with Bonferroni correction at alpha level of 0.05.

[c] Adjusted linear regression models only include non-zero coefficients from lasso

regression models that include all covariates in full model.

[d] Higher Graffar index values indicate lower socioeconomic status

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Figure 1 caption: Type of change in random effects relative to the sample mean trajectory in weight growth curve trajectories following a shape invariant model (SIM).

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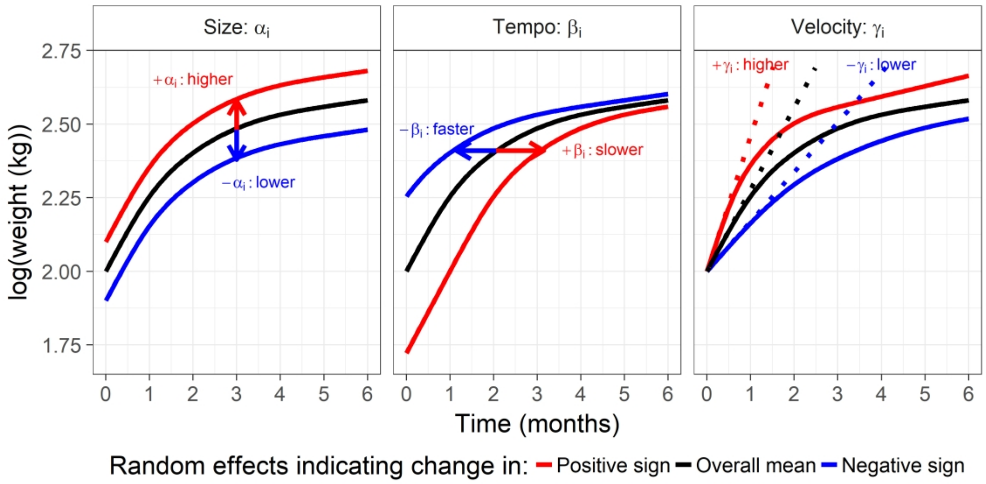

Figure 1. Type of change in random effects relative to the sample mean trajectory in weight growth curve trajectories following a shape invariant model (SIM).

Appendix Table 1. Description of items used for Graffar index

Graffar item	Scale	n(%)
N		1412
No. people in hh 'eating from 1 pot' (%)	1: 1-3	230 (16.3)
	2: 4-6	865 (61.3)
	3: 7-9	254 (18.0)
	4: 10-12	55 (3.9)
	5: 13-15	6 (0.4)
	6: over 16	2 (0.1)
Father's presence in household (%)	1: father is present; not left hh	1197 (84.8)
	3: left hh but sends money	66 (4.7)
	4: partially left hh	38 (2.7)
	6: completely gone	111 (7.9)
Head of household's highest educational level (%)	1: university completed	12 (0.9)
	2: university not completed	9 (0.6)
	3: h.s. or technical studies completed	325 (23.0)
	4: completed 8th grade	664 (47.1)
	5: did not reach 8th grade	382 (27.1)
	6: no schooling	19 (1.3)
Property ownership (%)	1: owned	269 (19.1)
	2: home mortgage	83 (5.9)
	3: rent	243 (17.2)
	4: given to you as a gift	117 (8.3)
	5: squatters w tents or construction	7 (0.5)
	6: lving in back of main house	693 (49.1)
Type of house construction (%)	1: very large house	15 (1.1)
	2: smaller house	181 (12.8)
	3: tiny concrete house	330 (23.4)

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Appendix Table 1. Description of items used for Graffar index

Graffar item	Scale	n(%)
	4: self-constructed home	398 (28.2)
	5: wooden house	94 (6.7)
	6: wooden house w/ less than three rooms	394 (27.9)
Characteristics of the kitchen (%)	1: independent kitchen in one room	931 (65.9)
	6: kitchen in a room with multiple uses	481 (34.1)
Sewage,plumbing (%)	1: inside plumbing	1402 (99.3)
	5: out house	9 (0.6)
	6: just go in woods	1 (0.1)
Water (%)	1: water from inside home faucet	949 (67.2)
	6: water from outside faucet	463 (32.8)
No. times garbage collected per week (%)	1: more than 4x/week	6 (0.4)
	2: 3 times/week	1288 (91.2)
	3: 2 times/week	117 (8.3)
	6: never	1 (0.1)
Total count of previous six goods,possessions (tv, washing machine, stereo, refrig., car) (%)	1: 13-15 (own all six goods)	77 (5.5)
	2: 10-12	311 (22.3)
	3: 7-9	302 (21.6)
	4: 4-6	277 (19.9)
	5: 1-3	374 (26.8)
	6: 0	54 (3.9)

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Appendix Table 2: Nonlinear mixed effects model fit evaluation: BIC for all evaluated models

Trajectory type	Model ID	Model description	BIC[a]
Weight	no random effects	no random effects	NA
	m2	random size (alpha0)	-19546.4
	m3	random tempo (beta0)	-17232
	m4	random velocity (beta1)	-18323
	m5	random tempo and velocity (beta0 and beta1)	-21901.5
	m5.strat	m5 + sex-spec effects	-22123.4
	m5.strat2	m5.strat + sex-spec corr structure	-22107.5
	m6	random size and tempo (alpha0 and beta0)	-21740.4
	m7	random size and velocity (alpha0 and beta1)	-21629.8
	m8	random size, tempo and velocity (alpha0, beta0, and beta1)	**-22940.66**
Height	no random effects	no random effects	NA
	m2	random size (alpha0)	-37399.5
	m3	random tempo (beta0)	-36684.1
	m4	random velocity (beta1)	-34985.7
	m5	random tempo and velocity (beta0 and beta1)	-37820
	m5.strat	m5 + sex-spec effects	**-38000.74**
	m5.strat2	m5.strat + sex-spec corr structure	-37978.2
	m6	random size and tempo (alpha0 and beta0)	-37381.5
	m7	random size and velocity (alpha0 and beta1)	-37819.9
WFL	no random effects	no random effects	NA
	m2	random size (alpha0)	-21147.2
	m3	random tempo (beta0)	-18852.1
	m4	random velocity (beta1)	-20549.9
	m5	random tempo and velocity (beta0 and beta1)	-22598
	m5.strat	m5 + sex-spec effects	-22761.2
	m5.strat2	m5.strat + sex-spec corr structure	-22751.3
	m6	random size and tempo (alpha0 and beta0)	**-22808.5**
	m7	random size and velocity (alpha0 and beta1)	-22484.6

[a]Bold values indicate lowest value within a trajectory evaluation.

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Reporting checklist for cohort study.

Based on the STROBE cohort guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the STROBE cohortreporting guidelines, and cite them as:

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		Reporting Item	Page Number
Title and abstract			
Title	#1a	Indicate the study’s design with a commonly used term in the title or the abstract	1

Abstract	#1b	Provide in the abstract an informative and balanced summary of what was done and what was found	3
Introduction			
Background / rationale	#2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	#3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	#4	Present key elements of study design early in the paper	5
Setting	#5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Eligibility criteria	#6a	Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up.	5
Eligibility criteria	#6b	For matched studies, give matching criteria and number of exposed and unexposed	na
Variables	#7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5
Data sources / measurement	#8	For each variable of interest give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than	5

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		one group. Give information separately for for exposed and unexposed groups if applicable.	
Bias	#9	Describe any efforts to address potential sources of bias	6
Study size	#10	Explain how the study size was arrived at	5
Quantitative variables	#11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	6
Statistical methods	#12a	Describe all statistical methods, including those used to control for confounding	6
Statistical methods	#12b	Describe any methods used to examine subgroups and interactions	na
Statistical methods	#12c	Explain how missing data were addressed	7
Statistical methods	#12d	If applicable, explain how loss to follow-up was addressed	na
Statistical methods	#12e	Describe any sensitivity analyses	na
Results			
Participants	#13a	Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-	7

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		up, and analysed. Give information separately for for exposed and unexposed groups if applicable.	
Participants	#13b	Give reasons for non-participation at each stage	7
Participants	#13c	Consider use of a flow diagram	na
Descriptive data	#14a	Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders. Give information separately for exposed and unexposed groups if applicable.	7
Descriptive data	#14b	Indicate number of participants with missing data for each variable of interest	7
Descriptive data	#14c	Summarise follow-up time (eg, average and total amount)	na
Outcome data	#15	Report numbers of outcome events or summary measures over time. Give information separately for exposed and unexposed groups if applicable.	na
Main results	#16a	Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	7-8
Main results	#16b	Report category boundaries when continuous variables were categorized	na
Main results	#16c	If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	na

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Other analyses	#17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	na
Discussion			
Key results	#18	Summarise key results with reference to study objectives	8-9
Limitations	#19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias.	10
Interpretation	#20	Give a cautious overall interpretation considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence.	10
Generalisability	#21	Discuss the generalisability (external validity) of the study results	10
Other Information			
Funding	#22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	10

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