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Body Mass Index Trajectories from Birth to 23 years by Cardiometabolic Risks in Young Adulthood

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Disclosure of potential conflicts/competing Interests

The authors declare no conflicts of interest.

Study Importance

What is already known about this subject?

- Large increases in body mass and overweight/obesity relate to poor cardiometabolic outcomes.

What this study adds?

- This study analyzed body mass at 9 time points from birth to age 23 years in 1,000 Chileans and found that individuals with adult cardiometabolic risks had a specific constellation of early-life growth (faster growth after infancy, lower body mass decline approaching age 5, absence of a definitive body mass nadir in early childhood, higher 5-year body mass) and a distinct mid-life growth pattern (larger body mass increases from childhood to young adulthood and lower levels of expected growth deceleration approaching young adulthood).

- Larger and faster increases in BMI and a failure of BMI growth to decline or decelerate at specific developmental periods differentiated individuals who would and would not have adult cardiometabolic risks.

What this study adds?

- Current findings call for further understanding of discernible patterns of BMI growth across development, from birth to young adulthood, that precede cardiometabolic risk.

- Obesity interventions implemented from infancy to late adolescence may be effective for reducing cardiometabolic risks.

Keywords: BMI trajectories, BMI growth, cardiometabolic risks, metabolic syndrome

ABSTRACT

Objective: To investigate whether the level, rate, and acceleration of BMI growth differ according to the presence or absence of adult cardiometabolic (CM) risks.

Methods: BMI was measured in 1,000 Chileans at nine time points from birth to 23 years and metabolic syndrome (MetS) and its components were assessed at young adulthood. BMI growth was analyzed in three developmental periods: birth to 6 months; 6 months to 5 years, and 5 to 23 years.

Results: Individuals with CM risks had a specific constellation of early-life growth (faster growth after infancy, lower BMI decline approaching age 5, absence of a definitive BMI nadir in early childhood, higher 5-year BMI) and distinct young adult growth (larger BMI increases from childhood to young adulthood and lower levels of expected growth deceleration approaching young adulthood). Those with CM risks also attained a BMI ≥ 25 at significantly younger ages than those absent risks (MetS: 12.3y v 20.1y; hyperglycemia: 13.1y v 18.9y; hypertension: 13.2y v 19.4y; hypertriglyceridemia: 14.3y v 19.5y; inflammation: 15.9y v 20.6y).

Conclusions: Larger and faster increases in BMI and a failure of BMI growth to decline or decelerate at specific developmental periods distinguished individuals who would and would not have adult cardiometabolic risks.

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INTRODUCTION

Obesity during childhood is a known risk factor for poor adult cardiometabolic (CM) functioning.[1,2] Recently, body mass index (BMI) growth trajectories have been examined in relation to cardiovascular health. These studies generally have linked specific BMI growth patterns to later CM risks,[3-7] or evaluated how age-specific changes in BMI relate to cardiovascular disease.[7-9] However, longitudinal studies where both BMI growth patterns and adult CM disease are known can also be useful for understanding how growth patterns differ according to the presence or absence of CM risks. A few studies have used this approach. Giudici and colleagues found that higher parent-reported child BMIs from age 4 to 10 years distinguished those who had metabolic syndrome (MetS) at 20-60 years of age.[10] Fall and colleagues found that those with MetS at ages 26-32 years had greater BMI gain from infancy to adolescence than those not having MetS.[11] Although such studies adopt an interesting approach of contrasting growth patterns by known CM risk, neither study compares the rate of BMI change or possible BMI growth acceleration or deceleration by subsequent CM risk. Yet larger and faster BMI increases have been associated with poorer cardiometabolic outcomes.[7,9,12] Thus, comparing BMI growth, as well as BMI at various ages, by subsequent CM risk allows one to determine not only whether distinct

growth patterns precede CM risk, but also quantifies how such growth patterns might diverge.

This study investigated whether the level, rate, and acceleration of BMI growth from birth to 23 years differ according to the presence or absence of CM risk factors in young adulthood. We also examined the age at which BMI first diverged by the presence or absence of CM risk, and the age at which BMI ≥ 25 and BMI ≥ 30 for those with and without specific CM risks. CM risks studied were metabolic syndrome and its components (hyperglycemia, hypertriglyceridemia [high TG], low high-density lipoprotein cholesterol [HDL-C], hypertension (HT), abdominal obesity), and inflammation (elevated C-reactive protein).

METHODS

Sample and study design

Data are from 1,000 participants of the Santiago Longitudinal Study (SLS), which initially involved 1,790 Chilean infants in an iron-deficiency anemia preventive trial and neuromaturation study.[13] Infants were recruited at 6 months (1991-1996) from community clinics serving low- to middle-income families. Eligible infants were healthy, term singletons with birth weight ≥ 3,000 g. The preventive trial involved random assignment of 1,657 non-anemic infants to receive an iron-fortified formula (12 mg/L, comparable to the level of iron in infant formulas available in the U.S.), a low iron-fortified formula (2.3 mg/L), or a no-added-iron formula.[13] An additional 133 infants participated in a neuro-maturation study involving laboratory assessments in addition to core components of the SLS. Weight and height (length) (converted to BMI: kg/m^2) were measured at birth, 3m, 6m, 1y, 5y, 10y, 21y, and 23y and up to three times in adolescence (between 11 and 18 years; $M = 15.3$ years). For participants assessed more than once during adolescence, height and weight from the assessment closest to age 15 years were used, excluding those < 14 years ($n = 52$) or > 16 years ($n = 123$). Cardiometabolic (CM) risk biomarkers were measured in 1,040 participants at age 23 years. Analyses utilize data from the 1,000 participants who had risk biomarker data at young adulthood and BMI at six or more time points (i.e., missing no more than three BMI values).[14] This criterion was based on having adequate data coverage on all variables in tandem with randomly distributed missingness.[14] Of the participants who had CM biomarker data at young adulthood, > 99% had BMI data at birth, 3 months, 6 months, 1 year, and 23 years. However, a substantial budget cut at the 5-year follow-up necessitated that the low-iron supplementation group ($n = 405$) as part of the infancy preventive trial was not studied. In order to maximize use of the available age 5 data, we employed the threshold requiring participants to have at least 6 complete BMI time points. This allowed us to utilize 69.1% of the data collected at age 5 and a minimum of 87.6% of data collected at the other time points (see Table 1). These are deemed acceptable levels of missing data when data are assumed to be missing completely at random.[14,15] The missing completely at random test provided evidence that data

within the current analytic sample were missing completely at random (Little's chi-square [df = 77] 90.33, p = 0.134).[15] (Sample follow-up and loss at each study time point are shown in Supplemental Figure 1.)

Characteristics of the sample (duration of breastfeeding, mothers' age, socioeconomic status [SES],[16] etc.) were assessed when participants were 1 year (Table 1). When children were 10 years, mothers self-reported their pre-pregnancy height and weight from which maternal BMI was calculated. Participants included in the current analyses were similar in background characteristics, age, and BMI at all time points to those not included. However, those analyzed here were more likely to be female, from higher socioeconomic families, and less likely to have received iron supplementation as part of the preventive trial (see Supplemental Table 1). Approval for this study was obtained from the authors' Institutional Review Boards in the U.S. and Chile. Informed written consent was obtained from children's parents at all time points prior to child age 21; participants gave written informed consent at ages 21 and 23 years. Participants received a stipend at the 23-year assessment. All study procedures were in accord with the Code of Ethics of the World Medical Association.[17]

Measurements

Anthropometric assessment

Weight and length at birth and 3 months were abstracted from medical records. Infants' unclothed weight at 6 months and 1 year was measured using an electronic scale (to the nearest 0.01 kg), and length was measured using a recumbent length board (to the nearest 0.1 cm) by a trained research clinician at the Institute for Nutrition and Food Technology (INTA) at the University of Chile. At all other time points, standardized procedures were used at INTA to measure height (cm) to the nearest 0.1 cm (using a Holtain stadiometer), and weight (kg) to the nearest 0.1 kg (using a Seca 703 scale, Seca GmbH & co. Hamburg, Germany). Measurements at 5 years and older were taken twice, with a third measurement if the difference between the first two exceeded 0.3 kg for weight or 0.5 cm for height. BMI was calculated from weight and height [kg/m^2] (or weight and length). Raw BMI scores at all time points were used in analyses for consistency in estimating the trajectory. Recent studies support the use of raw BMI scores as an indicator of obesity in children[18,19] and as a useful measure of adiposity change in longitudinal research that involves children and adults.[20] At the 23-year follow-up, waist circumference (WC) was measured with non-elastic flexible tape and recorded to 0.1 cm.

Cardiometabolic risk assessment

At the young adult assessment (*M* age = 23.0 years), after 15 min rest, systolic and diastolic blood pressures (SBP, DBP) were measured three times on the non-dominant arm using a standard mercury sphygmomanometer. The first measurement was discarded and the second two were averaged for analysis.[21] Fasting serum total glucose (mg/dL), total cholesterol (mg/dL), triglycerides (mg/dL), HDL-

cholesterol (HDL-C), and high-sensitivity C-reactive protein (hs-CRP) were measured after a 12-hour overnight fast. Serum glucose concentrations were measured with an enzymatic colorimetric test (Quimica Clinica Aplicada, Amposta, Spain). Cholesterol profile was determined by dry analytical methodology (Vitros®; Ortho Clinical Diagnostics Johnson & Johnson Inc., Raritan, NJ, USA). Hs-CRP was measured with a sensitive latex-based immunoassay, with elevated inflammation defined as CRP ≥ 3.0 mg/L.[22] MetS was based on the 2009 consensus definition,[23] which involves having at least three of the following five risk factors: abdominal obesity (WC ≥ 94 cm males; ≥ 80 cm females), high arterial blood pressure (SBP ≥ 130 mmHg or DBP ≥ 85 mmHg), high triglycerides (TG ≥ 150 mg/dL), low HDL-C (< 50 and < 40 mg/dL in females, males, respectively), and fasting hyperglycemia (Gli ≥ 100 mg/dL).[23] Additionally, we calculated a continuous score representing a composite cardiometabolic risk profile as the sum of the above five MetS risks (range: 0-5).

Covariate Selection

We selected covariates that could potentially confound the BMI-CM relationship:[24] participants' sex, maternal BMI, mothers' age at the participant's birth, duration of breastfeeding, iron supplementation as part of the preventive trial, and family SES. Covariates were included on the growth parameters.

Statistical Analysis

Given the number and timing of BMI measurements available within the current study, and the expectation of a variety of nonlinear change patterns,[25] we analyzed BMI growth within three developmental phases: birth to 6 months, 6 months to 5 years, and 5 to 23 years. These age phases were based on global BMI growth curves that show rapid BMI growth from birth to approximately 6 months, followed by decreases leading to a nadir at approximately 4 to 7 years, followed by steady increasing growth to young adulthood (age 20).[26,27] Piecewise latent growth curve analysis (LGCA) was conducted in M*plus* 8.2 to estimate the BMI trajectories within each age period for those with and without each CM risk.[28] We used BMI at birth as the intercept for the initial phase, 6-month BMI as intercept for the second phase, and 5-year BMI as the intercept for the third phase. We defined the intercept for each model at these time points because we were interested in BMI at these ages as well as in the growth following these ages, that is, in the three distinct developmental phases outlined above. LGCA quantifies slope (the degree of linear change in BMI) and nonlinear quadratic change (change in the rate of change), with the quadratic term indicating accelerated growth (a speeding up of BMI increase) or decelerated growth (a slowing down or flattening out of BMI growth).[25] The time scores for the quadratic slope factor are the squared values of the linear time scores, and these time scores are automatically computed by Mplus. We calculated the Satorra-Bentler scaled chi-square difference test[29] to determine whether a model that

included a quadratic term provided a better fit with the data than a nested model that omitted the quadratic. Chi-square difference tests were calculated for each of the three age periods. The chi-square difference test was significant for the last age period only (5 – 23 years). Thus, growth during the first two age periods was estimated by intercept and slope, and growth during the last phase (5-23y) was estimated by intercept, slope, and quadratic. The growth terms were evaluated in independent regression models. Model fit was evaluated based on well-established recommendations,[30,31] with comparative fit index (CFI) > .90, root mean square error of approximation (RMSEA) < .06, and standardized root mean square residual (SRMR) < .08. The CFI is the chi-square comparison of the target model to the baseline model (the model where all the regression paths are set to zero). The RMSEA is the average of the residuals between the observed sample covariance and the expected model estimated for the population. The SRMR is the standardized square root of the difference between the residuals of the observed and predicted covariance matrix. These indices comprise a combination of absolute fit indices (RMSEA, SRMR), an incremental fit index (CFI), and a parsimony-adjusted index (RMSEA).[30,31]

To test differences in growth according to the presence or absence of CM risk, we estimated the growth parameters, random effects derived from growth models) for each participant using the full sample. We report the means of each of these parameters stratified by CM risk (adjusted for covariates). Next, we assessed associations between the presence of each CM risk (1 = present, 0 = absent) and each growth factor. The growth factors were used as continuous latent variables and analyzed as dependent variables in multivariable linear regression models. In each model, the independent variable of interest was CM risk (presence vs. absence), adjusting for maternal BMI, breastfeeding duration, sex, SES, mothers' age, and iron supplementation. A statistically significant effect estimate indicates that the risk-present and risk-absent growth parameters are significantly different. Data were retained for all participants (N = 1,000) using the full information maximum likelihood (FIML) specification, which fits the model being tested directly onto the non-missing data for each participant and has been shown to be superior to other missing data strategies.[32] For descriptive purposes, we used SAS (version 9.4) mixed effects modeling (with a quadratic term for age) to plot BMI trajectories per each CM risk (Figure 1). We performed a sensitivity analysis to assess bias introduced by the missing data by re-estimating the growth analyses using data from participants who had BMI data at all 9 time points (*n* = 549). Analysis of covariance determined the age at which BMI first significantly diverged (*P* < 0.05) according to the presence or absence of each CM risk. We also extrapolated the ages at which BMI ≥ 25 and BMI ≥ 30 from known BMI values per each CM risk group to illustrate the disparity in age at which critical BMI milestones are attained for those with or without various CM risks.[33]

RESULTS

Sample Characteristics

At the 23-year follow-up, 12.2% of the sample was classified as having MetS and approximately 70% had at least one cardiometabolic risk (Table 1). The prevalence of low HDL-C, abdominal obesity, and inflammation were quite high (59.5%, 31.2% and 36.7%, respectively), whereas the prevalence of high triglycerides (14%), hypertension (9.3%), and hyperglycemia (3.5%) were moderate to low.

Growth Parameters for the Total Sample

The fit indices indicated that the model for each developmental phase fit the data: CFI: .951-.986, RMSEA: .080-.159, SRMR: .017-.042. The growth parameters for the total sample (Table 2) indicate an average BMI at birth of 13.75 and significant linear BMI increase from birth to 6 months (slope = 0.72). The parameters for the second phase (6m-5y) indicate an average 6-month BMI of 18.06, with significant linear decrease in BMI from 6 months to 5 years (slope = -0.11). The parameters for the third phase (5-23y) indicate a mean 5-year BMI of 16.98, with significant linear upward growth (slope = 3.34), followed by significant deceleration (a slowing down) of growth approaching young adulthood (quadratic = -0.10). (Supplemental Figure 2 shows the growth trajectory for the total sample.)

Growth Parameters by Cardiometabolic Risk

The growth parameters for each developmental phase by the presence or absence of each risk factor are shown in Table 2. At level of significance alpha = 0.05, our data do not provide evidence to suggest that the intercepts at birth varied by subsequent CM risk. However, those with young adult abdominal obesity had greater linear growth (a faster rise in BMI) from birth to 6 months than those without abdominal obesity. Regarding growth from 6 months to 5 years, none of the CM risks differed by 6-month BMI. However, the slope of BMI growth during this phase was significantly different by presence vs. absence of CM risk for all risks examined, with the risk-absent trajectories having a significant linear decrease in BMI growth, whereas the risk-present trajectories remained largely stable (flat). The parameters for the period from 5 to 23 years indicated that all CM risks were associated with a higher BMI at age 5. Five of the seven risks studied were also associated with greater linear growth from 5 to 23 years (high TG, low HDL-C, HT, abdominal obesity, MetS). Additionally, five of the risk-present trajectories had less decelerated growth than the risk-absent trajectories (i.e., differed in quadratic growth: hyperglycemia, low HDL-C, abdominal obesity, MetS, inflammation). Inspection of the quadratic parameters indicates that the risk-present trajectories showed nonsignificant growth deceleration, reflecting continued steady growth, or in the case of hyperglycemia, significant accelerated growth ($s = 0.45$, $p < .001$). In contrast, all of the quadratic terms for the risk-absent models were significant and negative, indicating significant growth deceleration, or a slowing down of growth approaching young adulthood. Thus, failure of BMI growth to decelerate when approaching young adulthood distinguished

those with versus without CM risks.

Growth Parameters by Number of Cardiometabolic Risks

When examining the growth parameters by number of CM risks (Table 3), compared to participants with no adult CM risks, those with one risk factor had a higher BMI at birth. No differences were found for linear growth from birth to 6 months by number of CM risks. However, compared to those with zero adult risks, those with two or more risks had flatter (less declining) growth from 6 months to 5 years, a higher 5-year BMI, faster linear growth from 5 to 23 years, and less decelerated growth approaching young adulthood.

Age at Growth Divergence by Cardiometabolic Risk

When examining the age at which BMI first diverged by subsequent CM risk, those with at least one risk factor had a significantly higher BMI at birth than those with zero risk factors, and those with adult abdominal obesity and high TG had a higher BMI at 3 months (Table 4). BMI diverged significantly at 1 year for individuals with or without MetS, and BMI diverged at 5 years for those with or without adult hyperglycemia, low HDL-C, hypertension, or inflammation.

Age BMI ≥ 25 and BMI ≥ 30 by Cardiometabolic Risk

Those with MetS in young adulthood attained a BMI ≥ 25 at 12.3 years on average, whereas those absent MetS achieved a BMI ≥ 25 approximately 8 years later, or at age 20.1 (Table 5). BMI ≥ 30 could not be estimated for any of the risk-absent groups, for those with inflammation or low HDL-C, or for those with zero or one CM risk because these individuals avoided a BMI ≥ 30 during the study period. Those with no CM risks avoided a BMI ≥ 25.

Sensitivity Analyses

The complete case analyses testing differences in growth parameter by the presence of CM risk using the 549 participants who had BMI at all 9 time points retained all but one of the significant effects found using the full analytic sample (Supplemental Table 2). Additionally, the growth parameters and magnitude of effect estimates were highly similar. When analyzing the growth parameter differences by number of CM risks, the complete case analyses retained 7 of the 9 significant effects found using the full analytic sample (Supplemental Table 3).

DISCUSSION

In this Chilean sample, individuals who had CM risk factors showed different patterns of BMI growth from birth to 23 years than those without CM risks. Individuals with adult CM risks had faster BMI growth from birth to 6 months, lower levels of expected BMI growth decline approaching age 5, a higher BMI at age 5, faster growth from 5 to 23 years, and lower levels of growth deceleration approaching young adulthood.

Unlike studies that have found differences in growth after only 4 years of age by subsequent CM risk,[12] current findings show that poor adult cardiometabolic health was preceded by specific growth patterns discernable from 6 months onward. Indeed, the growth pattern found in the current study reflecting faster growth from birth to 6 months and a smaller decline in BMI from 6 months to 5 years parallels the growth pattern believed to be responsible for an early age at adiposity rebound,[34,35] which itself is a well-established risk factor for later obesity and obesity-related morbidity.[34,36] The absence of a distinct BMI nadir can also be discerned in several of the risk-present trajectories (Figure 1). This constellation of early-life factors (faster growth after infancy, lower BMI decline approaching age 5, absence of a definitive BMI nadir in early childhood, higher 5-year BMI) consistently distinguished those who would develop cardiometabolic morbidities from those who would not. It is widely held that rapid weight gain during infancy plays an etiological role in programming later-life obesity which, in turn, is consequential for poor adult cardiovascular health.[37,38] Current findings augment such work by indicating that a constellation of early-life growth factors is directly associated with subsequent cardiometabolic morbidities.

Study findings also show that an absence of slowed growth approaching young adulthood discriminated the presence of several adult CM risk factors. This is consistent with findings by Attard and colleagues[5] who found that a high and increasing BMI from 13 to 21 years was associated with elevated blood pressure and insulin resistance, while a declining adiposity trajectory was protective.[5] Normally growing youth typically show decelerated growth during the transition to adulthood, as pubertal influences decline and skeletal growth subsides.[27,39] Preventive measures would, thus, involve achieving graduated linear growth from early childhood onward and a slowing down of growth approaching adulthood (i.e., successive reductions in BMI increases).

Findings also illustrate the disparity in age at which critical BMI milestones are attained for those with and without adult cardiometabolic risks. Avoiding a BMI ≥ 30 prior to age 23 served as a protective factor against all of the cardiometabolic risks studied, and individuals with zero risk factors maintained a BMI < 25 to age 23. Such findings, in alliance with other studies,[1,2] may be of value to clinicians and public health surveillance programs for identifying individuals at risk of cardiometabolic risk based on age-specific BMI.

Limitations and Strengths

Several factors should be considered when interpreting study findings. All participants were born at term and had birthweights ≥ 3.0 kg as eligibility criteria. Thus, premature and low-birth weight infants were not included, which likely affected this sample's BMI distribution and growth,[40] and, perhaps the likelihood of CM risk.[37] However, this sample restriction allowed us, by design, to control for

cardiovascular risk associated with preterm and low birthweight. The reduced data available at age 5 (due to a funding cut) limited selection of the analytic sample. However, the analytic strategy made use of all available data and we did not find evidence that the assumption of missing completely at random was violated. Moreover, a sensitivity analysis involving participants who had BMI at all nine study time points showed highly similar findings as the analytic sample, increasing confidence in the relations found. The absence of BMI measurements at closer age intervals precluded more specific estimates of growth change and limited the estimation of age at BMI growth divergence. The follow-up intervals between later visits were relatively large (5 years), which may cause biased estimations in the BMI growth curves. This study also did not have baseline measures of CM biomarkers or CRP. Thus, whether the associations found are independent of baseline levels of CM risk factors is not clear. Additionally, the sample was somewhat atypical in that approximately 60% of participants had low HDL-cholesterol in young adulthood. High prevalence of low HDL-C has been found in Latino populations,[41] with some finding a genetic predisposition to dyslipidemia.[42] Thus, findings should be considered within the racial/ethnic and cultural (diet, lifestyle) background of study participants. Finally, the relatively low numbers of participants with hyperglycemia may have reduced statistical power to detect differences between the growth parameters of those with and without this risk.

Study strengths include the availability of growth data from a large cohort studied from birth to young adulthood. Data on weight and height were measured objectively by trained clinical staff from age 6 months to 23 years, giving greater validity to the results. This study also had multiple objectively measured biomarkers of cardiometabolic health in early adulthood, when disease states often first appear.[43] The piecewise growth curve approach allowed us to determine the unique contribution of various parameters of growth during separate developmental periods for subsequent cardiometabolic health. Finally, several important confounders were controlled, reducing the possibility that study findings can be attributed to such factors.

In conclusion, how BMI changes across development is important for cardiometabolic health. Individuals with cardiometabolic risks in young adulthood had unique early-life growth patterns, indicating that an early-life preventive approach may be usful.[44] However, continued high and accelerated growth from early childhood to young adulthood also consistently related to many cardiometabolic risks, suggesting additional points of intervention into one's early 20s.

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Table 1. *Sample Characteristics (N = 1,000)*

	n	Mean or %	(SD)
Child sex (% female)	1000	51%	
Maternal BMI (kg/m2)[a]	835	28.9	(5.1)
Maternal age, (years)[b]	993	26.3	(6.0)
Family SES[c]	995	27.3	(6.3)
Received iron supplementation[d]	925	63.2%	
Duration breastfed (mos)[e]	979	3.6	(3.1)
Birth weight (g)	1000	3545.34	(365.76)
BMI (kg/m²)[f]			
Birth	1000	13.8	(1.1)
3m	997	17.5	(1.4)
6m	1000	18.0	(1.5)
1y	1000	17.8	(1.4)
5y	691	17.0	(2.2)
10y	876	19.4	(3.3)
15y	962	23.1	(4.4)
21y	916	26.4	(5.3)
23y	1000	26.7	(5.6)
Cardiometabolic risks at young adulthood			
Hyperglycemia	1000	3.5%	
Glucose ≥ 100 mg/dL			
Hypertriglyceridemia	1000	14.3%	
Triglycerides ≥150 mg/dL			

Low HDL-C	1000	59.5%
< 40 mg/dL male		
< 50 mg/dL female		
Hypertension (mmHg)	1000	9.3%
≥ 130 SBP or ≥85 DBP		
Abdominal obesity	1000	31.2%
≥ 94 cm male		
≥ 80 cm female		
Metabolic syndrome[g]	1000	12.2%
Number CM risks (%)	1000	
0		30.2%
1		37.7%
2		19.9%
3		8.8%
4		3.1%
5		0.3%
Inflammation	1000	36.7%
CRP ≥ 3.0 mg/L		*Table continues.*

Note. HDL-C= high-density lipoprotein cholesterol; SBP = systolic blood pressure; DBP = diastolic blood pressure; CM = cardiometabolic; CRP = C-reactive proteins. [a]Maternal prepregnancy body mass index (BMI) was assessed retrospectively at child age 10. [b]Maternal age (years) at study intake. [c]Higher scores reflect greater family socioeconomic disadvantage at child age 1 (range 11-47). [d]Randomly assigned to receive iron supplemented formula at 6-12 months as part of the preventive trial. [e]Duration exclusively breastfed (i.e., age at first bottle). [f]We used calculated BMI scores at all time points for consistency in the trajectory. [g]Defined as at least 3 cardiometabolic risks.

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Table 2. *Adjusted Means of Growth Parameters for the Total Sample and by Cardiometabolic Risk at 23y (N = 1,000)*

Total sample	Adj. Means
Intercept $_B$	13.75*
Slope $_{B-6m}$	0.72*
Intercept$_{6m}$	18.06*
Slope $_{6m-5y}$	-0.11*
Intercept $_{5y}$	16.98*
Slope $_{5-23y}$	3.34*
Quadratic $_{5-23y}$	-0.10*

	Risk-present Adj. Means	Risk-absent Adj. Means	Unstd. effect estimate (SE)		*P*
Hyperglycemia	(*n* = 35)	(*n* = 965)			
Intercept $_B$	13.69*	13.76*	-0.09	(.19)	.619
Slope $_{B-6m}$	1.31*	1.23*	0.004	(.05)	.934
Intercept$_{6m}$	17.85*	18.07*	0.35	(.22)	.114
Slope $_{6m-5y}$	0.05	-0.12*	0.20	(06)	.003
Intercept $_{5y}$	18.05*	16.78*	1.47	(.45)	.001
Slope $_{5-23y}$	3.17*	2.93*	0.07	(.57)	.883
Quadratic $_{5-23y}$	0.45*	-0.13*	0.45	(.13)	.001
High TG	(*n* = 143)	(*n* = 857)			
Intercept $_B$	13.71*	13.76*	-0.07	(.10)	.461
Slope $_{B-6m}$	1.34*	1.22*	0.05	(.03)	.072
Intercept$_{6m}$	18.22*	18.03*	0.18	(.13)	.167
Slope $_{6m-5y}$	-0.003	-0.13*	0.10	(.03)	.002

	Risk-present Adj. Means	Risk-absent Adj. Means	Unstd. effect estimate (SE)		P
Intercept $_{5y}$	17.82*	16.69*	0.90	(.25)	.001
Slope $_{5-23y}$	3.76*	3.07*	0.74	(.26)	.004
Quadratic $_{5-23y}$	-0.02	-0.13*	0.05	(.06)	.441
Low HDL-C	(*n* = 595)	(*n* = 405)			
Intercept $_B$	13.81*	13.67*	0.12	(.07)	.077
Slope $_{B-6m}$	1.23*	1.25*	-0.02	(.02)	.348
Intercept $_{6m}$	18.04*	18.10*	-.0.06	(.09)	.556
Slope $_{6 m-5y}$	-0.09	-0.14*	0.05	(.02)	.007
Intercept $_{5y}$	17.02*	16.56*	0.38	(.15)	.007
Slope $_{5-23y}$	3.29*	2.99*	0.31	(.16)	.047
Quadratic $_{5-23y}$	-0.05	-0.20*	0.11	(.04)	.007

Table continues.

	Risk-present Adj. Means	Risk-absent Adj. Means	Unstd. effect estimate (SE)		P
Hypertension	(*n* = 93)	(*n* = 905)			
Intercept $_B$	13.77*	13.65*	0.16	(.09)	.092
Slope $_{B-6m}$	1.36*	1.23*	0.04	(.04)	.205
Intercept $_{6m}$	18.14*	18.06*	-0.18	(.16)	.267
Slope $_{6m-5y}$	0.04	-0.13*	0.20	(.04)	.001
Intercept $_{5y}$	18.54*	16.66*	1.88	(.34)	.001
Slope $_{5-23y}$	4.00*	3.09*	0.93	(.30)	.002
Quadratic $_{5-23y}$	-0.02	-0.12*	0.10	(.08)	.207
Abdominal Obesity	(*n* = 312)	(*n* = 688)			

BMI Trajectories by Cardiometabolic Risks

Intercept $_B$	13.80*	13.73*	0.002	(.07)	.846
Slope $_{B-6m}$	1.47*	1.23*	0.06	(.02)	.006
Intercept$_{6m}$	18.07*	18.06*	0.05	(.11)	.672
Slope $_{6m-5y}$	0.05	-0.17*	0.20	(.02)	.001
Intercept $_{5y}$	18.12*	16.25*	1.92	(.19)	.001
Slope $_{5-23y}$	4.20*	2.70*	1.49	(.19)	.001
Quadratic $_{5-23y}$	-0.03	-0.15*	0.13	(.05)	.009
Metabolic Syndrome (n = 122)		(n = 878)			
Intercept $_B$	13.79*	13.75*	0.02	(.11)	.831
Slope $_{B-6m}$	1.32*	1.23*	0.03	(.03)	.312
Intercept$_{6m}$	18.10*	18.06*	-0.06	(.14)	.644
Slope $_{6m-5y}$	0.07	-0.13*	0.20	(.04)	.001
Intercept $_{5y}$	18.44*	16.59*	1.71	(.26)	.001
Slope $_{5-23y}$	4.22*	3.03*	1.24	(.26)	.001
Quadratic $_{5-23y}$	0.02	-0.14*	0.13	(.07)	.050
Inflammation (n = 365)		(n = 629)			
Intercept $_B$	13.77*	13.75*	0.01	(.07)	.898
Slope $_{B-6m}$	1.21*	1.25*	-0.01	(.02)	.745
Intercept$_{6m}$	17.93*	18.13*	-0.15	(.10)	.117
Slope $_{6m-5y}$	-0.05	-0.14*	0.09	(.02)	.001
Intercept $_{5y}$	17.25*	16.61*	0.68	(.16)	.001
Slope $_{5-23y}$	3.34*	3.09*	0.20	(.18)	.253
Quadratic $_{5-23y}$	0.002	-0.18*	0.18	(.04)	.001

Note. B = birth. Unstd = unstandardized. SE = standard error. High TG = high triglycerides. HDL-C= high-density lipoprotein cholesterol. Models adjusted for sex, maternal BMI, maternal age, family SES,

iron supplementation 6-12m, and duration of breastfeeding on the intercept, slope, and quadratic. $^*P <$ 0.001.

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Table 3. *Adjusted Mean Growth Parameters by Number of Cardiometabolic Risks at 23y (N = 1,000)*

Number of risks:	0	1		2		≥ 3	
			P		*P*		*P*
	(*n* = 302)	(*n* = 377)	1 different	(*n* =199)	2 different	(*n* =122)	≥ 3 different
	Adj. mean	Adj. mean	from 0	Adj. Mean	from 0	Adj. mean	from 0
Intercept $_B$	13.66**	13.85**	.017	13.70**	.419	13.80**	.378
Slope $_{B-6m}$	1.25*	1.18*	.174	1.27*	.404	1.23*	.407
Intercept $_{6m}$	18.08**	18.00**	.673	18.16**	.713	18.10**	.980
Slope $_{6m-5y}$	-0.18*	-0.15*	.085	-0.01	.001	0.07	.001
Intercept $_B$	16.21**	16.40**	.143	17.49**	.001	18.44**	.001
Slope $_{5-23y}$	2.65**	2.94**	.142	3.81**	.001	4.22**	.001
Quadratic $_{5-23y}$	-0.21**	-0.13*	.077	-0.07	.016	0.02	.001

Note. B = birth. Models adjusted for sex, maternal BMI, maternal age, family SES, iron supplementation 6-12m, and duration of breastfeeding. *P < .01. **P < .001.

Table 4. *Age and BMI at Significant Growth Curve Divergence by Presence or Absence of Cardiometabolic Risk at 23 Years*

	Age at significant growth curve divergence	Adjusted BMI at age of divergence (95% CI)		*P*
		Risk present	Risk absent	
Number CM risks[a]	birth	13.89 (13.76, 14.01)	13.68 (13.55, 13.82)	.030

	0 v. 1			
Abdominal obesity	3m	17.61 (17.44, 17.77)	17.36 (17.24, 17.47)	.020
Hypertriglyceridemia	3m	17.68 (17.43, 17.93)	17.40 (17.30, 17.50)	.040
MetS	1y	18.04 (17.77, 18.32)	17.75 (17.65, 17.85)	.048
Hyperglycemia	5y	18.42 (17.32, 19.53)	17.02 (16.82, 17.21)	.014
Low HDL-C	5y	17.28 (17.03, 17.52)	16.73 (16.42, 17.04)	.008
Hypertension	5y	18.57 (17.97, 19.17)	16.89 (16.69, 17.09)	.001
Inflammation	5y	17.63 (17.30, 17.96)	16.77 (16.53, 17.01)	.001

Note. CI = confidence interval. CM = cardiometabolic. [a]Presence of 5 risk factors, summed: hyperglycemia, hypertriglyceridemia, low HDL-C, hypertension, abdominal obesity. MetS = metabolic syndrome. HDL-C= high-density lipoprotein cholesterol. Models adjusted for sex, maternal BMI, maternal age, family SES, iron supplementation 6-12m, and duration of breastfeeding. Slight differences in BMIs shown here and those shown in Tables 2 and 3 are due to the absence of full information maximum likelihood specification in the above estimates.

Table 5. *Mean Age at BMI ≥ 25 and BMI ≥ 30 by Cardiometabolic Risk*

	Risk present		Risk absent	
	BMI ≥ 25	BMI ≥ 30	BMI ≥ 25	BMI ≥ 30
MetS	12.3y	17.7y	20.1y	--
Abdominal obesity	13.0y	18.8y	--	--
Hyperglycemia	13.1y	18.4y	18.9y	--
Hypertension	13.2y	19.5y	19.4y	--
High TG	14.3y	21.5y	19.5y	--
Inflammation	15.9y	--	20.6y	--
Low HDL-C	16.9y	--	--	--
Number CM risks[a]				
0	--	--		
1	21.0y	--		
2	14.6y	22.0y		
3	13.1y	18.9y		
4 or 5	10.6y	14.7y		

Note. Ages were extrapolated from known BMI values per each CM risk group. MetS = metabolic syndrome. TG = triglycerides. HDL-C = high-density lipoprotein cholesterol. A dash indicates that the average BMI for individuals with that risk did not exceed 25 or 30. [a]Total number of cardiometabolic

BMI Trajectories by Cardiometabolic Risks

risks: hyperglycemia, hypertriglyceridemia, low HDL-C, hypertension, abdominal obesity.

Figure 1. Body mass index trajectories from birth to 23 years by cardiometabolic risk in young adulthood, adjusted for sex, maternal BMI, maternal age, family SES, iron supplementation 6-12m, and duration of breastfeeding. Dashes surrounding trajectories represent 95% confidence interval. High TG = high triglyceride. HDL-C = high-density lipoproteins cholesterol. MetS = metabolic syndrome. CM = cardiometabolic. Gli = glucose. SBP = systolic blood pressure. DBP = diastolic blood pressure. WC = waist circumference. CRP = C-reactive protein.

Table 1. Sample Characteristics (N = 1,000)

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15y	962	23.1	(4.4)
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23y	1000	26.7	(5.6)
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Glucose $\geq$ 100 mg/dL			
Hypertriglyceridemia	1000	14.3%	
Triglycerides $\geq$150 mg/dL			
Low HDL-C	1000	59.5%	
< 40 mg/dL male			
< 50 mg/dL female			
Hypertension (mmHg)	1000	9.3%	
$\geq$ 130 SBP or $\geq$85 DBP			

Abdominal obesity	1000	31.2%
≥ 94 cm male		
≥ 80 cm female		
Metabolic syndrome[g]	1000	12.2%
Number CM risks (%)	1000	
0		30.2%
1		37.7%
2		19.9%
3		8.8%
4		3.1%
5		0.3%
Inflammation	1000	36.7%
CRP ≥ 3.0 mg/L		

Note. HDL-C= high-density lipoprotein cholesterol; SBP = systolic blood pressure; DBP = diastolic blood pressure; CM = cardiometabolic; CRP = C-reactive proteins. [a]Maternal prepregnancy body mass index (BMI) was assessed retrospectively at child age 10. [b]Maternal age (years) at study intake. [c]Higher scores reflect greater family socioeconomic disadvantage at child age 1 (range 11-47). [d]Randomly assigned to receive iron supplemented formula at 6-12 months as part of the preventive trial. [e]Duration exclusively breastfed (i.e., age at first bottle). [f]We used calculated BMI scores at all time points for consistency in the trajectory. [g]Defined as at least 3 cardiometabolic risks.