Association between Number of Siblings and Cardiovascular Risk Factors in Childhood and in Adulthood: The Cardiovascular Risk in Young Finns Study

Jukka Pihlman, MD[1,2], Costan G. Magnussen, PhD[1,2,3], Suvi P. Rovio, PhD[1,2], Katja Pahkala, PhD[1,2,4], Eero Jokinen, MD, PhD[5], Tomi P. Laitinen, MD, PhD[6], Nina Hutri-Kähönen, MD, PhD[7], Päivi Tossavainen, MD, PhD[8], Leena Taittonen, MD, PhD[8,9], Mika Kähönen, MD, PhD[10], Jorma S. A. Viikari, MD, PhD[11,12], Olli T. Raitakari, MD, PhD[1,2,13], Markus Juonala, MD, PhD[11,12], and Joel Nuotio, MD, PhD[1,2,14]

Objective To determine the association of number of siblings on cardiovascular risk factors in childhood and in adulthood.

Study design In total, 3554 participants (51% female) from the Cardiovascular Risk in Young Finns Study with cardiovascular disease risk factor data at baseline 1980 (age 3-18 years) and 2491 participants with longitudinal risk factor data at the 2011 follow-up. Participants were categorized by number of siblings at baseline (0, 1, or more than 1). Risk factors (body mass index, physical activity, hypertension, dyslipidemia, and overweight, and metabolic syndrome) in childhood and in adulthood were used as outcomes. Analyses were adjusted for age and sex.

Results In childhood, participants without siblings had higher body mass index (18.2 kg/m^2, 95% CI 18.0-18.3) than those with 1 sibling (17.9 kg/m^2, 95% CI 17.8-18.0) or more than 1 sibling (17.8 kg/m^2, 95% CI 17.7-17.9). Childhood physical activity index was lower among participants without siblings (SD -0.08, 95% CI -0.16-0.00) compared with participants with 1 sibling (SD 0.06, 95%CI 0.01-0.11) or more than 1 sibling (SD -0.02, 95% CI -0.07-0.03). OR for adulthood hypertension was lower among participants with 1 sibling (OR 0.73, 95% CI 0.54-0.98) and more than 1 sibling (OR 0.71, 95% CI 0.52-0.97) compared with participants with no siblings. OR for obesity was lower among participants with 1 sibling (OR 0.72, 95% CI 0.54-0.95) and more than 1 sibling (OR 0.75, 95% CI 0.56-1.01) compared with those with no siblings.

Conclusions Children without siblings had poorer cardiovascular risk factor levels in childhood and in adulthood. The number of siblings could help identify individuals at increased risk that might benefit from early intervention. *(J Pediatr 2021;237:87-95)*.

Cardiovascular disease (CVD) is the leading cause of death worldwide and a major portion of these deaths could be prevented.[1] In addition to well known risk factors for CVD, family size, described by the number of offspring, has been shown to impact the prevalence of CVD among parents.[2,3] However, the available evidence has been contradictory, with some studies showing that the number of offspring associates with the risk of CVD in mothers,[4,5] or in both parents,[3] and other studies have found no[6,7] or nonlinear[8,9] associations.

Research on offspring in low- or middle-income countries has shown negative effects of a larger family size on child health in childhood/adolescence mainly through nutritional factors.[10,11] A Finnish study found no association between the number of inhabitants in the household and death from coronary heart

BMI	Body mass index
CVD	Cardiovascular disease
HDL	High-density lipoprotein
LDL	Low-density lipoprotein
YFS	Cardiovascular Risk in Young Finns Study

From the [1]Research Center of Applied and Preventive Cardiovascular Medicine, University of Turku, Turku, Finland; [2]Center for Population Health Research, University of Turku and Turku University Hospital, Turku, Finland; [3]Menzies Institute for Medical Research, University of Tasmania, Hobart, Tasmania, Australia; [4]Paavo Nurmi Center, Sports and Exercise Medicine Unit, Department of Physical Activity and Health, University of Turku, Turku, Finland; [5]Department of Paediatric Cardiology, Hospital for Children and Adolescents, University of Helsinki, Helsinki, Finland; [6]Department of Clinical Physiology, University of Eastern Finland and Kuopio University Hospital, Kuopio, Finland; [7]Department of Pediatrics, Faculty of Medicine and Health Technology, Tampere University, Tampere, Finland; [8]Department of Pediatrics, PEDEGO Research Unit and Medical Research Center Oulu, University of Oulu, Oulu, Finland; [9]Vaasa Central Hospital, Vaasa, Finland; [10]Department of Clinical Physiology, Faculty of Medicine and Health Technology, Tampere University, Tampere, Finland; [11]Department of Internal Medicine, University of Turku, Turku, Finland; [12]Division of Medicine, and [13]Department of Clinical Physiology and Nuclear Medicine, Turku University Hospital, Finland; and [14]Heart Center, Turku University Hospital and University of Turku, Turku, Finland

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disease.[12] Similarly, the association between growing up in a large family and adulthood mortality was not demonstrated.[13] Although, an earlier study found that children without siblings have higher blood pressure in adulthood compared with children with siblings.[14] Moreover, children from small families (ie, 1 or 2 child families) are more likely to graduate from high school in the US compared with large families because of intrafamilial resources diluting in larger families[15] and lower education has been shown to increase prevalence of risk behaviors such as smoking, obesity, physical inactivity, and unhealthy diet.[16] Most studies have focused on the effects of family size on parent's health, been performed in less developed countries, or studied mortality and the association between family size and the development of CVD in offspring remains unknown.

Therefore, we investigated if the number of siblings associates with cardiovascular health in childhood and in adulthood in the longitudinal Cardiovascular Risk in Young Finns Study (YFS). The YFS is a population-based cohort of well-characterized individuals, followed from childhood to adulthood for up to 31 years. We hypothesized that the number of siblings would affect cardiovascular risk factor levels in childhood and adulthood.

Methods

The YFS is an ongoing longitudinal population-based multicenter study of cardiovascular risk factors from childhood to adulthood, conducted in 5 university hospital cities in Finland (Helsinki, Kuopio, Oulu, Tampere, and Turku) and their rural surrounds. The baseline study was conducted in 1980 when 3596 randomly selected children and adolescents age 3, 6, 9, 12, 15, and 18 years participated. Since 1980, the cohort has been regularly followed up in 3- to 9-year intervals. A detailed description of the cohort has been published previously.[17] Participants or their parents provided written informed consent, and the study was approved by local ethics committees. Participants included in this study had childhood risk factor data available from baseline (n = 3420) and adult risk factor data (n = 2491) from the 2011 follow-up study (n between 1979 and 2441), or in case of missing information from the 2011 follow-up, data from the 2007 follow-up was used (n between 406 and 438).

Family Size, Number of Siblings

Information on the number of children in the family was collected from parents' self-report questionnaires at baseline in 1980. Participants were categorized by the number of children in the family as (1) 1 child/no siblings (n = 536), 15% of total cohort; (2) 2 children/1 sibling (n = 1543), 43% of total cohort; (3) 3 or more children/2 or more siblings (n = 1475), 42% of total cohort.

Blood Pressure and Weight

At baseline, brachial artery blood pressure was measured using a standard mercury sphygmomanometer for participants age ≥6 years. In case of missing information, data from the 1983 follow-up was used. Adult blood pressure measurements were collected in the 2011 follow-up using a random-zero sphygmomanometer (Hawksley and Sons Ltd). All measurements were taken from the right arm after the participant had been seated for 5 minutes. Three measurements were taken, and the average of these measurements was used.

At baseline and all follow-up visits, weight was measured without shoes in light clothes with a digital Seca weighing scale to nearest 0.1 kg. A Seca stadiometer was used for the measurement of height. Body mass index (BMI) was calculated as weight (kg) divided by height in meters squared (m^2). The baseline measurement was used as the primary indicator of childhood/adolescent BMI. In case of missing information, data from the year 1983 follow-up was used. For adulthood BMI, data were derived from the latest follow-up study in 2011. In case of missing information, data from the 2007 follow-up was used.

Physical Activity Index

At ages 3 and 6 years, a physical activity index was calculated from the parents' ratings of the amount and vigorousness of their child's play time and the child's general level of activity.[18] At ages 9-18 years, data on frequency and intensity of leisure-time physical activity, participation in sports club training, participation in sport competitions, and habitual leisure time was acquired with a self-administered questionnaire.[19] The values for the physical activity indices in childhood were standardized and combined. Adulthood physical activity index was calculated by assessing the frequency of physical activity, intensity of physical activity, frequency of vigorous physical activity, hours spent on vigorous physical activity, and average duration of physical activity.[19]

Blood Biochemistry

Fasting serum lipids such as serum total cholesterol, high-density lipoprotein (HDL)-cholesterol, and triglycerides were measured in the same laboratory at each follow-up with standard methods. Low-density lipoprotein (LDL)-cholesterol concentration was calculated using the Friedewald equation.[20] The applied methods have been reported previously.[21,22] Serum glucose concentration was determined by the enzymatic hexokinase method (Glucose reagent, Beckman Coulter Biomedical). The concentration of glycated hemoglobin A1c (HbA1c) was assayed with an immunoturbidimetric method (HbA1c assay, Abbot) on an architect ci8200 analyzer (Abbott) in 2011. Serum insulin was measured in 1980 with a modification of the immunoassay method of Herbert et al.[23]

Adverse Cardiovascular Health Metrics in Childhood

According to pediatric guidelines, we defined abnormal blood pressure in childhood as pediatric hypertension or prehypertension based on either systolic blood pressure being in the uppermost 90th percentile of the age-, sex-, and year-specific distribution.[24,25] Integrated guidelines[26] were used

to define high total cholesterol (≥5.17 mmol/L), low HDL-cholesterol (<1.03 mmol/L), high LDL-cholesterol (≥3.36 mmol/L), and high triglycerides (≥1.13 mmol/L for children age 3-9 years and ≥1.47 mmol/l for children age 10-18 years) in childhood. Centers for Disease Control and Prevention recommendations were used to determine overweight (85th to 95th percentile) and obesity (95th percentile or greater) in childhood.[27]

Adverse Cardiovascular Health Metrics in Adulthood

Systolic blood pressure >140 mm Hg, diastolic blood pressure >90 mm Hg, or self-reported use of blood pressure medication were used as criteria for hypertension in adulthood. Participants were considered to have type 2 diabetes if they had fasting glucose ≥7 mmol/L or HbA1c ≥48 mmol/L, or they self-reported diabetes or use of glucose-lowering medication. Participants who had fasting plasma glucose from 5.6 mmol/L to 6.9 mol/L or HbA1c from 39 mmol/L to 46 mmol/L, and no self-reported diabetes were assigned as individuals with prediabetes.[28] Classification for hypercholesterolemia was assigned for participants if they had LDL-cholesterol >3 mmol/L or used lipid-lowering medication. Classification for hypertriglyceridemia was assigned for participants if they had triglycerides >1.7 mmol/L.[29] Participants with BMI from 25 kg/m^2 to 29.9 kg/m^2 were assigned as being overweight and those with BMI ≥30 kg/m^2 as being obese.[30]

Covariates

Information on the family's socioeconomic status was derived from the participant's parents self-reported household income administered via questionnaire at baseline (1980) and categorized as (1) low (<17 840 euros/year), (2) lower middle class (17 840-28 040 euros/year), (3) upper middle class (28 041-38 230 euros/year), and (4) high (>38 230 euros/year). In case of missing information in 1980, data collected from the 1983 survey was used. Participants' household annual income in 2011 was considered as an indicator of adulthood SES and was categorized as (1) very low (<21 780 euros/year), (2) low (21 780-32 670 euros/year), (3) intermediate (32 671-54 440 euros/years, and (4) high (>54 440 euros/year). In case of missing information in 2011, data from the previous follow-up in 2007 were used. Adolescent smoking (ie, ever daily smoking between the ages 12 and 18 years) was defined from baseline (1980) or the subsequent follow-ups (1983, 1986, 1989, or 1992). Participants age under 12 years were considered as nonsmokers. Adulthood smoking (ie, current daily smoking) was obtained from the latest follow-up in 2011. Information on participants' smoking status was derived from the self-report questionnaires.

Statistical Analyses

Baseline characteristics of the study population are reported as mean (SD) or median (25th and 75th percentiles, if skewed distributions) for continuous variables or as proportions for categorical variables. The relationship between number of siblings and continuous outcome variables was assessed using the generalized linear model adjusted with Tukey-Kramer approximation and with logistic regression models for categorical outcome variables. All analyses were adjusted for sex and age.

Sensitivity analyses were conducted for both childhood and adulthood outcomes to study the robustness of our findings. First, we combined data on the number of siblings from baseline and the 1983 and 1986 follow-up surveys to take account for the possible misclassification of participants where the number of children increased after the baseline survey. Second, using combined data from baseline and data collected on the number of siblings from the parents of the participants when they contributed data to the latest YFS field study in 2018-2020 (n = 1274). The parents were enquired how many childbirths they have had. Participants were categorized by the number of children in the family as (1) 1 child/no siblings (n = 450), 13% of total cohort; (2) 2 children/1 sibling (n = 1438), 40% of total cohort; (3) 3 or more children/2 or more siblings (n = 1670), 47% of total cohort. Third, we evaluated the associations using different cut-points for the number of siblings as 1 child/no siblings, 1 sibling, 2 siblings, and 3 or more siblings. Fourth, additional adjustments for birth order, childhood/adulthood socioeconomic status, childhood living region categorized as urban or rural,[31] and total years of education were also analysed. Both sex × exposure and age × exposure interactions were individually studied to investigate if the associations were similar by sex and age groups. The investigations were made separately for childhood and adulthood outcomes. Except for adult hypertriglyceridemia and LDL-cholesterol concentration in childhood, we observed no interactions between number of siblings with sex or age on risk factor/outcome (P value >.05 for all).

All statistical analyses were performed using SAS v 9.4 (SAS Institute), and statistical significance was inferred at a 2-tailed P value of <.05.

Results

Characteristics of the participants are show in **Table I**. The total number of participants with data on the number of siblings and the covariates in childhood was 3554 (51% female). Of these, 2491 had at least 1 adulthood outcome measurement available. The mean age of the participants was 41.6 ± 5 years at the 2011 follow-up. Median number of children in the family was 2.0 (IQR 2.0-3.0, range 0-18).

Childhood Risk Factors

Of the childhood risk factors, the number of siblings was associated with childhood LDL-cholesterol, BMI, and physical activity (**Table II**, adjusted for sex and age). Participants without siblings had higher adjusted mean LDL-cholesterol level (3.43 mmol/L, 95% CI 3.36-3.49 mmol/L) compared with those with 1 sibling (3.38 mmol/L, 95% CI 3.34-3.42 mmol/L) but lower than

Table I. Participant characteristics in childhood (1980) and adulthood (2011) according to the number of siblings at baseline in 1980

Year	Variables		Number of siblings 0	1	≥2
1980					
	N (% of participants)		536 (15)	1543 (43)	1475 (42)
	Female sex (%)		50	51	51
	Age (y)		8.9 (4.9)	9.6 (4.8)	11.9 (4.7)
	Childhood in urban region (%)		57	56	39
	Family income (%)				
	Low		28	19	36
	Lower middle class		31	32	29
	Upper middle class		27	24	17
	High		14	25	18
	HDL-cholesterol (mmol/L)		1.6 (0.3)	1.6 (0.3)	1.5 (0.3)
	LDL-cholesterol (mmol/L)		3.5 (0.8)	3.4 (0.8)	3.4 (0.8)
	Triglycerides (mmol/L)		0.58 (0.45, 0.78)	0.58 (0.44, 0.76)	0.61 (0.46, 0.82)
	Systolic blood pressure (mm Hg)		113 (11)	113 (11)	115 (12)
	Diastolic blood pressure (mm Hg)		68 (9)	68 (10)	70 (10)
	BMI (kg/m^2)		17.5 (3)	17.4 (3)	18.4 (3.2)
	Fasting plasma glucose (mmol/L)*		4.6 (0.5)	4.7 (0.4)	4.7 (0.6)
	Physical activity index	Age 3-6 (range 9-23)	16 (14, 17)	16 (15, 18)	16 (14, 18)
		Age 9-18 (range 5-14)	9 (8, 10)	9 (8, 10)	9 (8, 10)
	Smoking (%)†		19	23	25
	Hypertension (%)‡		12	10	10
	High total cholesterol (%)		54	51	52
	Low HDL-cholesterol (%)		5	3	4
	High LDL-cholesterol (%)		52	49	50
	High triglycerides (%)		4	4	4
	Metabolic syndrome (%)		9	7	7
	Childhood overweight§ (%)		17	12	8
	Childhood obesity¶ (%)		5	5	5
2011					
	n (% of participants)		362 (15)	1095 (44)	1034 (42)
	Female sex (%)		55	54	55
	Age (y)		39.9 (4.9)	40.6 (4.8)	42.9 (4.7)
	Family income (%)				
	Low		19	16	17
	Lower middle class		29	27	33
	Upper middle class		38	37	35
	High		15	20	15
	HDL-cholesterol (mmol/L)		1.3 (0.4)	1.3 (0.3)	1.3 (0.3)
	LDL-cholesterol (mmol/L)		3.2 (0.9)	3.2 (0.8)	3.3 (0.9)
	Triglycerides (mmol/L)		1.15 (0.85, 1.56)	1.05 (0.75, 1.56)	1.05 (0.75, 1.56)
	Systolic blood pressure (mm Hg)		120 (15)	119 (14)	121 (15)
	Diastolic blood pressure (mm Hg)		74 (10)	75 (11)	75 (10)
	BMI (kg/m^2)		26.7 (5.1)	26.1 (4.9)	26.7 (5.1)
	Fasting plasma glucose (mmol/L)		5.3 (0.7)	5.3 (0.8)	5.4 (0.8)
	Physical activity index	Age >18 (range 5-15)	9 (8, 10)	9 (8, 10)	9 (8, 10)
	Smoking (%)		19	16	18
	Hypertension (%)		21	18	21
	Type 2 diabetes (%)		3	3	5
	Prediabetes (%)**		20	22	23
	Hypercholesterolemia (%)		53	56	62
	Hypertriglyceridemia (%)		22	19	21
	Overweight (%)		41	41	45
	Obese (%)		25	20	23
	Metabolic syndrome (%)		26	24	27

Data are mean (SD) or median (25th, 75th percentile) for continuous variables and percentages for categorical variables. Metabolic syndrome contains waist ≥102 cm in men and ≥88 cm in women, fasting plasma glucose ≥5.6 mmol/l or treatment, hypertriglyceridaemia ≥1.7 mmol/L and HDL-cholesterol levels <1.0 mmol/L in men and <1.3 in women and blood pressure ≥130/ ≥85 mmHg or treatment. A diagnosis requires ≥3 of the 5 criteria.

*Data from the 1986 follow-up was used.

†Data from 1980-1992 surveys was used, explains if the participant has smoked between 12 and 18 years of age.

‡85th to less than the 95th percentile.

§95th percentile or greater.

¶Fasting plasma glucose from 5.6 mmol/L to 6.9 mmol/L.

**Harmonizing definition included waist ≥102 cm in men and ≥88 cm in women, fasting plasma glucose ≥5.6 mmol/L or treatment, hypertriglyceridemia ≥1.7 mmol/L and HDL-cholesterol levels <1.0 mmol/L in men and <1.3 in women and blood pressure ≥130/≥85 mm Hg or treatment. A diagnosis requires ≥3 of the 5 criteria. Adult hypercholesterolemia was assigned for participants if they had LDL-cholesterol >3 mmol/L or use of lipid-lowering medication.

Table II. Childhood risk factors according to the number of siblings

	Number of siblings							
	0		1		≥2			
Risk factors	Adjusted mean	95% CI	Adjusted mean	95% CI	Adjusted mean	95% CI	*P* for trend	n
HDL-cholesterol (mmol/L)	1.56	(1.53 - 1.59)	1.56	(1.55 - 1.58)	1.55	(1.53 - 1.56)	.29	3521
LDL-cholesterol (mmol/L)	3.43	(3.36 - 3.49)	3.38	(3.34 - 3.42)	3.47	(3.43 - 3.52)	.005	3519
Triglycerides (mmol/L)	0.67	(0.64 - 0.70)	0.65	(0.64 - 0.67)	0.67	(0.66 - 0.69)	.13	3524
Systolic blood pressure (mm Hg)	114	(113 - 115)	114	(114 - 115)	114	(114 - 115)	.76	2988
Diastolic blood pressure (mm Hg)	69	(68 - 70)	68	(68 - 69)	69	(69 - 70)	.14	2976
BMI (kg/m^2)	18.2	(18.0 - 18.3)	17.9	(17.8 - 18.0)	17.8	(17.7 - 17.9)	.004	3537
Serum insulin (mU/l)	9.81	(9.4 - 10.23)	9.47	(9.23 - 9.72)	9.39	(9.14 - 9.64)	.23	3505
Physical activity index*	−0.08	(-0.16 - 0.00)	0.06	(0.01 - 0.11)	−0.02	(-0.07 - 0.03)	.01	3477
N†	534		1537		1467			

*Standardized mean difference.
†N varied between 392 and 534 in participants with no siblings, 1260 and 1534 in participants with 1 sibling, and 1336-1467 in participants with 2 or more siblings. Adjusted for age and sex.

those with 2 or more siblings (3.47 mmol/L, 95% CI 3.43-3.52 mmol/L) (*P* for trend .005). Participants without siblings had higher BMI (18.2 kg/m^2, 95% CI 18.0-18.3 kg/m^2) than those with 1 sibling (17.9 kg/m^2, 95% CI 17.8-18.0 kg/m^2) or those with 2 or more siblings (17.8 kg/m^2, 95% CI 17.7-17.9 kg/m^2) (*P* for trend .004). Participants without siblings had the lowest physical activity index (−0.08 SD, 95% CI -0.16 to 0.00) than those with 1 sibling (0.06 SD, 95% CI 0.01-0.11) or those with 2 or more siblings (−0.02 SD, −0.07-0.03) (*P* for trend .01). There were no significant differences between the groups for other risk factors.

ORs for adverse metrics in childhood are shown in Table III. Compared with participants without siblings, the odds of overweight among those with one sibling (OR 0.66, 95% CI 0.49-0.88), and those with 2 or more siblings (OR 0.44, 95% CI 0.32-0.61) were lower.

Adulthood Risk Factors

The ORs for adulthood outcomes by number of siblings at baseline are shown in Table IV. Compared with participants without siblings, the odds for hypertension among those with 1 sibling (OR 0.73, 95% CI 0.54-0.98), and those with 2 or more siblings (OR 0.71, 95% CI 0.52-0.97) were lower. Compared with participants without siblings, the odds of obesity among those with one sibling (OR 0.72, 95% CI 0.54-0.95), and those with 2 or more siblings (OR 0.75, 95% CI 0.56-1.01) were lower.

Results for the association between the number of siblings and adulthood risk factors are shown in Table V (available at www.jpeds.com). Participants without siblings had higher LDL-cholesterol (3.23 mmol/L, 95% CI 3.14-3.31 mmol/L) than those with 1 sibling (3.22 mmol/L, 95% CI 3.17-3.27 mmol/L) but lower than those with 2 or more siblings (3.30 mmol/L, 95% CI 3.25-3.35 mmol/L) (*P* for trend .08). No other significant associations between the number of siblings and adulthood risk factors were observed.

Sensitivity Analyses

In sensitivity analyses that additionally adjusted for family annual income and childhood living region (urban/rural), we observed no alterations in the main results (data not shown). In sensitivity analyses that adjusted further for birth order, the results for the association of adulthood obesity among participants with 2 or more siblings was diluted (OR 0.82, 95% CI 0.57-1.18), but adjustment had little effect on

Table III. OR and their 95% CIs for childhood smoking, hypertension, and adverse lipid profile in childhood according to the number of siblings

	Number of siblings								
	0			1		≥2			
Outcomes	n/N		OR	CI 95%	n/N	OR	CI 95%	n/N	n all
Hypertension*	Reference	47/394	0.88	(0.62 - 1.25)	134/1260	0.87	(0.61 - 1.24)	140/1337	2991
High total cholesterol	Reference	290/536	0.88	(0.72 - 1.08)	788/1543	1.06	(0.86 - 1.30)	770/1418	3554
Low HDL-cholesterol	Reference	28/536	0.70	(0.44 - 1.12)	53/1543	0.86	(0.53 - 1.39)	57/1418	3554
High LDL-cholesterol	Reference	279/536	0.87	(0.71 - 1.07)	750/1543	1.08	(0.88 - 1.33)	734/1418	3554
High triglycerides	Reference	21/536	0.95	(0.57 - 1.58)	58/1543	0.99	(0.59 - 1.67)	60/1418	3554
Overweight†	Reference	96/483	0.66	(0.49 - 0.88)	328/1405	0.44	(0.32 - 0.61)	349/1418	3198
Obesity‡	Reference	80/508	0.94	(0.58 - 1.50)	164/1473	1.13	(0.70 - 1.82)	111/1360	3366
Smoking	Reference	25/495	1.14	(0.88 - 1.48)	68/1453	1.15	(0.89 - 1.49)	75/1360	3361

n/N, case number/total number.
Adjusted for age and sex.
*90th percentile or greater.
†85th to less than the 95th percentile.
‡95th percentile or greater.

Table IV. ORs and their 95% CI for adulthood outcomes in 2011 according to the number of siblings at baseline (1980)

	Number of siblings								
	0		1			≥2			
Outcomes	n/N		OR	CI 95%	n/N	OR	CI 95%	n/N	n all
Hypertension	Reference	85/360	0.73	(0.54 - 0.98)	217/1093	0.71	(0.52 - 0.97)	254/992	2485
Type 2 diabetes	Reference	101/350	0.77	(0.39 - 1.53)	328/1065	1.12	(0.58 - 2.16)	316/983	2398
Prediabetes	Reference	71/353	1.02	(0.77 - 1.34)	242/1081	0.92	(0.69 - 1.22)	230/1007	2441
Hypercholesterolemia	Reference	193/362	1.05	(0.82 - 1.34)	615/1095	1.12	(0.87 - 1.44)	639/992	2449
Hypertriglyceridemia	Reference	79/362	0.79	(0.58 - 1.07)	210/1095	0.79	(0.58 - 1.08)	218/992	2449
Overweight	Reference	143/350	0.99	(0.77 - 1.27)	443/1069	1.13	(0.87 - 1.46)	460/982	2435
Obesity	Reference	89/350	0.72	(0.54 - 0.95)	213/1069	0.75	(0.56 - 1.01)	229/982	2435
Metabolic syndrome	Reference	90/347	0.86	(0.65 - 1.15)	258/1061	0.81	(0.61 - 1.09)	269/973	2415
Smoking	Reference	68/358	0.84	(0.61 - 1.14)	174/1076	0.97	(0.70 - 1.33)	182/856	2455

Adjusted for age and sex. Systolic blood pressure >140 mm Hg, diastolic blood pressure >90 mm Hg, or self-reported use of blood pressure medication were used as criteria for hypertension in adulthood. Participants were considered to have type 2 diabetes if they had fasting plasma glucose ≥7 mmol/L or HbA1c ≥48 mmol/L or they self-reported diabetes or use of glucose-lowering medication. Participants who had fasting plasma glucose from 5.6 mmol/L to 6.9 mol/L or HbA1c from 39 mmol/L to 46 mmol/L and no self-reported diabetes or use of glucose-lowering medication were assigned as individuals with prediabetes. Hypercholesterolemia was assigned for participants if they had LDL-cholesterol >3 mmol/L or use of lipid-lowering medication. Hypertriglyceridemia was assigned for participants if they had triglycerides >1.7 mmol/L. Participants with BMI from 25 kg/m^2 to 29.9 kg/m^2 were assigned as overweight and as obese if BMI was ≥30 kg/m^2.

our results reported in the main analysis (data not shown). As number of siblings was associated with both childhood BMI and physical activity index, we further examined these associations by mutually adjusting for each in the same multivariable model. The associations observed for both childhood BMI and physical activity index remained statistically significant and the effect for BMI and the effect for physical activity index remained consistent. Participants without siblings had higher BMI (18.2 kg/m^2, 95%CI 18.0-18.4 kg/m^2) than those with 1 sibling (17. 9 kg/m^2, 95% CI 17.7-18.0 kg/m^2) or those with 2 or more siblings (17.8 kg/m^2, 95% CI 17.7-17.9 kg/m^2) (*P* for trend .002). Participants with one sibling were physically more active (0.06 SD, 95% CI 0.01-0.11) than those without siblings (−0.09 SD, 95% CI -0.18 to −0.01) or those with 2 or more siblings (−0.03 SD, −0.08 to 0.02) (*P* for trend .01). There were no significant differences between the groups for other risk factors. For the adult outcomes, we additionally adjusted the analyses for participant's years of education, but the results (data not shown) remained consistent with our main findings. We also analyzed the association of number of siblings and adulthood hypertension additionally adjusting for childhood and adulthood BMI and the results remained essentially similar. Compared with participants without siblings, the odds for hypertension among those with one sibling (OR 0.76, 95% CI 0.55-1.04), and those with 2 or more siblings (OR 0.71, 95% CI 0.52-0.98) were lower. Results that used different cut-points for the number of siblings (ie, 1 child/no siblings, 1 sibling, 2 siblings, and 3 or more siblings) were similar to the main analyses. As we used number of siblings based on data collected at the 1980 baseline survey, misclassification of the number of siblings was possible. First, we combined data on the number of siblings from baseline and the 1983 and 1986 follow-up surveys to take account for the possible misclassification of participants, we observed no alterations in the main results (data not shown). Second, we used data collected on the number of siblings from the parents of the participants when they contributed data to the latest YFS field study in 2018-2020, the results were similar in cohort (data not shown). Because of the significant interaction observed between sex and adulthood hypertriglyceridemia, we conducted the analyses separately for women and men. In women, the number of siblings was not associated with the odds for hypertriglyceridemia. However, in men, the participants with 2 or more siblings had lower odds for hypertriglyceridemia (OR 0.63, 95% CI 0.42-0.93) compared with participants without siblings. Because of the significant interaction between age and childhood LDL-cholesterol, we conducted the analyses for LDL-cholesterol stratified by baseline age group (3-9 years and 12-18 years). No associations were found in the younger age group. In the older age group, participants with 1 sibling had the lowest adjusted mean serum LDL-cholesterol (3.21 mmol/L, 95% CI [3.15-3.28] mmol/L) compared with those without siblings (3.29 mmol/L, 95% CI 3.18-3.41 mmol/L) and those with 2 or more siblings (3.35 mmol/L, 95% CI 3.29-3.40 mmol/L) (*P* for trend .01). In addition, we performed sensitivity analyses separately for children (age 3-9 years) and adolescents (age 12-18 years). When the participants were categorized into these 2 age groups at baseline, we observed a statistically significant association between the number of siblings and LDL-cholesterol, BMI, and physical activity index in older participants (age 12-18 years at baseline) in childhood (**Table VI**; available at www.jpeds.com). Concerning hypertension in adulthood, among participants age 3-9 years at baseline, the odds for hypertension were higher among those participants without siblings compared with those with siblings (**Table VII**; available at www.jpeds.com). For adulthood obesity, an association between the number of siblings and this adult outcome was observed in participants age 12-18 years at baseline (**Table VII**).

Discussion

We observed that children without siblings tended to have, on average, higher BMI and LDL-cholesterol, lower physical

activity, and higher odds for overweight in childhood compared with those with siblings. In addition, children without siblings were also more likely than their counterparts with siblings to have obesity and hypertension as adults.

Our cross-sectional findings in childhood are in line with earlier studies that outlined children without siblings were more likely to be overweight in childhood than children with siblings.[32-34] Moreover, research on the influence of the number of siblings for adulthood morbidity has suggested that persons without siblings might be more likely to be hypertensive in adulthood,[35] which supports our observations of higher odds for having adult hypertension and obesity in those without siblings.

Childhood obesity[36] is strongly associated with adult obesity,[37] and elevated childhood BMI is associated with increased risk of other adult morbidities such as hypertension, diabetes, and coronary heart disease.[38-40] Although a review underlined that although childhood BMI is strongly associated with higher risk of adult obesity, it is not a good predictor of adult obesity or morbidity as most of the adult obesity and obesity-related adult morbidity occurs in adults who had a healthy childhood weight.[41] We found that compared with the children with at least 1 sibling, the children without siblings had higher childhood BMI, increased odds for overweight, and they were physically less active, all characteristics that impact adult health.[42] Because we did not observe associations between the number of siblings and other CVD risk factors in childhood, the mechanisms behind higher childhood BMI among children without siblings might be due to the increased amount of shared physical activity between siblings, such as sibling-to-sibling interactions, co-operative play, and shared interest in sports.[33] Conversely, in this study the association of the number of siblings and childhood BMI was independent of childhood physical activity index, suggesting only part of the effect was directed through physical activity index and the mechanism remains vague. However, in the absence of time and resource dilution, parents with less children could have more resources for helping with educational attainment[33] and, for instance, providing transportation for offspring to hobbies, allowing children's easier participation in sports club training,[13] and, thus, could prevent offspring's weight gain. Incidentally, a higher risk for adult morbidities (type 2 diabetes, hypertension, high risk HDL- and LDL-cholesterol levels, hypertriglyceridemia) induced by childhood overweight or obesity can largely be avoided or limited by resolving overweight or obesity between childhood and adulthood.[43,44]

An earlier study found that children without siblings have higher blood pressure in adulthood compared with children with siblings.[14] We observed that participants without siblings had higher odds of obesity in adulthood which is a known risk factor for type 2 diabetes and glycemic disorders, dyslipidemia, and hypertension.[42] Moreover, compared with the children with 1 or more siblings those without siblings had higher odds for developing hypertension which is known to increase the risk for CVD and coronary heart disease mortality over a long-term follow-up in young and middle-age adults with isolated systolic hypertension.[45] Although a systematic review and meta-analysis found that childhood obesity is directly associated with adult systolic and diastolic blood pressures, serum triglycerides, and inversely with adult serum HDL-cholesterol concentration,[38] in the present study we observed increased odds for adult hypertension in participants without siblings and the effect was not substantially mediated by BMI in childhood or adulthood. Therefore, knowing factors associated with childhood and adulthood obesity is important.

Lower education has been shown to increase prevalence of risk behaviors such as smoking, obesity, physical inactivity, and unhealthy diet.[16] Also, children from small families (ie, 1 child or 2 children families) have been shown to be more likely to graduate from high school in the US compared with large families because of intrafamilial resources diluting in larger families.[15] In addition, birth order has been speculated to influence child's education level and mortality in adulthood, especially among women. However, earlier studies suggest that the effect is modest in children with less than 4 siblings.[46,47] In this study, the majority of participants had 4 or less siblings and also birth order or additional adjustments for participant's years of education did not alter the results substantially.

Regardless of many studies providing arguments for the negative effects of having many siblings,[13] it is possible that siblings might be beneficial for health outcomes in adulthood because siblings provide a source of emotional support and practical aid.[48] In addition, results from a recent study from Sweden based on a register data demonstrated that individuals with no siblings had an elevated risk for mortality in adulthood compared in comparison with men and women from multichild families.[13] Finally, our results demonstrate the number of siblings associates with childhood overweight which is, as well as childhood obesity, associated with adverse long-term outcomes[43] and overweight and obesity in childhood/adolescence increases the risk to become overweight or obese adult.[37] Indeed, those who sustain overweight or obesity from childhood to adulthood have higher risk of hypertension in adulthood compared with individuals who were overweight or obese in childhood but nonobese as adults.[43] Because number of siblings is a nonmodifiable risk factor, at-risk individuals (ie, those without siblings) could benefit from an early intervention and support to tackle the issue.

The main strength of this study is the large study population with comprehensive data on lifestyle, biochemistry, and anthropometric measurements as well as on socioeconomic status starting from childhood and extending into adulthood with over 30 years follow-up. However, this study has limitations. As in all observational studies, an apparent limitation is that causality cannot be established based on our findings. However, using the existing population-based studies with extensive data on established major risk factors from childhood to adulthood is the only possibility to study the associations between the number of siblings and cardiovascular risk

factors and health outcomes as it is not possible to acquire a life-long trial on CVD progression in humans. Admittedly, findings from longitudinal studies might suffer from bias because of differential loss to follow-up of participants over the course of the study. However, the YFS study population has been dynamic, meaning that participants lost to follow-up at some point have re-joined the study in the later follow-ups.[49] Thus, the cohort remains largely representative of the original population.[17] In addition, we do not have information on the onset of the diseases (hypertension, type 2 diabetes, prediabetes, dyslipidemia, overweight/obesity, and metabolic syndrome), and, thus, logistic regression was used for longitudinal analysis. Moreover, given the overall relatively low number of siblings in our cohort, the generalizability of our findings is limited to populations where the typical family sizes are similar to our cohort. Equally, our findings might not apply in less developed or in poorer countries than Finland. Furthermore, data collected from self-reported questionnaires (diabetes, smoking, and physical activity index) are subject to recall bias. However, we also evaluated diabetes with objective factors such as blood biochemistry and national prescription database. Nevertheless, we acknowledge that this is subject to underestimation of smoking habits and possibly to overestimation of physical activity. Finally, we recognize the possibility of misclassification of our main exposure measure of number of siblings at baseline in 1980, especially for those of younger age. In age-stratified analyses, we observed more associations among adolescents (baseline age 12-18 years). This is in line with our prior report showing that associations of childhood and adulthood risk factors improve with advancing age.[50] Our findings concerning younger age groups at baseline should be interpreted with some caution, as their family size has been more likely to change after the baseline investigation. Although we prioritized the use of these data as it maintained the largest sample size, our sensitivity analyses that used information collected from the parents of participants in the recently completed (2018-2020) 3-generation YFS, and also, combined data on the number of siblings from the baseline and 2 subsequent follow-up studies, confirmed our findings.

In our representative sample of Finnish children and adolescents, we found that those without siblings had lower physical activity levels and higher BMI and LDL-cholesterol levels in childhood, and higher odds for hypertension and obesity in adulthood than those with 1 or more siblings. Number of siblings could be a simple and useful tool for identifying children at increased risk that might benefit from early intervention and prevention aimed at improving or maintaining cardiovascular health. ■

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Reprint requests: Jukka Pihlman, MD, Research Center of Applied and Preventive Cardiovascular Medicine, University of Turku. Kiinamyllynkatu 10, 20520, Turku, Finland. E-mail: jttpih@utu.fi

References

1. Abajobir AA, Abbafati C, Abbas KM, Abd-Allah F, Abera SF, Aboyans V, et al. Global, regional, and national age-sex specific mortality for 264 causes of death, 1980-2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet 2017;390:1151-210.
2. Sanghavi M, Kulinski J, Ayers CR, Nelson D, Stewart R, Parikh N, et al. Association between number of live births and markers of subclinical atherosclerosis: the Dallas Heart Study. Eur J Prev Cardiol 2016;23:391-9.
3. Magnus MC, Iliodromiti S, Lawlor DA, Catov JM, Nelson SM, Fraser A. Number of offspring and cardiovascular disease risk in men and women. Epidemiology 2017;28:1.
4. Ness RB, Harris T, Cobb J, Flegal KM, Kelsey JL, Balanger A, et al. Number of pregnancies and the subsequent risk of cardiovascular disease. N Engl J Med 1993;328:1528-33.
5. Koski-Rahikkala H, Hartikainen A. Does parity affect mortality among parous women ? J Epidemiol Commun Health 2006;60:968-73.
6. Gallagher LG, Davis LB, Ray RM, Psaty BM, Gao DL, Checkoway H, et al. Reproductive history and mortality from cardiovascular disease among women textile workers in Shanghai, China. Int J Epidemiol 2011;40:1510-8.
7. Jacobsen BK, Knutsen SF, Oda K, Fraser EG. Parity and total , ischemic heart disease and stroke mortality . The Adventist Health Study, 1976-1988. Eur J Epidemiol 2011;26:711-8.
8. Peters SAE, Yang L, Guo Y, Chen Y, Bian Z, Millwood IY, et al. Parenthood and the risk of cardiovascular diseases among 0 . 5 million men and women: findings from the China Kadoorie Biobank. Int J Epidemiol 2017;46:180-9.
9. Parikh NI, Cnattingius S, Dickman PW, Mittleman MA, Ludvigsson JF, Ingelsson E. Parity and risk of later-life maternal cardiovascular disease. Am Heart J 2010;159:215-21.e6.
10. Glick PJ, Marini A, Sahn DE. Estimating the consequences of unintended fertility for child health and education in Romania: an analysis using twins data. Oxf Bull Econ Stat 2007;69:667-91.
11. Millimet DL, Wang L. Is the quantity-quality trade-off a trade-off for all , none , or some ? Econ Dev Cult Change 2011;60:155-95.
12. Eriksson JG, Forsén T, Tuomilehto J, Winter PD, Osmond C, Barker DJP. Catch-up growth in childhood and death from coronary heart disease: longitudinal study. Br Med J 1999;318:427-31.
13. Baranowska-Rataj A, Barclay K, Kolk M. The effect of number of siblings on adult mortality: Evidence from Swedish registers for cohorts born between 1938 and 1972. Popul Stud (NY) 2017;71:43-63.
14. Trevisan M, Krogh V, Klimowski L, Bland S. Absense of siblings: a risk factor for hypertension? N Engl J Med 1991;325:293-302.
15. Blake J. Number of siblings and educational attainment. Science (80) 1989;245:32-6.
16. Khaing W, Vallibhakara SA, Attia J, McEvoy M, Thakkinstian A. Effects of education and income on cardiovascular outcomes: a systematic review and meta-analysis. Eur J Prev Cardiol 2017;24:1032-42.
17. Raitakari OT, Juonala M, Rönnemaa T, Keltikangas-Järvinen L, Räsänen L, Pietikäinen M, et al. Cohort profile: the cardiovascular risk in young Finns study. Int J Epidemiol 2008;37:1220-6.
18. Telama R, Yang X, Leskinen E, Kankaanpää A, Hirvensalo M, Tammelin T, et al. Tracking of physical activity from early childhood through youth into adulthood. Med Sci Sports Exerc 2014;46:955-62.
19. Telama R, Yang X, Viikari J, Välimäki I, Wanne O, Raitakari O. Physical activity from childhood to adulthood a 21-year tracking study. Am J Prev Med 2005;28:267-73.

20. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin Chem 1972;18:499-502.
21. Juonala M, Viikari JSA, Hutri-Kähönen N, Pietikäinen M, Jokinen E, Taittonen L, et al. The 21-year follow-up of the Cardiovascular Risk in Young Finns Study: Risk factor levels, secular trends and east-west difference. J Intern Med 2004;255:457-68.
22. Nuotio J, Oikonen M, Magnussen CG, Jokinen E, Laitinen T, Hutri Kähönen N, et al. Cardiovascular risk factors in 2011 and secular trends since 2007: The Cardiovascular Risk in Young Finns Study. Scand J Public Health 2014;42:563-71.
23. Herbert V, Lau KS, Gottlieb CW, Bleicher SJ. Coated charcoal immunoassay of insulin. J Clin Endocrinol Metab 1965;25:1375-84.
24. Falkner B, Daniels SR. Summary of the fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. Hypertension 2004;44:387-8.
25. Oikonen M, Nuotio J, Magnussen CG, Viikari JSA, Taittonen L, Laitinen T, et al. Repeated blood pressure measurements in childhood in prediction of hypertension in adulthood. Hypertension 2016;67:41-7.
26. Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents : Summary Report. Pediatrics 2011;128:S213-56.
27. Grossman DC, Bibbins-Domingo K, Curry SJ, Barry MJ, Davidson KW, Doubeni CA, et al. Screening for obesity in children and adolescents us preventive services task force recommendation statement. JAMA 2017;317:2417-26.
28. Care D, Suppl SS. 2. Classification and diagnosis of diabetes: standards of medical care in diabetes 2019. Diabetes Care 2019;42:S13-28.
29. Chapman MJ, Ginsberg HN, Amarenco P, Andreotti F, Borén J, Catapano AL, et al. Triglyceride-rich lipoproteins and high-density lipoprotein cholesterol in patients at high risk of cardiovascular disease: evidence and guidance for management. Eur Heart J 2011;32:1345-61.
30. Bentham J, Di Cesare M, Bilano V, Bixby H, Zhou B, Stevens GA, et al. Worldwide trends in body-mass index, underweight, overweight, and obesity from 1975 to 2016: a pooled analysis of 2416 population-based measurement studies in 128·9 million children, adolescents, and adults. Lancet 2017;390:2627-42.
31. Nuotio J, Vähämurto L, Pahkala K, Magnussen CG, Hutri-Kähönen N, Kähönen M, et al. CVD risk factors and surrogate markers: urban-rural differences. Scand J Public Health 2019;48:752-61.
32. Wang H, Sekine M, Chen X, Kanayama H, Yamagami T, Kagamimori S. Sib-size, birth order and risk of overweight in junior high school students in Japan: results of the Toyama Birth Cohort Study. Prev Med (Baltimore) 2007;44:45-51.
33. Chen AY, Escarce JJ. Family structure and childhood obesity, Early childhood longitudinal study: kindergarten cohort. Prev Chronic Dis 2010;7:A50.
34. Ochiai H, Shirasawa T, Ohtsu T, Nishimura R, Morimoto A, Obuchi R, et al. Number of siblings, birth order, and childhood overweight: a population-based cross-sectional study in Japan. BMC Public Health 2012;12:1.
35. Winkelstein WJ. Study of blood pressure in Buffalo, N. Y. Ann N Y Acad Sci 1963;107:570-5.
36. Wang Y, Lobstein T. Worldwide trends in childhood overweight and obesity. Int J Pediatr Obes 2006;1:11-25.
37. Singh AS, Mulder C, Twisk JWR, Van Mechelen W, Chinapaw MJM. Tracking of childhood overweight into adulthood: a systematic review of the literature. Obes Rev 2008;9:474-88.
38. Umer A, Kelley GA, Cottrell LE, Giacobbi P, Innes KE, Lilly CL. Childhood obesity and adult cardiovascular disease risk factors: a systematic review with meta-analysis. BMC Public Health 2017;17:1-24.
39. Llewellyn A, Simmonds M, Owen CG, Woolacott N. Childhood obesity as a predictor of morbidity in adulthood: a systematic review and meta-analysis. Obes Rev 2016;17:56-67.
40. Reilly JJ, Kelly J. Long-term impact of overweight and obesity in childhood and adolescence on morbidity and premature mortality in adulthood: systematic review. Int J Obes 2011;35:891-8.
41. Simmonds M, Burch J, Llewellyn A, Griffiths C, Yang H, Owen C, et al. The use of measures of obesity in childhood for predicting obesity and the development of obesity-related diseases in adulthood: a systematic review and meta-analysis. Health Technol Assess (Rockv) 2015;19:1-336.
42. Sowers JR. Obesity as a cardiovascular risk factor. Am J Med 2003;115:37-41.
43. Juonala M, Magnussen CG, Berenson GS, Venn A, Burns TL, Sabin MA, et al. Childhood adiposity, adult adiposity, and cardiovascular risk factors. N Engl J Med 2011;365:1876-85.
44. Buscot MJ, Thomson RJ, Juonala M, Sabin MA, Burgner DP, Lehtimäki T, et al. Distinct child-to-adult body mass index trajectories are associated with different levels of adult cardiometabolic risk. Eur Heart J 2018;39:2263-2270a.
45. Yano Y, Stamler J, Garside DB, Daviglus ML, Franklin SS, Carnethon MR, et al. Isolated systolic hypertension in young and middle-aged adults and 31-year risk for cardiovascular mortality: the Chicago Heart Association detection project in industry study. J Am Coll Cardiol 2015;65:327-35.
46. Black SE, Devereux PJ, Salvanes KG. The more the merrier? The effect of family size and birth order on children's education. Q J Econ 2005;669:669-700.
47. Barclay K, Kolk M. Birth order and mortality: a population-based cohort study. Demography 2015;52:613-39.
48. Rostila M, Saarela J, Kawachi I. The forgotten griever: a nationwide follow-up study of mortality subsequent to the death of a sibling. Am J Epidemiol 2012;176:338-46.
49. Juonala M, Viikari JSA, Raitakari OT. Main findings from the prospective Cardiovascular Risk in Young Finns Study. Curr Opin Lipidol 2013;24:57-64.
50. Koskinen J, Magnussen CG, Sinaiko A, Woo J, Urbina E, Jacobs DR, et al. Childhood age and associations between childhood metabolic syndrome and adult risk for metabolic syndrome, type 2 diabetes mellitus and carotid intima media thickness: the international childhood cardiovascular cohort consortium. J Am Heart Assoc 2017;6:1-16.

Table V. Adult risk factors according to the number of siblings

	Number of siblings							
	0		1		≥2			
Risk factors	Adjusted mean	95% CI	Adjusted mean	95% CI	Adjusted mean	95%CI	*P* for trend	n
HDL-cholesterol (mmol/L)	1.31	(1.28 - 1.34)	1.32	(1.30 - 1.33)	1.33	(1.31 - 1.35)	.61	2439
LDL-cholesterol (mmol/L)	3.23	(3.14 - 3.31)	3.22	(3.17 - 3.27)	3.30	(3.25 - 3.35)	.08	2417
Triglycerides (mmol/L)	1.42	(1.32 - 1.52)	1.33	(1.27 - 1.38)	1.37	(1.31 - 1.43)	.25	2441
Systolic blood pressure (mm Hg)	121	(120 - 122)	119	(119 - 120)	120	(119 - 121)	.17	2441
Diastolic blood pressure (mm Hg)	77	(75 - 78)	75	(75 - 76)	75	(75 - 76)	.10	2440
BMI (kg/m^2)	26.9	(26.4 - 27.4)	26.3	(26.0 - 26.6)	26.5	(26.2 - 26.8)	.09	2435
Serum glucose (mU/l)	5.41	(5.33 - 5.50)	5.36	(5.31 - 5.40)	5.36	(5.32 - 5.41)	.54	2441
Serum HbA1c (mmol/mol)	36.5	(36.0 - 37.1)	36.5	(36.2 - 36.8)	36.6	(36.3 - 36.9)	.88	2016
Physical activity index	8.9	(8.6 - 9.1)	9.0	(8.9 - 9.1)	8.9	(8.8 - 9.0)	.21	2353
N*	351		1073		1018			

*N varied between 280 and 351 in participants with no siblings, 888 and 1073 in participants with one sibling, and 848 and 1018 in participants with 2 or more siblings. Adjusted for age and sex.

Table VI. LDL-cholesterol levels, BMI, and physical activity index in childhood according to the number of siblings (1980) in different age groups

		Number of siblings							
		0		1		≥2			
Age	Risk factors	Adjusted mean	95% CI	Adjusted mean	95%CI	Adjusted mean	95% CI	*P* for trend	n
3-9	LDL-cholesterol (mmol/L)	3.56	(3.47 - 3.64)	3.54	(3.48 - 3.59)	3.59	(3.53 - 3.66)	.42	1749
12-18	LDL-cholesterol (mmol/L)	3.29	(3.18 - 3.41)	3.21	(3.15 - 3.28)	3.35	(3.29 - 3.40)	.01	1770
3-9	BMI (kg/m^2)	16.1	(15.9 - 16.3)	15.9	(15.7 - 16.0)	15.9	(15.7 - 16.0)	.17	1765
12-18	BMI (kg/m^2)	20.3	(19.9 - 20.6)	19.9	(19.7 - 20.1)	19.7	(19.5 - 19.9)	.01	1772
3-9	Physical activity index*	−0.07	(−0.18 - 0.03)	0.05	(−0.02 - 0.11)	−0.04	(−0.12 - 0.05)	.11	1761
12-18	Physical activity index*	−0.10	(−0.24 - 0.03)	0.07	(−0.01 - 0.15)	−0.01	(−0.08 - 0.05)	.06	1716

‡Standardized mean difference. Adjusted for sex and age.

Table VII. ORs for adult hypertension according to number of siblings (1980) in different age groups

		Number of siblings							
		0		1			≥2		
Age	Outcomes	n		OR	CI 95%	n	OR	CI 95%	n	n all
3-9	Hypertension	Reference	230	0.56	(0.36 - 0.87)	630	0.56	(0.34 - 0.92)	347	1207
12-18	Hypertension	Reference	130	0.86	(0.56 - 1.32)	463	0.75	(0.49 - 1.13)	685	1278
3-9	Obesity	Reference	223	0.84	(0.57 - 1.24)	616	0.77	(0.50 - 1.20)	341	1180
12-18	Obesity	Reference	127	0.59	(0.38 - 0.90)	453	0.69	(0.45 - 1.03)	675	1255

Adjusted for sex and age. Systolic blood pressure >140 mm Hg, diastolic blood pressure >90 mm Hg, or self-reported use of blood pressure medication were used as criteria for hypertension in adulthood. Participants with BMI from 25 kg/m^2 to 29.9 kg/m^2 were assigned as overweight and as obese if BMI was equal or over 30 kg/m^2.