

Childhood psychosocial environment and adult cardiac outcomes: A causal mediation approach

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Abstract

Introduction. This study used causal mediation analysis to assess the life-course associations of favorable childhood psychosocial environment with left ventricular (LV) mass and diastolic function in adulthood, and to which extent adult health behaviors mediate these associations.

Methods. The sample included 880 participants (56% women) from the Young Finns Study who had data on childhood environment from 1980, adult health behaviors (smoking, physical activity, diet and BMI) from 2001 and echocardiographic assessment of LV mass ($\text{g}/\text{m}^{2.7}$) and diastolic function (E/e' ratio; higher values indicating lower diastolic function) from 2011. The associations of childhood environment with LV mass and E/e' ratio and mediation pathways through health behaviors were assessed using marginal structural models controlling for age, sex and time-dependent confounding by adult socioeconomic position (SEP; measured as educational attainment) via inverse probability weighting. Data were analyzed in 2018-2019.

Results. Mean age in 2011 was 41 (ranging 34-49). Those above the median of the childhood score versus below the median had 1.28 $\text{g}/\text{m}^{2.7}$ lower LV mass (95% CI=-2.63, 0.07) and 0.18 lower E/e' ratio (95% CI=-0.39, 0.03). There was no evidence for indirect effects from childhood environment to LV outcomes through adult health behaviors after controlling for time-dependent confounding by adult SEP (indirect effect $b=-0.30$, 95% CI=-1.22, 0.63 for LV mass, $b=-0.04$, 95% CI=-0.18, 0.11 for E/e' ratio). Results after multiple imputation were similar.

Conclusions. Favorable childhood environment was associated with more optimal cardiac structure and function in adulthood. After accounting for SEP, adult health behaviors explained little of the associations.

INTRODUCTION

While several studies have shown that early-life psychosocial adversity is associated with cardiovascular risks in adulthood,¹⁻³ recent investigations have turned the focus toward favorable psychosocial factors that may help maintaining optimal cardiac health.⁴⁻⁹ Adult cardiovascular health has been linked to various early-life psychosocial factors, including family socioeconomic position,^{10,11} emotional climate,^{12,13} health behaviors,^{14,15} environmental safety and stability,^{2,16} and child's self-regulation skills.^{4,17,18} In the Cardiovascular Risk in Young Finns Study, cumulative presence of favorable psychosocial factors in childhood and adolescence was associated with lower risk of type II diabetes⁹ and coronary artery calcification,⁷ more optimal BMI development⁶ and a more ideal overall cardiovascular profile.⁸ Similar findings have been reported in cohorts from the U.S.^{4,12}

Favorable childhood environment may influence cardiovascular outcomes through direct biological pathways, e.g., by supporting optimal regulation of immune, metabolic, neuroendocrine and autonomic nervous systems¹⁹ and enhancing restorative physiological processes.⁵ Childhood environment may also influence cardiovascular health through behavioral pathways. For instance, adverse childhood environment has been associated with smoking, overweight, physical inactivity and substance use in adulthood,^{3,20} that in turn are associated with cardiovascular outcomes. If adult behavioral factors lie on the causal pathway from childhood conditions to later-life cardiovascular health, they can represent modifiable means to reverse adverse effects of early-life circumstances. However, the degree to which childhood environment causes adulthood cardiac outcomes through adult health behaviors is not well known.

This study extended previous studies by assessing longitudinal associations of favorable childhood psychosocial environment with two established risk factors for cardiovascular morbidity and mortality: adult left ventricular (LV) mass and LV diastolic function.^{21–23} The aim was to identify potential behavioral mechanisms through which childhood environment may be associated with adult cardiac outcomes. To this end, a counterfactual approach was used to assess whether ideal cardiovascular health behaviors in adulthood explained the associations of favorable childhood environment with more optimal LV mass and diastolic function.

METHODS

Sample

The Cardiovascular Risk in Young Finns Study is a prospective cohort study on the precursors of atherosclerosis among Finnish children and adolescents.²⁴ The initial sample included 3596 participants aged 3-18 years in 1980. For this study, 2067 individuals who had data on childhood psychosocial environment in 1980 were included. Of these 2067 individuals, 864 were excluded because of missing behavioral and covariate (educational attainment) data in 2001, and further 323 were excluded due to missing data on LV mass and diastolic function in 2011, resulting in 880 participants. The study was conducted according to the Declaration of Helsinki and it was approved by the Ethics Committee of the Hospital District of Southwest Finland. The Harvard T.H. Chan School of Public Health IRB reviewed this protocol and determined that this activity is exempt under 45 CFR 46.101(b)(4). All participants gave written informed consent.

Echocardiography

Echocardiograms were performed in 2011. Standard echocardiographic examinations^{25,26} were produced from the standardized image planes and modes: parasternal long and short axis in 2-dimensional and M-mode and apical 4-chamber view.²⁵ Left ventricular mass was calculated as $(0.8[1.04((LV \text{ end-diastolic diameter} + \text{posterior wall thickness} + \text{interventricular septum thickness})^3 - LV \text{ end-diastolic diameter}^3)] + 0.6 \text{ g})$, and it was indexed by height raised to the allometric power of 2.7 (indexed LV mass = LV mass/height^{2.7}) as this indexation performs better in the context of overweight and obesity.^{26,27} LV diastolic function in the LV filling pressure was measured by using E/e' ratio (higher values indicating lower diastolic function), assessed with continuous and pulsed-wave Doppler measuring transmitral flow and tissue velocities.^{25,26}

Psychosocial factors in childhood

As described previously,⁶⁻⁹ childhood environment was assessed with six factors proposed as central components of childhood psychosocial environment:^{28,29} socioeconomic environment, emotional environment, parental health behaviors, stressful events, child's self-regulation and social adjustment (**Table S2**). These data were collected from parents of the study participants via questionnaires in 1980 (**Table S1**). The six psychosocial factors were constructed from several dichotomous variables (0/1). For this purpose, continuous data were first dichotomized. Selection of cutoffs is described in detail in **Table S2**. The scores from the six domains were standardized (z-scores) and then added together.⁶⁻⁹ Favorable psychosocial factor score was treated both as a continuous score and a dichotomous variable with a cutoff at the 50th percentile.

Cardiovascular health behaviors in adulthood

Four health behaviors – smoking, BMI, physical activity and diet – were assessed in 2001

following the AHA definitions of ideal cardiovascular health.³⁰ Smoking, physical activity and diet were self-reported. BMI (kg/m^2) was measured during a study visit. The total number of ideal behaviors was the count of ideal scores on smoking (never smoked or quit >1 year ago), BMI ($<25 \text{ kg}/\text{m}^2$), physical activity (120 min/week moderate-intensity or 60 min/week vigorous-intensity activity or a combination) and diet (2/3 of following components: fruits and vegetables every day; fish ≥ 2 times/week; soft drinks ≤ 2 times/week).^{30,31} A dichotomized measure of ideal cardiovascular behaviors (≥ 2 vs <2 ideal behaviors) was used in analyses.

Confounders

All analyses were adjusted for sex and age. Self-reported educational attainment (highest level of educational attendance or completed education in 2001; dichotomized into no college vs. college or higher) was used to assess adult socioeconomic position (SEP).

Statistical analysis

Linear regression analysis was used to examine the overall associations of childhood psychosocial factors score with LV mass and diastolic function. LV mass and E/e' ratio were examined in separate models, both without adjustments and adjusted for age and sex. The childhood psychosocial score was first used as a continuous score, and the estimates were scaled to 1 SD of the score. Then the childhood score was assessed as a dichotomous variable with a cutoff at the median (50th percentile). Associations of adult health behaviors with LV mass and E/e' ratio were assessed in a separate linear regression analysis adjusted for age, sex, adult SEP and the childhood score.

A counterfactual approach was used to assess the direct and indirect effects of childhood environment on LV outcomes through health behaviors in adulthood. The hypothetical causal model is presented in **Figure 1**. Here, favorable psychosocial childhood environment is the exposure and ideal health behaviors the proposed mediator. Age and sex were included as potential confounders of both the exposure–outcome and the mediator–outcome associations.^{32–38} In addition, adult SEP was included as a potential exposure-induced confounder of the mediator–outcome association. This causal structure was hypothesized based on established associations of childhood psychosocial environment with adult SEP and the associations of adult SEP with both health behaviors and LV structure and function.^{39–41}

In the presence of exposure-induced confounding, natural direct and indirect effects are not identified, but randomized interventional analogues for natural direct and indirect effects can be estimated.^{42,43} In this study, exposure-induced confounding was controlled in marginal structural models by inverse probability weighting following the approach described by VanderWeele et al.⁴³ The weights were constructed based on logistic regression models for childhood psychosocial environment, adult SEP and ideal health behaviors (all treated as dichotomous variables), and the estimates of direct and indirect effects were obtained from weighted linear regression models regressing the LV outcomes on the exposure. The effect decomposition has been described previously.⁴³ Standard errors and CIs were obtained with robust variance estimation to account for sampling error in estimating the weights.⁴⁴ LV mass and E/e' ratio were analyzed in separate models.

Multiple imputation with chained equations was performed to account for missing data (**Table S3**).⁴⁵ The imputation model included measures of LV mass, E/e' ratio, educational attainment in 2001, 2007 and 2011, ideal health behaviors in 1986, 2001, 2007 and 2011, sex, age and childhood psychosocial factors in 1980. All study variables with missing data were imputed and all analyses were repeated in 10 imputed datasets. The six childhood psychosocial factors were imputed as separate variables. Participants with imputed outcomes were excluded from the analysis of imputed data.⁴⁵ As sensitivity analyses, all analyses were repeated with data on health behaviors and education assessed in 2007. Additionally, the analyses were conducted after excluding participants with self-reported diagnoses of cardiac disease/events in 2001. Finally, mediation was assessed through each health behavior separately. All analyses were conducted in Stata 13.1 (StataCorp, LP, College Station, TX, USA) in 2018-2019.

RESULTS

Table 1 shows the sample characteristics (see also **Table S4**). Compared to those excluded due to missing data, included participants were almost one year older, more often women (56% vs 48%) and from more favorable childhood psychosocial environments (mean 0.7 vs 0.4) (**Table S5**). Descriptive statistics after multiple imputation are presented in **Table S6**.

Unadjusted linear regression analyses showed that the favorable childhood psychosocial score was associated with lower LV mass and E/e' ratio. 1 SD difference in the childhood psychosocial score was associated with 0.83 g/m^{2.7} difference in LV mass (95% CI, -1.27 to -0.38) and 0.08 difference in E/'e ratio (CI=-0.15 to -0.01). These associations remained significant after adjusting for age and sex (b=-0.66, 95% CI, -1.09 to -0.23 for LV mass, b=-0.08, 95% CI, -0.15 to -0.02 for E/'e ratio) and age, sex and adult SEP (b=-0.52, 95% CI, -0.96 to -0.08 for LV mass,

$b=-0.08$, 95% CI, -0.15 to -0.02 for E/e' ratio). Of the six psychosocial factors, socioeconomic environment, parental health behaviors and child's self-regulatory behavior were associated with LV outcomes (**Table S7**). The associations of the childhood psychosocial score with LV mass and E/e' ratio did not differ according to age (psychosocial score by age interaction $p=0.79$ for LV mass, $p=0.63$ for E/e' ratio) or sex (psychosocial score by sex interaction $p=0.52$ for LV mass, $p=0.34$ for E/e' ratio). Those with childhood psychosocial score above the median had 84% higher sex- and age-adjusted odds for having ≥ 2 ideal health behaviors in adulthood compared to those below the median (OR=1.84, 95% CI, 1.35, 2.51). Having ≥ 2 ideal health behaviors in adulthood was associated with 2.17 $\text{g/m}^{2.7}$ lower LV mass (95% CI, -3.14, -1.20) and 0.23 lower E/e' ratio (95% CI, -0.38 to -0.09) compared to having < 2 ideal behaviors after adjusting for sex, age, childhood psychosocial environment and adult SEP.

Differences in LV mass and E/e' ratio above and below the median of the childhood psychosocial score are presented in **Table 2**. The age- and sex-adjusted differences from linear regression models coincided with the total effect estimates from marginal structural models controlling for age, sex and time-dependent confounding by adult SEP (total effect $b=-1.28$, 95% CI, -2.63, 0.07 for LV mass, $b=-0.18$, 95% CI, -0.39, 0.03 for E/e' ratio). The marginal randomized interventional analogue of the direct effect indicated a difference of 0.98 $\text{g/m}^{2.7}$ in LV mass among those above the median of the childhood score versus those below the median (95% CI, -1.97, 0.00). The analogue for the direct effect on LV diastolic function indicated a corresponding difference of 0.14 in E/e' ratio (95% CI, -0.29, 0.01). Approximately 23% and 21% of the associations of childhood environment with LV mass and E/e' ratio were estimated to be mediated through adult health behaviors ($b=-0.30$, 95% CI, -1.22, 0.63 for LV mass, $b=-0.04$,

95% CI, -0.18, 0.11 for E/e' ratio). However, these estimates were not statistically significant (natural indirect effect $p=0.53$ for LV mass, $p=0.61$ for E/e' ratio). (**Table 2**). Results with imputed data concurred with those from the primary analyses (**Table 2**). Although estimates for LV mass were somewhat greater, no indirect effects were observed in imputed data.

In the complete case analysis using health behavior and educational data from 2007, all associations were somewhat stronger for LV mass and weaker for E/e' ratio compared to the primary analysis, but no indirect associations were observed (**Table S8**). Imputed analyses with data from 2007 yielded similar results to those from the imputed analyses with data from 2001 (**Table S8**). All results were substantially similar after excluding participants with cardiac disease or events (**Table S9**). No indirect associations were seen in analyses estimating the indirect effect through each health behavior separately (**Table S10**).

DISCUSSION

This prospective cohort study found that favorable psychosocial environment in childhood and youth was associated with better cardiovascular health 31 years later, as measured by cardiac structure (LV mass) and diastolic function (E/e' ratio). Compared to those with childhood psychosocial score below the median, those above the median had $1.2 \text{ g/m}^{2.7}$ lower LV mass and 0.2 lower E/e' ratio. After accounting for adult SEP, there was no consistent evidence of health behaviors mediating the association of childhood psychosocial environment with LV mass and E/e' ratio; the associations of childhood environment were largely explained by other factors besides ideal health behaviors.

Previous studies have demonstrated associations of psychosocial factors in childhood with several important cardiometabolic risk factors in adulthood.^{4,6-9,12} This study extends these findings to LV mass and diastolic function. Increased LV mass and LV diastolic dysfunction measured as the filling pressure of the left ventricle have been found to be prognostic of the risk of cardiovascular events and premature morbidity, independently of cardiovascular comorbidities and beyond traditional risk factor assessment, and thus they are clinically relevant markers for cardiovascular risk stratification.²¹⁻²³ A 11.8 g/m^{2.7} increase in LV mass has been associated with a 40% increased rate of adverse cardiovascular events.⁴⁶ In this study, difference between those with unfavorable vs favorable childhood score was 1.2 g/m^{2.7}, which would thereby correspond to a 3% higher rate of cardiovascular events. Although the incubation time from childhood exposures to disease manifestation may be long, some evidence suggests that childhood psychosocial exposures are associated with progression of cardiovascular risk factors over time.^{2,6} Future studies with repeated measurements of cardiac structure and function are needed to elucidate the timing of etiologically relevant pathophysiological changes.

Several pathways can connect childhood environment with adulthood cardiac health. Childhood and youth are developmental periods during which important regulatory systems and physiological responses are programmed.^{19,47} Childhood psychosocial environment may initiate differences in immune, metabolic, neuroendocrine and autonomic nervous systems relevant to cardiovascular health across life.¹⁹ Behavioral factors are suggested as a potentially important, modifiable mechanism explaining the association of childhood psychosocial environment with cardiovascular outcomes.^{3,5,19} However, the extent to which this occurs is not well understood.¹⁹ This study used marginal structural models to assess the associations of childhood environment

with adult cardiac outcomes through ideal cardiovascular health behaviors while controlling for time-dependent confounding by adult SEP. After accounting for age, sex and adult SEP, there was no evidence of an indirect association of childhood environment with LV mass and diastolic function through ideal cardiovascular health behaviors. Nevertheless, health behaviors are considered as a major contributor of the socioeconomic gradient in health. A pathway from childhood environment to LV mass and diastolic function may involve a sequence of exposures,⁴⁷ whereby childhood environment influences adult SEP which in turn drives the association of health behaviors with cardiac outcomes. This is feasible given that some evidence suggests an indirect association from childhood environment to adult cardiovascular outcomes through adult SEP.^{12,16} Furthermore, a recent study examining associations of childhood psychosocial adversity with adult cardiac outcomes did suggest an indirect association through health behaviors.¹⁶ A relevant question is whether favorable and adverse childhood exposures tap into different intermediate mechanisms, with the role of health behaviors possibly accentuating with childhood adversity. Further work recognizing potentially distinct pathways initiated by favorable vs adverse early-life exposures is needed to explain the psychosocial origins of lifetime cardiovascular health. Future research should also evaluate the degree to which standard cardiovascular risk factors, e.g., blood pressure or insulin resistance, may explain the associations of childhood psychosocial environment with adult cardiac structure and function.

Limitations

Assessment of mediation in a life-course perspective using longitudinal observational designs is complex. For the estimates of direct and indirect effects to have causal interpretation, strong assumptions regarding confounding are needed.^{42,43} In particular, longitudinal settings often

involve long time intervals between measurements of the exposure and the mediator. This introduces the possibility of intermediate, time-dependent confounding of the mediator–outcome association.⁴² In this study, time-dependent confounding was addressed by using a recently developed method for effect decomposition in the causal mediation framework. This approach is based on inverse probability weighting in marginal structural models, which requires estimating additional parameters, inevitably decreasing statistical power. The precision of estimates obtained from this analysis may thus be compromised by the methodological approach that was chosen in order to accurately represent the underlying causal structure.

Some other limitations should be noted. The analysis is based on observational data, and the possibility of residual or unmeasured confounding cannot be ruled out. Causal mediation analysis helped to improve the specification of the causal model, although the variables were dichotomous which decreased measurement precision.⁴⁸ This study is a long-running cohort study and loss to follow-up cannot be avoided. The complete case and multiple imputation analyses gave similar results for the lack of indirect effect through health behaviors, but it is possible that selective loss to follow-up biased the estimates. Although no established standard currently exists for measuring childhood psychosocial environment, the six factors included are theoretically sound^{28,29} and have been associated with relevant cardiometabolic outcomes.^{2,4,18,10–}
¹⁷ Likewise, no clear cutoffs exist for defining favorable vs adverse psychosocial experiences, and the childhood score cannot fully differentiate the relative contributions of beneficial vs adverse aspects of childhood environment. Although diet was measured using validated FFQs and the physical activity questionnaire has shown acceptable convergent validity against pedometer data,^{49–51} self-reported health behaviors involve a risk of reporting bias based on

childhood background or adult SEP. Finally, the participants were a white, ethnically homogeneous cohort residing in Finland, which limits generalizability of these findings. The strengths of this study include prospective, encompassing data on childhood psychosocial circumstances and application of recently developed methods to assess mediation.

CONCLUSIONS

This study found that favorable childhood environment is associated with more optimal LV mass and diastolic function in adulthood. Findings from the causal mediation analysis suggest this association is not explained by ideal cardiovascular health behaviors in adulthood once age, sex and adult SEP are accounted for. At present, these results highlight the importance of early-life environments in initiating pathways of long-term cardiovascular health, and motivate further application of rigorous designs to assess the causal pathways from childhood psychosocial environment to adult cardiovascular endpoints.

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K.K. and L.P.-R. had full access to the data and take responsibility for the integrity of the data and the accuracy of the data analysis.

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Table 1. Characteristics of 880 participants from the Cardiovascular Risk in Young Finns Study

	Mean (SD)	n [%]	N
Age in 2011	41.4 (4.9)		880
Sex (women)		493 [56%]	880
Educational attainment in 2001			880
No college		616 [70%]	
College or higher		264 [30%]	
Psychosocial factors in 1980			
Favorable socioeconomic environment (range, 0-4)	1.7 (1.2)		880
Favorable emotional environment (range, 0-4)	2.5 (0.9)		880
Favorable health behaviors of parents (range, 0-6)	4.9 (1.1)		880
Lack of stressful events (range, 0-5)	4.8 (0.5)		880
High self-regulatory behavior (range, 0-7)	6.7 (0.7)		880
High social adjustment (range, 0-2)	1.5 (0.7)		880
Childhood psychosocial factors score	0.7 (2.6)		880
Ideal health behaviors in 2001			880
≥2 ideal behaviors		613 [70%]	
<2 ideal behaviors		267 [30%]	
Non-smoking		608 [69%]	
BMI <25 kg/m ²		519 [59%]	
Ideal physical activity		480 [55%]	
Ideal diet		231 [26%]	
Left ventricular mass (g/m ^{2.7})	30.4 (6.7)		853
E/e' ratio	4.8 (1.0)		860

All values except for left ventricular mass (LV) and E/e' ratio calculated for participants with data on LV mass, E/e' ratio or both.

Mean LV mass (g/m^{2.7}) 29.6 (SD=6.2) and 31.2 (7.1) among those above vs below the median of the childhood psychosocial score.

Mean E/e' ratio 4.7 (0.9) vs 4.9 (1.0) among those above vs below the median of the childhood psychosocial score.

Table 2. Differences in LV outcomes between those above and below the median of childhood psychosocial score

	Complete cases		Multiple imputation	
	LV mass (g/m^{2.7}) Difference (95% CI)	E/e' ratio Difference (95% CI)	LV mass (g/m^{2.7}) Difference (95% CI)	E/e' ratio Difference (95% CI)
Linear regression				
Unadjusted	-1.61 (-2.51, -0.71)	-0.15 (-0.28, -0.02)	-1.67 (-2.34, -1.01)	-0.17 (-0.26, -0.07)
Sex- and age-adjusted	-1.16 (-2.02, -0.29)	-0.16 (-0.29, -0.03)	-1.37 (-2.01, -0.72)	-0.16 (-0.25, -0.06)
Marginal structural model^a				
Total effect	-1.28 (-2.63, 0.07)	-0.18 (-0.39, 0.03)	-1.36 (-2.27, -0.44)	-0.17 (-0.31, -0.03)
Direct effect	-0.98 (-1.97, 0.00)	-0.14 (-0.29, 0.01)	-1.05 (-1.74, -0.36)	-0.14 (-0.25, -0.04)
Indirect effect	-0.30 (-1.22, 0.63)	-0.04 (-0.18, 0.11)	-0.31 (-0.90, 0.29)	-0.02 (-0.12, 0.07)

Abbreviations: LV, left ventricular.

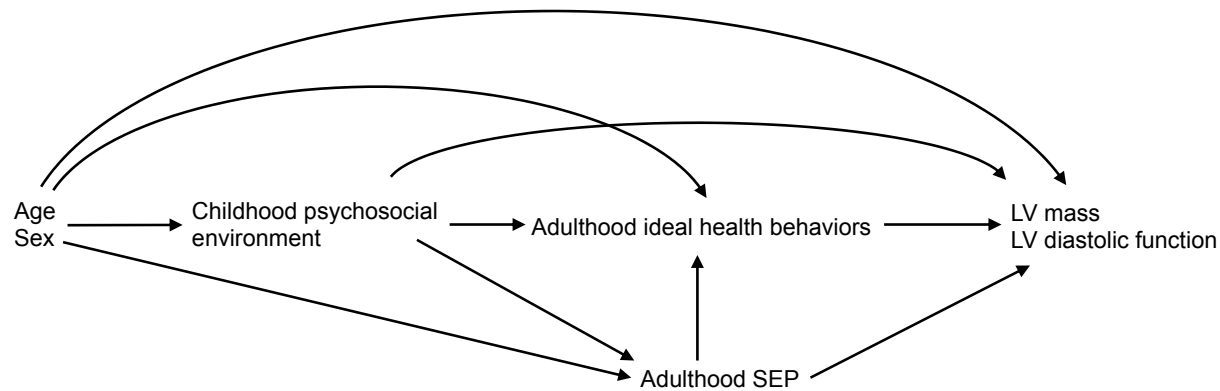
^a Estimates from the marginal structural model adjusted for age, sex and time-dependent confounding by adult socioeconomic position (SEP).

Sample sizes differ due to available data (n=853 for LV mass, n=860 for E/e' ratio in the complete case analysis, n=1908 for LV mass, n=1939 for E/e' ratio after multiple imputation).

In complete case analysis, those above the median of the childhood psychosocial score had 0.90 g/m^{2.7} lower LV mass (95% CI, -1.78, -0.02) and 0.16 lower E/e' ratio (95% CI, -0.29, -0.03) compared to those below the median of the childhood score after adjusting for age, sex and adult SEP.

In analyses with imputed data, those above the median of the childhood psychosocial score had 1.16 g/m^{2.7} lower LV mass (95% CI, -1.34, -0.99) and 0.15 lower E/e' ratio (95% CI, -0.18, -0.12) compared to those below the median of the childhood score after adjusting for age, sex and adult SEP.

Figure 1. Directed acyclic graph depicting the conceptual model of the relationships between childhood environment, health behaviors and SEP in adulthood and the outcomes of LV mass and diastolic function



Abbreviations: SEP, socioeconomic position; LV, left ventricular

Appendix Items

Appendix Table S1. Description of the childhood psychosocial variables as they appeared in the baseline questionnaire (year 1980) in the Cardiovascular Risk in Young Finns Study

Appendix Table S2. Process chart of the construction of the childhood psychosocial factors score

Appendix Table S3. Complete and missing/imputed observations of variables used in multiple imputation

Appendix Table S4. Characteristics of 880 participants from the Cardiovascular Risk in Young Finns Study

Appendix Table S5. Differences in demographic and childhood psychosocial factors between included and not included participants

Appendix Table S6. Characteristics of 1984 participants from the Cardiovascular Risk in Young Finns Study after multiple imputation

Appendix Table S7. Associations of the six psychosocial factors with LV outcomes

Appendix Table S8. Differences in LV outcomes between those above and below the median of the childhood psychosocial score among participants with health behavior and educational data recorded in 2007

Appendix Table S9. Differences in LV outcomes between those above and below the median of the childhood psychosocial score excluding participants with a history of cardiac disease or cardiac events

Appendix Table S10. Effect decomposition for indirect effects through each health behavior

Appendix Table S1. Description of the childhood psychosocial variables as they appeared in the baseline questionnaire (year 1980) in the Cardiovascular Risk in Young Finns Study

Item	Scoring	Range
Variables of the socioeconomic environment		
Occupational status	1=manual, 2=lower nonmanual, 3=higher nonmanual	1-3
Mother's education	Total number of years of education	3-22
Father's education	Total number of years of education	2-28
Family income	Total annual income (Finnish marks), 7-point scale	0-7
Mother's employment	0=unemployed, retired, or sick-leave, 1=employed	0-1
Father's employment	0=unemployed, retired, or sick-leave, 1=employed	0-1
Variables of the emotional environment		
Mother's mental health	0=diagnosis of mental disorder, 1=free of diagnosis	0-1
Father's mental health	0=diagnosis of mental disorder, 1=free of diagnosis	0-1
Caregiving nurturance	7-item scale ($\alpha=0.70$):	
	"I lose my nerve with my child. (reversed)"	1-5 ^b
	"My child is burdensome in difficult situations. (reversed)"	1-5 ^b
	"My child takes too much of my time (reversed)"	1-5 ^b
	"My child is important to me."	1-5 ^b
	"I am important to my child."	1-5 ^b
	"I enjoy spending time with my child."	1-5 ^b
	"I am able to self-actualize myself when being with my child."	1-5 ^b
Parental life satisfaction	3-item scale ($\alpha=0.71$):	
	"I am satisfied with myself as a mother/father."	1-5 ^b
	"I am satisfied with myself as a spouse/life companion."	1-5 ^b

	"I am satisfied with myself as an employee."	1-5 ^b
Mother's alcohol use	Frequency of intoxication, 8-point scale	1-8 ^c
Father's alcohol use	Frequency of intoxication, 8-point scale	1-8 ^c

Variables indicating parental health behaviors

Mother's BMI	kg/m ²	
Father's BMI	kg/m ²	
Mother's smoking	0=smoker, 1=non-smoker	0-1
Father's smoking	0=smoker, 1=non-smoker	0-1
Mother's exercise	1=no exercise, 2=some (irregular) exercise, 3=regular weekly	1-3
Father's exercise	1=no exercise, 2=some (irregular) exercise, 3=regular weekly	1-3

Variables indicating stressful events

Change of residence	0=yes, 1=no	0-1
Change of school	0=yes, 1=no	0-1
Parental divorce/separation	0=yes, 1=no	0-1
Death of family member	0=yes, 1=no	0-1
Long-term hospitalization	0=yes, 1=no	0-1

Variables indicating self-regulatory behavior of the child

Self-control	<i>Please, choose the option that most accurately describes your child:</i> 1=My child is always on the move, restless, and unable to control him/herself 2=My child is more restless and less controlled than children of same age 3=My child is restless/poorly controlled only when tired or bored, but mostly within normal limits. 4=My child is very controlled and stays calm even in situations where most children would become restless and out of control.	1-4
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Aggression control

6-item scale ($\alpha=0.60$):

"Other children say that my child gets easily into fights."	1-2 ^b
"My child hits/pushes other children "by accident."	1-2 ^b
"My child needs a lot of discipline to control aggression."	1-2 ^b
"My child uses swear words very often."	1-2 ^b
"Other children complain often about my child's behavior."	1-2 ^b
"Other parents have complained about my child's behavior."	1-2 ^b

Variables indicating social adjustment of the child

<i>Please, choose the option that most accurately describes your child:</i>	0-1
0=I am worried about my child's behavior and I am afraid he/she will become a problem child.	
1=I am not particularly worried about my child's behavior.	
<i>Please, choose the option that most accurately describes your child:</i>	0-1
0=I am worried about my child's behavior and I am afraid he/she will become a problem child.	
1=My child is well-adjusted and copes well with life's challenges.	

^a 1=extremely seldom, 2=seldom, 3=in between, 4=often, 5=very often.

^b 1=true, 2=not true

^c 1=daily, 2=approx. two times/week, 3=one time/week, 4=approx. two times/month, 5=approx. one time/month, 6=approx. one time/two months, 7=max three or four times/year, 8=never

Appendix Table S2. Process chart of the construction of the childhood psychosocial factors score

Factor	Definition of favorable level	Absent	Present
Favorable socioeconomic environment			
Occupational status	Upper white collar ^a	0	1
Educational level	Academic or college degree ^a	0	1
Family income	Annual income in the highest quartile	0	1
Occupational stability	Steady employment ^b	0	1
Favorable emotional environment			
Parental mental health	Free of diagnosis for mental disorder ^b	0	1
Parental nurturance	Positive reply to the nurturance scale ^c	0	1
Parental life satisfaction	Positive reply to the satisfaction scale ^c	0	1
Reasonable alcohol use	Intoxication ≤ 3 -4 times/year ^b	0	1
Optimal health behaviors of parents			
Energy intake (mother)	Body-mass index < 30.0	0	1
Energy intake (father)	Body-mass index < 30.0	0	1
Smoking (mother)	No daily smoking	0	1
Smoking (father)	No daily smoking	0	1
Physical activity (mother)	Exercise ≥ 1 times per week	0	1
Physical activity (father)	Exercise ≥ 1 times per week	0	1
Lack of stressful events			
Stability of living environment	No change of residence during youth	0	1
Stability of school environment	No change of school during youth	0	1
Stability of family environment	No parental divorce or separation	0	1
Loss of significant persons	No death of family member	0	1
Health-related events	No long-term hospitalization/disease ^a	0	1
Self-regulatory behavior of the child			
Self-control scale	High ability to tolerate frustration	0	1
Aggression control	(1) Doesn't fight	0	1
	(2) Doesn't hit	0	1
	(3) Doesn't need much discipline	0	1
	(4) Doesn't swear	0	1
	(5) Other children haven't complained	0	1
	(6) Other parents haven't complained	0	1
Social adjustment of the child			
Social adjustment scale	(1) Not worried about my child	0	1
	(2) I consider my child as well adjusted	0	1

^a Either parent had to meet this criterion.

^b Both parents had to meet this criterion.

^c Main caregiver replied in 2-parent households, and the available parent replied in single-parent households.

1. Favorable socioeconomic environment comprised 4 components: upper white collar occupation (1 point); academic/college degree (1 point), family income in the highest 25% (1 point) and occupational stability (no unemployment spells/retirement due to disability/long-term sick-leave) (1 point). Thus the scale ranged from 0 to 4.

2. Favorable emotional environment comprised 4 components. The first was absence of previously diagnosed parental mental disorder (1 point). The second was high parental nurturance, measured with a 7-item scale ($\alpha = 0.70$). A reply of “very often” to all times (shown in **Table S1**) gave 1 point. The third component was high parental life satisfaction, measured with a 3-item scale ($\alpha = 0.71$, **Table S1**). A positive reply to all 3 items gave 1 point. Fourth, reasonable alcohol use of both parents was included as evidence indicates that unhealthy drinking is harmful to child’s emotional development.¹ Parents reporting intoxication “never or maximum 3-4 times/a year were classified as reasonable drinkers. Altogether the scale range was 0 to 4.

3. Optimal health behaviors of parents were reported independently by each parent. As data on parental diet was not available, BMI >30 kg/m² was used as a proxy of excess energy intake (1 point for non-obesity). Other health behaviors were being a nonsmoker (1 point) and regular physical activity (1 point). Mother’s and father’s health behaviors were summed together. Thus the scale ranged from 0 to 6.

4. Lack of stressful events included events that may threaten a child’s sense of stability and continuity. These were moving residence, changing school, parental divorce or separation, death of a family member and serious disease in the family. Non-presence of each gave 1 point. Thus the scale ranged from 0 to 5.

5. Self-regulatory behavior of the participant consisted of 2 scales measuring high self-control and high aggression control. The self-control scale consisted of 1 question (**Table S1**). Children described as being very controlled “always or most of the time” received 1 point. Aggression control ($\alpha=0.60$) was measured with 6 items (shown in **Table S1**), each giving 1 point. The total score was formed by combining scores from self-control and aggression control. Thus the scale ranged from 0 to 7.

6. Social adjustment was assessed by a question about parental worry about the child’s adjustment (1 point) and parental evaluation of the child’s general level of adjustment (1 point) (**Table S1**). The social adjustment scale ranged from 0 to 2.

The scores from these six domains were standardized (z-scores) and then summed together. Thus, the favorable psychosocial factors score represents the cumulative score of the 6 psychosocial factors, each contributing equal weight. The favorable psychosocial factor score

was treated both as a continuous score and a dichotomous variable with a cutoff at the 50th percentile in the analysis.

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Appendix Table S3. Complete and missing/imputed observations in variables used in multiple imputation

	Complete	Missing/ Imputed	Total
Age	3956	0	3956
Sex	3956	0	3956
Favorable socioeconomic environment	3001	595	3596
Favorable emotional environment	2654	942	3596
Favorable health behaviors of parents	2839	757	3596
Lack of stressful events	3441	155	3596
High self-regulatory behavior	3065	531	3596
High social adjustment	3408	188	3596
Educational attainment in 2001 ^a	2606	990	3596
Educational attainment in 2007 ^b	2228	1368	3596
Educational attainment in 2011 ^c	2002	1594	3596
Number of ideal health behaviors in 1986 ^c	1951	1645	3596
Number of ideal health behaviors in 2001 ^a	2034	1562	3596
Number of ideal health behaviors in 2007 ^b	1906	1690	3596
Number of ideal health behaviors in 2011 ^c	1391	2205	3596
Left ventricular mass (g/m ^{2.7})	1908	1688	3596
E/e' ratio	1939	1657	3596

After excluding participants with missing data on left ventricular (LV) mass and E/e' ratio, the total number of included observations was 1908 in analyses on LV mass and 1939 in analyses on E/e' ratio.

^a Used as an auxiliary variable when performing multiple imputation for the analysis among participants with health behavior and educational data recorded in 2007.

^b Used as an auxiliary variable when performing multiple imputation for the analysis among participants with health behavior and educational data recorded in 2001.

^c Used as an auxiliary variable in the imputation.

Appendix Table S4. Characteristics of 880 participants from the Cardiovascular Risk in Young Finns Study

	≥ 2 ideal behaviors (n=613)		<2 ideal behaviors (n=267)		p for difference
	Mean (SD)	n [%]	Mean (SD)	n [%]	
Age in 2011	41.3 (5.0)		41.7 (4.6)		0.286
Sex (women)		382 [62%]		111 [42%]	<0.001
Educational attainment in 2001					
No college		393 [64%]		223 [84%]	<0.001
College or higher		220 [36%]		44 [16%]	
Psychosocial factors in 1980					
Favorable socioeconomic environment (range, 0-4)	1.8 (1.2)		1.5 (1.0)		0.001
Favorable emotional environment (range, 0-4)	2.6 (0.9)		2.4 (0.9)		0.020
Favorable health behaviors of parents (range, 0-6)	5.0 (1.1)		4.7 (1.2)		<0.001
Lack of stressful events (range, 0-5)	4.8 (0.5)		4.8 (0.5)		0.924
High self-regulatory behavior (range, 0-7)	6.7 (0.7)		6.6 (0.8)		0.003
High social adjustment (range, 0-2)	1.5 (0.6)		1.4 (0.7)		0.008
Childhood psychosocial factors score	1.0 (2.6)		0.0 (2.6)		<0.001
Ideal health behaviors in 2001					
Non-smoking		513 [84%]		95 [36%]	<0.001
BMI <25 kg/m ²		456 [74%]		63 [24%]	<0.001
Ideal physical activity		435 [71%]		45 [17%]	<0.001
Ideal diet		222 [36%]		9 [3%]	<0.001
Left ventricular mass (g/m ^{2.7})	29.4 (6.2)		32.6 (7.4)		<0.001
E/e' ratio	4.7 (1.0)		4.9 (1.0)		0.026

All values except for left ventricular mass (LV) and E/e' ratio are calculated for participants with data on LV mass, E/e' ratio or both.

Appendix Table S5. Differences in demographic and childhood psychosocial factors between included and not included participants

	Included (n=880)		Not included ^a (n=1187)	
	Mean (SD)	n [%]	Mean (SD)	n [%]
Sex (women)		493 [56%]		571 [48%]
Age in 1980	10.4 (4.9)		9.3 (4.8)	
Favorable socioeconomic environment	1.7 (1.2)		1.6 (1.2)	
Favorable emotional environment	2.5 (0.9)		2.4 (1.0)	
Favorable parental health behaviors	4.9 (1.1)		4.8 (1.2)	
Lack of stressful events	4.8 (0.5)		4.8 (0.4)	
High self-regulatory behavior	6.7 (0.7)		6.6 (0.8)	
High social adjustment	1.5 (0.7)		1.5 (0.7)	
Childhood psychosocial factors score	0.7 (2.6)		0.4 (2.8)	

Participants with data on childhood psychosocial factors measured in 1980 (n=2067) were initially eligible for this study.

^a Not included due to missingness

Appendix Table S6. Characteristics of 1984 participants from the Cardiovascular Risk in Young Finns Study after multiple imputation

	Mean (SD)	n [%]	N
Age in 2011	41.9 (5.0)		1984
Sex (women)		1076 [54%]	1984
Educational attainment in 2001			1984
No college		1458 [73%]	
College or higher		526 [73%]	
Educational attainment in 2007			1984
No college		1281 [65%]	
College or higher		703 [35%]	
Psychosocial factors in 1980			
Favorable socioeconomic environment (range, 0-4)	1.6 (1.2)		1984
Favorable emotional environment (range, 0-4)	2.5 (1.0)		1984
Favorable health behaviors of parents (range, 0-6)	4.8 (1.2)		1984
Lack of stressful events (range, 0-5)	4.6 (0.7)		1984
High self-regulatory behavior (range, 0-7)	6.6 (0.8)		1984
High social adjustment (range, 0-2)	1.5 (0.7)		1984
Childhood psychosocial factors score	0.2 (2.9)		1984
Ideal health behaviors in 2001			1984
≥2 ideal behaviors		1240 [62%]	
<2 ideal behaviors		744 [38%]	
Ideal health behaviors in 2007			1984
≥2 ideal behaviors		1097 [55%]	
<2 ideal behaviors		887 [45%]	
Left ventricular mass (g/m ^{2.7})	30.8 (6.6)		1908
E/e' ratio	4.8 (1.0)		1939

All estimates are pooled over 10 imputed datasets.

Mean left ventricular mass (g/m^{2.7}) 30.1 (SD=6.4) vs 31.7 (6.8) among those above vs below the median of the childhood psychosocial score.

Mean E/e' ratio 4.7 (1.0) vs 4.9 (1.0) among those above vs below the median of the childhood psychosocial score.

Appendix Table S7. Associations of the six psychosocial factors with LV outcomes

LV mass		
	B (95% CI)	p
Favorable socioeconomic environment	0.67 (0.47, 0.97)	0.033
Favorable emotional environment	0.72 (0.46, 1.13)	0.156
Favorable health behaviors of parents	0.59 (0.40, 0.86)	0.006
Lack of stressful events	1.36 (0.51, 3.60)	0.538
High self-regulatory behavior	0.46 (0.25, 0.84)	0.012
High social adjustment	1.03 (0.54, 1.94)	0.938
E/e' ratio		
	B (95% CI)	p
Favorable socioeconomic environment	0.92 (0.87, 0.97)	0.002
Favorable emotional environment	1.05 (0.98, 1.12)	0.167
Favorable health behaviors of parents	0.95 (0.89, 1.00)	0.056
Lack of stressful events	0.91 (0.79, 1.05)	0.214
High self-regulatory behavior	0.93 (0.85, 1.02)	0.104
High social adjustment	0.97 (0.88, 1.06)	0.479

Abbreviations: LV, left ventricular.

All estimates are from separate linear regression analyses adjusted for age and sex.

All estimates calculated among participants with health behavior and educational data recorded in 2001.

Appendix Table S8. Differences in LV outcomes between those above and below the median of the childhood psychosocial score among participants with health behavior and educational data recorded in 2007

	Complete cases		Multiple imputation	
	LV mass (g/m^{2.7})	E/e' ratio	LV mass (g/m^{2.7})	E/e' ratio
	Difference (95% CI)	Difference (95% CI)	Difference (95% CI)	Difference (95% CI)
Linear regression				
Unadjusted	-1.77 (-2.64, -0.89)	-0.10 (-0.24, 0.04)	-1.67 (-2.34, -1.01)	-0.17 (-0.26, -0.07)
Sex- and age-adjusted	-1.44 (-2.29, -0.60)	-0.11 (-0.25, 0.02)	-1.37 (-2.01, -0.72)	-0.16 (-0.25, -0.06)
Marginal structural model^a				
Total effect	-1.41 (-2.66, -0.15)	-0.12 (-0.32, 0.08)	-1.29 (-2.20, -0.38)	-0.16 (-0.29, -0.02)
Direct effect	-1.26 (-2.17, -0.36)	-0.10 (-0.25, 0.05)	-1.05 (-1.75, -0.36)	-0.14 (-0.24, -0.04)
Indirect effect	-0.14 (-1.01, 0.72)	-0.02 (-0.16, 0.12)	-0.24 (-0.82, 0.35)	-0.01 (-0.10, 0.08)

Abbreviations: LV, left ventricular.

^a Estimates from the marginal structural model adjusted for age, sex and time-dependent confounding by adult socioeconomic position.

Diet in 2007 was measured as 4/5 of the following components in 2007: ≥ 450 g/day of fruits and vegetables; \geq two servings (100 g) of fish/week; \geq three servings (30 g) of whole grain rye bread/day; < 1500 mg of sodium/day; ≤ 450 kcal of sugar-sweetened beverages/week. All other measures were similar in 2001 and 2007.

Sample sizes differ due to available data (n=875 for LV mass, n=876 for E/e' ratio in the complete case analysis, n=1908 for LV mass, n=1939 for E/e' ratio after multiple imputation).

Appendix Table S9. Differences in LV outcomes between those above and below the median of the childhood psychosocial score excluding participants with a history of cardiac disease or cardiac events

	LV mass (g/m^{2.7}) Difference (95% CI)	E/e' ratio Difference (95% CI)
Linear regression		
Unadjusted	-1.58 (-2.51, -0.65)	-0.18 (-0.32, -0.04)
Sex- and age-adjusted	-1.12 (-2.02, -0.22)	-0.19 (-0.33, -0.06)
Marginal structural model^a		
Total effect	-1.28 (-2.67, 0.10)	-0.21 (-0.42, 0.00)
Direct effect	-0.98 (-1.99, 0.03)	-0.17 (-0.33, -0.02)
Indirect effect	-0.30 (-1.25, 0.65)	-0.04 (-0.18, 0.11)

Abbreviations: LV, left ventricular.

^a Estimates from the marginal structural model adjusted for age, sex and time-dependent confounding by adult socioeconomic position.

All estimates calculated among participants with health behavior and educational data recorded in 2001.

Sample sizes differ due to available data (n=803 for LV mass, n=807 for E/e' ratio).

Appendix Table S10. Effect decomposition for indirect effects through each health behavior

	LV mass (g/m^{2.7}) Difference (95% CI)	E/e' ratio Difference (95% CI)
Non-smoking		
Total effect	-1.26 (-2.50, -0.03)	-0.15 (-0.34, 0.04)
Direct effect	-1.19 (-2.10, -0.29)	-0.13 (-0.27, 0.00)
Indirect effect	-0.07 (-0.90, 0.77)	-0.02 (-0.15, 0.11)
Ideal BMI		
Total effect	-1.27 (-2.51, -0.02)	-0.17 (-0.36, 0.01)
Direct effect	-0.95 (-1.86, -0.03)	-0.17 (-0.31, -0.03)
Indirect effect	-0.32 (-1.17, 0.53)	0.00 (-0.13, 0.13)
Ideal physical activity		
Total effect	-1.27 (-2.51, -0.02)	-0.17 (-0.36, 0.02)
Direct effect	-1.36 (-2.27, -0.45)	-0.17 (-0.31, -0.03)
Indirect effect	0.09 (-0.75, 0.94)	0.00 (-0.13, 0.13)
Ideal diet		
Total effect	-1.33 (-2.56, -0.11)	-0.16 (-0.35, 0.03)
Direct effect	-1.33 (-2.23, -0.43)	-0.14 (-0.28, -0.01)
Indirect effect	0.00 (-0.83, 0.83)	-0.02 (-0.15, 0.11)

All estimates are from separate marginal structural models adjusted for age, sex and time-dependent confounding by adult educational attainment.

All estimates calculated among participants with health behavior and educational data recorded in 2001.

Sample sizes differ due to available data (n=853 for LV mass, n=860 for E/e' ratio).