ARTICLE

Socially Isolated Children 20 Years Later

Risk of Cardiovascular Disease

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Objective: To test the hypothesis that children who occupy peripheral or isolated roles in their peer groups (isolated children) are at risk of poor adult health.

Design: Longitudinal study of an entire birth cohort.

Setting: Dunedin, New Zealand.

Participants: A total of 1037 children who were followed up from birth to age 26 years.

Interventions: Measurement of social isolation in childhood, adolescence, and adulthood.

Main Outcome Measures: When study members were 26 years old, we measured adult cardiovascular multifactorial risk status (overweight, elevated blood pressure, elevated total cholesterol level, low high-density lipoprotein level, elevated glycated hemoglobin concentration, and low maximum oxygen consumption).

Results: Socially isolated children were at significant risk of poor adult health compared with nonisolated children (risk ratio, 1.37; 95% confidence interval, 1.17-1.61). This association was independent of other well-established childhood risk factors for poor adult health (low childhood socioeconomic status, low childhood IQ, childhood overweight), was not accounted for by health-damaging behaviors (lack of exercise, smoking, alcohol misuse), and was not attributable to greater exposure to stressful life events. In addition, longitudinal findings showed that chronic social isolation across multiple developmental periods had a cumulative, dose-response relationship to poor adult health (risk ratio, 2.58; 95% confidence interval, 1.46-4.56).

Conclusions: Longitudinal findings about children followed up to adulthood suggest that social isolation has persistent and cumulative detrimental effects on adult health. The findings underscore the usefulness of a life-course approach to health research, by focusing attention on the effect of the timing of psychosocial risk factors in relation to adult health.

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THE NEED TO BELONG IS A fundamental human motivation that, when thwarted, compromises psychological health.[1,2] Loneliness and social isolation can also compromise physical health. Prospective studies have documented that lack of social support and social isolation in adulthood predict the future onset of coronary artery disease[3-5] and are related to the prognosis for adult patients with preexisting coronary artery disease.[6,7] However, emerging evidence from life-course epidemiology points to the importance of early life experiences in shaping adult disease.[8-10] In the present study, we observed a 1972-1973 cohort of children from birth to young adulthood and tested the hypothesis that children who occupy peripheral or isolated roles in their peer group are at significant risk of poor adult health. Because the cohort was still too young to present adverse clinical end points of cardiovascular disease (eg, myocardial infarction), we focused on multiple risk-factor clustering as a measure of adverse cardiovascular risk.[11-13]

Our first aim was to test whether childhood social isolation was an independent risk factor for poor adult health. We thus tested 3 alternative explanations for the link between social isolation and poor adult health.

A first alternative explanation, the *co-occurring risk hypothesis*, is that links between childhood isolation and poor adult health are spurious because both are associated with other well-established childhood risk factors for adult disease. We tested 4 such risk factors. First, some children may be socially isolated from their peers because they come from socioeconomically disadvantaged families, and children who grow up in families with low socioeconomic status (SES) have poor health in adulthood.[14] Second, some children may be

isolated because they are overweight,[15] and childhood overweight is a risk factor for poor adult health.[16,17] Third, some children may be isolated because they are mentally retarded or simply not very bright, and recent longitudinal research suggests that intelligence (as measured by IQ tests) predicts adult morbidity and mortality, including cardiovascular diseases.[18] Fourth, some children are isolated because they are aggressive and are thus rejected by their peers,[19] and longitudinal research suggests that aggression may be a risk factor for all-cause morbidity.[20] If childhood social isolation is an independent risk factor for adult poor health, it should survive controlling for all of these co-occurring childhood risk factors.

A second alternative explanation, the *health-behavior hypothesis,* is that socially isolated children develop poor health because they engage in health-compromising behaviors as adolescents or adults.[21] For example, they may become so socially disengaged that they lead increasingly sedentary lives and refrain from exercise. In addition, lonely children may smoke and drink more, possibly as a form of self-medication or as a way to gain approval from peers. In the present study, we measured these behaviors and tested whether childhood social isolation is related to poor adult health because isolated young people engage in more health-compromising behaviors.

According to the *differential-exposure hypothesis*, lonely children grow up to be exposed to more stress.[21] In the present study, we measured 3 potential stressors (low status attainment, stressful life events, and depression) and tested whether childhood social isolation is related to poor adult health because lonely children experience more stressful lives when they grow up.

Our second aim was to test the cumulative effects of social isolation on adult health, testing 2 interrelated hypotheses. First, we examined the *early-timing hypothesis,* testing whether childhood social isolation has an influence on adult health because it contributes to adult social isolation or because it may establish psychological and biological tendencies that independently affect adult health.[22] If childhood social isolation is linked to poor adult health simply because it is a developmental precursor of later social isolation, the association between childhood social isolation and poor adult health should be attenuated once adult social isolation is factored into the longitudinal analysis. If the longitudinal association remains significant, it would suggest that the distress created by social isolation early in life may erode health over time. Second, we examined the *cumulative stress hypothesis*, testing whether the duration of social isolation across multiple developmental periods bears a dose-response relationship to poor adult health.

METHODS

SAMPLE

Participants were members of the Dunedin Multidisciplinary Health and Development Study, a longitudinal investigation of health and behavior in a complete birth cohort.[23] Study members were born in Dunedin, New Zealand, between April 1, 1972, and March 31, 1973. Of these, 1037 children (91% of eligible births; 52% male) participated in the first follow-up assessment at age 3 years, constituting the base sample for the remainder of the study. Cohort families represented the full range of SES in the general population of New Zealand's South Island and were primarily white. Follow-up examinations were carried out at ages 5, 7, 9, 11, 13, 15, 18, 21, and, most recently, 26 years, when we assessed 980 (96.2%) of the 1019 study members still alive. Participants attended the research unit within 60 days of their birthday for a full day of individual data collection. The unit assumed study members' costs to remove all barriers to their participation, eg, travel, lost wages, and child care. The Otago Ethics Committee granted ethical approval for each phase of this longitudinal study. Study members gave informed consent before participating.

SOCIAL ISOLATION MEASURES

Childhood Social Isolation

When study members were 5, 7, 9, and 11 years old, their parents and teachers completed the Rutter Child Scales.[24] Two items measure peer problems ("tends to do things on his/her own; is rather solitary" and "not much liked by other children"). Scores on these 2 items were averaged across the 4 time periods and by 2 reporters (Cronbach $\alpha = 0.77$). Evidence shows that children who chronically experience negative peer relations have the worst prognosis, and repeated assessments of children's peer experiences are recommended for research purposes.[25]

Adolescent Social Isolation

When study members were 15 years old, they completed the inventory of peer attachment,[26,27] which assesses the extent to which adolescents feel integrated with their peers (eg, "I feel alone or apart when I am with friends" and "friends are concerned about my well-being" [reverse coded]). Scores were summed to derive a scale of adolescent social isolation (Cronbach $\alpha = 0.80$).

Adult Social Isolation

When study members were 26 years old, we used 2 sources of information to identify socially isolated study members. First, we identified those who were not involved with any partner and/or had not dated at all in the past year (5%). Second, study members were interviewed about their social support networks and asked how many people (1) "make you feel liked or loved," (2) "can comfort you or calm you down," (3) "you can trust to keep the things you talk about private," and (4) "you can talk to when you are feeling down or blue." We identified those who said they had no one to provide any one of these emotional support roles (4%). We classified as "isolated" those who said they were not involved with any partner and had not dated at all in the past year or those who had no one to provide emotional support; 8% of the sample was so classified.

CO-OCCURRING RISK FACTORS AND POTENTIAL MEDIATING VARIABLES

The SES of study members' families was measured with a 6-point scale assessing parents' occupational status. The scale places each occupation into 1 of 6 categories (from 1, professional to 6, unskilled laborer) on the basis of educational levels and income associated with that occupation in data from the New Zealand census.[9]

Height and weight measurements were taken at ages 5, 7, 9, and 11 years. Body mass index was calculated and standardized within each age and averaged across the 4 time periods to yield an index of childhood overweight.

The Wechsler Intelligence Scale for Children[28] was administered by trained psychometrists at ages 7, 9, and 11 years.[29] We averaged scores from the 3 age periods to form an overall score (mean, 106.4; SD, 14.46).

When study members were 5, 7, 9, and 11 years old, their parents and teachers rated whether each child "frequently fights with other children."[24] We created a childhood aggression scale by averaging these ratings (Cronbach $\alpha = 0.70$).[23]

We measured 3 health-damaging behaviors. First, the lack of vigorous exercise was assessed at age 26 years by asking study members to report how much time, in a typical week, they spent engaged in physical activity that "caused you to breathe hard or puff a lot, eg, working out at the gym, playing [a] sport, digging in the garden, or activity at work."[30] Because of the skewed nature of reported activity levels, quartiles were formed. Second, heavy smoking at age 26 years was defined as smoking 20 or more cigarettes per day (10% of the sample). Third, alcohol dependence was assessed at age 26 years using a reporting period of the past 12 months; 17% of the study members met *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*[31] criteria for alcohol dependence.

We measured 3 adult stressors. First, low adult SES was measured with a 6-point scale assessing occupational status, as described in the first paragraph of this section. Second, stressful life events during the past 5 years (including problems with employment, finances, housing, disabling injuries, and partner relationships) were assessed at age 26 years.[32] Third, depression was assessed at age 26 years using a reporting period of the past 12 months; 17% of the study members met *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*[31] criteria for a major depressive disorder.

ADULT PHYSICAL HEALTH MEASURES

Physical examinations were conducted at age 26 years. We assessed health risk-factor clustering by measuring 6 biomarkers: weight, blood pressure, total cholesterol level, high-density lipoprotein cholesterol level, glycated hemoglobin concentration, and maximum oxygen consumption. (Pregnant women were excluded from the reported analyses.)

To determine overweight, we assessed body mass index (calculated as weight in kilograms divided by the square of height in meters) and waist girth (in centimeters). Study members were considered overweight if their body mass index was 30 or more or if their waist measurement was 88 cm or more for women or 102 cm or more for men[33,34]; 16% of the women and 10% of the men in the sample met this criterion.

Blood pressure (in millimeters of mercury) was assessed according to standard protocols.[35] Study members were considered to have high blood pressure if their systolic reading was 130 mm Hg or higher or if their diastolic reading was 85 mm Hg or higher[34]; 6% of the women and 26% of the men met this criterion.

Venipuncture was conducted at the same time each day (4:15-4:45 PM). Ninety percent of the sample consented. Nonfasting total cholesterol, high-density lipoprotein cholesterol, and glycated hemoglobin levels were measured in the serum.

Study members were considered to have an elevated total cholesterol level if their total cholesterol reading was 240 mg/dL (6.22 mmol/L) or greater[34]; 12% of the women and 12% of the men met this criterion.

Study members were considered to have a low high-density lipoprotein cholesterol level if the value was 40 mg/dL (1.04 mmol/L) or lower for men and 50 mg/dL (1.3 mmol/L) or less for women[34]; 32% of the women and 27% of the men met this criterion.

Glycated hemoglobin concentrations (expressed as a percentage of total hemoglobin) were measured by ion exchange high-performance liquid chromatography (Variant II; Bio-Rad, Hercules, Calif) (coefficient of variation, 2.4%), a method certified by the US National Glycohemoglobin Standardization Program (http://www.missouri.edu/~diabetes/ngsp.html). Following Blake et al,[36] study members were designated as having this health risk if their scores were in the top quartile ($\geq$5.2%) of the cohort's distribution.

Maximum oxygen consumption adjusted for body weight (in milliliters per minute per kilogram) was assessed by measuring heart rate in response to a submaximal exercise test on a friction-braked cycle ergometer, and calculated by standard protocols.[37] Sex-specific quartiles were formed. Following Carnethon et al,[38] study members in the lowest quartile were considered to have this health risk.

We assessed multiple risk-factor clustering by summing the number of biomarkers on which the study member was at risk (range, 0-6; 35% of the study members had 0 risks; 35%, 1 risk; 16%, 2 risks; 10%, 3 risks; 3%, 4 risks; and 1%, $\geq$5 risks). Study members were "clustered" if they had at least 3 risk factors: 14% of the study members were clustered (13% of the women and 15% of the men).

DATA ANALYSIS

We estimated the effect of social isolation on adult health, controlling for sex. We then expanded the regression equation to control for co-occurring childhood risk factors, health-damaging behaviors, and adult stress exposure. For these analyses linking childhood social to adult health outcomes, the total number in the cohort was 841. For sensitivity analyses, we conducted all analyses twice. First, we estimated regression models where the outcome was binary (1, clustered; 0, nonclustered), and in this article we report risk ratios (RRs) and 95% confidence intervals (CIs). Second, we estimated negative binomial regressions where the outcome was the summed number of biomarkers (0-6). The same pattern of associations was observed across both methods examined; tables showing the results from negative binomial regressions are available from the authors.

We tested the cumulative effects of social isolation on multiple risk-factor clustering in adulthood by using 2 steps. First, we conducted a regression analysis to estimate the unique effects of childhood social isolation, adolescent social isolation, and adult social isolation on adult clustering. Second, we estimated the effect of the linear combination of these 3 variables on adult risk-factor clustering. For these analyses, we had complete data for 810 study members.

RESULTS

CHILDHOOD ISOLATION AND ADULT HEALTH

Table 1 shows the biomarker and risk-factor characteristics of nonclustered vs clustered participants. The regression analysis in **Table 2** (model 1) shows that a 1-SD change in childhood social isolation increased the risk of adult risk-factor clustering (defined as having adverse levels of $\geq$3 of the 6 adult biomarkers) by 1.37 (95% CI, 1.17-1.61). We tested whether the longitudinal association between childhood social isolation and adult clustering was confounded by 4 well-established risk factors for poor adult health (the co-occurring risk hypothesis). The regression analysis in Table 2 (model 2) shows that, even after controlling for these 4 childhood risk factors for poor adult health, the association between child-

Table 1. Biomarker Characteristics and Risk-Factor Characteristics of Study Participants, According to Adult Cardiovascular Multifactorial Risk Status (Nonclustered vs Clustered)*

	Full Sample (n = 841)	Nonclustered (n = 722)	Clustered (n = 119)
Biomarkers			
Overweight			
BMI	25.1 (4.4)	24.2 (3.5)	30.2 (5.5)
Waist girth, cm	80.3 (10.0)	78.4 (8.2)	92.1 (11.7)
Blood pressure, mm Hg			
Systolic	116.9 (11.0)	115.8 (10.1)	123.8 (13.7)
Diastolic	71.8 (9.4)	71.1 (8.9)	76.0 (11.5)
Total cholesterol, mg/dL	193.0 (38.7)	189.5 (34.8)	224.3 (46.4)
HDL cholesterol, mg/dL	54.1 (15.5)	54.1 (15.5)	42.5 (11.6)
Glycated hemoglobin, % of total hemoglobin	5.0 (0.3)	4.9 (0.3)	5.1 (0.3)
$\dot{V}O_{2max}$, mL/min per kilogram	44.4 (11.1)	46.1 (10.6)	34.1 (8.5)
Risk factors			
Sex, % F	46.8	47.5	42.5
Childhood social isolation†	0 (1)	−0.11 (0.9)	0.30 (1.1)
Low childhood social class†	0 (1)	−0.05 (1.0)	0.11 (1.1)
Childhood overweight†	0 (1)	−0.07 (0.9)	0.57 (1.3)
Low childhood IQ†	0 (1)	−0.12 (0.9)	0.14 (1.0)
Childhood aggression†	0 (1)	−0.05 (1.0)	0.26 (1.1)
Alcohol dependence, %‡	17.7	18.0	15.8
Lack of exercise†	0 (1)	−0.06 (1.0)	0.22 (1.0)
Heavy smoking, %‡	10.2	9.5	14.3
Low adult SES†	0 (1)	−0.07 (1.0)	0.20 (1.0)
Adult stressors†	0 (1)	−0.01 (1.0)	0.04 (1.0)
Diagnosis of depression, %‡	16.6	16.6	16.7
Adolescent social isolation†§	0 (1)	−0.04 (1.0)	0.25 (1.1)
Adult social isolation, %‡§	7.6	6.5	14.3

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by the square of height in meters); HDL, high-density lipoprotein; SES, socioeconomic status; $\dot{V}O_{2max}$, maximum oxygen consumption.

SI conversion factor: To convert cholesterol values to millimoles per liter, multiply by 0.0259.

*Multiple risk-factor clustering was defined in terms of a study member having at least 3 of the following 6 risk factors: overweight, elevated systolic and/or diastolic blood pressure, elevated serum total cholesterol level, low serum HDL cholesterol level, elevated glycated hemoglobin level, and low $\dot{V}O_{2max}$. Values are mean (SD) unless otherwise specified.

†These predictor variables were measured as continuous variables and entered into the analyses as *z* scores.

‡These predictor variables were measured as binary variables and entered into the analyses as dummy variables.

§For analyses using these social isolation variables, n = 810.

hood social isolation and adult clustering remained statistically significant: RR, 1.34; 95% CI, 1.10-1.64. Thus, the link between childhood social isolation and adult risk-factor clustering appeared to be independent of other well-established childhood risk factors for poor health.

We also tested whether the longitudinal association between childhood social isolation and adult risk-factor clustering was accounted for by the fact that isolated children later engaged in more health-damaging behaviors (the health-behavior hypothesis). After controlling for these potential health-damaging behaviors, the association between childhood social isolation and adult risk-factor clustering remained statistically significant: RR, 1.33; 95% CI, 1.13-1.56 (Table 2; model 3).

Finally, we tested whether the longitudinal association between childhood social isolation and adult clustering was mediated by isolated children's greater exposure to stress in adulthood (the differential-exposure hypothesis). After controlling for these potential mediators, the association between childhood isolation and adult risk-factor clustering remained statistically significant: RR, 1.37; 95% CI, 1.16-1.62 (Table 2; model 4).

CUMULATIVE INFLUENCE OF SOCIAL ISOLATION ON ADULT HEALTH

Social isolation showed some continuity across the life course. Children who were rated by adults as socially isolated were likely to self-report that they were socially isolated in adolescence ($r=0.16$, $P<.001$), and social isolation in both childhood and adolescence increased the risk of social isolation in adulthood (RR, 1.37; 95% CI, 1.13-1.66; and RR, 1.61; 95% CI, 1.30-1.99, respectively).

Table 3 shows the links between these 3 developmentally distinct assessments of social isolation and adult risk-factor clustering. The table highlights 4 findings. First, column A shows that social isolation was robustly linked to adult risk-factor clustering, whether isolation was assessed in childhood (RR, 1.37; 95% CI, 1.17-1.60), in adolescence (RR, 1.26; 95% CI, 1.04-1.52), or in adulthood (RR, 2.01; 95% CI, 1.20-3.36). Second, column A also shows that social isolation was linked to adult risk-factor clustering, whether isolation was measured via adults' reports about children's social isolation or via adolescents' and adults' own self-reports. Third, column B shows that, even after taking into account adult social isolation, child-

Table 2. Association Between Childhood Social Isolation and Adult Cardiovascular Multifactorial Risk Status*

Predictor Variables	RR (95% CI)			
	Model 1: Baseline Bivariate Associations	Model 2: Co-occurring Childhood Risk Factors Hypothesis†	Model 3: Health-Damaging Behavior Hypothesis‡	Model 4: Differential Stress-Exposure Hypothesis§
Sex	1.19 (0.83-1.71)	1.19 (0.80-1.86)	1.27 (0.87-1.86)	1.17 (0.79-1.74)
Childhood isolation‖	1.37 (1.17-1.61)	1.34 (1.10-1.64)	1.33 (1.13-1.56)	1.37 (1.16-1.62)
Low childhood social class‖	1.15 (0.96-1.38)	0.93 (0.76-1.15)	. . .	. . .
Childhood overweight‖	1.56 (1.35-1.81)	1.54 (1.32-1.79)	. . .	. . .
Low childhood IQ‖	1.30 (1.07-1.58)	1.27 (1.02-1.58)	. . .	. . .
Childhood aggression‖	1.27 (1.08-1.49)	0.98 (0.79-1.21)	. . .	. . .
Alcohol dependence¶	0.88 (0.54-1.43)	. . .	0.81 (0.48-1.36)	. . .
Lack of exercise‖	1.29 (1.07-1.55)	. . .	1.24 (1.02-1.49)	. . .
Heavy smoking¶	1.47 (0.88-2.46)	. . .	1.36 (0.80-2.32)	. . .
Low adult SES‖	1.27 (1.05-1.53)	. . .	. . .	1.20 (0.98-1.47)
Adult stressors‖	1.05 (0.88-1.25)	. . .	. . .	0.99 (0.81-1.20)
Diagnosis of depression¶	1.00 (0.62-1.62)	. . .	. . .	1.03 (0.62-1.72)

Abbreviations: CI, confidence interval; RR, risk radio; SES, socioeconomic status; ellipses, variable not included in model.
*Multiple risk-factor clustering was defined in terms of a study member having at least 3 of the following 6 risk factors: overweight, elevated systolic and/or diastolic blood pressure, elevated serum total cholesterol level, low serum high-density lipoprotein cholesterol level, elevated glycated hemoglobin level, and low maximum oxygen consumption.
†For model 2, –2 (log likelihood) = 594.1.
‡For model 3, –2 (log likelihood) = 675.2.
§For model 4, –2 (log likelihood) = 637.6.
‖These predictor variables were measured as continuous variables and entered into the regression equations as *z* scores.
¶These predictor variables were measured as binary variables and entered into the regression equations as dummy variables.

Table 3. Cumulative Influence of Social Isolation on Adult Cardiovascular Multifactorial Risk Status*

	RR (95% CI)	
	A. Individual Contributions at Each Age†	B. Independent Contributions From All Ages‡
Measured in childhood, via adults' reports§	1.37 (1.17-1.60)	1.31 (1.11-1.56)
Measured in adolescence, via self-reports§	1.26 (1.04-1.52)	1.16 (0.95-1.40)
Measured in adulthood, via self-reports‖	2.01 (1.20-3.36)	1.70 (0.98-2.95)
Cumulative isolation across all ages¶	. . .	2.58 (1.46-4.56)

Abbreviations: CI, confidence interval; RR, risk ratio; ellipses, variable not included in model.
*Multiple risk-factor clustering was defined in terms of a study member having at least 3 of the following 6 risk factors: overweight, elevated systolic and/or diastolic blood pressure, elevated serum total cholesterol level, low serum high-density lipoprotein cholesterol level, elevated glycated hemoglobin level, and low maximum oxygen consumption.
†The individual contributions were estimated in 3 separate regression models, with sex as a covariate.
‡The independent contributions were estimated in a multivariate regression, with all measures of social isolation entered simultaneously along with sex as a covariate.
§These predictor variables were measured as continuous variables and entered into the regression equations as *z* scores.
‖This predictor variable was measured as a binary variable and entered into the regression equation as a dummy variable.
¶The effect of cumulative isolation was estimated as the combined effect of childhood social isolation plus adolescent social isolation plus adult social isolation, with sex as a covariate.

hood social isolation continued to be linked significantly to adult risk-factor clustering (RR, 1.31; 95% CI, 1.11-1.56). Fourth, the bottom row of Table 3 shows that social isolation was cumulatively linked to adult clustering; study members who occupied peripheral or isolated roles in their networks at multiple developmental periods were in worse health in adulthood (RR, 2.58; 95% CI, 1.46-4.56). The **Figure** documents the association between cumulative social isolation and adult clustering.

COMMENT

The findings from this prospective longitudinal study are novel in 2 ways. First, whereas clinical and research interest in the association between social isolation and poor health has been generated by studies of adults,[7] the findings from this study provide, to our knowledge, the first evidence linking childhood social isolation to poor adult health. Our findings are consistent with a handful of retrospective studies reporting associations between chronic health conditions in adulthood and adults' retrospective reports of a perceived lack of social support in childhood.[39,40] There has been concern about the accuracy of long-term recall of childhood experiences,[41] but that is not an issue in this study because we collected data about childhood social isolation contemporaneously during childhood in the context of the longitudinal prospective investigation. In addition, the association between childhood social isolation and poor adult health was independent of other well-established childhood risk fac-

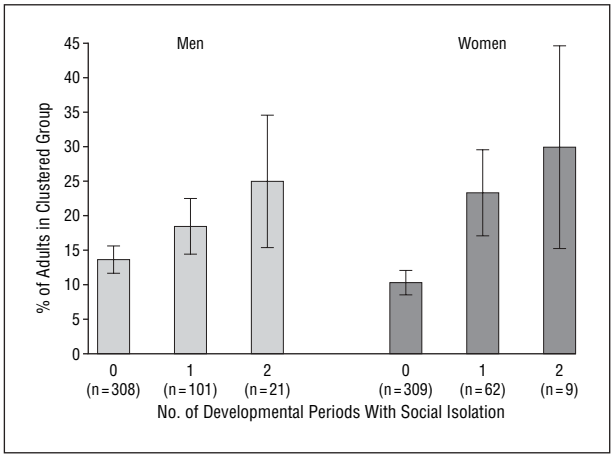

Figure. Association between cumulative social isolation and risk-factor clustering in adulthood. For illustrative purposes, study participants were considered isolated if they were in the top decile in each developmental period. Limit lines indicate standard error.

tors for poor adult health, including low childhood SES, low childhood IQ, and childhood overweight. Moreover, health-damaging behaviors did not account for the association between childhood social isolation and poor adult health. This is consistent with studies of adults[21,42] in which health-damaging behaviors did not account for the poor health of socially isolated individuals. Finally, the association between childhood social isolation and poor adult health was not accounted for by a greater exposure to stressful life circumstances among isolated children in adulthood.

Second, whereas studies of adults have pointed to an inverse gradient between social support and clinical outcomes,[7] the present study additionally documents that social isolation during multiple developmental periods (in childhood, adolescence, and adulthood) had a cumulative, dose-response relationship to poor adult health. A useful concept for understanding how repeated social isolation can lead to poor health is allostatic load,[43] which refers to the cumulative wear and tear caused by repeated adaptations to psychosocial stressors (such as social isolation) in childhood, adolescence, and adulthood. The experience of social isolation may be a form of chronic stress that activates the sympathetic nervous and hypothalamic-pituitary-adrenocortical systems and induces a variety of pathophysiologic responses that contribute to the clustering of risk factors for coronary artery disease (hypertension, insulin resistance, and central adiposity).[44,45] It is also possible that social isolation disrupts constructive and restorative processes that enhance physiological capacities, as suggested by evidence that lonely individuals experience disrupted sleep[46] and engage in passive rather than active coping strategies in their everyday lives.[47]

The new findings should be evaluated alongside several limitations. First, because we studied a cohort of children born only in the early 1970s, we are not yet able to assess disease outcomes; the study members are still too young. Instead, we focused on intermediate health risks that are known to predict future disease in midlife and old age.[11,12] Second, findings from this New Zealand cohort require replication in other parts of the world. However, there is reason to believe that these findings about the effect of childhood social isolation may be generalizable to other settings, given that our findings about the significance of other well-established childhood risk factors for poor adult health (eg, low childhood SES and childhood overweight) are consistent with findings reported from North American and European population-based studies.[48] Third, we do not know whether these findings can be generalized to all ethnic groups.

The findings from the present study underscore the usefulness of a life-course approach to health research.[8] The influence of psychosocial risk factors on the course of coronary artery disease is now well documented.[49] However, adult risk factors are the target of most research into the effect of psychosocial risk factors on poor adult health and on the pathogenesis of cardiovascular disease in particular. In contrast, a life-course perspective focuses attention on the effect of the developmental timing of psychosocial factors on adult health.[50,51] The findings from this longitudinal, observational study of children followed up from childhood to adulthood suggest that social isolation has persistent and cumulative effects on poor adult health. The findings appear to meet several criteria suggestive of a causal association between social isolation and adult health[52]: social isolation preceded the outcome, the association between isolation and health appeared to be independent of a wide range of correlated risk factors, the findings were consistent with reports from studies of adults about the link between their social isolation and poor health, and there was evidence of a dose-response relationship between duration of exposure to social isolation and poor adult health. The epidemiologic evidence cannot identify the mechanisms involved but is consistent with emerging evidence that social isolation and social exclusion may have tangible neurobiological effects on lifelong development.[2,53,54]

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