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Physical and Sexual Abuse in Childhood as Predictors of Early-Onset Cardiovascular Events in Women

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Background—Although child abuse is widespread and has been associated with cardiovascular disease (CVD) risk factors, its association with CVD events is not established.

Methods and Results—We examined associations of child abuse with CVD events among 66 798 women in the Nurses' Health Study 2. Proportional hazards models estimated hazard ratios and 95% confidence intervals (CIs) for myocardial infarction (n=262), stroke (n=251), and total CVD (n=513). Severe physical abuse was reported by 9% and forced sex by 11% of participants. After adjustment for age, race, childhood body type, parental education, and family CVD history, the hazard ratios for CVD events were 0.91 (95% CI, 0.70–1.17) for mild physical abuse, 1.02 (95% CI, 0.82–1.26) for moderate physical abuse, and 1.46 (95% CI, 1.11–1.92) for severe physical abuse compared with no abuse. Compared with women without childhood sexual abuse, the hazard ratio was 1.10 (95% CI, 0.88–1.35) for unwanted sexual touching and 1.56 (95% CI, 1.23–1.99) for forced sex. After adjustment for adult lifestyle and medical risk factors, the hazard ratio for severe physical abuse was 1.13 (95% CI, 0.85–1.51) and that for forced sex was 1.25 (95% CI, 0.98–1.60); these intermediates accounted for much of the association of severe child abuse with CVD. Associations were similar for retrospectively and prospectively reported events. Women with abuse were less likely to release medical records. The associations were stronger for unconfirmed self-reported events than end points that were corroborated with additional information or medical record review.

Conclusion—Severe child abuse is a prevalent risk for early adult CVD that is partially mediated by preventable risk factors. (*Circulation*. 2012;126:920-927.)

Key Words: epidemiology ■ myocardial infarction ■ stroke ■ women ■ violence

Cardiovascular disease (CVD) remains the leading cause of death and disability among women in the United States despite advances in treatment and secondary prevention.¹ Recognizing that CVD has roots in early life, the American Academy of Pediatrics now recommends that cardiovascular screening, prevention, and treatment begin in childhood.² Interventions to alter CVD risk in childhood require an understanding of the early social contexts that shape risk trajectories.³

Clinical Perspective on p 927

Physical abuse and sexual abuse are widespread and understudied early exposures that have been associated with adult obesity, hypertension, and diabetes mellitus.^{4–7} The National Violence Against Women (NVAWS) survey by the National Institute of Justice and the Centers for Disease Control and Prevention reported that 40% of women had been

physically assaulted by an adult caretaker and 9% had been raped before 18 years of age.⁸ Women and men surveyed by the Adverse Childhood Experiences (ACE) Study reported a 45% prevalence of physical and 21% prevalence of sexual abuse. Abuse of children by adults has remained stable over time.⁹

With 1 exception,¹⁰ existing studies examining child abuse and CVD risk have been limited by modest samples,^{11–13} retrospective design,^{11–15} and self-reported outcomes without medical record confirmation,^{11–15} making them susceptible to misclassification and recall bias. The 2 largest studies suggest that sexual abuse is associated with heart disease risk^{14,15}; one of them also reported an association of physical abuse with heart disease.¹⁴ The exceptional study that examined childhood adversity as a predictor of incident, confirmed CVD cases included 23 916 Finns. Although “serious conflicts in the family” and

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“fear of a family member” were considered, it is not clear the extent to which these exposures reflect child abuse.¹⁰

We tested whether early physical or sexual abuse is associated with CVD cases of various levels of confirmation. We compared the association in retrospectively versus prospectively reported data. We hypothesized that associations of early abuse with adult CVD would be partially mediated by adult lifestyle and medical risk factors. We used data from the Nurses’ Health Study 2 (NHS2), a longitudinal cohort of women from whom we collected data on lifetime abuse history in 2001 and for whom medical record–confirmed CVD events were available from 1989 through 2007.

Methods

Sample

The NHS2 cohort includes 116 430 registered nurses 25 to 42 years of age at the 1989 baseline. Participants are followed up by biennial questionnaires on risk factors and disease incidence. In 2001, a Violence Questionnaire was mailed to 91 297 participants, excluding those who had requested short questionnaires or required >4 mailings of the 1999 biennial questionnaire. Participants returned 68 376 Violence Questionnaires. The institutional review board of Partners Health Care System (Boston, MA) approved this study and accepted the return of the questionnaire as implied consent.

Participants contributed person-time from 1989 until their last returned questionnaire, CVD event, or the end of follow-up. Data were analyzed in 2011, after the 2007 questionnaire cycle was closed in 2009, and medical records for CVD events were obtained, reviewed, and coded. For the main analysis, we examined 513 cases of myocardial infarction (MI) and stroke that accrued from 1989 to 2007, the follow-up period during which self-reported cases were confirmed by the process described below. To assess potential recall bias, we examined subsets of 363 events that occurred before and 150 events that occurred after the Violence Questionnaire data were collected.

Exclusions

For the main analysis from 1989 to 2007, we excluded women who reported MI (n=272) or stroke (n=184) before the 1989 baseline questionnaire because events that occurred before baseline were not confirmed. At baseline (n=606) and throughout follow-up, women were censored at the report of cancer (except nonmelanoma skin cancer). We excluded 516 women missing data on childhood abuse, yielding 66 798 women in the main analysis.

Exposure Assessment

The Violence Questionnaire covers 3 time periods: up to 11 years of age, 11 to 17 years of age, and adulthood. We combined abuse before 18 years of age as childhood abuse. Adult experiences of abuse¹⁶ were used to exclude women for analysis of abuse that was limited to childhood. The derivation of abuse categories is described elsewhere¹⁷ and explained briefly here.

Physical abuse was assessed by the revised Conflict Tactics Scale, which queried specific acts of a parent, stepparent, or adult guardian.¹⁸ We created categories of physical abuse severity based on item factor loadings from principal-components factor analysis and the reported frequency of each abuse item.¹⁷ Physical abuse was categorized into 4 groups: no physical abuse (none); being “pushed, grabbed, or shoved” at any frequency or being “kicked, bitten, or punched” once or “hit with something” once (mild); being “hit with something” more than once or “physically attacked” once (moderate); being “kicked, bitten, or punched” or “physically attacked” more than once or ever “choked or burned” (severe).

Sexual abuse was measured by questions adapted from Finkelhor et al^{19,20}: “Were you ever touched in a sexual way by an adult or an older child or were you forced to touch an adult or an older child in a sexual way when you did not want to?” And “Did an adult or older child ever force you or attempt to force you into any sexual activity

by threatening you, holding you down, or hurting you in some way when you did not want to?” Exposure was categorized as no sexual abuse, unwanted sexual touching only, and forced sexual activity.

Cardiovascular End-Point Assessment

On the 1989 baseline questionnaire, participants indicated whether they had ever experienced physician-diagnosed “MI or angina” and “stroke (CVA [cerebrovascular accident]) or TIA [transient ischemic attack].” These baseline self-reports constituted exclusion criteria for the main analysis. For each biennial follow-up, participants were asked if they were diagnosed by a physician in the past 2 years as having “myocardial infarction (heart attack)” or “stroke (CVA) or TIA”; separate questions were posed regarding angina pectoris and coronary revascularization. Permission was requested from participants (or next of kin in the case of death) to review medical records after report of CVD events. Medical records were reviewed by physicians blinded to exposure status. MI was confirmed if it met the criteria of the World Health Organization based on symptoms plus diagnostic ECG changes or elevated cardiac enzyme concentrations.²¹ Stroke was classified by National Survey of Stroke criteria as a neurological deficit with sudden or rapid onset that persisted for >24 hours or until death.²² Cerebrovascular pathology resulting from infection, trauma, or malignancy was excluded, as were “silent” strokes discovered only by radiology.

We attempted to confirm self-reported CVD cases reported during study follow-up from 1989 to 2007. Events confirmed by medical records were designated as definite (n=340). Events for which confirmatory information was obtained by interview or letter but for which medical records could not be reviewed were designated as probable (n=173). We examined 3 levels of case confirmation: (1) the 2836 self-reported CVD events regardless of confirmation status or whether they occurred before or after 1989 baseline (to replicate the extant literature that has used unconfirmed self-reports), (2) the 513 probable or definite CVD cases occurring from 1989 to 2007 (combined to maximize statistical power as our main analysis), and (3) the 340 definite CVD cases occurring from 1989 to 2007 that were confirmed by blinded medical record review.

Covariates

Factors in early childhood were evaluated as potential confounders, including race/ethnicity (white, nonwhite), birth weight (5 categories), maternal and paternal history of MI or stroke before 60 years of age, maternal and paternal occupation (3 categories each), maternal and paternal education at the participant’s birth (years), home ownership when the participant was an infant, and aspects of high school diet (glycemic load, glycemic index, animal and vegetable fat consumption).²³ A somatogram scale at 5 years of age was used to estimate early childhood adiposity.²⁴ Recall of child somatogram scores is sufficiently accurate for epidemiological studies.²⁵

Cardiovascular risk factors arising after childhood were considered potential mediators because these factors may have been influenced by earlier abuse. Except when otherwise noted, these time-varying covariates were updated biennially, including adult body mass index (continuous; kg/m²), cigarette smoking (current, past, never), alcohol use (none, <15 g daily, ≥15 g daily), physical activity (5 categories, updated every 4 years), hypertension, type 2 diabetes mellitus, parity (0, 1), oral contraceptive use (current, past, never), hormone replacement therapy (premenopausal use, postmenopausal use, both), and aspects of diet (animal fat intake, vegetable fat intake, glycemic load, glycemic index, updated every 4 years). Lifetime depression status was first measured on the 2001 questionnaire as a positive response to both of these questions: “In your lifetime, have you ever had 2 weeks or longer when nearly every day you felt sad, blue, or depressed for most of the day?” and “Did you ever tell a doctor or mental health specialist that you were feeling depressed?” From the 2003 questionnaire onward, we considered depression to be an endorsement of clinician-diagnosed depression.

Statistical Analysis

We used Cox proportional hazards models to estimate hazard ratios (HRs) and 95% confidence intervals (CIs).²⁶ Global tests of the

Table 1. Age-Standardized* Characteristics of the Study Population by History of Childhood Physical and Sexual Abuse

	Physical Abuse				Sexual Abuse		
	None (n=31 122, 47%)	Mild (n=12 450, 19%)	Moderate (n=17 500, 26%)	Severe (n=5726, 9%)	None (n=44 517, 67%)	Sexual Touching Only (n=14 798, 22%)	Forced Sexual Activity (n=7483, 11%)
Age in 1989, y†	35 (5)	35 (5)	35 (5)	35 (5)	35 (5)	35 (5)	35 (5)
Maternal education, y‡	13 (2)	12 (2)	12 (2)	12 (2)	12 (2)	12 (2)	12 (2)
Paternal education, y‡	13 (3)	13 (2)	12 (3)	12 (3)	13 (2)	12 (3)	12 (3)
Body mass index at 18 y of age, kg/m ²	21 (3)	21 (3)	21 (3)	22 (4)	21 (3)	21 (3)	22 (4)
Body mass index in 1989, kg/m ²	24 (5)	24 (5)	24 (5)	25 (6)	24 (5)	24 (5)	25 (6)
Somatotype at 5 y of age§	2 (2–3)	2 (2–3)	2 (2–3)	2 (1–3)	2 (2–3)	2 (2–3)	2 (2–3)
White, %	95	95	93	93	95	93	93
Parental history of MI at <60 y of age, %	18	18	19	22	18	19	22
Parental history of stroke at <60 y of age, %	4	4	4	6	4	5	5
Daily alcohol consumption, %							
None	38	33	37	39	37	37	39
<15 g alcohol daily	59	63	59	57	61	59	58
≥15 g alcohol daily	3	3	3	4	3	3	3
Cigarette smoking status, %							
Never smoker	71	64	64	56	69	64	57
Past smoker	19	23	23	27	20	23	26
Current smoker	10	13	13	17	11	12	17
Exercise weekly, %	78	79	78	79	79	77	79
Ever depression, %#	25	31	34	48	26	35	45
Hypertension in 1989, %	5	5	5	7	5	5	7
Diabetes mellitus in 1989, %	<1	<1	<1	<1	<1	<1	1
Adult abuse, %	36	48	53	67	41	50	63
Childhood sexual abuse, %	26	34	39	57			
Childhood physical abuse, %					48	59	74

MI indicates myocardial infarction. Values are mean (SD) and mean (interquartile range) as appropriate.

*Values are standardized to the age distribution of the study population. Values do not add to 100% because of missing values. Fewer than 2% were missing any given variable, with the exception of maternal (11.5% missing) and paternal (12.7% missing) education.

†Value is not age adjusted.

‡Mean years of education at the time of the participant's birth, reported in 2005.

§Median somatogram score at age 5 year of age; range is 0 to 9.

#Lifetime depression reported in 2001.

association of physical and sexual abuse were conducted by a likelihood ratio test comparing nested models with and without abuse parameters. Factors that preceded childhood abuse and were theoretically or empirically associated with abuse and cardiovascular risk were retained in the models, including race, parental education at the time of the participant's birth, somatotype at 5 years of age, and parental CVD history. This model including potential confounders that preceded the exposure is our main model. Lifestyle and CVD risk factors arising in adulthood were tested as potential mediators of the childhood abuse and CVD associations by examining the extent to which their inclusion in models diminished the abuse effect estimates. The proportion of the abuse association potentially explained by adult covariates was estimated with the SAS macro of Spiegelman as the mediation proportion with 95% CI.^{27,28}

Results

Table 1 summarizes characteristics by child abuse history. Overall, 65% of women reported some abuse, predominately mild physical abuse or unwanted sexual touching. However, 9% reported severe physical abuse and 11% reported forced sex; 17% experienced either severe physical or sexual abuse.

A history of abuse was associated with higher adult body mass index, cigarette smoking, depression, and intimate partner violence in adulthood. Parents of women reporting abuse had less education and were more likely to have suffered early CVD events.

From 1989 through 2007, there were 513 definite or probable CVD events, including 262 MIs and 251 strokes. The details of case confirmation status are presented in Table 2 by abuse history. Increasing severity of physical abuse was associated with a lower likelihood that a CVD case was confirmed by study staff; this was driven by a tendency of participants with a history of physical abuse to deny access to medical records. Differences in case confirmation status across sexual abuse history were weak and lacked statistical significance.

Compared with women reporting no history of childhood physical abuse, those who reported experiencing physical abuse in childhood were at increased risk of CVD events ($P=0.03$, adjusted for childhood risk factors). This was driven by an association of severe physical abuse with CVD; women report-

Table 2. Percent of Cardiovascular Disease Cases With Various Degrees of Case Confirmation Status for Cases Reported From 1989 to 2007 by History of Child Abuse, Nurses' Health Study 2

	Probable Cases: On Recontact or Participant- Kin-Confirmed Questionnaire Report of CVD, but Case Was Not Definite Because:				
	Definite Cases Confirmed by Medical Record Review, %	Confirmed Only by Death Certificate Autopsy Report, %	Medical Records Unavailable, %	Too Little Information From Participant to Retrieve Records, %	Participant Denied Permission to Review Records, %
Physical abuse					
None	72	0	10	8	10
Mild	65	0	10	9	17
Moderate	66	0	9	9	16
Severe	50	1	12	6	31
<i>P</i> *	0.009	0.09	0.96	0.91	0.0006
Sexual abuse					
None	66	0	12	8	15
Sexual touching	72	0	7	8	13
Forced sex	59	1	8	10	22
<i>P</i> *	0.14	0.09	0.23	0.70	0.22

CVD indicates cardiovascular disease.
 * χ^2 Test across abuse categories. The *P* value across all confirmation status categories was 0.01 for physical abuse and 0.15 for sexual abuse.

ing mild or moderate physical abuse were not at increased CVD risk (Table 3). The 9% of women reporting severe physical abuse were at a 46% higher risk of adult CVD events after childhood risk factors were accounted for (model 2). Further adjustment for lifestyle and medical risk factors arising in adulthood, particularly adult body mass index, hypertension, and diabetes mellitus, attenuated the association of severe physical abuse with CVD risk (model 3). The estimated mediation proportion indicated that adult risk factors accounted for as

much as 79% (95% CI, 25–98) of the association of severe childhood physical abuse and risk of CVD.

Women who had experienced sexual abuse had increased risk of CVD events (*P*=0.002, adjusted for childhood risk factors). This elevated risk was apparent only for the 11% of women who reported forced sex in childhood, who experienced a 56% increased risk of adult CVD after adjustment for childhood risk factors (model 2). As with physical abuse, the association of forced sex with adult CVD was attenuated by

Table 3. Adjusted Hazard Ratios (95% Confidence Intervals) for the Association of Physical and Sexual Abuse in Childhood With Risk of Cardiovascular Events in Adulthood, Nurses' Health Study 2, 1989 to 2007

	Cases, n (person-y)	Hazard Ratio (95% Confidence Interval)		
		Model 1: Adjusted for Age	Model 2: Adjusted for Age and Childhood Covariates Preceding Abuse*	Model 3: Model 2 Plus Adult Covariates†
Physical abuse				
None	226 (537 165)	1.00	1.00	1.00
Mild	82 (214 508)	0.91 (0.71–1.18)	0.91 (0.70–1.17)	0.87 (0.68–1.13)
Moderate	137 (301 260)	1.06 (0.85–1.31)	1.02 (0.82–1.26)	0.93 (0.74–1.15)
Severe	68 (97 860)	1.59 (1.21–2.08)	1.46 (1.11–1.92)	1.13 (0.85–1.51)
<i>P</i> ‡		0.006	0.03	0.40
Sexual abuse				
None	306 (767 975)	1.00	1.00	1.00
Sexual touching	119 (254 752)	1.13 (0.91–1.40)	1.10 (0.88–1.35)	1.02 (0.82–1.27)
Forced sex	88 (128 066)	1.71 (1.35–2.17)	1.56 (1.23–1.99)	1.25 (0.98–1.60)
<i>P</i> ‡		0.0002	0.002	0.22

*Model 2 is adjusted for age, race, age 5 somatotype, parental education, and parental myocardial infarction or stroke.
 †Model 3 is adjusted for variables in model 2 plus adult body mass index, smoking, alcohol use, depression, intimate partner violence, quintiles of animal fat consumption, vegetable fat consumption, glycemic index in high school and updated throughout adulthood, oral contraceptive use, parity, menopausal status, postmenopausal hormone use, physical activity, and incident hypertension and diabetes mellitus.
 ‡*P* value for differences across abuse categories derived from a likelihood ratio test contrasting nested models with and without the set of abuse covariates.

Table 4. Adjusted* Hazard Ratios (95% Confidence Intervals) for the Association of Abuse in Childhood With Risk of Cardiovascular Events in Adulthood by Follow-Up Period, Nurses' Health Study 2

CVD Model 2	Total, 1989–2007 (513 Cases)	Retrospective,† 1989–2003 (363 Cases)	Prospective,† 2003–2007 (150 Cases)
Physical abuse			
None	1.00	1.00	1.00
Mild	0.91 (0.70–1.17)	1.05 (0.78–1.40)	0.60 (0.36–1.03)
Moderate	1.02 (0.82–1.26)	1.01 (0.78–1.31)	1.04 (0.71–1.52)
Severe	1.46 (1.11–1.92)	1.51 (1.09–2.09)	1.35 (0.81–2.24)
<i>P</i> ‡	0.03	0.11	0.09
Sexual abuse			
None	1.00	1.00	1.00
Sexual touching	1.10 (0.88–1.35)	1.06 (0.82–1.37)	1.19 (0.80–1.75)
Forced sex	1.56 (1.23–1.99)	1.53 (1.14–2.03)	1.66 (1.06–2.58)
<i>P</i> ‡	0.002	0.02	0.10

*Adjusted for age, race, somatotype at 5 years of age, parental education, and parental myocardial infarction or stroke.

†Retrospective analysis includes follow-up time through May 2003; exposures and cardiovascular disease events could have preceded violence reports during this period. Prospective analysis includes follow-up time and incident events after May 2003, after all violence reports had been collected.

‡*P* value for differences across abuse categories derived from a likelihood ratio test contrasting nested models with and without the set of abuse covariates.

adjustment for adult risk factors. As much as 63% (95% CI, 39–82) of the association of forced sex with CVD risk was explained by adult covariates.

Most women who reported severe physical abuse also reported sexual abuse and vice versa (Table 1). The association of severe physical abuse with CVD events after adjustment for sexual abuse (and covariates in model 2) was 1.30 (95% CI, 0.97–1.73), and the association for forced sex after adjustment for physical abuse was 1.47 (95% CI, 1.14–1.89).

Childhood abuse was associated with an increased likelihood of adult abuse (Table 1). For women who reported no adult abuse, among whom there were 233 CVD events, severe physical abuse in childhood was associated in model 2 with an HR of 1.86 (95% CI, 1.18–2.91), and forced sexual activity in childhood was associated with an HR of 1.67 (95% CI, 1.09–2.53).

The comparison of the retrospective analysis (events reported before the Violence Questionnaire) and prospective analysis (events occurring after the Violence Questionnaire) in Table 4 shows similar patterns of elevated CVD risk for the more severe forms of child abuse, albeit with less statistical power in the shorter prospective follow-up period. The findings for forced sex were somewhat stronger in the prospective analysis; the findings for severe physical abuse were somewhat stronger in the retrospective analysis.

Table 5 repeats the analysis with various levels of CVD case confirmation status. Associations of abuse with CVD events were stronger when we considered all 2836 self-reported CVD cases. Associations were intermediate for the combined group of 513 definite and probable cases documented as described above. Findings were weakest when restricted to the 340 cases that we were able to confirm by record review. Notably, the analysis of all self-reported end

points yielded associations of moderate and severe abuse with CVD events.

We examined associations of abuse separately for definite and probable MI (n=262) and stroke (n=251), presented in Table I in the online-only Data Supplement. Although physical abuse was unassociated with increased risk of MI, there was a suggestion of an increased risk of MI among women with a history of forced sex in childhood (HR, 1.36; 95% CI, 0.96–1.93). Severe physical abuse and sexual abuse were each associated with increased risk of stroke, with HRs of 1.86 (95% CI, 1.29–2.68) for severe physical abuse and 1.82 (95% CI, 1.31–2.54) for forced sex.

Discussion

The 17% of women who experienced severe physical or sexual abuse in childhood had 46% to 56% higher risks of cardiovascular events in early adulthood after adjustment for childhood CVD risk factors. Adult risk factors known to be associated with early abuse, including adult experiences of intimate partner violence, smoking, body mass index, hypertension, diabetes mellitus, and depression, accounted for as much as 60% to 80% of the associations of severe early abuse with CVD risk. This suggests that a large portion of the association of childhood abuse with adult CVD risk could be eliminated or reduced by targeted prevention efforts that have been successful in reducing CVD incidence among US women.¹

The structure of our data set allowed us to examine several methodological questions. Similar results of prospectively and retrospectively reported cases (Table 4) indicate that recall bias is unlikely to explain the associations. However, examination of all self-reported disease yielded considerably stronger associations than did examination of cases confirmed by additional data or medical record review. There could be several reasons for this gradient across case confir-

Table 5. Adjusted* Hazard Ratios (95% Confidence Intervals) for the Association of Abuse in Childhood With Risk of Cardiovascular Events in Adulthood by Case Confirmation Status, Nurses' Health Study 2

CVD Model 2	All Lifetime Self-Reports (n=2836 Cases)	Probable and Definite Cases 1989–2007 (n=513 Cases)	Definite Cases, 1989–2007 (n=340 Cases)
Physical abuse			
None	1.00	1.00	1.00
Mild	1.08 (0.97–1.21)	0.91 (0.70–1.17)	0.81 (0.60–1.11)
Moderate	1.31 (1.20–1.44)	1.02 (0.82–1.26)	0.94 (0.73–1.22)
Severe	2.04 (1.83–2.29)	1.46 (1.11–1.92)	1.03 (0.71–1.49)
P†	<0.0001	0.03	0.58
Sexual abuse			
None	1.00	1.00	1.00
Sexual touching	1.26 (1.15–1.37)	1.10 (0.88–1.35)	1.19 (0.92–1.53)
Forced sex	2.07 (1.88–2.28)	1.56 (1.23–1.99)	1.44 (1.06–1.96)
P†	<0.0001	0.002	0.06

CVD indicates cardiovascular disease.

*Adjusted for age, race, somatotype at 5 years of age, parental education, and parental myocardial infarction or stroke.

†P value for differences across abuse categories derived from a likelihood ratio test contrasting nested models with and without the set of abuse covariates.

mation status. There was less statistical power to examine confirmed cases. Alternatively, the stronger estimates for the unconfirmed cases reported at baseline in 1989 could result from early, prebaseline CVD events of women with a history of child abuse. However, such “attrition of susceptibles” over time seems a less likely explanation than simple differences by case confirmation status, especially because we observed contrasts between probable and definite cases and definite cases observed over the same follow-up period (1989–2007). Women with a history of childhood physical abuse tended to deny permission to review medical records (Table 2), precluding their classification as definite cases. Unfortunately, it is unclear whether risk estimates based on probable and definite cases or only definite cases best reflect the association of abuse history with CVD risk: On the one hand, restriction to women willing to release records could induce a bias to the null if that restriction eliminates the very women whose abuse history is severe enough to affect CVD risk; on the other hand, the restriction to medically confirmed cases could be an appropriate way to eliminate any tendency of abused women to overreport disease outcomes. Because analyses restricted to definite, record-confirmed CVD events in women exposed to severe physical abuse were null, the findings for physical abuse cannot be considered robust. However, the increased risk of CVD with forced sex was consistent and statistically significant, even with the strictest case confirmation status.

Our findings are generally consistent in direction, if not magnitude, with 2 large studies of child abuse.^{14,15} Differences between studies in assessment of abuse exposures and CVD outcomes make close comparisons problematic. The present study included 66 798 women 43 to 60 years of age at the end of follow-up, of whom 0.8% experienced CVD events confirmed by corroborating medical information or records. The ACE study included 17 337 men and women 56 years of age on

average, of whom 10.6% reported a history of ischemic heart disease in response to queries on history of heart attack, chest pain, or heavy chest pressure with exertion or the use of nitroglycerine.¹⁴ Self-reports of ischemic heart disease were not confirmed. The focus of the ACE study is a 10-item childhood trauma score that includes 2 items on physical abuse and 2 items on sexual abuse. Results were not stratified by sex. Our finding of a 46% increased risk of CVD events with severe physical abuse appears to agree with the ACE report of 50% (95% CI, 40–90) increased risk of ischemic heart disease with physical abuse, although in our data the association of physical abuse with CVD was driven by a stronger association with stroke than with MI. The ACE study estimated a 40% (95% CI, 30–60) increased ischemic heart disease risk among individuals who experienced either sexual touching or intercourse; this appears to be intermediate between our null estimate for sexual touching and 56% increased risk of CVD with forced sex. Again, we observed stronger associations of sexual abuse with stroke than with MI.

The National Comorbidity Survey (NCS) questioned 5877 men and women 15 to 54 years of age; 0.4% of women endorsed an item regarding “heart attack or serious heart trouble” in the past 12 months.¹⁵ There was little evidence that women who indicated that they had been “physically abused as a child” were more likely to report heart disease; on the other hand, women who reported a history of child or adolescent “rape or sexual molestation” were 5 times more likely to report heart disease.¹⁵ Our estimates for sexual abuse are consistent in direction with those of the NCS, although much smaller in magnitude.

The only study to examine exclusively confirmed events in a prospective analysis, the Health and Social Support (HeSSup) study in Finland, was focused on child adversities as a whole rather than on child abuse in particular.¹⁰ Among the roughly 14 000 women studied, there were 91 CVD events. The risk

of CVD events increased with the number of childhood adversities reported. When the adversity score was dissected into its components, the “serious conflicts in the family” item was associated with an age-adjusted HR for CVD of 1.71 (95% CI, 1.07–2.73). However, “fear of a family member” was associated with an HR of 1.33 (95% CI, 0.79–2.23). As in our study, adjustment for adult CVD risk factors attenuated these estimates. Although these exposures do not correspond directly to physical and sexual child abuse, they do suggest that childhood social environment is associated with adult CVD risk and that much of this association is mediated by preventable risk factors that are elevated in women with a history of childhood adversity.

Several strengths of the present study are notable. We were able to examine CVD events variously self-reported by nurses, corroborated by additional details, and/or confirmed by medical record review. The fact that some associations were weaker when restricted to definite cases suggests that the use of unconfirmed self-reports may overestimate associations of abuse with CVD risk. Previous studies have been too small to permit more fine-grained examination of severity of abuse. In contrast, the NHS2 cohort is several times larger than the next largest study; distinguished between mild, moderate, and severe abuse; examined CVD events that were confirmed by medical record or other evidence; and tested whether associations were similar among cases that occurred before and after the abuse assessment, permitting evaluation of the potential role of recall bias. Another strength that distinguishes the present study is the 18 years of prospectively collected data on risk factors such as family history, socioeconomic position, smoking, body mass index, hypertension, and diabetes mellitus that enabled testing of confounders and intermediates.

Like most large abuse studies, our participants self-reported their abuse history. We used instruments used by national surveys^{18,19} that reduce bias by querying specific acts of violence rather than nominal questions on “abuse” or “rape.”²⁹ The alternative to self-report is police, court, or other administrative records of abuse. However, only the minority of child abuse cases are reported to authorities; officially documented abuse cases are almost certainly a nonrandom sample of all cases; and it is impractical, if not impossible, to assemble a cohort of documented abuse cases large enough (and long ago enough) to study CVD end points. Given these issues, self-report is the gold standard abuse measurement for large cohort studies. The nurses in our cohort reported somewhat more mild and moderate abuse than women in the NVAWS telephone survey.⁸ The NHS2 abuse prevalence is similar to that reported by ACE study, suggesting that survey methodology may explain some discrepancies.

We did not document other childhood neglect or traumas such as marital discord, mental illness, or criminal activity in the home. Such factors are correlated with child abuse and are also associated with CVD risk.^{10,14,15} In this analysis, we did not consider emotional abuse. The NHS2 participants are predominantly white women with at least a college degree. Our findings need to be replicated in more diverse settings to determine their generalizability. Finally, because participants were 43 to 60 years of age at the end of follow-up, these

findings pertain to early CVD; further follow-up is necessary to determine whether early abuse also predicts CVD during the peak incidence period.

Several lines of evidence suggest that abuse in early life may increase cardiovascular risk. Preclinical and clinical studies demonstrate profound and lasting effects of early stress on the hypothalamic-pituitary-adrenal and noradrenergic stress systems, including heightened glucocorticoid, norepinephrine, and autonomic stress reactivity, as well as altered dopaminergic and serotonergic function.^{30–34} Survivors of childhood sexual abuse have increased heart rate and blood pressure response to cognitive and social challenges.³⁵ Supporting, if indirect, evidence that abuse increases cardiovascular risk can be drawn from literature on posttraumatic stress disorder, which is prevalent among abused women³⁶ and is associated with increased risks of coronary heart disease,³⁷ smoking,^{38–41} overweight,⁴² dyslipidemia,⁴³ diabetes mellitus,⁴⁴ hypertension,⁴⁵ and possibly inflammation.⁴⁶ This is consistent with literature that documents increased adiposity,^{6,7} hypertension,⁴ diabetes mellitus,⁵ and smoking^{38–41} with a history of child abuse.

Studies consistently document widespread physical and sexual abuse of children and adolescents. Early abuse is associated with behavioral and physiological risk factors for CVD. The evidence is now growing that early abuse, especially sexual abuse, also predicts CVD events in adulthood. However, our findings suggest that this field may be vulnerable to differential reporting of disease end points by abuse status. We need to understand the complex physiological and behavioral pathways through which abuse leads to true CVD events so that interventions that aim to alter CVD risk trajectories from childhood can be maximally effective.

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Disclosures

None.

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CLINICAL PERSPECTIVE

Women with a history of severe sexual abuse in childhood are at increased risk for cardiovascular disease as adults. Severe physical abuse may also increase risk of future cardiovascular disease. More than 10% of women have a history of severe physical or sexual abuse as girls. A large proportion of the cardiovascular disease risk associated with child abuse is explained by adverse lifestyle and medical risk factors for cardiovascular disease in adulthood among women abused as children. This suggests that targeted prevention and treatment of risk factors would reduce the incidence of cardiovascular disease in this high-risk population. Future research should examine whether specialized therapies can be developed to help girls and women with a history of child abuse reduce their cardiovascular risk.

SUPPLEMENTAL MATERIAL

Supplemental Table. Adjusted hazard ratios (95% confidence interval) for the association of abuse in childhood with risk of myocardial infarction and stroke in adulthood, Nurses' Health Study 2, 1989-2007

	Myocardial Infarction			Stroke		
	Cases Person- Years	Model 1: Adjusted for age	Model 2: Adjusted for age, race, age 5 somatotype, parental education, and parental MI or stroke	Cases Person- Years	Model 1: Adjusted for age	Model 2: Adjusted for age, race, age 5 somatotype, parental education, and parental MI or stroke
Physical Abuse						
None	117 537,949	1.00	1.00	109 537,862	1.00	1.00
Mild	43 214,765	0.93 0.65-1.32	0.92 0.65-1.31	39 214,794	0.90 0.62-1.29	0.89 0.61-1.28
Moderate	75 301,642	1.10 0.82-1.47	1.06 0.79-1.42	62 301,745	1.01 0.74-1.38	0.98 0.72-1.35
Severe	27 98,137	1.22 0.80-1.85	1.11 0.73-1.69	41 97,997	1.99 1.38-2.85	1.86 1.29-2.68
p-value*		0.57	0.69		0.004	0.01
Sexual Abuse						
None	159 768,997	1.00	1.00	147 768,995	1.00	1.00
Sexual touching	62 255,116	1.13 0.84-1.52	1.09 0.81-1.47	57 255,136	1.13 0.83-1.53	1.10 0.81-1.50
Forced sex	41 128,380	1.52 1.07-2.15	1.36 0.96-1.93	47 128,267	1.92 1.38-2.67	1.82 1.31-2.54
p-value*		0.05	0.18		0.001	0.003

* p-value for differences across abuse categories, derived from a likelihood ratio test contrasting nested models with and without the set of abuse covariates