

Childhood Adversities and Adult Psychiatric Disorders in the National Comorbidity Survey Replication I

Associations With First Onset of DSM-IV Disorders

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Context: Although significant associations of childhood adversities (CAs) with adult mental disorders have been documented consistently in epidemiological surveys, these studies generally have examined only 1 CA per study. Because CAs are highly clustered, this approach results in overestimating the importance of individual CAs. Multivariate CA studies have been based on insufficiently complex models.

Objective: To examine the joint associations of 12 retrospectively reported CAs with the first onset of DSM-IV disorders in the National Comorbidity Survey Replication using substantively complex multivariate models.

Design: Cross-sectional community survey with retrospective reports of CAs and lifetime DSM-IV disorders.

Setting: Household population in the United States.

Participants: Nationally representative sample of 9282 adults.

Main Outcome Measures: Lifetime prevalences of 20 DSM-IV anxiety, mood, disruptive behavior, and substance use disorders assessed using the Composite International Diagnostic Interview.

Results: The CAs studied were highly prevalent and intercorrelated. The CAs in a maladaptive family functioning (MFF) cluster (parental mental illness, substance abuse disorder, and criminality; family violence; physical abuse; sexual abuse; and neglect) were the strongest correlates of disorder onset. The best-fitting model included terms for each type of CA, number of MFF CAs, and number of other CAs. Multiple MFF CAs had significant subadditive associations with disorder onset. Little specificity was found for particular CAs with particular disorders. Associations declined in magnitude with life course stage and number of previous lifetime disorders but increased with length of recall. Simulations suggest that CAs are associated with 44.6% of all childhood-onset disorders and with 25.9% to 32.0% of later-onset disorders.

Conclusions: The fact that associations increased with length of recall raises the possibility of recall bias inflating estimates. Even considering this, the results suggest that CAs have powerful and often subadditive associations with the onset of many types of largely primary mental disorders throughout the life course.

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SIGNIFICANT ASSOCIATIONS between retrospectively reported childhood adversities (CAs) and adult illness have been documented in numerous studies.^{1,2} The first such studies focused on only a single CA, such as

*See also pages 111
and 124*

parental death or neglect,^{3,4} and 1 mental disorder, most often depression.^{5,6} Subsequent studies showed that retrospectively reported CAs are often highly clustered,^{7,8} requiring examination of multiple CAs to avoid overestimating asso-

ciations involving particular CAs.^{2,9,10} These studies also found that CAs are often non-specific in their associations with many different mental disorders,¹⁰⁻¹² making it useful to examine multiple outcomes to avoid overly narrow interpretations.

Subsequent studies¹³⁻¹⁵ created summary CA scales and documented dose-response relationships with adult outcomes. However, such indices implicitly assumed that each CA has the same effect and that joint effects are additive. These assumptions are almost certainly incorrect.¹⁶ Indeed, a preliminary examination of these assumptions in the National Comorbidity Survey (NCS)¹⁷ showed that some CAs have stronger associations with

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adult outcomes than do others and that joint associations are nonadditive.¹⁰ That study also found that these associations sometimes attenuate with age, a specification generally, but not always,^{12,18} ignored in subsequent studies.

The present study builds on these earlier NCS findings by analyzing the CAs assessed in the NCS Replication (NCS-R).¹⁹ Associations between retrospectively reported CAs and mental disorders can be upwardly biased owing to recall failure, nevertheless, it is useful to examine associations based on such retrospective data because they provide upper estimates that avoid the problem of downward bias due to systematic sample attrition in estimates based on long-term prospective data. We examine associations of CAs with the first onset of diverse DSM-IV disorders based on several competing multivariate models. A companion study²⁰ examines associations of CAs with lifetime persistence of the same disorders.

METHODS

SAMPLE

The NCS-R is a face-to-face survey of English-speaking adults performed between February 5, 2001, and April 7, 2003, in a multistage clustered area probability sample of the US household population.¹⁹ The response rate was 70.9%. Recruitment began with a letter and a study fact brochure followed by in-person interviewer visits to explain study aims and procedures before obtaining informed consent. Respondents were paid \$50 for participation. Recruitment and consent procedures were approved by the human subjects committees of Harvard Medical School, Boston, Massachusetts, and the University of Michigan, Ann Arbor.

The survey was administered in 2 parts. Part I included a core diagnostic assessment and was administered to all the respondents (n=9282). Part II, which was generally administered on the same occasion as part I, included questions about correlates and additional disorders administered to all part I respondents who met lifetime criteria for any part I disorder plus a probability subsample of other part I respondents (n=5692). The part I sample was weighted to adjust for differential probabilities of selection and intensity of recruitment effort in hard-to-recruit cases. The part II sample, the focus of the present study, was additionally weighted for the lower selection probabilities of part I respondents without a mental disorder. A final weight adjusted the sample to match the 2000 census population on the cross-classification of numerous geographic and sociodemographic variables. All the analyses used these weights. As a result, the sociodemographic characteristics of the weighted part II sample closely match those of the population (eg, 42% female, 71% non-Hispanic white, 24% aged 18-29 years, and 21% ≥60 years old). More detailed information on NCS-R sampling, design, weighting, and sociodemographic distribution is reported elsewhere.²¹

DIAGNOSTIC ASSESSMENT

The NCS-R lifetime diagnoses are based on the World Health Organization Composite International Diagnostic Interview (CIDI),²² a fully structured, lay-administered interview that generates diagnoses according to the definitions and criteria of the *International Classification of Diseases, 10th Revision* and the DSM-IV. The DSM-IV criteria are used herein. The lifetime di-

agnoses include 4 broad classes of 20 specific disorders: mood disorders (major depressive disorder, dysthymic disorder, bipolar I disorder, bipolar II disorder, and subthreshold bipolar disorder), anxiety disorders (panic disorder, agoraphobia without a history of panic disorder, generalized anxiety disorder, specific phobia, social phobia, posttraumatic stress disorder, and separation anxiety disorder), disruptive behavior disorders (intermittent explosive disorder, attention-deficit/hyperactivity disorder, oppositional-defiant disorder, and conduct disorder), and substance use disorders (alcohol abuse, alcohol dependence with abuse, drug abuse, and drug dependence with abuse). Diagnostic hierarchy rules and organic exclusion rules were used in making diagnoses. The DSM-IV/CIDI disorder prevalence estimates in sociodemographic subsamples are reported elsewhere (<http://www.hcp.med.harvard.edu/ncs>). An NCS clinical reappraisal study²³ found generally good concordance between diagnoses based on the CIDI and those based on blinded clinical reinterviews using the Structured Clinical Interview for DSM-IV.²⁴

The CIDI assessed age at onset of the disorder retrospectively. Based on evidence that retrospective age-at-onset reports are often erroneous,²⁵ a special question sequence was used to improve the accuracy of reporting. This began with questions designed to emphasize the importance of accurate responses: "Can you remember your exact age the *very first time* [emphasis in original] when you had [the symptom/the syndrome]?" Respondents who answered "no" were then probed for a bound of uncertainty by asking the earliest age at which they could clearly remember having the disorder. Onset was set at the upper end of the bound of uncertainty. Experimental research²⁶ has shown that this approach yields more plausible age-at-onset distributions than do standard age-at-onset questions.

CHILDHOOD ADVERSITIES

Twelve dichotomous CAs occurring before age 18 years were assessed in the NCS-R. The selection of CAs was based on a review of the literature. These CAs include 3 types of interpersonal loss (parental death, parental divorce, and other separation from parents or caregivers), 4 types of parental maladjustment (mental illness, substance abuse, criminality, and violence), 3 types of maltreatment (physical abuse, sexual abuse, and neglect), and 2 other CAs (life-threatening childhood physical illness in the respondent and extreme childhood family economic adversity). The measures of parental death, divorce, and other separation (eg, respondent placed in foster care) focus only on the biological parents, not on stepparents or other caregivers. Respondents who were born to a single mother and never experienced any further disruption of this parenting arrangement were coded as not experiencing any parental separation. We did not include information about the number of caregiver disruptions (eg, multiple divorces) or separations (eg, multiple foster care placements) but rather coded respondents dichotomously as having any vs no such disruptions because the rarity of multiple disruptions made estimates of dose-response relationships unstable.

Parental criminality, family economic adversity, and sexual abuse were assessed using a short question series developed for the baseline NCS.¹⁰ Parental criminality was assessed using questions about whether a parent either engaged in criminal activities, such as burglary or selling stolen property, or was ever arrested for criminal activity. Economic adversity was assessed using questions about whether the family received welfare or other government assistance and whether the family often lacked enough money to pay for the basic necessities of living. Sexual abuse was assessed using questions about repeated fondling, attempted rape, and rape. Parental mental

illness (major depression, generalized anxiety disorder, and prior to panic disorder) and substance abuse were assessed using the Family History Research Diagnostic Criteria interview²⁷ and its extensions.²⁸ Family violence and physical abuse of the respondent by parents were assessed using a modified version of the Conflict Tactics Scales.²⁹ Neglect was assessed using questions used in studies of child welfare about the frequency of not having adequate food, clothing, or medical care; having inadequate supervision; and having to do age-inappropriate chores.³⁰ Life-threatening physical illness was assessed using a standard chronic conditions checklist.³¹

ANALYSIS METHODS

Tetrachoric factor analysis (promax rotation) was used to examine intercorrelations among CAs. Associations of CAs with lifetime disorders were estimated using discrete-time survival analysis, with person-years as the unit of analysis,³² controlling for respondent age at interview, sex, race/ethnicity (non-Hispanic white, non-Hispanic black, Hispanic, and other), and other DSM-IV/CIDI disorders with onset before the age at onset of the disorder under investigation and before age 18 years. The controls for early-onset disorders were included to adjust for the associations of CAs with temporally secondary disorders through earlier-onset disorders that affected secondary disorders. Person-years began at age 4 years, the youngest age evaluated for possible disorder onset. Person-years were coded "0" on the dependent variables until the age at onset and "1" at the year of onset and were censored after the year of onset. Several multivariate models were estimated, with each including dummy predictor variables for CAs plus controls. The first model was additive; that is, it included a separate predictor variable for each of the 12 CAs without interaction terms. The second multivariate model included predictor variables for number of CAs without variables for types of CAs experienced. A third model included 12 predictors for type of CA and additional predictors for number of CAs, with the latter starting at exactly 2 rather than 1 because the variable for exactly 1 CA was perfectly predicted by the 12 dummy variables for the individual CAs. A variant of this third model distinguished between 2 types of CAs as described in the "Associations of CAs With the First Onset of DSM-IV/CIDI Disorders" subsection. Another variant included interactions between types of CAs and number of CAs. Finally, we considered more complex, inherently nonlinear models, but these did not improve on the fit of the simpler models and are consequently not discussed herein.

The Akaike information criterion³³ was used to select the best multivariate model for the overall data array (ie, the consolidated data file that stacked the 20 separate disorder-specific person-year files and included 19 dummy predictor variables to distinguish among these files, thereby forcing the estimated slopes of disorders on CAs to be constant across disorders). This best-fitting model was then estimated again in subsamples defined by disorder, class of disorder (mood, anxiety, disruptive behavior, and substance use disorders), life course stage, and the conjunction of life course stage with class of disorder. Survival coefficients and their standard errors were exponentiated and are reported as odds ratios (ORs) and 95% confidence intervals, respectively.

The population-attributable risk proportion (PARP) of the outcomes was computed for the best-fitting model. The PARP is the proportion of observed outcomes that would have been prevented in the absence of CAs if the ORs were due to causal effects of CAs.³⁴ In the more realistic case in which the associations of CAs with outcomes are partly due to common causes, the PARP reflects overall associations. All of the

PARPs were calculated using simulation methods to generate individual-level predicted probabilities of the outcome disorders from the coefficients in the best-fitting model with and without coefficients for CAs. The PARP is 1 minus the ratio of the predicted prevalence estimates in the 2 specifications. The PARP for a pooled data set is the average PARP across all disorders included in the calculation based on a constant model across disorders.

All statistical significance tests were evaluated using 2-sided tests ($P < .05$). Because the NCS-R data are clustered and weighted, the design-based Taylor series method³⁵ implemented in the SUDAAN software system³⁶ was used to estimate standard errors of ORs.

RESULTS

PREVALENCE AND CO-OCCURRENCE OF CAs

Approximately 53.4% of NCS-R respondents reported having at least 1 CA (**Table 1**). The most common CAs were parental divorce (17.5%), family violence (14.0%), family economic adversity (10.6%), and parental mental illness (10.3%). Multiple CAs were the norm in respondents with each CA, from 51.2% in those with death of a parent to 95.1% in those with parental neglect; there were a mean of 3.2 CAs in respondents with more than 1 CA.

Most tetrachoric correlations between pairs of CAs (94%) are positive. (Detailed results are available on request from the corresponding author.) Negative values are small (range, -0.09 to -0.01). Positive values have a median of 0.11 and an interquartile range (25th-75th percentiles) of 0.04 to 0.19. Factor analysis found 3 meaningful factors (Table 1). Most CAs have significant loadings on the first factor of maladaptive family functioning (MFF) (eg, parental substance abuse, criminality, domestic violence, and abuse and neglect), with factor loadings of 0.32 to 0.67. The second factor represents parental death and other loss with associated economic adversity (factor loadings, 0.50-0.67). The third factor represents parental divorce with associated economic adversity (factor loadings, 0.48-0.83). The CAs in factor 1 are referred to herein as MFF CAs and the remaining CAs as other CAs.

ASSOCIATIONS OF CAs WITH THE FIRST ONSET OF DSM-IV/CIDI DISORDERS

In the bivariate models (ie, only 1 CA considered at a time) of the pooled associations of CAs with the first onset of the 20 DSM-IV/CIDI disorders, all but 1 CA (parental death) was significant, with ORs of 1.5 to 1.9 for MFF CAs and 1.0 to 1.5 for other CAs (**Table 2**). The ORs are generally smaller in the additive multivariate model, with 8 CAs significant and ORs of 1.0 to 1.4 for MFF CAs and 1.0 to 1.3 for other CAs. The χ^2 test for associations of all CAs is significant ($\chi^2_{12} = 884.5$, $P < .001$), although the ORs are substantively modest. We can reject the hypothesis that the ORs are the same for all CAs ($\chi^2_{11} = 286.6$, $P < .001$).

The multivariate model that considers only number rather than type of CAs shows generally increasing ORs with number of CAs, from 1.3 for 1 CA (compared with

Table 1. Prevalence of Retrospectively Reported CAs and Promax-Rotated Tetrachoric Factor Loadings (Standardized Regression Coefficients) of CAs Based on a 3-Factor Model (n=5692)^a

	Individual CAs, % (SE)	Respondents With a Given CA Who Also Had ≥1 Other CA, % (SE)	CAs in Those With >1 CA, Mean No. (SE)	Factor (F) Loadings		
				F1 ^b	F2 ^c	F3 ^c
Interpersonal loss						
Parental death	9.9 (0.5)	51.2 (2.8)	3.1 (0.1)	-0.09	0.67	-0.34
Parental divorce	17.5 (0.8)	63.2 (2.2)	3.4 (0.1)	-0.02	0.00	0.83
Other parental loss	6.7 (0.4)	75.9 (2.7)	3.8 (0.1)	0.07	0.58	0.09
Family maladaptation						
Parental mental illness	10.3 (0.6)	71.7 (2.1)	3.9 (0.1)	0.62	-0.14	-0.20
Parental substance use	8.5 (0.5)	85.5 (1.5)	4.1 (0.1)	0.67	-0.14	-0.01
Parental criminality	7.2 (0.3)	85.3 (1.7)	4.1 (0.1)	0.51	-0.11	0.19
Family violence	14.0 (0.7)	86.6 (1.8)	3.8 (0.1)	0.59	0.10	0.18
Abuse and neglect						
Physical abuse	8.4 (0.5)	87.6 (2.4)	4.3 (0.1)	0.62	0.21	-0.09
Sexual abuse	6.0 (0.2)	72.3 (3.3)	4.1 (0.1)	0.32	0.19	-0.07
Neglect	5.6 (0.4)	95.1 (1.1)	4.6 (0.1)	0.59	0.24	-0.04
Other CAs						
Physical illness	5.8 (0.5)	60.7 (4.2)	3.3 (0.1)	0.14	0.10	-0.17
Economic adversity	10.6 (0.5)	83.4 (2.2)	3.5 (0.1)	-0.01	0.50	0.48
Any adversity	53.4 (1.2)	49.6 (1.1)	3.2 (0.0)			

Abbreviation: CA, childhood adversity.

^aCorrelations among factors: F1-F2: 0.15; F1-F3: 0.24; and F2-F3: 0.07.

^bFactor 1 refers to maladaptive family functioning CAs.

^cFactors 2 and 3 are combined and refer to other CAs.

respondents who had no CAs) to highs of 3.4 for 6 CAs and 3.2 for 7 or more CAs. The χ^2 test for the joint associations is significant ($\chi^2_7=822.0, P<.001$). The model that includes measures of types of CAs and number of CAs fits the data better than the previous models in terms of Akaike information criterion, as indicated by the types-of-CA measures being significant after controlling for number of CAs ($\chi^2_{12}=86.9, P<.001$) and the number of CAs measures being significant after controlling for types ($\chi^2_6=63.7, P<.001$). (Detailed results of model fitting are available on request from the author.) The hypothesis that the ORs are the same for all types of CAs can be rejected ($\chi^2_{11}=60.0, P<.001$). The MFF CAs consistently have higher ORs than do other CAs. The ORs associated with types are mostly higher than in the additive model, indicating that the additivity assumption led to a downward bias in the estimated associations of individual CAs with the outcome. The reason for this is that the ORs associated with number of CAs in the more complex model are for the most part less than 1.0 and become increasingly smaller as number of CAs increases. This means that although the odds of disorder onset increase with increasing number of CAs, they increase at a significantly decreasing rate.

We also evaluated more complex models but found that they generally did not fit as well as the model with types and number of CAs. One refinement did improve fit, although by distinguishing number of MFF CAs from number of other CAs. The significant subadditive interactions associated with number of CAs are found for MFF CAs ($\chi^2_6=61.7, P<.001$) but not for other CAs ($\chi^2_7=5.2, P=.16$). (The test had only 3 *df* because no respondents had all 5 MFF CAs.) This was the model used in subsequent disaggregated analyses.

DIFFERENTIAL ASSOCIATIONS BY CLASS OF DSM-IV/CIDI DISORDER

Disaggregation shows that CAs are significantly associated with the first onset of each class of disorders (mood, anxiety, disruptive behavior, and substance use). The ORs associated with types of CAs are always associated with increased odds ($\chi^2_{12}=44.5-193.7, P<.001$). Those for MFF CAs are more consistently significant ($\chi^2_7=38.2-115.2, P<.001$) than are those for other CAs ($\chi^2_5=7.4-57.5, P=.19$ to $<.001$) (**Table 3**). The ORs associated with number of CAs are always associated with decreased odds, although they are largely confined to MFF CAs ($\chi^2_6=19.4-50.9, P=<.001$ to $.004$).

Close inspection finds what seems to be meaningful variation in the ORs associated with some MFF CAs, such as parental criminality consistently having its lowest OR and parental substance abuse its highest OR predicting respondent substance use disorders. The more striking pattern, though, is that each MFF CA is significantly associated with each disorder class with rather consistent ORs. The ORs of other CAs are less consistent, with only 25% significant at $P<.05$. Again, there seems to be some meaningful variation, most notably family economic adversity and respondent physical illness associated with anxiety but not mood disorders, but these differences are not statistically significant.

DIFFERENTIAL ASSOCIATIONS BY LIFE COURSE STAGE AND NUMBER OF PREVIOUS DISORDERS

Disaggregation by life course stage (childhood: aged 4-12 years, adolescence: aged 13-19 years, early adulthood: aged 20-29 years, and middle-later adulthood: aged ≥ 30 years)

Table 2. Bivariate and Multivariate Associations Between CAs and the Subsequent First Onset of DSM-IV/CIDI Disorders (n=5692)^a

	OR (95% CI)			
	Bivariate ^b	Multivariate (Additive) ^c	Multivariate (No. of CAs) ^d	Multivariate (Interactive) ^e
Maladaptive family functioning CAs				
Parental mental illness	1.7 (1.5-1.8) ^f	1.3 (1.2-1.4) ^f	NA	1.4 (1.3-1.6) ^f
Parental substance abuse	1.8 (1.6-1.9) ^f	1.3 (1.2-1.4) ^f	NA	1.4 (1.2-1.6) ^f
Parental criminality	1.5 (1.4-1.7) ^f	1.0 (1.0-1.2)	NA	1.2 (1.0-1.4) ^f
Family violence	1.8 (1.7-2.0) ^f	1.4 (1.2-1.5) ^f	NA	1.5 (1.3-1.7) ^f
Physical abuse	1.8 (1.7-2.0) ^f	1.2 (1.1-1.4) ^f	NA	1.4 (1.2-1.6) ^f
Sexual abuse	1.8 (1.6-2.0) ^f	1.4 (1.3-1.6) ^f	NA	1.6 (1.4-1.9) ^f
Neglect	1.9 (1.7-2.1) ^f	1.2 (1.0-1.3) ^f	NA	1.4 (1.2-1.6) ^f
χ^2_7	NA	411.2 ^f	NA	59.0 ^f
Other CAs				
Parental death	1.0 (0.9-1.2)	1.0 (0.9-1.1)	NA	1.1 (0.9-1.2)
Parental divorce	1.1 (1.0-1.3) ^f	1.0 (0.9-1.1)	NA	1.1 (0.9-1.2)
Other parental loss	1.5 (1.4-1.6) ^f	1.2 (1.1-1.3) ^f	NA	1.3 (1.1-1.5) ^f
Physical illness	1.3 (1.2-1.5) ^f	1.3 (1.2-1.4) ^f	NA	1.4 (1.2-1.6) ^f
Economic adversity	1.3 (1.2-1.4) ^f	1.0 (0.9-1.1)	NA	1.1 (1.0-1.3)
χ^2_5	NA	31.7 ^f	NA	21.9 ^f
χ^2_{12}	NA	884.5 ^f	NA	86.9 ^f
No. of childhood adversities				
1	NA	NA	1.3 (1.2-1.5) ^f	NA
2	NA	NA	1.8 (1.6-2.0) ^f	1.1 (0.9-1.3)
3	NA	NA	1.9 (1.7-2.2) ^f	0.8 (0.6-1.1)
4	NA	NA	2.4 (2.1-2.7) ^f	0.8 (0.5-1.1)
5	NA	NA	2.8 (2.5-3.1) ^f	0.6 (0.4-1.0)
6	NA	NA	3.4 (2.8-4.1) ^f	0.6 (0.3-1.1)
≥7	NA	NA	3.2 (2.8-3.6) ^f	0.3 (0.2-0.7) ^f
χ^2_7	NA	NA	822.0 ^f	$\chi^2_6=63.7f$

Abbreviations: CA, childhood adversity; CI, confidence interval; CIDI, Composite International Diagnostic Interview; NA, not applicable; OR, odds ratio.

^aA separate person-year file was created for each of the 20 disorders, and these 20 files were then stacked. The models were estimated in a discrete-time survival framework with person-year as the unit of analysis using this stacked data set, thereby forcing the slopes to be constant across the 20 disorders. Each model controlled for person-year, age category, sex, 19 dummy variables for the outcome disorder category (ie, for the 20 disorders in the stacked data set), and controls for the previous onset of comorbid conditions that began up to age 17 years. The 5692 respondents had 11 047 disorder onsets, ranging from a low of 101 onsets for bipolar I disorder to a high of 1573 onsets for major depressive disorder. A total of 4 700 780 noncase (ie, not involving 1 of the 11 047 onsets) person-years existed across all disorders in the stacked data set. A 10% stratified probability subsample of these person-years was used as controls, each with a weight of 10 to decrease computation time. No bias in the estimation of ORs is introduced by sampling on the outcome owing to the fact that the sampling fraction cancels out in the estimation of ORs.³⁷ Estimates of population-attributable risk proportions, though, are biased by subsampling. The weight of 10 (ie, 1 / 10% = 10) was added to correct for this bias. Data on the prevalence of individual CAs and the distribution of the number of CAs separately in person-years with and without onsets of the disorders are available on request. For person-years with an onset, these prevalence estimates range from a low of 9.0% (physical illness) to a high of 28.5% (family violence).

^bModels were estimated with 1 CA at a time in addition to the controls noted in the previous footnote.

^cThe model was estimated with all 12 CAs in addition to the controls noted in the first footnote.

^dThe model was estimated with dummy predictors for the number of CAs without any information about types of CAs. The same controls used in earlier models were included as well.

^eThe model was estimated with dummy predictors for the number of CAs and information about types of CAs. The same controls used in earlier models were included as well.

^fSignificant at $P < .05$, 2-tailed.

shows that the significant ORs of some, but not all, CAs persist throughout the life course (**Table 4**). The ORs associated with other CAs decline with age, but these declines are generally not statistically significant. The exceptions are significant declines with age in ORs for parental death ($\chi^2_3=8.1$, $P=.04$), physical abuse ($\chi^2_3=22.9$, $P<.001$), sexual abuse ($\chi^2_3=40.3$, $P<.001$), and physical illness ($\chi^2_3=13.7$, $P=.003$). The persistence of the OR for other parental loss throughout the life course is striking compared with the OR for parental death being significant only in childhood. More highly disaggregated analyses showed that age-related declines involving sexual abuse were consistent across all disorder classes (although significant only for mood disorders), whereas declines associated with physical abuse, parental death, and physical illness varied by class of disorder. (Detailed results are available on request.)

We also examined differential associations of CAs with the first onset of DSM-IV/CIDI disorders as a function of the number of previous lifetime disorders. (Detailed results are available on request from the author.) We found that the ORs associated with most CAs become smaller as the number of previous disorders becomes larger. This means that CAs are more strongly associated with the onset of temporally primary vs secondary disorders. The sign pattern of the associations between types of CAs and onset of disorders remains largely positive (ie, ORs >1.0) when number of previous disorders is 0 (11 of 12 ORs >1.0, 9 of 12 significant at $P < .05$), 1 (7 of 12 ORs >1.0, 0 of 12 significant at $P < .05$), or 2 or more (7 of 12 ORs >1.0, 6 of 12 significant at $P < .05$), but the magnitude of ORs is considerably stronger when number of previous disorders is 0, with median (interquartile range) values of the ORs being higher when number of previous

Table 3. Multivariate Associations Between CAs and the Subsequent First Onset of DSM-IV/CIDI Classes of Disorders Based on a Simple Interactive Model (n=5692)^a

	OR (95% CI)				
	Mood	Anxiety	Substance Use	Disruptive Behavior ^b	All
MFF CAs					
Parental mental illness	1.8 (1.4-2.3) ^c	1.7 (1.5-2.0) ^c	1.4 (1.0-1.9) ^c	1.8 (1.4-2.3) ^c	1.7 (1.5-1.9) ^c
Parental substance abuse	1.7 (1.4-2.1) ^c	1.4 (1.2-1.6) ^c	2.3 (1.7-3.1) ^c	2.0 (1.5-2.5) ^c	1.7 (1.5-1.9) ^c
Parental criminality	1.3 (1.0-1.7) ^c	1.3 (1.2-1.5) ^c	1.4 (1.1-2.0) ^c	1.7 (1.2-2.3) ^c	1.4 (1.2-1.7) ^c
Family violence	1.4 (1.1-1.8) ^c	1.6 (1.4-1.9) ^c	1.8 (1.4-2.4) ^c	2.0 (1.6-2.6) ^c	1.7 (1.5-2.0) ^c
Physical abuse	1.5 (1.2-1.8) ^c	1.6 (1.3-1.8) ^c	1.6 (1.2-2.1) ^c	2.0 (1.6-2.6) ^c	1.6 (1.4-1.9) ^c
Sexual abuse	2.1 (1.6-2.6) ^c	1.9 (1.6-2.4) ^c	1.7 (1.1-2.4) ^c	1.6 (1.2-2.1) ^c	1.8 (1.5-2.2) ^c
Neglect	1.8 (1.3-2.4) ^c	1.6 (1.3-1.9) ^c	1.8 (1.3-2.5) ^c	1.8 (1.3-2.4) ^c	1.7 (1.4-2.0) ^c
χ^2_7	46.4 ^{ac}	115.2 ^c	38.2 ^c	53.0 ^c	88.0 ^c
Other CAs					
Parental death	1.0 (0.8-1.2)	1.2 (1.0-1.4)	1.0 (0.8-1.3)	1.0 (0.8-1.2)	1.1 (0.9-1.2)
Parental divorce	1.0 (0.9-1.2)	1.0 (0.8-1.1)	1.0 (0.8-1.2)	1.1 (0.9-1.3)	1.0 (0.9-1.1)
Other parental loss	1.1 (0.9-1.4)	1.1 (1.0-1.3)	1.5 (1.1-2.0) ^c	1.6 (1.3-2.1) ^c	1.3 (1.1-1.4) ^c
Physical illness	1.2 (1.0-1.5)	1.5 (1.3-1.7) ^c	1.0 (0.8-1.4)	1.5 (1.2-1.9) ^c	1.3 (1.2-1.5) ^c
Economic adversity	1.1 (0.9-1.4)	1.2 (1.0-1.5) ^c	0.9 (0.6-1.2)	1.0 (0.8-1.3)	1.1 (1.0-1.3)
χ^2_5	7.5	57.5 ^c	7.4 (0.19)	36.4 ^c	35.3 ^c
χ^2_{12}	52.5 ^c	193.7 ^c	44.5 ^c	84.2 ^c	120.3
No. of MFF CAs					
0-1					
2	0.7 (0.5-1.1)	0.8 (0.6-1.0) ^c	0.6 (0.4-0.9) ^c	0.6 (0.4-0.8) ^c	0.7 (0.6-0.9) ^c
3	0.5 (0.3-0.9) ^c	0.6 (0.5-0.9) ^c	0.4 (0.2-0.7) ^c	0.4 (0.2-0.8) ^c	0.5 (0.4-0.7) ^c
4	0.4 (0.2-0.8) ^c	0.4 (0.3-0.7) ^c	0.2 (0.1-0.5) ^c	0.3 (0.2-0.6) ^c	0.4 (0.2-0.6) ^c
5	0.3 (0.1-0.7) ^c	0.4 (0.2-0.7) ^c	0.2 (0.1-0.6) ^c	0.2 (0.1-0.5) ^c	0.3 (0.1-0.5) ^c
6	0.1 (0.0-0.4) ^c	0.3 (0.1-0.6) ^c	0.1 (0.0-0.3) ^c	0.1 (0.0-0.3) ^c	0.2 (0.1-0.3) ^c
≥7	0.0 (0.0-0.2) ^c	0.2 (0.1-0.3) ^c	0.0 (0.0-0.2) ^c	0.1 (0.0-0.2) ^c	0.1 (0.0-0.2) ^c
χ^2_6	39.8 ^c	50.9 ^c	19.4 ^c	23.9 ^c	61.7 ^c
No. of other CAs					
0-1					
2	0.7 (0.5-1.0) ^c	0.8 (0.7-1.0) ^c	0.9 (0.7-1.3)	1.0 (0.7-1.2)	0.8 (0.7-1.0) ^c
3	0.8 (0.5-1.3)	0.7 (0.5-1.0) ^c	1.0 (0.6-1.7)	0.9 (0.6-1.4)	0.8 (0.6-1.0)
≥4	0.7 (0.3-1.6)	1.3 (0.6-2.6)	0.6 (0.2-1.8)	0.5 (0.2-1.2)	0.9 (0.6-1.3)
χ^2_3	4.7 (0.20)	13.3 (0.004)	1.2 (0.75)	3.0 (0.39)	5.2
χ^2_{21}	316.9 ^c	1727.0 ^c	206.2 ^c	465.6 ^c	2184.8 ^c

Abbreviations: CA, childhood adversity; CI, confidence interval; CIDI, Composite International Diagnostic Interview; MFF, maladaptive family functioning; OR, odds ratio.

^aSee footnote "a" to Table 2 for a description of the data set and overall modeling approach. The model used herein was estimated with predictors for types of CAs and number of CAs (distinguishing number of MFF CAs from number of other CAs) in addition to the controls used in the models described in Table 2. Note that no term was included in the model for having exactly 1 CA. This means that the coefficients for types of CAs can be interpreted as the associations of pure CAs (ie, having 1 and only 1 particular type of CA compared with having none) with onset, whereas the associations with number of CAs represent the extent to which the incremental associations of co-occurring CAs (ie, the added risk of an additional CA in respondents who are otherwise equivalent in terms of the number of other CAs they experienced, controlling for types of other CAs) differ from the associations of pure CAs. The 5692 respondents had 11 047 disorder onsets, including 4545 onsets of an anxiety disorder, 2366 of a substance use disorder, 2357 of a mood disorder, and 1621 of a disruptive behavior disorder. Data on the prevalence of individual CAs and the distribution of the number of CAs separately in person-years with and without onsets of the disorders are available on request. For person-years with an onset, these prevalence estimates range from a low of 7.7% (physical illness associated with onset of a substance use disorder) to a high of 33.5% (family violence associated with onset of a disruptive behavior disorder).

^bDisruptive behavior disorders are restricted to respondents 44 years and younger at interview.

^cSignificant at $P < .05$, 2-sided test.

disorders is 0 (1.6 [1.2-1.7]) rather than either 1 (1.2 [1.1-1.2]) or 2 or more (1.2 [1.1-1.3]).

POPULATION-LEVEL ASSOCIATIONS OF CAs WITH DISORDER ONSET

We calculated the PARPs associated with CAs based on the best-fitting model. Results show that CAs explain (in a predictive sense) 32.4% of all disorders, 41.2% of disruptive behavior disorders, 32.4% of anxiety disorders, 26.2% of mood disorders, and 21.0% of substance use disorders (**Table 5**). The CAs explain a higher proportion of childhood-onset disorders (44.6%) than adolescent-

onset disorders (32.0%) and adult-onset disorders (28.6% and 25.9%). This decline is largely explained by the PARPs for mood disorders decreasing with age from a high of 57.1% for childhood-onset cases to a low of 20.5% for onsets in the age range of 30 years or older. The PARPs also decrease with age for anxiety disorders, but less dramatically than for mood disorders (from 39.5% of childhood-onset cases to 29.8% of onsets in the age range of ≥30 years). The PARPs do not decrease with age, in comparison, for substance use disorders. The number of disruptive behavior disorders that occur for the first time in adulthood is so small that we could not calculate the PARPs for these disorders beyond adolescence.

Table 4. Multivariate Associations Between CAs and the Subsequent First Onset of DSM-IV/CIDI Disorders in 4 Life Course Stages Based on a Simple Interactive Model^a

	OR (95% CI)			
	Childhood, Aged 4-12 y	Adolescence, Aged 13-19 y	Young Adulthood, Aged 20-29 y	Middle-Later Adulthood, Aged ≥30 y
MFF CAs				
Parental mental illness	1.8 (1.5-2.2) ^b	1.7 (1.4-2.1) ^b	1.5 (1.3-1.9) ^b	1.6 (1.3-1.9) ^b
Parental substance abuse	1.6 (1.3-1.9) ^b	1.8 (1.5-2.2) ^b	1.8 (1.2-2.6) ^b	1.7 (1.3-2.1) ^b
Parental criminality	1.4 (1.1-1.8) ^b	1.6 (1.2-2.0) ^b	1.4 (1.1-1.8) ^b	1.2 (0.9-1.6)
Family violence	1.6 (1.4-1.9) ^b	1.8 (1.4-2.2) ^b	1.8 (1.5-2.3) ^b	1.8 (1.3-2.4) ^b
Physical abuse	1.9 (1.6-2.2) ^b	1.8 (1.4-2.2) ^b	1.5 (1.2-1.9) ^b	1.3 (1.0-1.6)
Sexual abuse	2.3 (1.9-2.7) ^b	1.8 (1.4-2.3) ^b	1.7 (1.3-2.2) ^b	1.4 (1.1-1.9) ^b
Neglect	1.6 (1.3-2.0) ^b	1.8 (1.4-2.3) ^b	1.9 (1.4-2.6) ^b	1.4 (1.0-2.0) ^b
χ^2_7	139.1 ^b	49.3 ^b	49.5 ^b	42.3 ^b
Other CAs				
Parental death	1.2 (1.0-1.4) ^b	1.0 (0.8-1.2)	1.0 (0.8-1.4)	1.1 (0.9-1.3)
Parental divorce	1.0 (0.9-1.2)	1.0 (0.9-1.2)	1.0 (0.8-1.2)	1.0 (0.8-1.2)
Other parental loss	1.3 (1.1-1.5) ^b	1.2 (1.0-1.5) ^b	1.2 (0.9-1.6)	1.4 (1.1-1.8) ^b
Physical illness	1.6 (1.4-1.9) ^b	1.2 (1.0-1.4)	1.1 (0.8-1.4)	1.3 (1.0-1.7)
Economic adversity	1.2 (1.0-1.4) ^b	1.0 (0.8-1.2)	1.2 (0.9-1.5)	1.2 (0.9-1.6)
χ^2_5	71.1 ^b	12.9 ^b	4.2	10.3
χ^2_{12}	342.6 ^b	85.9 ^b	61.7 ^b	81.8 ^b
No. of MFF CAs				
0-1				
2	0.8 (0.6-1.0)	0.7 (0.5-0.9) ^b	0.6 (0.4-0.8) ^b	0.7 (0.5-1.1)
3	0.6 (0.4-0.9) ^b	0.5 (0.3-0.7) ^b	0.4 (0.2-0.8) ^b	0.5 (0.3-0.8) ^b
4	0.4 (0.3-0.8) ^b	0.3 (0.1-0.5) ^b	0.3 (0.1-0.5) ^b	0.5 (0.2-0.9) ^b
5	0.3 (0.2-0.7) ^b	0.2 (0.1-0.4) ^b	0.2 (0.1-0.7) ^b	0.4 (0.2-1.1)
6	0.2 (0.1-0.5) ^b	0.1 (0.0-0.2) ^b	0.2 (0.1-0.5) ^b	0.3 (0.1-0.9) ^b
≥7	0.1 (0.0-0.4) ^b	0.0 (0.0-0.2) ^b	0.1 (0.0-0.3) ^b	0.2 (0.0-0.8) ^b
χ^2_6	37.2 ^b	47.8 ^b	26.4 ^b	8.4
No. of other CAs				
0-1				
2	0.9 (0.8-1.1)	0.8 (0.6-1.0)	0.7 (0.5-1.0)	0.8 (0.5-1.2)
3	0.8 (0.6-1.1)	0.8 (0.5-1.2)	0.7 (0.4-1.2)	0.6 (0.3-1.2)
≥4	1.0 (0.4-2.4)	0.5 (0.2-1.2)	0.4 (0.1-1.3)	0.8 (0.3-2.4)
χ^2_3	2.6	4.9	5.4	2.6
χ^2_{21}	1167.8 ^b	182.4 ^b	472.0 ^b	163.0 ^b

Abbreviations: CA, childhood adversity; CI, confidence interval; CIDI, Composite International Diagnostic Interview; MFF, maladaptive family functioning; OR, odds ratio.

^aSee footnote "a" to Table 2 for a description of the data set and the overall modeling approach. The model used herein was estimated using predictors for types of CAs and number of CAs (distinguishing number of MFF CAs from number of other CAs) in addition to the controls used in the models described in Table 2. See footnote "a" in Table 3 for a description of the interpretation of the joint effects of type and number of CAs. The 5692 respondents had a total of 11 047 disorder onsets, including 3550 in the age range of 4 to 12 years, 3401 in the age range of 13 to 19 years, 2093 in the age range of 20 to 29 years, and 1845 in the age range of 30 years and older. Data on the prevalence of individual CAs and the distribution of the number of CAs separately in person-years with and without onsets of the disorders are available on request. For person-years with an onset, these prevalence estimates range from a low of 7.7% (physical illness associated with onsets in the age range of 20-29 years) to a high of 31.0% (family violence with onsets in the age range of 4-12 years).

^bSignificant at $P < .05$, 2-sided test.

EFFECTS OF TIME TO RECALL

The use of retrospective data introduces the possibility of recall bias. We investigated this possibility by examining age differences in the reported prevalence of CAs and in the ORs of CAs with disorder onset. (Detailed results are available on request from the author.) Reported death of a parent when the respondent was a child was positively related to age, whereas parental divorce when the respondent was a child was inversely related to age. These patterns are consistent with historical trends. Respondent age was unrelated, in comparison, to reports of other parental loss, neglect, or life-threatening childhood physical illness. Respondent age of 65 years and older was significantly related to low reports of parental mental illness, substance abuse, criminality, fam-

ily violence, physical abuse, and sexual abuse, whereas age was generally unrelated to these CAs in the age range 18 to 64 years. These patterns could be due to a genuinely low prevalence of some CAs in older respondents, underrepresentation of elderly people with these CAs in the sample (due to early death or differential participation), or underreporting of these CAs in elderly respondents (due to differential recall or differential willingness to report). Although we have no way to know which of these processes are at work, any bias in prevalence estimates is likely conservative in the total sample because of lower reporting in the elderly respondents.

Analysis of age differences in associations at given life course stages found generally good consistency between ORs estimated in the youngest cohorts only (aged 18-29 years at interview) and in the entire sample. Of the

Table 5. Population-Attributable Risk Proportions (PARPs) of Lifetime *DSM-IV*/CIDI Disorder Types Associated With Childhood Adversities by Life Course Stage^a

	PARPs				
	Overall	Childhood, Aged 4-12 y	Adolescence, Aged 13-19 y	Early Adulthood, Aged 20-29 y	Middle-Later Adulthood, Aged ≥30 y
Mood	26.2	57.1	30.5	24.7	20.5
Anxiety	32.4	39.5	28.7	31.3	29.8
Substance use	21.0	^b	26.1	25.6	32.1
Disruptive behavior ^c	41.2	34.4	38.9	^b	^b
Any	32.4	44.6	32.0	28.6	25.9

Abbreviation: CIDI, Composite International Diagnostic Interview.

^aThe PARPs were calculated using simulation methods to generate individual-level predicted probabilities of the outcome disorders twice from the coefficients in the best-fitting model: the first time using all the coefficients in the model (probability of the disorder in those exposed to childhood adversities) and the second time assuming that the coefficients associated with the childhood adversities were all zero (probability of the disorder in those unexposed). One minus the ratio of the predicted prevalence estimates in the 2 specifications was then used to calculate PARP. In the pooled data set, the PARP value is the average PARP across all disorders included in the calculation based on a constant model across disorders.

^bToo few cases available to estimate the PARP.

^cDisruptive behavior disorders are restricted to respondents 44 years and younger at interview.

48 coefficients for individual CAs (12 CAs associated with disorder onsets in the person-year ranges of 4-12, 13-19, 20-29, and ≥30), 36 were positive and 21 were significant in the youngest cohorts, compared with 41 positive and 31 significant in the total sample. Median (interquartile range) ORs were also similar in the youngest cohorts (1.3 [1.1-1.5]) and the total sample (1.4 [1.2-1.7]). In 8 of 48 cases, the ORs differed significantly for the youngest vs the older cohorts. The OR was significant but was lower in magnitude in the younger (1.2-1.8) vs the older (1.4-1.4) cohorts in 3 of these cases. The OR changed from greater than 1.0 (1.1-1.1) in the older cohorts to less than 1.0 (0.7-0.9) in the younger cohorts in 2 other cases but was nonsignificant in both. The OR was nonsignificant in the youngest cohorts (0.8-1.1) but was significant in older cohorts (1.4-1.7) in the other 3 cases, which involved associations of childhood sexual abuse with disorder onsets in the age ranges of 20 to 29 years and 30 years and older and of parental substance abuse with disorder onsets in the age range of 30 years and older. These findings are not definitive because recall failure could exist even for respondents with the shortest recall intervals, but they nonetheless show that the results are stable across a range of recall times.

COMMENT

Despite these results, this study is limited by the retrospective nature of the data. Methodological research suggests that recall bias can lead to underreporting of CAs,³⁸ which would be expected to make the estimates of PARPs conservative. However, bias could be anticonservative in estimating ORs if the same respondents who did not report CAs also underreported disorders. A long-term prospective study is needed to resolve these uncertainties. Several such studies³⁹⁻⁴² exist that could be used to evaluate these results, but these studies generally have non-trivial attrition. If this attrition is systematic (ie, respondents with the highest risk of disorders also have the highest attrition), estimates of CA effects could be bi-

ased downward. The best way to guard against this possibility is to think of retrospective and prospective studies as bounding the true values of associations (ie, retrospective studies giving upper bound estimates and prospective studies lower bound estimates).

A second study limitation is that the list of CAs, although larger than that in most previous studies, is not exhaustive. We also did not consider the timing, sequencing, persistence, recurrence, or severity of individual CAs. In some cases, such as parental mental illness, there could be complex associations remaining to be discovered that involve the number of ill parents, the number of illnesses, and the persistence and severity of these illnesses. A related limitation is that the analysis of joint CA effects did not include fine-grained evaluation of interactions but focused only on broad interaction patterns. This broad-gauged approach is probably desirable as a first approximation but inevitably misses important subtleties. For example, some research⁴³⁻⁴⁵ suggests that parental divorce is associated with a reduced risk of subsequent psychiatric disorders if it facilitates escape from exposure to maladaptive parenting. Future analyses need to examine such specifications against the backdrop of the broader preliminary patterns found in the present study.

In the context of these limitations, the present results are consistent with those of previous studies in suggesting that most US children are exposed to childhood family adversities that are often clustered.^{7,9} Neglect, in particular, almost always appears with other CAs. Even the CAs most likely to be independent co-occur with at least one other CA in most cases. Because of this high co-occurrence, it is critical for future research not to focus on one CA without considering others, because bivariate analyses artificially inflate estimates of individual CA effects.¹³ There are implications as well for more subtle analyses. For example, some previous research¹¹ suggested that childhood neglect exacerbates the predictive effects of other CAs, but the present results raise the possibility that this finding is due to neglect being associated with an especially large number of other un-

controlled CAs rather than itself creating a high risk of psychiatric disorders.

The present finding that the multivariate structure of the associations between CAs and disorder onset is broadly subadditive has, to our knowledge, never before been examined. This subadditive pattern has important implications for intervention because it means that prevention or amelioration of only a single CA in youths exposed to many CAs is unlikely to have important preventive effects. The finding that this nonadditivity is confined to MFF CAs is reminiscent of the finding in the child maltreatment literature that the most severe CAs tend to be chronic intrafamilial adversities involving the use of physical force.⁴⁶ This finding also reinforces the importance of considering CA persistence and severity in future research because the finding that people exposed to many co-occurring MFF CAs have a very high risk of lifetime disorders might be due at least partly to the effects of unmeasured CA persistence and severity.

Despite considerable early theorizing to suggest unique effects of particular CAs on particular mental disorders, such as of childhood parental death on adult depression,⁴⁷ we found remarkably little specificity of this sort in the NCS-R data. Most CAs we studied, especially MFF CAs, were associated with all the disorder classes we considered. This pattern was found even in the models that controlled for number of CAs, in which ORs associated with specific CA types can be interpreted under the model as the associations of pure CAs (ie, having a particular 1 and only 1 CA vs none) with disorder onset, thereby removing the confounding effects of CA co-occurrences. We also controlled for comorbid child-adolescent disorders to increase the ability to detect specificities of this sort. Previous studies^{48,49} found some evidence of specificity in predicting prevalent cases, but inspection of coefficients in the best-fitting models at the level of disorder class and the level of individual disorders (the latter results are available on request) yielded little evidence of specificity. The obvious implication is that the causal pathways that link CAs to the onset of psychiatric disorders are quite general.

In considering the theme of causal pathways, note that these results do not confirm that CAs have causal effects. An alternative possibility is that unmeasured third variables caused CAs and subsequent mental disorders. Genetic factors are possible confounding variables of this type. This is most obviously true for parental mental illness, which can predict respondent mental illness through genetic pathways unrelated to CAs, but the same might be true for other CAs to the extent that they are indicators of genetic liability. Gene \times environment interactions could also be involved to the extent that the people exposed to CAs have an elevated genetic risk of psychiatric disorders and are exposed to stressful experiences related to their CAs that potentiate this genetic liability. Genetically informative designs (eg, twin-family and adoption studies) are needed to evaluate these possibilities rigorously.

Another class of potentially important third variables is respondent behaviors and behavioral predispositions that elicit some CAs, such as abuse, and cause the subsequent onset of respondent mental disorders. Prospective studies that measure these proposed constructs repeatedly would be in the best position to evaluate this

possibility. In the ideal case, such studies would have multiple informants to assess reporting bias.

A final noteworthy finding is that the associations of many, but not all, CAs with first onset of *DSM-IV* disorders persist into adulthood. Future research needs to investigate the causal pathways responsible for this specification. Although previous research^{15,50} has documented long-term associations of some CAs with adult disorders, these studies almost entirely focused on prevalent cases rather than on first onsets. It is much more striking to document, as we did herein, that CAs continue to be related to first onsets of *DSM-IV* disorders beyond early adulthood. Indeed, the PARPs calculated herein suggest that CAs are associated with more than one-fourth of all new disorders in adulthood. Although several hypotheses could be advanced to explain this finding,⁵⁰⁻⁵² nothing in these results sheds light on them. The indirect retrospective documentation of long-term multivariate associations is nonetheless important in providing an empirical justification for conducting further analyses to explore such hypotheses to investigate mediators, developmental sequences, and dynamic relationships between CAs and adult-onset disorders.

Future research also needs to distinguish between associations of CAs with disorder onset and disorder persistence. As reported in a companion article,²⁰ we found a rather different association of CAs with disorder persistence than reported herein with disorder onset. In addition, future research should integrate the kind of broad-based analyses of joint effects presented herein with more focused investigations of specific adversities^{53,54} and important adversity clusters.^{2,55} Future studies should also examine the moderating effects of early disorders on the associations of CAs with later disorders,⁵⁶ a line of study that could be important in focusing clinical attention on preventing the onset of secondary disorders. Finally, future studies should try to identify risk and protective factors in adulthood (eg, personality, social support, and adult stressors) that mediate or modify the relationships of CAs with adult disorders.

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