ORIGINAL ARTICLE

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

Associations With Persistence of DSM-IV *Disorders*

Katie A. McLaughlin, PhD; Jennifer Greif Green, PhD; Michael J. Gruber, MS; Nancy A. Sampson, BA; Alan M. Zaslavsky, PhD; Ronald C. Kessler, PhD

Context: Although significant associations of childhood adversities (CAs) with adult mental disorders have been widely documented, associations of CAs with onset and persistence of disorders have not been distinguished. This distinction is important for conceptual and practical purposes.

Objective: To examine the multivariate associations of 12 retrospectively reported CAs with persistence of adult *DSM-IV* disorders in the National Comorbidity Survey Replication.

Design: Cross-sectional community survey.

Setting: Household population in the United States.

Participants: Nationally representative sample of 5692 adults.

Main Outcome Measures: Recency of episodes was assessed separately for each of 20 lifetime *DSM-IV* mood, anxiety, disruptive behavior, and substance use disorders in respondents with a lifetime history of these disorders using the Composite International Diagnostic Interview. Predictors of persistence were examined using backward recurrence survival models to predict time since most recent episode controlling for age at onset and time since onset.

Results: The CAs involving maladaptive family functioning (parental mental illness, substance use disorder, criminality, family violence, physical and sexual abuse, and neglect) but not other CAs were significantly but modestly related to persistence of mood, substance abuse, and anxiety disorders. Number of maladaptive family functioning CAs had statistically significant, but again substantively modest, subadditive associations with the same outcomes. Exposure to multiple other CAs was significantly associated with persistence of mood and anxiety disorders. Associations remained statistically significant throughout the life course, although the substantive size of associations indicated by simulations showing time to most recent episode would increase by only 1.6% (from a mean of 8.3 years to a mean of 8.4 years) in the absence of CAs.

Conclusions: The overall statistically significant associations of CAs with adult *DSM-IV*/Composite International Diagnostic Interview disorders are due largely to component associations with onsets rather than with persistence, indirectly suggesting that the greatest focus of public health attention on CAs should be aimed at primary rather than secondary prevention.

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Significant associations between retrospectively reported childhood adversities (CAs) and diverse adult mental disorders have been documented in numerous epidemiological surveys.[1-4] These associations are substantial, with more than 30% of adult mental disorders estimated to be directly related to CAs.[5,6] Previous studies[7-9] have suggested that the associations are due to increased stress sensitivity that persists into adulthood, making individuals with a history of CAs especially vulnerable to mental disorders triggered by adult stressors. If this is the case, we would expect that CAs would be associated with disorder persistence because most adult episode onsets are recurrences rather than first onsets.[10-12] However, previous epidemiological studies have largely focused on prevalent disorders[1,13-15] or lifetime disorders,[15-17] with no attempt to distinguish associations of CAs with disorder first onset vs persistence. It would be useful to make this distinction to advance our understanding of the associations of CAs with adult mental disorders. A companion article[6] to this one takes a first step in doing this by analyzing data from the

See also pages 111 and 113

Author Affiliations: Department of Health Care Policy, Harvard Medical School, Boston, Massachusetts.

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National Comorbidity Survey Replication (NCS-R)[18] and showing that the number of CAs is, in fact, associated with first onsets of a wide range of *DSM-IV* disorders throughout the life course. The present study takes the next logical step in this line of investigation by examining associations of CAs with persistence of the same *DSM-IV* disorders in the NCS-R.

Although a handful of previous studies have examined the associations of CAs with illness course, the results have been inconsistent. Some of these studies found significant associations of CAs with illness course,[10,11,19,20] whereas others did not.[3,21] Limitations of these studies are that they used relatively primitive methods to measure and analyze these associations and that they generally focused on a single mental health outcome. We address the first limitation in 2 ways. First, we use a novel statistical approach to examine the separate and joint associations of CAs with disorder persistence[6] to address the fact that CAs are highly co-occurring[22-24] and that multivariate associations of co-occurring CAs are generally nonadditive.[25] Second, we use an innovative approach to measure illness course based on a special class of survival models known as *backward recurrence models*.[26,27] These models allow us to study the associations of CAs with illness course more sensitively than in previous retrospective studies. We address the second limitation by examining associations of CAs with persistence of a wide range of *DSM-IV* disorders.

METHODS

SAMPLE

The NCS-R is a face-to-face household survey of 9282 English-speaking respondents 18 years and older performed between February 5, 2001, and April 7, 2003, in a nationally representative multistage clustered area probability sample of the US household population.[18] The response rate was 70.9%. 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 (n=9282). Part II included questions about risk factors, consequences, and other correlates along with assessments of additional disorders. The CAs were assessed in part II, which was administered to all part I respondents who met the 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 differences in intensity of the recruitment effort in hard-to-recruit cases. The part II sample, which is the focus of the present study, was additionally weighted for the undersampling of part I respondents without a part I disorder. A final weight adjusted the part II sample to match the 2000 census population on a cross-classification of a variety of geographic and sociodemographic variables. All the analyses reported in this article use these weights. More details about the NCS-R sample and design are reported elsewhere.[25]

DIAGNOSTIC ASSESSMENT

The NCS-R diagnoses are based on version 3.0 of the World Health Organization Composite International Diagnostic Interview (CIDI),[28] a fully structured lay-administered interview that generates diagnoses according to *International Classification of Diseases, 10th Revision* and *DSM-IV* criteria. The *DSM-IV* criteria are used herein. The 20 lifetime diagnoses include mood disorders (major depressive disorder, dysthymic disorder, and bipolar disorder [bipolar I disorder, bipolar II disorder, and subthreshold bipolar disorder, each treated in the analysis as a separate 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. As detailed elsewhere,[29] blinded clinical reappraisal interviews found generally good concordance between *DSM-IV* diagnoses based on the CIDI and those based on the Structured Clinical Interview for *DSM-IV*.[30] The CIDI assessed age at onset (AAO) of disorders retrospectively using a special question sequence documented experimentally to improve the accuracy of AAO reporting compared with conventional methods.[31] Recency was assessed by asking respondents if they had an episode of the disorder in the 12 months before interview and, if not, asking their age at the time of their most recent episode. Time since onset was calculated by subtracting AAO from age at interview.

CHILDHOOD ADVERSITIES

Twelve dichotomously measured CAs were assessed in the NCS-R: 3 types of interpersonal loss (parental death, parental divorce, and other loss of contact with parents), 4 types of parental maladjustment (psychiatric disorder, substance abuse, criminality, and violence), 3 types of maltreatment (physical abuse, sexual abuse, and neglect), and 2 other CAs (serious physical illness in respondent and family economic adversity). The measures used to assess these CAs are described in a companion article,[6] where we also show that factor analysis found that 7 of these 12 CAs (the 4 indicators of parental maladjustment and the 3 indicators of maltreatment) were strongly interrelated. We refer to this cluster of CAs as the maladaptive family functioning (MFF) cluster.

PERSISTENCE OF DISORDERS

Persistence of disorders, the proportion of time since onset that a person with a history of the disorder is in episode, is a joint function of episode duration and recurrence risk in people with a history of episodes. It is possible for longitudinal studies to calculate persistence directly by recording complete information about duration of incident episodes, time to recurrence after offset of incident episodes, duration of second episodes, time to recurrence of third episodes after offset of second episodes, and so on, although this is difficult logistically even in long-term multiwave prospective studies.[32-34] It is impossible to obtain this kind of direct assessment of persistence using retrospective assessments in a cross-sectional survey such as the NCS-R, but persistence can be estimated indirectly from the ratio of current prevalence to lifetime prevalence. This ratio is only an approximation of persistence because differential mortality and recall failure can lead the ratio to differ from true mean persistence.

ANALYSIS METHODS

Given that persistence can be indirectly estimated as the ratio of current to lifetime prevalence, the associations of CAs with persistence can be estimated approximately by using information

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about CAs to predict current prevalence in lifetime cases. However, that approach would use only part of the information about recency of disorders available in the CIDI. In addition to assessing current prevalence in lifetime cases, the CIDI obtains information from other lifetime cases about age at offset of the most recent episode. This information can be used to study associations of CAs with disorder persistence using a special class of survival models known as *backward recurrence models*.[26,27] These models use a person-year survival approach[35] to predict current prevalence in lifetime cases and time since termination of the most recent episode in lifetime cases who are not in episode at the time of interview. In the present application, we use a discrete-time person-year survival approach in which the dependent variable in each person-year is coded 1 for respondents with a most recent episode in that year and 0 for respondents with a most recent episode in an earlier year.

As in conventional survival analysis, person-years before the most recent episode are censored. The number of person-years in the data file for a given disorder for a particular respondent equals 1 of the 2 following values: (1) Respondents who had at least 1 episode at an age later than their AAO are represented with 1 more person-year than the number of years since the respondent's most recent episode. For example, a respondent with an episode in the year of interview is represented by only 1 person-year, which is coded 1 on the outcome, whereas a respondent with a most recent episode y years before the interview is represented by $y + 1$ person-years, only the last of which is coded 1. (2) Respondents with no episode subsequent to AAO are represented by a number of person-years equal to time since onset (beginning with the year of interview and ending with the year after AAO), each coded 0.

The 20 disorder-specific person-year files were stacked into a consolidated data file, each file containing a yes-no outcome variable for the most recent episode of the focal disorder. Logistic regression analysis was used to estimate the associations of CAs with this outcome variable with 19 dummy control variables to distinguish among the 20 disorders and nonlinear controls for person-year (ie, time since interview), AAO, time since onset, sex, race/ethnicity (non-Hispanic white, non-Hispanic black, Hispanic, and other), and lifetime history of other disorders as of AAO of the focal disorder. The same range of bivariate and multivariate models was examined as in the companion analysis of the associations of CA with disorder onset.[6] The initial model coefficients were constrained to be the same for all 20 disorders. The most complex model, which included predictors of type and number of CAs and which differentiated MFF CAs from other CAs, was then used to estimate coefficients in subsamples defined by life-course stage and class of disorders.

Backward recurrence models, although, to our knowledge, never before used to study the persistence of mental disorders, have been used extensively by demographers to predict such demographic transitions as probability of having an additional child or of changing marital status as a function of respondent age at first making a related transition (eg, age at first child birth or age at first marrying), current age, and number of years since most recent transition (eg, years since last having a child or years in current marital status).[36,37] Empirical comparison of predictor coefficients in such models with the coefficients in prospective time-to-next-event survival models (ie, models that use the more detailed information needed to study transitions prospectively by recording the age of each of the respondent's children and the time between births of each child or the respondent's age at each marital transition, including marriages, separations, and divorces, and time in state for each of these transitions) shows that recurrence model coefficients are generally good approximations to the survival coefficients obtained in prospective analyses.[38]

We assessed the overall associations of all CAs combined with disorder persistence by simulating, based on the most complex model, the extent to which the most recent episode would have been pushed backward in time if none of the CAs had occurred and if the odds ratios (ORs) in the model were due to causal effects of the CAs. This simulation, which was performed using an SAS macro written explicitly for this purpose, generated individual-level predicted probabilities of recurrence at each person-year twice from the coefficients in the model: the first time using all the coefficients in the model and the second time assuming that the coefficients associated with the CAs were all zero. The ratio of the mean time-to-most-recent-episode estimates in the 2 specifications was used to calculate the effects of CAs on time since most recent episode recurrence.

The coefficients and standard errors in the backward recurrence survival models were exponentiated for ease of interpretation and are reported herein as ORs and 95% confidence intervals. Statistical significance was consistently evaluated using $P < .05$-level 2-sided tests. Because the NCS-R data are clustered and weighted, the design-based Taylor series method[39] implemented in the SUDAAN software system[40] was used to estimate standard errors and to evaluate the statistical significance of coefficients.

RESULTS

ASSOCIATIONS OF CAs WITH PERSISTENCE OF *DSM-IV*/CIDI DISORDERS

Two-thirds of the CAs are significantly associated with greater persistence of disorders in bivariate backward recurrence models that examine 1 CA at a time and that pool across the 20 *DSM-IV*/CIDI disorders (**Table 1**). These ORs are all weak in substantive terms (range, 1.1-1.3), indicating that persistence in a given year is only modestly higher in people with vs without a history of CAs. Furthermore, most significant bivariate ORs become nonsignificant in a multivariate model that includes all CAs. The 2 CAs that remain significant in the multivariate additive model (physical abuse and sexual abuse) have weak ORs (range, 1.1-1.2). In addition, only a weak dose-response relationship exists between number of CAs and disorder persistence in the multivariate model of number of CAs, with ORs of 1.3 to 1.4 for respondents who experienced a high number of CAs (compared with respondents who experienced no CAs). We can, nevertheless, reject the hypothesis that the 2 significant ORs occurred by chance in the set of 12 ($\chi^2_{12}=63.1$, $P<.001$) and the hypothesis that the 12 ORs do not differ significantly among themselves ($\chi^2_{11}=41.6$, $P<.001$). The latter result means that we would have underestimated the associations of CAs with persistence by using a simple 0 to 12 summary count measure.

The most complex model we considered, a multivariate interactive model, includes separate predictors for type of CA (ie, 1 predictor for each of the 12 CAs) and number of CAs (ie, separate predictors for respondents who were exposed to exactly 1, exactly 2, exactly 3, etc, CAs) and distinguishes between MFF CAs and other CAs (**Table 2**). This model shows that type ($\chi^2_7=31.1$, $P<.001$) but not number ($\chi^2_6=6.0$, $P=.43$) of MFF CAs is significantly associated with disorder persistence, whereas neither type ($\chi^2_5=4.6$, $P=.47$) nor number ($\chi^2_5=3.2$, $P=.36$) of non-MFF CAs is associated with persistence. The significant MFF CAs include parental mental illness, physical abuse, sexual abuse, and neglect, each of which has a modestly elevated

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Table 1. Bivariate and Multivariate Associations Between CAs and the Persistence of *DSM-IV*/CIDI Disorders (n=10 915)[a]

	Odds Ratio (95% Confidence Interval)			
	Bivariate[b]	Multivariate (Additive)[c]	Multivariate (No. of CAs)[d]	Multivariate (Interactive)[e]
Maladaptive family functioning CAs				
Parental mental illness	1.2 (1.0-1.4)[f]	1.1 (1.0-1.3)	NA	1.1 (1.0-1.2)
Parental substance abuse	1.1 (1.0-1.2)[f]	1.0 (0.9-1.1)	NA	1.0 (0.9-1.2)
Parental criminality	1.0 (0.9-1.1)	0.9 (0.8-1.0)	NA	0.9 (0.8-1.1)
Family violence	1.2 (1.1-1.3)[f]	1.0 (1.0-1.1)	NA	1.0 (0.9-1.1)
Physical abuse	1.3 (1.2-1.4)[f]	1.2 (1.1-1.3)[f]	NA	1.2 (1.0-1.3)[f]
Sexual abuse	1.2 (1.1-1.4)[f]	1.1 (1.0-1.3)[f]	NA	1.2 (1.0-1.3)
Neglect	1.2 (1.1-1.4)[f]	1.1 (1.0-1.2)	NA	1.1 (0.9-1.3)
χ^2_7	NA	44.8[f]	NA	23.9[f]
χ^2_6	NA	NA	NA	23.0[f]
Other CAs				
Parental death	1.0 (0.9-1.1)	1.0 (0.9-1.1)	NA	1.0 (0.9-1.2)
Parental divorce	1.1 (1.0-1.2)[f]	1.1 (1.0-1.2)	NA	1.0 (0.9-1.2)
Other parental loss	1.0 (1.0-1.2)	1.0 (0.9-1.1)	NA	1.0 (0.8-1.1)
Physical illness	1.0 (0.9-1.2)	1.0 (0.9-1.1)	NA	1.0 (0.9-1.1)
Economic adversity	1.1 (1.0-1.2)[f]	1.1 (1.0-1.2)	NA	1.1 (0.9-1.2)
χ^2_5	NA	5.1	NA	4.1
χ^2_{12}	NA	63.1[f]	NA	32.8[f]
χ^2_{11}	NA	NA	NA	41.6[f]
No. of CAs				
0	NA	NA	NA	NA
1	NA	NA	NA	NA
2	NA	NA	1.2 (1.1-1.3)[f]	1.1 (1.0-1.2)
3	NA	NA	1.1 (1.0-1.3)[f]	1.0 (0.8-1.3)
4	NA	NA	1.3 (1.1-1.6)[f]	1.1 (0.8-1.6)
5	NA	NA	1.4 (1.2-1.7)[f]	1.1 (0.7-1.8)
6	NA	NA	1.3 (1.2-1.5)[f]	1.0 (0.6-1.7)
7	NA	NA	1.3 (1.0-1.5)[f]	0.9 (0.5-1.8)
χ^2_7	NA	NA	46.6[f]	χ^2_6 = 9.8

Abbreviations: CA, childhood adversity; CIDI, Composite International Diagnostic Interview; NA, not applicable.

[a] A separate backward recurrence person-year file was created for respondents with a lifetime history of each of the 20 disorders. These 20 files were then stacked. The models were estimated using this stacked data set in a backward recurrence discrete-time survival framework with person-year as the unit of analysis to predict recency of the outcome disorder, thereby forcing the slopes to be constant across the 20 disorders. Each model controlled for person-year (number of years since interview), age at onset, time since onset, sex, 19 dummy variables for the outcome disorder category (ie, for the 20 disorders in the stacked data set), and controls for the previous (to the age at onset of the focal disorder) onset of comorbid disorders. The 5692 respondents had 11 047 lifetime disorder onsets, of which 132 started in the year of interview, and 9301 of the remaining 10 915 had most recent occurrences at a later age than age at onset, ranging from 80 for bipolar I disorder to 1140 for specific phobia. There were 71 783 person-years across all disorders without onsets. Data on the prevalence of individual CAs and the distribution of number of CAs separately in person-years with and without most recent episodes are available on request. For person-years with most recent episodes, these prevalence estimates range from 9.1% (physical illness) to 29.1% (family violence).

[b] The model was estimated with 1 CA at a time in addition to the controls noted in the previous footnote.

[c] The model was estimated using all 12 CAs in addition to the controls noted in the first footnote.

[d] The model was estimated using dummy predictors for number of CAs without any information about types of CAs. The same controls used in earlier models were included as well.

[e] The model was estimated using dummy predictors for the number of CAs and types of CAs. The same controls used in earlier models were included as well.

[f] Significant at $P<.05$, 2-sided test.

OR (range, 1.2-1.2). The ORs associated with number of MFF CAs become increasingly smaller and less than 1.0 in this model as number increases, documenting significant subadditive interactions in the MFF CAs (ie, that the joint effects of multiple MFF CAs are significantly less than the product of the ORs associated with the individual CAs in the cluster).

DISAGGREGATION BY TYPE OF DISORDER

Disaggregation of the final model by type of disorder reveals differential associations of CAs with persistence of mood, anxiety, disruptive behavior, and substance use disorders (Table 2). Type of MFF CA is significantly associated with persistence of mood, anxiety, and substance abuse disorders (χ^2_7=19.8-52.8, P=.006 to <.001) but not with disruptive behavior disorders (χ^2_7=8.5, P=.29). All MFF CAs other than parental criminality are associated with mood, anxiety, or substance use disorders, with significant ORs of 1.2 to 1.9. Only 2 of these ORs vary significantly across the 3 types of disorders: (1) a higher OR of parental substance abuse disorders with respondent substance use disorders (1.5) than with the other disorders (1.0-1.1) and (2) a higher OR of physical abuse with mood disorders (1.9) than with the other disorders (1.0-1.3). Type of non-MFF CA is associated with persistence of disruptive behavior disorders (χ^2_5=12.9, P=.03) but not with mood, anxiety, or substance use disorders (χ^2_5=1.0-6.0, P=.31-.96), although none of the individual CAs is significantly associated with disruptive

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Table 2. Multivariate Associations Between CAs and the Persistence of *DSM-IV*/CIDI Classes of Disorders Based on a Simplei Interactive Model (n=10 915)[a]

	Odds Ratio (95% Confidence Interval)				
	Mood	Anxiety	Substance Use	Disruptive Behavior[b]	Any
MFF CAs					
Parental mental illness	1.3 (1.0-1.6)[c]	1.1 (1.0-1.3)	1.2 (0.9-1.5)	1.2 (0.9-1.7)	1.2 (1.0-1.3)[c]
Parental substance abuse	1.1 (0.9-1.4)	1.0 (0.8-1.2)	1.5 (1.1-2.0)[c]	1.0 (0.7-1.4)	1.1 (0.9-1.2)
Parental criminality	1.1 (0.8-1.5)	1.0 (0.8-1.2)	1.1 (0.8-1.5)	0.9 (0.6-1.3)	1.0 (0.8-1.1)
Family violence	1.3 (1.0-1.7)[c]	1.0 (0.8-1.2)	1.4 (1.1-1.7)[c]	1.1 (0.8-1.6)	1.1 (1.0-1.2)
Physical abuse	1.9 (1.5-2.4)[c]	1.1 (1.0-1.4)	1.3 (1.1-1.7)[c]	1.0 (0.8-1.4)	1.2 (1.1-1.4)[c]
Sexual abuse	1.3 (1.0-1.6)[c]	1.2 (1.0-1.4)	1.6 (1.2-2.1)[c]	1.2 (0.9-1.7)	1.2 (1.0-1.4)[c]
Neglect	1.2 (0.9-1.6)	1.4 (1.0-1.9)[c]	1.1 (0.8-1.5)	1.1 (0.8-1.4)	1.2 (1.0-1.4)[c]
χ^2_7	52.8[c]	19.8[c]	28.0[c]	8.5	31.1[c]
χ^2_6	28.5[c]	18.6[c]	9.9	6.2	23.0[c]
Other CAs					
Parental death	1.1 (0.9-1.4)	1.1 (0.9-1.3)	1.0 (0.8-1.2)	0.9 (0.7-1.2)	1.0 (0.9-1.1)
Parental divorce	1.1 (0.9-1.3)	1.1 (0.9-1.2)	1.0 (0.8-1.2)	1.1 (1.0-1.3)	1.0 (0.9-1.1)
Other parental loss	1.0 (0.7-1.4)	0.9 (0.7-1.2)	0.8 (0.6-1.0)[c]	0.9 (0.7-1.2)	0.9 (0.8-1.0)
Physical illness	1.0 (0.7-1.4)	1.0 (0.8-1.2)	0.8 (0.6-1.1)	1.3 (0.9-1.9)	1.0 (0.8-1.1)
Economic adversity	1.0 (0.8-1.4)	1.1 (0.8-1.4)	0.9 (0.7-1.2)	1.0 (0.8-1.3)	1.0 (0.9-1.2)
χ^2_5	1.0	1.6	6.0	12.9[c]	4.6
χ^2_{12}	57.7[c]	21.9[c]	33.4[c]	24.9[c]	43.3[c]
χ^2_{11}	44.9[c]	20.6[c]	35.1[c]	23.9[c]	41.6[c]
No. of MFF CAs					
0-1	NA	NA	NA	NA	NA
2	0.7 (0.5-0.9)[c]	1.0 (0.7-1.3)	0.8 (0.6-1.2)	1.1 (0.8-1.7)	0.9 (0.8-1.2)
3	0.5 (0.3-0.7)[c]	1.0 (0.7-1.5)	0.7 (0.4-1.2)	1.4 (0.8-2.7)	0.9 (0.7-1.2)
4	0.6 (0.3-1.1)	0.8 (0.4-1.6)	0.4 (0.2-0.8)[c]	1.2 (0.5-2.5)	0.8 (0.5-1.2)
5	0.2 (0.1-0.5)[c]	0.8 (0.4-1.8)	0.5 (0.2-1.1)	1.9 (0.7-5.2)	0.8 (0.4-1.4)
6	0.3 (0.1-0.9)[c]	0.7 (0.3-1.7)	0.2 (0.1-0.6)[c]	1.2 (0.3-5.1)	0.6 (0.3-1.0)
7	0.3 (0.1-2.1)	0.9 (0.2-3.5)	0.2 (0.1-0.5)[c]	2.1 (0.3-13.7)	0.7 (0.3-1.8)
χ^2_6	20.4[c]	3.2	29.5[c]	7.8	6.0
No. of other CAs					
0-1	NA	NA	NA	NA	NA
2	0.9 (0.6-1.3)	1.0 (0.8-1.3)	1.4 (1.0-1.9)	1.0 (0.7-1.4)	1.0 (0.9-1.3)
3	1.6 (0.8-3.1)	1.1 (0.6-1.9)	1.3 (0.7-2.5)	1.0 (0.6-1.5)	1.2 (1.0-1.5)
>4	3.8 (1.1-12.6)[c]	1.5 (0.5-4.4)	2.0 (0.7-6.1)	1.4 (0.3-5.9)	1.5 (0.7-3.1)
χ^2_3	13.5[c]	0.7	3.5	0.6	3.2
χ^2_{21}	171.1[c]	66.1[c]	120.8[c]	94.6[c]	148.8[c]

Abbreviations: CA, childhood adversity; CIDI, Composite International Diagnostic Interview; MFF, maladaptive family functioning; NA, not applicable.

[a] See footnote "a" to Table 1 for a description of the data set and 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 the number of other CAs) in addition to the controls used in the models described in Table 1. 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 persistence, whereas the associations with the number of CAs represent the extent to which the incremental associations of comorbid CAs (ie, the added risk of having a particular type of CA or not in respondents who are otherwise equivalent in having a given number of other CAs controlling for the types of those other CAs) differ from the associations of pure CAs. Data on the prevalence of individual CAs and the distribution of the number of CAs separately in person-years with and without most recent episodes are available on request. For person-years with most recent episodes, these prevalence estimates range from 7.5% (physical illness associated with episodes of substance use disorder) to 34.6% (family violence associated with disruptive behavior disorders).

[b] Disruptive behavior disorders are restricted to those 44 years and younger.

[c] Significant at $P<.05$, 2-sided test.

behavior disorders. Results of a test of the joint associations of the 21 type and number of CA variables with disorder persistence across the 4 disorder classes are significant ($\chi^2_{63}=95.7$, $P=.005$), indicating differential associations by disorder type.

The ORs for number of MMF CAs are significantly related to persistence of mood and substance use disorders ($\chi^2_6=20.4$-29.5, $P=.002$ to $<.001$) but not anxiety and disruptive behavior disorders ($\chi^2_7=3.2$-7.8, $P=.25$-$.78$). As in the aggregate model, the ORs associated with number of CAs are negative, indicating subadditive interactions. The ORs for number of non-MFF CAs, in comparison, are significantly related to persistence of mood disorders ($\chi^2_3=13.5$, $P=.004$) but not any of the other types of disorders ($\chi^2_3=0.6$-3.5, $P=.33$-$.90$) and are greater than 1.0. This means that although none of the non-MFF CAs, when occurring alone, is significantly related to persistence of mood disorders, persistence is significantly higher in respondents who experienced several of these CAs than in respondents who experienced none.

In terms of overall strength of associations, simulations suggest that mean duration between time of interview and time of most recent episode would have increased by 4.9% for mood disorders, 0.6% for anxiety disorders, and 2.1% for substance use disorders and would be largely unaffected for disruptive behavior disorders

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Table 3. Multivariate Associations Between CAs and the Persistence of *DSM-IV*/CIDI Disorders by Age at Interview Based on a Simple Interactive Model (n=10 915)[a]

	Odds Ratio (95% Confidence Interval)			
	Age 18-29 y	Age 30-44 y	Age 45-59 y	Age ≥60 y
MFF CAs				
Parental mental illness	1.2 (1.0-1.5)	1.2 (1.0-1.5)[b]	1.1 (0.9-1.3)	1.1 (0.8-1.4)
Parental substance abuse	1.0 (0.7-1.3)	1.2 (1.0-1.4)	1.2 (0.9-1.5)	0.9 (0.6-1.3)
Parental criminality	0.9 (0.6-1.3)	1.0 (0.8-1.4)	0.9 (0.7-1.2)	1.0 (0.5-2.1)
Family violence	1.0 (0.8-1.3)	1.4 (1.2-1.6)[b]	1.1 (0.8-1.4)	0.8 (0.4-1.6)
Physical abuse	1.0 (0.7-1.4)	1.4 (1.2-1.7)[b]	1.3 (1.0-1.7)[b]	1.0 (0.7-1.6)
Sexual abuse	1.1 (0.8-1.5)	1.4 (1.1-1.7)[b]	1.3 (1.0-1.7)[b]	0.7 (0.4-1.2)
Neglect	1.0 (0.7-1.3)	1.4 (1.1-1.9)[b]	1.1 (0.9-1.4)	0.8 (0.5-1.2)
χ^2_7	4.9	33.3[b]	14.3[b]	4.8
χ^2_6	4.0	14.9[b]	11.8	3.8
Other CAs				
Parental death	0.9 (0.7-1.1)	1.0 (0.8-1.3)	0.9 (0.8-1.1)	1.1 (0.8-1.6)
Parental divorce	1.1 (0.9-1.3)	1.0 (0.9-1.1)	1.0 (0.8-1.3)	0.9 (0.6-1.3)
Other parental loss	1.0 (0.7-1.3)	0.8 (0.6-1.1)	1.1 (0.8-1.4)	0.6 (0.4-1.0)
Physical illness	0.9 (0.6-1.4)	1.0 (0.6-1.4)	1.1 (0.9-1.4)	0.8 (0.6-1.1)
Economic adversity	1.1 (0.9-1.4)	0.9 (0.7-1.1)	1.0 (0.7-1.4)	1.1 (0.7-1.8)
χ^2_5	7.1	6.4	2.5	10.6
χ^2_{12}	10.8	43.0[b]	26.7[b]	19.0
χ^2_{11}	9.8	55.3[b]	22.6[b]	9.5
No. of MFF CAs				
0-1	NA	NA	NA	NA
2	0.9 (0.6-1.4)	0.9 (0.7-1.1)	0.8 (0.6-1.2)	1.5 (0.7-2.9)
3	1.1 (0.6-2.0)	0.7 (0.5-1.0)[b]	0.7 (0.5-1.2)	1.3 (0.4-3.9)
4	0.9 (0.4-1.9)	0.6 (0.3-0.9)[b]	0.9 (0.5-1.7)	1.4 (0.4-6.0)
5	1.4 (0.5-3.9)	0.5 (0.2-1.0)	0.5 (0.3-1.1)	2.0 (0.4-11.0)
6	1.3 (0.4-4.4)	0.3 (0.1-0.6)[b]	0.5 (0.1-1.6)	2.5 (0.3-19.6)
7	1.4 (0.3-7.2)	0.4 (0.1-1.1)	0.6 (0.2-2.2)	NA
χ^2_6	5.2	15.6[b]	12.9[b]	2.5
No. of other CAs				
0-1	NA	NA	NA	NA
2	1.0 (0.7-1.5)	1.2 (0.9-1.6)	1.0 (0.6-1.4)	1.1 (0.5-2.1)
3	1.2 (0.7-2.0)	1.4 (0.9-2.3)	1.0 (0.6-1.7)	3.8 (1.4-10.3)[b]
>4	1.1 (0.4-3.2)	0.0 (0)[b]	2.7 (1.1-6.8)[b]	
χ^2_3	0.7	238.4[b]	27.3[b]	6.8[b]
χ^2_{21}	59.0[b]	419.7[b]	195.9[b]	57.3[b]

Abbreviations: CA, childhood adversity; CIDI, Composite International Diagnostic Interview; MFF, maladaptive family functioning; NA, not applicable.

[a] See footnote "a" to Table 1 for a description of the data set and 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 the number of other CAs) in addition to the controls used in the models described in Table 1. See footnote "a" in Table 2 for a description of the interpretation of the joint effects of type and number of CAs. Data on the prevalence of individual CAs and the distribution of the number of CAs separately in person-years with and without most recent episodes are available on request. For person-years with most recent episodes, these prevalence estimates range from 5.1% (parent criminality in respondents 60 years and older) to 33.8% (family violence in respondents aged 30-44 years).

[b] Significant at $P<.05$, 2-sided test.

if none of the CAs had occurred and the ORs were due to causal effects of CAs.

DISAGGREGATION BY AGE AT INTERVIEW

Disaggregation of the final model by respondent age at interview shows that the significant associations described previously herein are more pronounced in midlife (ages 30-44 and 45-59 years) than in either earlier (ages 18-29 years) or later (ages ≥60 years) ages (**Table 3**). It is only in the groups aged 30 to 44 and 45 to 59 years that we find significantly elevated ORs associated with type of MFF CA (χ^2_7=14.3-33.3, P=.045 to <.001) and significantly decreasing ORs associated with number of MFF CAs (χ^2_6=12.9-15.6, P=.045-.02). As might be expected, the significant ORs associated with type are somewhat larger in respondents in the significant age range (range, 1.2-1.4) than in the total sample (1.2). Type of non-MFF CA is not related to disorder persistence in any age group (χ^2_5=2.5-10.6, P=.78-.06), whereas number of non-MFF CAs is significantly and positively related to persistence in the groups aged 30 to 44, 45 to 59, and 60 years or older (χ^2_3=6.8-238.4, P=.03 to <.001). Simulations suggest that mean duration between time of interview and time of most recent episode would have increased by 1.3% in respondents aged 18 to 29 years, 2.6% in those aged 30 to 44 years, 1.9% in those aged 45 to 59 years, and 1.3% in those 60 years and older if none of the CAs had occurred and the ORs were due to causal effects of CAs.

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Table 4. Simulated Effects of CAs on Proportional Increase in Mean Duration Between Time of Interview and Time of Most Recent Episode in Subsamples Defined by the Cross-classification of Disorder Type and Respondent Age at Interview[a]

	Overall			Age 18-29 y			Age 30-44 y			Age 45-59 y			Age ≥60 y		
	$Mean_r$	$Mean_u$	Difference, %	$Mean_r$	$Mean_u$	Difference, %	$Mean_r$	$Mean_u$	Difference, %	$Mean_r$	$Mean_u$	Difference, %	$Mean_r$	$Mean_u$	Difference, %
Mood	3.8	3.7	4.9	1.4	1.3	6.2	2.6	2.3	12.5	6.0	5.8	4.0	11.8	11.3	5.1
Anxiety	10.9	10.8	0.6	2.0	2.0	−1.5	9.3	9.1	1.5	15.6	15.7	−0.6	32.2	32.0	3.7
Substance use	7.4	7.3	2.1	1.8	1.8	2.2	6.9	6.6	3.3	11.3	11.0	2.7	15.2	13.7	10.7
Disruptive behavior[b]	9.2	9.3	−1.2	4.7	4.8	−2.5	11.5	12.3	−6.5	NA	NA	NA	NA	NA	NA
Any	8.4	8.3	1.6	3.0	2.9	1.4	8.1	7.9	2.7	11.4	11.2	2.0	20.0	19.7	1.3

Abbreviations: CA, childhood adversity; $mean_r$, mean number of years in the restricted model; $mean_u$, mean number of years in the unrestricted model; NA, not applicable.

[a]The restricted model is one in which the odds ratios associated with CAs were restricted to 1.0, simulating a situation in which CAs were completely unrelated to duration between time of interview and time of most recent episode. The unrestricted model is one in which the empirically observed associations between CAs and the outcome were retained. If CAs are associated with more recent episodes, we would expect the estimated mean duration in the restricted model to be larger than that in the unrestricted model, that is, for the amount of time since the most recent episode to be longer in the absence of CAs. This is, in fact, the general pattern in the table, with differences between $mean_r$ and $mean_u$ being mostly positive.

[b]Disruptive behavior disorders are restricted to those 44 years and younger at interview.

DISAGGREGATION BY THE CROSS-CLASSIFICATION OF AGE AT INTERVIEW AND TYPE OF DISORDER

Further disaggregation of the final model by the cross-classification of respondent age at interview and type of disorder shows further variation. (Detailed results are available on request from the authors.) The significantly elevated ORs associated with type of MFF CAs extend into the age range of 60 years and older for mood and substance use disorders, and the significantly decreasing ORs associated with number of MFF CAs appear as early as 18 to 29 years of age for mood and substance use disorders and extend into the age range of 60 years and older for anxiety and substance use disorders. The MFF CAs are more consistently significant (15% of ORs) than are non-MFF CAs (2.5% of ORs), although no single MFF CA stands out as most consistently significant. Each MFF CA is significant in at least 1 subsample, and none are significant in more than 4 of the 16 subsamples created by cross-classifying the 4 types of disorders with the 4 age ranges considered herein. Number of non-MFF CAs predicts greater persistence of anxiety disorders in 3 of 4 life-course subsamples. The hypothesis can be rejected that all MFF CAs have the same OR in most subsamples.

SIMULATED AGGREGATE ASSOCIATIONS OF CAs WITH TIME SINCE MOST RECENT EPISODE

We evaluated the overall importance of CAs for disorder persistence using the simulation method described in the "Analysis Methods" subsection. This simulation estimated the extent to which most recent episodes might have been pushed backward in time (ie, time since most recent episode increased) in the absence of CAs (**Table 4**). The mean observed time since the most recent episode under the model is 8.3 years. This mean value includes respondents who were in episode at the time of interview, who were coded as having a time of 0 years since their most recent episode. This mean value increases only very slightly, to 8.4 years, in the simulated data that restricts the ORs associated with CAs to 1.0. This change represents a 1.6% increase in the mean duration of time since most recent episode associated with the absence of CA effects, documenting that although the associations of CAs with persistence are significant in a statistical sense, the overall substantive importance of CAs is quite modest. Simulations suggest that mean duration between time of interview and time of most recent episode would have increased by no more than 12.5% (for mood disorders in respondents aged 30-44 years) in the absence of CA effects across subsamples defined by the cross-classification of disorder and age at interview.

COMMENT

This study is limited because it is based on retrospective reports of CAs and lifetime disorders; because we evaluated a nonexhaustive set of CAs that did not consider timing, sequencing, persistence, or severity; and because we assessed disorder persistence indirectly from information about recency of last episode rather than by reconstructing or prospectively assessing a complete history of episodes. Results of backward recurrence models might be biased, especially if the disorders under study are associated with early mortality,[41] in which case we would expect the associations of CAs with persistence to be underestimated.[42] A preferable approach might be to assess CAs in childhood and to follow up respondents prospectively into adulthood with low attrition to chart the persistence and severity of their disorders across time. Several long-term prospective general population studies[13,43-45] of this sort exist that could be used to evaluate the generalizability of the results reported herein, although it is important to note that attrition bias in these studies (ie, decreasing response rates with time that might be more pronounced for original respondents with more persistent mental disorders) can lead to errors in estimates that in some cases could be as great as those due to recall bias in retrospective studies. The ideal approach, in light of these

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limitations of retrospective and prospective studies, is to compare results from the 2 kinds of studies and to have the most faith in results that are consistent across the two.

Additional study limitations are that the list of CAs, although larger than in most previous studies, is not exhaustive and did not consider timing, sequencing, severity, or duration of individual CAs. In addition, the analysis of joint CA effects focused only on broad patterns of interactions in dichotomous CA measures and did not include fine-grained evaluation of targeted interactions. Future analyses need to examine targeted interactions against the backdrop of the broader patterns found in the present study. Future research is also needed to examine disorder persistence in childhood and adolescence. We could not do this because the NCS-R included only respondents older than 18 years.

In the context of these limitations, these findings extend the previous literature on the associations of CAs with disorder course in several important ways. First, we found clear evidence that CAs predict disorder persistence significantly, albeit with small effect sizes, and that these significant associations can be detected throughout the life course, including in elderly people. Second, we found that CAs associated with MFF are stronger predictors of persistence than are other CAs. A similar specification was found in the analysis of the association between CAs and first onset of mental disorders[6] and in previous research on the associations of CAs with prevalent cases of adult disorders.[46,47] Third, we found that the effects of CAs on persistence are larger for mood and substance use disorders than for anxiety disorders. Fourth, we found that the joint effects of co-occurring MFF CAs on persistence are subadditive, whereas the effects of other CAs are largely confined to people who experienced multiple other CAs. Consistent with recent work,[25] these results show that the simple summary count measures of CAs used in much of the previous literature on multivariate CA effects[41,48,49] are inadequate to capture the true effects of multiple CAs. Moreover, these findings suggest that the dozens of previous studies that have examined associations between specific CAs and specific mental and physical health outcomes[50-53] have most likely overestimated these associations by failing to account for co-occurring CAs and comorbid outcomes.

Perhaps the most important finding of this study comes from the simulations, which found that although the associations of CAs with persistence are significant in a statistical sense, they are small in substantive terms. The largest effect size is 5% for mood disorders. To translate this into substantive terms, a 5% increase in time since most recent episode occurrence means that a person with a history of depression who has not had an episode in the past 20 years would be expected to have had a most recent episode 21 years ago rather than 20 years ago were it not for a history of CAs. Effects of CAs on anxiety and substance abuse disorders are even smaller. These results indirectly suggest that the public health implications of CAs are greater for primary than for secondary prevention because the associations of CAs with disorder onset are much stronger than the associations with persistence.[6]

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Correspondence: Ronald C. Kessler, PhD, Department of Health Care Policy, Harvard Medical School, 180 Longwood Ave, Boston, MA 02115 (kessler@hcp.med.harvard.edu).

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Additional Information: A complete list of WMH publications can be found at http://www.hcp.med.harvard.edu/wmh/. A complete list of NCS publications and the

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