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Association of Childhood Adversities and Early-Onset Mental Disorders With Adult-Onset Chronic Physical Conditions

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Context: The physical health consequences of childhood psychosocial adversities may be as substantial as the mental health consequences, but whether this is the case remains unclear because much prior research has involved unrepresentative samples and a selective focus on particular adversities or physical outcomes. The association between early-onset mental disorders and subsequent poor physical health in adulthood has not been investigated.

Objective: To investigate whether childhood adversities and early-onset mental disorders are independently associated with increased risk of a range of adult-onset chronic physical conditions in culturally diverse samples spanning the full adult age range.

Design: Cross-sectional community surveys of adults in 10 countries.

Setting: General population.

Participants: Adults (ie, aged ≥18 years; N=18 303), with diagnostic assessment and determination of age at onset of *DSM-IV* mental disorders, assessment of childhood familial adversities, and age of diagnosis or onset of chronic physical conditions.

Main Outcome Measures: Risk (ie, hazard ratios) of adult-onset (ie, at age >20 years) heart disease, asthma, diabetes mellitus, arthritis, chronic spinal pain, and chronic headache as a function of specific childhood adversities and early-onset (ie, at age <21 years) *DSM-IV* depressive and anxiety disorders, with mutual adjustment.

Results: A history of 3 or more childhood adversities was independently associated with onset of all 6 physical conditions (hazard ratios, 1.44 to 2.19). Controlling for current mental disorder made little difference to these associations. Early-onset mental disorders were independently associated with onset of 5 physical conditions (hazard ratios, 1.43 to 1.66).

Conclusions: These results are consistent with the hypothesis that childhood adversities and early-onset mental disorders have independent, broad-spectrum effects that increase the risk of diverse chronic physical conditions in later life. They require confirmation in a prospectively designed study. The long course of these associations has theoretical and research implications.

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THE DELETERIOUS MENTAL health consequences of childhood psychosocial adversities, such as abuse and neglect, have been well documented.[1] Although less extensively researched, childhood adversities have been hypothesized to increase the risk of adult onset of a spectrum of chronic physical diseases.[2,3] A recent meta-analysis[4] of the effects of child abuse on medical outcomes in adulthood reached that exact conclusion, finding that the increased risk of selected adverse physical health outcomes was comparable to that observed for poor mental health outcomes. However, the evidence base for the association of child maltreatment with subsequent physical health has significant limitations, which include lack of control for the potentially biasing effects of current mental disorder on recall of childhood adversities, a predominant focus on a single adversity (ie, sexual abuse), and a lack of sample diversity in terms of race/ethnicity (ie, mostly white), age (ie, mostly young adults), and sex (ie, mostly female). The relatively young age of current prospective cohorts with childhood maltreatment data is a particular limitation because it greatly restricts the range of disease outcomes studied and truncates the full expression of disease risk, potentially biasing findings toward the null.

In prior research that has considered the influence of the early psychosocial environment on later physical health, mental dis-

orders have generally been out of the frame of consideration, which may be an important oversight. It is possible that early-onset mental disorders may function as a type of endogenous psychosocial stressor, associated with later poor physical health not only through risky health behaviors but also through direct biological mechanisms. Mental disorders have been hypothesized to contribute to allostatic load,[5] a chronic imbalance in the hormonal and neurotransmitter mediators of the stress response[6] that has been linked to a range of adverse metabolic, cardiovascular, immune, and cognitive effects.[7,8] Research suggests that the stressors that occur early in life have the most potential to contribute to allostatic load through dysregulation of the hypothalamic-pituitary-adrenal axis.[9-11] This finding generates a hypothesis that associations might exist between early-onset mental disorders and chronic physical conditions in adulthood. Although associations between depression and anxiety measured in midlife and the subsequent onset of heart disease and other chronic conditions are well established,[12,13] the associations between diagnosed early-onset mental disorders and adult-onset physical conditions have not been studied previously, to our knowledge. The span of time during which mental-physical sequential associations may be developing has important implications for the understanding of mechanisms and the planning of interventions.

We further suggest the need to investigate the independent associations of childhood adversities and mental disorders with subsequent physical health. Childhood adversities are associated with mental and physical health outcomes and so may confound sequential associations between mental health and subsequent physical health.[14] Moreover, current mental disorders may bias recall of childhood adversities[15] and so may potentially inflate associations between childhood adversities and physical conditions in retrospective studies (ie, most studies rely on retrospective recall of childhood adversities, such as abuse and neglect).

In this study using data from 10 countries participating in the World Health Organization (WHO) World Mental Health (WMH) Surveys initiative, we sought to answer the following question: Are childhood adversities and early-onset mental disorders independently associated with increased risk of adult-onset chronic physical conditions in nationally representative, culturally diverse survey samples of men and women spanning the full adult age range? We also assessed the associations between childhood adversities and physical health outcomes after controlling for current mental disorder. Although the surveys are cross-sectional, they collected information on the age at onset of mental disorders and age at onset or diagnosis of chronic physical conditions, which allowed the use of survival analyses examining predictive associations.

METHODS

SAMPLES

Ten surveys were performed in the Americas (ie, Colombia, Mexico, and the United States), Europe (ie, Belgium, France, Germany, Italy, the Netherlands, and Spain), and Asia (ie, Ja-

pan) between January 1, 2001, and December 31, 2004. All surveys were based on multistage, clustered, area probability household samples and were conducted face to face by trained lay interviewers. Sample sizes range from 2372 (in the Netherlands) to 9282 (in the United States). Response rates range from 45.9% (in France) to 87.7% (in Colombia), with a weighted average of 66.7%. Internal subsampling was used to reduce respondent burden. Part 1 included the core diagnostic assessment of mental disorders. Part 2 included additional information relevant to a wide range of survey aims, including assessment of chronic physical conditions and childhood adversities. All respondents completed part 1. All part-1 respondents who met the criteria for any mental disorder and a probability sample of other respondents were administered part 2. Part-2 respondents were weighted by the inverse of their probability of selection for part 2 of the interview to adjust for differential sampling. Analyses in this article were based on the weighted part 2 subsample (N=18 303). Additional weights were used to adjust for differential probabilities of selection within households, to adjust for nonresponse, and to match the samples to population sociodemographic distributions. Further detail regarding the survey samples is provided elsewhere.[16]

TRAINING AND FIELD PROCEDURES

The central WMH staff trained bilingual supervisors in each country. The WHO translation protocol was used to translate instruments and training materials. Some surveys were performed in bilingual form and others were performed exclusively in the country's official language or languages. Quality control protocols, described in more detail elsewhere,[16] were standardized across countries to check interviewer accuracy and to specify data cleaning and coding procedures. Each country followed national procedures for gaining study approval by institutional review board or ethics committees and for obtaining informed consent and protecting human cohort individuals.

MENTAL DISORDER STATUS

All surveys used the WMH Survey version of the WHO Composite International Diagnostic Interview (WMH-CIDI, now known as CIDI 3.0),[17] a fully structured diagnostic interview, to assess mental disorders. Methodologic evidence collected in clinical calibration studies has shown that all the disorders considered herein were assessed with acceptable reliability and validity.[18] Disorders were assessed using the definitions and criteria of the *DSM-IV*. The CIDI organic exclusion rules were imposed. This article includes anxiety disorders (ie, generalized anxiety disorder, panic disorder and/or agoraphobia, posttraumatic stress disorder [PTSD], and social phobia) and depression (ie, major depressive disorder). Prior WMH Survey analyses showed that these disorders were associated most strongly with physical condition comorbidity and also demonstrated that despite the variation in frequency of both mental disorders and physical conditions across WMH surveys, the associations between mental disorders and physical conditions are remarkably consistent across countries.[19,20]

CHILDHOOD FAMILY ADVERSITIES

The following childhood adversities were assessed: physical abuse, sexual abuse, neglect, parental death, parental divorce, other parental loss, parental mental disorder, parental substance use, parental criminal behavior, family violence, and family economic adversity. The aim was to assess the occurrence of childhood adversities occurring in the context of the family (rather than all possible childhood adversities) because these

are more likely to be sustained for long periods and to contribute to chronic health effects. Those respondents who reported that the experience occurred before the age of 18 years and met the criteria specified for a given adversity were coded as having experienced childhood family adversity. Assessment of the adversities is detailed in prior publications.[20,21]

CHRONIC PHYSICAL CONDITIONS

Chronic physical conditions were assessed using a checklist adapted from the US Health Interview Schedule. The medical diagnoses were ascertained by the following question: "Did a doctor or other health professional ever tell you that you had . . . heart disease, asthma, diabetes or high blood sugar . . . ?" Symptomatic conditions were ascertained with the question: "Have you ever had . . . arthritis or rheumatism, chronic back or neck problems, frequent or severe headaches . . . ?" For all conditions reported, respondents were asked how old they were when their condition was first diagnosed (for the medical diagnoses) or when they first had experienced the condition (for the symptomatic conditions).

STATISTICAL ANALYSIS

The association of childhood adversities and early-onset mental disorders with adult-onset physical conditions was studied with survival analyses, using retrospectively reported age at diagnosis or onset of the physical condition (reported in whole years). Survival analyses of retrospective data have been used previously to study the predictors of onset or survival of medical conditions.[22,23] The start of the period at risk of the physical conditions was set at age 20 years. Time to age of onset of the physical condition from age 20 was the dependent variable. Data from individuals who had not developed the physical condition were censored at their current age. Data from individuals who reported that the physical condition developed before age 21 years were excluded. Cox proportional hazards models estimated the risk of each of the physical conditions as a function of number and type of childhood adversities and early-onset (ie, at age <21 years) depressive or anxiety disorder status. Specific childhood adversities, specific early-onset mental disorders, and the number of childhood adversities (0, 1, 2, and ≥3) were the predictor variables. The no-adversities category and that of individuals without early-onset depression or anxiety disorder served as the reference groups. Childhood adversities and early-onset mental disorders were included in the Cox models separately and then simultaneously to investigate to what extent they were independently associated with the risk of onset of each physical condition.

All associations are expressed as hazard ratios (HRs), measuring the relative risk of the physical condition after adjustment for current age and sex. The main analyses were repeated, additionally controlling for educational level, but because the results were consistently similar to those not controlling for educational level, the simpler model results are reported herein. Models of asthma and heart disease additionally controlled for smoking status (ie, ever, never, or current). Further analyses of the association between adversities and each physical condition adjusted for current (ie, 12-month) anxiety or mood disorder. We also assessed for the interaction of childhood adversities with early-onset mental disorders in predicting the onset of each physical condition, but these interaction effects were not significant, so only main effects are reported herein. Country was included in all analyses as a stratifying variable, which allowed each country to have a unique hazard function. The assumption of proportional hazards was assessed by inspecting log-minus-log plots of the survival functions. Statistical significance was evaluated with $P > .049$ for a 2-sided test. The analyses were performed using the SURVIVAL procedure in SUDAAN[24] statistical software to account for the complex sample design.

ASSOCIATIONS OF SPECIFIC EARLY-ONSET MENTAL DISORDERS AND CHILDHOOD ADVERSITIES WITH ONSET OF PHYSICAL CONDITIONS

Data regarding the distribution of childhood adversities, mental disorders, and chronic physical conditions across the 10 countries have been published previously.[20] All 5 early-onset mental disorders were associated with the onset of the 3 chronic pain conditions in adulthood, with HRs between 1.52 and 2.27 (**Table 1**). Early-onset major depressive disorder, PTSD, and panic disorder also predicted the subsequent onset of heart disease and asthma, and social phobia predicted the onset of heart disease. No early-onset mental disorders were associated with the onset of diabetes mellitus. Table 1 also lists the associations between specific childhood adversities and the onset of the 6 health outcomes. Physical abuse was the only childhood adversity associated with onset of each of the chronic disease outcomes. Other loss of parent and parental mental disorder were associated with onset of 5 of the 6 health outcomes. The magnitude of risk of health condition onset associated with childhood adversities was similar to that associated with early-onset mental disorders, with most HRs being less than 2. The exception to this was the association between sexual abuse and heart disease onset, which was considerably stronger (HR, 3.91).

INDEPENDENT ASSOCIATIONS BETWEEN EARLY-ONSET MENTAL DISORDERS AND CHILDHOOD ADVERSITIES WITH ONSET OF PHYSICAL CONDITIONS

Even after adjustment for childhood adversities, early-onset depressive and anxiety disorders (ie, any early-onset mental disorder) were associated with the onset of 5 of the 6 physical conditions in adulthood (**Table 2**). Similarly, 3 or more childhood adversities were associated with all outcomes after adjustment for early-onset mental disorders, and 2 or more childhood adversities were associated with 5 of the 6 outcomes. Table 2 shows a dose-response relationship between the number of childhood adversities experienced and the likelihood of later physical-condition onset. We also assessed the associations between the number of childhood adversities and the onset of health outcomes after adjustment for current mental disorder to control for the potentially biasing effects of mood on recall of adversities (data not shown; available on request from the authors). The magnitude of these associations adjusted for current mental disorder was similar to that given in Table 2, with 3 or more childhood adversities associated with all physical condition outcomes and 2 or more adversities associated with all outcomes except diabetes mellitus.

Table 1. Associations Between Specific Early-Onset Mental Disorders and Childhood Adversities With the Subsequent Onset of Chronic Physical Conditions in Adulthood[a]

Variable	HR (95% CI)[b]					
	Heart Disease	Asthma	Diabetes Mellitus	Osteoarthritis	Chronic Spinal Pain (Back or Neck)	Frequent or Severe Headache
Early-onset (ie, at age <21 years) mental disorders						
Major depressive disorder	**1.82** (1.07-3.09)	**2.11** (1.51-2.93)	1.14 (0.88-1.47)	**1.52** (1.26-1.85)	**1.59** (1.37-1.85)	**1.68** (1.40-2.03)
Generalized anxiety disorder	1.42 (0.78-2.59)	1.46 (0.89-2.38)	1.02 (0.57-1.80)	**1.69** (1.32-2.17)	**2.01** (1.64-2.45)	**1.65** (1.32-2.06)
Social phobia	**1.80** (1.30-2.50)	1.19 (0.85-1.67)	1.07 (0.78-1.46)	**1.54** (1.34-1.76)	**1.52** (1.34-1.73)	**1.61** (1.35-1.91)
Posttraumatic stress disorder	**2.39** (1.51-3.79)	**1.95** (1.07-3.58)	1.08 (0.67-1.73)	**1.91** (1.50-2.43)	**2.27** (1.76-2.92)	**1.65** (1.19-2.30)
Panic disorder or agoraphobia	**2.32** (1.49-3.63)	**2.06** (1.34-3.18)	1.32 (0.80-2.18)	**1.68** (1.38-2.03)	**1.62** (1.32-1.99)	**1.76** (1.37-2.25)
Childhood adversity						
Physical abuse	**1.82** (1.37-2.43)	**1.92** (1.32-2.81)	**1.52** (1.16-2.00)	**1.42** (1.22-2.09)	**1.61** (1.43-1.82)	**1.64** (1.44-1.88)
Sexual abuse	**3.91** (2.40-6.39)	1.26 (0.84-1.82)	0.99 (0.63-1.55)	**1.64** (1.28-2.09)	**1.62** (1.28-2.06)	**1.73** (1.38-2.17)
Neglect	1.37 (0.98-1.91)	1.02 (0.70-1.49)	1.02 (0.74-1.42)	**1.29** (1.08.1.55)	**1.33** (1.15-1.34)	**1.21** (1.02-1.43)
Parental death	**1.34** (1.05-1.70)	**1.34** (1.01-1.77)	0.91 (0.71-1.18)	1.02 (0.89-1.18)	1.08 (0.95-1.22)	1.10 (0.93-1.31)
Parental divorce	1.31 (0.95-1.80)	1.23 (0.84-1.82)	**1.37** (1.01-1.86)	1.02 (0.86-1.22)	**1.16** (1.01-1.34)	1.01 (0.84-1.22)
Other loss of parent[c]	**1.41** (1.03-1.93)	1.36 (0.94-1.97)	**1.58** (1.12-2.23)	**1.26** (1.04-1.54)	**1.26** (1.08-1.48)	**1.29** (1.06-1.58)
Parental mental disorder	**1.58** (1.18-2.12)	**1.50** (1.05-2.17)	1.04 (0.74-1.47)	**1.27** (1.07-1.51)	**1.42** (1.24-1.63)	**1.52** (1.25-1.83)
Parental substance use disorder	**1.75** (1.18-2.60)	1.28 (0.83-1.97)	1.30 (0.92-1.84)	**1.38** (1.14-1.67)	**1.31** (1.12-1.54)	**1.42** (1.18-1.71)
Violence in family	1.31 (0.95-1.82)	**1.51** (1.05-2.17)	1.16 (0.87-1.55)	**1.39** (1.16-1.67)	**1.52** (1.32-1.74)	**1.51** (1.30-1.76)
Criminal behavior in family	1.47 (0.87-2.47)	1.37 (0.82-2.31)	**1.81** (1.26-2.59)	**1.36** (1.07-1.71)	**1.32** (1.08-1.62)	**1.44** (1.10-1.88)
Family economic adversity	1.41 (0.96-2.07)	0.90 (0.61-1.33)	**1.44** (1.04-1.98)	1.08 (0.93-1.26)	1.13 (0.95-1.34)	1.21 (0.98-1.48)

Abbreviations: CI, confidence interval; HR, hazard ratio.
[a] All models were adjusted for age, sex, and country, and models for heart disease and asthma were additionally adjusted for smoking status.
[b] Bold HRs are significant at $P < .05$.
[c] For example, adoption, foster care, or leaving home before the age of 16 years.

Table 2. Independent Associations Between Early-Onset Mental Disorders and Number of Childhood Adversities With the Subsequent Onset of Chronic Physical Conditions in Adulthood[a]

Variable	HR (95% CI)[b]					
	Heart Disease	Asthma	Diabetes Mellitus	Osteoarthritis	Chronic Spinal Pain (Back or Neck)	Frequent or Severe Headache
Any early-onset (ie, at age <21 years) mental disorder	**1.66** (1.26-2.18)	**1.54** (1.17-2.03)	1.08 (0.88-1.33)	**1.43** (1.28-1.61)	**1.56** (1.40-1.73)	**1.62** (1.42-1.89)
Number of childhood adversities						
1	1.23 (0.98-1.52)	1.21 (0.96-1.54)	1.06 (0.84-1.34)	1.00 (0.88-1.14)	**1.13** (1.02-1.25)	**1.40** (1.22-1.60)
2	**1.55** (1.19-2.03)	**1.43** (1.04-1.98)	1.19 (0.88-1.62)	**1.27** (1.08-1.50)	**1.34** (1.17-1.54)	**1.41** (1.19-1.67)
≥3	**2.19** (1.59-3.01)	**1.55** (1.06-1.28)	**1.59** (1.20-2.09)	**1.44** (1.24-1.67)	**1.59** (1.36-1.82)	**1.63** (1.37-1.95)

Abbreviations: CI, confidence interval; HR, hazard ratio.
[a] All models were adjusted for age, sex, and country, and models for heart disease and asthma were additionally adjusted for smoking status. Models with early-onset mental disorders as predictors were adjusted for childhood adversities; models with childhood adversities as predictors were adjusted for early-onset mental disorders.
[b] Bold HRs are significant at $P < .05$.

COMMENT

In this 10-country study, multiple childhood adversities and early-onset mental disorders were found to be independent predictors of a range of adult-onset chronic physical conditions. It is notable that the predictors were as strongly associated with the diagnosed medical conditions as they were with the symptomatic pain conditions. The association between 3 or more childhood adversities and the physical condition outcomes was generalized, occurring for all outcomes included in the study. It was largest in magnitude for heart disease, but all associations were within a fairly narrow range (HR, 1.44-2.19).

Similarly, some early-onset mental disorders (especially major depressive disorder, PTSD, and panic disorder) were associated with the onset of all physical health outcomes except diabetes mellitus. These analyses did not take into account the severity or the precise timing of onset of the childhood adversities or the early-onset mental disorders. These associations should therefore be considered averages. Such averaged estimates probably underestimate the strength of association between the more severe adversities or mental dis-

orders occurring at critical childhood developmental stages.

Several limitations need to be borne in mind when interpreting these results. This cross-sectional study relies on retrospective reports of mental disorders and their age at onset. Recall of mental disorders, particularly during long intervals, leads to false-negative results (ie, underreporting due to forgetting), although false-positive results are rare.[25] Bias also exists regarding recall of the age at onset of mental disorders.[26] The WMH Surveys revised the method of asking about age at onset to reduce this bias, but some bias probably remains. However, data regarding age at onset or diagnosis of medical conditions have been found to be accurate and reliable.[27] Childhood adversities also were assessed retrospectively. Reviews of the validity of such reports conclude that retrospectively reported events that are clearly operationalized are sufficiently valid to warrant their use, although a considerable degree of underreporting and possibly some bias exist.[28] Bias can result from current mental state influencing recall,[15] but this study accounted for that possibility by assessing associations between childhood adversities and the health outcomes after adjustment for current mental disorders.

Another considerable limitation is that the medical conditions were assessed on the basis of self-report of diagnoses rather than independent verification by a medical professional. This limitation is mitigated somewhat by the generally strong agreement between self-report of medical diagnoses and physician or medical record confirmation of those diagnoses[29,30] and by the fact that although affective traits and states have been found to bias the self-report of physical symptoms, they have not been found to bias the self-report of diagnosed physical conditions.[31,32] The WMH Survey samples may have better mental or physical health than nonrespondents or may be biased because of differential selection out of the population through early mortality. These sample selection factors would probably lead to downward (ie, conservative) bias in estimating the strength of associations. Lastly, although most estimates were significant at very low P values, the large number of statistical comparisons undertaken increases the likelihood that some individual estimates may be chance findings. More weight should be placed on the overall pattern of findings than on the significance (or lack thereof) of any single estimate.

This study also has important strengths. It addresses the limitations of much prior research in its ability to investigate the physical health outcomes of a wide range of childhood adversities in a large, culturally diverse general population sample spanning the entire adult age range. It also provides the first investigation of associations between early-onset diagnosed mental disorders with a range of adult-onset physical conditions, independent of the effects of childhood adversities. Our findings are consistent with the results of prospective research linking depression with the subsequent onset of medical conditions. For example, we observed an HR of 1.82 between early-onset major depressive disorder and adult heart disease onset, which is within the 1.50 to 2.00 range from meta-analyses of the prospective association between depression measured in adulthood and subsequent heart

disease onset.[12,13] Our findings also are consistent with extant research pertaining to associations between retrospectively reported childhood adversities and health outcomes.[2] It is noteworthy that we found significant associations between abuse in childhood and pain outcomes in adulthood where prospective studies have failed to find this.[33] Although one interpretation of this null finding from prospective studies is that the memories of abuse rather than the abuse itself are linked to later health,[1,33] another explanation is that the prospective studies in question were based on too-young samples (ie, aged <30 years) to observe the relationship. Evidence for this latter interpretation comes from the survival curves of the association between childhood adversities and onset of spinal pain from this study (data not shown; available on request from the authors), which showed that the association did not emerge until approximately age 40 years.

Given the cross-sectional nature of this study, it should be considered exploratory in nature. A definitive study of causal relationships among early-onset mental disorders, childhood adversities, and the subsequent onset of a spectrum of chronic physical conditions requires a prospective design. This is logistically challenging because such a study would necessitate a large sample followed up during the lifetime of the study participants. Unfortunately, data from such a definitive study will not be forthcoming in the foreseeable future. Therefore, scientific inference regarding these relationships will depend on interpreting results from diverse study designs, each with its own significant flaws and limitations—some retrospective with potentially biased ascertainment of exposures and outcomes and others prospective with limitations on sample size, diversity, breadth of coverage of exposures and outcomes, and duration of follow-up.

This study found that childhood adversities and early-onset mental disorders were independently associated with a range of health outcomes. The results are consistent with the theory that early adverse environments can influence the setting of the stress response and shape behavioral responses and subsequent environmental exposures in a way that may increase risks of a spectrum of chronic physical conditions in later life.[34] Depression and anxiety may further embed risky health behaviors through an individual's attempts at emotional regulation[35] and make independent contributions to allostatic load.[5] How childhood adversities and early-onset mental disorders might combine to increase the risk of physical condition onset will be the work of future research using prospective data that can disentangle the temporal sequence of the predictors and the potential mediators (eg, behavioral, biological, and socioeconomic). Although the magnitude of risk associated with specific childhood adversities and early-onset mental disorders was generally modest, many estimates are of a similar magnitude to the association between serum cholesterol and heart disease. The public health significance of the latter has less to do with its magnitude than with the prevalence of elevated serum cholesterol levels in the general population, and the same argument can be made for the risk factors of childhood adversities and depressive and anxiety disorders. Moreover, if the results reported herein were confirmed by prospective studies, they would constitute broad-spectrum effects across a range of common

chronic physical conditions, expanding their population impact.

In conclusion, the results of this cross-national study are consistent with the hypothesis that childhood adversities and early-onset mental disorders have independent associations with adult onset of a spectrum of chronic physical conditions. Although the retrospective nature of these data precludes strong causal inference, the results are consistent with current theories of the role of allostatic load in the theorized cause of diverse chronic physical conditions. This study indicates a need for existing and future prospective studies to investigate the role of both childhood adversities and early-onset mental disorders in predicting a range of chronic physical conditions, while taking into account the potentially long time frame for the expression of associations between these early-life psychosocial risk factors and later disease outcomes.

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REFERENCES

1. Gilbert R, Widom CS, Browne K, Fergusson DM, Webb E, Janson S. Burden and consequences of child maltreatment in high-income countries. *Lancet*. 2009; 373(9657):68-81.

2. Felitti VJ, Anda RF, Nordenberg D, Williamson DF, Spitz AM, Edwards V, Koss MP, Marks JS. Relationship of childhood abuse and household dysfunction to many of the leading causes of death in adults: the Adverse Childhood Experiences (ACE) Study. *Am J Prev Med*. 1998;14(4):245-258.

3. Anda RF, Felitti VJ, Bremner JD, Walker JD, Whitfield C, Perry BD, Dube SR, Giles WH. The enduring effects of abuse and related adverse experiences in childhood: a convergence of evidence from neurobiology and epidemiology. *Eur Arch Psychiatry Clin Neurosci*. 2006;256(3):174-186.

4. Wegman HL, Stetler C. A meta-analytic review of the effects of childhood abuse on medical outcomes in adulthood. *Psychosom Med*. 2009;71(8):805-812.

5. McEwen BS. Mood disorders and allostatic load. *Biol Psychiatry*. 2003;54(3):200-207.

6. McEwen BS. Protective and damaging effects of stress mediators. *N Engl J Med*. 1998;338(3):171-179.

7. Miller GE, Cohen S, Ritchey AK. Chronic psychological stress and the regulation of pro-inflammatory cytokines: a glucocorticoid resistance model. *Health Psychol*. 2002;21(6):536-541.

8. Chrousos GP, Kino T. Glucocorticoid action networks and complex psychiatric and/or somatic disorders. *Stress*. 2007;10(2):213-219.

9. Heim C, Newport DJ, Heit S, Graham YP, Wilcox M, Bonsall R, Miller AH, Nemeroff CB. Pituitary-adrenal and autonomic responses to stress in women after sexual and physical abuse in childhood. *JAMA*. 2000;284(5):592-597.

10. Teicher MH, Andersen SL, Polcari A, Anderson CM, Navalta CP. Developmental neurobiology of childhood stress and trauma. *Psychiatr Clin North Am*. 2002; 25(2):397-426, vii-viii.

11. Sanchez MM. The impact of early adverse care on HPA axis development: non-human primate models. *Horm Behav*. 2006;50(4):623-631.

12. Wulsin LR, Singal BM. Do depressive symptoms increase the risk for the onset of coronary disease? a systematic quantitative review. *Psychosom Med*. 2003; 65(2):201-210.

13. Nicholson A, Kuper H, Hemingway H. Depression as an aetiologic and prognostic factor in coronary heart disease: a meta-analysis of 6362 events among 146 538 participants in 54 observational studies. *Eur Heart J*. 2006;27(23):2763-2774.

14. Goodwin RD, Fergusson DM, Horwood LJ. Asthma and depressive and anxiety disorders among young persons in the community. *Psychol Med*. 2004;34 (8):1465-1474.

15. Williams JMG, Watts FN, MacLeod C, Mathews A. *Cognitive Psychology and Emotional Disorders*. 2nd ed. Chichester, England: John Wiley & Sons Ltd; 1997.

16. Kessler RC, Ustun TB, eds. *The WHO World Mental Health Surveys: Global Perspectives on the Epidemiology of Mental Disorders*. New York, NY: Cambridge University Press; 2008.

17. Kessler RC, Ustün TB. The World Mental Health (WMH) Survey Initiative version of the World Health Organization (WHO) Composite International Diagnostic Interview (CIDI). *Int J Methods Psychiatr Res*. 2004;13(2):93-121.

18. Haro JM, Arbabzadeh-Bouchez S, Brugha TS, de Girolamo G, Guyer ME, Jin R, Lepine JP, Mazzi F, Reneses B, Vilagut G, Sampson NA, Kessler RC. Concordance of the Composite International Diagnostic Interview Version 3.0 (CIDI 3.0) with standardized clinical assessments in the WHO World Mental Health surveys. *Int J Methods Psychiatr Res*. 2006;15(4):167-180.

19. Scott KM, Bruffaerts R, Tsang A, Ormel J, Alonso J, Angermeyer MC, Benjet C, Bromet E, de Girolamo G, de Graaf R, Gasquet I, Gureje O, Haro JM, He Y, Kessler RC, Levinson D, Mneimneh ZN, Oakley Browne MA, Posada-Villa J, Stein DJ, Takeshima T, Von Korff M. Depression-anxiety relationships with chronic physical conditions: results from the World Mental Health Surveys. *J Affect Disord*. 2007; 103(1-3):113-120.

20. Von Korff M, Scott KM, Gureje O, eds. *Global Perspectives on Mental-Physical Comorbidity in the WHO World Mental Health Surveys*. New York, NY: Cambridge University Press; 2009.

21. Scott KM, Von Korff M, Alonso J, Angermeyer MC, Benjet C, Bruffaerts R, de Girolamo G, Haro JM, Kessler RC, Kovess V, Ono Y, Ormel J, Posada-Villa J. Childhood adversity, early-onset depressive/anxiety disorders, and adult-onset asthma. *Psychosom Med*. 2008;70(9):1035-1043.

22. Sainsbury R, Johnston C, Haward B. Effect on survival of delays in referral of patients with breast-cancer symptoms: a retrospective analysis. *Lancet*. 1999; 353(9159):1132-1135.

23. Smith GCS, Pell JP, Walsh D. Pregnancy complications and maternal risk of ischaemic heart disease: a retrospective cohort study of 129 290 births. *Lancet*. 2001; 357(9273):2002-2006.

24. *SUDAAN: Software for the Statistical Analysis of Correlated Data*. Research Triangle Park, NC: Research Triangle Institute; 2001.

25. Wells JE, Horwood LJ. How accurate is recall of key symptoms of depression? a comparison of recall and longitudinal reports. *Psychol Med*. 2004;34(6): 1001-1011.

26. Simon GE, VonKorff M. Recall of psychiatric history in cross-sectional surveys: implications for epidemiologic research. *Epidemiol Rev*. 1995;17(1):221-227.

27. Torén K, Palmqvist M, Löwhagen O, Balder B, Tunsäter A. Self-reported asthma was biased in relation to disease severity while reported year of asthma onset was accurate. *J Clin Epidemiol*. 2006;59(1):90-93.

28. Hardt J, Rutter M. Validity of adult retrospective reports of adverse childhood experiences: review of the evidence. *J Child Psychol Psychiatry*. 2004;45(2): 260-273.

29. Kriegsman DMW, Penninx BWJH, Van Eijk JTM, Boeke AJP, Deeg DJH. Self-reports and general practitioner information on the presence of chronic diseases in community dwelling elderly: a study on the accuracy of patients' self-reports and on determinants of inaccuracy. *J Clin Epidemiol*. 1996;49(12): 1407-1417.

30. Baumeister H, Kriston L, Bengel J, Härter M. High agreement of self-report and physician-diagnosed somatic conditions yields limited bias in examining mental-physical comorbidity. *J Clin Epidemiol*. 2010;63(5):558-565.

31. Kolk AMM, Hanewald GJFP, Schagen S, Gijsbers van Wijk CMT. Predicting medically unexplained physical symptoms and health care utilization: a symptom-perception approach. *J Psychosom Res*. 2002;52(1):35-44.

32. Vassend O, Skrondal A. The role of negative affectivity in self-assessment of health: a structural equation approach. *J Health Psychol*. 1999;4(4):465-482.

33. Raphael KG, Widom CS, Lange G. Childhood victimization and pain in adulthood: a prospective investigation. *Pain*. 2001;92(1-2):283-293.

34. Scott KM. The development of mental-physical comorbidity. In: Von Korff MR, Scott KM, Gureje O, eds. *Global Perspectives on Mental-Physical Comorbidity in the WHO World Mental Health Surveys*. New York, NY: Cambridge University Press; 2009:97-107.

35. Hertzman C. The biological embedding of early experience and its effects on health in adulthood. *Ann N Y Acad Sci*. 1999;896:85-95.