



Published in final edited form as:

Arch Gen Psychiatry. 2011 August ; 68(8): 838–844. doi:10.1001/archgenpsychiatry.2011.77.

The association of childhood adversities and early onset mental disorders with adult onset chronic physical conditions

Kate M. Scott, PhD,

Department of Psychological Medicine, School of Medicine and Health Sciences, University of Otago, Wellington, New Zealand

Michael Von Korff, ScD,

Group Health Research Institute, Seattle, Washington, United States

Matthias C. Angermeyer, MD, PhD,

Center for Public Mental Health, Gösing am Wagram, Austria

Corina Benjet, PhD,

National Institute of Psychiatry, Mexico City, Mexico

Ronny Bruffaerts, PhD,

University Hospital Gasthuisberg, Leuven, Belgium

Giovanni de Girolamo, MD,

IRCCS Centro S. Giovanni di Dio Fatebenefratelli, Brescia, Italy

Josep Maria Haro, MD, MPH, PhD,

Parc Sanitari Sant Joan de Déu, CIBERSAM, Sant Boi de Llobregat, Barcelona, Spain

Jean-Pierre Lépine, MD, HDR,

Hôpital Lariboisière Fernand Widal, Assistance Publique Hôpitaux de Paris INSERM U 705, CNRS UMR 7157 University Paris Diderot and Paris Descartes Paris, France

Johan Ormel, MA, PhD,

Department of Psychiatry and Psychiatric Epidemiology, University Medical Center Groningen, University Center for Psychiatry, Groningen, Netherlands

José Posada-Villa, MD,

Colegio Mayor de Cundinamarca University, Bogota, Colombia

Hisateru Tachimori, PhD, and

National Institute of Mental Health, National Center of Neurology and Psychiatry, Japan

Ronald C. Kessler, PhD

Author for correspondence: Kate Scott, PhD, Associate Professor, Registered Clinical Psychologist, Department of Psychological Medicine, Otago University, PO Box 913, Dunedin, NEW ZEALAND, Tel 64 3 4740999 ext 7369, Fax 64 3 4747934.

Conflicts of Interest - K Scott has no conflicts of interest to declare. M Von Korff is principal investigator of a grant from Johnson and Johnson Inc. to Group Health Research Institute. R Kessler has been a consultant for GlaxoSmithKline Inc., Kaiser Permanente, Pfizer Inc., Sanofi-Aventis, Shire Pharmaceuticals, and Wyeth-Ayerst; has served on advisory boards for Eli Lilly & Company and Wyeth-Ayerst; and has had research support for his epidemiological studies from Bristol-Myers Squibb, Eli Lilly & Company, GlaxoSmithKline, Johnson & Johnson Pharmaceuticals, Ortho-McNeil Pharmaceuticals Inc., Pfizer Inc., and Sanofi-Aventis. The remaining authors have no conflicts of interest to declare.

Author contributions - KMS and MVK contributed equally to the study concept and design; KMS drafted the paper and contributed to the planning of the analyses and interpretation of the results; MVK contributed to the drafting of the paper, had overall responsibility for the analysis plan and its execution and obtained the funding for analyses; MVK had full access to all the data and takes responsibility for the integrity and accuracy of the data analysis; all other authors had responsibility for the conduct of the surveys in their respective countries and reviewed the draft manuscript for intellectual content. KMS had full access to all the data and had final responsibility for the decision to submit for publication.

Department of Health Care Policy, Harvard Medical School, Boston, Massachusetts, United States

Abstract

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 ten countries.

Setting—General population.

Participants—Adults (≥ 18 years; $n = 18,303$), with diagnostic assessment and determination of age of onset of DSM-IV mental disorders; assessment of childhood familial adversities; and age of diagnosis/onset of chronic physical conditions.

Main Outcome Measures—Risk (hazard ratios) of adult onset ($> \text{age } 20$) heart disease, asthma, diabetes, arthritis, chronic spinal pain, and chronic headache as a function of specific childhood adversities and early onset ($< \text{age } 21$) DSM-IV depressive and anxiety disorders, with mutual adjustment.

Results—A history of three or more childhood adversities was independently associated with onset of all six physical conditions (hazard ratios from 1.44–2.19). Controlling for current mental disorder made little difference to these associations. Early onset mental disorders were independently associated with onset of five physical conditions (hazard ratios from 1.43–1.66).

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

Introduction

The deleterious mental health consequences of childhood psychosocial adversities such as abuse and neglect have been well documented.¹ Although less extensively researched, it has been hypothesized that childhood adversities may also increase risk of adult onset of a spectrum of chronic physical diseases.^{2–3} A recent meta-analysis of the effects of child abuse on medical outcomes in adulthood reached just that conclusion: it found that the increased risk of selected adverse physical health outcomes was comparable to that observed for poor mental health outcomes.⁴ However, the evidence base for the association of child maltreatment with subsequent physical health has significant limitations; these 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 (sexual abuse), and a lack of sample diversity in terms of race/ethnicity (mostly Caucasian), age (mostly young adults) and sex (mostly female). The relatively young age of current prospective cohorts with childhood maltreatment data is a particular limitation both because it greatly restricts the range of disease outcomes studied and also because it truncates the full expression of disease risk, potentially biasing findings towards the null.

In prior research that has considered the influence of the early psychosocial environment on later physical health, mental disorders have generally been out of the frame. This 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 response⁶ that has been linked with a range of adverse metabolic, cardiovascular, immune and cognitive effects.⁷⁻⁸ Research suggests that it is the stressors occurring early in life that have the most potential to contribute to allostatic load through dysregulation of the hypothalamic-adrenal-pituitary axis.⁹⁻¹¹ This generates a hypothesis that there might be associations between early onset mental disorders and chronic physical conditions in adulthood. Although there are well established associations between depression and anxiety measured in mid-life and the subsequent onset of heart disease and other chronic conditions,¹²⁻¹³ the associations between diagnosed early onset mental disorders and adult onset physical conditions have not previously been studied. The time course of mental-physical sequential associations has important implications for the understanding of mechanisms.

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 both 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 (the vast majority of studies rely on retrospective recall of childhood adversities such as abuse and neglect).

In this study using data from ten countries participating in the World Mental Health Surveys initiative, we sought to answer the following question: are both 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 of onset of mental disorders and age of onset or diagnosis of chronic physical conditions which allowed the use of survival analyses examining predictive associations.

Methods

Samples

Ten surveys were carried out in the Americas (Colombia, Mexico, United States), Europe (Belgium, France, Germany, Italy, Netherlands, Spain), and Asia (Japan) over the period 2001–2004. All surveys were based on multi-stage, clustered, area probability household samples and were conducted face-to-face by trained lay interviewers. Sample sizes range from 2372 (Netherlands) to 9282 (United States). Response rates range from 45.9% (France) to 87.7% (Colombia), with a weighted average of 66.7%. Internal sub-sampling 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 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 non-response and to match the samples to population socio-demographic distributions. Further detail on 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 carried out in bilingual form while others were carried out exclusively in the country's official language. Quality control protocols, described in more detail elsewhere,¹⁶ were standardized across countries to check on interviewer accuracy and to specify data cleaning and coding procedures. Each country followed national procedures for gaining study approval by IRB or ethics committees and for obtaining informed consent and protecting human subjects.

Mental disorder status

All surveys used the WMH Survey version of the WHO Composite International Diagnostic Interview (WMH-CIDI, now CIDI 3.0),¹⁷ a fully structured diagnostic interview, to assess mental disorders. Methodological 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 *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV)*. CIDI organic exclusion rules were imposed. This paper includes anxiety disorders (generalized anxiety disorder, panic disorder and/or agoraphobia, post-traumatic stress disorder, and social phobia) and depression (major depressive disorder). Prior World Mental Health Surveys analyses showed that these were the disorders most strongly associated 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, parent 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 (not all possible childhood adversities), as these are more likely to be sustained over long periods of time and so to have chronic health effects. Those respondents who reported that the experience occurred before the age of 18 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

These 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 they were first diagnosed with the condition (for the medical diagnoses) or first 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 using survival analyses, using retrospectively reported age of 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. Persons who had not developed the physical condition were censored at their current age. Persons who reported that the physical condition developed before age 21 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 (< 21 years of age) depressive/anxiety disorder status. Specific childhood adversities, specific early onset mental disorders and the number of childhood adversities (none, one, two, and three or more), were the predictor variables. The no adversities category and persons 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 first 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 education, but as the results were consistently similar to those not controlling for education, the simpler model results are reported here. Models of asthma and heart disease additionally controlled for smoking status (ever, never, current). Further analyses of the association between adversities and each physical condition adjusted for current (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 here. 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 $p = 0.05$ for a two-sided test. The analyses were performed using the SURVIVAL procedure in SUDAAN²⁴ statistical software to account for the complex sample design.

Results

Associations between specific early onset mental disorders and childhood adversities with onset of physical conditions

Data on the distribution of childhood adversities, mental disorders and chronic physical conditions across the ten countries has been published previously.²⁰ All five early onset mental disorders were associated with the onset of the three chronic pain conditions in adulthood with hazard ratios 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. Table 1 also shows associations between specific childhood adversities and the onset of the six health outcomes. Physical abuse was the one 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 five out of the six 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 hazard ratios being under 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/anxiety disorders ('any') were associated with the onset of five of the six physical conditions in adulthood (Table 2). Similarly, three or more childhood adversities were associated with all outcomes after adjustment for early onset mental disorders, and two or more childhood adversities were associated with five of the six 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 the 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). The magnitude of these associations adjusted for current mental disorder was very similar to that shown in Table 2, with three or more childhood adversities associated with all physical condition outcomes and two or more adversities associated with all outcomes except diabetes.

Discussion

In this ten-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 three 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 fell within a fairly narrow range (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. These analyses did not take into account the severity or the precise timing of onset of either the childhood adversities or the early onset mental disorders. These associations should therefore be considered as 'averages'. Such averaged estimates probably underestimate the strength of association between the more severe adversities or mental disorders occurring at critical childhood developmental stages.

Several limitations need to be borne in mind in interpreting these results. This cross-sectional study relies on retrospective reports of mental disorders and their age of onset. Recall of mental disorders, particularly over long intervals, leads to false negatives (under-reporting due to forgetting), though false positives are rare.²⁵ There is also bias in recall of the age of onset of mental disorders.²⁶ The WMH surveys revised the way of asking about age of onset to reduce this bias, but some bias probably remains. Age of onset or diagnosis of medical conditions on the other hand, has been found to be accurate and reliable.²⁷ Childhood adversities were also 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, though there is a considerable degree of underreporting and possibly some bias.²⁸ Bias can result from current mental state influencing recall,¹⁵ but this study took that into account by assessing associations between childhood adversities and the health outcomes after adjustment for current mental disorders.

It is also a considerable limitation that the medical conditions were assessed on the basis of self-report of diagnoses rather than independent verification by a medical practitioner. This limitation is mitigated somewhat by the generally good agreement between self-report of medical diagnoses and physician or medical record confirmation of those diagnoses.^{29,30} and by the fact that while 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} WMH survey samples may have better mental or physical health than non respondents or may be biased due to differential selection out of the population through early mortality. These sample selection factors would probably lead to downward (conservative) bias in estimating the strength of associations. Lastly, it should be noted that although the majority of 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 not) of any single estimate.

This study also has important strengths: it addresses the limitations of much prior research in being able 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 results of prospective research where these are available. For example, the hazard ratio we observed of 1.82 between early onset major depressive disorder and adult heart disease onset is within the 1.50–2.00 range from meta-analyses of the prospective association between depression measured in adulthood and subsequent heart disease onset.¹³¹² Our findings are also consistent with extant research on 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 is that it is the memories of abuse rather than abuse itself that is linked to later health,^{1, 33} another explanation is that the prospective studies in question were based on samples too young (< 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) which showed that the association did not emerge until around age 40.

Given the cross-sectional nature of this study, it should be considered exploratory in nature. A definitive study of causal relationships between 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 very large sample followed up over the lifetime of the study participants. Unfortunately, data from such a definitive study will not be forthcoming in the foreseeable future. Therefore, scientific inference about 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, 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 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 (behavioral, biological and socioeconomic). Although the magnitude of risk associated with specific

childhood adversities and early onset mental disorders was generally quite modest, many estimates are of a similar magnitude to the association between cholesterol and heart disease. The public health significance of the latter is less to do with its magnitude than with the prevalence of elevated cholesterol 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 here were confirmed by prospective studies, these 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. While 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 etiology 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 timeframe for the expression of associations between these early life psychosocial risk factors and later disease outcomes.

Acknowledgments

The World Health Organization World Mental Health (WMH) Survey Initiative is supported by the National Institute of Mental Health (NIMH; R01 MH070884), the Mental Health Burden Study: Contract number HHSN271200700030C, the John D. and Catherine T. MacArthur Foundation, the Pfizer Foundation, the US Public Health Service (R13-MH066849, R01-MH069864, and R01 DA016558), the Fogarty International Center (FIRCA R03-TW006481), the Pan American Health Organization, Eli Lilly and Company, Ortho-McNeil Pharmaceutical, GlaxoSmithKline, and Bristol-Myers Squibb. We thank the staff of the WMH Data Collection and Data Analysis Coordination Centres for assistance with instrumentation, fieldwork, and consultation on data analysis. None of the funders had any role in the design, analysis, interpretation of results, or preparation of this paper. This report was prepared under the auspices of the World Health Organization ICD-11 Chapter 5 (Mental and Behavioural Disorders) epidemiology working group, which is co-chaired by Chatterji and Kessler. The views and opinions expressed in this report are those of the authors and should not be construed to represent the views of the sponsoring organizations, agencies, or governments. The Colombian National Study of Mental Health (NSMH) is supported by the Ministry of Social Protection, with supplemental support from the Saldarriaga Concha Foundation. The European surveys were funded by the European Commission (Contracts QLG5-1999-01042; SANCO 2004123), the Piedmont Region (Italy), Fondo de Investigación Sanitaria, Instituto de Salud Carlos III, Spain (FIS 00/0028), Ministerio de Ciencia y Tecnología, Spain (SAF 2000-158-CE), Departament de Salut, Generalitat de Catalunya, Spain, Instituto de Salud Carlos III (CIBER CB06/02/0046, RETICS RD06/0011 REM-TAP), and other local agencies and by an unrestricted educational grant from GlaxoSmithKline. The World Mental Health Japan (WMHJ) Survey is supported by the Grant for Research on Psychiatric and Neurological Diseases and Mental Health (H13-SHOGAI-023, H14-TOKUBETSU-026, H16-KOKORO-013) from the Japan Ministry of Health, Labour and Welfare. The Mexican National Comorbidity Survey (MNCS) is supported by The National Institute of Psychiatry Ramon de la Fuente (INPRFMDIES 4280) and by the National Council on Science and Technology (CONACyT-G30544-H), with supplemental support from the PanAmerican Health Organization (PAHO). The US National Comorbidity Survey Replication (NCS-R) is supported by the National Institute of Mental Health (NIMH; U01-MH60220) with supplemental support from the National Institute of Drug Abuse (NIDA), the Substance Abuse and Mental Health Services Administration (SAMHSA), the Robert Wood Johnson Foundation (RWJF; Grant 044708), and the John W. Alden Trust. A complete list of all within-country and cross-national WMH publications can be found at <http://www.hcp.med.harvard.edu/wmh/>.

The funders had no input into the design and conduct of the study; collection, management, analysis, and interpretation of the data; or preparation, review or approval of the manuscript.

References

1. Gilbert R, Widom CS, Browne K, Fergusson DM, Webb E, Janson S. Child maltreatment I. Burden and consequences of child maltreatment in high-income countries. *Lancet*. 2009; 373:68–81. [PubMed: 19056114]

2. Felitti VJ. Relationship of childhood abuse and household dysfunction to many of the leading causes of death in adults. *Am J Prev Med.* 1998; 14:245–258. [PubMed: 9635069]
3. Anda RF, Felitti V, Bremner JD, et al. The enduring effects of abuse and related adverse experiences in childhood. *Eur Arch Psychiatry Clin Neurosci.* 2006; 256:174–186. [PubMed: 16311898]
4. Wegmen HL, Stetler C. A meta-analytic review of the effects of childhood abuse on medical outcomes in adulthood. *Psychosom Med.* 2009; 71:805–812. [PubMed: 19779142]
5. McEwen BS. Mood disorders and allostatic load. *Biol Psychiatry.* 2003; 54:200–207. [PubMed: 12893096]
6. McEwen BS. Protective and damaging effects of stress mediators. *N Engl J Med.* 1998; 338:171–179. [PubMed: 9428819]
7. Miller GE, Cohen S, Ritchey AK. Chronic psychological stress and the regulation of pro-inflammatory cytokines: a glucocorticoid resistance model. *Health Psychol.* 2002; 21:536–541.
8. Chrousos GP, Kino T. Glucocorticoid action networks and complex psychiatric and/or somatic disorders. *Stress.* 2007; 10:213–219. [PubMed: 17514590]
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; 284:592–597. [PubMed: 10918705]
10. Teicher MH, Andersen SL, Polcari A, Anderson CM, Navalta CP. Developmental neurobiology of childhood stress and trauma. *Psychiatr Clin North Am.* 2002; 25:397–426. [PubMed: 12136507]
11. Sanchez MM. The impact of early adverse care on HPA axis development: nonhuman primate models. *Horm Behav.* 2006; 50:623–631. [PubMed: 16914153]
12. Wulsin LR, Singla BM. Do depressive symptoms increase the risk for the onset of coronary disease: A systematic quantitative review. *Psychosom Med.* 2003; 65:201–210. [PubMed: 12651987]
13. Nicholson A, Kuper H, Hemingway H. Depression as an aetiological 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; 27:2763–2774. [PubMed: 17082208]
14. Goodwin RD, Fergusson DM, Horwood J. Asthma and depressive and anxiety disorders among young persons in the community. *Psychol Med.* 2004; 34:1465–1474. [PubMed: 15724877]
15. Williams, JMG.; Watts, FN.; MacLeod, C.; Mathews, A., editors. *Cognitive Psychology and Emotional Disorders.* 2. Chichester: John Wiley and Sons; 1997.
16. Kessler, RC.; Ustun, TB., editors. *The WHO World Mental Health Surveys: Global Perspectives on the Epidemiology of Mental Disorders.* New York: Cambridge University Press; 2008.
17. Kessler RC, Ustun B. The World Mental Health (WMH) Survey Initiative version of the World Health Organization (WHO) Composite International Diagnostic Interview (CIDI). *Int J Methods Psychiatr Res.* Feb.2004 13:93–121. [PubMed: 15297906]
18. Haro JM, Arbabzadeh-Bouchez S, Brugha TS, de Girolamo G, Guyer ME, Jin R, Lepine J-P, 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; 15:167–180. [PubMed: 17266013]
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, Gureye 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; 103:113–120. [PubMed: 17292480]
20. Von Korff, M.; Scott, KM.; Gureje, O., editors. *Global Perspectives on Mental-Physical Comorbidity in the WHO World Mental Health Surveys.* New York: Cambridge University Press; 2009.
21. Scott KM, Von Korff M, Alonso J, et al. Childhood adversity, early-onset depressive/anxiety disorders, and adult-onset asthma. *Psychosom Med.* 2008; 70:1035–1043. [PubMed: 18941133]

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. [PubMed: 10209976]
23. Smith GC, Dell JP, Walsh D. Pregnancy complications and maternal risk of ischaemic heart disease: a retrospective cohort study. *Lancet*. 2001; 357(9273):2002–2006. [PubMed: 11438131]
24. SUDAAN: Software for the statistical analysis of correlated data. Research Triangle Park; North Carolina, USA: 1999.
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. [PubMed: 15554571]
26. Simon GE, Von Korff M. Recall of psychiatric history in cross-sectional surveys: implications for epidemiological research. *Epidemiol Rev*. 1995; 17:221–227. [PubMed: 8521941]
27. Toren K, Palmqvist M, Lowhagen O, Balder B, Tunsater A. Self-reported asthma was biased in relation to disease severity while reported year of asthma onset was accurate. *J Clin Epidemiol*. 2006; 59:90–93. [PubMed: 16360566]
28. Hardt J, Rutter M. Validity of adult retrospective reports of adverse childhood experiences: review of the evidence. *J Child Psychol Psychiatry*. 2004; 45:260–273. [PubMed: 14982240]
29. Kriegsman DM, Penninx BW, Van Eijk JT, Boeke AJ, Deeg DJ. Self-reports and general practitioner information on the presence of chronic diseases in community dwelling elderly. *J Clin Epidemiol*. 1996; 49:1407–1417. [PubMed: 8970491]
30. Baumeister H, Kriston L, Bengel J, Harter M. High agreement of self-report and physician-diagnosed somatic conditions yields limited bias in examining mental-physical comorbidity. *J Clin Epidemiol*. 2010
31. Kolk AM, Hanewald GJ, Schagen S, Gijsbers van Wijk CM. Predicting medically unexplained physical symptoms and health care utilization. A symptom-perception approach. *J Psychosom Res*. 2002; 52(1):35–44. [PubMed: 11801263]
32. Vassend O, Skrandal A. The role of negative affectivity in self-assessment of health. *J Health Psychol*. 1999; 4:465–482. [PubMed: 22021640]
33. Raphael KG, Widom CS, Lange G. Childhood victimization and pain in adulthood: a prospective investigation. *Pain*. 2001; 92:283–293. [PubMed: 11323150]
34. Scott, KM. The development of mental-physical comorbidity. In: Von Korff, M.; Scott, KM.; Gureje, O., editors. *Global Perspectives on Mental-Physical Comorbidity in the WHO World Mental Health Surveys*. New York: Cambridge University Press; 2009. p. 97-107.
35. Hertzman C. The biological embedding of early experience and its effects on health in adulthood. *Ann NY Acad Science*. 1999; 896:85–95.

Table 1

Associations between specific early onset mental disorders and childhood adversities with the subsequent onset of chronic physical conditions in adulthood.¹

	Heart disease HR² (95%CI)	asthma HR (95%CI)	diabetes HR (95%CI)	Osteo arthritis HR (95%CI)	Spinal pain (back or neck) HR (95%CI)	Chronic or severe headache HR (95%CI)
Early Onset Mental Disorders (< 21 years)						
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)
Generalised 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)
Post-traumatic 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 /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 adversities						
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)
Parent died	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)
Parents divorced	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 ³	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)

¹ All models adjust for age, sex, country, and models for heart disease and asthma additionally adjust for smoking status.

² HR = hazard ratio.

Bolded HRs are significant at p < 0.05.

³ For example: adoption, foster care, or leaving home before the age of sixteen.

Table 2

Independent associations between early onset mental disorders and number of childhood adversities with the subsequent onset of chronic physical conditions in adulthood.¹

	Heart disease HR² (95%CI)	asthma HR (95%CI)	diabetes HR (95%CI)	Osteo arthritis HR (95%CI)	Spinal pain (back or neck) HR (95%CI)	Chronic or severe headache HR (95%CI)
Any early onset mental disorder (< 21 years)	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)
One childhood adversity	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)
Two childhood adversities	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)
Three or more childhood adversities	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)

¹ All models adjust for age, sex, country, and models for heart disease and asthma additionally adjust for smoking status. Models with early onset mental disorders as predictors adjust for childhood adversities; models with childhood adversities as predictors adjust for early onset mental disorders.

² HR = hazard ratio.

Bolded HRs are significant at p < 0.05.