



HHS Public Access

Author manuscript

Mol Psychiatry. Author manuscript; available in PMC 2018 November 22.

Published in final edited form as:

Mol Psychiatry. 2018 September ; 23(9): 1–8. doi:10.1038/mp.2017.194.

The associations of earlier trauma exposures and history of mental disorders with PTSD after subsequent traumas

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Disclaimer: The views and opinions expressed in this article are those of the authors and should not be construed to represent the views of any of the sponsoring organizations or agencies.

Conflict of Interest Disclosures: In the past 3 years, Dr. Kessler received support for his epidemiological studies from Sanofi Aventis; was a consultant for Johnson & Johnson Wellness and Prevention, Shire, Takeda; and served on an advisory board for the Johnson & Johnson Services Inc. Lake Nona Life Project. Kessler is a co-owner of DataStat, Inc., a market research firm that carries out healthcare research. In the past 3 years, Dr. Stein has received research grants and/or consultancy honoraria from Biocodex, Lundbeck, Servier, and Sun. The remaining authors declare no conflicts of interest.

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Abstract

Although earlier trauma exposure is known to predict post-traumatic stress disorder (PTSD) after subsequent traumas, it is unclear if this association is limited to cases where the earlier trauma led to PTSD. Resolution of this uncertainty has important implications for research on pre-trauma vulnerability to PTSD. We examined this issue in the WHO World Mental Health (WMH) Surveys with 34,676 respondents who reported lifetime trauma exposure. One lifetime trauma was selected randomly for each respondent. DSM-IV PTSD due to that trauma was assessed. We reported in a previous paper that four earlier traumas involving interpersonal violence significantly predicted PTSD after subsequent random traumas (OR=1.3–2.5). We also assessed 14 lifetime DSM-IV mood, anxiety, disruptive behavior, and substance disorders prior to random traumas. We show in the current report that only prior anxiety disorders significantly predicted PTSD in a multivariate model (OR=1.5–4.3) and that these disorders interacted significantly with three of the earlier traumas (witnessing atrocities, physical violence victimization, rape). History of witnessing atrocities significantly predicted PTSD after subsequent random traumas only among respondents with prior PTSD (OR=5.6). Histories of physical violence victimization (OR=1.5) and rape after age 17 (OR=17.6) significantly predicted only among respondents with no history of prior anxiety disorders. Although only preliminary due to reliance on retrospective reports, these results suggest that history of anxiety disorders and history of a limited number of earlier traumas might usefully be targeted in future prospective studies as distinct foci of research on individual differences in vulnerability to PTSD after subsequent traumas.

INTRODUCTION

Only a minority of people ever develops post-traumatic stress disorder (PTSD)¹ despite traumas occurring to the vast majority of the population.² This suggests that individual differences exist in vulnerability to traumas.^{3–5} Increased understanding of these differences could help inform intervention development.⁶ In addition, measurement of these differences shortly after trauma exposure could help target high-risk individuals for preventive interventions.⁷ Epidemiological research shows that earlier trauma exposure and history of psychopathology are the two strongest pre-trauma predictors PTSD after subsequent traumas.⁸ Earlier trauma exposure is particularly interesting because, unlike

psychopathology, earlier traumas are external to the individual and presumably predict future PTSD because (i) exposure to these traumas is influenced by stable vulnerability factors and/or (ii) exposure to these traumas causes biological and/or psychological vulnerabilities to subsequent PTSD. Childhood adversities (CAs) have been of special interest, as they occur early in life and are strongly associated with increased risk of psychopathology throughout the life course.^{9, 10} However, it is difficult to tease apart the effects of pre-existing vulnerability factors and intervening biological and psychological processes in studying CAs. There are two reasons for this. First, CAs are strongly associated with parental psychopathology and, by extension, genetic risk.¹¹ Second, a high proportion of the most severe CAs are associated with child- and adolescent-onset mental disorders and long-term neurobiological and psychological changes due to those disorders that are associated with risk of a range of later disorders.¹²

The effects of earlier traumas not involving CAs on PTSD after subsequent traumas might be easier to study than CAs to the extent that exposure to earlier traumas is more independent than CAs of prior psychopathology and genetic risk. A potential limitation, though, is that some,^{13, 14} although not all,¹⁵ epidemiological studies suggest that associations of earlier traumas with PTSD after subsequent traumas are limited to people who developed PTSD due to the earlier traumas. If true, this specification would reintroduce the same complication as in research on CAs. Resolution of this uncertainty could have important implications for future research on the environmental determinants of individual differences in vulnerability to PTSD.¹⁶

We attempt to take a first step in resolving this uncertainty here by analyzing data from a unique sample of 34,676 respondents who reported lifetime exposure to one or more traumas in the WHO World Mental Health (WMH) Surveys.⁷ In a previous report,¹⁷ we showed that four trauma groups/types, all involving interpersonal violence, had significantly elevated relative-odds of predicting DSM-IV PTSD after subsequent traumas. We also showed in that report that these associations did not vary depending on type of subsequent trauma. However, in that earlier report we did not explore the possibility that the associations of these earlier traumas with later PTSD might depend on history of PTSD or other common DSM-IV disorders related to the earlier traumas. We do this in the current report.

METHODS AND MATERIALS

Sample

Data come from 22 community epidemiological surveys in the larger WMH series that assessed lifetime PTSD after *randomly-selected* traumas. By *randomly selected* we mean that one occurrence of one lifetime trauma reported by each respondent was selected at random for retrospective assessment of PTSD. We adjusted for individual differences in number of lifetime trauma exposures by weighting random trauma data at the individual level by the respondent's number of lifetime traumas, generating a weighted sample representative of all trauma occurrences in the population rather than of all individuals in the population. The joint associations of earlier lifetime traumas and history of psychopathology with PTSD after the subsequent random trauma are the focus of the current report

Three of the 22 surveys were in low/lower-middle income countries (Colombia, Peru, Ukraine), seven in upper-middle income countries (Brazil, Bulgaria, Colombia [administered after the previously-mentioned Colombian survey, when the World Bank country income rating had increased], Lebanon, Mexico, Romania, South Africa), and 12 in high income countries (Belgium, France, Germany, Israel, Italy, Japan, Netherlands, New Zealand, Northern Ireland, Spain [separate national and regional surveys], United States)¹⁸ Each survey was based on a multi-stage clustered area probability sample of adult household residents. Three surveys were limited to all urbanized areas in their countries (Colombia, Mexico, Peru), four others to specific Metropolitan areas (Sao Paulo Brazil; Medellin Colombia, Murcia Spain, six cities in Japan), and the remaining 15 represented the full household populations in their countries.

Interviews were administered face-to-face in respondent homes by trained lay interviewers after obtaining informed consent using procedures approved by local Institutional Review Boards.¹⁹ The weighted (by sample size) mean response rate was of 71.3% across surveys (from 45.9% in France to 97.2% in Medellin). The interview was in two parts. Part I, administered to all n=101,454 respondents, assessed core DSM-IV mental disorders. Part II, administered to Part I respondents with core disorders and a probability subsample of other respondents (n=54,600), assessed additional disorders and correlates. Traumas and PTSD were assessed in Part II. The analysis sample considered here includes the 34,676 Part II respondents who reported lifetime trauma exposure. Each Part II respondent was weighted by the inverse of his/her selection probability into Part II, within-household variation in selection probabilities (due to one respondent being selected per household regardless of household size), between-household variation in selection probabilities (due to under-sampling hard-to-reach respondents in the last recruitment phase), and to match the sample with the population on Census geographic/socio-demographic variables. Details about these weights are presented elsewhere.²⁰

Measures

Traumas—Twenty-nine trauma types were assessed. These included traumas involving *exposure to organized violence* (e.g., civilian in war zone, relief worker in war zone, refugee), *participation in organized violence* (e.g., combat experience, witnessed atrocities), *physical violence victimization* (e.g., beaten by caregiver as child; beaten by someone else), *sexual violence victimization* (e.g., raped, sexually assaulted, beaten by romantic partner), *accidents/injuries* (e.g., natural disaster, automobile accident), and unexpected death of loved one).² Age of first exposure was recorded for each trauma type reported.

DSM-IV disorders—Fourteen lifetime DSM-IV disorders were assessed with the fully-structured Composite International Diagnostic Interview (CIDI):²¹ two mood disorders (major depressive disorder/dysthymic disorder and broadly-defined bipolar disorder [bipolar I and II and sub-threshold bipolar disorder, defined using criteria described elsewhere]);²² six anxiety disorders (generalized anxiety disorder, panic disorder and/or agoraphobia, posttraumatic stress disorder, separation anxiety disorder, social phobia, specific phobia); four disruptive behavior disorders (attention-deficit/hyperactivity disorder, conduct disorder, intermittent explosive disorder, oppositional-defiant disorder); and two substance disorders

(alcohol and drug abuse with or without dependence). PTSD was unique in being assessed twice: once for the random trauma and a second time for the lifetime trauma nominated by the respondent as having caused the most distress-impairment. Age-of-onset of each disorder was assessed using probing techniques shown experimentally to improve recall accuracy,²³ allowing us to determine whether respondents had a history of each disorder prior to exposure to the random trauma. DSM-IV organic exclusion and diagnostic hierarchy rules were not used in making diagnoses. As detailed elsewhere,²⁴ generally good concordance was found between diagnoses based on the CIDI and blinded clinical diagnoses based on SCID reappraisal interviews.²⁵

Analysis Methods

Random trauma reports were weighted by the inverse of their within-person probability of selection multiplied by the Part II weight to generate a sample representative of all traumas experienced by all respondents. This composite weight was standardized within surveys to equal the number of respondents reporting lifetime traumas and then pooled across surveys. Logistic regression was used to estimate associations of earlier traumas and random trauma types with subsequent PTSD after random traumas controlling sex, age at random trauma exposure, and survey. This model, the results of which were reported previously,¹⁷ was then expanded in the analyses reported here to evaluate whether temporally prior (to the random trauma) lifetime DSM-IV/CIDI disorders influenced associations of earlier traumas with PTSD after subsequent random traumas. We considered both additive models where prior lifetime disorders were controls and models that included interactions of earlier traumas with lifetime disorders.

Temporal ordering between earlier traumas and lifetime disorders was complex due to many respondents having multiples of both. As a result, the main effects of mental disorders as predictors were explained without attempting to distinguish between mental disorders as risk markers (i.e., temporally primary predictors of both earlier traumas and PTSD after subsequent traumas) versus as mediators (i.e., earlier traumas predicted later mental disorders, which, in turn, predicted PTSD after subsequent random traumas). However, in cases where interactions were found and the association of the earlier trauma with the outcome was significant in the presence of mental disorders, we decomposed the association to determine if the OR associated with the earlier traumas depended on whether the mental disorders occurred before or only after those traumas.

Statistical significance was consistently evaluated using .05-level two-sided design-based tests. The Taylor series method²⁶ implemented in the SAS software system²⁷ was used to adjust estimates of standard errors for survey design effects. Logistic regression coefficients and their standard errors were exponentiated to create odds-ratios (ORs) and 95% confidence intervals (CIs). Design-based Wald χ^2 tests were used to evaluate significance of predictor sets.

RESULTS

Associations of DSM-IV/CIDI disorders with PTSD after subsequent random traumas

All 14 prior lifetime DSM-IV/CIDI disorders had increased ORs predicting PTSD after random traumas in bivariate models. (Table 1, Bivariate Model) The highest OR was for prior PTSD (5.7) and the lowest for conduct disorder (1.1). Ten of the 14 bivariate ORs were statistically significant. However, in a multivariate model containing all 14 disorders (Table 1, Model 1.1), only the anxiety disorders remained significant as a set ($\chi^2_6=112.1$, $p<.001$). The ORs for the 6 individual anxiety disorders differed significantly among themselves ($\chi^2_5=26.8$, $p<.001$), with 5 of the 6 ORs significant (the exception was panic/agoraphobia) and in the range between 4.3 for PTSD and 1.5 for social phobia.

A global interaction test for number of anxiety disorders was non-significant in an expanded model that included separate coefficients for history of each individually significant anxiety disorder and a count variable. (Model 1.2) The interaction was also non-significant in a revised model that included separate dummy variables for respondents with histories of between 2 and all 5 significant anxiety disorders. (Model 1.3) These results demonstrated clearly that the joint associations of prior anxiety disorders with PTSD after subsequent traumas were additive on a logistic scale (Model 1.4).

Interactions between earlier traumas and history of anxiety disorders

As noted in the introduction, we showed in a previous report that four earlier trauma groups/types, all involving interpersonal violence, predicted DSM-IV PTSD after subsequent random traumas. The first of these earlier traumas was participation in organized violence (OR=1.3; a composite of five trauma types with a combined prevalence of 26.1%, including combat experience; purposefully injuring, torturing, or killing someone; accidentally injuring or killing someone; witnessing serious injury/death or discovering a dead body; and witnessing atrocities). The second was physical violence victimization (OR=1.4; a composite of three trauma types with a combined prevalence of 26.4% that included witnessing physical violence at home as a child; physical abuse by a caregiver as a child; beaten up by someone else). The third and fourth were rape (OR=2.5; 4.5% prevalence) and other sexual assault (OR=1.6; 7.6% prevalence).¹⁷

Based on the results in Table 1, we investigated how much the gross associations of earlier traumas with PTSD after subsequent random traumas (Table 2, Model 2.1) were due to the anxiety disorders in Model 1.4. We began with an additive model. (Model 2.2) The ORs of all four earlier trauma groups/types became non-significant in that model (OR=1.1–1.6) and those of all five anxiety disorders remained significant with ORs in the range between 4.3 for PTSD and 1.5 for social phobia. We then tested the significance of interactions between earlier traumas and a three-category anxiety disorder profile score: (i) prior PTSD regardless of presence/absence of any other anxiety disorders (2.8% of the sample); (ii) no prior PTSD, but one or more other significant anxiety disorders (16.1% of the sample), and (iii) none of the prior anxiety disorders (81.1% of the sample). These interactions were significant overall ($\chi^2_8=32.5$, $p<.001$), with significant component interactions for participation in organized violence ($\chi^2_2=10.1$, $p=.006$) and physical violence victimization ($\chi^2_2=10.5$, $p=.005$), a near-

significant interaction for rape ($\chi^2_2=5.8$, $p=.056$), and a non-significant interaction for other sexual assault ($\chi^2_2=0.2$, $p=.89$).

Subgroup coding of the significant and near-significant interactions showed that the OR of participation in organized violence was significant only among respondents with prior PTSD (OR=2.0) and that the ORs of physical violence victimization and rape were significant only among respondents with no prior anxiety disorders (OR=1.5 for physical violence victimization and 3.4 for rape; Model 2.3). The OR of other sexual assault, in comparison, was non-significant in all three subgroups. Further analyses described next then investigated the significant within-subgroup associations that accounted for the interactions.

Participation in organized violence—As noted above, participation in organized violence was a composite of five trauma types. Disaggregation showed that only one of these five, witnessing atrocities, accounted for the significant subgroup OR of the composite among respondents with a history of prior PTSD. The OR for witnessing atrocities (with or without any of the other four traumas in the composite) predicting PTSD after subsequent random traumas was OR=5.6 (95% CI=1.6–20.3), whereas the OR for one or more of the other four traumas in the composite was OR=0.8 (95% CI=0.4–1.5). We also investigated whether the significant OR for witnessing atrocities among people with a history of prior PTSD varied significantly by whether age at first witnessing atrocities was before or after age-of-onset of PTSD. It did not ($\chi^2_1=0.0$, $p=.95$), although the number of respondents with a history of both witnessing atrocities and having PTSD prior to the random trauma was small ($n=40$).

Physical violence victimization—We also noted above that physical violence victimization was a composite of three trauma types. Disaggregation failed to find evidence that these three differed in importance in accounting for the significant subgroup OR of the composite among respondents with no prior anxiety disorders ($\chi^2_2=2.9$, $p=.24$).

Rape—Although the WMH surveys collected information about circumstances surrounding the rapes selected as random traumas,²⁸ the only information collected about other rapes was age at first exposure. Disaggregation of the subgroup OR of rape among respondents with no history of anxiety disorder was limited to adult-onset (ages 18+) rapes (OR=17.6, 95% CI=6.6–47.1). The OR associated with childhood-onset (ages 4–17) rapes was not significant (OR=1.5, 95% CI=0.8–2.9). It is noteworthy, though, that this disaggregation is based on an earlier interaction that was only near-significant.

Population distributions

It is instructive to project the above results to the population by dividing the total WMH sample (i.e., including respondents with no history of earlier trauma exposure) into the three subgroups of: (i) individuals with a history of any anxiety disorder that predicted PTSD; (ii) individuals without any such disorder but with exposure to the earlier traumas found to predict PTSD after subsequent traumas (i.e., witnessing atrocities and adult rape victimization); and (iii) other respondents. (Table 3) These three subgroups made up 13.8%, 12.3%, and 73.9% respectively, of the total sample. When we classified each WMH

respondent using this scheme as of 5 years before interview, we found a significantly higher rate of new trauma exposure among respondents in the first (71.9/100 respondents) and second (72.7/100) subgroups than the third (27.5/100) subgroups ($\chi^2_2=1,359.5$, $p<.001$).

We also saw from the trauma-level sample that conditional PTSD prevalence after random traumas was much higher among respondents in the first (10.6%) than second (3.5%) or third (2.2%) subgroups ($\chi^2_2=182.0$, $p<.001$). Based on these distributions, we estimated that approximately 57.9% of PTSD cases occur among people in the first subgroup, 17.4% in the second, and 24.7% in the third subgroup. We also estimated that 7.6 new cases of PTSD would be found per 100 respondents by following respondents in the first subgroup over a period of 5 years compared to 2.6/100 in the second and 0.6/100 in the third subgroup. The roughly 2-fold higher number of PTSD cases in the first than second subgroup is due entirely to higher PTSD risk after trauma exposure. The nearly 4-fold higher number of cases in the second than third subgroup, in comparison, is due to a combination of a substantially higher rate of trauma exposure and a significantly higher PTSD risk after trauma exposure.

DISCUSSION

The main advantage of the WMH design over previous studies in examining the associations of earlier traumas with PTSD after subsequent traumas is its large size, which allows more fine-grained assessments of intervening and interactive associations than previous studies. The WMH surveys were limited, though, by being cross-sectional, raising the possibility of biased recall about history of earlier traumas. Other limitations were that comorbid physical disorders and treatments were not taken into consideration and diagnoses of mental disorders were made with fully-structured interviews rather than semi-structured clinical interviews.

Within the context of these limitations, our finding that numerous mental disorders had significant gross associations with PTSD after subsequent traumas is broadly consistent with previous research.^{8, 29, 30} Although no previous study examined the full range of mental disorders considered here, prospective studies of pre-trauma biological and psychological vulnerabilities are indirectly consistent with our finding that anxiety disorders are the most important class of prior disorders in predicting subsequent PTSD.^{3, 30, 31} More direct evaluation of this variation is needed in future prospective studies, though, possibly in conjunction with an investigation of the unanticipated finding in Table 3 that prior anxiety disorders were associated with increased risk of subsequent trauma exposure and the possibility that this pattern is due to stress-generating effects of anxiety disorders.

Our finding that history of exposure to traumas involving interpersonal violence is associated with significantly elevated risk of PTSD after subsequent traumas is also consistent with previous research.^{8, 29} However, previous research was more equivocal on whether earlier traumas are important only when they result in PTSD. Breslau et al.¹⁴ first documented this specification in a prospective epidemiological sample of young adults, documenting that the significant association of a dichotomous measure of baseline trauma history with increased PTSD risk after subsequent traumas was limited to respondents with a

baseline history of PTSD. Cougle et al.,¹⁵ in a larger prospective study of adolescent assaultive violence (physical or sexual) subsequently showed that respondents with a baseline history assaultive violence victimization without PTSD were significantly more likely than others to develop PTSD after a subsequent trauma. Breslau and Peterson¹³ then reported a failure to replicate this specification in a cross-sectional community epidemiological survey that, like the WMH surveys, assessed PTSD separately for each respondent's most upsetting lifetime trauma and a randomly selected lifetime trauma. However, trauma history was defined in the Breslau-Peterson sample only in terms of most upsetting lifetime trauma, resulting in some respondents classified as having a history of only nonviolent trauma exposure actually being exposed to assaultive violence.

It is somewhat surprising given the potential importance of this specification that no subsequent studies carried out more definitive investigations. If the association of trauma history with PTSD after subsequent traumas is due entirely to the mediating effects of PTSD caused by earlier traumas, then trauma history cannot be considered an environmental risk factor for future PTSD. On the other hand, if history of at least some trauma types in the absence of history of mental disorder reliably predicts PTSD after subsequent traumas, individuals with a history of exposure to these earlier traumas could be targeted for intensive baseline evaluation and prospective study of premorbid modifiable biological and psychological vulnerabilities to PTSD in future prospective studies of trauma victims.

Our results provide the first evidence that at least two earlier traumas -- physical violence victimization and, more provisionally (due to the total-sample p value only being near-significant), adult rape -- are associated with PTSD after subsequent traumas among people who did not have anxiety disorders either before or after the earlier traumas. Although only provisional because they are based on cross-sectional data, these results raise the possibility that investigators designing future prospective studies might profit from over-sampling baseline respondents who had these earlier traumas but did not have a history of anxiety disorders for purposes of enriching prospective analyses of vulnerability factors for subsequent PTSD. Why these individuals might be at elevated risk of subsequent PTSD is unclear, but a number of suggestions exist in the literature about developmental, psychosocial, and neurobiological factors that could either be risk factors for exposure to or consequences of these earlier traumas.^{3, 6, 30} We showed that a meaningful proportion of the population falls into this subgroup, making over-sampling feasible to enrich investigation of vulnerabilities that are independent of prior anxiety disorders. Replicating results regarding predictive associations of biological and psychological vulnerabilities in such an enriched over-sample could help evaluate the independence of presumed causal factors from earlier mental disorders in a way that substantially improves on more standard approaches of using multivariate methods to control for such potential confounders.³¹

Acknowledgments

Funding/Support: The World Health Organization World Mental Health (WMH) Survey Initiative is supported by the National Institute of Mental Health (NIMH; R01 MH070884 and R01 MH093612-01), 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, Inc., 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. The views and opinions expressed in this paper are those of the authors and do not necessarily represent the views or policies of the World Health Organization, other sponsoring organizations, agencies or governments.

A complete list of all within-country and cross-national WMH publications can be found at <http://www.hcp.med.harvard.edu/wmh/>. The São Paulo Megacity Mental Health Survey is supported by the State of São Paulo Research Foundation (FAPESP) Thematic Project Grant 03/00204–3. The Bulgarian Epidemiological Study of common mental disorders EPIBUL is supported by the Ministry of Health and the National Center for Public Health Protection. The Colombian National Study of Mental Health (NSMH) is supported by the Ministry of Social Protection. The Mental Health Study Medellín – Colombia was carried out and supported jointly by the Center for Excellence on Research in Mental Health (CES University) and the Secretary of Health of Medellín. The ESEMeD project is funded by the European Commission (Contracts QLG5-1999-01042; SANCO 2004123, and EAHC 20081308), (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 Israel National Health Survey is funded by the Ministry of Health with support from the Israel National Institute for Health Policy and Health Services Research and the National Insurance Institute of Israel. 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 Lebanese Evaluation of the Burden of Ailments and Needs Of the Nation (L.E.B.A.N.O.N.) is supported by the Lebanese Ministry of Public Health, the WHO (Lebanon), National Institute of Health/Fogarty International Center (R03 TW006481-01), anonymous private donations to IDRAAC, Lebanon, and unrestricted grants from, Algorithm, AstraZeneca, Benta, Bella Pharma, Eli Lilly, Glaxo Smith Kline, Lundbeck, Novartis, Servier, OmniPharma, Phenicia, Pfizer, UPO. 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). Te Rau Hinengaro: The New Zealand Mental Health Survey (NZMHS) is supported by the New Zealand Ministry of Health, Alcohol Advisory Council, and the Health Research Council. The Northern Ireland Study of Mental Health was funded by the Health & Social Care Research & Development Division of the Public Health Agency. The Peruvian World Mental Health Study was funded by the National Institute of Health of the Ministry of Health of Peru. The Romania WMH study projects “Policies in Mental Health Area” and “National Study regarding Mental Health and Services Use” were carried out by National School of Public Health & Health Services Management (former National Institute for Research & Development in Health), with technical support of Metro Media Transilvania, the National Institute of Statistics-National Centre for Training in Statistics, SC. Cheyenne Services SRL, Statistics Netherlands and were funded by Ministry of Public Health (former Ministry of Health) with supplemental support of Eli Lilly Romania SRL. The South Africa Stress and Health Study (SASH) is supported by the US National Institute of Mental Health (R01-MH059575) and National Institute of Drug Abuse with supplemental funding from the South African Department of Health and the University of Michigan. The Psychiatric Enquiry to General Population in Southeast Spain – Murcia (PEGASUS-Murcia) Project has been financed by the Regional Health Authorities of Murcia (Servicio Murciano de Salud and Consejería de Sanidad y Política Social) and Fundación para la Formación e Investigación Sanitarias (FFIS) of Murcia. The Ukraine Comorbid Mental Disorders during Periods of Social Disruption (CMDPSD) study is funded by the US National Institute of Mental Health (R01-MH61905). 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. Dr. Dan Stein is supported by the Medical Research Council of South Africa (MRC). Liu’s work was supported in part by a training grant from the National Institute of Mental Health (T32 MH017119).

References

1. Atwoli L, Stein DJ, Koenen KC, McLaughlin KA. Epidemiology of posttraumatic stress disorder: prevalence, correlates and consequences. *Curr Opin Psychiatry*. 2015; 28:307–311. [PubMed: 26001922]
2. Benjet C, Bromet E, Karam EG, Kessler RC, McLaughlin KA, Ruscio AM, et al. The epidemiology of traumatic event exposure worldwide: results from the World Mental Health Survey Consortium. *Psychol Med*. 2016; 46:327–343. [PubMed: 26511595]
3. Bomyea J, Risbrough V, Lang AJ. A consideration of select pre-trauma factors as key vulnerabilities in PTSD. *Clin Psychol Rev*. 2012; 32:630–641. [PubMed: 22917742]
4. Liberzon I, Abelson JL. Context processing and the neurobiology of post-traumatic stress disorder. *Neuron*. 2016; 92:14–30. [PubMed: 27710783]

5. Smoller JW. The genetics of stress-related disorders: PTSD, depression, and anxiety disorders. *Neuropsychopharmacology*. 2016; 41:297–319. [PubMed: 26321314]
6. Horn SR, Charney DS, Feder A. Understanding resilience: new approaches for preventing and treating PTSD. *Exp Neurol*. 2016; 284(Pt B):119–132. [PubMed: 27417856]
7. Kessler RC, Rose S, Koenen KC, Karam EG, Stang PE, Stein DJ, et al. How well can post-traumatic stress disorder be predicted from pre-trauma risk factors? An exploratory study in the WHO World Mental Health Surveys. *World Psychiatry*. 2014; 13:265–274. [PubMed: 25273300]
8. DiGangi JA, Gomez D, Mendoza L, Jason LA, Keys CB, Koenen KC. Pretrauma risk factors for posttraumatic stress disorder: a systematic review of the literature. *Clin Psychol Rev*. 2013; 33:728–744. [PubMed: 23792469]
9. Kessler RC, McLaughlin KA, Green JG, Gruber MJ, Sampson NA, Zaslavsky AM, et al. Childhood adversities and adult psychopathology in the WHO World Mental Health Surveys. *Br J Psychiatry*. 2010; 197:378–385. [PubMed: 21037215]
10. Nemeroff CB. Paradise lost: the neurobiological and clinical consequences of child abuse and neglect. *Neuron*. 2016; 89:892–909. [PubMed: 26938439]
11. Green JG, McLaughlin KA, Berglund PA, Gruber MJ, Sampson NA, Zaslavsky AM, et al. Childhood adversities and adult psychiatric disorders in the national comorbidity survey replication I: associations with first onset of DSM-IV disorders. *Arch Gen Psychiatry*. 2010; 67:113–123. [PubMed: 20124111]
12. McLaughlin KA, Greif Green J, Gruber MJ, Sampson NA, Zaslavsky AM, Kessler RC. Childhood adversities and first onset of psychiatric disorders in a national sample of US adolescents. *Arch Gen Psychiatry*. 2012; 69:1151–1160. [PubMed: 23117636]
13. Breslau N, Peterson EL. Assaultive violence and the risk of posttraumatic stress disorder following a subsequent trauma. *Behav Res Ther*. 2010; 48:1063–1066. [PubMed: 20673870]
14. Breslau N, Peterson EL, Schultz LR. A second look at prior trauma and the posttraumatic stress disorder effects of subsequent trauma: a prospective epidemiological study. *Arch Gen Psychiatry*. 2008; 65:431–437. [PubMed: 18391131]
15. Cougle JR, Resnick H, Kilpatrick DG. Does prior exposure to interpersonal violence increase risk of PTSD following subsequent exposure? *Behav Res Ther*. 2009; 47:1012–1017. [PubMed: 19647229]
16. Harkness KL, Hayden EP, Lopez-Duran NL. Stress sensitivity and stress sensitization in psychopathology: an introduction to the special section. *J Abnorm Psychol*. 2015; 124:1–3. [PubMed: 25688427]
17. Liu H, Petukhova MV, Sampson NA, Aguilar-Gaxiola S, Alonso J, Andrade LH, et al. Association of DSM-IV posttraumatic stress disorder with traumatic experience type and history in the World Health Organization World Mental Health Surveys. *JAMA Psychiatry*. 2017; 74:270–281. [PubMed: 28055082]
18. World Bank. World Bank list of economies (July 2009). The World Bank; Washington, D.C: 2009. (Available at http://www.iqla.org/joining/World-Bank_Classification-List_2009.pdf) [Accessed 01 June 2017]
19. Pennell B-E, Mneimneh ZN, Bowers A, Chardoul S, Wells JE, Viana MC. , et al. Implementation of the World Mental Health Surveys. In: Kessler RC, Üstün TB, editors *The WHO World Mental Health Surveys: Global Perspectives on the Epidemiology of Mental Disorders*. Cambridge University Press; New York, NY: 2008. 33–57.
20. Heeringa SG, Wells JE, Hubbard F, Mneimneh ZN, Chiu WT, Sampson NA. , et al. Sample designs and sampling procedures. In: Kessler RC, Üstün TB, editors *The WHO World Mental Health Surveys: Global Perspectives on the Epidemiology of Mental Disorders*. Cambridge University Press; New York, NY: 2008. 14–32.
21. Kessler RC, Ustun 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; 13:93–121. [PubMed: 15297906]
22. Kessler RC, Akiskal HS, Angst J, Guyer M, Hirschfeld RM, Merikangas KR, et al. Validity of the assessment of bipolar spectrum disorders in the WHO CIDI 3. 0. *J Affect Disord*. 2006; 96:259–269. [PubMed: 16997383]

23. Knäuper B, Cannell CF, Schwarz N, Bruce ML, Kessler RC. Improving accuracy of major depression age-of-onset reports in the US National Comorbidity Survey. *Int J Methods Psychiatr Res.* 1999; 8:39–48.
24. Haro JM, Arbabzadeh-Bouchez S, Brugha TS, de Girolamo G, Guyer ME, Jin R, et al. 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]
25. First MB, Spitzer RL, Gibbon M, Williams BJ. Structured Clinical Interview for Axis I DSM-IV Disorders. New York State Psychiatric Institute Biometrics Research Department; New York: 1994.
26. Wolter KM. Introduction to Variance Estimation. Springer-Verlag; New York: 1985.
27. SAS Institute Inc. SAS Software, Version 9.2 [computer program]. SAS Institute Inc; Cary, NC: 2008.
28. Scott KM, Koenen KC, King A, Petukhova MV, Alonso J, Bromet EJ, et al. Post-traumatic stress disorder associated with sexual assault among women in the WHO World Mental Health Surveys. *Psychol Med.* 2017; e-pub ahead of print 19 June 2017. doi: 10.1017/S0033291717001593
29. Ozer EJ, Best SR, Lipsey TL, Weiss DS. Predictors of posttraumatic stress disorder and symptoms in adults: a meta-analysis. *Psychol Bull.* 2003; 129:52–73. [PubMed: 12555794]
30. Sayed S, Iacoviello BM, Charney DS. Risk factors for the development of psychopathology following trauma. *Curr Psychiatry Rep.* 2015; 17:70.
31. Ogle CM, Siegler IC, Beckham JC, Rubin DC. Neuroticism increases PTSD symptom severity by amplifying the emotionality, rehearsal, and centrality of trauma memories. *J Pers.* 2016; e-pub ahead of print 12 August 2016. doi: 10.1111/jopy.12278

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Table 1

The associations of prior lifetime (to random trauma exposure) DSM-IV/CIDI disorder history with PTSD after random traumas (n = 34,676)^f

	Prevalence of prior disorders		Associations of prior lifetime disorders with PTSD after random traumas											
	%	(SE)	Bivariate associations		Model 1.1 ²		Model 1.2 ³		Model 1.3 ⁴		Model 1.4 ⁵			
			OR	(95% CI)	p	OR	(95% CI)	p	OR	(95% CI)	p	OR	(95% CI)	p
I. Mood disorders														
MDD or dysthymia disorder	9.0	(0.3)	2.3	(1.7–3.1)	<.001	1.3	(0.9–1.7)	.13						
Bipolar disorder	1.8	(0.2)	1.7	(0.9–3.3)	.10	0.8	(0.5–1.4)	.47						
Any mood	10.0	(0.4)	2.1	(1.6–2.8)	<.001									
χ^2_3						2.6	--	.27						
χ^2_2						1.8	--	.18						
II. Anxiety disorders														
Agor/panic	3.7	(0.3)	1.8	(1.2–2.9)	.008	1.0	(0.7–1.4)	.92	1.0	--	--	1.0	--	--
GAD	3.5	(0.2)	4.1	(2.3–7.2)	<.001	2.8	(1.4–5.4)	.002	3.4	(1.5–7.5)	.003	3.3	(1.5–7.5)	.004
PTSD	2.8	(0.2)	5.7	(3.8–8.6)	<.001	4.3	(2.8–6.6)	<.001	4.9	(2.8–8.4)	<.001	4.8	(2.7–8.5)	<.001
Social phobia	6.2	(0.3)	2.5	(1.9–3.2)	<.001	1.5	(1.1–2.0)	.008	1.8	(1.1–2.8)	.02	1.8	(1.1–2.8)	.02
Specific phobia	9.9	(0.4)	2.6	(2.0–3.4)	<.001	1.9	(1.4–2.5)	<.001	2.1	(1.4–3.0)	<.001	2.1	(1.4–3.0)	<.001
SAD	3.3	(0.2)	3.0	(2.0–4.5)	<.001	2.1	(1.5–3.1)	<.001	2.5	(1.5–4.3)	<.001	2.6	(1.5–4.4)	<.001
Number ^g	20.3	(0.6)	2.3	(1.9–2.6)	<.001				0.9	(0.6–1.2)	.48			
$\chi^2_{6/5}$						112.1	--	<.001	35.8	--	<.001	33.4	--	<.001
$\chi^2_{5/4}$						26.8	--	<.001	17.4	--	.002	16.0	--	.003
Exactly 1	13.8	(0.5)	2.5	(1.6–3.7)	<.001									
Exactly 2	3.6	(0.2)	4.8	(3.2–7.3)	<.001							0.8	(0.4–1.6)	.53
Exactly 3	1.2	(0.1)	9.7	(5.5–17.1)	<.001							0.6	(0.2–1.9)	.38
Exactly 4	0.2	(0.0)	50.8	(19.8–130.5)	<.001							1.1	(0.2–5.7)	.94
Exactly 5	0.0	(0.0)	48.5	(3.0–774.2)	.006							0.3	(0.0–10.0)	.54
χ^2_4			63.8		<.001							2.2	--	.70
III. Disruptive behavioral disorders														
ADHD	2.2	(0.2)	2.4	(1.5–3.8)	<.001	1.7	(1.0–3.0)	.04						

Associations of prior lifetime disorders with PTSD after random traumas

	Prevalence of prior disorders		Bivariate associations			Model 1.1 ²			Model 1.2 ³			Model 1.3 ⁴			Model 1.4 ⁵		
	%	(SE)	OR	(95% CI)	p	OR	(95% CI)	p	OR	(95% CI)	p	OR	(95% CI)	p	OR	(95% CI)	p
Conduct	2.1	(0.2)	1.1	(0.6–2.0)	.67	0.6	(0.3–1.1)	.10									
IED	2.8	(0.3)	1.4	(0.8–2.3)	.25	0.8	(0.5–1.4)	.51									
ODD	2.6	(0.2)	1.6	(0.9–3.1)	.14	0.9	(0.5–1.7)	.77									
Number	7.0	(0.4)	1.3	(1.1–1.6)	.02												
χ^2_4						5.3	--	.25									
χ^2_3						5.3	--	.15									
IV. Substance disorders																	
Alcohol	8.0	(0.4)	1.5	(1.0–2.3)	.03	1.0	(0.6–1.5)	.93									
Drug	3.2	(0.2)	1.9	(1.1–3.3)	.02	1.3	(0.7–2.3)	.35									
Any	8.9	(0.5)	1.5	(1.1–2.2)	.02												
χ^2_2						1.0	--	.62									
χ^2_1						0.5	--	.49									
χ^2_{14}						136.8	--	<.001									
χ^2_{13}						60.0	--	<.001									

¹ Each model was estimated using logistic regression with controls for respondent age at random trauma exposure, sex, survey, random trauma type, and earlier traumas.

² Model 1.1 estimates the association of prior mental disorders with PTSD after the random trauma.

³ Model 1.2 retains the significant anxiety disorders from Model 1.1 and includes a continuous variable for the number of anxiety disorders.

⁴ Model 1.3 recodes the number of anxiety disorders in Model 1.2 into separate dummy variables for between 2 to 5 anxiety disorders.

⁵ Model 1.4 omits the number-of-anxiety-disorders variables that were in Models 1.2 and 1.3.

⁶ Coded as a 0–5 continuous variable.

Table 3

Estimated population distributions of trauma and DSM-IV/CIDI PTSD among WMH respondents (i) with prior PTSD or other anxiety disorders that predict PTSD, (ii) with history of traumas that predict PTSD in the absence of anxiety disorders, and (iii) other respondents (n = 54,600)¹.

	Prior PTSD or other anxiety disorders ²		Earlier traumas but no prior anxiety disorders ³		All others	
	Est	(se)	Est	(se)	Est	(se)
Proportion of respondents in the sample	13.8%	(0.2)	12.3%	(0.2)	73.9%	(0.3)
Traumas/100 people over 5 years	71.9	(1.5)	72.7	(1.8)	27.5	(0.5)
PTSD prevalence associated with random traumas	10.6	(0.9)	3.5	(0.7)	2.2	(0.2)
Proportion of PTSD cases over 5 years	57.9	(2.9)	17.4	(2.9)	24.7	(2.0)
Number of PTSD cases/100 people over 5 years	7.6	(0.7)	2.6	(0.5)	0.6	(0.0)

¹The results in the first two rows are based on the total weighted (to be representative of people in the population) Part II WMH sample of individuals (n = 54,600). The results in the third row are based on the weighted (to be representative of all traumas that occur in the population) random trauma sample (n = 34,676). The results in the last two rows are based on jackknife repeated replications simulations using the data in the first three rows.

²Limited to prior anxiety disorders found to predict PTSD. See the text for details.

³Limited to earlier traumas found to predict subsequent PTSD among respondents without any of the prior anxiety disorders that predict subsequent PTSD. See the text for details.