



Psychiatric disorders and risk for multiple adverse outcomes: a national prospective study

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Abstract

Most psychiatric disorders, when examined individually, are associated with a broad range of adverse outcomes. However, psychiatric disorders often co-occur and their co-occurrence is well explained by a limited number of transdiagnostic factors. Yet it remains unclear whether the risk of these adverse outcomes is due to specific psychiatric disorders, specific dimensions of psychopathology (i.e., internalizing and externalizing dimensions), a general psychopathology factor, or a combination of these explanations. In a large nationally representative prospective survey, the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), we used structural equation modeling to examine the shared and specific effects of common Axis I and Axis II disorders on the risk of ten adverse outcomes (unemployment; financial crisis; low income; poorer general health; worse mental and physical health; legal problems; divorce; problems with a neighbor, friend, or relative; and violence) in the general adult population. Effects of psychiatric disorders were exerted mostly through a general psychopathology factor representing the shared effect across all disorders, independent of sociodemographic characteristics and the presence of the adverse outcomes at baseline. Violence and legal problems were further associated with the externalizing factor, but there were no independent associations of the internalizing factor or any individual psychiatric disorders with any of the adverse outcomes. Our findings reveal that associations between psychiatric disorders and adverse outcomes occur through broad psychological dimensions. Understanding the biological and psychological mechanisms underlying these dimensions should yield key intervention targets to decrease the individual suffering and societal burden associated with common psychiatric disorders.

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Introduction

Persistently increasing national rates of suicide attempts [1] and deaths [2] and opioid overdoses [3, 4] along with decreasing life expectancy [5, 6] and quality of life [7] in some demographic groups have reignited interest in relationships between psychiatric disorders and adverse outcomes. Most psychiatric disorders, when examined individually, are associated with a broad range of adverse outcomes [8–10]. However, psychiatric disorders often co-occur and their co-occurrence is well explained by a limited number of underlying dimensions or transdiagnostic factors [11, 12]. In a previous study, we found that the association of psychiatric disorders with increased risk of suicide attempt was mediated almost exclusively through a general psychopathology factor representing the shared effect across common psychiatric disorders [8]. It is unknown, though, whether similar general associations exist for other adverse outcomes and whether the strength of such associations vary by adverse outcome.

This prospective study sought to generalize the findings of our study on risk of suicide attempt and address broader questions by examining the shared and specific associations of a wide range of DSM-IV Axis I and Axis II disorders with multiple adverse outcomes assessed in a large, nationally representative sample. Since dimensions underlying psychopathology are correlated [11, 12], we used a bifactor latent variable approach to disentangle the effects shared by all psychiatric disorders (i.e., general psychopathology), those specific to dimensions of psychopathology (e.g., internalizing dimension) and those specific to individual psychiatric disorders (e.g., major depressive episode). To our knowledge, this is the most extensive assessment in a nationally representative sample of associations between psychiatric disorders and adverse outcomes. Based on prior research [8–10], we hypothesized that psychiatric disorders would be associated with a broad range of adverse outcomes and that these associations would be mediated primarily by broad underlying dimensions of psychopathology.

Materials and methods

Sample

Data were drawn from the Wave 1 and Wave 2 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), a nationally representative face-to-face survey of the U.S. adult population, conducted in 2001–2002 (Wave 1) and 2004–2005 (Wave 2) by the National Institute on Alcoholism and Alcohol Abuse [13]. The target population included the civilian noninstitutionalized population, aged 18 years and older, residing in the United States. The cumulative response rate at Wave 2 was 70.2%, resulting in 34,653 Wave 2 interviews [13]. The Wave 2 NESARC data were weighted to be representative of the U.S. civilian population based on the 2000 census [13]. The research protocol, including written informed consent procedures, received full human subjects review, and approval from the U.S. Census Bureau and the Office of Management and Budget.

Measures

Assessments of DSM-IV Axis I and Axis II disorders

Psychiatric disorders were assessed using the Alcohol Use Disorder and Associated Disabilities Interview Schedule, DSM-IV version (AUDADIS-IV), a valid and reliable structured diagnostic instrument [13–18]. Axis I diagnoses included substance use disorders (alcohol use disorder, drug use disorder, and nicotine dependence), mood disorders (major depressive disorder, dysthymic disorder, and bipolar disorder), anxiety disorders (panic disorder, social anxiety

disorder, specific phobia, and generalized anxiety disorder), and pathological gambling. All Axis I disorder diagnoses were based on the past 12 months prior to Wave 1. Axis II disorders (including avoidant, dependent, obsessive-compulsive, histrionic, paranoid, schizoid, and antisocial personality disorders) were assessed on a lifetime basis [13].

Assessments of adverse outcomes

We included all adverse outcomes assessed in the demographic and background information section of the AUDA-DIS in Waves 1 and 2. Adverse outcomes included unemployment; financial crisis; income below the median; poorer general health; worse mental and physical health; legal problems; divorce/separation; having problems with a neighbor, friend, or relative; and violence. In Wave 1, all outcomes were assessed using a past-year timeframe, except violence, which was assessed using a lifetime timeframe. In Wave 2, all outcomes were also assessed using a past-year timeframe, except violence, which included any occurrence since the Wave 1 interview.

Respondents were considered unemployed if they answered “yes” to either: “Were you fired or laid off from a job?” or “Were you unemployed and looking for a job for more than a month?” Having a financial crisis was assessed with the question: “Have you experienced a major financial crisis, declared bankruptcy, or more than once been unable to pay your bills on time?”. Income was assessed by self-report. Participants also completed version 2 of the Short Form 12 Health Survey (SF-12v2) [19], a 12-item measure that assesses life satisfaction and current functioning over the last 4 weeks and has demonstrated sensitivity to change in clinical status [10, 20]. The SF-12v2 can be scored to generate a norm-based physical component summary score (PCS) and a norm-based mental component summary score (MCS). Higher scores indicate better functioning. General health perception was assessed with the following question: “In general, would you say your health is excellent, very good, good, fair, or poor?” which was recoded as fair/poor, good, or very good/excellent.

Participants were considered to have had legal problems if they answered positively to any of the following three questions: “Did you or a family member have trouble with the police, got arrested, or sent to jail?”, “Have you gotten arrested, held at a police station, or had any other legal problems because of your drinking?”, and “Have you gotten arrested, held at a police station, or had any other legal problems because of your medicine or drug use?”. Marital status was assessed by self-report. In accord with prior work [21], violence was assessed using nine questions (e.g., “Have you used a weapon like a stick, knife, or gun in a fight?”, “Have you hit someone so hard that you injured them or they had to see a doctor?”). Having problems with a neighbor was assessed by asking: “Have you had serious problems with a neighbor,

friend, or relative?" To examine whether selective loss to follow-up between waves could bias the results, we compared the distribution of adverse outcomes among all individuals who participated in Wave 1, versus those who participated in both waves. For all outcomes, the difference in prevalence was less than 2%, indicating that loss to follow-up did not substantially influence the distribution of adverse outcomes. Because the prevalence of psychiatric disorders differs by age group, sex, and across ethnicities, all analyses were adjusted for these variables [8].

Statistical analysis

Odds ratios (ORs) were calculated between each pair adverse events. ORs, population attributable fractions (PAFs), and their 95% confidence intervals were calculated between each psychiatric disorder at Wave 1 with each adverse outcome at Wave 1 at the bivariate level. While the OR assesses the strength of association between two variables, the PAF is the proportional reduction in population adverse outcome that would occur if exposure to a risk factor were eliminated. Thus, the magnitude of the PAF depends on the strength of association between the risk factor (in this case, each psychiatric disorder) and each adverse outcome, as well as the prevalence of the risk factor. For the analyses of ORs and PAFs, continuous variables (i.e., income, SF-12 scores and general health status) were dichotomized at the median.

Because bivariate analyses do not properly model comorbidity and can lead to an inflation of type I error due to multiple comparisons (i.e., each disorder times each outcome), we used confirmatory factor analysis (CFA) to identify the latent structure underlying individual mental disorders assessed at Wave 1, based on the previous models used to examine the relationship of psychiatric disorders with suicide attempts in these data [8]. Specifically, we performed a bifactor CFA model to determine whether a general psychopathology factor measured by all psychiatric disorders in addition to disorder-specific factors [22, 23] fit the underlying structure of psychiatric disorders. We examined measures of goodness-of-fit, including the comparative fit index (CFI), the Tucker–Lewis index (TLI), and the root mean squared error of approximation (RMSEA). CFI and TLI values >0.95 and values of RMSEA <0.06 are commonly used to indicate good model fit and were used as cutoffs [24].

Finally, we used a structural equation model, based on our previous work on the relationship of psychiatric disorders to risk of suicide attempt [8], to assess shared and specific associations of psychiatric disorders at Wave 1 on each Wave 2 adverse outcome, while controlling for demographic characteristics and each adverse outcome at Wave 1 and each corresponding outcome at Wave 2. Specifically, we examined three sets of relationships: (1) the association of the general

psychopathology liability factor (representing the effects shared across all mental disorders) with adverse outcomes, (2) the associations of each dimension of psychopathology with adverse outcomes beyond its association with the general psychopathology factor, and (3) the associations of individual psychiatric disorders with the adverse outcomes above and beyond the shared effects of psychiatric disorders through the latent factors.

Since internalization and externalization dimensions are positively correlated [11, 12], an advantage of modeling a bifactor model is that a general psychopathology factor accounts for a substantial proportion of this correlation, is orthogonal to these dimensions and saturates each psychiatric disorder diagnosis directly [22, 23]. The bifactor model allows a disambiguation from each of the other associations shared by all psychiatric disorders (represented by the general psychopathology factor), those shared by disorders within each dimension of psychopathology (e.g., externalizing dimension) and the specific associations of each psychiatric disorder per se [25].

The relationships between the general psychopathology factor and adverse outcomes are interpreted as the association of the overall shared psychiatric disorder liability predictor with the risk of the adverse outcome. By contrast, the relationships examined between the specific dimensions of psychopathology or specific individual disorders and adverse events are interpreted as the direct associations, because they indicate associations that are not mediated through the general psychopathology factor. To determine if a particular psychiatric disorder is associated with an adverse outcome above and beyond the association attributable to the latent variables, modification indices (i.e., χ^2 tests with 1 df) were examined to test if any residuals associated with psychiatric disorders are correlated with the risk of the adverse outcome. To avoid including associations that could be significant due to multiple testing (3 factors and 18 disorders times 10 outcomes), we consistently used as threshold for inclusion in the model associations with Bonferroni-corrected p -value = $0.05/210$, i.e., $p \leq 0.00024$ [26]. To assess the robustness of our results and facilitate comparisons with other work, we conducted a sensitivity analysis using two additional parameterizations of the model used in our previous work on suicide attempts: one in which the internalizing factor is subdivided in to separate internalizing factors, and another using the distress–fear–externalizing model that includes antisocial personality disorder, but not other personality disorders.

PAFs were computed using the Punaf program [27, 28] for STATA software (Svy routines in Stata, version 11.0; StataCorp) [28, 29]. This program implements the method for estimating PAFs recommended by Greenland and Drescher for cohort studies [30]. All other analyses were conducted in Mplus Version 7.3 [26]. The default estimator

Table 1 Associations of past-year Axis I disorders and lifetime personality disorders (assessed in Wave 1) on the occurrence of adverse outcomes in Wave 2 of the National Epidemiological Survey on Alcohol and Related Conditions ($N = 34,653$)

Wave 1 disorders	(%)	Divorced or separated	Problems with neighbor	Unemployment	Financial crisis	Income ^a	General health ^b	MCS ^c	Violence	PCS ^c	Legal problems
		OR	OR	OR	OR	OR	OR	OR	OR	OR	OR
MDE	(7.02)	2.20	3.20	2.00	3.04	1.64	1.67	3.34	3.02	1.49	2.29
Dysthymia	(1.23)	3.10	3.68	1.80	3.79	2.26	2.63	4.98	1.91	2.78	1.99
GAD	(2.05)	2.24	3.37	1.75	3.73	1.59	2.39	4.81	1.65	2.16	2.15
Panic disorder	(2.14)	1.83	3.37	1.70	2.79	1.89	2.00	2.76	2.21	2.00	2.03
SAD	(2.83)	1.51	2.44	1.30	2.18	1.50	1.59	3.13	1.72	1.50	1.74
Specific phobia	(7.16)	1.23	2.14	1.20	1.83	1.44	1.23	1.83	1.66	1.32	1.62
Mania/hypomania	(2.66)	1.74	3.45	2.23	3.54	1.96	1.80	3.66	5.13	1.43	3.39
Avoidant PD	(2.32)	1.65	2.96	2.01	3.09	2.04	2.02	4.43	2.95	1.67	2.03
Dependent PD	(0.43)	1.43*	2.60	2.50	4.32	5.17	4.45	8.24	5.01	3.94	2.94
OCPD	(8.07)	1.22	2.29	1.48	1.96	0.99*	1.24	1.88	1.92	1.29	1.70
Paranoid PD	(4.33)	1.99	3.91	2.37	3.65	1.95	1.98	3.14	4.50	1.62	2.75
Schizoid PD	(3.06)	1.80	2.50	1.89	3.04	1.51	1.98	2.35	3.42	1.79	2.44
Histrionic PD	(1.80)	1.50	3.13	2.46	3.23	1.49	1.29	2.92	5.94	1.16*	3.09
AUD	(8.27)	1.33	1.60	1.91	1.74	0.66	0.84	1.20	6.22	0.65	3.35
DUD	(1.94)	1.33	2.66	3.11	3.44	1.34	1.13*	2.06	10.08	0.73	5.32
Nicotine Dep	(12.41)	1.93	1.86	2.09	2.75	1.15	1.67	1.68	4.08	1.42	2.48
Pathological gambling	(0.16)	2.12	1.98*	3.64	2.91	0.74*	1.26*	1.69*	4.31	0.75	2.99
Antisocial PD	(3.63)	1.44	2.06	2.84	3.22	1.12*	1.57	1.82	6.39	1.29	3.59

Results are significant (two-sided p -value < 0.05) unless marked with the asterisk

CI confidence interval, GAD generalized anxiety disorder, SAD social anxiety disorder, MDE major depressive episode, OCPD obsessive-compulsive personality disorder, OR odds ratio, PD personality disorder, AUD alcohol use disorder, DUD drug use disorder, MCS mental component summary score, PCS physical component summary score

^aThe income variable is dichotomized as follows: under the median versus equal or over the median (median = \$21,690)

^bThe general health variable is dichotomized as follows: poor or good health versus very good or excellent health

^cThese variables are dichotomized as follows: under the mean versus equal or over the mean (mean = 50)

for the analysis was the variance-adjusted weighted least squares, a robust estimator appropriate for ordered categorical and dichotomous observed variables such as the ones used in this study [26]. All analyses accounted for the NESARC's complex sampling design.

Results

Associations of mental disorders with adverse outcomes

All adverse consequences increased the odds of all other adverse consequences except the association of SF-12 PCS and unemployment, which decreased the odds; and the associations of income with marital status, SF-12 physical component score and violence and SF-12 physical component score and legal problems, all of which had ORs that were not statistically significant (Supplementary Table 1).

The psychiatric disorders with the highest 12-month prevalence were nicotine dependence (12.4%) and major depressive disorder (7.0%). All psychiatric disorders, except

alcohol use disorder and pathological gambling, were positively associated with all adverse outcomes examined. The largest ORs were for the association between drug use disorder and violence and for the association between dependent personality disorder and scoring below the mean in the MCS of the SF-12. Alcohol use disorder, drug use disorder, and pathological gambling were also associated with increased ORs for most adverse outcomes, but had decreased ORs for having a score below the mean in the PCS of the SF-12. In addition, alcohol use disorder was associated with lower odds of having an income below the median and general health that was good, fair, or poor as opposed to very good or excellent. Drug use disorder had decreased odds of scoring below the mean on the PCS of the SF-12 (Table 1).

The PAFs followed a slightly different pattern because their magnitude depends both on the prevalence of the psychiatric disorders, as well as on strength of the association between psychiatric disorders and adverse outcomes (Table 2). All psychiatric disorders, except alcohol use disorder, drug use disorder, pathological gambling, and obsessive-compulsive personality disorder, were associated with increased PAFs for all adverse outcomes. The largest

Table 2 Population attributable fractions (PAF) of the Axis I disorders and lifetime personality disorders (assessed in Wave 1) on the occurrence of adverse outcomes in Wave 2 of the National Epidemiological Survey on Alcohol and Related Conditions ($N = 34,653$)

Wave 1 disorders	(%)	Divorced or Separated		Problems with neighbor		Unemployment		Financial crisis		Income ^a		General health ^b		MCS ^c		Violence		PCS ^c		Legal problems	
		PAF (%)	PAF (%)	PAF (%)	PAF (%)	PAF (%)	PAF (%)	PAF (%)	PAF (%)	PAF (%)	PAF (%)	PAF (%)	PAF (%)	PAF (%)	PAF (%)	PAF (%)	PAF (%)	PAF (%)	PAF (%)	PAF (%)	PAF (%)
MDE	(7.02)	4.75	12.18	5.12	8.94	1.83	1.89	6.01	11.71	1.70	6.95										
Dysthymia	(1.23)	1.48	2.52	0.57	1.96	0.64	0.77	1.47	1.23	1.00	0.99										
GAD	(2.05)	1.42	3.90	1.14	3.17	0.60	0.95	2.17	2.09	1.09	1.80										
Panic disorder	(2.14)	1.23	4.02	1.11	2.48	0.69	0.78	1.59	2.42	0.98	1.72										
SAD	(2.83)	0.96	3.20	0.73	2.36	0.56	0.70	2.06	1.90	0.77	1.68										
Specific phobia	(7.16)	0.99	6.30	0.90	3.82	1.18	0.89	2.86	4.38	1.16	3.26										
Mania/hypomania	(2.66)	1.31	5.39	2.66	4.16	0.95	0.81	2.31	8.88	0.63	4.58										
Avoidant PD	(2.32)	0.99	4.24	1.97	3.30	1.06	0.99	2.26	4.13	0.92	2.41										
Dependent PD	(0.43)	0.10	0.62	0.37	0.75	0.32	0.30	0.51	1.28	0.35	0.42										
OCPD	(8.07)	1.04	8.05	2.74	5.37	-0.43	0.92	3.34	7.45	0.98	4.75										
Paranoid PD	(4.33)	2.77	9.87	4.52	7.20	1.59	1.73	3.72	13.69	1.36	5.80										
Schizoid PD	(3.06)	1.55	3.99	1.96	3.84	0.62	1.01	1.88	5.89	1.03	3.22										
Histrionic PD	(1.80)	0.58	3.25	1.61	2.66	0.21	0.29	1.22	6.85	0.14	3.00										
AUD	(8.27)	1.64	4.67	5.29	4.23	-2.03	-0.96	0.84	24.75	-2.35	11.07										
DUD	(1.94)	0.22	2.65	2.44	2.42	0.27	0.06	0.76	11.13	-0.34	4.66										
Nicotine Dep	(12.41)	6.22	9.32	8.30	12.27	1.03	3.13	4.23	24.33	2.25	11.81										
Pathological gambling	(0.16)	0.11	0.21	0.24	0.22	-0.03	0.05	0.07	0.62	0.03	0.25										
Antisocial PD	(3.63)	0.78	4.01	4.03	4.78	0.16	0.67	1.38	14.76	0.36	6.61										

Results are significant (two-sided p -value < 0.05) unless marked with the asterisk

CI confidence interval, *GAD* generalized anxiety disorder, *SAD* social anxiety disorder, *MDE* major depressive episode, *OCPD* obsessive-compulsive personality disorder, *OR* odds ratio, *PD* personality disorder, *AUD* alcohol use disorder, *DUD* drug use disorder, *MCS* mental component summary score, *PCS* physical component summary score

^aThe income variable is dichotomized as follows: under the median versus equal or over the median (median = \$21,690)

^bThe general health variable is dichotomized as follows: poor or good health versus very good or excellent health

^cThese variables are dichotomized as follows: under the mean versus equal or over the mean (mean = 50)

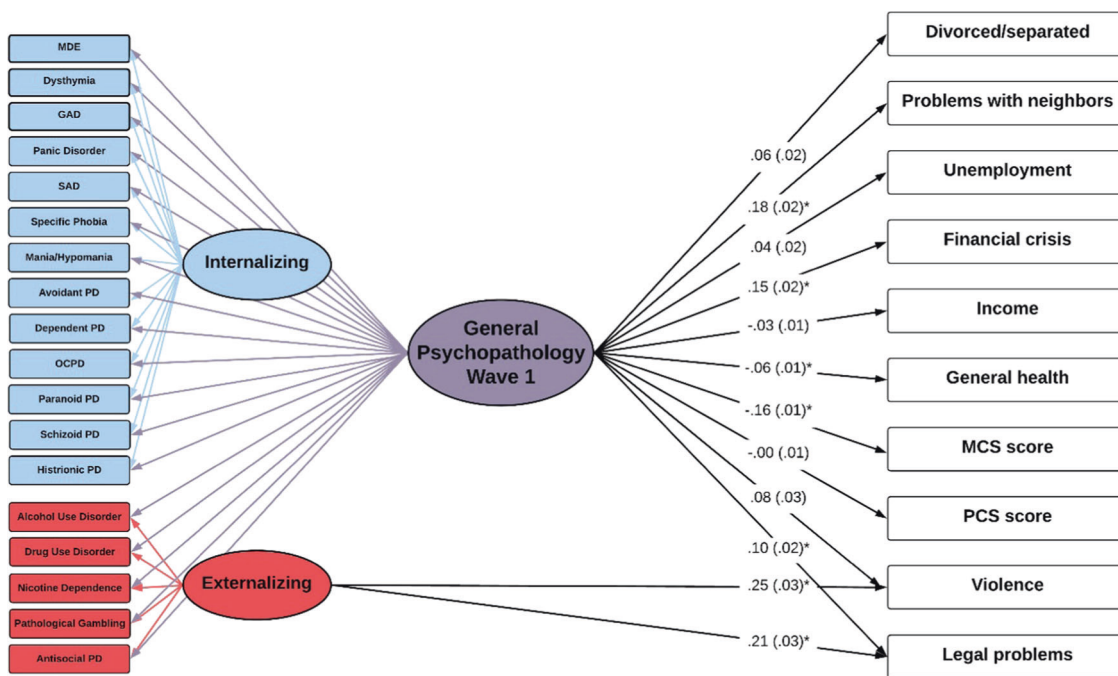


Fig. 1 Bifactor model with one internalizing and one externalizing factors testing the shared and specific effects of past-year Axis I disorders and lifetime personality disorders (assessed in Wave 1) on the

occurrence of adverse outcomes in Wave 2 of the National Epidemiological Survey on Alcohol and Related Conditions ($N = 34,653$)

PAFs were for associations of alcohol use disorder and nicotine dependence with violence. The size of these PAFs indicate that although other associations were stronger (as measured by the ORs presented in Table 1), the higher prevalence of these disorders resulted in a greater impact at the population level (Table 2). Obsessive–compulsive personality disorder, alcohol use disorder and pathological gambling had small negative PAFs, indicating that at the population level, they were associated with increases in median income. Alcohol and drug use disorders were associated with negative PAFs on the physical component score of the SF-12 and alcohol use disorder was further associated with a negative PAF for general health.

Association of transdiagnostic factors with adverse outcomes

A bifactor model (left side of Fig. 1) of Wave 1 psychiatric disorders provided a good fit to the data (CFI = 0.957, TLI = 0.943, and RMSEA = 0.013). After adjusting for sex, age, and race/ethnicity and Wave 1 adverse outcomes, the general psychopathology factor at Wave 1 was significantly associated with all adverse outcomes at Wave 2, except divorce/separation, unemployment, income, violence, and PCS. In addition, the externalizing factor was associated with violence and legal problems in the last 12 months (nonsignificant paths from the internalizing and externalizing factors to the Wave 2 outcomes are shown in Supplementary Table 2). Furthermore,

there were no direct associations with any individual psychiatric disorder with Wave 2 outcomes (Fig. 1). Sex, age, and race-ethnicity had significant associations with Wave 2 outcomes beyond that of the general psychopathology factor (Table 3) and the proportion of explained variance for each Wave 2 progressively increased from considering the general psychopathology alone to considering also the contribution of the specific factors, the Wave 1 outcomes, and the socio-demographic characteristics (Supplementary Table 3). In the sensitivity analysis, the model with two separate internalizing factors yielded nearly identical results to the main model (Supplemental Fig. 1). The fear–distress–externalizing model results (Fig. 2) were also very similar although there were direct effects from the internalizing factor to problems with neighbors and from the distress factor to the MCS of the SF-12 and there were no direct effects of the externalizing factor to any adverse outcome.

Discussion

In a large, nationally representative sample, we found that psychiatric disorders were prospectively associated with a broad range of adverse outcomes assessed 3 years later. These associations were primarily mediated by a general psychopathology factor representing the shared effects across all psychiatric disorders, independent of socio-demographic characteristics, and the presence of the adverse

Table 3 Effects of sex, age, and race/ethnicity on the general psychopathology factor and adverse outcomes in the bifactor model

	GPF β (SE)	Divorced or separated β (SE)	Problems with neighbor β (SE)	Unemployment β (SE)	Financial crisis β (SE)	Income β (SE)	General health MCS β (SE)	PCS β (SE)	Violence β (SE)	Legal problems β (SE)
Age	-0.35 (0.02)	-0.03 (0.02)*	-0.07 (0.02)	-0.31 (0.02)	-0.21 (0.02)	-0.07 (0.01)	-0.20 (0.01)	-0.21 (0.01)	-0.33 (0.02)	-0.19 (0.02)
Men	-0.08 (0.02)	-0.04 (0.01)	-0.08 (0.02)	0.04 (0.01)	-0.05 (0.01)	0.10 (0.01)	-0.06 (0.01)	-0.01 (0.01)*	0.17 (0.02)	0.03 (0.01)
White	0.12 (0.01)	-0.04 (0.01)	0.03 (0.02)*	-0.08 (0.01)	-0.10 (0.01)	0.03 (0.01)	0.10 (0.01)	0.01 (0.01)	-0.03 (0.02)*	-0.04 (0.01)

Regression coefficients (β) are standardized. Results are significant (two-sided $p < 0.05$) unless indicated by the asterisk
SE standard error, MCS mental component summary score, PCS physical component summary score

outcomes at baseline. Violence and legal problems were further associated with the externalizing factor, but there were no independent associations of the internalizing factor or any individual psychiatric disorders with any of the adverse outcomes. Sensitivity analysis indicated that the results were generally robust to model specification, with small differences probably due to differences in parameterization and to the exclusion of most personality disorders from the fear–distress–externalizing model.

Although previous studies have shown that individual psychiatric disorders are associated with a broad range of adverse outcomes [1, 7, 9], our findings demonstrate that these associations are mostly mediated by a general liability to psychopathology rather than being specific to any single disorder. Our results help reconcile findings that both internalizing disorders (such as major depressive disorder) and externalizing disorders (such as substance use disorders) are associated with multiple adverse outcomes. These patterns, which are consistent with current dimensional models of psychopathology and highlight the role of comorbidity, replicate and extend prior analyses on the risk of suicide attempt [8]. The new results generalize to a wide of adverse outcomes associations of psychiatric disorders with a broad range of adverse outcomes through a common psychological factor. Shared genetic [31] and environmental influences [32] may contribute to this common psychological factor, whose underlying neurocircuitry is being actively pursued [33, 34]. It is also possible that the associations between psychopathology at Wave 1 and Wave 2 outcomes may be partially explained by shared genetic factors, given the substantial contribution of genetic influences to several of the adverse outcomes examined in the study [35, 36].

To our knowledge, this is the first study to examine prospectively differential associations of multiple outcomes across a broad range of psychiatric disorders. Although the general psychopathology factor was associated with all adverse outcomes, the strength of this association varied across outcomes. Furthermore, the externalizing factor was independently associated with violence and legal problems beyond the effect of the general psychopathology factor. These findings suggest that there is some specificity in the associations of psychopathological dimensions and adverse outcomes. The risk of adverse outcomes likely depends to different degrees on influences other than psychopathology. A previous analysis of the NESARC that established the validity of the bifactor model of psychopathology examined four validators (personal income, disability income, pain, and lifetime history of incarceration) [37]. It found large effects of the specific factors beyond the general factor, also suggesting specificity of associations between different psychopathological dimensions and adverse outcomes. Despite its valuable contribution, because this study

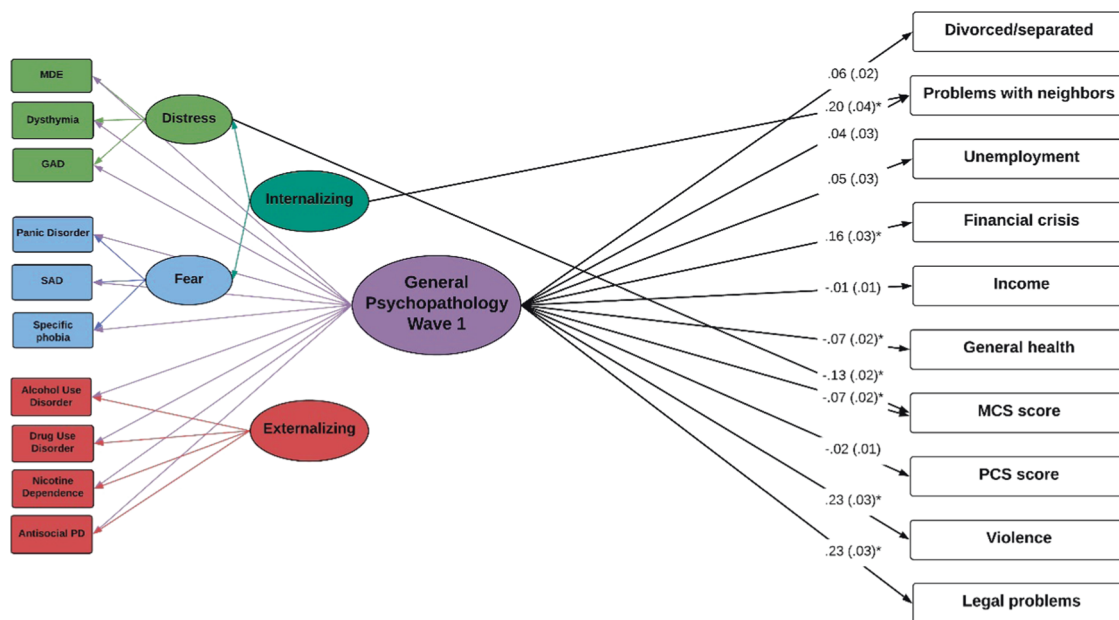


Fig. 2 Bifactor model with fear, distress, and externalizing factors testing the shared and specific effects of past-year Axis I disorders and antisocial personality disorder (assessed in Wave 1) on the occurrence

of adverse outcomes in Wave 2 of the National Epidemiological Survey on Alcohol and Related Conditions ($N = 34,653$)

combined current and lifetime outcomes and did not control for those outcomes at Wave 1, it did not assess the effects of psychopathology on the development of adverse outcomes.

The bivariate analyses showed a clear pattern of associations between all psychiatric disorders and adverse outcomes. Of the 180 ORs examined (18 disorders times 10 adverse outcomes), 166 (92.2%) were significantly above 1, which is greater than 18-fold the number of significant ORs ($180 \times 0.05 = 9$) that would be expected by chance. Even in the rare cases where some disorders, such as alcohol or drug use disorders were associated with decreased odds of some adverse outcomes (PCS of the SF-12), these disorders were associated with increased risks for most adverse outcomes. Consistent with this pattern, there were no direct effects of individual disorders on adverse outcomes in the bifactor model, indicating that after taking into account the presence of other disorders and the broader dimensions of psychopathology, all psychiatric disorders were consistently associated with the adverse outcomes examined in this study.

From the clinical and preventive perspective, the results highlight the central role of comorbidity in accounting for associations between psychiatric disorders and their adverse functional consequences and the limitations of examining individual disorders in isolation. The findings raise the possibility that transdiagnostic interventions [38], which are directed at broad psychopathological dimensions, may have greater effects than those directed at individual disorders. The results are also consistent with the observation that remission of one disorder decreases the risk of new onset or relapse of other disorders [39] and with evidence of

transdiagnostic biomarkers [40]. The recent identification of neurocircuitry associated with broad psychopathology factors is also consistent with the results and may suggest promising targets for therapeutic interventions [33, 34]. Linking transdiagnostic domains such as affect, cognition, and behavior and their underlying neurobiology with the adverse outcomes on which psychopathology exerts its strongest effects may also help identify novel therapeutic targets.

From the public health perspective, our findings suggest that studies which narrowly focus on disorder-specific outcomes may underestimate effects on functional outcomes. Some interventions may help to improve several functional domains in addition to the individual's symptoms. The study results further suggest that addressing public health crises as isolated disorder-specific events may be less fruitful than addressing their shared neurobiological or environmental causes.

Our findings should be interpreted in light of some limitations. First, although Wave 1 of the NESARC examined a wide range of Axis I and Axis II psychiatric disorders, several disorders, including psychotic disorders and borderline personality disorder, were not included. However, the structure of psychiatric disorders seems to be robust to the inclusion of a broad range of disorders as indicators [8]. Second, our list of adverse outcomes, although extensive and providing a consistent pattern of results, is not exhaustive. Third, despite its prospective design, because of the possibility of uncontrolled confounds, our study cannot establish causal relationships

between psychiatric disorders and adverse outcomes. Last, our study examined associations between psychiatric disorders and adverse events over a 3-year period and the pattern of associations may differ over different time intervals.

Despite these limitations, the results underscore that associations between psychiatric disorders and adverse outcomes occur primarily through broad psychological dimensions. Understanding the biological and psychological mechanisms underlying these dimensions should yield important intervention targets to decrease the individual suffering and societal burden of psychiatric disorders.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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