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Mental Disorders, Comorbidity and Suicidal Behavior:

Results from the National Comorbidity Survey Replication

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Abstract

Mental disorders are among the strongest predictors of suicide attempts. However, little is known about which disorders are uniquely associated with suicidal behavior due to high levels of psychiatric comorbidity. We examined the unique associations between individual disorders and subsequent suicidal behavior (suicide ideation, plans, and attempts) using data from the National Comorbidity Survey Replication, a nationally representative household survey of 9,282 US adults. Results revealed that approximately 80% of suicide attempters in the US have a temporally prior mental disorder. Anxiety, mood, impulse-control, and substance disorders all significantly predict subsequent suicide attempts in bivariate analyses (odds ratios=2.7-6.7); however, these associations decrease substantially in multivariate analyses controlling for comorbidity (odds ratios=1.5-2.3) but remain statistically significant in most cases.

Disaggregation of the observed effects reveals that depression predicts suicide ideation, but not suicide plans or attempts among those with ideation. Instead, disorders characterized by severe anxiety/agitation (e.g., PTSD) and poor impulse-control (e.g., conduct disorder, substance disorders) predict which suicide ideators go on to make a plan or attempt. These results advance understanding of the unique associations between mental disorders and different forms of suicidal behavior. Future research must further delineate the mechanisms through which people come to think about suicide and progress from suicidal thoughts to attempts.

INTRODUCTION

Suicide is among the leading causes of death worldwide.^{1,2} Although the etiology of suicide is not well-understood, numerous studies have shown that the presence of mental disorders is one of the strongest risk factors for suicide attempts and suicide deaths.^{3,4} Indeed, psychological autopsy studies suggest that more than 90% of people who die by suicide have a diagnosable mental disorder,⁵ with similar figures reported among clinical samples of suicide attempters.^{6,7}

Although it is clear that mental disorders in general are associated with suicidal behavior, research has not yet revealed which disorders uniquely predict these outcomes. This is because most studies have examined the associations between individual disorders and suicidal behavior.⁸⁻¹⁰ When examined in this way, virtually all mental disorders are associated with suicidal behavior.^{3,11-13} However, because mental disorders are highly comorbid,¹⁴ these bivariate associations could be due to the true effects of only a small number of disorders. As just one example, several early reports suggested that panic disorder predicts suicide attempts^{8,15} even after controlling for comorbid depression and substance abuse.^{15,16} However, follow-up studies have reported that the association of panic disorder with suicide attempts is no longer significant when controls are introduced for a broader range of comorbid disorders.¹⁷⁻¹⁹ Effects of comorbidity need to be taken into consideration in a more rigorous way to clarify the unique associations of mental disorders with suicidal behaviors. Knowledge of which disorders are uniquely predictive of suicidal behaviors, and how comorbidity contributes to these outcomes, is needed to better understand the mechanisms through which mental disorders lead to suicidal behaviors.

Another area of uncertainty is regarding what aspect of suicidal behavior mental disorders actually predict. Although decades of research have documented a strong association between mental disorders and suicide, several recent epidemiological studies suggest that mental disorders predict the onset of suicide ideation, but may have weaker effects in predicting suicide plans or attempts among people with suicide ideation.^{12,20} Family and genetic studies similarly have suggested that the the co-occurrence of suicide ideation within family members is explained by the presence of mental disorders, but that the tendency to act on suicidal thoughts is not, and instead may result of a distinct genetic component perhaps related to the presence of impulsive-aggressive traits.²¹⁻²³ Despite these recent findings, surprisingly little is known about what which mental disorders are uniquely related to suicide ideation, and which predict the progression to suicide attempts.

The current study was designed to address these limitations by carefully testing the associations between the presence of DSM-IV Axis I mental disorders and subsequent suicidal behavior in a nationally representative sample of the US household population. Axis II (i.e., personality) disorders and specific aspects of mental disorders, such as their severity and chronicity, also are likely to influence the occurrence of suicidal behavior; however, the current study focused specifically on the presence of Axis I disorders as an initial step toward better understanding how and why mental disorders predict subsequent suicidal behavior. This study extends prior research on this topic by simultaneously examining a wide range of DSM-IV Axis I disorders, by testing more complex statistical models of the effects of comorbidity than in previous studies, and by carefully decomposing the associations between mental disorders and suicide attempts.

MATERIALS AND METHODS

Sample

Data are from the National Comorbidity Survey-Replication (NCS-R), a nationally-representative face-to-face household survey of the US household population conducted between February 2001 and April 2003. The NCS-R used a multi-stage clustered area probability design to interview 9,282 English-speaking adults (18+ years-old) in order to assess the prevalence and correlates of *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV)*²⁴ mental disorders.²⁵ Interviewer contacts were preceded by an advance letter that explained the purposes of the study and included a toll-free telephone number for respondents who wanted more information or who wanted to opt out. Interviewers then visited the homes of designated respondents and answered remaining questions about participation before obtaining informed consent. Respondents were paid \$50 for participation. The NCS-R response rate was 70.9%. A probability sub-sample of initial non-respondents was asked to participate in a brief telephone non-respondent survey to check for systematic non-response bias. A \$100 incentive was offered for participation in this survey. Data in the main survey were weighted using a propensity score weight.²⁶ The university human subjects committee approved all procedures.

The NCS-R interview was administered in two parts. Part I included a core diagnostic assessment of DSM-IV mental disorders along with questions on suicidal behaviors administered to all 9,282 respondents. Part II included questions about correlates and additional disorders and was administered to a probability sub-sample of 5,692 Part I respondents that included 100% of those who met lifetime criteria for any Part I disorder and a probability sub-sample of other respondents. The Part II sample was weighted to adjust for differential probabilities of selection within households, over-sampling of Part I respondents with a mental disorder, systematic non-

response, and residual differences between the sample and the 2000 Census of the Population on a variety of socio-demographic and geographic variables. Further details about the weighting procedures used are presented elsewhere.²⁷

Measures

DSM-IV Mental Disorders. Mental disorders were assessed using the World Health Organization (WHO) Composite International Diagnostic Interview (CIDI) Version 3.0, a fully structured diagnostic interview administered by trained lay interviewers.²⁸ The 16 mental disorders included in our analysis were anxiety disorders (panic disorder, generalized anxiety disorder, phobias, posttraumatic stress disorder [PTSD], and separation anxiety disorder), mood disorders (major depressive disorder, dysthymic disorder, and bipolar disorder), impulse-control disorders (oppositional defiant disorder, conduct disorder, attention-deficit/hyperactivity disorder, and intermittent explosive disorder), and substance use disorders (alcohol and illicit drug abuse or dependence). A clinical reappraisal study revealed generally good concordance between CIDI diagnoses and those obtained using the research version of the Structured Clinical Interview for DSM-IV (SCID).^{29,30}

Suicidal behavior. Suicidal behaviors were assessed using the Suicidality Module of the CIDI.²⁸ This module includes an assessment of the lifetime occurrence and age-of-onset of suicide ideation, plans, and attempts. Consistent with our goal of examining relationships of mental disorders with a continuum of suicidal behaviors, we considered five dated lifetime history outcomes in a series of nested survival analyses (see below for analysis methods): (i) suicide ideation in the total sample; (ii) suicide attempt in the total sample; (iii) suicide plan among respondents with ideation; (iv) suicide attempt among those with a plan; and (v) suicide attempt among those with ideation in the absence of a plan (impulsive attempt).

Analysis methods

The prevalence of temporally prior mental disorders among respondents with each of the five outcomes was estimated using cross-tabulations. Temporal precedence of mental disorders was examined using individual-level retrospective age-of-onset reports. Predictive associations between temporally prior mental disorders and subsequent suicidal behaviors were estimated using discrete-time survival models with person-years as the unit of analysis.³¹ Mental disorders were treated as time-varying covariates in these models. Survival coefficients were exponentiated to generate odds-ratios (ORs) and their standard errors for ease of interpretation.

We estimated survival models that were bivariate (in which only one disorder was considered at a time) as well as multivariate (in which all disorders were considered simultaneously) in predicting each suicidal behavior. We also estimated a series of models that allowed for multiplicative interactions among comorbid disorders. Because 16 disorders were included in the analyses, the number of logically possible interactions ($2^{16}-17=65,519$) greatly exceeded the number of observations, which meant that we needed to impose some structure on the interactions in order to generate models with stable estimates. We began with a model that included summary dummy predictor variables for total number of comorbid disorders experienced by each respondent (e.g., separate dummy predictor variables to distinguish respondents with exactly two disorders, exactly three, . . . , etc.). This model assumed that interactions were constant across types of disorder and were influenced only by number of disorders (i.e., that the 120 ORs of the $16 \times 15 / 2$ logically possible two-way interactions could all be considered the same; that the 560 ORs of the $16 \times 15 \times 14 / 6$ logically possible three-way interactions could all be considered the same; etc.). More complex models were then estimated that allowed for separate interactions between each type of disorder and number of comorbid

disorders. The simple model that assumed constant interactions was a good approximation of the data, so we focused on that model in subsequent analyses. Population attributable risk proportions (PARPs) due to each disorder and to all disorders combined were then calculated based on the results of that simple interaction model. Standard errors of prevalence estimates and survival coefficients were estimated with the Taylor series method³² using SUDAAN software³³ to adjust for the weighting and clustering of the NCS-R sample design. Multivariate significance was evaluated with Wald χ^2 tests based on design-corrected coefficient variance–covariance matrices. All significance tests were evaluated using .05-level two-sided tests.

RESULTS

Prevalence of temporally prior disorders among those with suicidal behaviors

Approximately two-thirds (66.0%) of people who have seriously considered killing themselves report having a prior DSM-IV/CIDI disorder. History of mental disorders is even higher among respondents who go on to make a suicide plan (77.5%) and to make a suicide attempt (79.6%). History of mental disorders is higher among respondents who make a planned attempt (83.4%) compared to an unplanned attempt (74.1%), suggesting that the latter may be influenced to a greater extent by other factors such as stressful life events (more detailed results reported by each disorder and suicidal behavior are available on request).

Associations of temporally primary DSM-IV/CIDI disorders with suicide attempts

Bivariate survival models show that each of the 16 lifetime DSM-IV/CIDI disorders examined is significantly associated with increased risk of the subsequent first onset of a suicide attempt, with ORs from a low of 2.7 (agoraphobia) to a high of 6.7 (bipolar disorder). (**Table 1**) The inter-quartile range (IQR) of the ORs is 4.1-4.9. The bivariate ORs associated with broad classes of disorder are similar to each other: 4.6 for any anxiety disorder; 5.2 for any mood

disorder; 4.8 for any impulse-control disorder; and 4.8 for any substance use disorder. The bivariate OR associated with having any disorder is even higher (7.0).

As expected, the ORs all become much smaller in an additive multivariate model (IQR decreases to 1.3-1.9), although 14 of the 16 ORs remain greater than 1.0 and 10 are statistically significant. Next, a simple interactive multivariate model was estimated that included one dummy variable for each of the 16 disorders plus additional dummy variables for each number of disorders (e.g., exactly one prior disorder, exactly two, etc.). The ORs for individual disorders in this model can be interpreted as the relative-odds of a subsequent suicide attempt among respondents with a history of a pure disorder (i.e., only this one disorder) versus those with no disorders. Similar to the additive multivariate model, a number of pure disorders have statistically significant ORs that are comparable in magnitude (ORs=1.5-2.3; IQR=1.4-1.9) with all 16 ORs greater than 1.0 and 10 statistically significant.

Associations of number of comorbid disorders with suicide attempts

Next, we examined the association between comorbidity and suicide attempts in isolation by estimating a model in which the only substantive predictors were dummy variables for number of disorders temporally prior to the first suicide attempt. A strong positive association was found, with ORs increasing from 3.7 for any one disorder, 6.8 for two, 12.1 for three, up through 29.0 for six or more (compared to respondents with no disorders). (**Table 2**) However, the ORs associated with having a large number (five or more) of disorders either do not increase, or increase at a decreasing rate, compared to the ORs associated with fewer disorders. As a result, the ORs for high numbers of disorders in a more elaborate model that also included predictors for the 16 types of disorders (i.e., as in Table 1) are lower than 1.0, indicating the existence of sub-additive effects of comorbidities involving large numbers of disorders. In other

words, as the number of comorbid disorders increase, the relative-odds of a suicide attempt increase at a decreasing rate.

As noted above, the model that included as predictors both 16 dummy variables for types of disorder and dummy variables for number of disorders implicitly assumes that interactions are identical for all comorbid profiles involving the same number of disorders. We evaluated more elaborate models that considered distinct interactions for specific disorders with numbers of other disorders, but these models did not improve appreciably over the simpler interactive model (more detailed results are available on request). As a result, we based our subsequent analysis of intermediate outcomes (i.e., suicide ideation and plans) on the simple interactive model.

Interactive associations of comorbid disorders with intermediate outcomes

To disaggregate the observed effects and examine whether the association between mental disorders and suicide attempts is explained by the intermediate outcomes of suicide ideation and plan, we estimated models predicting each of the five suicidal behaviors studied. **(Table 3)** Examining the model coefficients in parallel, we see that the most powerful and consistent associations are with suicide ideation (15 of the 16 ORs positive, 11 statistically significant, IQR=1.3-1.8). Conditional associations with suicide plans among ideators are both less consistent and less powerful (11 of the 16 ORs positive, only 2 statistically significant, IQR=1.0-1.2). Conditional associations with planned attempts (14 of the 16 ORs positive, 5 statistically significant, IQR=1.2-1.6) and unplanned attempts (12 of the 16 ORs positive, 4 statistically significant, IQR=1.1-1.9) are intermediate in strength and consistency.

As in the model predicting suicide attempts in the total sample, ORs significantly less than 1.0 exist for comorbidities involving large numbers of disorders in predicting suicide ideation and planned attempts. These sub-additive comorbidities involving large numbers of

disorders are not found in predicting plans among ideators, where ORs for number of disorders are all close to 1.0. This suggests that the multivariate effects of comorbid disorders are additive. A non-significant trend pattern of sub-additive coefficients for high comorbidity is found in predicting unplanned attempts.

Examination of the associations between individual disorders and each suicidal behavior reveals that although major depression is among the strongest predictors of suicide ideation (OR=2.3), it does not significantly predict suicide plans or attempts among ideators (ORs=1.0-1.3). Instead, suicide plans and attempts are predicted by anxiety, impulse-control, and substance use disorders. The ORs for these disorders are generally stronger for unplanned (i.e., impulsive) suicide attempts (ORs=2.1-2.9) than for the occurrence of suicide plans or planned attempts among ideators (ORs=1.6-1.9).

Population attributable risk proportions

The results presented above focus on ORs describing individual-level associations without taking into consideration either the prevalence of the predictors or the distribution of comorbidity. We calculated population attributable risk proportions (PARPs) to examine these population-level effects. PARPs represent the proportion of observed cases of the outcome that would be prevented if specific predictor variables could be prevented based on the assumption that the ORs in the model accurately represent causal effects of the predictors. The PARP estimates show even more clearly than the ORs that the predictive effects of the disorders considered here on suicide attempts are largely due to effects on ideation rather than on the transitions from ideation to plans or attempts.

Focusing first on PARPs for all disorders combined, we estimate that roughly three-fourths (76.5%) of all suicide attempts are associated with prior DSM-IV/CIDI disorders.

However, this strong aggregate association is due largely to the prediction of suicide ideation (78.9%), with much smaller PARPs of disorders predicting the onset of a suicide plan among ideators (10.5%), attempts among ideators with a plan (25.4%), and attempts among ideators without a plan (36.9%). **(Table 4)** Mood and anxiety disorders play the largest roles in accounting for the onset of ideation, whereas anxiety disorders play the largest roles in accounting for attempts both among ideators with and without a plan.

DISCUSSION

Three important limitations should be borne in mind when interpreting these results. First, the NCS-R data are based on retrospective self-reports of the occurrence and timing of mental disorders and suicidal behavior and so these reports may be subject to systematic recall bias.³⁴ On balance, systematic reviews have suggested that people can recall past experiences with sufficient accuracy to provide valuable information³⁵ and that retrospective data are especially useful when, as in the current case, prospective data are not available.³⁶ Nonetheless, it is important to be cautious in interpreting the results because recall bias almost certainly exists to some extent in the retrospective reports used to generate the data. Second, although the NCS-R examined a wide range of mental disorders, several disorders known to be linked to suicidal behaviors were not included, most notably nonaffective psychosis and personality disorders. Third, we did not examine the severity or chronicity of each disorder, which might have led to an underestimation in the strength of the associations between disorders and suicidal behavior.

These limitations notwithstanding, these results advance our understanding of suicidal behavior in several important ways. Our study extends findings from psychological autopsy studies that people who die by suicide have very high rates of mental disorders⁵ and the consistent finding of similarly high rates of mental disorders among suicide attempters in clinical

settings.^{6,7} These results suggest that in the general population, the rate of temporally prior mental disorders, while elevated among people with each suicidal behavior, is slightly lower than in psychological autopsy studies and studies of clinical samples.

The elevated rates of prior mental disorders among people with suicidal behavior are most pronounced for suicide ideators compared to people who never considered suicide. Importantly, differences in rates of prior mental disorders between ideators who did versus did not make a plan or attempt are much more modest. This pattern of results is consistent across each disorder. These results indicate that although the presence of mental disorders predict the onset of suicidal ideation, they are less useful in determining which people with suicide ideation will make a suicide attempt.

The finding that every mental disorder measured predicts suicide attempts in bivariate analyses replicates results from prior studies.^{11,12,20} Our multivariate analysis showed that the incremental predictive effects of individual disorders are much less powerful and that a general pattern of sub-additive interactive effects exists for comorbidities involving a large number of disorders. One possible explanation for this pattern is that some disorders are correlated with suicide attempts because they are comorbid with disorders that are independently associated with suicide attempts. In the current study, the disorders with the lowest ORs in multivariate analyses were generalized anxiety disorder, social phobia, agoraphobia, separation anxiety disorder, and dysthymia—all of which are strongly comorbid with major depression.^{37,38} These disorders also were among those showing the largest decay in their association with suicide attempts in the presence of comorbid disorders, suggesting they are not uniquely associated with suicide attempts. Interestingly, the significant bivariate association between panic disorder and subsequent suicide attempts, although decreased substantially in multivariate analyses, continued

to be statistically significant and substantial in magnitude (OR=1.9), arguing for a middle ground in the long-standing debate as to whether panic disorder is⁸ or is not¹⁷ uniquely related to suicide attempts. These results suggest that future studies should consider the effects of comorbid disorders when examining predictive effects of mental disorders on suicide attempts.

Another plausible interpretation of this pattern is that much of the association between mental disorders and suicide attempts is explained by some factor common to most disorders, such as the experience of distress or impairment. Such an interpretation is consistent with an escape model of suicide, which suggests that people attempt suicide in an effort to escape intolerable distress regardless of the specific source of that distress.^{39,40} Such a model also may help explain the strong dose-response relationship observed between number of disorders and risk of subsequent suicide attempt. The presence of multiple disorders (i.e., multimorbidity³⁸) is associated with higher levels of distress, impairment, and disease burden,^{38,41} and these factors may be intolerable for some people when they occur at high levels. Taken together, these findings highlight one potential pathway through which mental disorders may lead to suicidal behaviors and provide a point of departure for future studies aimed at expanding our understanding of this pathway.

The unique relations that emerged between specific disorders and the progression to suicide attempts are especially noteworthy. Results suggest that the onset of suicide ideation is best predicted by depression, but depression does not predict further progression to suicide attempt. Instead, disorders characterized by anxiety/agitation (e.g., PTSD) and poor impulse-control (e.g., bipolar disorder, conduct disorder, substance disorders) emerged as the strongest predictors of which ideators make suicide plans and attempts. These results synthesize earlier findings on the association of depression,⁹ anxiety,⁴² and impulse-control disorders^{12,42,43} with

suicide attempts and suggest that some disorders may elevate suicide risk by increasing the desire for death or suicide, while others characterized by impulsiveness and poor behavioral control may elevate risk by increasing the likelihood of acting on suicidal thoughts.^{21-23,42-45}

Studies examining genetic, biological, and other risk factors for suicide should carefully consider which form of suicidal behavior is being examined in a given study, as these findings suggest that associations are likely to differ when predicting suicide ideation versus suicide attempts.

Taken together, these results underscore the importance of carefully considering comorbidity in the study of suicidal behavior, illuminate the ways in which different types of mental disorders may contribute to the risk of suicidal behavior, and point toward modifiable targets for decreasing the morbidity and mortality associated with suicidal behavior.

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Additional information: A complete list of NCS publications and the full text of all NCS-R instruments can be found at <http://www.hcp.med.harvard.edu/ncs>. Send correspondence to ncs@hcp.med.harvard.edu.

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