# Anxiety Disorders and Risk for Suicidal Ideation and Suicide Attempts

## *A Population-Based Longitudinal Study of Adults*

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**Context:** Controversy exists whether anxiety disorders are independently associated (ie, after adjusting for comorbid mental disorders) with suicidal ideation and suicide attempts.

**Objective:** To examine whether anxiety disorders are risk factors for suicidal ideation and suicide attempts in a large population-based longitudinal study.

**Methods:** Data come from the Netherlands Mental Health Survey and Incidence Study, a prospective population-based survey with a baseline and 2 follow-up assessments over a 3-year period. The Composite International Diagnostic Interview was used to assess *DSM-III-R* mental disorders. Lifetime diagnoses of anxiety disorders (social phobia, simple phobia, generalized anxiety disorder, panic disorder, agoraphobia, obsessive-compulsive disorder) were assessed at baseline. Multiple logistic regression analyses were used to examine whether anxiety disorders were associated with suicidal ideation and attempts at baseline (n = 7076) and whether anxiety disorders were risk factors for subsequent onset of suicidal ideation and attempts (n = 4796).

**Results:** After adjusting for sociodemographic factors and all other mental disorders assessed in the survey, base-line presence of any anxiety disorder was significantly associated with suicidal ideation and suicide attempts in both the cross-sectional analysis (adjusted odds ratio for suicidal ideation, 2.29; 95% confidence interval, 1.85-2.82; adjusted odds ratio for suicidal attempts, 2.48; 95% confidence interval, 1.70-3.62) and longitudinal analysis (adjusted odds ratio for suicidal ideation, 2.32; 95% confidence interval, 1.31-4.11; adjusted odds ratio for suicide attempts, 3.64; 95% confidence interval, 1.70-7.83). Further analyses demonstrated that the presence of any anxiety disorder in combination with a mood disorder was associated with a higher likelihood of suicide attempts in comparison with a mood disorder alone.

**Conclusions:** This is the first study to demonstrate that a preexisting anxiety disorder is an independent risk factor for subsequent onset of suicidal ideation and attempts. Moreover, the data clearly demonstrate that comorbid anxiety disorders amplify the risk of suicide attempts in persons with mood disorders. Clinicians and policymakers need to be aware of these findings, and further research is required to delineate whether treatment of anxiety disorders reduces the risk of subsequent suicidal behavior.

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S UICIDAL IDEATION (SI) AND suicide attempts (SAs) are highly prevalent in the community (11%-14% and 2.8%-4.6%, respectively)[1,2] and are strong risk factors for completed suicide.[3] Psychological autopsy studies have demonstrated that the majority of suicides occur on the individual's first SA.[3,4] Thus, it is highly important to understand risk factors for suicidal behavior and intervene prior to the individual making the first SA. A well-established risk factor for suicidal behavior is the presence of mental disorders, especially mood disorders,[1,5,6] substance use disorders,[7] and schizophrenia.[8,9]

Although there has been significant interest in whether anxiety disorders are risk factors for suicidal behavior, this remains a controversial area.[1,10-12] Cross-sectional community[1,13-15] and clinical studies[10,16-24] have repeatedly demonstrated in univariate models that anxiety disorders are associated with SI, SAs, and completed suicides. Among the anxiety disorders, panic disorder has received the greatest attention. In multivariate models, it has been questioned whether panic disorder is associated with suicidal behavior after adjusting for other anxiety disorders and other mental disorders.[18,23,25-28] Because anxiety disorders are highly comorbid with other anxiety disorders and tend to clus-

ter together,[29,30] we suggest that it is important to address whether anxiety disorders as a group of mental disorders have an impact on suicidal behavior after adjusting for other types of mental disorders (especially mood and substance use disorders). To date, none of the published studies using large community samples on anxiety disorders and suicidal behavior have examined whether anxiety disorders as a group, after adjusting for other mental disorders, are associated with suicidal behavior.

An even more important limitation of the literature on this topic is that most studies, with the exception of a few,[23,31] have used cross-sectional, retrospective data. Such retrospective reports have been criticized for the lack of temporal information on whether anxiety disorders preceded the onset of suicidal behavior[24] among those with comorbidity. Prospective longitudinal evaluation of whether anxiety disorders are risk factors for new-onset suicidal behavior is required.

The current study addresses whether anxiety disorders have a significant impact on suicidal behavior using data from the Netherlands Mental Health and Incidence Survey (NEMESIS),[32,33] a large, Dutch, general population survey. We examined the impact of anxiety disorders on suicidal behavior in 2 stages. First, we estimated whether the presence of lifetime anxiety disorder diagnoses had a cross-sectional association with lifetime suicidal behavior at baseline assessment. Second, we examined whether anxiety disorders at baseline had a significant impact on first-ever incidence of SI and SAs at follow-up assessments. To the best of our knowledge, this represents the first prospective examination of whether anxiety disorders predict subsequent onset of suicidal behavior in a large population-based sample.

## METHODS

### BASELINE AND FOLLOW-UP SAMPLES

The NEMESIS[32-34] is a population-based study with repeated measurements among the same respondents. A stratified, random sampling procedure was used. First, a sample was drawn from 90 Dutch municipalities stratified by urbanicity and a sufficient distribution over the 12 provinces of the Netherlands. Post office records were used to draw a sample of private households (addresses). The number of households selected in each municipality was in proportion to its population. One respondent in each household was selected randomly, according to whose birthday was most recent, on the condition that he or she was between 18 and 64 years of age and sufficiently fluent in Dutch. To maximize the response rate and to compensate for any seasonal influences, the initial data collection phase was spread over the entire period from February to December 1996.

At baseline, a total of 7076 people (response rate of 69.7%) were interviewed and are referred to as the baseline sample. Two follow-up assessments were conducted, once at 1 year after the baseline and once at 3 years after the baseline. Of the 7076 participants at baseline, 5618 respondents were available for reinterview at the first follow-up assessment and 4848 respondents at the second follow-up assessment. A total of 4796 respondents had valid information at all 3 assessments. Previous analysis[35] of the NEMESIS data has demonstrated that the presence of a *DSM-III-R* mental disorder was only a modest predictor of attrition in this sample.

## MEASURES

### Mental Disorders

The *DSM-III-R*[36] Axis I mental disorders were diagnosed with version 1.1 of the Composite International Diagnostic Interview (CIDI).[37] A computerized version of the CIDI was used for all waves of the NEMESIS. The CIDI is a structured interview developed by the World Health Organization, based on the Diagnostic Interview Schedule and the Present State Examination, and administered by trained interviewers.[38] The CIDI has documented reliability and validity for all mental disorders examined in the current survey.[38-40]

Lifetime *DSM-III-R* diagnoses were assessed at baseline. The individual anxiety disorders included in the analysis were obsessive-compulsive disorder (OCD), generalized anxiety disorder (GAD), simple phobia, social phobia, agoraphobia, and panic disorder. The anxiety disorder diagnoses assessed in this survey were highly reliable based on previous methodological studies of the CIDI.[40] A variable that measured the presence of any anxiety disorder was also created. As well, having any lifetime mood disorder (major depression, bipolar disorder, and dysthymia) measured at baseline was also included in the analysis. Other mental disorders assessed in the survey included lifetime alcohol abuse or dependence, drug abuse or dependence, eating disorders (bulimia, anorexia), and schizophrenia. All respondents who screened positive on the psychosis subsection of the CIDI in this survey were reinterviewed by a trained clinician to diagnose the presence or absence of psychosis. Based on this clinical reappraisal, the lifetime prevalence of schizophrenia in the NEMESIS was 0.4%.[32,41,42]

### Suicidality

Items from the CIDI questionnaire were used to measure SI and SAs and were the same questions used in the Epidemiologic Catchment Area survey[13] and the US National Comorbidity Survey (NCS).[1] At baseline, SI was assessed by the following question: "Have your ever felt so low you thought about committing suicide?" Similarly, the presence of at least 1 lifetime SA was measured using a question that asked, "Have you ever attempted suicide?" At the 2 follow-up assessments, the same questions were repeated with the time frame limited to the intervening period between assessments.

Prevalence of lifetime SI and SAs at baseline assessment (n=7076) was 11.1% and 2.7%, respectively. The first-ever incidence of SI was defined when a person did not report SI or SAs at baseline but endorsed SI at either follow-up period. At the first and second follow-up periods, there were 41 and 44 new cases of SI, respectively. Thus, the total number of new cases of SI at either follow-up assessment was 85 (2.0% of the sample at risk, n=4246).

Similarly, the first-ever incidence of an SA was defined when a person did not report an SA at baseline but endorsed making an SA at either follow-up period. We included individuals endorsing SI at baseline in the sample at risk for the SA analysis. At the first and second follow-up periods, there were 24 and 15 new cases of SAs, respectively. Thus, the total number of new cases of SAs at either follow-up was 39 (0.8% of the sample at risk, n=4670).

### SOCIODEMOGRAPHIC VARIABLES

Age was measured in number of years and was used as a continuous variable in the analyses. Education was measured by highest level of attainment as indicated by 3 categories: primary/lower vocational, secondary/middle vocational, higher voca-

| Anxiety Disorder at Baseline | Suicidal Ideation and Suicide Attempts at Baseline | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | No Suicidal Ideation (n = 6265), No. (%)* | Suicidal Ideation (n = 809), No. (%) | OR (95% CI) | AOR-1 (95% CI)† | AOR-2 (95% CI)‡ | No Suicide Attempts (n = 6868), No. (%) | Suicide Attempts (n = 205), No. (%) | OR (95% CI) | AOR-1 (95% CI) | AOR-2 (95% CI) |
| Social phobia | 371 (5.6) | 204 (25.0) | 5.57 (4.56-6.81)§ | 2.01 (1.54-2.64)§ | 1.56 (1.16-2.10)‖ | 515 (7.2) | 60 (27.7) | 4.92 (3.53-6.86)§ | 1.16 (0.75-1.80) | 0.74 (0.45-1.23) |
| Simple phobia | 529 (8.2) | 205 (25.0) | 3.74 (3.09-4.53)§ | 1.57 (1.22-2.02)§ | 1.20 (0.91-1.59) | 660 (9.3) | 74 (36.4) | 5.55 (4.06-7.59)§ | 1.94 (1.33-2.83)§ | 1.79 (1.20-2.68)‖ |
| Generalized anxiety disorder | 234 (3.5) | 170 (20.0) | 7.01 (5.60-8.78)§ | 1.96 (1.45-2.64)§ | 1.59 (1.16-2.19)‖ | 355 (4.8) | 49 (22.7) | 5.87 (4.12-8.35)§ | 1.33 (0.86-2.05) | 1.07 (0.67-1.70) |
| Obsessive-compulsive disorder | 27 (0.4) | 34 (4.5) | 10.57 (6.21-18.00)§ | 3.09 (1.42-6.72)§ | 2.12 (0.99-4.55) | 48 (0.7) | 13 (6.7) | 10.01 (5.17-19.39)§ | 2.01 (0.88-4.62) | 1.63 (0.69-3.88) |
| Panic disorder | 159 (2.3) | 127 (15.7) | 7.85 (6.07-10.16)§ | 2.73 (1.96-3.80)§ | 2.23 (1.56-3.20)§ | 245 (3.3) | 41 (20.6) | 7.62 (5.20-11.16)§ | 1.91 (1.20-3.05)‖ | 2.01 (1.23-3.28)‖ |
| Agoraphobia without panic | 179 (2.6) | 78 (9.4) | 3.87 (2.88-5.20)§ | 1.64 (1.12-2.41)‖ | 1.52 (1.01-2.28)¶ | 228 (3.1) | 29 (13.8) | 5.04 (3.19-7.96)§ | 1.97 (1.12-3.47)‖ | 2.12 (1.16-3.86)‖ |
| Any anxiety disorder | 1077 (16.5) | 429 (52.4) | 5.57 (4.74-6.55)§ | 2.29 (1.85-2.82)§ | NA | 1375 (19.2) | 131 (64.1) | 7.49 (5.50-10.20)§ | 2.48 (1.70-3.62)§ | NA |

Abbreviations: AOR, adjusted odds ratio; CI, confidence interval; OR, odds ratio (unadjusted); NA, not applicable.

*All numbers were unweighted, and all percentages were weighted.

†AOR-1 indicates adjustments for age, sex, education, marital status, urban/rural status, major depression, bipolar disorder, dysthymia, eating disorder, alcohol use disorder, drug use disorder, and schizophrenia (each diagnosis was entered separately in the same regression).

‡AOR-2 indicates adjustments for all variables in AOR-1 and simultaneous adjustments for each of the other anxiety disorders.

§*P*<.001.

‖*P*<.01.

¶*P*<.05.

tional/academic. Marital status was divided into 4 categories: never married, married/common-law, widowed, or separated/divorced. Urbanicity was dichotomized into 2 categories: municipalities with fewer than 500 addresses per square kilometer[2] were considered rural, and larger municipalities were considered urban.

## STATISTICAL ANALYSIS

In all analyses, the appropriate statistical weight was used to ensure the data were representative of the national population. Standard errors were calculated by using the Taylor series linearization method in the SUDAAN program.[43]

First, we examined the relationship between anxiety disorders and SI and SAs in the baseline sample (ie, cross-sectional analysis). Second, among the subsamples at risk, we examined whether lifetime anxiety disorder diagnosis at baseline was associated with subsequent onset SI and SAs (at either follow-up time period). We conducted 3 sets of regressions: unadjusted; adjusted for sociodemographics and other mental disorders; and adjusted for sociodemographics, other mental disorders, and each of the other anxiety disorders. It is important to underscore that we used the more stringent approach of adjusting for comorbidity in aggregate (similar to Hornig and McNally[26] and Vickers and McNally[25]), where we simultaneously entered the presence or absence of each of the following lifetime *DSM-III-R* mental disorders in the same regression: major depression, bipolar disorder, dysthymia, eating disorder, alcohol abuse or dependence, drug abuse or dependence, and schizophrenia.

We also examined whether stratification by mood disorder affected the relationship between anxiety disorders and suicide variables. We stratified the sample into 4 groups based on lifetime diagnoses at baseline: (1) both anxiety disorder and mood disorder, (2) anxiety disorder only, (3) mood disorder only, and (4) neither mood disorder nor anxiety disorder. Using multiple logistic regression, we calculated the odds of SI and SAs for each of the first 3 groups with reference to the group with neither anxiety nor mood disorder. Next, we compared respondents with a lifetime mood disorder only with those with lifetime mood and anxiety disorders on suicide variables. All analyses were conducted unadjusted and then adjusted for sociodemographic variables and other mental disorders at baseline (alcohol use disorders, drug use disorders, eating disorders, schizophrenia).

## RESULTS

### CROSS-SECTIONAL ANALYSIS OF ANXIETY DISORDERS AND SUICIDE VARIABLES AT BASELINE

It is noteworthy that, among all respondents with SI at baseline, 52.4% had at least 1 anxiety disorder (**Table 1**). Similarly, among all respondents reporting SAs at baseline, 64.1% had at least 1 anxiety disorder. After adjusting for sociodemographics and mental disorders assessed in the survey, the presence of at least 1 anxiety disorder diagnosis at baseline was significantly associated with lifetime SI and SAs at baseline. Examination of specific anxiety disorders (Table 1) demonstrated that each lifetime anxiety disorder was strongly associated with lifetime SI (odds ratio, 3.74-10.57) and lifetime SAs (odds ratio, 4.92-10.01). For lifetime SI, when adjusting for sociodemographic factors and other mental disorders and simultaneously adjusting for each of the other anxiety disorders, all of the anxiety disorders (except simple phobia and OCD) remained significantly associated with SI. A slightly different pattern was found for lifetime SAs at baseline. In multivariate analyses, we found that panic disorder, agoraphobia without panic and simple phobia (not OCD, GAD, or social phobia) were significantly associated with lifetime SAs, even after adjusting for other mental disorders and sociodemographic variables.

| | New-Onset Suicidal Ideation and Suicide Attempts at Follow-up Assessments | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Anxiety Disorder at Baseline** | **No Suicidal Ideation (n = 4161), No. (%)\*** | **Suicidal Ideation (n = 85), No. (%)** | **OR (95% CI)** | **AOR-1 (95% CI)†** | **AOR-2 (95% CI)‡** | **No Suicide Attempts (n = 4631), No. (%)** | **Suicide Attempts (n = 39), No. (%)** | **OR (95% CI)** | **AOR-1 (95% CI)** | **AOR-2 (95% CI)** |
| Social phobia | 217 (5.0) | 13 (16.7) | 3.87 (2.01-7.44)§ | 2.73 (1.40-5.30)‖ | 2.55 (1.20-5.39)‖ | 317 (6.6) | 7 (22.5) | 3.95 (1.58-9.82)‖ | 1.78 (0.61-5.15) | 1.27 (0.41-4.00) |
| Simple phobia | 335 (7.8) | 12 (15.5) | 2.08 (1.06-4.09)¶ | 1.43 (0.71-2.85) | 1.10 (0.53-2.28) | 428 (9.0) | 11 (30.8) | 4.71 (2.19-10.10)§ | 2.87 (1.15-7.16)‖ | 2.71 (1.07-6.6.87)¶ |
| Generalized anxiety disorder | 144 (3.2) | 9 (12.0) | 4.23 (1.96-9.16)§ | 2.48 (1.02-6.06)¶ | 2.71 (1.09-6.72)‖ | 227 (4.5) | 7 (20.5) | 5.24 (2.10-13.06)§ | 2.35 (0.78-7.10) | 2.30 (0.64-8.25) |
| Obsessive-compulsive disorder | 16 (0.4) | 3 (3.6) | 9.63 (2.70-34.37)§ | 6.52 (1.26-33.86)‖ | 6.33 (1.11-35.96)‖ | 29 (0.6) | 2 (5.1) | 7.99 (1.82-35.16)‖ | 1.93 (0.14-26.06) | 1.57 (0.15-16.33) |
| Panic disorder | 104 (2.3) | 3 (2.4) | 1.15 (0.35-3.78) | 0.57 (0.16-2.13) | 0.31 (0.07-1.35) | 166 (3.3) | 4 (10.3) | 3.11 (1.08-8.98)¶ | 1.10 (0.26-4.66) | 0.64 (0.09-4.36) |
| Agoraphobia without panic | 112 (2.4) | 5 (4.8) | 1.94 (0.73-5.12) | 1.13 (0.36-3.51) | 0.92 (0.31-2.77) | 145 (2.8) | 4 (7.7) | 3.02 (1.04-8.72)¶ | 1.75 (0.55-5.60) | 1.22 (0.29-5.20) |
| Any anxiety disorder | 678 (15.6) | 31 (36.9) | 3.13 (1.95-5.02)§ | 2.32 (1.31-4.11)‖ | NA | 889 (18.4) | 21 (55.0) | 5.49 (2.82-10.67)§ | 3.64 (1.70-7.83)‖ | NA |

Abbreviations: AOR, adjusted odds ratio; CI, confidence interval; OR, odds ratio (unadjusted); NA, not applicable.

\*All numbers were unweighted, and all percentages were weighted.

†AOR-1 indicates adjustments for age, sex, education, marital status, urban/rural status, major depression, bipolar disorder, dysthymia, eating disorder, alcohol use disorder, drug use disorder, and schizophrenia (each diagnosis was entered separately in the same regression).

‡AOR-2 indicates adjustments for all variables in AOR-1 and simultaneous adjustments for each of the other anxiety disorders.

§$P<.001$.

‖$P<.01$.

¶$P<.05$.

## IMPACT OF BASELINE ANXIETY DISORDER ON FIRST-EVER INCIDENCE OF SUICIDE VARIABLES

**Table 2** demonstrates that, similar to the pattern found in the cross-sectional analysis, the presence of an anxiety disorder at baseline was significantly associated with first-ever incidence of SI and SAs in multivariate models. Among those respondents with first-ever incidence of SAs, 55.0% had at least 1 anxiety disorder at baseline. Similarly, among those respondents with first-ever incidence of SI, 37% had at least 1 anxiety disorder at baseline. The impact of specific anxiety disorders on first-ever incidence of SI and SAs is also illustrated in Table 2. After adjusting for other mental disorders and sociodemographic variables, social phobia, GAD, and OCD remained associated with first-ever incidence of SI. In addition, when adjusting for all the mental disorders and each of the other anxiety disorders, social phobia, GAD, and OCD remained significantly associated with first-ever incidence of SI. In multivariate models, baseline simple phobia was the only anxiety disorder diagnosis that remained significantly associated with first-ever incidence of an SA.

## CROSS-SECTIONAL ANALYSIS OF ANXIETY DISORDERS AND SUICIDE VARIABLES STRATIFIED BY MOOD DISORDER

**Table 3** demonstrates that stratification by presence of mood disorder affected the relationship between anxiety disorders and suicide variables. Importantly, the respondents with 1 or more lifetime anxiety disorders at baseline who had never met criteria for a mood disorder remained at significantly higher risk of lifetime SI (adjusted odds ratio [AOR], 3.26) and SAs (AOR, 3.63), even after adjusting for comorbid mental disorders (alcohol or drug use disorders, eating disorders, and schizophrenia) and sociodemographic factors. Although individuals with mood disorders without anxiety disorders had higher odds of SI and SAs than persons without mood disorders, respondents meeting criteria for both a mood and an anxiety disorder had substantially increased odds of SI (AOR, 17.60) and SAs (AOR, 16.96) compared with persons with neither.

We further analyzed whether the presence of an anxiety disorder in combination with a mood disorder elevated the risk of suicidal behavior in comparison with those with a mood disorder alone. Compared with the mood disorder without anxiety disorder group, we found a significantly elevated risk of SI and SAs in those with both a mood and anxiety disorder. These findings remained significant (SI AOR, 1.86; SA AOR, 2.17) after adjusting for sociodemographic factors and other mental disorders (schizophrenia, eating disorders, and substance use disorders).

## IMPACT OF BASELINE ANXIETY DISORDER ON FIRST-EVER INCIDENCE OF SUICIDE VARIABLES STRATIFIED BY MOOD DISORDER

Compared with individuals with neither mood nor anxiety disorders at baseline, the presence of an anxiety disorder, with or without a mood disorder, was associated with substantially higher likelihood of first-ever SI (AOR, 3.34) and SA (AOR, 3.24) (**Table 4**). These findings re-

**Table 3. Cross-sectional Analysis Relationship Between Anxiety Disorders and Suicide Variables Stratified by Mood Disorder in the Baseline Sample**

| Disorders at Baseline | Suicidal Ideation and Suicide Attempts at Baseline | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | No Suicidal Ideation (n = 6265), No. (%)* | Suicidal Ideation (n = 809), No. (%) | OR (95% CI) | AOR-1 (95% CI)† | No Suicide Attempts (n = 6868), No. (%) | Suicide Attempts (n = 205), No. (%) | OR (95%CI) | AOR-1 (95% CI) |
| Neither anxiety disorder nor mood disorder | 4705 (76.4) | 179 (23.6) | 1.00 | 1.00 | 4852 (72.1) | 32 (16.5) | 1.00 | 1.00 |
| Anxiety disorder only | 646 (10.0) | 85 (10.7) | 3.46 (2.60-4.59)‡ | 3.26 (2.42-4.40)‡ | 708 (10.1) | 23 (9.8) | 4.34 (2.48-7.61)‡ | 3.63 (2.05-6.43)‡ |
| Mood disorder only | 483 (7.1) | 201 (24.1) | 10.97 (8.67-13.88)‡ | 9.56 (7.45-12.28)‡ | 641 (8.7) | 42 (19.6) | 9.80 (5.98-16.05)‡ | 7.62 (4.48-12.99)‡ |
| Anxiety and mood disorder | 431 (6.5) | 344 (41.7) | 20.91 (16.81-26.01)‡ | 17.60 (13.90-22.29)‡ | 667 (9.1) | 108 (54.1) | 25.89 (16.94-39.58)‡ | 16.96 (10.84-26.54)‡ |
| Anxiety and mood disorder (reference group: mood disorder only) | NA | NA | 1.91 (1.52-2.38)‡ | 1.86 (1.47-2.36)‡ | NA | NA | 2.64 (1.79-3.89)‡ | 2.17 (1.45-3.25)‡ |

Abbreviations: AOR, adjusted odds ratio; CI, confidence interval; OR, odds ratio (unadjusted); NA, not applicable.

*All numbers were unweighted, and all percentages were weighted.

†AOR-1 indicates adjustments for age, sex, education, marital status, urban/rural status, major depression, bipolar disorder, dysthymia, eating disorder, alcohol use disorder, drug use disorder, and schizophrenia (each diagnosis was entered separately in the same regression).

‡*P*<.001.

**Table 4. Incidence of Suicide Variables in Relation to Baseline Anxiety Disorder (Stratified by Mood Disorder) Among Those at Risk**

| Disorders at Baseline | New-Onset Suicidal Ideation and Suicide Attempts at Follow-up Assessments | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | No Suicidal Ideation (n = 4161), No. (%)* | Suicidal Ideation (n = 85), No. (%) | OR (95% CI) | AOR-1 (95% CI)† | No Suicide Attempts (n = 4631), No. (%) | Suicide Attempts (n = 39), No. (%) | OR (95% CI) | AOR-1 (95% CI) |
| Neither anxiety disorder nor mood disorder | 3160 (77.1) | 38 (46.4) | 1.00 | 1.00 | 3295 (72.6) | 14 (33.3) | 1.00 | 1.00 |
| Anxiety disorder only | 418 (9.8) | 16 (19.0) | 3.28 (1.78-6.05)‡ | 3.34 (1.75-6.40)‡ | 469 (10.0) | 5 (15.4) | 3.24 (1.11-9.45)‡ | 3.24 (1.09-9.69)§ |
| Mood disorder only | 323 (7.2) | 16 (16.7) | 4.00 (2.17-7.39)‡ | 3.46 (1.78-6.72)‡ | 447 (9.1) | 4 (10.3) | 2.39 (0.78-7.37) | 2.44 (0.79-7.55) |
| Anxiety and mood disorder | 260 (5.8) | 15 (17.9) | 5.03 (2.59-9.77)‡ | 4.64 (2.28-9.43)‡ | 420 (8.4) | 16 (41.0) | 9.99 (4.65-21.49)‡ | 10.05 (4.33-23.32)‡ |
| Anxiety and mood disorder (reference group, mood disorder only) | NA | NA | 1.26 (0.60-2.65) | 1.31 (0.60-2.87) | NA | NA | 4.18 (1.39-12.61)§ | 4.15 (1.34-12.90)§ |

Abbreviations: AOR, adjusted odds ratio; CI, confidence interval; OR, odds ratio (unadjusted); NA, not applicable.

*All numbers were unweighted, and all percentages were weighted.

†AOR-1 indicates adjustments for age, sex, education, marital status, urban/rural status, major depression, bipolar disorder, dysthymia, eating disorder, alcohol use disorder, drug use disorder, and schizophrenia (each diagnosis was entered separately in the same regression).

‡*P*<.05.

§*P*<.001.

mained significant after adjusting for comorbidity with other mental disorders and sociodemographic characteristics. Furthermore, respondents with mood and anxiety disorders had significantly higher likelihood of SAs (AOR, 4.15), but not SI, compared with respondents with a mood disorder without anxiety disorders.

### COMMENT

To the best of our knowledge, the current study is the first population-based, prospective, longitudinal examination of the impact of anxiety disorders on SI and SAs. The main finding from this study is that the presence of an anxiety disorder at baseline was a risk factor for subsequent onset of SI and SA, even after adjusting for common mental disorders. These findings contribute to resolving the contentious issue of whether anxiety disorders are risk factors for suicidal behavior.[13,18,25] Together with

strong evidence that anxiety disorders are highly underrecognized and undertreated in the community[44,45] and primary care,[46] the current findings suggest that untreated anxiety disorders might be missed opportunities for preventing suicidal behavior. Future randomized controlled trials are required to assess whether early intervention and treatment of anxiety disorders reduces the likelihood of subsequent suicidal behavior.

From a public health perspective, a very important finding of the current study is that mood disorders in combination with anxiety disorders had the highest likelihood of SI and SAs compared with those with neither anxiety nor mood disorders in both cross-sectional and longitudinal evaluation. Furthermore, the presence of a combination of a mood and anxiety disorder was associated with a higher risk for SAs compared with those with mood disorders alone. These findings are consistent with previous studies demonstrating that suicidal behavior is associ-

ated with presence of multiple mental disorders[1,5] and mood disorders in combination with anxiety disorders.[31,47] Overall, these findings imply that public health treatment strategies aimed at reducing suicidal behavior in the community should target individuals with mood disorders alone, anxiety disorders alone, and especially those with both an anxiety and a mood disorder.

Among the specific anxiety disorders, the current study found that OCD, social phobia, and GAD were strongly linked with SI at baseline and follow-up. Adjusted models did not find an association between these anxiety disorders and SAs. Previous work[14] has also found that social phobia was associated with SI but not SAs in the Epidemiologic Catchment Area study. However, SAs were found to be associated with uncomplicated OCD in the Epidemiologic Catchment Area study.[15] It is possible that the relationship between these anxiety disorders and suicidal behavior may differ. Suicidal ideation may be directly related to GAD, social phobia, and OCD. However, SAs may be indirectly mediated through comorbidity with other mental disorders.

Among the anxiety disorders studied in the NEMESIS, simple phobia was found to be associated with SI and SAs in unadjusted models, but only SAs in multivariate models adjusting for other mental disorders. These findings were consistent in cross-sectional and longitudinal analyses and fit with previous analysis of the NCS data showing a positive association between simple phobia and SI and SAs.[1] There are at least 4 possible explanations for these findings. First, simple phobia might have a direct association with suicidal behavior due to its association with significant distress. Previous work from the NCS[29] demonstrated that simple phobia often has an early age of onset and even in its noncomorbid form is associated with significant role impairment.

Second, simple phobia might be indirectly associated with suicidal behavior through an interaction with other comorbid disorders assessed here. In the NCS, simple phobia was shown to be highly comorbid with other mental disorders (83.4% have at least 1 other disorder, most commonly another anxiety disorder or a mood disorder).[29] We found partial support for this hypothesis: simple phobia was not associated with increased risk for SI, although it was associated with increased risk for SAs. The sample lacked the power to test for interactions in a more definitive, disorder-by-disorder fashion.

Third, simple phobia might be indirectly associated with suicidal behavior through another diagnosis not assessed in the current survey. For example, posttraumatic stress disorder (PTSD) has been positively associated with suicidal behavior in a range of clinical and epidemiologic studies.[48-52] Using the NCS data, multivariate models adjusting for the effects of all other anxiety disorders found that PTSD was the only anxiety disorder that remained associated with suicidal behavior.[25] We suggest that the lack of assessment of PTSD in the NEMESIS may be an important explanation of why simple phobia remained associated with suicidal behavior in the current study; specifically, we hypothesize that some of the diagnoses of simple phobia in the NEMESIS are really cases of PTSD-related phobic avoidance that are not adequately categorized in this regard.

Finally, it is possible that the diagnosis of simple phobia in community samples may be a marker for a subthreshold anxiety disorder. Because the criteria for simple phobia (strong, unreasonable fear of a situation) are relatively easier to meet compared with other anxiety diagnoses, individuals diagnosed with simple phobia in community samples may have subthreshold presentations of other anxiety disorders (PTSD, panic disorder, agoraphobia). There is emerging evidence that individuals suffering with subthreshold (ie, *DSM* criteria) anxiety symptoms have significant impairment and suicidal behavior.[53] Overall, we believe that the most likely reason for the association of simple phobias with suicidal behaviors is comorbidity with other unmeasured or subthreshold mental disorders. Further epidemiologic studies are required to replicate and better understand the current findings. Broader assessment of a wider range of mental disorders (especially PTSD) in community samples would be important in such inquiries.

Unlike previous studies of the Epidemiologic Catchment Area[26] and NCS,[25] we found a cross-sectional association of panic disorder with SI and SAs in multivariate models. A potential reason for the discrepancy between our findings and previous work is based on how agoraphobia was entered in the multivariate model. In previous studies,[25,26] all cases meeting criteria for agoraphobia (with or without panic disorder) were categorized as agoraphobia, rather than as panic disorder, thus potentially obfuscating the relationship between panic disorder and suicidality. We believe that panic disorder with agoraphobia is a severe form of panic disorder[54] and therefore created 2 mutually exclusive categories: (1) panic disorder with or without agoraphobia and (2) agoraphobia without panic disorder. In doing so, we found strong cross-sectional relationships between panic disorder and SI and SAs, even when adjusting for all other covariates. In the cross-sectional evaluation, agoraphobia without panic disorder was also associated with suicidal behavior. However, neither agoraphobia nor panic disorder was associated with first-ever incidence of suicidal behavior (except in the unadjusted SA models). There are 2 possible explanations for these findings: (1) an association between these anxiety disorders and follow-up suicidal behavior exists but was not found because of the small number of new cases of SI and SAs (ie, power was too low to detect this association prospectively) or (2) suicidal behavior may occur prior to the onset of panic disorder and agoraphobia. Future studies are required in adolescent and young adult samples to determine the order of onset of panic disorder and suicidal behavior.

## ETIOLOGIC MECHANISMS

There are a number of possible explanations for the relationship between anxiety disorders and suicidal behavior. First, direct effects may be present such that individuals suffering with high levels of anxiety, worry, and fear may seek escape from their suffering by considering or attempting suicide. Possible indirect mechanisms include comorbidity with other mental disorders, such as substance use disorders or mood disorders, that may mediate the relationship between anxiety disorders

and suicide variables. Our current analysis does provide some support for this hypothesis because some associations between anxiety disorders and suicidal behavior were effected when adjusting for comorbidity. Common factors such as childhood trauma,[55,56] genetic factors,[57] and personality factors (neuroticism,[2] impulsivity,[51] and self-criticism[58]) may explain some of the risk of anxiety and suicidal behavior. Childhood maltreatment has been associated with mental disorders[56,59] and suicidal behavior.[55] Some of the biologic factors, such as low levels of hydroxyindoleacetic acid in the cerebrospinal fluid (CSF-HIAA, a metabolite of serotonin), may link both anxiety disorders and suicidal behavior.[60-62] Finally, a whole host of factors, such as no religious affiliation,[2,63] poor social support,[1] and experiences of traumatic events,[64] may interact with the presence of a mental disorder to lead to suicidal behavior. In summary, suicidal behavior is a complex process because of numerous interrelated factors, and although the present study suggests that anxiety disorders play an important role, the mechanism of the increase in suicidal behavior associated with anxiety disorders remains to be determined.

## STUDY LIMITATIONS

First, although SI and SAs are linked with completed suicide, the current study cannot comment on whether anxiety disorders are associated with completed suicides. Future studies using psychological autopsy design[4] are required to systematically assess for a broad range of anxiety disorders among those who have completed suicide. Second, this study did not assess for important variables known to be associated with suicidal behavior such as PTSD and Axis II personality disorders (eg, borderline and antisocial). Some of the findings in the current study may have been affected if these variables had been included in the models. Third, although the reliability of the CIDI-based diagnoses used in the current survey have been demonstrated to be high,[38] they are unlikely to match the accuracy of clinician-based diagnoses. Fourth, because the baseline assessment of suicidal behavior was based on a longer time frame (lifetime) than the follow-up assessments (1-year and 2-year periods), it is possible that recall errors of SI and SAs may be more likely in the baseline assessment than the follow-up assessments. This issue could affect the number of incident cases of SI and SAs. Fifth, the short period of follow-up led to a low total number of cases with incident SI and SAs. Therefore, in the longitudinal analysis, we may not have had enough power to detect some effects. For example, in the incidence analysis, the presence of a mood disorder without anxiety disorders (Table 4) was associated with SI but not SAs. The latter finding is counterintuitive and is likely a type II error due to the small sample size in these categories. There is ample evidence that mood disorders are associated with SAs at follow-up.[4] Nonetheless, it is important to underscore that even in the context of a small number of new cases of SI and SAs, we were able to demonstrate that anxiety disorders were risk factors for new onset SI and SAs. Future studies are required to replicate and extend our findings using longer follow-up periods, larger samples, and adolescent cohorts and elderly cohorts. Finally, although the presence of an anxiety disorder elevated the risk of SI and SAs at follow-up assessments, it must be considered that, because SI and SAs are low base-rate phenomena, most individuals with anxiety disorder did not develop SI or SAs at follow-up. Further work is required to delineate the clinical and sociodemographic features that differentiate between anxious subjects who go on to develop suicidal behavior vs those who do not develop suicidal behavior.

## CONCLUSIONS

The current study demonstrated that as a group of disorders, anxiety disorders were highly prevalent among those with suicidal behavior in a large community sample with repeated assessments. We also found that anxiety disorders are independent risk factors for suicidal behavior, even after adjusting for comorbidity with common mental disorders. Furthermore, stratified analysis based on the presence of an anxiety or mood disorder demonstrated that the presence of at least 1 anxiety disorder without a mood disorder was associated with an increased likelihood of suicidal behavior. Finally, the presence of an anxiety disorder in combination with a mood disorder was associated with increased likelihood of suicidal behavior compared with those with a mood disorder alone. These findings underscore the importance of early recognition and treatment of anxiety disorders, especially those with comorbid mood disorders.

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