

The Epidemiology of Panic Attacks, Panic Disorder, and Agoraphobia in the National Comorbidity Survey Replication

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Context: Only limited information exists about the epidemiology of *DSM-IV* panic attacks (PAs) and panic disorder (PD).

Objective: To present nationally representative data about the epidemiology of PAs and PD with or without agoraphobia (AG) on the basis of the US National Comorbidity Survey Replication findings.

Design and Setting: Nationally representative face-to-face household survey conducted using the fully structured World Health Organization Composite International Diagnostic Interview.

Participants: English-speaking respondents (N=9282) 18 years or older.

Main Outcome Measures: Respondents who met *DSM-IV* lifetime criteria for PAs and PD with and without AG.

Results: Lifetime prevalence estimates are 22.7% for isolated panic without AG (PA only), 0.8% for PA with

AG without PD (PA-AG), 3.7% for PD without AG (PD only), and 1.1% for PD with AG (PD-AG). Persistence, lifetime number of attacks, and number of years with attacks increase monotonically across these 4 subgroups. All 4 subgroups are significantly comorbid with other lifetime *DSM-IV* disorders, with the highest odds for PD-AG and the lowest for PA only. Scores on the Panic Disorder Severity Scale are also highest for PD-AG (86.3% moderate or severe) and lowest for PA only (6.7% moderate or severe). Agoraphobia is associated with substantial severity, impairment, and comorbidity. Lifetime treatment is high (from 96.1% for PD-AG to 61.1% for PA only), but 12-month treatment meeting published treatment guidelines is low (from 54.9% for PD-AG to 18.2% for PA only).

Conclusion: Although the major societal burden of panic is caused by PD and PA-AG, isolated PAs also have high prevalence and meaningful role impairment.

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EPIDEMIOLOGICAL SURVEY INVESTIGATORS have helped advance understanding of panic by studying the prevalence and distribution,¹⁻³ onset and course,⁴ associations with comorbid disorders,⁵⁻⁷ and societal costs.^{8,9} Despite these advances, important questions remain unanswered about the epidemiology of panic,¹⁰ among the most important of them regarding the finding that many people have isolated panic attacks (PAs) that do not meet criteria for panic disorder (PD). These people have elevated prevalence of other mental disorders.^{6,11} They report greater impairment, use of psychotropic medication, and psychiatric help-seeking than people with many Axis I disorders.⁸ Such findings have led to the view that PAs are fairly nonspecific risk markers for psychopathology.¹²

Some people with isolated PAs meet criteria for agoraphobia (AG).¹³ It is not

known, though, whether the persistent course and poor outcome associated with AG among people with PD¹⁴ also apply to PAs with AG. As a result, the boundary between PA and PD and the relative role of AG within each are not well understood. Investigation and comparison of these symptom presentations in community samples might help clarify these issues. The current report presents initial data of this sort from the recently completed US National Comorbidity Survey Replication (NCS-R).

METHODS

SAMPLE

The NCS-R is a nationally representative survey of 9282 English-speaking household residents 18 years or older in the coterminous United States. Face-to-face interviews were performed between February 2001 and April 2003. The response rate was 70.9%. Consent was oral rather

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than written to parallel the baseline NCS procedures. The human subjects committees of Harvard Medical School (Boston, Mass) and the University of Michigan (Ann Arbor) approved the NCS-R recruitment and consent procedures. Respondents were interviewed in 2 parts. The part 1 interview, administered to all respondents, included the core diagnostic assessment. The part 2 interview, administered to all part 1 respondents who met criteria for any lifetime core disorder plus a probability subsample of others (for a total of 5692 part 2 respondents), was used to assess correlates and disorders of secondary interest. The part 1 sample is used here to examine prevalence and course, clinical severity and role impairment, and most aspects of comorbidity. The part 2 sample is used to examine comorbidity with disorders of secondary interest to the survey, sociodemographic correlates, and treatment. The part 1 sample was weighted to adjust for differential probability of selection and discrepancies between the sample and the US population concerning census sociodemographic and geographic variables. The part 2 sample was weighted additionally to adjust for differential probability of selection from the part 1 sample. More details on NCS-R sampling and weights are reported elsewhere.¹⁵

PANIC AND AG

Panic and AG were assessed using the World Mental Health Survey Initiative version of the World Health Organization Composite International Diagnostic Interview (CIDI),¹⁶ a fully structured lay-administered diagnostic interview (available at www.hcp.med.harvard.edu/wmhcdi). The assessment of panic was comparable to that in previous versions of the CIDI, except that a distinction was made between uncued PAs (described as occurring "out of the blue" with no triggering event) and cued PAs. A series of parallel questions was asked about each of these 2 types of attacks. Panic disorder was defined as the occurrence of 4 or more uncued PAs not caused by substance use or a general medical condition accompanied by 1 month or more of persistent concern about recurrence, worry about the implications of the attacks, or significant change in behavior because of the attacks. Agoraphobia was defined as anxiety about 2 or more situations that had to include *being in crowds, going to public places, traveling by yourself, or traveling away from home* associated with a fear of having a PA and fear that it might be difficult or embarrassing to escape. This fear had to result in avoidance of the feared situations, distress when exposed to these situations, or the necessity of a companion during these situations. We used these classifications to define 4 subgroups for comparative analysis: PA without PD or AG (PA only), PA with PD and AG (PA-AG), PD without AG (PD only), and PD with AG (PD-AG). The PA-only category is not a codable DSM-IV¹² disorder; PA-AG is a subset of the DSM-IV category AG without a history of PD, excluding respondents with AG who never had a PA. This latter subgroup is not considered in this report because we focus exclusively on people with a history of panic.

As detailed elsewhere,^{17,18} blinded clinical reappraisal interviews using the lifetime nonpatient version of the Structured Clinical Interview for DSM-IV (SCID)¹⁹ were administered to a probability subsample of 325 NCS-R respondents to assess concordance with CIDI diagnoses. The CIDI-SCID concordance for PD diagnosis had an area under the receiver operating characteristic curve of 0.72, a moderate κ value (standard error) of 0.45 (0.15), and a high odds ratio (OR) of 56.3 (95% confidence interval, 15.5-204.6). No bias was found in the CIDI prevalence estimate compared with that in the SCID by using a McNemar test ($\chi^2=0$, $P=.82$). The CIDI-SCID concordance was not assessed for PA because PA was not evaluated separately in the SCID; concordance also was not assessed for AG because AG occurred too infrequently in the

clinical reappraisal study for reliable analysis of concordance. The DSM-IV requires recurrent uncued PAs, which could be interpreted as 2 or more, for a PD diagnosis. However, CIDI respondents who reported 2 or 3 lifetime uncued PAs generally were found in the SCID to have had only 1 full PA with additional limited-symptom attacks. Validity of the CIDI in relation to the SCID consequently was improved when we required at least 4 lifetime uncued attacks in the CIDI. The McNemar test result documents that the CIDI PD prevalence estimate does not differ significantly from the SCID estimate despite the SCID requiring only 2 attacks.

COURSE, SEVERITY, AND IMPAIRMENT

Respondents who met DSM-IV lifetime criteria for PA were asked to estimate the age of onset (AOO) of their first attack and AOO of having 4 uncued attacks with a month of persistent worry. They also were asked to estimate their age at the most recent attack, lifetime number of uncued and cued attacks, and number of years with at least 1 attack. Clinical severity was assessed only for 12-month cases by using a fully structured version of the 7-question Panic Disorder Severity Scale (PDSS) that was developed specifically for the NCS-R. (Question wording is posted at www.hcp.med.harvard.edu/ncs.) The clinician-administered version of the PDSS yields a reliable and valid assessment of overall PD clinical severity.²⁰ A separate fully structured version of the PDSS, developed independently of the NCS-R version but with similar wording, has excellent concordance with the clinician-administered version.²¹ Published PDSS cut points (none, mild, moderate, or severe) were used to define severity.

Although 2 of the 7 PDSS questions assess role impairment, a more generic measure of role impairment, the Sheehan Disability Scale (SDS),²² also was included in each section of the CIDI. The SDS asked respondents with 12-month panic to focus on the 1 month in the past year when their panic, their worry about having another PA, or their restriction of activity because of this worry interfered most with their life and activities and to rate this interference on a 0 to 10 visual analog scale with response options of none (0), mild (1-3), moderate (4-6), severe (7-9), or very severe (10). Interference ratings were obtained for 4 role domains: home management, work, social life, and personal relationships. Responses were combined by taking the highest score across the 4 ratings and collapsing the severe and very severe response categories.

COMORBID DSM-IV DISORDERS

The NCS-R was used to assess a number of other DSM-IV disorders: other anxiety disorders (generalized anxiety disorder, specific phobia, social phobia, posttraumatic stress disorder, obsessive-compulsive disorder, and adult manifestations of separation anxiety disorder), mood disorders (major depressive disorder, dysthymic disorder, and bipolar disorder I or II), substance use disorders (alcohol and illicit drug abuse and dependence, in which abuse and dependence on specific illicit drugs were combined with polysubstance abuse and dependence), and impulse-control disorders (intermittent explosive disorder and adult manifestations of 3 child-adolescent impulse-control disorders: attention-deficit/hyperactivity disorder, oppositional-defiant disorder, and conduct disorder). Organic exclusion rules and diagnostic hierarchy rules were used in making all diagnoses. As reported in more detail elsewhere,¹⁸ blinded clinical reappraisal interviews using the nonpatient version of the SCID¹⁹ showed generally good concordance between CIDI and SCID diagnoses of anxiety, mood, and substance use dis-

orders, with area under the receiver operating characteristic curve in the range of 0.65 to 0.81, κ in the range of 0.33 to 0.70, and ORs in the range of 6.3 to 877.0. Diagnoses of impulse-control disorders were not validated because the SCID does not assess these disorders.

TREATMENT

Two questions about lifetime and 12-month treatment of panic were asked at the end of the panic section. Part 2 respondents additionally were asked more general questions about whether they ever received treatment for any *problems with your emotions or nerves or your use of alcohol or drugs* and, if so, about types of professionals seen.²³ Treatment was distinguished in 5 sectors: psychiatry, nonpsychiatry mental health specialty, general medical, human services, and complementary-alternative. Questions about treatment in the 12 months before interview asked about number and duration of visits; number and duration of psychotherapy sessions; and name, dose, and duration of each medication used. No information was obtained about the content of psychotherapy. A rough measure of 12-month guideline-concordant treatment of panic was developed using these reports on the basis of available evidence-based guidelines.²⁴ Guideline-concordant treatment was defined as receiving either pharmacotherapy (at least 2 months of an appropriate medication, defined as antidepressants or anxiolytics,²⁵ plus at least 4 visits to any type of medical physician) or psychotherapy (at least 8 visits with any health care or human services professional lasting an average of at least 30 minutes). The decision to require at least 4 physician visits for pharmacotherapy was based on the recommendation of at least 4 visits for medication evaluation, initiation, and monitoring during the early and continuation phases of PD medication treatment.²⁴ The decision to require at least 8 psychotherapy sessions was based on the fact that clinical trials demonstrating effectiveness generally have included at least 8 psychotherapy visits.²⁴ Because respondents who began a course of treatment only shortly before the interview could not fulfill the requirements, we counted respondents with at least 2 visits to an appropriate treatment sector if they were in treatment at the time of interview.

ANALYSIS METHODS

Cross-tabulations were used to estimate prevalence and patterns of treatment. The actuarial method²⁶ was used to estimate AOO distributions. Mean comparisons were used to examine illness course and severity or impairment. Logistic regression analysis²⁷ was used to estimate associations with sociodemographic variables and comorbid *DSM-IV* disorders. Because the NCS-R sample design featured weighting and clustering, all analyses used the Taylor series design-based method,²⁸ implemented in the SUDAAN software system.²⁹ Significance tests of sets of coefficients in the logistic regression equations were made using Wald χ^2 tests based on design-corrected coefficient variance-covariance matrices. Statistical significance was evaluated using 2-sided, design-based $P < .05$ -level tests.

RESULTS

PREVALENCE

Twenty-eight percent (standard error) (28.3% [1.0]) of respondents met criteria for lifetime PA and 11.2% (0.5) for 12-month PA, whereas 4.7% (0.3) of respondents (roughly one sixth of those with lifetime PA) met criteria for life-

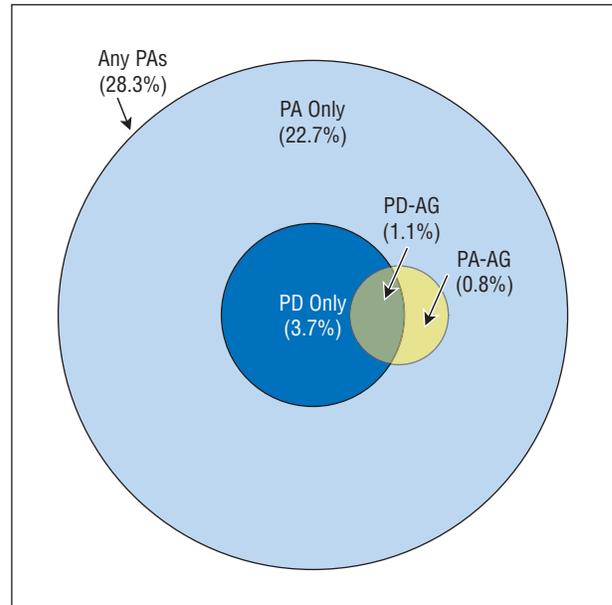


Figure 1. Lifetime prevalence estimates of *DSM-IV* panic attacks (PAs) and panic disorder (PD) with and without agoraphobia (AG). PA only indicates lifetime history of PA but not PD or AG; PA-AG, lifetime history of PA with AG but not PD; PD only, lifetime history of PD without AG; PD-AG, lifetime history of PD with AG. The prevalence estimates of PD only (3.7%) and PD-AG (1.1%) sum to more than the observed 4.7% prevalence of all PD because of rounding.

time PD and 2.8% (0.2) for 12-month PD. Eight tenths of 1% of all respondents (roughly 3% of those with a lifetime PA) met criteria for lifetime PA-AG and 0.4% (0.1) for 12-month PA-AG, whereas 1.1% (0.1) of respondents (approximately one fifth of those with lifetime PD and 60% of those with lifetime PA-AG) met criteria for lifetime PD-AG and 0.4% (0.1) for 12-month PD-AG.

COURSE OF ILLNESS

As described, respondents with lifetime panic were placed into 4 mutually exclusive subgroups (**Figure 1**): PA only, 22.7% of the sample; PA-AG, 0.8%; PD only, 3.7%; and PD-AG, 1.1%. A small proportion of respondents without PD (12.0% with PA only and 10.7% with PA-AG) reported a sufficient number of uncued attacks to qualify for PD (with means of 31.0 and 131.4 lifetime uncued attacks, respectively) but failed to meet other requirements for a PD diagnosis (**Table 1**). Most respondents in 3 of the 4 subgroups, the exception being PD only, reported at least 1 cued lifetime attack (from 67.9% in PD-AG to 87.6% in PA-AG). A significantly lower 46.8% of PD-only cases reported any cued lifetime attack. Mean number of cued attacks among those with any varies significantly across subgroups ($F_{3,1568} = 18.2, P < .001$). Panic disorder is associated with a significantly higher mean number of cued attacks than PA among those without (121.8 vs 38.3, $z = 6.6, P < .001$) and those with (134.4 vs 78.2, $z = 2.1, P = .03$) AG. Agoraphobia is associated with a significantly higher mean number of cued attacks among those with PA (78.2 vs 38.3, $z = 2.4, P = .02$) but not among those with PD (134.4 vs 121.8, $z = 0.53, P = .60$). In the subsample of respondents who reported ever

Table 1. Prevalence, Persistence, and Course of Panic Among Respondents in 4 Mutually Exclusive Lifetime Panic Subgroups

Parameter	PA Only (n = 1672)	PA-AG (n = 71)	PD Only (n = 344)	PD-AG (n = 105)	χ^2
Lifetime prevalence and persistence*					
Prevalence	22.7 (1.0)	0.8 (0.1)	3.7 (0.2)	1.1 (0.1)	NA
≥1 Lifetime cued attacks	76.2 (1.2)	87.6 (4.4)	46.8 (3.0)	67.9 (5.5)	90.7‡
≥4 Lifetime uncued attacks	12.0 (1.1)	10.7 (4.1)	100.0 (0)	100.0 (0)	0.1‡
					$F_{3,9278}$
Age of onset of PA†	22.7 (0.5)	22.1 (1.7)	22.7 (0.8)	21.5 (1.0)	0.9
PD onset†	NA	NA	23.6 (0.9)	22.9 (1.0)	0.5
AG onset†	NA	19.3 (1.8)	NA	17.0 (1.4)	0.9
Course of illness*					
12-mo persistence*	35.7 (1.5)	41.1 (5.5)	57.4 (3.7)	62.6 (4.4)	48.7‡
					$F_{3,9278}$
Years with attacks†	4.7 (0.2)	6.6 (1.1)	8.3 (0.6)	10.7 (1.1)	20.4‡
≥1 Lifetime cued attacks†	38.3 (4.5)	78.2 (16.0)	121.8 (11.9)	134.4 (20.7)	18.2‡
≥4 Lifetime uncued attacks†	31.0 (4.5)	131.4 (29.4)	31.3 (2.7)	46.0 (7.8)	4.3‡
Median ≥1 lifetime cued attacks†	6.0 (0.3)	9.2 (2.2)	17.2 (8.8)	34.1 (70.4)	NA
Median ≥4 lifetime uncued attacks†	11.5 (0.9)	100.2 (48.3)	10.0 (0.7)	16.6 (3.5)	NA

Abbreviations: AG, agoraphobia; NA, not applicable; PA, panic attack; PD, panic disorder; PA only, lifetime history of PA but not of PD or AG; PA-AG, lifetime history of PA with AG but not of PD; PD only, lifetime history of PD without AG; PD-AG, lifetime history of PD with AG.

*Data are given as percentage (standard error).

†Data are given as mean (standard error) unless otherwise indicated.

‡Significant at $P = .05$, 2-sided test.

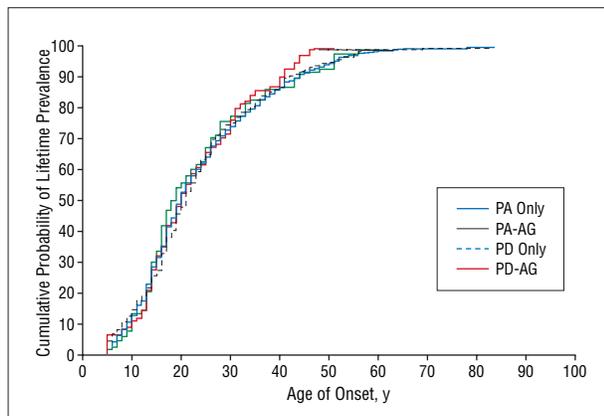


Figure 2. Age of onset of first lifetime panic attack in 4 mutually exclusive lifetime panic subgroups ($\chi^2_3=6.9$, $P=.07$). See legend to Figure 1 for an explanation of abbreviations.

having a cued attack, the mean number of such attacks substantially exceeds the mean number of uncued attacks in the PD-only subgroup (121.8 vs 31.3, $z=7.4$, $P<.001$) and in the PD-AG subgroup (134.4 vs 46.0, $z=4.0$, $P<.001$).

No meaningful difference exists in mean AOO of PA among the 4 subgroups (21.5-22.7; $F_{3,2188}=0.9$, $P=.44$); the entire PA AOO distribution is similar across these subgroups (**Figure 2**). Mean AOO of PD is only about 1 year later than mean AOO of PA and does not differ significantly between the PD-only and PD-AG subgroups (23.6 vs 22.9, $F_{3,1568}=0.5$, $P=.62$). Persistence (12-month prevalence of PA among lifetime cases), however, varies substantially, from 35.7% in PA only to 62.6% in PD-AG ($\chi^2_3=48.7$, $P<.001$). Persistence is significantly higher in the PD than PA subgroups in the absence of AG (57.4% vs 35.7%, $z=5.4$, $P<.001$) and the presence of AG (62.6% vs 41.1%, $z=3.0$, $P=.002$) but does

not vary as a function of AG either in the 2 PA subgroups (41.1% vs 35.7%, $z=0.9$, $P=.34$) or in the 2 PD subgroups (62.6% vs 57.4%, $z=0.9$, $P=.36$). Mean number of years with attacks also varies significantly across the subgroups ($F_{3,2188}=46.7$, $P<.001$) with the same rank ordering as persistence.

SOCIODEMOGRAPHIC CORRELATES

We failed to find consistent variation in magnitude of significant sociodemographic correlates of lifetime prevalence across the 4 subgroups, although the ORs associated with being female are noticeably higher for the PD than the PA subgroups, whereas the ORs associated with *other* employment status are noticeably higher for the AG than non-AG subgroups (**Table 2**). Age of 60 years or older (vs younger ages) and non-Hispanic blacks (vs non-Hispanic whites) have reduced odds of panic in all 4 subgroups, although not all are significant. Women and previously married people have consistently elevated odds of panic in all 4 subgroups. Respondents classified as having *other* employment status, made up largely of the unemployed and disabled, have elevated odds of all outcomes other than PA only, whereas retired people have elevated odds of PD-AG but not the other 3 outcomes. None of these associations is strong in substantive terms, though, as indicated by the Pearson contingency coefficients for the set of sociodemographic predictors all being quite small (in the range of 0.01 to 0.02).

COMORBIDITY

Respondents in all 4 panic subgroups have significantly increased odds of virtually all other lifetime DSM-IV disorders assessed in the survey (**Table 3**). One or more comorbid conditions are found in 71.9% of the PA-only

Table 2. Sociodemographic Correlates of 4 Mutually Exclusive Lifetime Panic Subgroups*

Characteristic	Odds Ratio (95% Confidence Interval)			
	PA Only (n = 5172)	PA-AG (n = 3572)	PD Only (n = 3844)	PD-AG (n = 3604)
Age, y				
18-29	1.0	1.0	1.0	1.0
30-44	1.0 (0.7-1.3)	1.6 (0.6-4.4)	1.5† (1.1-2.1)	1.7 (1.0-2.8)
45-59	0.9 (0.7-1.2)	1.7 (0.5-6.0)	1.3 (0.9-1.8)	1.3 (0.7-2.4)
≥60	0.4† (0.2-0.6)	0.5 (0.1-3.7)	0.4† (0.2-0.7)	0.1† (0-0.2)
χ ²	29.2†	4.0	24.2†	35.5†
Sex				
Male	1.0	1.0	1.0	1.0
Female	1.4† (1.2-1.7)	1.3 (0.8-2.3)	2.3† (1.8-3.0)	2.0† (1.3-3.2)
χ ²	16.5†	1.2	38.6†	9.1†
Race				
Hispanic	0.6† (0.4-0.8)	1.0 (0.3-3.2)	0.8 (0.5-1.3)	0.8 (0.3-2.1)
Black	0.7† (0.5-0.8)	0.6 (0.3-1.5)	0.4† (0.3-0.6)	0.5† (0.2-1.0)
Other	1.0 (0.6-1.5)	2.1 (0.6-7.0)	1.1 (0.6-2.0)	0.6 (0.2-1.9)
White	1.0	1.0	1.0	1.0
χ ²	27.7†	2.5	23.5†	5.1
Education, y				
0-11	1.0	1.0	1.0	1.0
12	1.0 (0.7-1.3)	0.7 (0.3-1.7)	0.9 (0.6-1.3)	0.9 (0.4-2.1)
13-15	0.9 (0.7-1.2)	0.9 (0.4-2.0)	1.2 (0.8-1.9)	0.8 (0.3-1.9)
≥16	0.9 (0.7-1.2)	0.5 (0.2-1.5)	0.8 (0.5-1.2)	0.7 (0.3-2.1)
χ ²	0.7	1.9	10.3†	0.7
Marital status				
Married/cohabitating	1.0	1.0	1.0	1.0
Separated/widowed/divorced	1.1 (0.8-1.4)	2.2† (1.1-4.2)	1.6† (1.2-2.1)	1.3 (0.7-2.3)
Never married	1.0 (0.8-1.2)	1.2 (0.5-3.2)	1.2 (0.8-1.8)	0.9 (0.4-2.0)
χ ²	0.5	6.3†	10.3†	1.2
Employment status				
Working	1.0	1.0	1.0	1.0
Student	0.8 (0.5-1.4)	0.8 (0.2-3.5)	0.4 (0.1-1.4)	1.5 (0.5-4.9)
Homemaker	0.8 (0.5-1.3)	2.0 (0.8-5.1)	1.1 (0.7-1.7)	1.3 (0.5-3.7)
Retired	1.0 (0.6-1.5)	1.2 (0.2-6.6)	1.0 (0.5-1.9)	4.3† (1.6-11.3)
Other	1.1 (0.9-1.5)	3.6† (1.8-7.1)	1.5† (1.0-2.2)	3.8† (2.1-6.8)
χ ²	1.7	18.4†	15.1†	30.9†
Annual family income				
Low	1.2 (0.9-1.6)	1.0 (0.5-2.3)	1.3 (0.9-2.0)	1.4 (0.6-3.2)
Low-average	1.0 (0.8-1.2)	0.9 (0.4-2.0)	1.4 (0.9-2.1)	0.8 (0.4-1.7)
High-average	1.2† (1.0-1.4)	0.7 (0.3-1.7)	1.3 (0.8-2.1)	0.9 (0.5-1.6)
High	1.0	1.0	1.0	1.0
χ ²	8.4†	0.9	2.5	2.2

Abbreviations: AG, agoraphobia; PA, panic attack; PD, panic disorder; PA only, lifetime history of PA but not PD or AG; PA-AG, lifetime history of PA with AG but not PD; PD only, lifetime history of PD without AG; PD-AG, lifetime history of PD with AG.

*Based on multivariate logistic regression analyses that separately compare respondents in each of the 4 panic subgroups with respondents who have no lifetime history of panic; the sample sizes differ because respondents in each of the 4 mutually exclusive panic subgroups (1672 PA only, 72 PA-AG, 344 PD only, and 104 PD-AG) are compared separately with the 3500 respondents who have no history of panic.

†Significant at the $P < .05$ level, 2-sided test.

subgroup, 83.1% of the PD-only subgroup, and 100% of the other 2 subgroups. The ORs for particular comorbid conditions differ significantly across the 4 subgroups, with the lowest ORs consistently in the PA-only subgroup. In the case of comorbidity with other anxiety disorders and major depression, AG is more important than PD, as shown by the PA-AG ORs (4.4-24.0) consistently being higher than the PD-only ORs (2.0-5.4) and often as high as the PD-AG ORs (2.5-25.8). In the case of the other mood disorders and alcohol use disorders, the PA-AG ORs (3.2-5.1) are comparable to the PD-only ORs (3.5-5.4), whereas the PD-AG ORs (5.6-13.6) are considerably larger. A distinct pattern for drug use disorders for the

ORs is associated with all 3 AG or PD subgroups to be comparable in magnitude (3.4-5.8).

TWELVE-MONTH CLINICAL SEVERITY AND ROLE IMPAIRMENT

Summary PDSS ratings of clinical severity vary significantly across the four 12-month panic subgroups ($\chi^2_3 = 34.3-102.9$, $P < .001$), with the highest ratings in the PD-AG subgroup (86.3% with moderate or severe rating, and 42.4% with severe rating) and the lowest in the PA-only subgroup (6.7% with moderate or severe rating, and 0.3% with severe rating) (**Table 4**). Re-

Table 3. Comorbidities of 4 Mutually Exclusive Lifetime Panic Subgroups With Other *DSM-IV* Disorders*

Disorder	PA Only		PA-AG		PD Only		PD-AG		χ^2
	Percentage	OR (95% CI)	Percentage	OR (95% CI)	Percentage	OR (95% CI)	Percentage	OR (95% CI)	
Other anxiety disorders									
Generalized anxiety disorder	10.0	2.4† (1.7-3.2)	31.9	8.5† (4.9-14.6)	21.3	4.4† (2.9-6.8)	15.0	2.6† (1.4-4.8)	33.6†
Specific phobia	21.0	2.4† (2.0-3.0)	73.7	24.0† (13.8-41.4)	34.3	3.8† (2.7-5.3)	75.2	25.8† (14.3-46.6)	153.8†
Social phobia	18.8	1.9† (1.6-2.4)	65.5	16.6† (7.7-35.8)	31.1	3.1† (2.3-4.2)	66.5	15.5† (9.3-25.8)	82.4†
Posttraumatic stress disorder	12.0	3.0† (2.3-3.9)	24.2	5.8† (2.3-14.6)	21.6	5.0† (3.4-7.5)	39.6	11.6† (6.8-19.7)	40.7†
Obsessive-compulsive disorder	2.1	1.5 (0.5-4.3)	0	NA‡	8.2	5.4† (1.8-16.1)	19.6	20.2† (5.5-73.9)	20.8†
Separation anxiety disorder	7.7	3.1† (2.3-4.0)	13.8	6.3† (2.7-14.5)	11.0	4.4† (2.6-7.5)	23.5	11.6† (7.1-19.0)	40.6†
Any other anxiety disorder	45.0	3.2† (2.7-3.8)	94.9	77.9† (24.9-244.1)	66.0	7.2† (5.5-9.3)	93.6	56.2† (22.4-141.0)	143.7†
Mood disorders									
Major depressive disorder	28.2	2.1† (1.8-2.4)	48.7	4.4† (2.6-7.4)	34.7	2.0† (1.5-2.7)	38.5	2.5† (1.5-4.0)	8.2†
Dysthymia	5.0	3.2† (2.4-4.3)	10.0	5.0† (2.1-12.0)	9.6	5.0† (2.9-8.8)	14.6	8.9† (4.2-18.8)	6.9
Bipolar disorder I or II	7.1	2.8† (2.3-3.5)	15.5	5.1† (2.7-9.6)	14.4	5.4† (3.6-7.9)	33.0	13.6† (8.0-23.2)	52.3†
Any mood disorder	36.0	2.5† (2.2-2.8)	64.2	7.1† (4.1-12.3)	50.0	3.3† (2.4-4.5)	73.3	10.0† (5.0-19.9)	35.3†
Impulse-control disorders									
Attention-deficit/hyperactivity disorder	11.7	2.3† (1.6-3.3)	28.8	NA‡	13.0	2.6† (1.5-4.5)	36.2	NA‡	20.0†
Oppositional defiant disorder	13.6	2.5† (1.8-3.5)	12.2	NA‡	13.0	2.4† (1.5-3.7)	27.6	NA‡	7.3
Conduct disorder	12.3	1.9† (1.4-2.6)	12.4	NA‡	21.7	4.2† (2.8-6.4)	22.5	NA‡	18.8†
Intermittent explosive disorder	7.8	1.7† (1.3-2.2)	21.8	5.3† (2.4-11.6)	11.8	2.5† (1.4-4.4)	9.0	1.7 (0.8-3.6)	9.5†
Any impulse-control disorder	33.7	2.3† (1.8-2.8)	63.2	NA‡	47.2	4.3† (2.8-6.6)	59.5	NA‡	24.6†
Substance use disorders									
Alcohol abuse or dependence	19.3	2.2† (1.8-2.7)	27.0	3.2† (1.5-6.7)	25.0	3.5† (2.5-4.9)	37.3	5.6† (2.7-11.5)	11.5†
Alcohol dependence	8.5	2.4† (1.8-3.2)	14.2	4.0† (1.6-9.7)	12.8	4.1† (2.6-6.3)	23.4	7.3† (3.0-17.6)	12.1†
Illicit drug abuse or dependence	13.0	2.4† (1.8-3.0)	17.7	3.4† (1.6-7.3)	17.5	3.6† (2.3-5.4)	20.6	3.9† (2.1-7.2)	7.3
Illicit drug dependence	5.6	3.0† (2.0-4.4)	10.6	5.8† (2.1-16.0)	9.1	5.2† (3.1-8.7)	9.3	4.6† (1.9-10.9)	6.0
Any substance use disorder	21.4	2.2† (1.8-2.6)	31.4	3.5† (1.8-6.9)	27.0	3.3† (2.4-4.5)	37.3	4.8† (2.4-9.5)	9.8†
Any disorder	71.9	3.3† (2.8-4.1)	100.0	NA	83.1	6.5† (3.7-11.7)	100.0	NA	5.3†

Abbreviations: AG, agoraphobia; CI, confidence interval; NA, not applicable; OR, odds ratio; PA, panic attack; PD, panic disorder; PA only, lifetime history of PA but not PD or AG; PA-AG, lifetime history of PA with AG but not PD; PD only, lifetime history of PD without AG; PD-AG, lifetime history of PD with AG.

*Based on a separate multivariate logistic regression equation for each row of the table in which dummy variables defining the 4 panic subgroups are used to predict lifetime occurrence of the comorbid disorder controlling for age at interview (in 5-year age intervals), sex, and race-ethnicity. The ORs compare respondents in each of the 4 panic subgroups with respondents who have no lifetime history of panic.

†Significant at the $P < .05$ level, 2-sided test.

‡Insufficient precision for estimation because of the low prevalence of PA-AG and PD-AG.

spondents in the PA-AG subgroup have higher PDSS ratings (45.3% with moderate or severe rating, and 20.2% with severe rating) than those in the PD-only subgroup (46.1% with moderate or severe rating, and 6.0% with severe rating).

Summary SDS ratings of role impairment are similar to PDSS ratings in being highest in the PD-AG subgroup (95.0% with moderate or severe rating, and 84.7% with severe rating) and lowest in the PA-only subgroup (21.3% with moderate or severe rating, and 11.1% with severe rating). Unlike PDSS ratings, however, the PA-AG subgroup has lower SDS ratings (58.8% with moderate or severe rating, and 39.0% with severe rating) than the PD-only subgroup (76.8% with moderate or severe rating, and 56.2% with severe rating), although the modal rating is severe in all 3 subgroups other than in the PA-only subgroup. In the latter, the modal rating is no disability (70.6%).

TREATMENT

Most patients with PD obtained lifetime treatment for psychiatric problems, although somewhat more so among those with AG (96.1%) than without (84.8%) (**Table 5**).

Lifetime treatment proportions are lower in the PA-AG (74.7%) and PA-only (61.1%) subgroups. The proportions that obtained panic-specific treatment are only slightly lower than overall treatment in the PD-only (70.3% vs 84.8%) and PD-AG (85.0% vs 96.1%) subgroups, but substantially lower in the PA-only (16.2% vs 61.1%) and PA-AG (37.6% vs 74.7%) subgroups. The most common site of treatment was the general medical sector in 3 of the 4 subgroups (32.3%-70.4%). The exception is PA-AG, in which nonmedical mental health treatment (46.1%) is slightly more common than general medical treatment (42.7%).

As with lifetime treatment, the proportion of 12-month cases that received treatment in the year before interview is highest in the PD-AG subgroup (72.6%), lowest in the PA-only subgroup (45.7%), and intermediate in the PA-AG (60.8%) and PD-only (66.9%) subgroups. Also similar to the lifetime treatment data, 12-month panic-specific treatment made up a higher proportion of all treatment in the PD-only (43.9% vs 66.9%) and PD-AG (52.7% vs 72.6%) subgroups than in the PA-only (14.7% vs 45.7%) and PA-AG (29.7% vs 60.8%) subgroups. Twelve-month treatment was obtained in the general medical sector more often than in any other sector in each

of the 4 subgroups (25.5%-46.0%). The proportions that obtained treatment consistent with basic treatment guidelines did not differ markedly across the 3 subgroups with PD or AG (40.6%-54.9%). Although treatment meeting basic guidelines was received by a substantially lower proportion of patients in the PA-only subgroup (18.2%), published treatment guidelines apply to PD and AG, not to isolated PAs.

COMMENT

These results should be interpreted in light of several limitations. First, the response rate was only 70%. As described in more detail elsewhere,¹⁵ we assessed this problem in a nonrespondent survey in which a subsample of initial nonrespondents was offered a large financial incentive (\$100) to complete a short (15-minute) telephone interview that included CIDI diagnostic stem questions. No significant difference was found in panic stem question endorsement compared with responses in the main survey sample, indirectly arguing against large non-response bias on the basis of panic. Second, although good concordance with SCID PD diagnoses was found, no validity data were obtained for PA or AG. Third, possibly biased information about AOO, persistence, and other important course and treatment variables were obtained retrospectively. As described in more detail elsewhere,¹⁶ a number of strategies were used in the NCS-R to reduce recall bias. Evidence exists that these strategies improved the accuracy of retrospective AOO reports,³⁰ but we have no data about effects on other aspects of recall.

With these limitations as a backdrop, the NCS-R lifetime prevalence estimates of DSM-IV PD and PD-AG (4.7% and 1.1%, respectively) are similar to the DSM-III-R¹ estimates in the baseline NCS (3.5% and 1.5%, respectively). The NCS-R estimate of PD-only prevalence (3.7%) is substantially higher than in the NCS (2.0%).² Although higher than in earlier epidemiological surveys,³¹ the concordance of the NCS-R PD prevalence estimate with an independent SCID estimate argues against upward bias. In the case of AG, the concern is more with downward than upward bias because the CIDI requirement of anxiety about multiple situations is stricter than the DSM-IV requirement.

Estimates of persistence, sociodemographic correlates, and psychiatric comorbidity are broadly consistent with the baseline NCS^{1,2,32} and other previous epidemiological surveys,^{14,31,33-35} although direct comparison is not possible because previous surveys did not disaggregate panic into the 4 subgroups considered here. High prevalence among women, low prevalence among the elderly, and strong comorbidity with other anxiety and mood disorders are all noteworthy consistencies with previous survey findings. One notable difference is a much higher estimated lifetime prevalence of PAs in the NCS-R (28.3%) than in the NCS (7.3%), a discrepancy presumably caused by the more detailed stem questions in the DSM-IV version of the CIDI than in the DSM-III-R version that suggests PAs were underestimated in the baseline NCS.

Table 4. Clinical Severity and Role Impairment Among Respondents in 4 Mutually Exclusive 12-Month Panic Subgroups

Parameter	Percentage (Standard Error)				χ^2
	PA Only (n = 701)*	PA-AG (n = 37)*	PD Only (n = 120)*	PD-AG (n = 41)*	
Clinical severity†					
Severe	0.3 (0.2)	20.2 (7.1)	6.0 (2.5)	42.4 (8.0)	34.3‡
Moderate	6.4 (0.8)	25.1 (7.9)	40.1 (4.8)	43.9 (10.1)	102.9‡
Mild	14.9 (2.0)	25.1 (5.6)	37.8 (5.7)	13.7 (4.5)	61.9‡
None	78.4 (2.2)	29.6 (8.3)	16.1 (4.4)	0	NA
Impairment§					
Severe	11.1 (1.1)	39.0 (7.9)	56.2 (5.0)	84.7 (5.3)	108.4‡
Moderate	10.2 (1.5)	19.8 (8.0)	20.6 (4.4)	10.3 (5.0)	119.8‡
Mild	8.1 (1.2)	11.7 (5.9)	13.8 (3.1)	5.0 (3.0)	62.9‡
None	70.6 (2.0)	29.4 (8.8)	9.4 (3.3)	0	62.9‡

Abbreviations: AG, agoraphobia; NA, not applicable; PA, panic attack; PD, panic disorder; PA only, lifetime history of PA but not PD or AG; PA-AG, lifetime history of PA with AG but not PD; PD only, lifetime history of PD without AG; PD-AG, lifetime history of PD with AG.

*The number of respondents in each subgroup who reported 12-month prevalence does not equal the sample size in Table 1 multiplied by the estimate of 12-month persistence in that table because persistence is estimated on weighted data and the sample sizes report the actual numbers of (unweighted) cases.

†The original Panic Disorder Severity Scale categories of severe and very severe were collapsed to define the severe category reported here.

‡Significant at the $P < .05$ level, 2-sided test.

§Responses to the 4 Sheehan Disability Scale questions (impairments in work, home, social, and personal relationship functioning) were combined by assigning respondents their most severe score across the 4. The original Sheehan Disability Scale categories of severe and very severe were collapsed to define the severe category reported here.

||Because the number of respondents with at least mild impairment is the additive inverse of the number with no impairment, the χ^2 value in this row is identical to the value in the preceding row.

We are aware of no previous general population research in which investigators compared the prevalence and correlates of isolated PAs vs PD with and without AG. The most striking results of this comparison are that isolated PAs are common and significantly comorbid with other DSM-IV disorders. These results are consistent with results from clinical studies.^{36,37} Most people with isolated PAs fail to meet PD criteria because they never had recurrent uncued attacks, although they typically had numerous cued attacks. Another notable subgroup result is that cued attacks are more common than uncued attacks even among people with PD. This finding is especially striking given that probing often uncovers initially unrecognized panic cues,^{38,39} which means that the NCS-R probably leads to underestimating the proportion of attacks that are cued. We also found that persistence and lifetime number of attacks are more strongly related to PD than to AG; that comorbidity, especially with other anxiety disorders, is more strongly related to AG than to PD; and that isolated PAs are associated with substantial role impairment when they occur in conjunction with AG.

The subgroup results suggest that AG and PD are to some extent distinct, as about 40% of all respondents with PA and AG never met criteria for PD. This finding is consistent with family aggregation studies, which show that

Table 5. Lifetime and 12-Month Treatment of Respondents in 4 Mutually Exclusive Panic Subgroups

Treatment	Percentage (Standard Error)				$\chi^2_{3^*}$
	PA Only	PA-AG	PD Only	PD-AG	
Lifetime treatment	(n = 1672)	(n = 71)	(n = 344)	(n = 105)	
Psychiatrist	24.2 (1.2)	39.4 (6.6)	37.9 (2.5)	58.4 (4.9)	58.5†
Other mental health	26.5 (1.3)	46.1 (7.1)	38.0 (2.8)	48.1 (4.2)	32.7†
General medical	32.3 (1.2)	42.7 (6.4)	56.0 (2.9)	70.4 (4.9)	88.1†
Human services	15.1 (1.3)	26.6 (6.1)	17.6 (2.3)	16.5 (4.1)	4.7
Complementary-alternative	15.9 (1.0)	35.5 (7.1)	19.1 (1.9)	28.3 (4.7)	31.0†
Panic-specific treatment	16.2 (1.2)	37.6 (6.6)	70.3 (2.8)	85.0 (4.3)	101.1†
Any treatment	61.1 (1.3)	74.7 (5.4)	84.8 (1.8)	96.1 (1.7)	107.5†
12-mo treatment	(n = 701)	(n = 36)	(n = 120)	(n = 42)	
Psychiatrist	12.1 (1.8)	21.6 (7.4)	27.2 (4.7)	34.6 (7.1)	24.7†
Other mental health	15.2 (1.4)	21.1 (8.1)	28.7 (4.7)	41.0 (6.4)	33.8†
General medical	25.5 (1.7)	30.6 (7.9)	46.0 (5.0)	45.1 (7.4)	25.1†
Human services	8.5 (1.2)	21.6 (7.3)	12.7 (3.0)	14.3 (6.1)	7.7
Complementary-alternative	6.2 (1.0)	11.7 (5.7)	9.7 (3.0)	15.9 (5.8)	7.5
Panic-specific treatment	14.7 (1.4)	29.7 (8.9)	43.9 (4.5)	52.7 (7.3)	123.7†
Any treatment	45.7 (2.4)	60.8 (8.4)	66.9 (4.6)	72.6 (6.5)	24.3†
Guideline-concordant treatment	18.2 (1.7)	40.6 (9.0)	45.1 (5.0)	54.9 (6.3)	54.5†

Abbreviations: AG, agoraphobia; PA, panic attack; PD, panic disorder; PA only, lifetime history of PA but not PD or AG; PA-AG, lifetime history of PA with AG but not PD; PD only, lifetime history of PD without AG; PD-AG, lifetime history of PD with AG.

*This set of statistics tests the significance of the differences among the 4 percentages in each row.

†Significant at the $P < .05$ level, 2-sided test.

risk of AG is significantly elevated among relatives of people with PA-AG⁴⁰ and relatives of people with PD-AG compared with those with PD only.^{39,41} Family genetic studies also suggest that AG and PD may have at least some distinct pathogenic mechanisms.^{42,43} At the same time, our finding of higher conditional prevalence of AG among people with PD than PA is consistent with the strong association between AG and PD long observed in clinical settings.

The subgroup results document monotonic increases from PA only to PD-AG in number of attacks, comorbidity, clinical severity, role impairment, and treatment seeking, with intermediate values for PA-AG and PD only. Together with the finding that a high proportion of AG is associated with PA, these results could be interpreted as suggesting that panic exists along a continuum in which PA and PD differ in degree rather than in kind. This interpretation is consistent with prior findings that infrequent, spontaneous PAs are common in the general population,^{41,42} that these attacks typically include fewer and less severe symptoms than those in patients with PD,⁴³ and that infrequent PA aggregates with PD in families.^{40,44}

The distinction between cued and uncued attacks might be called into question as part of this same line of thinking based on the view that most PAs are to some extent cued.^{37,45,46} It would be premature to conclude from these results that the boundary between PA and PD is arbitrary. Nevertheless, given the high prevalence of PA only and the negative outcomes associated with PA only, future research might profitably attempt to study PA only and evaluate whether diagnostic criteria or symptom thresholds for PD should be modified to improve differentiation between pathological and normal panic experiences.

An innovation of the NCS-R was the use of a fully structured version of the PDSS to assess clinical severity. Al-

though lower than in clinical samples, 86.3% of respondents with PD-AG and 45.3% to 46.1% of those with PA-AG and PD only were in the clinically important range on the PDSS. A related finding is that clinical severity assessed in the PDSS and role impairment assessed in the SDS appear to be influenced nearly as much by AG (PA-AG vs PA only) as by PD (PD only vs PA only). This finding is consistent with prior findings that AG is associated with panic severity, anticipatory anxiety, and cognitive correlates of severity^{41,47-49} and our finding that AG is more common among people with PD than PA. Also consistent with this pattern is the higher average lifetime number of PAs among respondents with vs those without AG in both the PA and PD samples. One possible interpretation of this pattern is that AG is a severity marker of panic, although this is at least superficially inconsistent with the notion in previous paragraphs that AG is distinct from PD disorder. Another possibility is that AG has a direct effect on impairment.

The treatment results are consistent with previous NCS-R reports that most people with PD eventually obtain treatment,²³ that most active cases receive treatment in a given year,⁵⁰ and that most current treatment (45%-60% across the 3 PD and/or AG subgroups) fails to meet basic treatment guidelines.⁵⁰ The latter result is all the more striking in that our definition of treatment quality is liberal. For example, no distinction was made among psychotherapies despite much more evidence for the effectiveness of some types of psychotherapy than others in treating panic,⁵¹⁻⁵³ nor was a distinction made among antidepressants or anxiolytics despite much more evidence for the effectiveness of some than others.^{54,55} In interpreting the finding that many patients fail to receive guideline-concordant treatment, some patients were so classified because they dropped

out of treatment prematurely rather than because treatment providers delivered inappropriate care. Both problems need to be addressed in future practice-oriented research.

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