ILL: 77847090

Call Number: v.61-(2000-)

Location:

Maxcost: $25IFM

DateReq: 5/18/2011

Date Rec: 5/19/2011

Borrower: GWC

☐ Yes ☐ No ☐ Conditional

Request Type:

Source: ILLiad

LenderString: *GMA,FTU,FCM,EBC,EBC

OCLC Number: 3661773

Affiliation: Free Lender/LVIS/Lyra/Gold/Soline/So6/Galileo/Arche

Staff Email: ill@westga.edu

Billing Notes: fein 586002055; IFM preferred

N/C

Title: The Journal of clinical psychiatry.

Uniform Title:

Author:

Edition:

Imprint: [Memphis, Tenn., Physicians Postgraduate Press]

Article: Grant, Bridget F: The Epidemiology of DSM-IV Panic Disorder and Agoraphobia in the United States: Results From the National Epidemiologic Survey on Alcohol and Related Conditions

Vol: 67 No.: 3 Pages: 363- Date: 2006

Dissertation:

Verified: <TN:84762><ODYSSEY:206.107.42.161/ILL> OCLC 0160-6689

Borrowing Notes: ARIEL IP 160.10.98.75; ODYSSEY 206.107.42.161

ShipTo: ILL/Library/University of West Georgia/1601 Maple Street/Carrollton GA 30118

E-delivery Addr: 678-839-6511; ARIEL IP 160.10.98.75

Ship Via: Best Method

ShipVia: ~~Best Method~~ Ariel

Return To:

Monroe F. Swilley, Jr. Library ILL
Mercer University
3001 Mercer University Dr
Atlanta GA 30341

Ship To:

ILL
Library
University of West Georgia
1601 Maple Street
Carrollton GA 30118

NeedBy: 6/17/2011

Borrower: GWC

ILL: 77847090 Lender: GMA

Req Date: 5/18/2011 OCLC #: 3661773

Patron:

Author:

Title: **The Journal of clinical psychiatry.**

Article: Grant, Bridget F: The Epidemiology of DSM-IV Panic Disorder and Agoraphobia in the United States: Results From the National Epidemiologic

Vol.: 67 No.: 3

Date: 2006 Pages: 363-

Verified: <TN:84762><ODYSSEY:206.107.42.161/I

Maxcost: $25IFM Due Date:

Lending Notes:

Bor Notes: ARIEL IP 160.10.98.75; ODYSSEY 206.107.42.161

The Epidemiology of DSM-IV Panic Disorder and Agoraphobia in the United States: Results From the National Epidemiologic Survey on Alcohol and Related Conditions

Bridget F. Grant, Ph.D., Ph.D.; Deborah S. Hasin, Ph.D.; Frederick S. Stinson, Ph.D.; Deborah A. Dawson, Ph.D.; Rise B. Goldstein, Ph.D., M.P.H.; Sharon Smith, Ph.D.; Boji Huang, M.D., Ph.D.; and Tulshi D. Saha, Ph.D.

Objective: To present nationally representative data on the prevalence, correlates, and comorbidity of DSM-IV panic disorder (PAN), including the differentiation between panic with agoraphobia (PDA) and without agoraphobia (PDWA) and agoraphobia without a history of panic disorder (AG).

Method: The data were derived from the 2001–2002 National Epidemiologic Survey on Alcohol and Related Conditions (N = 43,093). Prevalence, correlates, and comorbidity of PAN, PDA, and PDWA with Axis I and II disorders were determined.

Results: Prevalences of 12-month and lifetime PAN were 2.1% and 5.1%. Rates of 12-month and lifetime PDWA were 1.6% and 4.0%, exceeding those of 12-month (0.6%) and lifetime (1.1%) PDA. Rates of 12-month and lifetime AG were extremely low, 0.05% and 0.17%. Being female, Native American, middle-aged, widowed/separated/divorced, and of low income increased risk, while being Asian, Hispanic, or black decreased risk for PAN, PDA, and PDWA. Individuals with PDA were more likely to seek treatment and had earlier ages at onset and first treatment, longer episodes, and more severe disability, impairment, panic symptomatology, and Axis I and II comorbidity than those with PDWA.

Conclusion: PDA may be a more severe variant of PAN. Overrepresentation of PDA in treatment settings reflects increased treatment seeking and the severity of PDA relative to PDWA. The very low prevalence of AG leaves open questions about the meaning of the disorder as a distinct clinical entity as defined in the DSM-IV.

(J Clin Psychiatry 2006;67:363–374)

Received June 2, 2005; accepted Aug. 30, 2005. From the Laboratory of Epidemiology and Biometry, Division of Clinical and Biological Intramural Research, National Institute on Alcohol Abuse and Alcoholism, National Institutes of Health, Bethesda, Md. (Drs. Grant, Stinson, Dawson, Goldstein, Smith, Huang, and Saha); and the Department of Epidemiology and Psychiatry, Columbia University and New York State Psychiatric Institute, New York, N.Y. (Dr. Hasin).

The National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) is funded by the National Institute on Alcohol Abuse and Alcoholism (NIAAA), with supplemental support from the National Institute on Drug Abuse. Dr. Hasin acknowledges support from NIAAA grant K05 AA014223, National Institute on Drug Abuse grant R01DA018652, and the New York State Psychiatric Institute.

The authors report no other financial affiliation relevant to the subject of this article.

The views and opinions expressed in this report are those of the authors and should not be construed to represent the views of any of the sponsoring organizations, agencies, or the U.S. government.

Corresponding author and reprints: Bridget F. Grant, Ph.D., Ph.D., Laboratory of Epidemiology and Biometry, Room 3077, Division of Intramural Clinical and Biological Research, National Institute on Alcohol Abuse and Alcoholism, National Institutes of Health, M.S. 9304, 5635 Fishers Lane, Bethesda, MD 20892-9304 (e-mail: bgrant@willco.niaaa.nih.gov).

Panic disorder is characterized by unexpected repeated episodes of intense fear accompanied by physical symptoms that may include chest pain, heart palpitations, shortness of breath, dizziness, or abdominal distress, as well as intense interepisode anxiety. The disorder is chronic, recurring, and disabling and is comorbid with many other psychiatric disorders.[1–7] Agoraphobia, the fear of being in places or situations from which escape might be difficult or help unavailable in the event of panic attacks or symptoms, has been linked with panic disorder since the early versions of modern nomenclatures.[8–11] In those earlier writings, agoraphobia was described as a consequence of recurrent panic attacks. According to that concept, agoraphobia accompanying panic disorder indicates a more severe form of panic disorder and, given the specific nature of the fear, would seldom occur among those without a history of panic disorder. Empirically, however, the nature of the relationship between panic disorder and agoraphobia is not well understood, and thus

current and accurate information on the epidemiology and comorbidity of panic disorder and agoraphobia in the United States is needed.

The DSM-III-R[12] and DSM-IV[13] included 3 relevant categories: panic disorder with agoraphobia (PDA), panic disorder without agoraphobia (PDWA), and agoraphobia without a history of panic disorder (AG). No large-scale epidemiologic survey conducted in the United States has reported separate rates for DSM-IV PDA, PDWA, and AG. Five surveys from other countries[14–20] combined PDA and PDWA, showing 12-month rates of 0.8% to 2.3% and lifetime rates of 2.1% to 3.9%. One survey[15] reported rates of 12-month PDA (0.9%) and PDWA (1.3%). International epidemiologic studies using DSM-III-R criteria also combined PDA and PDWA, showing slightly higher rates than DSM-IV criteria for 12-month (1.1%–2.6%) and lifetime (2.3%–4.5%) panic disorder,[21–25] similar to current and lifetime U.S. rates of 2.3% and 3.5% reported in the National Comorbidity Survey (NCS)[26] conducted from 1990 to 1992.

Concerning DSM-IV AG, reliable, semistructured clinician assessments in an Italian community sample indicated rates of 0.1% for 12-month and 0.4% for lifetime disorders.[17,18] These low rates are consistent with samples of AG in U.S. patients[3,4,27] and families participating in genetics studies.[28] In contrast, many epidemiologic surveys showed surprisingly high rates of DSM-III-R or DSM-IV 6-month/12-month (1.6%–5.1%) and lifetime (3.4%–5.3%) rates of AG.[15,20,22,23,25,26]

To better understand these unexpectedly high rates of AG, we considered the assessment methodology shared by the surveys producing the high rates. This methodology was found in the World Health Organization-Composite International Diagnostic Interview (WHO-CIDI),[29] used in 2 of the studies[15,23]; the University of Michigan (UM)-CIDI,[30] used in 2 other studies[22,25,26]; and the Munich-CIDI,[31] used in 1 study.[20] All included items covering typical agoraphobic situations (e.g., crowds, tunnels/bridges, public transportation). However, none included questions asking if the situations were feared due to anticipated difficulty of escape or gaining help in the case of a panic attack or symptom, the aspect of agoraphobia that primarily differentiates it from specific phobia of the same situations.[32–35] Thus, these studies may have combined cases of true agoraphobia and specific phobia, artifactually inflating rates of AG. This possibility is supported by clinical reappraisal studies showing that 62% to 95% of individuals diagnosed with AG by the WHO-CIDI,[15,36] UM-CIDI,[37] and Munich-CIDI[38] and the direct predecessor of these instruments, the Diagnostic Interview Schedule (DIS),[39] were found on reinterview to be rediagnosed as representing cases of specific phobia.[40,41]

In addition to the possibility of overestimated rates, since the early 1980s only 2 epidemiologic surveys that included DSM-III-R or DSM-IV panic disorder and agoraphobia[15,25] have presented information on an array of sociodemographic characteristics. Further, none examined onset, course, or treatment seeking or comorbidity with specific disorders, especially personality disorders. Thus, a gap in knowledge exists concerning accurate and detailed information about the prevalence, correlates, course, treatment seeking, and comorbidity of panic disorder and agoraphobia.

This gap in knowledge affects a number of important areas, 2 in particular. The first concerns policy, as the information is needed in order to initiate accurate evaluation of treatment needs and the economic costs of the disorders. The second concerns etiologic research, in particular molecular genetics studies. In these studies, phenotype choice is crucial to the success of the study, and investigators have explicitly addressed the uncertainty in characterizing probands and relatives as affected if they have PDA, PDWA, or AG,[28] especially in light of the epidemiologic survey findings.[42] The concept of agoraphobia as an indicator of severe panic disorder would be supported by showing that compared to PDWA, PDA is less common and has earlier onset, more severe panic symptomatology, and greater comorbidity, disability, chronicity, and likelihood of treatment. Further support would arise by finding very low rates of AG in the general population.

The National Epidemiologic Survey on Alcohol and Related Conditions (NESARC)[43,44] was designed, in part, to overcome the limitations of previous epidemiologic surveys on panic disorder and agoraphobia and to provide accurate information on the epidemiology and comorbidity of panic disorder, PDA, PDWA, and AG. The large NESARC sample size (N = 43,093) and excellent response rate (81.0%) allows precise estimation of rates of rare disorders, detailed examination of these disorders across a range of sociodemographic and clinical correlates, and a more detailed analysis of comorbidity.

METHOD

Sample

The 2001–2002 NESARC is a representative sample of the United States conducted by the National Institute on Alcohol Abuse and Alcoholism (NIAAA).[43,44] The NESARC target population was the civilian population, aged 18 years and older, residing in households and group quarters. Face-to-face interviews were conducted with 43,093 respondents. The survey response rate was 81%. Blacks, Hispanics, and young adults (aged 18–24 years) were oversampled, with data adjusted for oversampling and household- and person-level nonresponse. The weighted data were then adjusted to represent the U.S. civilian population based on the 2000 census.

DSM-IV Diagnostic Interview

The diagnostic interview used to generate diagnoses was the NIAAA Alcohol Use Disorder and Associated Disabilities Interview Schedule-DSM-IV Version (AUDADIS-IV).[45] This structured diagnostic interview, designed for lay interviewers, was developed to advance measurement of substance use and mental disorders in large-scale surveys.

Panic Disorder and Agoraphobia

An episode of panic disorder (PAN) was diagnosed when recurrent unexpected panic attacks occurred and at least 1 attack was followed by at least 1 month of persistent concern about having additional attacks, worry about the implications/consequences of the attacks, or a significant change in behavior related to the attacks.[13] In the AUDADIS-IV, panic attacks were operationalized as discrete periods of intense fear/discomfort in which at least 4 of the 13 DSM-IV panic attack symptoms developed abruptly and reached a peak within 10 minutes. Diagnoses of PDA also required the presence of agoraphobia, while diagnoses of PDWA required the absence of agoraphobia. Consistent with the DSM-IV, agoraphobia was defined as anxiety about being in situations from which escape might be difficult/embarrassing or in which help might not be available in the event of having an unexpected or situationally predisposed panic attack or panic-like symptoms and avoiding such situations, enduring them with marked distress/anxiety about having a panic attack or panic-like symptoms, or requiring the presence of a companion. *Unexpected* panic attack is defined as in DSM-IV, i.e., not associated with a situational trigger, as is *situationally predisposed*, i.e., likely although not invariably occurring in the presence of a situational trigger.

Diagnoses of AG required the presence of agoraphobia (defined above) related to the fear of developing panic attacks or symptoms that might be incapacitating or embarrassing in the corresponding situations. Diagnoses of AG also required that the full criteria for panic disorder not be met on a lifetime basis. Among respondents with lifetime PDA, PDWA, and AG thus defined, respondents with at least 1 episode during the year before the interview were classified with 12-month diagnoses. All PDA, PDWA, and AG diagnoses required that the clinical significance criterion of the DSM-IV (p. 7)[13] be met. Unlike other instruments used in epidemiologic surveys,[27–31,46] the diagnoses of PDA, PDWA, and AG were primary (or independent) diagnoses[44]; substance-induced disorders or those due to medical conditions were excluded (DSM-IV, p. 192).[13]

Other Psychiatric Disorders

The AUDADIS-IV also assessed 3 other DSM-IV anxiety disorders—social phobia, specific phobia, and generalized anxiety disorder—and 4 major mood disorders, namely, dysthymia and major depressive, bipolar I, and bipolar II disorders. Diagnosis of all of these disorders followed DSM-IV criteria, required the clinical significance criteria to be met, and ruled out substance-induced episodes or those due to a medical condition. Agoraphobic fears (e.g., being in a crowd, standing in a line, closed spaces, bridges, buses, trains) not involving fear of difficulty in escaping or getting help in the event of a panic attack or symptoms were diagnosed as specific phobia if they met all other criteria for specific phobia.

AUDADIS-IV questions operationalize DSM-IV criteria for alcohol and drug-specific abuse and dependence for 10 drug classes[44] (aggregated in this report). Consistent with DSM-IV, 12-month and lifetime AUDADIS-IV diagnoses of alcohol abuse required at least 1 of the 4 criteria for abuse either in the 12-month period preceding the interview or previously. AUDADIS-IV lifetime alcohol dependence diagnoses required at least 3 of the 7 DSM-IV criteria for dependence during the past year or prior. For prior diagnoses of alcohol dependence, at least 3 criteria must have occurred within a 1-year period, following DSM-IV. Drug abuse and dependence and nicotine dependence[47] diagnoses used the same algorithms.

AUDADIS-IV assessments of DSM-IV personality disorders (PDs) have been described in detail previously.[48,49] These include avoidant, dependent, obsessive-compulsive, paranoid schizoid, histrionic, and antisocial PDs. DSM-IV PD diagnoses require evaluating long-term patterns of functioning. AUDADIS-IV PD diagnoses were made accordingly. To receive a DSM-IV PD diagnosis, respondents needed the required number of DSM-IV symptoms for the specific PD, with at least 1 symptom causing distress and/or social or occupational dysfunction. Diagnoses of antisocial personality disorder required the specified number of DSM-IV symptoms for conduct disorder before age 15 and adult antisocial personality disorder since age 15.

As reported elsewhere, test-retest reliability of panic disorder and agoraphobia diagnoses was fair to good ($\kappa = 0.42–0.52$),[50] and reliability ($\kappa > 0.74$)[50–53] and validity[54–62] were good to excellent for substance use disorders. Reliability was fair to good for mood and other anxiety disorders ($\kappa = 0.40–0.60$) and PDs ($\kappa = 0.40–0.67$).[50] In addition, validity of PDA, PDWA, and AG diagnoses was assessed using the 12-Item Short Form Health Survey, version 2 (SF-12v2), a reliable and valid impairment measure in population surveys.[63] Controlling for sociodemographic factors and other mental disorders, both PDA and PDWA showed highly significant relationships ($p < .00001$) with domains measured by SF-12v2 scales (Mental Health Summary, Social Functioning, Role Emotional Functioning, Mental Health). Respondents with PDA demonstrated significantly greater ($p < .03$ to $.0001$) disability and mental impairment on all 4 SF-12v2 scales than respondents with PDWA. Similar relation-

Table 1. Prevalence of 12-Month and Lifetime DSM-IV PAN, PDA, and PDWA by Sociodemographic Characteristics[a]

	PAN				PDA				PDWA			
	12-Month (N = 907)[b]		Lifetime (N = 2,116)		12-Month (N = 254)		Lifetime (N = 463)		12-Month (N = 635)		Lifetime (N = 1,653)	
Characteristic	%	SE	%	SE	%	SE	%	SE	%	SE	%	SE
Total	2.1	0.09	5.1	0.15	0.6	0.05	1.1	0.07	1.6	0.07	4.0	0.13
Sex												
Male	1.3	0.10	3.3	0.17	0.3	0.05	0.7	0.08	1.0	0.08	2.6	0.15
Female	2.9	0.15	6.7	0.23	0.8	0.07	1.4	0.10	2.1	0.13	5.3	0.21
Race/ethnicity												
White	2.3	0.11	5.6	0.18	0.7	0.06	1.2	0.08	1.7	0.09	4.4	0.16
Black	1.5	0.18	3.5	0.30	0.4	0.08	0.8	0.12	1.1	0.15	2.7	0.26
Native American	4.6	0.89	9.3	0.38	1.2	0.45	2.5	0.69	3.5	0.83	6.8	1.17
Asian/Pacific Islander	0.7	0.24	2.1	0.36	0.1	0.06	0.3	0.15	0.7	0.23	1.8	0.33
Hispanic	1.6	0.18	3.6	0.33	0.3	0.09	0.7	0.17	1.3	0.14	2.9	0.25
Age, y												
18–29	2.2	0.19	3.9	0.26	0.6	0.10	0.9	0.13	1.6	0.17	3.0	0.22
30–44	2.6	0.19	6.0	0.27	0.8	0.10	1.4	0.14	1.8	0.14	4.6	0.22
45–64	2.3	0.16	6.1	0.26	0.6	0.07	1.3	0.12	1.7	0.14	4.9	0.25
65+	0.8	0.12	2.8	0.24	0.1	0.03	0.3	0.07	0.7	0.12	2.5	0.24
Marital status												
Married/cohabiting	1.9	0.10	4.9	0.18	0.5	0.05	1.0	0.08	1.4	0.09	3.9	0.16
Widowed/separated/divorced	2.8	0.21	6.6	0.31	0.6	0.09	1.3	0.15	2.2	0.20	5.4	0.29
Never married	2.1	0.19	4.3	0.27	0.6	0.11	1.1	0.14	1.5	0.16	3.2	0.22
Education												
Less than high school	2.4	0.22	5.0	0.37	0.6	0.10	1.2	0.17	1.8	0.21	3.8	0.31
High school	2.0	0.16	5.2	0.26	0.6	0.09	1.2	0.12	1.4	0.13	4.1	0.23
College or higher	2.1	0.11	5.0	0.18	0.5	0.05	1.0	0.08	1.6	0.10	4.0	0.17
Personal income, $/y												
0–19,999	2.8	0.15	6.2	0.24	0.7	0.08	1.4	0.12	2.1	0.13	4.7	0.21
20,000–34,999	1.7	0.15	4.3	0.26	0.5	0.08	0.8	0.11	1.2	0.13	3.5	0.24
35,000–69,999	1.5	0.16	4.2	0.25	0.5	0.09	0.8	0.11	1.0	0.14	3.4	0.24
70,000+	0.8	0.17	3.3	0.43	0.1	0.03	0.5	0.16	0.7	0.16	2.8	0.39
Urbanicity												
Urban	2.2	0.10	5.1	0.17	0.6	0.05	1.1	0.08	1.6	0.07	4.0	0.15
Rural	2.0	0.18	5.0	0.32	0.5	0.09	1.0	0.13	1.6	0.08	4.0	0.30
Region												
Northeast	2.4	0.19	5.6	0.37	0.8	0.12	1.4	0.17	1.6	0.14	4.2	0.35
Midwest	2.2	0.19	5.3	0.33	0.6	0.10	1.2	0.15	1.5	0.15	4.2	0.29
South	2.0	0.14	4.6	0.24	0.5	0.07	0.9	0.10	1.5	0.12	3.7	0.22
West	2.0	0.20	5.1	0.31	0.4	0.90	1.0	0.14	1.6	0.18	4.1	0.26

[a]Percentages reported here are based on weighted data.
[b]Based on unweighted data.
Abbreviations: PAN = panic disorder (with and without agoraphobia), PDA = panic disorder with agoraphobia, PDWA = panic disorder without agoraphobia.

ships have been found between other AUDADIS-IV anxiety, mood, and personality disorders and SF-12v2 domains.[44,48,49,54,64]

Statistical Analyses

Weighted means, medians, and cross-tabulations were computed to compare PDA and PDWA groups for age at onset, course, severity of panic symptomatology, impairment, and treatment seeking. Odds ratios (ORs) derived from linear logistic regression analyses indicated bivariate associations between lifetime PAN, PDA, and PDWA and (1) sociodemographic correlates and (2) other psychiatric disorders, adjusted for sociodemographic factors. Two-sided t tests were used to compare beta coefficients (associated with ORs) between PDA and PDWA and each other psychiatric disorder. Prevalences and associations for PAN allow comparison with other epidemiologic surveys that combined PDA and PDWA. Hazard rates reflecting the cumulative risk of PDA and PDWA onset at specific ages among the population at risk at those ages were calculated using standard life table methods.[65] Standard errors and 95% confidence intervals were estimated using SUDAAN,[66] which adjusts for characteristics of complex sample surveys.

RESULTS

Prevalence and Sociodemographic Characteristics

Overall, 12-month and lifetime prevalences of PAN were 2.1% and 5.1%, with rates of PDWA exceeding those of PDA on a 12-month (1.6% vs. 0.6%) and lifetime basis (4.0% vs. 1.1%) (Table 1). Rates of AG (12-month, 0.05%; lifetime, 0.17%) were extremely low, precluding further analyses due to precision concerns.

Table 2. Odds Ratios (ORs) of Lifetime DSM-IV PAN, PDA, and PDWA and Sociodemographic Characteristics

	PAN		PDA		PDWA	
Characteristic	OR	95% CI	OR	95% CI	OR	95% CI
Sex						
Male	0.5	0.42 to 0.54	0.5	0.42 to 0.55	0.5	0.37 to 0.63
Female	1.0		1.0		1.0	
Race/ethnicity						
White	1.0		1.0		1.0	
Black	0.6	0.50 to 0.74	0.6	0.48 to 0.73	0.7	0.50 to 0.97
Native American	1.7	1.23 to 2.39	1.6	1.07 to 2.29	2.1	1.19 to 3.85
Asian/Pacific Islander	0.4	0.26 to 0.51	0.4	0.27 to 0.57	0.3	0.10 to 0.70
Hispanic	0.6	0.52 to 0.77	0.7	0.54 to 0.79	0.6	0.36 to 0.95
Age, y						
18–29	1.4	1.14 to 1.74	1.2	0.96 to 1.55	2.8	1.66 to 4.80
30–44	2.2	1.82 to 2.70	1.9	1.52 to 2.34	4.5	2.81 to 7.26
45–64	2.3	1.86 to 2.75	2.0	1.61 to 2.50	4.0	2.50 to 6.39
65+	1.0		1.0		1.0	
Marital status						
Married/cohabiting	1.0		1.0		1.0	
Widowed/separated/divorced	1.4	1.24 to 1.54	1.4	1.23 to 1.59	1.3	0.96 to 1.67
Never married	0.9	0.74 to 1.01	0.8	0.69 to 0.95	1.1	0.82 to 1.47
Education						
Less than high school	0.9	0.83 to 1.17	0.9	0.77 to 1.12	1.2	0.87 to 1.65
High school	1.0	0.92 to 1.17	1.0	0.89 to 1.16	1.2	0.91 to 1.48
College or higher	1.0		1.0		1.0	
Personal income, $/y						
0–19,999	1.9	1.42 to 2.55	1.7	1.26 to 2.35	2.7	1.46 to 5.18
20,000–34,999	1.3	0.96 to 1.75	1.2	0.90 to 1.71	1.6	0.80 to 3.08
35,000–69,999	1.3	0.95 to 1.69	1.2	0.88 to 1.64	1.6	0.83 to 3.08
70,000+	1.0		1.0		1.0	
Urbanicity						
Urban	1.0		1.0		1.0	
Rural	1.0	0.88 to 1.20	1.0	0.84 to 1.20	1.1	0.82 to 1.54
Region						
Northwest	1.1	0.91 to 1.34	1.0	0.82 to 1.27	1.5	0.98 to 2.14
Midwest	1.1	0.88 to 1.27	1.0	0.84 to 1.24	1.2	0.80 to 1.80
South	0.9	0.77 to 1.08	0.9	0.76 to 1.09	0.9	0.64 to 1.36
West	1.0		1.0		1.0	

Abbreviations: PAN = panic disorder (with and without agoraphobia), PDA = panic disorder with agoraphobia, PDWA = panic disorder without agoraphobia.

The odds of having PAN, PDA, and PDWA were significantly greater for women than men (Table 2). Compared to whites, Native Americans had significantly greater odds, while the odds for blacks, Hispanics, and Asians were lower than for whites. Compared with respondents aged 65 and older, all others had higher odds of PAN, PDA, and PDWA, with the highest odds found among 30- to 64-year-olds. The odds of PAN and PDA, but not PDWA, were significantly greater among respondents who were widowed/separated/divorced compared with those who were married/cohabiting. Compared with those in the highest income bracket, respondents in the lowest income bracket had significantly greater odds of PAN, PDA, and PDWA.

Age at Onset, Course, Severity, and Treatment Seeking

The mean age at onset of PDA (28.0 years, 95% CI = 22.7 to 29.3 years) was significantly earlier than for PDWA (31.8 years, 95% CI = 31.0 to 32.6 years). The hazard rate curve for PDA (Figure 1) peaked at about age 25 and declined slowly over the next 4 decades of life. The hazard rates for PDWA (Figure 2) peaked at age 35 and remained generally stable until age 50, when the rates began to decline. Respondents with PDA (71.6%, 95% CI = 69.6% to 73.8%) were significantly more likely than those with PDWA (63.2%, 95% CI = 60.2% to 65.3%) to seek treatment, receive medication, and consult a physician or other health professional for their disorders and were significantly younger (31.7 years, 95% CI = 30.2 to 33.2 years vs. 34.5 years, 95% CI = 33.6 to 35.4 years) at mean age at first treatment.

As shown in Table 3, respondents with PDA were significantly more likely than those with PDWA to experience trembling/shaking, feelings of choking, nausea/abdominal distress, feeling dizzy/unsteady/light-headed/faint, chills/hot flashes, depersonalization/derealization, and fear of losing control during their worst panic attack. Respondents with PDA were also significantly more likely to have at least 1 month of persistent concern about having another panic attack, the implications of having another attack, or a significant behavioral change related to the at-

Figure 1. Hazard Rate for Age at Onset of Panic Disorder With Agoraphobia

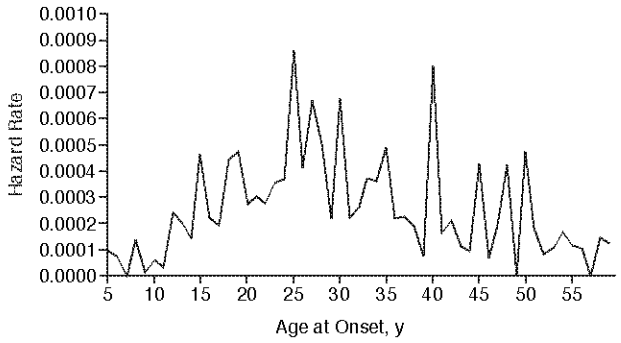

Figure 2. Hazard Rate for Age at Onset of Panic Disorder Without Agoraphobia

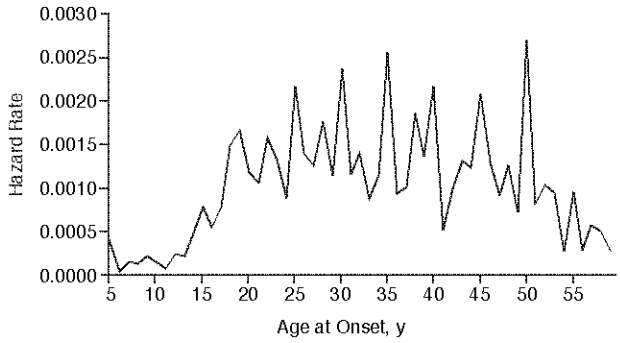

Table 3. Prevalence of Panic Attack Symptoms and Criteria and Distress/Impairment During Worst Panic Attack Among Respondents With PAN, PDA, and PDWA

	PAN		PDA		PDWA		
Criteria/Impairment	%	SE	%	SE	%	SE	p Value[a]
Panic attack symptoms							
Palpitations/pounding heart/accelerated heart rate	94.6	0.55	95.7	0.90	94.5	0.67	.7621
Sweating	73.7	1.15	77.1	2.41	72.8	1.29	.3254
Trembling/shaking	70.5	1.28	77.3	2.67	68.7	1.46	.0066
Sensation of shortness of breath/ smothering	83.9	0.93	86.5	2.02	83.2	1.06	.6927
Feelings of choking	37.7	1.25	47.4	2.72	35.1	1.43	.0002
Chest pain/discomfort	57.3	1.34	58.0	2.77	57.1	1.51	.8724
Nausea/abdominal distress	51.6	1.27	57.8	2.75	50.0	1.49	.0173
Feeling dizzy/unsteady/light-headed/faint	71.4	1.31	79.4	2.27	69.2	1.52	.0003
Derealization/depersonalization	60.6	1.39	71.3	2.60	57.7	1.55	.0001
Fear of losing control/going crazy	58.7	1.25	71.6	2.45	55.2	1.41	.0001
Fear of dying	54.5	1.28	58.7	2.54	53.4	1.49	.0781
Paresthesias	46.5	1.42	49.8	2.90	45.6	1.56	.4021
Chills/hot flashes	64.0	1.38	73.3	2.73	61.6	1.51	.0002
Other panic disorder criteria							
Worry for at least 1 month of having another panic attack	75.0	1.20	84.6	1.99	72.5	1.38	.0001
Worry for at least 1 month about complications/consequences of having another panic attack	64.6	1.38	81.8	2.17	59.9	1.54	.0001
Significant change in behavior related to attacks for at least 1 month	59.9	1.54	75.8	2.45	60.1	1.52	.0001
Distress/impairment							
Were uncomfortable or upset by panic disorder symptoms	79.3	1.08	91.5	1.43	76.1	1.32	.0001
Serious problems getting along with other people	21.1	1.14	37.9	2.73	16.6	1.09	.0001
Serious problems in social/occupational functioning	32.3	1.28	55.5	2.79	26.1	1.29	.0001
Restricted daily activities	44.3	1.44	71.7	2.35	37.0	1.52	.0001
Unable to carry out daily activities	37.8	1.31	63.7	2.52	30.8	1.35	.0001

[a]All statistical comparisons between PDA and PDWA.
Abbreviations: PAN = panic disorder (with and without agoraphobia), PDA = panic disorder with agoraphobia, PDWA = panic disorder without agoraphobia.

tacks than those with PDWA. Compared with respondents with PDWA, those with PDA reported significantly more distress concerning their panic disorder symptoms and were significantly more likely to experience disorder-specific occupational and role dysfunction.

Psychiatric Comorbidity

Associations of PAN, PDA, and PDWA with other psychiatric disorders are shown in Table 4 in the form of ORs adjusted for sociodemographic characteristics. ORs were overwhelmingly positive and statistically significant between PAN, PDA, and PDWA and each specific disorder examined, except for alcohol abuse.

For 12-month and lifetime disorders, adjusted ORs indicated considerably stronger associations for PDA than PDWA. The magnitude of the lifetime association for PDA compared with PDWA was significantly greater for drug dependence, bipolar I disorder, social phobia, specific phobia, generalized anxiety, and each PD except antisocial PD. Similar results were found for 12-month

Table 4. Twelve-Month and Lifetime Odds Ratios of DSM-IV PAN, PDA and PDWA and Other DSM-IV Psychiatric Disorders[a]

	12-Month						Lifetime					
	PAN		PDWA		PDA		PAN		PDWA		PDA	
Other Psychiatric Disorder	OR[b]	95% CI	OR	95 %CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Any alcohol use disorder	2.3	1.9 to 3.0	2.2	1.7 to 2.8	2.7	1.8 to 4.1	2.4	2.2 to 2.7	2.3	2.0 to 2.6	2.5	2.1 to 3.1
Alcohol abuse	1.1	0.7 to 1.5	0.9	0.6 to 1.4	1.5	0.8 to 2.9	1.1	1.0 to 1.3	1.2	1.0 to 1.4	1.0	0.7 to 1.4
Alcohol dependence	3.7	2.8 to 4.8	3.5	2.6 to 4.9	3.6	2.1 to 6.1	3.2	2.9 to 3.6	3.0	2.6 to 3.3	3.6	2.8 to 4.6
Any drug use disorder	4.2	3.1 to 5.6	3.4	2.3 to 4.9	5.6	3.6 to 8.8	3.4	2.9 to 3.9	2.9	2.5 to 3.4	4.4	3.4 to 5.8[c]
Any drug abuse	2.0	1.3 to 3.2	1.6	0.8 to 3.0	3.1	1.6 to 6.1	1.9	1.6 to 2.4	1.9	1.6 to 2.3	1.9	1.3 to 2.7
Any drug dependence	8.3	5.3 to 13.1	6.8	4.1 to 11.5	9.3	4.9 to 17.5	6.3	5.1 to 7.8	4.6	3.7 to 5.8	8.6	6.0 to 12.3[c]
Nicotine dependence	3.5	3.0 to 4.2	3.4	2.7 to 4.2	3.6	2.7 to 4.9	3.0	2.6 to 3.4	2.9	2.5 to 3.3	2.9	2.3 to 3.7
Any mood disorder	9.9	8.1 to 12.0	8.8	7.2 to 10.9	10.7	7.6 to 15.2	6.2	5.5 to 6.9	5.2	4.6 to 5.9	9.2	7.1 to 12.1[c]
Major depression	5.2	4.2 to 6.5	5.4	4.2 to 7.0	4.1	2.8 to 6.0	3.3	2.9 to 3.8	3.2	2.7 to 3.7	3.3	2.5 to 4.3
Dysthymia	5.4	4.0 to 7.3	5.3	3.7 to 7.6	4.5	2.6 to 7.7	3.4	2.8 to 4.2	3.2	2.6 to 4.0	3.2	2.4 to 4.5
Bipolar I	10.3	8.2 to 13.1	8.1	6.0 to 10.9	12.5	8.7 to 18.0	6.7	5.8 to 7.8	5.1	4.2 to 6.1	8.7	6.7 to 11.3[c]
Bipolar II	5.4	3.5 to 8.4	4.9	3.1 to 7.6	5.5	2.9 to 10.4	4.6	3.4 to 6.3	4.1	3.0 to 5.8	4.4	2.7 to 7.2
Any other anxiety disorder	8.1	6.8 to 9.6	5.0	4.0 to 6.1	23.4	15.9 to 34.5[c]	5.9	5.3 to 6.7	3.6	3.2 to 4.1	29.9	21.8 to 39.5[c]
Social phobia	8.6	6.8 to 10.8	3.3	2.4 to 4.5	29.6	21.7 to 40.6[c]	5.7	4.9 to 6.6	2.5	2.1 to 3.0	23.2	18.5 to 29.2[c]
Specific phobia	5.8	4.9 to 6.9	3.6	2.9 to 4.5	16.4	12.5 to 22.2[c]	4.8	4.3 to 5.5	2.8	2.4 to 3.2	19.3	15.3 to 24.4[c]
Generalized anxiety	12.9	10.2 to 16.2	8.7	6.5 to 11.7	19.2	13.6 to 27.3[c]	7.3	6.3 to 8.4	4.8	4.0 to 5.7	13.5	10.2 to 17.7[c]
Any personality disorder[d]	5.9	5.0 to 6.9	4.3	3.6 to 5.3	12.3	8.9 to 17.2[c]	5.0	4.5 to 5.7	3.8	3.3 to 4.3	10.4	8.2 to 13.2[c]
Avoidant	7.3	5.8 to 9.3	4.1	2.9 to 5.7	16.1	11.6 to 22.4[c]	7.6	6.2 to 9.3	3.9	3.0 to 5.1	17.1	13.0 to 22.8[c]
Dependent	10.9	7.4 to 16.0	4.0	2.3 to 6.9	27.3	16.4 to 45.4[c]	12.2	8.3 to 18.0	3.7	2.5 to 5.7	28.9	18.2 to 45.9[c]
Obsessive-compulsive	4.5	3.7 to 5.4	3.5	2.7 to 4.6	6.8	5.2 to 8.9[c]	4.2	3.7 to 4.8	3.2	2.7 to 3.8	7.2	5.8 to 9.0[c]
Paranoid	6.3	5.1 to 8.0	4.6	3.4 to 6.2	10.7	8.1 to 14.1[c]	5.9	5.0 to 7.1	4.0	3.2 to 5.0	10.5	8.3 to 13.2[c]
Schizoid	5.9	4.7 to 7.4	3.7	2.7 to 5.1	11.8	8.8 to 16.1[c]	5.2	4.3 to 6.2	3.3	2.6 to 4.1	10.0	7.7 to 13.0[c]
Histrionic	5.0	3.8 to 6.6	3.9	2.8 to 5.5	7.1	4.5 to 11.2	6.0	4.8 to 7.5	4.0	3.1 to 5.2	9.5	6.6 to 13.8[c]
Antisocial	4.7	3.6 to 6.2	4.0	2.9 to 5.6	6.0	4.0 to 9.0	4.7	3.8 to 5.7	3.9	3.2 to 4.9	5.5	4.0 to 7.5

[a]The ORs represent the odds of having the specific comorbid disorder among individuals with PAN (or PDA or PDWA) relative to the odds of having the specific comorbid disorder among individuals without PAN (or PDA or PDWA).
[b]ORs adjusted for age, sex, race/ethnicity, marital status, education, income, urbanicity, and geographic region.
[c]$p < .001$, difference between PDA and PDWA.
[d]Personality disorders assessed on a lifetime basis only.
Abbreviations: PAN = panic disorder (with and without agoraphobia), PDA = panic disorder with agoraphobia, PDWA = panic disorder without agoraphobia.

associations, with the exception of drug dependence, bipolar I disorder, and histrionic PD.

Drug dependence was the most strongly associated substance use disorder among respondents with PDA and PDWA, and bipolar I was the most strongly associated mood disorder. All other anxiety disorders were strongly related to PDA. Generalized anxiety disorder was more strongly related to PDWA than were the remaining other anxiety disorders. While PDs and PDWA were associated, there was little variation in the magnitude of the associations. In contrast, stronger and more variable associations were found between PDs and PDA, with odds ratios indicating highly significant relationships with personality disorders, especially avoidant and dependent PDs.

DISCUSSION

Twelve-month and lifetime prevalences of DSM-IV PAN in this general population survey were 2.1% and 5.1%. Twelve-month and lifetime rates of PDA were 0.6% and 1.1%, lower than the corresponding rates of PDWA (1.6% and 4.0%). Twelve-month (0.05%) and lifetime (0.17%) rates of AG were extremely low in this survey, mirroring those found in well-designed, large clinical studies[3,4] in which AG was uncommon, constituting less than 8% of patients with PDA, PDWA, and AG combined.

This study identified population subgroups at greater risk of PAN, PDA, and PDWA, many not identified in previous epidemiologic surveys. The odds of PAN, PDA, and PDWA were greater among women compared with men, a finding consistent with previous surveys. The odds of PAN, PDA, and PDWA were also greater among the 3 youngest age groups compared to the oldest age group and greatest among 30- to 64-year-olds, a finding at variance with the NCS,[25] which found no age differences among individuals with PAN. However, the sample size for PAN (N = 77) in the NCS was small, precluding the assessment of age differences. The hazard results for PDA and PDWA demonstrated an early onset distribution similar to other anxiety disorders. Age-related differential recall or willingness to disclose, or other methodological factors could have played a role in this pattern, although increases in the prevalence of PDA and PDWA in recent cohorts might have occurred. Longitudinal evaluation is necessary to resolve these issues.

The odds of PAN, PDA, and PDWA were also greater among widowed/separated/divorced individuals and among individuals falling within the lowest income bracket. In contrast, the NCS[25] did not find income differ-

ences among individuals with PAN or PDA, and an Australian survey[15] found an increased odds of PDA and PDWA among individuals who were cohabiting relative to those who were never married. However, the numbers of cases of PDA (N = 81) and PDWA (N = 154) in the Australian survey were also small, limiting power to detect differences.

The NESARC provides more precise information on race/ethnic differences in panic disorder than any other source due to the sample size. The findings disclosed greater odds of PAN, PDA, and PDWA among Native Americans compared with whites. Although this was the first survey to examine the odds of these disorders among Native Americans, information on diagnosable mental disorders among Native Americans is scarce and attention to the mental health needs of this group appears warranted. The NCS[25] and an earlier survey[41] did not find race/ethnic differences in the odds of PAN or PDA among blacks, Hispanics, and whites, but the large sample size of the NESARC revealed the lower odds for blacks and Hispanics. That rates of PAN, PDA, and PDWA also were lower among Asians compared with whites represents a new finding. Interestingly, low rates of PD have been found in international studies among Asian samples.[67] Analyses are needed to understand protective factors in these minority groups and whether disparities in treatment for PDA and PDWA among these minorities exist despite lower rates. Research is also critically needed to ascertain the degree to which language bias, differential response patterns, and other cultural factors influenced the rates of panic disorder and agoraphobia among subgroups of the population defined in terms of race/ethnicity.

In the clinical studies noted above,[3,4] the proportion of cases with PDA exceeded those with PDWA. This study of the general population found the reverse. However, clinical and general population findings are reconciled by the fact that, in the NESARC, individuals with PDA were more likely to seek treatment. Further, compared to NESARC cases of PDWA, those with PDA had greater disability, as previously described on all SF-12v2 mental impairment scores, more severe panic symptomatology, longer durations, earlier onsets, and greater Axis I and II comorbidity compared with individuals with PDWA. These results suggest that the overrepresentation of individuals with PDA in clinical samples reflects increased treatment-seeking behavior among severe cases.

A striking finding from this survey was the greater psychiatric comorbidity among individuals with PDA compared to those with PDWA. Prior results on this difference have been unavailable because PAN with and without agoraphobia were combined in past surveys. The results also provide, for the first time, new information on the comorbidity of PAN, PDA, and PDWA and specific Axis I and II disorders, including strong associations with alcohol, drug, and nicotine dependence, in contrast to weaker associations with drug and alcohol abuse. These results highlight the importance of not lumping abuse and dependence together when studying comorbidity and the utility of the DSM-IV system of diagnosing dependence, a disorder with a strong theoretical basis and abundant validity evidence.[58,59,68] The NESARC findings advance knowledge over the Epidemiologic Catchment Area (ECA) survey,[69] which used DSM-III[70] criteria to diagnose panic disorder, agoraphobia, and substance use disorders, and over the NCS,[25,26] NCS-R,[71] and NCS-2,[71] which involved smaller samples and measurement issues in alcohol[72] and drug dependence[73] and major depressive disorder.[74]

Among mood disorders, the magnitude of association with PAN, PDA, and PDWA was much greater for bipolar I disorder than other mood disorders. However, PDA was strongly associated with all other anxiety disorders, whereas PDWA was most strongly related to generalized anxiety disorder. Failure to differentiate PDA and PDWA in prior studies has obscured the relationships between specific mood and other anxiety disorders that relate in important, but different, ways to PDA and PDWA. Determining the reason for these variations in magnitude is important. The information in this report can provide a strong starting point for such investigation.

Information on PDs among U.S. adults was not previously available and is highly relevant to PAN as indicated by clinical studies.[5–7] The magnitudes of the associations were much greater for PDA than PDWA. There was little variability in the strength of associations of specific PDs and PDWA. Consistent with clinical findings,[5–7] 2 Cluster C PDs (dependent and avoidant) showed the strongest associations with PDA, while 2 Cluster A (paranoid and schizoid) and 1 Cluster B (histrionic) PD showed intermediate associations. Future work will address the structure of comorbidity of PDA and PDWA and PDs with a view toward examining a state-trait spectrum.[75]

Perhaps one of the most striking findings of this study compared to other epidemiologic surveys was the very low prevalence of AG. While this is consistent with clinical samples[2–4] and a community survey using clinician assessments,[17,18] most epidemiologic surveys[15,20,22,23,25,26] found considerably higher rates of agoraphobia without panic disorder. As noted above, the key feature differentiating specific phobia of particular situation(s) and agoraphobia involving the same situations is that, in the case of agoraphobia, the fear is due to anticipated difficulty escaping or getting help in case of a panic attack or symptoms. The NESARC instrument, the AUDADIS-IV, includes questions on this key differentiation, while the instruments used in the other general population surveys[19–31,46] do not. Taken together with the results on PDA and PDWA, the results of this study demonstrate support for earlier theories on the etiology of panic disorder.[8–11,76]

These models predicted low rates of AG as well as more severe disability, panic symptomatology, distress, and impairment; earlier onsets; longer duration; and greater treatment seeking and Axis I and II comorbidity among individuals with PDA compared with those with PDWA. These findings suggest that initial panic attacks may be important in the development of PDA or that PDA may represent a more severe variant of PAN. However, there is some evidence that the functional relationship exists between agoraphobia and PAN and not vice versa.[77,78] Thus, there is a need for detailed longitudinal surveys to resolve this issue.[79]

The extremely low prevalence of AG in this study also raises questions about agoraphobia as a distinct clinical entity as defined in the DSM-IV. In the DSM-IV, the diagnostic criteria for AG require the presence of agoraphobia related only to the anxiety and avoidance of developing panic attacks or panic-like symptoms. Although panic attacks and symptoms are experienced by a substantial proportion of individuals with agoraphobia, not all agoraphobic anxiety and avoidance can be attributed to panic or panic-like symptoms. It has been suggested that the current emphasis on panic attacks and symptoms is a potential obstacle to investigating factors other than those related to panic that may give rise to agoraphobic anxiety and avoidance.[79] To examine this issue, we assessed, as part of the present study, a number of other potential motivational factors that might give rise to agoraphobia. Of all respondents who met all other criteria for AG except fear of inability to escape or get help related to panic attack or symptoms, 0.63% reported a different motivation for their agoraphobic fear. These motivations included embarrassment resulting from a physical problem that was not under the respondent's control; embarrassment resulting from eating habits; embarrassment resulting from a physical illness or deformity; separation anxiety; fear of being contaminated by dirt or germs; embarrassment of performing repetitive behaviors in public like counting, checking, or ordering; and the result of thinking about an extremely traumatic event. Inclusion of these individuals among those with AG as defined in the DSM-IV would raise the lifetime prevalence of AG in this study from 0.17% to 0.5% and the prevalence of PDA from 1.1% to 1.4%. Detailed analyses addressing the clinical concept of agoraphobic anxiety as a more generalized response to unsafety is currently ongoing using these NESARC data.

Uncertainty regarding the meaning of the agoraphobia rates in previous epidemiologic surveys has influenced the design of molecular genetics studies of panic disorder. Commenting on the inconsistency between clinical and epidemiologic findings regarding agoraphobia without panic disorder, Gelernter et al.[42] conducted a linkage genome scan for loci predisposing to panic disorder or agoraphobia. Two genomic regions met criteria for suggestive linkage for panic disorder across the sample, while results for agoraphobia arose primarily from a single family. Following Gelernter and colleagues' approach, Hamilton et al.[28] investigated genetic linkage between polymorphisms in the adenosine 2A receptor and panic disorder and/or agoraphobia. This study showed several suggestive LOD (logarithm of the odds) scores for the panic with agoraphobia phenotype, but little evidence of linkage for panic disorder alone or agoraphobia alone, the latter being exceedingly rare. Until agoraphobia without a history of panic is better understood clinically, the above findings suggest a focus on panic disorder with agoraphobia, perhaps in comparison to panic disorder without agoraphobia.

The findings of this study have several implications. With regard to public health, this study has determined the magnitude of PAN, PDA, and PDWA confronting the nation and identified important subgroups of the population at risk for the disorder. This information is critical to the planning of local and national mental health services and the design of prevention and intervention programs. With regard to clinical implications, PDA and PDWA were found to be highly comorbid with substance use, other anxiety, mood, and personality disorders. Comprehensive evaluation of patients with PDWA, and especially PDA, should also include a systematic assessment of these and other comorbid disorders.

Differentiating individuals with PDA and PDWA is important since the 2 main types of nonpharmacologic treatment, exposure treatment and cognitive therapy, may be differentially effective in modifying avoidance and panic attacks, respectively. Awareness of the extent of psychiatric comorbidity among individuals with PDA and PDWA also has important treatment implications. Selective serotonin reuptake inhibitors,[80–84] tricyclic antidepressants,[81,82,85–89] and benzodiazepines[85,86,89–98] are of comparable efficacy in PAN.[1] However, when PAN is associated with comorbid mood and/or other anxiety disorders (as was frequently shown in this study), serotonergic antidepressants have been shown to be more effective than benzodiazepines.[1,80,86,97]

In sum, this study provides the most comprehensive information on the epidemiology of DSM-IV PAN, PDA, and PDWA among U.S. adults to date. Limitations of this cross-sectional survey (e.g., recall bias) are better addressed in longitudinal studies of the general population. Accordingly, the 3-year NESARC Wave 2 now in the field will allow use of Wave 1 results as a platform for prospective investigations regarding the relationship between panic disorder and agoraphobia. Given the seriousness of agoraphobia and panic disorder with agoraphobia, the importance of examining motivational factors other than panic attacks or symptoms that can give rise to agoraphobic anxiety and avoidance cannot be underestimated. This study provides information that will

form the basis for further investigation in a number of directions.

REFERENCES

1. Ballenger JC, Davidson JRT, Lecrubier Y, et al. Consensus statement on panic disorder from the International Consensus Group on Depression and Anxiety. J Clin Psychiatry 1998;59(suppl 8):47–54
2. Goisman RM, Warshaw MG, Peterson LG, et al. Panic, agoraphobia and panic with agoraphobia: data from a multicenter anxiety disorders study. J Nerv Ment Dis 1994;182:72–79
3. Massion AO, Warshaw MG, Keller MB. Quality of life and psychiatric morbidity in panic disorder and generalized anxiety disorder. Am J Psychiatry 1993;150:600–607
4. Dyke IR, Phillips KA, Warshaw MG, et al. Patterns of personality pathology in patients with generalized anxiety disorder, panic with and without agoraphobia, and social phobia. J Personal Disord 2001; 15:60–71
5. Mulder RT, Sellman JD, Joyce PR. The comorbidity of anxiety disorders with personality, depressive, alcohol and drug use disorders. Int Rev Psychiatry 1991;3:253–263
6. Renneberg B, Chambless DL, Gracely EJ. Prevalence of SCID-diagnosed disorders in agoraphobic outpatients. J Anxiety Disord 1992;6:111–118
7. Skodol AE, Oldham JM, Hyler SE, et al. Patterns of anxiety and personality disorder comorbidity. J Psychiatr Res 1995;29:361–374
8. Klein DF. Anxiety reconceptualized. Compr Psychiatry 1980;21: 411–427
9. Klein DF, Klein HM. The nosology, genetics and theory of spontaneous panic and phobia. In: Tyrer P, ed. Psychopharmacology of Anxiety. Oxford, England: Oxford University Press; 1989:163–195
10. Klein DF, Klein HM. The status of panic disorder. Curr Opin Psychiatry 1988;1:177–183
11. Klein DF, Klein HM. The substantive effect of variations in panic measurement and agoraphobia definition. J Anxiety Disord 1989;3:45–56
12. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised. Washington, DC: American Psychiatric Association; 1987
13. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition. Washington, DC: American Psychiatric Association; 1994
14. Alonso J, Angermeyer MC, Bernert S, et al. Prevalence of mental disorders in Europe: results from the European Study of the Epidemiology of Mental Disorders (ESEMeD) project. Acta Psychiatr Scand Suppl 2004: 21–27
15. Andrews G, Slade T. Agoraphobia without a history of panic disorder may be part of the panic disorder syndrome. J Nerv Ment Dis 2002;190: 624–630
16. ESEMeD/MHEDEA Investigators. 12-month comorbidity patterns and associated factors in Europe: results from the European Study of the Epidemiology of Mental Disorders (ESEMeD) project. Acta Psychiatr Scand 2004;109:28–37
17. Faravelli C, Abrardi L, Bartolozzi D, et al. The Sesto Fiorentino study: background, methods and preliminary results. Lifetime prevalence of psychiatric disorders in an Italian community sample using clinical interviewers. Psychother Psychosom 2004;73:216–225
18. Faravelli C, Abrardi L, Bartolozzi D, et al. The Sesto Fiorentino study: point and one-year prevalences of psychiatric disorders in an Italian community sample using clinical interviewers. Psychother Psychosom 2004;73:226–234
19. Jacobi F, Wittchen H-U, Holting C, et al. Prevalence, co-morbidity and correlates of mental disorders in the general population: results from the German Health Interview and Examination Survey (GHS). Psychol Med 2004;34:597–611
20. Meyer C, Rumpf H-J, Hapke U, et al. Lebenszeitprevalenz psychischer sterunger in der erwachsenen Allgemein-bevolkerung: ergebnisse der TACOS studie. Nervenarzt 2000;71:535–542
21. Bijl RV, Ravelli A, Zessen GV. Prevalence of psychiatric disorder in the general population: results of the Netherlands Mental Health Survey and Incidence Survey (NEMESIS). Soc Psychiatry Psychiatr Epidemiol 1998;33:587–595
22. Offord DR, Boyle MH, Campbell D, et al. One-year prevalence of psychiatric disorder in Ontarians 15 to 64 years of age. Can J Psychiatry 1996;41:559–563
23. Kringlen E, Torgersen S, Cramer B. A Norwegian psychiatric epidemiological study. Am J Psychiatry 2001;158:1091–1098
24. Faravelli C, Guerrini B, Degl'Innocenti BG, et al. Epidemiology of anxiety disorders in Florence. Acta Psychiatr Scand 1989;79:308–312
25. Eaton WW, Kessler RC, Wittchen H-U, et al. Panic and panic disorder in the United States. Am J Psychiatry 1994;151:413–420
26. Kessler RC, McGonagle KA, Zhao S, et al. Lifetime and 12-month prevalence of DSM-III-R psychiatric disorders in the United States: results from the National Comorbidity Survey. Arch Gen Psychiatry 1994;51: 8–19
27. Yonkers KA, Bruce SE, Dyke IR, et al. Chronicity, relapse and illness-course of panic disorder, social phobia, and generalized anxiety disorder: findings in men and women from 8 years of follow-up. Depress Anxiety 2003;17:173–179
28. Hamilton SP, Slager SL, de Leon AB, et al. Evidence of genetic linkage between polymorphism in the adenosine 2A receptor and panic disorder. Neuropsychopharmacology 2004;29:558–565
29. World Health Organization. Composite International Diagnostic Interview, Version 2.0. Geneva, Switzerland: World Health Organization; 1997
30. Kessler RC, Wittchen H-U, Abelson F, et al. Methodological studies of the Composite International Diagnostic Interview (CIDI) in the US National Comorbidity Survey (NCS). Int J Methods Psychol Res 1999;7: 33–55
31. Wittchen H-U, Essau CA, von Zerssen D, et al. Lifetime and six-month prevalence of mental disorders in the Munich Follow-Up Study. Eur Arch Psychiatry Clin Neurosci 1992;241:247–258
32. Chapman TF. The epidemiology of fears and phobias. In: Davey GCL, ed. A Handbook of Theory, Research and Treatment. New York, NY: John Wiley & Sons; 1997:415–434
33. Chapman TF, Mannuzza S, Fyer AJ. Epidemiologic and family studies of social phobia. In: Heimber MR, Liebowitz MR, Hope D, et al, eds. Social Phobia: Diagnosis, Assessment and Treatment. New York, NY: Guilford; 1995:163–189
34. Mannuzza S, Fyer AJ, Liebowitz MR, et al. Defining the boundaries of social phobia: its relationship to panic disorder and agoraphobia. J Anxiety Disord 1990;4:41–59
35. Fyer AJ, Klein DF. Agoraphobia, social phobia, and simple phobia. In: Michels R, Cooper AM, Guze SB, eds. Psychiatry, vol. 1. Philadelphia, Pa: Lippincott; 1992:276–302
36. Friend P, Andrews G. Agoraphobia without panic attacks. In: McNaughton N, Andrews G, eds. Anxiety. Dunedin, New Zealand: University of Otago Press; 1990:27–39
37. Sareen J, Chartier M, Kjernisted KD, et al. Comorbidity of phobic disorders with alcoholism in a Canadian community sample. Can J Psychiatry 2001;46:733–740
38. Wittchen H-U, Reed V, Kessler RC. The relationship between agoraphobia and panic in a community sample of young adults. Arch Gen Psychiatry 1998;55:1017–1024
39. Robins LN, Helzer JE, Croughan J, et al. National Institute of Mental Health's Diagnostic Interview Schedule (DIS): its history, characteristics and validity. Arch Gen Psychiatry 1981;38:381–389
40. Horwath E, Lish JD, Johnson J, et al. Agoraphobia without panic: clinical reappraisal of an epidemiologic finding. Am J Psychiatry 1993;150: 1496–1501
41. Weissman MM, Merikangas KR. The epidemiology of anxiety and panic disorders: an update. J Clin Psychiatry 1986;47(6, suppl):11–17
42. Gelernter J, Bonvicini K, Page G, et al. Linkage genome scan for loci predisposing to panic disorder or agoraphobia. Am J Med Genet 2001; 105:548–557
43. Grant BF, Moore TC, Shepard J, et al. Source and Accuracy Statement, Wave 1 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC). Available at: http://www.niaaa.census.gov/pdfs/source_and_accuracy_statement.pdf. Access verified January 10, 2006
44. Grant BF, Stinson FS, Dawson DA, et al. Prevalence and co-occurrence of substance use disorders and independent mood and anxiety disorders: results from the National Epidemiologic Survey on Alcohol and Related Conditions. Arch Gen Psychiatry 2004;61:807–816
45. Grant BF, Dawson DA, Hasin DS. The Alcohol Use Disorder and Associated Disabilities Interview Schedule-DSM-IV Version. Bethesda, MD:

National Institute on Alcohol Abuse and Alcoholism; 2001
46. Alonso J, Angermeyer MC, Bernert S, et al. Sampling and methods of the European Study of the Epidemiology of Mental Disorders (ESEMeD) project. Acta Psychiatr Scand Suppl 2004:8–20
47. Grant BF, Hasin DS, Chou SP, et al. Nicotine dependence and psychiatric disorders in the United States: results from the national epidemiologic survey on alcohol and related conditions. Arch Gen Psychiatry 2004;61:1107–1115
48. Grant BF, Hasin DS, Stinson FS, et al. Prevalence, correlates, and disability of personality disorders in the United States: results from the National Epidemiologic Survey on Alcohol and Related Conditions. J Clin Psychiatry 2004;65:948–958
49. Grant BF, Hasin DS, Stinson FS, et al. Co-occurrence of DSM-IV personality disorders in the US: results from the National Epidemiologic Survey on Alcohol and Related Conditions. Compr Psychiatry 2005; 46:1–5
50. Grant BF, Dawson DA, Stinson FS, et al. The Alcohol Use Disorder and Associated Disabilities Interview Schedule-IV (AUDADIS-IV): reliability of alcohol consumption, tobacco use, family history of depression and psychiatric diagnostic modules in a general population sample. Drug Alcohol Depend 2003;71:7–16
51. Canino GJ, Bravo M, Ramfrez R, et al. The Spanish Alcohol Use Disorder and Associated Disabilities Interview Schedule (AUDADIS): reliability and concordance with clinical diagnoses in a Hispanic population. J Stud Alcohol 1999;60:790–799
52. Grant BF, Harford TC, Dawson DA, et al. The Alcohol Use Disorder and Associated Disabilities Interview schedule (AUDADIS): reliability of alcohol and drug modules in a general population sample. Drug Alcohol Depend 1995;39:37–44
53. Vrasti R, Grant BF, Chatterji S, et al. The reliability of the Romanian version of the alcohol module of the WHO Alcohol Use Disorder and Associated Disabilities Interview Schedule-Alcohol/Drug-Revised (AUDADIS-ADR). Eur Addict Res 1997;40:89–97
54. Compton WM, Grant BF, Colliver JD, et al. Prevalence of marijuana use disorders in the United States: 1991–1992 and 2001–2002. JAMA 2004;291:2114–2121
55. Cottler LB, Grant BF, Blaine J, et al. Concordance of DSM-IV alcohol and drug use disorder criteria and diagnoses as measured by AUDADIS-ADR, CIDI and SCAN. Drug Alcohol Depend 1997;47: 195–205
56. Grant BF, Dawson DA, Stinson FS, et al. The 12-month prevalence and trends in DSM-IV alcohol abuse and dependence: United States, 1991–1992 and 2001–2002. Drug Alcohol Depend 2004;74:223–234
57. Hasin DS, Paykin A. Alcohol dependence and abuse diagnoses: concurrent validity in a nationally representative sample. Alcohol Clin Exp Res 1999;23:144–150
58. Hasin DS, Muthen B, Grant BF. The dimensionality of DSM-IV alcohol abuse and dependence: factor analysis in a clinical sample. Drug Alcohol Depend 1993;88:10079–11090
59. Hasin DS, Schuckit MA, Martin CS, et al. The validity of DSM-IV alcohol dependence: what do we know and what do we need to know? Alcohol Clin Exp Res 2003;27:244–252
60. Nelson CB, Rehm J, Ustun B, et al. Factor structure of DSM-IV substance disorder criteria endorsed by alcohol, cannabis, cocaine and opiate users: results from the World Health Organization Reliability and Validity Study. Addiction 1999;94:843–855
61. Pull CB, Saunders JB, Mavreas V, et al. Concordance between ICD-10 alcohol and drug use disorder criteria and diagnoses as measured by the AUDADIS-ADR, CIDI and SCAN: results of a cross-national study. Drug Alcohol Depend 1997;47:207–216
62. Ustun B, Compton W, Mager D, et al. WHO Study on the reliability and validity of the alcohol and drug use disorder instruments: overview of methods and results. Drug Alcohol Depend 1997;47:161–169
63. Ware JE, Kosinski M, Turner-Bowker DM, et al. How to Score Version 2 of the SF-12 Health Survey. Lincoln, RI: Quality Metric; 2002
64. Grant BF, Stinson FS, Hasin DS, et al. Immigration and lifetime prevalence of DSM-IV psychiatric disorders among Mexican Americans and non-Hispanic whites in the United States: results from the National Epidemiologic Survey on Alcohol and Related Conditions. Arch Gen Psychiatry 2004;61:1226–1233
65. Lee ET. Statistical Methods for Survival Analysis. Belmont, Calif: Lifetime Learning Publications; 1980:88–96
66. Research Triangle Institute. Software for Survey Data Analysis (SUDAAN) Version 9.0. Research Triangle Park, NC: Research Triangle Institute; 2004
67. Weissman MM, Bland RC, Canino GJ, et al. The cross-national epidemiology of panic disorder. Arch Gen Psychiatry 1997;54:305–309
68. Deroch-Gamonet V, Belin D, Piazza VP. Evidence for addiction-like behavior in the rat. Science. 2004;305:1014–1017
69. Robins LN, Regier DA. Psychiatric Disorders in America. New York, NY: The Free Press; 1991
70. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Third Edition. Washington, DC: American Psychiatric Association; 1980
71. Kessler RC, Walters EE. The National Comorbidity Survey. In: Tsuang MT, Tohen M, eds. Textbook in Psychiatric Epidemiology. 2nd ed. New York, NY: John Wiley & Sons; 2002:343–362
72. Hasin DS, Grant BF. The co-occurrence of DSM-IV alcohol abuse in DSM-IV alcohol dependence: results of the National Epidemiologic Survey on Alcohol and Related Conditions on heterogeneity that differ by population subgroup. Arch Gen Psychiatry 2004;61:891–896
73. Hasin DS, Grant BF. The co-occurrence of DSM-IV drug abuse in drug dependence: results from the National Epidemiologic Survey on Alcohol and Related Conditions. Drug Alcohol Depend. In press
74. Hasin DS, Goodwin RD, Stinson FS, et al. The epidemiology of major depressive disorder: results from the National Epidemiologic Survey on Alcohol and Related Conditions. Arch Gen Psychiatry. In press
75. Siever LJ, Davis KL. A psychobiological perspective on the personality disorders. Am J Psychiatry 1991;148:1647–1658
76. Klein DF, Klein HM. The definition and psychopharmacology of spontaneous panic and phobia: a critical review. In: Tyrer PJ, ed. Psychopharmacology of Anxiety. New York, NY: Oxford University Press; 1989
77. Marks IM. Behavioral aspects of panic disorder. Am J Psychiatry 1987;144:1160–1165
78. Marks IM. Fears, Phobias and Rituals. New York, NY: Oxford University Press; 1987
79. Davey GCL. A Handbook of Theory, Research and Treatment. New York, NY: John Wiley; 1998
80. Ballenger JC, Wheadon DE, Steiner M, et al. Double-blind, fixed-dose, placebo-controlled study of paroxetine in the treatment of panic disorder. Am J Psychiatry 1998;155:36–42
81. Lecrubier Y, Bakker A, Dunbar G, et al. A comparison of paroxetine, clomipramine and placebo in the treatment of panic disorder. Acta Psychiatr Scand 1997;95:145–152
82. Lecrubier Y, Judge R, Investigators CPPS. Long-term evaluation of paroxetine, clomipramine and placebo in panic disorder. Acta Psychiatr Scand 1997;95:153–160
83. Oehrberg S, Christiansen PE, Behnke K, et al. Paroxetine in the treatment of panic disorder: a randomized, double-blind, placebo-controlled study. Br J Psychiatry 1995;167:374–379
84. Wade AG, Lepola U, Koponen HJ, et al. The effect of citalopram in panic disorder. Br J Psychiatry 1997;170:549–553
85. Andersch S, Rosenberg NK, Kullingsjo H, et al. Efficacy and safety of alprazolam, imipramine and placebo in treating panic disorder: a Scandinavian multicenter study. Acta Psychiatr Scand 1991;365:18–27
86. Cross National Collaborative Panic Study SPI. Drug treatment of panic disorder. Br J Psychiatry 1992;160:191–202
87. Fahy TJ, O'Rourke D, Brophy J, et al. The Galway Study of Panic Disorder, 1: clomipramine and lofepramine in DSM-III-R panic disorder: a placebo controlled trial. J Affect Disord 1992;25:63–75
88. Modigh K, Westberg P, Eriksson E. Superiority of clomipramine over imipramine in the treatment of panic disorder: a placebo-controlled trial. J Clin Psychopharmacol 1992;12:251–261
89. Schweitzer E, Rickels K, Weiss S, et al. Maintenance drug treatment of panic disorder: results of a prospective, placebo-controlled comparison of alprazolam and imipramine. Arch Gen Psychiatry 1993;50:51–60
90. Ballenger JC, Burrows GD, DuPont RL, et al. Alprazolam in panic disorder and agoraphobia: results from a multicenter trial, 1: efficacy in short-term treatment. Arch Gen Psychiatry 1988;45:413–422
91. Lydiard RB, Lesser IM, Ballenger JC, et al. A fixed-dose study of alprazolam 2 mg, alprazolam 6 mg, and placebo in panic disorder. J Clin Psychopharmacol 1992;12:96–103
92. Munjack DD, Crocker B, Cobe D. Alprazolam, propranolol and placebo in the treatment of panic disorder and agoraphobia with panic attacks.

J Clin Psychopharmacol 1989;9:22–27
93. Noyes R Jr, Burrows GD, Reich JH, et al. Diazepam versus alprazolam for the treatment of panic disorder. J Clin Psychiatry 1996;57:349–355
94. Pecknold JC, Swinson RP, Kuch K, et al. Alprazolam in panic disorder and agoraphobia: results from a multicenter trial, 3: discontinuation effects. Arch Gen Psychiatry 1988;45:429–436
95. Rosenbaum JF, Moroz G, Bowden CL. Clonazepam in the treatment of panic disorder with or without agoraphobia: a dose-response study of efficacy, safety and discontinuance. J Clin Psychopharmacol 1997;17:390–400
96. Tesar GE, Rosenbaum JF, Pollack MH, et al. Double-blind, placebo-controlled comparison of clonazepam and alprazolam for panic disorder. J Clin Psychiatry 1991;52:69–76
97. den Boer JA. Pharmacotherapy of panic disorder: differential efficacy from a clinical viewpoint. J Clin Psychiatry 1998;59(suppl 8):30–36
98. Lecrubier Y. The impact of comorbidity on the treatment of panic disorder. J Clin Psychiatry 1998;59(suppl 8):11–14

