

Prevalence and Correlates of Panic Attacks in Postmenopausal Women

Results From an Ancillary Study to the Women's Health Initiative

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Background: Panic attacks are known to be more common in women than in men, but the prevalence and correlates of panic in the postmenopausal period have not been well defined.

Methods: Cross-sectional survey of 3369 community-dwelling postmenopausal women enrolled between December 1, 1997, and November 30, 2000, in the Myocardial Ischemia and Migraine Study, a 10-center ancillary study of the 40-center Women's Health Initiative. Participants, aged 50 to 79 years and predominantly white (73%), completed questionnaires about the occurrence of panic attacks in the previous 6 months and about migraine headaches and underwent 24-hour ambulatory electrocardiographic monitoring. The 6-month prevalences of full-blown and limited-symptom panic attacks were calculated, and their associations with other socio-demographic and clinical variables were examined in multivariate analyses.

Results: One of the panic attack types was reported by

17.9% (95% confidence interval, 16.6%-19.2%) of women (full-blown attacks, 9.8%; limited-symptom attacks, 8.1%). Adjusting for age and race or ethnicity, full-blown panic attacks were more common in women with a history of migraine, emphysema, cardiovascular disease, chest pain during ambulatory electrocardiography, and symptoms of depression. Full-blown panic attacks were associated in a dose-response manner with negative life events during the past year. Panic attacks were associated with functional impairment even after adjusting for comorbid medical conditions and depression. There was no significant association with self-reported use of hormone replacement therapy.

Conclusions: Panic attacks may be relatively common among postmenopausal women and seem to be associated with stressful life events, medical comorbidity, and functional impairment.

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PREVIOUS RESEARCH has established that panic attacks and panic disorder are more common in women than in men,¹ but relatively little is known about the frequency of panic after menopause. The most recent large-scale epidemiologic survey of psychiatric disorders in the United States, the National Comorbidity Survey (NCS),² did not include individuals older than 54 years. The earlier Epidemiologic Catchment Area (ECA) study³ included older adults and found the lowest prevalence of panic attacks and panic disorder in those 65 years and older. In an analysis of 3 ECA sites, the 6-month prevalence of simple panic attacks ranged from 0% to 3.7%,⁴ and the lifetime prevalence of panic disorder in women 65 years and older across 5 ECA sites was only 0.67%.⁵ During perimenopause, a period of change in reproductive hormone levels, somatic symptoms (eg, vasomotor symptoms and sleep

disturbance) and psychological symptoms (eg, dysphoria, anxiety, and irritability) are relatively common.⁶ Although some studies have reported a perimenopausal increase in depression (for reviews see Pearlstein et al⁷ and Burt et al⁸), the prevalence of anxiety and panic during this period has received less attention. In a Scottish population-based survey⁶ of 8000 women aged 45 to 54 years, 23% of respondents who had experienced natural menopause reported that anxiety had been a problem for them during the past 6 months. However, 2 prospective studies^{9,10} in which women were assessed before and after the onset of menopause found no significant increase in anxiety symptoms. Panic attacks are a distinctive form of anxiety, and, to our knowledge, their prevalence specifically among postmenopausal women has not been documented.

We surveyed a subset of women participating in the largest-ever study of post-

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menopausal women in the United States, the Women's Health Initiative (WHI).¹¹ More than 3000 women participating in the Myocardial Ischemia and Migraine Study (MIMS), an ancillary study of the WHI, were surveyed about the occurrence of panic attacks in the previous 6 months. This article describes the prevalence and correlates of panic attacks in these women. Further analyses of the relationship between panic and cardiovascular and other health measures will be described in future articles.

METHODS

PARTICIPANTS

Participants in the MIMS were drawn from among the 93676 postmenopausal women aged 50 to 79 years enrolled in the observational study (OS) of the WHI.¹¹ The WHI is a 40-center study of the major health problems affecting older women. The study has 2 components: a set of randomized controlled clinical trials and a parallel, long-term OS. The clinical trials will evaluate the effect of a low-fat dietary pattern, the effects of hormone replacement therapy, and the effect of calcium and vitamin D supplementation on the various outcomes of breast and colorectal cancer, coronary heart disease, and osteoporotic fractures. Women were enrolled in the concurrent long-term OS to delineate new risk factors and biological markers for disease in women. The MIMS is a 10-center ancillary study of the WHI to investigate the relationship among 3 putative risk factors for cardiovascular disease in a subsample of WHI-OS participants: migraine headaches, panic attacks, and daily life ischemia as measured by 24-hour ambulatory electrocardiography (AECG).

Women were recruited into the MIMS at their baseline or first follow-up visit for the WHI-OS. All women in the OS who agreed to 24-hour AECG and who completed the additional questionnaires were eligible. After a complete description of the study, written informed consent was obtained. There were 3372 women enrolled in the MIMS who completed the migraine questionnaire and had WHI baseline data, of whom 3132 had AECGs that were read at the ECG center; 3369 women completed the panic questionnaire. These data were collected between December 1, 1997, and November 30, 2000.

PROCEDURE

Participants were asked to complete an Anxiety Questionnaire, which begins with 2 screening questions adapted from those used in the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV)*, panic disorder field trial^{12,13} referring to the past 6 months. The first question asks whether the participant has experienced a sudden attack of feeling frightened, anxious, or extremely uncomfortable; the second asks whether she has experienced a sudden episode of rapid or irregular heartbeats. If the answer to either of these questions is "yes," the participant is asked which panic attack symptoms occurred during the most recent bad episode. Owing to a clerical error, the panic symptom of sweating was inadvertently omitted from this symptom list (see the "Definition of Variables" subsection), so that the panic symptom checklist included 12 rather than 13 panic attack symptoms.

Participants were also asked to complete a 13-item Migraine Status Questionnaire that asked about the history and features of headaches lasting more than 4 hours, history of physician-diagnosed migraine headache, and family history of migraine.

Finally, participants were fitted with an AECG Holter monitor, which they wore for 24 hours, including during usual daily activities. Participants were instructed to press the event marker on the AECG recorder if they experienced chest pain while wearing the Holter monitor. At the end of the 24-hour recording period, participants completed a questionnaire asking about any episodes of chest pain, headaches lasting 4 or more hours, medications, and ratings on their peak and average levels of physical activity and mental stress during the recording period. The AECG recordings were made using a Zymed 2010/2010 plus series Holter analysis system, which uses the digitrak Holter monitor (Zymed, Camarillo, Calif) and were transmitted over telephone lines to the AECG Core Laboratory at the University of Florida, Gainesville.

In addition to the data described previously, sociodemographic and clinical covariates obtained as part of the WHI-OS were examined in the MIMS women. Clinical variables included history of comorbid medical conditions and medical treatments, a measure of current depression,¹⁴ quality of life as measured by the Rand 36-Item Health Survey,¹⁵ and self-reported history of smoking, alcohol and coffee intake, and hormone use.

The measure of depression¹⁴ was an 8-item screening instrument that incorporates 6 items from the Center for Epidemiological Studies Depression Scale¹⁶ and 2 items from the Diagnostic Interview Schedule.¹⁷ A logistic regression prediction equation was used to assign a scale score based on a weighted combination of item responses. A cutoff score of 0.06 has demonstrated good sensitivity and specificity for detecting depressive disorder in the past month in primary care and mental health user populations¹⁴ and was therefore used to define positive depression screen findings in our sample.

DEFINITION OF VARIABLES

Two types of panic episodes were defined on the basis of responses to the anxiety questionnaire. *Full-blown panic* was defined as reporting an attack of sudden fear, anxiety, or extreme discomfort during the past 6 months accompanied by 4 or more panic attack symptoms from the 12-symptom checklist. *Limited-symptom panic* was defined as full-blown panic except that fewer than 4 panic symptoms were endorsed. A third response category, "indeterminate panic," comprised women who endorsed only the second screening question (a sudden episode of rapid or irregular heartbeats in the past 6 months but not an attack of fear, anxiety, or extreme discomfort) accompanied by 4 or more panic symptoms. This second screening question had been included in the *DSM-IV* field trial of panic disorder based on previous evidence that it might detect individuals with true panic attacks or panic disorder who do not endorse the traditional screening question about anxiety attacks.¹⁸ Thus, the group that endorsed only this autonomic symptom screen along with 4 or more panic symptoms likely included a mixture of women with and without true panic attacks, and we considered their status indeterminate with respect to panic. *Any panic* was defined as a 6-month history of either full-blown or limited-symptom episodes of panic. The *no panic* group, used as a comparison group in logistic regression analyses, consisted of women who were not classified as having either of the 2 types of panic defined in the previous sentences and who were not in the indeterminate category. As noted in the "Procedure" subsection, the symptom of sweating was inadvertently omitted from the panic symptom checklist. We therefore calculated panic attack prevalence in 2 ways: (1) "conservative" prevalence was the proportion of women who met the respective panic attack type criteria using the 12-symptom checklist (without sweating), and (2) "upper-bound" prevalence was the prevalence of the respective panic attack types assuming that

all women would have endorsed sweating as a symptom of their panic episodes. Multivariate analyses were performed using only the conservative definitions of panic attacks.

Migraine variables were defined using modified International Headache Society criteria.¹⁹ Migraine with aura was defined as headaches lasting more than 4 hours, with pain mostly on one side of the head or a headache that was throbbing, pulsating, or pounding, and accompanied by nausea or vomiting or being bothered by bright lights and having such headaches for more than 1 year or having 5 or more in 1 year and having spots, jagged lines, or "heat waves" in either or both eyes before the headache. Migraine with no aura was defined similarly except for the last item, that is, no spots before headache were reported.

We hypothesized that panic attacks would be associated with several medical comorbidities that have been linked to panic in studies of other age groups and populations: obstructive pulmonary disease,²⁰ cardiovascular disease (and related symptoms and risk factors),²¹ thyroid disease,²² and migraine headache.²³ Self-report of physician-diagnosed conditions (in answer to the question, "Has a doctor ever told you that you had [condition]?") was used to assess a history of emphysema, asthma, cardiovascular disease, angina, hypertension, diabetes mellitus, and thyroid problems (including overactive and underactive thyroid). Body mass index was measured at the first clinic visit, and migraine headaches and chest pain during AECG monitoring were assessed as described in the "Procedure" subsection.

Because panic attacks and panic disorder have previously been associated with functional limitations and impairments in quality of life,²⁴ we examined whether panic attacks were associated with impaired social and role functioning in this sample of postmenopausal women. Impairment in social functioning was assessed by 2 questions from the RAND 36-Item Health Survey¹⁵ asking to what extent and how much of the time physical health or emotional problems interfered with usual social activities with family, neighbors, friends, or groups in the past 4 weeks. Role limitations due to emotional problems were assessed with the question, "In the past 4 weeks, as a result of any emotional problems (feeling depressed or anxious), have any of the following occurred: (1) you cut down on the amount of time you spent on work or other activities, (2) you accomplished less than you would have liked, or (3) you did work or other things less carefully than usual?" These variables were dichotomized to indicate no role limitations or any role limitations.

Life events were assessed by 12 items asking about the death or serious illness of a spouse, partner, family member, friend, or pet; divorce or a friend's or family member's divorce; problems with money; major conflicts with children or grandchildren; accidents, muggings, disasters, and unwanted sexual experiences; job loss or a close friend's or family member's job loss or retirement; and physical or verbal abuse by a close friend or family member. The scale is based on that used in the Alameda County Study,²⁵ which was later modified and used in the β -Blocker Heart Attack Trial in patients after myocardial infarction²⁶ and modified by the WHI to add items on domestic violence. The score used for analysis was the sum of the life events.

DATA ANALYSIS

Prevalence estimates (and their 95% confidence intervals [CIs]) of any, full-blown, or limited-symptom panic were determined for the overall sample of 3369 women and by age and race or ethnicity. Multivariate logistic regression was used to compute odds ratios (ORs) adjusted for age and race or ethnicity. Odds ratios were computed by comparing each panic

Table 1. Sociodemographic Characteristics of Women in the MIMS Sample and of the Full Cohort of the WHI-OS

Characteristic	MIMS Sample, No. (%) (n = 3372)*	Full WHI-OS Cohort, % (n = 93 676)*
Age, y		
50-59	1165 (34.6)	31.7
60-69	1516 (45.0)	44.0
70-79	691 (20.5)	24.3
Race or ethnicity		
American Indian or Alaskan native	11 (0.3)	0.5
Asian or Pacific Islander	542 (16.1)	2.9
Black	193 (5.7)	8.2
Hispanic	80 (2.4)	3.9
White, not of Hispanic origin	2474 (73.4)	83.3
Unknown	72 (2.1)	1.1
Annual income, \$		
<10 000	100 (3.0)	4.2
10 000-19 999	291 (8.6)	10.8
20 000-34 999	701 (20.8)	21.6
35 000-49 999	612 (18.1)	18.6
50 000-74 999	687 (20.4)	18.7
≥75 000	793 (23.5)	18.8
Marital status		
Never married	168 (5.0)	4.2
Divorced or separated	495 (14.7)	15.7
Widowed	510 (15.1)	17.4
Presently married or living together	2194 (65.1)	61.7
Education		
0-8 y	36 (1.1)	1.7
Some high school	104 (3.1)	3.5
High school or general equivalency diploma	521 (15.5)	16.1
School after high school	1160 (34.4)	36.2
College degree or higher	1533 (45.5)	41.6

Abbreviations: MIMS, Myocardial Ischemia and Migraine Study; WHI-OS, Women's Health Initiative Observational Study.

*Percentages may not sum to 100 because of missing data for some variables.

group with the reference group of women who reported no panic, that is, excluding those with full-blown, limited-symptom, or indeterminate panic, except as otherwise noted.

RESULTS

BASELINE CHARACTERISTICS

Table 1 gives the sociodemographic composition of the MIMS sample and of the entire OS cohort for comparison. Approximately two thirds of the sample was 60 years or older. The women were predominantly white (73%) and relatively well educated (46% had a college degree or higher). Nevertheless, 32% of the sample had low-middle incomes (<\$35 000 annual household income) and 12% had incomes of less than \$20 000. The MIMS sample is enriched for Asians and Pacific Islanders (16.1%) compared with the WHI-OS population (2.9%) because 1 of the 10 clinics participating in the MIMS was in Honolulu, Hawaii, where 69% of the overall OS population is Asians and Pacific Islanders. In other respects, the MIMS sample is similar to the full OS cohort of 93 676 women. The OS cohort is somewhat healthier than a probability sample of US women aged 50 to 79 years in the NHANES

Table 2. Six-Month Prevalence of Panic Attacks, by Age and Race or Ethnicity

Variable	Participants, No. (n = 3369)	Panic Attacks, % (95% CI)		
		Any	Full-blown	Limited-Symptom
Age at screening, y				
50-59	1164	21.6 (19.2-23.9)	13.8 (11.8-15.8)	7.7 (6.2-9.3)
60-69	1515	16.0 (14.1-17.8)	7.7 (6.3-9.0)	8.3 (6.9-9.7)
70-79	690	15.9 (13.2-18.7)	7.7 (5.7-9.7)	8.3 (6.2-10.3)
Race or ethnicity				
American Indian or Alaskan native	10	20.0	20.0	0.0
Asian or Pacific Islander	542	11.8 (9.1-14.5)	5.7 (3.8-7.7)	6.1 (4.1-8.1)
Black	192	21.9 (16.0-27.7)	13.5 (8.7-18.4)	8.3 (4.4-12.2)
Hispanic or Latino	80	25.0 (15.5-34.5)	16.3 (8.2-24.3)	8.8 (2.6-14.9)
White, not of Hispanic origin	2473	18.7 (17.1-20.2)	10.1 (8.9-11.3)	8.6 (7.5-9.7)
Unknown	72	18.1 (9.2-26.9)	11.1 (3.9-18.4)	6.9 (1.1-12.8)

Abbreviation: CI, confidence interval.

III (third National Health and Nutrition Examination Survey) cohort.²⁷ In that cohort, 10.0% of participants reported receiving treatment for diabetes mellitus with insulin or pills, 5.6% reported they had been told by a physician that they had a previous myocardial infarction, and 4.6% were told that they had a previous stroke (compared with our OS cohort, for which the values are 4.2%, 2.5%, and 1.5%, respectively).

PREVALENCE OF PANIC ATTACKS

Of the 3369 women who completed the panic questionnaire, 17.9% (95% CI, 16.6%-19.2%) reported experiencing 1 of 2 panic attack types in the past 6 months. Full-blown panic attacks were reported by 9.8% (95% CI, 8.8%-10.8%) of participants, whereas limited-symptom attacks were reported by 8.1% (95% CI, 7.2%-9.0%). The upper-bound prevalence values (assuming all women who endorsed the panic attack stem question would have also endorsed sweating had it been included) were 19.6% (95% CI, 18.3%-20.9%) for any panic, 13.0% (95% CI, 11.9%-14.2%) for full-blown attacks, and 6.6% (95% CI, 5.7%-7.4%) for limited-symptom attacks. All subsequent analyses use the conservative definition of panic attacks in which it is assumed that none of the women would have endorsed sweating as a panic symptom. The prevalence of full-blown panic attacks was highest in the youngest age group (aged 50-59 years) (**Table 2**).

SOCIODEMOGRAPHIC ASSOCIATIONS WITH PANIC ATTACKS

Table 3 gives the association between panic attack subtypes and sociodemographic and lifestyle characteristics. Compared with women in the 50- to 59-year-old group, adjusting for race or ethnicity, older women were significantly less likely to report full-blown panic attacks but not limited-symptom panic attacks. White, black, or Hispanic race or ethnicity was not significantly associated with panic attacks after adjustment for age, but Asians and Pacific Islanders were significantly less likely to report full-blown or limited-symptom panic attacks than were white women. There were only 11 women who self-reported being American Indian or Alaskan native.

Consequently, their data were combined with those of women whose race or ethnicity was unspecified to use the full data set in stable multivariate models, but results for this combined group itself are not meaningful and are omitted from Table 3. Lower-income women (annual income <\$20000) were 2.7 times more likely to report full-blown panic attacks, after adjustment for race or ethnicity and age, than those with higher incomes. There was no significant relationship between marital status and 6-month prevalence of panic attacks and no consistent relationship with education level.

ASSOCIATION WITH HABITS, LIFESTYLE VARIABLES, AND USE OF HORMONE REPLACEMENT THERAPY

Current smoking, after adjustment for age and race or ethnicity, was associated with full-blown panic (OR, 2.00; 95% CI, 1.30-3.06), whereas alcohol and coffee intake were not (Table 3). Consistent with the idea that adverse life events may trigger panic attacks, the number of life events during the past year was strongly associated with 6-month prevalence of panic attacks. Full-blown and limited-symptom panic attacks were highly and significantly related to the number of negative life events during the past year, with those having 5 or more such events being 6.9 times more likely to report full-blown panic attacks (95% CI, 4.05-11.65) and 3.1 times more likely to report limited-symptom attacks (95% CI, 1.61-6.02).

Finally, we also examined whether the prevalence of panic attacks is associated with hormone replacement therapy in postmenopausal women. Adjusting for age and race or ethnicity, we found no significant relationship between self-reported past or current hormone replacement therapy and panic attacks.

COMORBIDITY

We examined whether comorbid medical conditions were associated with risk of panic attacks in these women (**Table 4**). Consistent with previous evidence²⁸ that pulmonary disease may be a risk factor for the development of panic disorder, we found that panic attacks were

more likely to be reported by women with a history of emphysema (OR, 4.13; 95% CI, 2.65-6.43). Women with a history of asthma were also more likely to report limited-symptom and full-blown panic attacks. We also found an association between full-blown panic and a history of cardiovascular disease (OR, 2.92; 95% CI, 2.24-3.80), angina (OR, 4.13; 95% CI, 2.68-6.38), and reported chest pain during 24-hour AECG monitoring (OR, 2.55; 95% CI, 1.87-3.48). Of the 3 cardiovascular risk factors examined, body mass index was also associated with full-blown panic (OR, 1.03 per unit increase in body mass index; 95% CI, 1.01-1.05), whereas hypertension and diabetes mellitus were not. Full-blown panic attacks were associated with a history of thyroid problems (OR, 1.47; 95% CI, 1.14-1.89), including a self-reported history of underactive thyroid problems (OR, 1.51; 95% CI, 1.12-2.04) and overactive thyroid (OR, 1.80; 95% CI, 1.02-3.17).

The strongest association with panic attacks was observed for a history of migraine with aura. Women who reported such a history were more than 6 times more likely to report full-blown panic than were women without headaches (OR, 6.44; 95% CI, 4.68-8.85). Migraine without aura was also associated with full-blown panic, although less strongly (OR, 2.83; 95% CI, 2.00-4.00). Finally, current depression, as defined by the depression screening instrument, was significantly associated with full-blown panic attacks (OR, 5.32; 95% CI, 4.01-7.05) but not with limited-symptom panic. Thirty-one percent of women with full-blown panic had accompanying symptoms of depression compared with 10% of those with limited-symptom panic and 7.3% of those with no panic ($P < .001$ for both).

ASSOCIATION OF PANIC ATTACKS WITH SOCIAL IMPAIRMENT AND ROLE LIMITATIONS

Table 5 indicates that women who reported full-blown panic attacks in the previous 6 months were more likely to report impairment in social functioning in the past 4 weeks (OR, 2.51; 95% CI, 1.86-3.39) and role limitations due to emotional problems (OR, 1.84; 95% CI, 1.35-2.50), after controlling for age and race or ethnicity and other variables that were univariately associated with panic attacks and each of these 2 quality-of-life outcomes. Limited-symptom panic attacks also seemed to be associated with impaired social functioning (OR, 1.42; 95% CI, 1.04-1.94) and role limitations (OR, 1.56; 95% CI, 1.12-2.17), although to a lesser degree than full-blown panic attacks.

COMMENT

To our knowledge, this study is the largest survey of the prevalence and correlates of panic attacks in postmenopausal women.

PREVALENCE OF PANIC ATTACKS

In this sample of 3369 women, 9.8% reported a full-blown panic attack within the past 6 months. Limited-symptom panic attacks, which have been reported to confer a similar risk of phobic and functional complica-

Table 3. Sociodemographic and Lifestyle Variables Associated With Panic Attacks

Variable	Odds Ratio (95% CI)*	
	Full-blown Panic	Limited-Symptom Panic
Age, y†		
50-59	1.00	1.00
60-69	0.51 (0.39-0.65)	0.98 (0.74-1.30)
70-79	0.53 (0.38-0.74)	1.00 (0.70-1.41)
Race or ethnicity‡		
White, not of Hispanic origin	1.00	1.00
Asian or Pacific Islander	0.52 (0.35-0.76)	0.64 (0.44-0.94)
Black	1.46 (0.94-2.28)	1.07 (0.63-1.84)
Hispanic or Latino	1.69 (0.91-3.15)	1.13 (0.51-2.52)
Annual income, \$\$		
50 000	1.00	1.00
20 000-49 999	1.44 (1.10-1.89)	0.91 (0.68-1.22)
<20 000	2.71 (1.88-3.89)	1.50 (1.00-2.23)
Marital status§		
Presently married	1.00	1.00
Never married	1.44 (0.91-2.30)	0.86 (0.46-1.64)
Divorced or separated	1.00 (0.72-1.39)	1.13 (0.79-1.60)
Widowed	1.05 (0.73-1.50)	1.10 (0.77-1.58)
Education§		
College degree or higher	1.00	1.00
School after high school	1.78 (1.38-2.31)	1.47 (1.11-1.94)
High school diploma	1.20 (0.82-1.75)	1.36 (0.94-1.96)
<High school diploma	2.44 (1.41-4.21)	0.82 (0.37-1.84)
Employment§		
Currently working	1.00	1.00
Not working	1.77 (1.29-2.43)	0.92 (0.62-1.37)
Retired	1.21 (0.89-1.66)	1.08 (0.78-1.48)
Smoking§		
Never	1.00	1.00
Past	0.91 (0.71-1.17)	1.19 (0.92-1.55)
Current	2.00 (1.30-3.06)	1.25 (0.71-2.20)
Alcohol intake§		
None	1.00	1.00
Past	1.40 (0.94-2.08)	0.81 (0.51-1.30)
Rarely	1.03 (0.70-1.52)	1.16 (0.77-1.75)
1-6 drinks/wk	0.70 (0.45-1.07)	1.01 (0.65-1.57)
≥7 drinks/wk	0.95 (0.59-1.52)	1.19 (0.73-1.95)
Coffee intake§		
None	1.00	1.00
1-3 cups/d	1.05 (0.81-1.37)	1.28 (0.97-1.69)
≥4 cups/d	1.21 (0.76-1.93)	1.46 (0.91-2.34)
Life events during past year, No.§		
None	1.00	1.00
1-2	1.48 (1.02-2.15)	1.56 (1.08-2.26)
3-4	4.67 (3.16-6.89)	3.10 (2.06-4.66)
≥5	6.86 (4.05-11.65)	3.11 (1.61-6.02)
Hormone replacement therapy§		
Never	1.00	1.00
Past	1.29 (0.90-1.84)	1.48 (1.00-2.17)
Current	1.05 (0.78-1.41)	1.17 (0.84-1.62)

Abbreviation: CI, confidence interval.

*Comparison is for panic attack type vs no panic (indeterminate cases excluded).

†Adjusted for race or ethnicity.

‡Adjusted for age.

§Adjusted for race or ethnicity and age.

tions,^{29,30} were reported by an additional 8.1% of participants. This prevalence is higher than that reported in other population-based samples that have included women in a similar age range. For example, an analysis⁴ from 3 ECA

Table 4. Association of Panic Attacks With Comorbid Conditions

Variable	Odds Ratio (95% CI)*	
	Full-blown Panic	Limited-Symptom Panic
History of emphysema or chronic bronchitis	4.13 (2.65-6.43)	0.80 (0.34-1.86)
History of asthma	1.71 (1.17-2.50)	1.58 (1.03-2.42)
History of cardiovascular disease	2.92 (2.24-3.80)	1.65 (1.21-2.25)
History of angina	4.13 (2.68-6.38)	2.15 (1.25-3.70)
Chest pain during AECG (with or without ST depression)	2.55 (1.87-3.48)	1.20 (0.78-1.83)
History of hypertension	1.27 (0.96-1.67)	0.90 (0.67-1.21)
History of diabetes mellitus	1.57 (1.00-2.48)	1.27 (0.75-2.16)
Body mass index (per unit increase)	1.03 (1.01-1.05)	1.02 (1.00-1.05)
History of thyroid problems	1.47 (1.14-1.89)	0.87 (0.65-1.18)
Overactive thyroid	1.80 (1.02-3.17)	0.74 (0.32-1.73)
Underactive thyroid	1.51 (1.12-2.04)	0.87 (0.60-1.25)
Migraine with aura (vs no headaches)	6.44 (4.68-8.85)	2.18 (1.49-3.21)
Migraine without aura (vs no headaches)	2.83 (2.00-4.00)	1.42 (0.96-2.10)
Depression screen positive findings	5.32 (4.01-7.05)	1.42 (0.93-2.16)

Abbreviations: AECG, ambulatory electrocardiography; CI, confidence interval.

*Comparison is for panic attack type vs no panic (indeterminate cases excluded).

sites found the unadjusted 6-month prevalence of simple panic attacks to range from 0% to 3.7% among women older than 65 years and from 4.5% to 7.9% among those aged 45 to 64 years. In fact, the 6-month prevalence of panic attacks in the present study was comparable to the overall lifetime prevalence (9.7%) reported in the ECA study.⁵ The more recent NCS included only individuals aged 15 to 54 years and estimated the lifetime prevalence of panic attacks to be 7.3%.¹ The discrepancy in prevalence estimates in our study compared with the ECA and NCS studies may be due in part to differences in methods of assessment. The ECA and NCS studies used structured diagnostic interviews, in contrast to the self-report questionnaire used in the present study. It may be that women are less likely to report panic symptoms in a face-to-face interview than on a questionnaire. In addition, the definition of a full-blown panic attack used in this study is somewhat broader than that used in the ECA and NCS studies. The stem question in the Diagnostic Interview Schedule used in the ECA study was, "Have you ever had a spell or attack when all of a sudden you felt frightened, anxious, or very uneasy *in a situation when most people wouldn't be afraid?*" Individuals diagnosed as having "simple panic attacks" were those who responded positively to this stem question and endorsed at least 4 of 12 symptoms of panic. The italicized phrase in the stem question implies that the panic episode is spontaneous. The panic attacks reported by women in the present study did not include the italicized phrase and thus may have captured "situationally bound" panic attacks (eg, in the presence of a phobic stimulus). The

NCS study used a modified version of the Composite International Diagnostic Interview² and defined panic attacks as unexplained fearful spells (which corresponded to the ECA concept of simple panic attacks) but also required a crescendo quality to the panic symptoms (ie, they are limited to only a few minutes).¹ The lifetime prevalence of intense fearful spells (sudden unexplained fear without the crescendo feature) was 11.3% in the NCS.¹ In the present study, we based our panic screen on screening questions used in the DSM-IV field trial¹³ supplemented by the checklist of panic attack symptoms corresponding to those used to define panic attacks in the DSM-IV.³¹ In the field trial, 72% of individuals who screened positive met DSM-III-R or DSM-IV criteria for panic disorder on structured clinical interview, whereas 28% were "infrequent panickers" who did not meet disorder criteria.¹³ Panic disorder and infrequent panic were associated with excess functional disability in that study.¹² Thus, our panic screen seems likely to have identified women with functionally significant panic symptoms.

Our results might also differ from those of previous epidemiologic studies because the WHI-OS, from which the MIMS sample was derived, is somewhat healthier than the probability sample of the US population as determined in NHANES III.²⁷ To the extent that comorbid medical conditions are associated with panic attacks, this difference might be expected to result in an underestimate of panic attack prevalence. Thus, we believe that the rates we observed may be a conservative estimate of panic in postmenopausal women.

Our data suggest that the occurrence of panic attacks in older women is relatively common, consistent with findings from previous smaller studies of panic in later life. In a study of 70 older adults (mean age >80 years, 83% women) from retirement communities, Deer and Calamari³² reported a 1-year prevalence of 27% for panic attacks, although no cases of panic disorder were observed. In that study, anxiety sensitivity (a fear of somatic anxiety-related symptoms) was a predictor of panic symptoms. Among women with high anxiety sensitivity, somatic symptoms associated with perimenopause or menopause and medical illness in the elderly may potentiate panic attacks. Other predisposing features of the postmenopausal period may include stressful life transitions (eg, retirement and widowhood), and, consistent with this, we observed a dose-response relationship between the number of negative life events in the preceding year and the 6-month prevalence of panic attacks.

Because the present data are cross-sectional, we do not know whether the onset of panic attacks in the women we studied was premenopausal or postmenopausal. The age of onset for panic attacks and panic disorder is typically in the second or third decade of life,^{4,33} although there may be a bimodal distribution with a later peak between ages 45 and 54 years.¹ However, a 13- to 15-year follow-up of 1920 participants in the Baltimore ECA study³⁴ found no new cases of panic disorder among those older than 65 years. In a clinical sample, more than half of the elderly individuals with panic attacks and panic disorder reported symptom onset after age 60 years.³⁵ Compared with earlier-onset cases, late onset of panic

Table 5. Association of Panic Attacks With Functional Impairment

	Odds Ratio (95% CI)			
	Impairment in Social Functioning Due to Physical or Emotional Problems		Role Limitations Due to Emotional Problems	
	Crude	Adjusted*	Crude	Adjusted†
Full-blown (vs no panic)	3.87 (3.06-4.91)	2.51 (1.86-3.39)	3.04 (2.41-3.83)	1.84 (1.35-2.50)
Limited-symptom panic (vs no panic)	1.31 (1.01-1.70)	1.42 (1.04-1.94)	1.42 (1.08-1.85)	1.56 (1.12-2.17)

Abbreviation: CI, confidence interval.

*Adjusted for age, race or ethnicity, income, education, employment, life events, smoking, depression screen positive findings, body mass index, chest pain during ambulatory electrocardiography, and history of asthma, emphysema, cardiovascular disease, angina, diabetes mellitus, thyroid problems, and migraine headaches (with and without aura).

†Adjusted for the variables listed in the previous footnote except for history of migraine headaches, which was not univariately associated with role limitations due to emotional problems.

attacks and panic disorder (after age 50-60 years) has been associated with lesser severity,³⁶ less use of mental health services,³⁷ and lower levels of psychiatric comorbidity³⁷ but higher levels of medical comorbidity.³⁵

We found that panic attack prevalence was highest in the youngest age group of these postmenopausal women. This is consistent with data from the ECA study,⁵ which found the lowest prevalence of panic disorder in individuals older than 65 years. In our sample, the highest prevalence was observed in women aged 50 to 59 years, the group likely to be closest to perimenopause, a time when hormonal changes, psychological distress, and somatic symptoms may be greatest.⁷ If panic, like depression, is associated with increased mortality rates in older adults, the age-dependent decline in panic prevalence might also be attributable in part to decreased survival, although longitudinal studies are required to evaluate this hypothesis. Consistent with the ECA and NCS studies,^{1,5} we found little evidence for an effect of race or ethnicity on panic attack prevalence but, as in the NCS, a higher prevalence of attacks in women in the lowest income group. The relationship between education level and panic attack prevalence was nonlinear, with the highest risk in those who had not completed high school.

RELATIONSHIP TO COMORBID DISORDERS

There has been considerable interest in the association between panic attacks and medical comorbidities, particularly pulmonary and cardiovascular disease. Previous studies have documented an excess risk of panic disorder in patients with obstructive airways disease (including asthma and emphysema),³⁸ and there is evidence that pulmonary disease may be a risk factor for the development of panic disorder.²⁸ Consistent with this literature, we found that women with a reported history of asthma or emphysema were more likely to report panic attacks. In the absence of data on the age of onset of panic and pulmonary disease in these women, we cannot address whether there is a temporal or causal relationship between the two.

An excess risk of panic disorder among patients with coronary heart disease has also been reported previ-

ously.²¹ In our sample, a history of cardiovascular disease was associated with a nearly 3-fold increased likelihood of panic attacks in the past 6 months. An association of similar magnitude was seen between chest pain during AECG monitoring and panic attacks. Because cardiopulmonary symptoms are central features of panic attacks, it is possible that panic attacks reported by women with a history of cardiac or pulmonary disease were actually symptoms of their underlying medical illness. However, results of previous studies,³⁹⁻⁴³ most of which have examined men, have suggested that anxiety is a risk factor for subsequent fatal or nonfatal coronary heart disease. The present study is the first, to our knowledge, to document an association between panic and cardiovascular disease specifically in postmenopausal women. The mechanisms behind this relationship are the subject of ongoing investigation. In patients with a history of coronary artery disease, mental stress-induced myocardial ischemia has been shown to be a predictor of fatal and nonfatal cardiac events.⁴⁴ In addition, numerous studies⁴⁵⁻⁴⁸ have documented evidence of altered cardiac autonomic balance (decreased vagal tone or increased sympathetic heart rate control) in individuals with panic or phobic anxiety, suggesting a possible explanation for an elevated risk of sudden death.

The strongest relationship between panic attacks and comorbid medical conditions was observed for migraine headaches with aura. Women who reported such headaches were 6.4 times more likely to report full-blown panic attacks than were women without headaches. Several studies have previously documented excess comorbidity between panic disorder and migraine and other chronic daily headache syndromes,^{23,49-51} and some have suggested shared genetic or environmental causes.^{23,49,52} Consistent with previous research,⁴⁹ migraine with aura was somewhat more strongly associated with panic attacks than was migraine without aura. Previous studies have addressed the etiologic relationship between panic and migraine. Longitudinal data from community samples have documented that panic and other anxiety disorders may either precede the onset of migraine^{23,49,51} or follow it.⁴⁸ In a recent analysis of a population-based sample of 1287 persons aged 25 to 55 years, Breslau and colleagues²³ found that migraine headaches

were a risk factor for and a sequela of panic disorder. This bidirectional relationship is consistent with the hypothesis that genetic or environmental effects on the 2 conditions are overlapping. Thus far, however, family study data⁴⁹ have not supported the hypothesis that migraine and anxiety/affective disorders represent alternate expressions of a common genetic diathesis. Migraine and panic disorder have been associated with dysregulation of serotonergic neurotransmitter systems,^{53,54} suggesting a possible neurobiological connection between them. Although the cross-sectional nature of the present data does not allow us to evaluate whether the observed association between migraine and panic represents a causal relationship, this study is the first to extend the reported connection between migraine and panic to a large sample of postmenopausal women.

Our study also documented the well-established association between depression and panic attacks.^{55,56} Women who screened positive on the depression screening instrument were 5 times more likely to report full-blown panic attacks in the past 6 months than were those who did not, although this relationship did not exist for limited-symptom panic. The screening instrument is not intended to establish a clinical diagnosis of major depression. In a recent study⁵⁷ of a sample of WHI participants, the positive predictive value of the screen was relatively low for a diagnosis of current major depression or dysthymia when measured against a structured clinical interview. Thus, the association we observed may apply to depressive symptoms rather than clinically diagnosable major depression.

FUNCTIONAL SIGNIFICANCE OF PANIC

The significance of panic attacks in these postmenopausal women is underscored by the finding that full-blown panic attacks are strongly associated with limitations in social and emotional functioning (Table 5), even after controlling for psychiatric (depression) and medical comorbidities. Our results accord with previous research¹² documenting that even infrequent panic attacks are associated with substantial comorbidity and disability. In a study of primary care patients, Katon and colleagues¹² found that patients who had at least 1 panic attack within the past 6 months resembled those with *DSM-III-R* panic disorder in having greater psychiatric comorbidity and functional disability compared with control patients without panic.

The limitations of this study should be considered in interpreting these results. First, as noted in the "Procedure" subsection, the panic checklist we used did not include the symptom of sweating. This omission might be expected to result in a conservative estimate of panic attack prevalence among women who most recently reached menopause because "night sweats" is a common perimenopausal and postmenopausal symptom.^{6,9} We evaluated this by calculating an upper-bound estimate, assuming that all women who endorsed the panic attack stem question would have also endorsed sweating. The prevalence of panic attacks using this assumption was slightly higher for any panic attack (19.6% vs 17.9% without this assumption) and full-blown panic at-

tacks (13.0% vs 9.8%). The prevalence of limited-symptom attacks was correspondingly lower (4.9% vs 8.1%) because some proportion of women who endorsed only 3 panic symptoms would now reach full-blown panic attack criteria with the fourth symptom of sweating. Second, the data are based on a cross-sectional, self-report measure of panic attack symptoms. It is possible that the prevalence estimates would differ if a diagnostic interview were used to assess panic attacks. Third, there may be substantial heterogeneity in the frequency and severity of panic among women who reported attacks. Our prevalence estimate of full-blown panic attacks would include women who experienced a single threshold attack and women with recurrent, severe panic attacks occurring as part of panic disorder. Screening positive for panic episodes within the past 6 months is likely to be a sensitive, although not a specific, indicator of underlying panic disorder.⁵⁸ The differential diagnosis of panic attacks includes not only panic disorder but also other psychiatric and medical disorders and panic in response to medication or illicit substance use. Because panic attacks can occur in these contexts and sporadically, the prevalence of panic attacks is necessarily greater than that of panic disorder. On the other hand, individuals with infrequent panic attacks have been reported^{12,29,30} to be similar to those with frequent, recurrent attacks or panic disorder in terms of clinical profiles and levels of disability. Fourth, the temporal relationship between the onset of panic attacks and some of the comorbid conditions examined is unknown, making it difficult to determine the causal directionality (if any) between panic and these variables. Finally, because this study was intended to be descriptive and to highlight areas deserving further study, our statistical tests were not corrected for multiple comparisons, raising the possibility of type I error in some findings.

In summary, we found that the 6-month prevalence of panic attacks in a large sample of postmenopausal women was substantial (9.8% for full-blown attacks and 17.9% for full-blown or limited-symptom attacks). The higher prevalence of attacks in this study compared with previous large epidemiologic surveys may be due in part to differences in methods of assessment and differences in the target populations. Panic attacks were associated with younger age, lower income, recent negative life events, a history of medical comorbidity (especially cardiopulmonary disease, thyroid problems, and migraine headache), and depression as well as self-reported limitations in social functioning. Future studies of this sample will further characterize the association of panic attacks with cardiac and other health outcomes. Given previous research¹² suggesting that the occurrence of panic attacks within the past 6 months can be an indicator of significant psychiatric comorbidity and functional disability, primary care clinicians treating postmenopausal women may wish to screen for such attacks using the questionnaire applied in this study or even briefer available instruments (eg, the 2-item Autonomic Nervous System Questionnaire developed by Stein and colleagues⁵⁸). However, panic attacks include a cluster of symptoms that can be associated with a variety of physical and mental disorders so that their diagnostic and treatment implications depend on a

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more thorough evaluation of a given patient. Further research is needed to clarify the frequency and severity of panic symptoms in postmenopausal women and their impact on quality of life.

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