ORIGINAL ARTICLE

Prevalence and Predictors of Depressive Symptoms in Older Premenopausal Women

The Harvard Study of Moods and Cycles

Bernard L. Harlow, PhD; Lee S. Cohen, MD; Michael W. Otto, PhD; Donna Spiegelman, ScD; Daniel W. Cramer, MD, ScD

Background: The Harvard Study of Moods and Cycles is a community-based cohort study designed to evaluate the relationship between major depression and changes in menstrual and ovarian function.

Methods: All women aged 36 to 44 years with a verifiable address from 7 Boston, Mass, metropolitan communities were selected from the Massachusetts Town Books. A self-administered questionnaire assessed demographic characteristics and menstrual history, depression history, and current depressive symptoms (Center for Epidemiologic Studies Depression Scale [CES-D]) in 4161 women.

Results: We observed a score of 16 or more on the CES-D in 22.4% of women surveyed, and 8.6% scored 25 or more. Widowed, divorced, or separated women were twice as likely as married women to have depression scores greater than 16 (95% confidence interval, 1.6-2.8), and smokers in the upper tertile of pack-years were 1.9 times more likely to have CES-D scores of 16 or more (95% confidence interval, 1.5-2.3). Relative to nulliparous women, those with 1 or 2 children had a 30% lower risk of historic mood disorder, and those with 3 or more children had an even greater reduction in risk (odds ratio, 0.4; 95% confidence interval, 0.3-0.6). Menstrual cycle irregularities were largely unassociated with current or past depression. However, 5 of 8 premenstrual symptoms were significantly associated with CES-D scores of 16 or more.

Conclusions: These findings corroborate the prevalence of depression reported by other community-based studies, and also support a relationship between depressive symptoms and marital status, cigarette smoking, nulliparity, and premenstrual symptoms.

Arch Gen Psychiatry. 1999;56:418-424

From Harvard Medical School (Drs Harlow, Cohen, Otto, and Cramer), the Obstetrics and Gynecology Epidemiology Center, Brigham and Women's Hospital (Drs Harlow and Cramer), the Perinatal Psychiatry Clinical Research Program, Massachusetts General Hospital (Drs Cohen and Otto), and the Departments of Epidemiology and Biostatistics, Harvard School of Public Health (Dr Spiegelman), Boston, Mass.

CROSS-SECTIONAL population-based studies consistently report the highest prevalence of major depression in women entering their late premenopausal years.[1,2] Coincidental with these prevalence estimates was a report suggesting that women with a self-reported history of depression were at twice the risk of undergoing a natural menopause before age 47 years.[3] In an effort to determine whether depression is a preceding risk factor for early cessation of menstrual periods, or a consequence of a more rapid decline in ovarian function that may precede by many years the cessation of menstrual periods, we established a cohort of premenopausal women with and without past or current major depressive disorder (the Harvard Study of Moods and Cycles). These women will be prospectively followed up through the menopausal transition. As part of the screening process to identify eligible cohort members, we had an opportunity to (1) assess the prevalence of past and current depression in a large community-based sample and (2) evaluate potential correlates of depressive symptoms, including menstrual history, demographic data, and cigarette smoking. Although some of these factors have been reportedly associated with depressive symptoms in earlier studies,[4-7] they have rarely been assessed simultaneously.

RESULTS

The prevalence of depressive symptoms is shown in **Table 1** by a matrix of 5 rows of past depression categories (numbered 1-5) and 3 columns of CES-D current depression scores (lettered *a-c*). Prevalence categories (1*a* through 5*c*) are described throughout this report. Just less than half (45.9%) of all women reported no lifetime history of past or current depression. Regardless of current depressive symptoms, 43.2% of all women (sum of prevalence 3*a-c*, 4*a-c*, and 5*a-c*) reported a continuous 2-week period of having felt depressed or down at some time. Of these women, about 58% sought psychotherapy or pharmacotherapy for their depression (sum of 4*a-c* and 5*a-c*, about 25% overall). Approximately 22% of all women had scores on the CES-D exceeding 16, while 8.6% reported scores of 25 or greater.

©1999 American Medical Association. All rights reserved.
Downloaded From: http://archpsyc.jamanetwork.com/ on 07/23/2016

SUBJECTS AND METHODS

SAMPLED POPULATION

All women between the ages of 36 and 44 years, identified from Massachusetts Town Books (annual publications that list residents by name, age, and address according to voter precincts), were selected from 7 communities in the Boston, Mass, metropolitan area. Women with verified addresses and telephone numbers were mailed a 1-page, 2-sided, optically scannable questionnaire to assess characteristics of their menstrual cycle (eg, age at menarche, cycle length, flow, and regularity), menopausal status, past depression, and current depressive symptoms. To signal a refusal, women were asked to return the blank questionnaire in the envelope provided. After 2 mailings, a follow-up telephone call prompted the return of the questionnaire. Of 6222 questionnaires mailed, 4572 (73.5%) were completed. After excluding 165 women outside the 36- to 44-year age range (ages that were incorrectly reported in the Town Books) and 243 women surgically or naturally menopausal, we were left with 4164 completed questionnaires.

MEASURES OF DEMOGRAPHICS, DEPRESSION, AND REPRODUCTIVE EVENTS

The Center for Epidemiologic Studies Depression Scale (CES-D), a 20-item inventory specifically designed to assess depressive symptoms in the general population,[8] was used to screen for current depressive disorder during the past month. Although this scale is designed to screen but not diagnose major depression, a score of 16 or more is highly suggestive of depressive symptoms. Community-based studies suggest that approximately 65% of women with scores of 16 or more meet more formal diagnostic criteria for major depression.[9] In one validation study conducted in a private psychiatric facility, a mean CES-D score of 24.4 was strongly associated with major depression.[10] Thus, to better delineate the variability of depressive symptoms, we elected to stratify women in our sample by means of 3 ranges: less than 16, 16-24, and 25 or greater.

Past depression was evaluated by 4 questions. Women were asked (1) whether there had ever been a time when they were feeling depressed or down most of the day, nearly every day, for a period of at least 2 weeks; (2) whether they had seen a professional who said they were depressed; (3) whether they had sought treatment for depression; and (4) whether they had ever taken antidepressants for a period of 6 months or longer (a period selected to include a positive response only for those who could tolerate psychiatric medication). Three women who failed to complete the CES-D and questions on history of depression were eliminated.

We also collected demographic (age, race, education), medical, and reproductive history (height, weight, cigarette smoking, history of oral contraceptive use, menstrual cycle characteristics) variables. Women were asked to characterize their current menstrual cycles with respect to cycle regularity (predictable within 10 days) and usual cycle length. The 8-item Moos Premenstrual Inventory was also administered. The Moos premenstrual syndrome (PMS) assessment[11] requests that subjects rate on a 4-point scale (0, rarely; 1, some of the time; 2, much of the time; and 3, most of the time) the degree to which 8 groups of premenstrual symptoms usually occur the week before their menstrual period. Each symptom was evaluated dichotomously (rarely or some of the time vs much or most of the time), and then in categorical quartiles based on the entire summary score (ranging from 0 if all 8 questions are answered as rarely, to 24 if all 8 questions are answered as most of the time), and finally in a similar summary score fashion with the use of quartiles that include only questions pertaining to physical symptoms.

A specific question asked subjects to rate on the same 4-point scale the extent to which premenstrual symptoms as a whole interfered with their social or occupational functioning.

STATISTICAL ANALYSIS

We calculated the 1-month and cumulative age-adjusted incidence of varying severity of current and past depression, and then assessed differences in demographic characteristics, lifestyle measures, and reproductive history between those with current or past depressive disorder and women with no history of past depression and CES-D scores less than 16. Stratified analyses were used to compare the distribution of background and menstrual and reproductive histories between the groups with past or current depressive symptoms. We used logistic regression models to calculate adjusted odds ratios and 95% confidence intervals, and the χ^2 test for linear trend was calculated on the basis of the change in deviance in logistic regression models with and without continuous exposure variables.[12]

We separated the entire sample into 4 categories and refer to women as "nondepressed" if they scored less than 16 on the CES-D and reported no history of a 2-week period of depression (the sum of 1*a* and 2*a* in Table 1). Women not currently depressed (CES-D scores <16) were separated into those who never sought a diagnosis or treatment (3*a* in Table 1) and those who sought diagnosis and/or treatment of their depressive symptoms (the sum of 4*a* and 5*a* in Table 1). Women with CES-D scores of 16 or greater were considered separately as a group with current depressive symptoms.

We assessed, in comparison with nondepressed women, differences in the demographic characteristics, background, and menstrual and reproductive histories of women in the 3 groups with varying past and current depression as described above (**Table 2** and **Table 3**). Across all categories, we observed little difference by age and race. In comparison with women achieving at most a high school education, higher educational achievement slightly decreased the risk of current depressive symptoms, but strongly increased the association with a history of depression. Relative to married women, those who never married or were divorced, widowed, or separated were significantly more likely to have a history of depression that required diagnosis or therapy, or be among those scoring 16 or greater on the CES-D. Women currently employed and those living in the towns with higher per capita income were less likely to report a history of depression and more likely to have CES-D scores less than 16. Body mass index was not associated with risk of past depression, but the association with

©1999 American Medical Association. All rights reserved.
Downloaded From: http://archpsyc.jamanetwork.com/ on 07/23/2016

Table 1. Age-Adjusted* 1-Month and Lifetime Prevalence of Depressive Symptoms and Self-reported History of Depression Among Premenopausal Women 36 to 44 Years of Age in the Boston, Mass, Metropolitan Area

Depression History	Severity of Depressive Symptoms in Past Month, Prevalence (No. of Women)			Lifetime History of Depressive Symptoms, Prevalence (No. of Women)
	(*a*) CES-D Score <16	(*b*) CES-D Score 16-24	(*c*) CES-D Score ≥25	
1. No history of depression	45.9 (1908)	4.4 (181)	0.9 (38)	51.2 **(2127)**
2. No 2-wk period of feeling depressed or down but sought diagnosis or treatment for depression	4.1 (171)	1.1 (44)	0.5 (22)	5.7 **(237)**
Two-week period† of feeling depressed or down				
3. With no diagnosis or treatment sought	13.0 (551)	2.9 (119)	2.1 (88)	18.2 **(758)**
4. With diagnosis and psychotherapy	8.6 (358)	2.8 (116)	2.4 (100)	13.8 **(574)**
5. With diagnosis and pharmacotherapy	5.8 (244)	2.7 (113)	2.6 (108)	11.2 **(465)**
Distribution of past month score on CES-D	77.7 **(3232)**	13.8 **(573)**	8.6 **(356)**	**(4161)**

**Adjusted to the age distribution of women with no current or previous history of depression by means of the direct standardization method.[13]*
CES-D indicates Center for Epidemiologic Studies Depression Scale.
†Refers to any period, including the 1-month period in which current depressive symptoms were assessed.

current depressive symptoms increased modestly with increasing quartiles of body mass index. Women in the highest tertile of pack-years of cigarette smoking were significantly more likely than nonsmokers to have a history of depression or current depressive symptoms.

We observed a trend of decreasing risk for CES-D scores of 16 or more with increasing age at menarche, but not with respect to a history of depression (Table 3). Likewise, a trend of increasing risk of history of depression that required medical treatment was observed with increasing menstrual cycle length, but not with current depressive symptoms. These trends were modest but did remain even after adjustment for all menstrual variables together in the same logistic model (excluding pain during menstrual cycles and PMS symptoms). Since previous research supports a strong relationship between self-reported menstrual pain and/or worsening of premenstrual symptoms in patients with major depression,[14,15] adjustment for these variables, which may be a consequence of depression, could spuriously reduce other associations observed. No other differences across the 4 groups of past and current depression were observed with respect to menstrual cycle characteristics, even after additional adjustment for medical conditions such as hypothyroidism and endometriosis (data not shown).

Risk of both past and current depression decreased with increasing numbers of live births. However, this trend was significant only for past ($P<.001$) and not current depressive symptoms. Although use of oral contraceptives for less than 1 year was associated with greater likelihood of past and current depression compared with women who reported no previous use of oral contraceptives, this increased risk waned with increasing years of oral contraceptive use.

The independent effect of each premenstrual symptom group on past and current depression was assessed simultaneously in a single logistic regression model as a dichotomous variable (rarely or some of the time, vs much or most of the time; **Table 4**). Two of the 8 symptom groups were associated with a history of depression that required treatment or diagnosis, and 5 of the 8 symptom groups were significantly associated with women reporting CES-D scores of 16 or more. Quartiles of total score based on the distribution among the nondepressed women were calculated. Scores ranged from 0 in women who reported that all 8 symptom groups rarely or never occurred, to 24 in women who reported that all 8 symptom groups occurred most or all of the time.

Women with current depressive symptoms exhibited a significant trend of higher overall PMS scores compared with nondepressed women ($P<.001$). Likewise, women not currently depressed but who reported a history of treatment or having sought a diagnosis also exhibited a significant trend of higher overall PMS scores compared with the nondepressed women with no history of depression ($P<.001$). When we restricted the analysis to the 5 symptom groups dealing with physical as opposed to neurologic or psychological symptoms (items indicated by double dagger in Table 4), a similar pattern of increasing likelihood of current depression was observed with increasing PMS symptom scores. This same association was observed in the women with past depression as well. Finally, the greater degree to which premenstrual symptoms interfered with social and occupational functioning, the greater the likelihood of women reporting past or current depression.

COMMENT

Data obtained from the screening interview presented in this report provided us with a cross-sectional view of both the prevalence of depressive symptoms of varying severity across the sample and the relationship between various reproductive factors (menstrual history, presence of PMS symptoms, etc) and depression severity scores as measured by the CES-D. A limitation is that we cannot accurately determine which individuals in this sample met frank diagnostic criteria for major depression, and many who scored high on the CES-D may have done so for reasons other than full-blown major depression. However, if we assume that a cutoff of 16 or more on the CES-D has only a 33% predictive value for the detection of true major depression,[9] then our data suggest that, at a minimum, 7.4% ([929 women with CES-D ≥16 × 0.33]/4161) of this population is likely to be suffering from current major depressive disorder. This estimate is comparable with the 6.4%

©1999 American Medical Association. All rights reserved.
Downloaded From: http://archpsyc.jamanetwork.com/ on 07/23/2016

Table 2. Characteristics of Women With and Without Varying Depression History and Symptoms*

	CES-D <16 and No History of 2-wk Period of Feeling Depressed, % (n = 2079)	Not Currently Depressed (CES-D <16), History of 2-wk Period of Feeling Depressed: No Reported Treatment or Diagnosis Sought (n = 551)		History of Treatment or Diagnosis Sought (n = 602)		CES-D ≥16 (n = 929)	
		%	OR† (95% CI)	%	OR† (95% CI)	%	OR† (95% CI)
Age, y							
36-37	22.6	21.7	1.0	20.4	1.0	22.3	1.0
38-39	24.3	24.1	1.0 (0.7-1.3)	23.9	1.0 (0.7-1.3)	23.0	0.9 (0.7-1.2)
40-41	23.5	22.1	1.0 (0.7-1.3)	23.1	1.1 (0.8-1.4)	23.1	1.0 (0.8-1.2)
42-44	29.6	32.1	1.1 (0.9-1.5)	32.6	1.2 (0.9-1.6)	31.6	1.0 (0.8-1.3)
Test of trend		$P > .10$		$P = .07$		$P > .10$	
Race							
White	92.8	93.6	1.0	94.5	1.0	91.5	1.0
Nonwhite	7.2	6.4	0.8 (0.6-1.3)	5.5	0.7 (0.5-1.1)	8.5	1.1 (0.8-1.5)
Education							
≤High school	11.3	8.7	1.0	3.2	1.0	15.6	1.0
Some college/vocational	19.1	16.2	1.1 (0.7-1.6)	16.3	3.2 (1.9-5.5)	22.1	0.9 (0.6-1.1)
College graduate	69.6	75.1	1.5 (1.0-2.1)	80.5	4.5 (2.7-7.5)	62.3	0.8 (0.6-1.0)
Test of trend		$P = .002$		$P < .001$		$P = .03$	
Marital status							
Married	69.9	69.0	1.0	55.6	1.0	56.7	1.0
Never married	21.6	22.0	1.0 (0.8-1.3)	29.6	1.6 (1.3-2.0)	27.8	1.6 (1.3-2.0)
Divorced/separated/widowed	8.5	9.0	1.1 (0.7-1.5)	14.8	2.1 (1.6-2.8)	15.5	2.2 (1.7-2.8)
Test of trend		$P > .10$		$P < .001$		$P < .001$	
Currently employed							
No	16.9	19.1	1.0	16.0	1.0	19.7	1.0
Yes	83.1	80.9	0.8 (0.6-1.0)	84.0	0.8 (0.6-1.0)	80.3	0.7 (0.6-0.9)
Per capita income of town of residence, $1000							
<30	15.3	19.2	1.0	26.7	1.0	18.0	1.0
30-39	24.8	26.0	0.9 (0.6-1.1)	23.3	0.6 (0.5-0.8)	29.5	0.9 (0.7-1.1)
40-49	36.4	31.9	0.7 (0.5-0.9)	29.1	0.5 (0.4-0.6)	34.7	0.8 (0.6-1.1)
≥50	22.5	22.9	0.7 (0.6-1.1)	20.9	0.6 (0.4-0.8)	17.8	0.9 (0.6-1.6)
Test of trend		$P = .03$		$P < .001$		$P > .10$	
Quartiles of self-reported body mass index, kg/m^2							
<21.0	25.9	30.3	1.0	26.2	1.0	25.6	1.0
21.0-22.9	24.1	20.4	0.7 (0.6-1.0)	23.1	1.0 (0.8-1.3)	19.8	0.8 (0.7-1.1)
23.0-26.4	25.3	26.5	0.9 (0.7-1.2)	25.3	1.0 (0.8-1.4)	23.3	0.9 (0.7-1.1)
≥26.5	24.7	22.8	0.8 (0.6-1.1)	25.4	1.1 (0.8-1.5)	31.3	1.2 (0.9-1.5)
Test of trend		$P > .10$		$P > .10$		$P = .01$	
Tertiles of cigarette smoking, pack-years							
None	58.2	58.1	1.0	52.5	1.0	48.8	1.0
<913	13.1	10.2	0.8 (0.6-1.1)	13.6	1.2 (0.9-1.6)	11.7	1.1 (0.9-1.5)
913-3650	14.7	14.5	1.0 (0.9-1.4)	16.3	1.3 (1.0-1.7)	14.8	1.2 (0.9-1.5)
>3650	14.0	17.2	1.3 (1.0-1.8)	17.6	1.5 (1.1-2.0)	24.7	1.9 (1.5-2.3)
Test of trend		$P > .10$		$P = .001$		$P < .001$	

*CES-D indicates Center for Epidemiologic Studies Depression Scale; OR, odds ratio; and CI, confidence interval.
†Adjusted for age (continuous), race, marital status, education, whether currently employed, per capita income, and pack-years of cigarette smoking.

©1999 American Medical Association. All rights reserved.
Downloaded From: http://archpsyc.jamanetwork.com/ on 07/23/2016

Table 3. Menstrual History and Other Reproductive Characteristics of Women With and Without Varying Depression History and Symptoms*

	CES-D <16 and No History of 2-wk Period of Feeling Depressed, % (n = 2079)	Not Currently Depressed (CES-D <16), History of 2-wk Period of Feeling Depressed: No Reported Treatment or Diagnosis Sought (n = 551)		History of Treatment or Diagnosis Sought (n = 602)		CES-D ≥16 (n = 929)	
		%	OR† (95% CI)	%	OR† (95% CI)	%	OR† (95% CI)
Age at menarche, y							
≤10	4.8	6.5	1.4 (0.9-2.1)	4.3	0.8 (0.5-1.3)	6.7	1.3 (0.9-1.8)
11-13	70.6	69.5	1.0	74.3	1.0	71.0	1.0
14-15	19.9	19.6	1.0 (0.8-1.3)	16.9	0.8 (0.6-1.1)	18.6	0.9 (0.7-1.1)
≥16	4.7	4.4	0.9 (0.6-1.5)	4.5	1.0 (0.6-1.6)	3.7	0.7 (0.5-1.1)
Test of trend		$P>.10$		$P>.10$		$P=.03$	
Interval between menstrual cycles, d							
≤24	8.4	8.7	1.1 (0.8-1.5)	8.5	1.0 (0.7-1.5)	10.2	1.2 (0.9-1.5)
25-26	13.1	13.4	1.1 (0.8-1.4)	11.3	0.9 (0.7-1.2)	10.5	0.8 (0.6-1.1)
27-29	54.8	53.0	1.0	53.0	1.0	53.3	1.0
30-32	15.6	16.5	1.1 (0.9-1.5)	18.1	1.3 (1.0-1.7)	17.2	1.2 (0.9-1.5)
≥33	8.1	8.4	1.1 (0.7-1.6)	9.1	1.3 (0.9-1.9)	8.8	1.1 (0.8-1.5)
Test of trend		$P>.10$		$P=.05$		$P>.10$	
Days of menstrual flow							
2-3	13.7	14.3	1.1 (0.8-1.4)	16.9	1.3 (1.0-1.7)	15.6	1.1 (0.9-1.4)
4-5	62.1	60.2	1.0	56.1	1.0	59.6	1.0
6-7	22.2	22.0	1.0 (0.8-1.3)	24.3	1.3 (1.0-1.6)	20.8	0.9 (0.8-1.2)
≥8	2.0	3.5	1.9 (1.1-3.3)	2.7	1.9 (1.0-3.5)	4.0	2.0 (1.2-3.2)
Test of trend		$P>.10$		$P>.10$		$P>.10$	
Cycle regularity							
Usually regular	94.2	94.0	1.0	95.2	1.0	91.6	1.0
Usually irregular	5.8	6.0	1.0 (0.6-1.5)	4.8	0.7 (0.4-1.1)	8.4	1.4 (1.0-1.9)
Pain with periods‡							
None	22.4	17.6	1.0	14.5	1.0	12.7	1.0
Mild	49.2	51.4	1.2 (0.9-1.6)	49.0	1.3 (1.0-1.7)	40.9	1.0 (0.8-1.3)
Moderate	25.6	27.2	1.1 (0.8-1.5)	29.7	1.2 (0.9-1.6)	37.1	1.1 (0.8-1.5)
Severe	2.8	3.8	1.2 (0.7-2.2)	6.8	2.4 (1.4-3.9)	9.3	1.6 (1.0-2.5)
Test of trend		$P>.10$		$P=.05$		$P=.09$	
Live births, No.							
0	34.3	36.6	1.0	49.3	1.0	40.3	1.0
1-2	43.9	45.6	1.0 (0.8-1.3)	40.9	0.7 (0.6-0.9)	41.5	0.9 (0.8-1.2)
≥3	21.8	17.8	0.8 (0.6-1.1)	9.8	0.4 (0.3-0.6)	18.2	0.8 (0.6-1.1)
Test of trend		$P>.10$		$P<.001$		$P>.10$	
OC use, y							
Never	31.7	31.8	1.0	28.4	1.0	27.9	1.0
<1	10.4	12.3	1.2 (0.8-1.6)	14.1	1.5 (1.1-2.1)	15.7	1.7 (1.3-2.2)
1-<3	20.1	17.8	0.9 (0.7-1.2)	21.1	1.2 (0.9-1.5)	18.6	1.1 (0.8-1.4)
≥3	37.8	38.1	1.0 (0.8-1.3)	36.4	1.1 (0.8-1.4)	37.8	1.1 (0.9-1.4)
Test of trend		$P>.10$		$P>.10$		$P>.10$	

*CES-D indicates Center for Epidemiologic Studies Depression Scale; OR, odds ratio; CI, confidence interval; and OC, oral contraceptive.
†Adjusted for age (continuous), education, marital status, pack-years of cigarette smoking, and each variable in the table except pain during menstrual periods.
‡Adjusted for premenstrual symptom score in addition to the above-listed factors.

estimate reported in the National Comorbidity Survey for women of similar ages.[1] In addition, 25% of this population reported a 2-week period of feeling depressed or down that caused them to seek a diagnosis as well as psychotherapy or pharmacotherapy for their depression. Although we cannot determine the extent to which depressed nonrespondents may have been more or less motivated to return the screener questionnaire, we achieved

©1999 American Medical Association. All rights reserved.
Downloaded From: http://archpsyc.jamanetwork.com/ on 07/23/2016

Table 4. Association Between Premenstrual Symptoms and Past or Current Depression*

Extent to Which the Following Symptoms Occur Much or Most of the Time	Not Currently Depressed (CES-D <16), History of 2-wk Period of Feeling Depressed: No Reported Treatment or Diagnosis Sought (n = 551)		Not Currently Depressed (CES-D <16), History of 2-wk Period of Feeling Depressed: History of Treatment or Diagnosis Sought (n = 602)		CES-D ≥16 (n = 929)	
	OR† (95% CI)	*P*	OR† (95% CI)	*P*	OR† (95% CI)	*P*
Muscle stiffness, headaches, cramps, or fatigue‡	0.8 (0.6-1.0)	.12	1.1 (0.8-1.3)	.64	1.1 (0.9-1.3)	.50
Insomnia, forgetfulness, or confusion	1.5 (1.0-2.2)	.05	2.3 (1.6-3.2)	<.001	2.5 (1.9-3.4)	<.001
Lowered performance or lack of energy	1.0 (0.7-1.3)	.75	1.0 (0.8-1.3)	.92	2.2 (1.8-2.7)	<.001
Dizziness, faintness, sweats, nausea, or flashes‡	1.6 (0.9-2.5)	.08	1.5 (0.9-2.3)	.11	1.8 (1.2-2.6)	.002
Weight gain, painful breasts, or swelling‡	1.2 (1.0-1.5)	.07	1.2 (1.0-1.5)	.12	1.0 (0.8-1.2)	.95
Tension, mood swings, irritability, or depression	1.2 (1.0-1.5)	.09	1.3 (1.0-1.6)	.03	3.3 (2.2-4.0)	<.001
Excitement, well-being, or bursts of energy‡	1.0 (0.7-1.4)	.89	0.7 (0.5-1.0)	.07	0.7 (0.5-1.0)	.07
Heart pounding, numbness, or ringing in ears‡	3.8 (1.7-8.7)	.001	2.4 (0.9-6.3)	.08	3.2 (1.6-6.6)	<.001
Total PMS score§						
≤3	1.0		1.0		1.0	
4-5	1.4 (1.0-1.8)	.02	1.3 (1.0-1.8)	.04	1.8 (1.3-2.5)	<.001
6-7	1.6 (1.2-2.1)	.001	1.4 (1.1-1.9)	.02	3.2 (2.4-4.4)	<.001
≥8	1.6 (1.3-2.1)	<.001	2.0 (1.5-2.5)	<.001	9.3 (7.1-12.0)	<.001
Physical symptoms score§						
≤3	1.0		1.0		1.0	
4-5	1.3 (1.0-1.6)	.04	1.2 (0.9-1.5)	.13	2.0 (1.6-2.5)	<.001
6-7	1.5 (1.1-2.0)	.006	1.6 (1.2-2.1)	<.001	3.1 (2.5-3.9)	<.001
≥8	1.6 (1.1-2.5)	.03	1.6 (1.1-2.5)	.02	6.4 (4.8-8.6)	<.001
Extent to which these symptoms interfere with social or occupational functioning‖	1.5 (1.0-2.2)	.08	2.1 (1.4-3.1)	<.001	6.3 (4.8-8.3)	<.001

*CES-D indicates Center for Epidemiologic Studies Depression Scale; OR, odds ratio; CI, confidence interval; and PMS, premenstrual syndrome.

†Odds ratios are all relative to women with CES-D scores less than 16 and no history of 2-week period of feeling depressed and are adjusted for age, pack-years of cigarette smoking, education, marital status, and parity. All 8 symptoms were evaluated simultaneously in the same logistic regression model.

‡Included in physical symptom score below.

§All tests of trend are significant at P<.001.

‖Does not include adjustment for each of the 8 symptom categories.

a respectable response rate, and the estimated lifetime prevalence is comparable with the 23.8% lifetime prevalence reported in the National Comorbidity Survey.[1] The relatively large number of patients with apparent histories of depression of 2 weeks' duration who did not seek professional treatment is consistent with other reports describing the extent of untreated depression.[16-18] The apparent absence of change during the last 2 decades in numbers of patients who suffer from depression in the community, and who nonetheless fail to receive treatment, suggests a problem of considerable public health concern. Regardless of where the true division for the classification of current or past major depression exists, our data represent a comprehensive population-based sample of women within a defined age and geographic location.

Although the proportion of nonwhite women was highest among the currently depressed group of women in this dataset, there were no statistical differences by race. Thus, these results are suggestive of, but cannot confirm, the findings from several other studies that showed the lifetime prevalence of depression to be similar across racial groups but higher when assessed during a 1-month period.[1,19] Women with current depressive symptoms were somewhat less likely to be more highly educated. However, a significantly greater proportion of more highly educated women composed the group with history of depression. Coryell et al[20] reported that women with any college education were significantly more likely to develop depression than women with no college education. The fact that we saw only a modest reduction in the association between education and current depressive symptoms may indicate merely that those who are more highly educated sought treatment for their disorder, which would likely have resulted in a relatively normal CES-D score. We also cannot rule out the possibility that educational status may influence the reporting accuracy of depressive symptoms.

Our results support the findings of previous studies that suggest that marital disruption is strongly associated with a higher prevalence of major depression.[6,20-22] We did not have the opportunity in these data to determine whether marital disruption preceded or was a consequence of the onset of mood disorder. However, the cohort of women derived from these cross-sectional data will allow for the temporal assessment of mood disorder and changes in marital status over time. Our data also suggest that being underweight has little effect on mood disorder and that only those in the upper quartile of body mass index are at a somewhat greater risk of exhibiting current depressive symptoms.

The cross-sectional data presented in this analysis do not allow us to distinguish between cigarette smoking ex-

©1999 American Medical Association. All rights reserved.
Downloaded From: http://archpsyc.jamanetwork.com/ on 07/23/2016

posure before or after first diagnosis of depression. If a true association exists between depression and cigarette smoking, it is unlikely that such an association would be caused by cigarette smoking as a consequence of becoming depressed, since the greatest association was observed in women who smoked for more than 20 years (data not shown) and in the highest tertile of pack-years of exposure. Results from the Coronary Artery Risk Development in Young Adults study suggested that the association between cigarette smoking and depressive symptoms should become attenuated after adjustment for education.[23] Education was not associated with current depressive symptoms and therefore did not influence the association between cigarette smoking and CES-D score of 16 or more. Education was strongly and negatively correlated with both cigarette smoking and a history of depression that required diagnosis and treatment. However, statistical adjustment for education strengthened rather than attenuated the association between smoking and past depression.

We were somewhat puzzled by the finding of decreasing depressive symptoms with increasing age at menarche that should logically also have been observed for past depression. Likewise, risk of past depression increased with increasing cycle length, which should logically also have been observed for current depressive symptoms as well. These may, therefore, be merely chance findings. Although these data provide only limited information pertaining to oral contraceptive exposure, the association with short-term use of oral contraceptives may be a consequence of an attempt to control either pain with menstrual periods or premenstrual symptoms. However, our prospective study will provide much more detail pertaining to this association.

Several reports, including ours, describe a strong association between premenstrual dysphoria and depressive symptoms.[24-26] The extent to which PMS symptoms precede depressive disorder or are a consequence of worsening mood[14,15] could not be definitively determined in this analysis. Thus, to prevent the spurious reduction in the magnitude of other associations, we chose not to adjust for PMS symptoms when assessing other potential risk factors. We recognize in these data that the strength of the relationship between PMS and mood disorder dwarfs the influence of other menstrual and nonreproductive variables on depression prevalence. For example, more than 50% of women with Moos PMS scores greater than 5 had CES-D depression scores of 16 or more compared with only 15% of women with PMS scores less than 5. Thus, the fraction of the prevalence attributable to this exposure is about 73% ([55 – 15]/55), leaving little room for other causal pathways to exist in the presence of this exposure.[27] In these cross-sectional data, both total scores for PMS and scores derived from both psychological and somatic symptom clusters were strongly associated with past and current depressive symptoms. Although this might be explained by the overlap of symptoms in certain domains (ie, energy, instability, and mood swings), the strong association is also noted between somatic symptoms associated with PMS and depressive symptoms. We recognize that an obvious limitation of these data stems from the use of a retrospective inventory that is likely to be influenced by current premenstrual and/or depressive symptoms, recall, and other life events that are coincident at the time of the interview.

Future analyses will refine these preliminary observations as we prospectively evaluate reproductive hormonal function and course of mood disorder in an established cohort.

Accepted for publication January 27, 1999.

This research was supported by grant R01-MH-50013 from the National Institute of Mental Health, Bethesda, Md.

Reprints: Bernard L. Harlow, PhD, Obstetrics and Gynecology Epidemiology Center, Brigham and Women's Hospital, 221 Longwood Ave, Boston, MA 02115 (e-mail: bharlow@rics.bwh.harvard.edu).

REFERENCES

1. Blazer DG, Kessler RC, McGonagle KA, Swartz MS. The prevalence and distribution of major depression in a national community sample: the National Comorbidity Survey. *Am J Psychiatry*. 1994;151:979-986.
2. Regier DA, Farmer ME, Rae DS, Myers JK, Kramer M, Robins LN, George LK, Karno M, Locke BZ. One-month prevalence of mental disorders in the United States and sociodemographic characteristics. *Acta Psychiatr Scand*. 1993;88:35-47.
3. Harlow BL, Cramer DW, Annis KM. Association of medically treated depression and age at natural menopause. *Am J Epidemiol*. 1995;141:1170-1176.
4. Kendler KS, Neale MC, MacLean CJ, Heath AC, Eaves LJ, Kessler RC. Smoking and major depression: a causal analysis. *Arch Gen Psychiatry*. 1993;50:36-43.
5. Anda RF, Williamson DF, Escobedo LG, Mast EE, Giovino GA, Remington PL. Depression and the dynamics of smoking. *JAMA*. 1990;264:1541-1545.
6. Roy A. A case-control study of social risk factors for depression in American patients. *Can J Psychiatry*. 1997;42:307-309.
7. Endicott J. The menstrual cycle and mood disorders. *J Affect Disord*. 1993;29:193-200.
8. Roberts RE, Vernon SW. The Center for Epidemiologic Studies Depression Scale: its use in a community sample. *Am J Psychiatry*. 1983;140:41-46.
9. Boyd JH, Weissman MM, Thompson WD, Myers JK. Screening for depression in a community sample . *Arch Gen Psychiatry*. 1982;39:1195-1200.
10. Craig TJ, van Natta PA. Recognition of depressed affect in hospitalized psychiatric patients: staff and patient perceptions. *Dis Nerv Syst*. 1976;37:561-566.
11. Moos RH. Typology of menstrual cycle symptoms. *Am J Obstet Gynecol*. 1969;103:390-401.
12. Breslow NE, Day NE. *Statistical Methods in Cancer Research, Volume 1: The Analysis of Case-Control Studies*. Lyon, France: International Agency for Research on Cancer; 1980. IARC scientific publication 32.
13. Fleiss JL. *Statistical Methods for Rates and Proportions*. New York, NY: John Wiley & Sons Inc; 1973:162-164.
14. Fava M, Pedrazzi F, Guaraldi GP, Romano G, Genazzani AR, Fachinetti F. Comorbid anxiety and depression among patients with late luteal phase dysphoric disorder. *J Anxiety Disord*. 1992;6:1325-1335.
15. Tonkers KA. The association between premenstrual dysphoric disorder and other mood disorders. *J Clin Psychiatry*. 1997;58(suppl 15):19-25.
16. Keller MB, Harrison W, Fawcett JA, Gelenberg A, Hirschfeld RM, Klein D, Kocsis JH, McCullough JP, Rush AJ, Schatzberg A, et al. Treatment of chronic depression with sertraline or imipramine. *Psychopharmacol Bull*. 1995;31:205-212.
17. Hirschfeld RM, Keller MB, Panico S, Arons BS, Barlow D, Davidoff F, Endicott J, Froom J, Goldstein M, Gorman JM, Marek RG, Maurer TA, Meyer R, Phillips K, Ross J, Schwenk TL, Sharfstein SS, Thase ME, Wyatt RJ. The National Depressive and Manic-Depressive Association consensus statement on the undertreatment of depression. *JAMA*. 1997;277:333-340.
18. Keller MB, Lavori PW, Klerman GL, Andreason NC, Endicott J, Coryell W, Fawcett J, Rice JP, Hirschfeld RM. Low levels and lack of predictors of somatotherapy and psychotherapy received by depressed patients. *Arch Gen Psychiatry*. 1986;43:458-466.
19. Somervell PD, Leaf PJ, Weissman MM, Blazer DG, Bruce ML. The prevalence of major depression in black and white adults in five United States communities. *Am J Epidemiol*. 1989;130:725-735.
20. Coryell W, Endicott J, Keller M. Major depression in a nonclinical sample: demographic and clinical risk factors for first onset. *Arch Gen Psychiatry*. 1992;49:117-125.
21. Bruce ML, Kim KM. Differences in the effects of divorce on major depression in men and women. *Am J Psychiatry*. 1992;149:914-917.
22. Weissman MM, Bland RC, Canino GJ, Faravelli C, Greenwald S, Hwu HG, Joyce PR, Karam EG, Lee CK, Lellouch J, Lepine JP, Newman SC, Rubio-Stipec M, Wells JE, Wickramaratne PJ, Wittchen H, Yeh EK. Cross-national epidemiology of major depression and bipolar disorder. *JAMA*. 1996;276:293-299.
23. Son BK, Markovitz JH, Winders S, Smith D. Smoking, nicotine dependence, and depressive symptoms in the CARDIA study. *Am J Epidemiol*. 1997;145:110-116.
24. Graze PP, Nee J, Endicott J. Premenstrual depression predicts future major depressive disorder. *Acta Psychiatr Scand*. 1990:81:201-205.
25. Halbreich U, Endicott J. Relationship of premenstrual changes to depressive disorders. *Acta Psychiatr Scand*. 1985;71:331-338.
26. MacKenzie TB, Wilcox K, Baron H. Lifetime prevalence of psychiatric disease in women with premenstrual difficulties. *J Affective Disord*. 1986:10:15-19.
27. Rothman KJ. *Modern Epidemiology*. Boston, Mass: Little Brown & Co; 1986:36-40.

©1999 American Medical Association. All rights reserved.
Downloaded From: http://archpsyc.jamanetwork.com/ on 07/23/2016