Published in final edited form as:

Fertil Steril. 2013 December ; 100(6): 1667–1672. doi:10.1016/j.fertnstert.2013.08.020.

Prospective Evaluation of Hot Flashes during Pregnancy and Postpartum

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Abstract

Objective—To determine the prevalence, course, and risk factors for hot flashes during pregnancy and postpartum.

Study Design—Women (N=429) were assessed prospectively during pregnancy (weeks 20, 30, 36) and up to a year after delivery (weeks 2, 12, 26, 52). A clinical interview, physical measurements, and questionnaires were administered at each visit.

Results—Thirty-five percent of women reported hot flashes during pregnancy and 29% reported hot flashes after delivery. In multivariable binomial mixed effects models, women who were younger (per year: OR(95%CI): 0.94(0.88–0.99)), had a higher pre-pregnancy body mass index (BMI; per unit increase: OR(95%CI): 1.05(1.01–1.10)), and had less than a college education (OR(95%CI): 2.58(1.19–5.60); vs. college) were more likely to report hot flashes during pregnancy. Higher depressive symptoms were associated with hot flashes during pregnancy (per unit increase: OR(95%CI): 1.08(1.04–1.13)) and after birth (OR(95%CI): 1.19(1.14–1.25), multivariable models).

Conclusion—Hot flashes, typically considered a menopausal symptom, were reported by over a third of women during pregnancy and/or postpartum. Predictors of hot flashes during this reproductive transition, including depressive symptoms, low education, and higher BMI are similar to those experienced during menopause. Future work should investigate the role of hormonal and affective factors in hot flashes during pregnancy and postpartum.

Keywords

Hot flashes; pregnancy; postpartum; night sweats; vasomotor symptoms

Introduction

Hot flashes are the classic common menopausal symptom, with most women reporting hot flashes at some point during the menopausal transition (1). Hot flashes are associated with sleep disturbance (2), irritability and embarrassment (3), and overall impairments in physical, social, and emotional quality of life (4). Although the physiology of hot flashes is not well understood, they are thought to be thermoregulatory events occurring due to the dramatic hormonal transitions experienced during the menopause transition (5).

Although hot flashes are most commonly reported during menopause, they are also reported at other times of marked hormonal fluctuation, such as pregnancy or postpartum. In fact, hot flashes during pregnancy are commonly documented in the popular literature (e.g., (6)). However, there is a dearth of information about pregnancy-related hot flashes in the academic literature. Two cross-sectional surveys of pregnant women found that hot flashes were reported by a sizable number of pregnant women (7, 8), and one study found that 10% of women reported hot flashes within the first month postpartum (9). However, most of these studies assessed women at a single time point and hot flashes were reported retrospectively over a considerable period of time. No studies have tracked hot flashes prospectively across both pregnancy and after birth. Thus, the prevalence and course of these hot flashes have not been fully characterized.

Whether the risk factors for pregnancy-related hot flashes are similar to those for hot flashes experienced during the menopause is not known. Typical risk factors for menopausal hot flashes are smoking, depression, low education, and for women early in the menopause transition, obesity (1). Similar to menopausal hot flashes, one study found that increased negative affect was associated with elevated reporting of hot flashes during pregnancy (8). However, a more complete examination of predictors of hot flashes during pregnancy and postpartum is needed.

Our objective is to determine the prevalence, course, and risk factors for hot flashes during pregnancy and up to a year after delivery. We examined these questions in 464 women both with and without mood disorders assessed prospectively throughout pregnancy and after delivery.

Materials and Methods

Sample

The sample was comprised of women from two NIMH-supported observational investigations (Antidepressant Use during Pregnancy R01MH60335 and Antimanic Use during Pregnancy R01MH07592; *Wisner, PI*) with similar design that followed women throughout pregnancy and postpartum. Details of study design and procedures have been reported elsewhere (10). Briefly, women with a lifetime history of Major Depressive Disorder (MDD), Bipolar Disorder (BD) and a comparison group of women with neither psychiatric disorder were enrolled. For both studies, pregnant women aged 18–44 years old were recruited by self-referral, physician referral, advertising, and screening in the obstetrical ultrasound suite. The parent studies had a primary focus on fetal exposures to

disease or medication (10); therefore, women with active substance use disorder (identified by self-report or urine drug screen) or with gestational exposure to benzodiazepines or prescription drugs in the FDA-defined category of D or X were excluded. Approval was obtained from the Case Western Reserve University and University of Pittsburgh institutional review boards. All women provided written informed consent. Women were classified into non-overlapping groups based upon lifetime history of psychiatric disorders at study entry: Women with MDD (N=173); women with BD (N=151); and women with neither MDD nor BD (N=140).

Protocol

Baseline assessments (at week 20 of pregnancy) included a clinical interview, physical measurements, a urine drug screen, a blood draw, and completion of questionnaires. Women were thereafter assessed at 30 and 36 weeks of gestation and at 2, 12, 26, and 52 weeks after birth. These follow up assessments included the same measurements (with the exception of the urine drug screen) as those administered at baseline.

Measures

Demographic characteristics, including age, race, employment status (categorized as employed/unemployed), education (categorized as < or > college completion) were assessed at baseline via standard instruments. Hot flashes were assessed at each visit in response to a question about the presence of sleep-disturbing hot flashes (0=none; 1=mild, minimal disruption; 2=moderate, important sleep disturbances; 3=severe, major disruption; categorized as any/none due to small cell sizes). Psychiatric diagnosis was established at baseline via the Structured Clinical Interview for DSM-IV (SCID). The timeline technique (11) was adapted to chart mood episodes across time. For interviews after the baseline assessment, the longitudinal interval follow-up evaluation was used in conjunction with the SCID to assess for diagnostic status change. Depressive symptoms were assessed with the 29-item Structured Interview Guide for the Hamilton Depression Rating Scale with Atypical Depression Supplement (SIGH-ADS) (12). Psychotropic drug exposure was documented by charting the subject's drug doses at each visit (with verification of exposure by serum levels (10)). Use of tobacco, alcohol, and illicit drugs was assessed at each visit. Breastfeeding status was recorded at each postpartum assessment by the percent in deciles of feedings of breastmilk; 100% was fully breastfed and 0% was entirely formula fed. Due to small cell sizes at each decile, we categorized breastfeeding as breastfeeding (women who breastfed 50%) or not breastfeeding (<50% breastfed). Pre-pregnancy BMI was calculated as weight (lbs)/height (in)² using the woman's reported pre-pregnancy height and weight.

Data Analysis

Pregnancy and postpartum (2–52 weeks after delivery) were considered separately due to their differing hormonal milieu. Bivariate and multivariate models of hot flashes were examined using repeated measures binomial mixed effect models with an unstructured covariance matrix. Retained covariates were selected via backward stepwise methods. Ethnicity, education, employment status, and BMI (pre-pregnancy) were considered as time-invariant covariates and smoking, alcohol use, illicit drug use, depressive symptoms, mania symptoms, and medication use were considered time-varying covariates. With respect to

medication, we specifically focused on serotonin selective reuptake inhibitor (SSRI) use since they are used to therapeutically reduce hot flashes (13). Pre-pregnancy lifetime diagnosis of depression, mania, or neither was forced into multivariate models. All tests were two-tailed, $\alpha=0.05$.

Results

Hot flashes were reported both during pregnancy and after delivery, with 35% of women reporting hot flashes at any point during pregnancy and 29% after delivery. At any given visit, their prevalence ranged from 18–24% during pregnancy and 10–20% after delivery (Tables 1, 2). Hot flashes varied significantly over time, peaking during pregnancy at week 30 and during postpartum at week 2, declining thereafter.

In bivariate analyses, risk factors for reporting hot flashes during pregnancy were younger age, minority race/ethnicity, having less than a college education, being unemployed, having a higher pre-pregnancy BMI, having a pre-pregnancy history of mania, being a smoker, and having higher current depressive symptoms. Risk factors for hot flashes after delivery were similar to those during pregnancy and included having less than a college education, being unemployed, having a pre-pregnancy history of mania, being a smoker, and having higher current depressive symptoms. There was some indication in the weeks after delivery that BMI, smoking, and education showed a time-dependent relation to hot flashes. For example, low pre-pregnancy BMI appeared associated with more hot flashes in the weeks directly postpartum, but not as time since delivery increased.

In multivariable models, factors that remained associated with hot flashes during pregnancy were younger age, a higher pre-pregnancy BMI, having less than a college education, and having higher depressive symptoms (Table 3). Higher depressive symptoms remained associated with the presence of hot flashes after delivery (Table 4).

Discussion

Hot flashes are typically considered a menopausal symptom. Hot flashes during pregnancy or postpartum are commonly discussed in the popular literature, yet there has been a relative silence about them in the academic literature. In this study, over a third of women reported hot flashes during pregnancy, peaking at week 30. Over a quarter of women reported hot flashes in the postpartum, peaking at week 2 and declining thereafter. Further, similar to menopausal hot flashes, key risk factors, such as elevated depressive symptoms, higher BMI, and lower education, were risk factors for hot flashes during pregnancy/postpartum.

A full understanding of the underlying physiology of hot flashes, including the well-documented menopausal hot flashes, remains elusive. However, the menopause transition is a time of marked hormonal changes, with large swings in gonadal hormones during the perimenopause with an ultimate leveling off to low endogenous estrogen levels during the postmenopause (14). These hormonal fluctuations and/or estrogen withdrawal are thought to be key permissive factors to hot flash occurrence, with the relative importance of low absolute levels versus fluctuations debated (14, 15). Notably, pregnancy and postpartum are also times of pronounced hormonal changes, with dramatic increases in estrogens and

progesterone during pregnancy, withdrawal during the postpartum, and ultimately normalization (16). The present findings suggest the importance of hormone fluctuations in hot flashes, providing further clues to their etiology. However, whereas all menopausal and pregnant/postpartum women experience pronounced hormonal changes, not all of these women report hot flashes. Thus, other systems are likely at play, such as central thermoregulatory and/or neuroendocrine systems (5), and peripheral autonomic nervous and vascular systems (17, 18).

Women were evaluated prospectively in this study, allowing characterization of the course of hot flashes over pregnancy and up to a year after delivery. Hot flashes were observed during both periods, increasing through pregnancy to reach a high during the 30th week, in which 24% of women reported hot flashes. Hot flashes were also experienced by 20% of women during postpartum, peaking in the 2nd week and decreasing thereafter, possibly as reproductive hormone levels normalized. Over a third of woman reported hot flashes at any point during pregnancy and 29% reported them during the weeks after delivery. The limited prior work on this topic has indicated a broad range of estimates, ranging from 24% in early pregnancy (7) to 55% at any point during pregnancy (8). One study found that 10% of women reported hot flashes at one month postpartum. The discrepancies between these findings are likely due to a range of factors, including time of assessment, differing sample compositions, method of assessing hot flashes, and frame of recall (e.g., current symptoms, past two weeks, any point). Most of these studies assessed hot flashes cross-sectionally at a single time point. The present study was unique in its prospective repeated assessment of hot flashes during both pregnancy and up to a year after birth.

In the present work, elevated depressive symptoms were the most consistent predictor of hot flashes in both pregnancy and after delivery. Elevated depressive symptoms are also a robust risk factor for menopausal hot flashes (1, 19). The reasons for relations between depressive symptoms and hot flashes are likely numerous. Depressive symptoms may predispose a woman to reporting hot flashes via changes in central neuroendocrine function (20), an elevated propensity to report physical symptoms (21), and/or in this case, sleep disturbance that may increase the likelihood of endorsing sleep-disturbing hot flashes (22). Hanisch et al similarly found elevated negative affect (anxious symptoms, typically highly correlated with depressive symptoms) to be one of the few predictors of pregnancy-related hot flashes (8). Thus, affective factors clearly play an important role in hot flash reporting across reproductive transitions for women.

Several other risk factors for pregnancy/postpartum hot flashes were low education and a higher pre-pregnancy BMI. Notably, low education is a consistent predictor of menopausal hot flashes for reasons not fully understood (1). Moreover, elevated BMI is associated with elevated hot flashes early in the menopausal transition (1, 23). During this time, body fat may both act as an insulator against the presumed thermoregulatory function of hot flashes to dissipate heat (24, 25), and possibly exert a deleterious effect on the hypothalamic-gonadal-axis (26, 27) to in turn increase hot flashes. These effects are less clear in the postmenopause, when body fat may be the primary source of estrogen (28) and mitigate hot flashes (23). Whether body size is operating similarly in women during pregnancy, blunting hormonal responses to increase hot flashes during pregnancy, yet protecting against some of

the dramatic hormonal withdrawal in the postpartum, is not entirely clear. It is important to note that pre-pregnancy, not pregnancy BMI, was used in our analysis as BMI measured during pregnancy is a poor proxy for adiposity at this time. However, the role of obesity in the hormonal dynamics of pregnancy and associated hot flashes deserves continued evaluation. In sum, our findings show a similarity of risk factors for hot flashes during pregnancy/postpartum and the menopause transition, suggesting a potentially similar underlying physiology.

This study had several limitations. First, the hot flashes measurement employed here was a brief global assessment of hot flashes experienced over the past two weeks, with limited assessment of their characteristics. Future work should utilize more detailed diary or physiologic hot flash measures and assess the phenomenology of these hot flashes to determine their comparability to menopausal hot flashes. The present study queried about hot flashes with respect to their disturbance on sleep, and thereby may represent only a subset of all hot flashes. These reports may be influenced by sleep problems. Further, pre-pregnancy BMI was reported, not measured, as women entered the study when they were pregnant. Thus, there is likely some error in these BMI reports, although it would not be expected to systematically vary by hot flash status. Finally, the overall higher prevalence of women with mood disorders and using psychotropic medications in our sample relative to the general population may have resulted in a differential prevalence of hot flashes, as both negative mood (1, 21) and SSRI antidepressant use (13) can impact hot flash reporting (although in opposing directions). Future work should consider a population-based sampling strategy.

A major strength of this study is that it is the first to assess hot flashes over both pregnancy and postpartum. Additionally, hot flashes were assessed prospectively multiple times during both time periods, allowing characterization of the course of these hot flashes. Finally, unlike many prior reports, the sample was relatively large and socioeconomically diverse.

Although hot flashes are typically only associated with the menopause transition, this study showed a markedly high prevalence of hot flashes during pregnancy and after delivery. This work underscores the potential importance of considering hot flashes during multiple female reproductive transitions. These findings may assist in better understanding the etiology of hot flashes, not fully understood at present. They point to consideration of how affective factors may influence the occurrence and reporting of hot flashes. Finally, these results underscore the importance of further investigating the phenomenology of hot flashes during pregnancy and postpartum, their underlying physiology, and their potential impact on women's lives during this important life transition.

Acknowledgments

This work was supported by National Institutes of Health grants R01 MH060335 and R01 MH075921 (PI: Wisner). This work was also supported by NIH grant K23 AG029216 (PI: Thurston).

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Table 1

Subject characteristics by sleep-disturbing hot flashes and weeks gestation of pregnancy

	Week 20 (N=429)		Week 30 (N=341)		Week 36 (N=304)	
	Hot Flashes		Hot Flashes		Hot Flashes	
	Yes (18%)	No (82%)	Yes (24%)	No (76%)	Yes (23%)	No (77%)
Age [†]	26.7 ± 5.5	29.1 ± 6.0	26.7 ± 5.5	29.8 ± 5.7	27.1 ± 6.3	30.1 ± 5.8
Race ^{††}						
White	44 (13.9)	272 (86.1)	51 (19.8)	207 (80.2)	48 (20.9)	182 (79.1)
Black	27 (29.3)	65 (70.7)	25 (36.2)	44 (63.8)	18 (30.5)	41 (69.5)
Other	7 (33.3)	14 (66.7)	5 (35.7)	9 (64.3)	4 (26.7)	11 (73.3)
Education ^{††}						
College	13 (6.5)	187 (93.5)	22 (12.6)	153 (87.4)	24 (15.0)	136 (85.0)
< College	64 (28.2)	163 (71.8)	59 (35.8)	106 (64.2)	45 (31.7)	97 (68.3)
Employment status [*]						
Yes	25 (11.4)	195 (88.6)	36 (20.2)	142 (79.8)	30 (18.1)	136 (81.9)
No	52 (26.0)	148 (74.0)	44 (28.0)	113 (72.0)	38 (29.0)	93 (71.0)
BMI ^{//*}	28.9 ± 7.2	26.4 ± 6.8	28.9 ± 8.8	26.0 ± 6.2	28.0 ± 7.4	26.1 ± 6.8
Diagnosis ^{//**†}						
Depression	23 (13.6)	146 (86.4)	21 (15.2)	117 (84.8)	19 (16.1)	99 (83.9)
Mania	41 (33.3)	82 (66.7)	36 (39.6)	55 (60.4)	34 (40.5)	50 (59.5)
Neither	14 (10.2)	123 (89.8)	24 (21.4)	88 (78.6)	17 (16.7)	85 (83.3)
Smoker ^{††}						
Yes	25 (29.4)	60 (70.6)	21 (41.2)	30 (58.8)	17 (43.6)	22 (56.4)
No	52 (16.0)	273 (84.0)	58 (21.3)	214 (78.7)	50 (20.2)	198 (79.8)
Alcohol use [*]						
Yes	17 (17.2)	82 (82.8)	3 (14.3)	18 (85.7)	1 (6.7)	14 (93.3)
No	60 (19.2)	253 (80.8)	75 (24.9)	226 (75.1)	67 (24.5)	206 (75.5)
Depressive symptoms ^{//**†}	18.5 ± 8.3	12.5 ± 8.2	16.8 ± 7.3	11.1 ± 7.4	15.6 ± 6.8	11.1 ± 6.9
SSRI use [†]						

	Week 20 (N=429)		Week 30 (N=341)		Week 36 (N=304)	
	Hot Flashes		Hot Flashes		Hot Flashes	
	Yes (18%)	No (82%)	Yes (24%)	No (76%)	Yes (23%)	No (77%)
Yes	9 (15.3)	50 (84.7)	14 (22.6)	48 (77.4)	9 (18.0)	41 (82.0)
No	69 (18.6)	301 (81.4)	67 (24.0)	212 (76.0)	61 (24.0)	193 (76.0)

// Pre-pregnancy value;

¶ Structured Interview Guide for the Hamilton Rating Scale for Depression-Atypical Depression Symptoms score

* Significantly associated with hot flash status $p<0.05$;

† Significantly varies by week $p<0.05$

Note: Descriptive statistics presented as mean $\pm$ standard deviation and n (%)

Table 2

Subject characteristics by sleep-disturbing hot flash status and weeks following birth

	Week 2 (N=291)		Week 12 (N=237)		Week 26 (N=218)		Week 52 (N=201)	
	Hot Flashes		Hot Flashes		Hot Flashes		Hot Flashes	
	Yes (20%)	No (80%)	Yes (14%)	No (86%)	Yes (11%)	No (89%)	Yes (10%)	No (90%)
Age [†]	28.3 ± 6.3	29.1 ± 5.7	28.4 ± 6.3	29.5 ± 5.4	28.6 ± 5.7	29.6 ± 5.3	27.9 ± 6.0	30.0 ± 5.5
Race [†]								
White	41 (18.8)	177 (81.2)	22 (12.4)	156 (87.6)	15 (9.0)	152 (91.0)	14 (8.8)	146 (91.3)
Black	14 (23.7)	45 (76.3)	9 (17.6)	42 (82.4)	9 (20.9)	34 (79.1)	6 (17.6)	28 (82.4)
Other	3 (21.4)	11 (78.6)	2 (25.0)	6 (75.0)	1 (12.5)	7 (87.5)	1 (14.3)	6 (85.7)
Education ^{*††}								
College	26 (17.0)	127 (83.0)	9 (6.6)	127 (93.4)	7 (5.5)	120 (94.5)	4 (3.3)	117 (96.7)
< College	32 (23.2)	106 (76.8)	24 (23.8)	77 (76.2)	18 (19.8)	73 (80.2)	17 (21.3)	63 (78.8)
Employed ^{*†}								
Yes	23 (15.8)	123 (84.2)	10 (8.4)	109 (91.6)	4 (3.2)	120 (96.8)	6 (5.4)	106 (94.6)
No	34 (24.6)	104 (75.4)	22 (19.5)	91 (80.5)	21 (22.8)	71 (77.2)	14 (16.5)	71 (83.5)
BMI [‡]	24.6 ± 5.7	26.8 ± 7.0	26.8 ± 6.7	26.6 ± 7.3	27.8 ± 6.7	25.7 ± 6.1	26.8 ± 5.9	26.2 ± 6.6
Diagnosis ^{†/††}								
Depression	23 (20.5)	89 (79.5)	7 (8.2)	78 (91.8)	7 (8.6)	74 (91.4)	5 (6.9)	67 (93.1)
Mania	24 (28.9)	59 (71.1)	18 (27.3)	48 (72.7)	14 (27.5)	37 (72.5)	13 (26.5)	36 (73.5)
Neither	11 (11.5)	85 (88.5)	8 (9.3)	78 (90.7)	4 (4.7)	82 (95.3)	3 (3.8)	77 (96.3)
Smoker ^{*††}								
Yes	9 (20.9)	34 (79.1)	16 (32.0)	34 (68.0)	10 (25.6)	29 (74.4)	10 (28.6)	25 (71.4)
No	43 (19.3)	180 (80.7)	17 (9.9)	155 (90.1)	14 (8.2)	157 (91.8)	10 (6.4)	146 (93.6)
Alcohol use [‡]								
Yes	13 (17.1)	63 (82.9)	16 (16.0)	84 (84.0)	14 (14.3)	84 (85.7)	10 (10.6)	84 (89.4)
No	40 (21.2)	149 (78.8)	15 (12.3)	107 (87.7)	10 (9.1)	100 (90.9)	10 (10.2)	88 (89.8)
Depressive symptoms ^{¶*}	17.3 ± 9.4	10.0 ± 6.1	16.3 ± 7.6	8.0 ± 7.0	19.4 ± 8.9	7.8 ± 6.9	20.3 ± 8.8	7.3 ± 6.6
Breastfeeding ^{‡†}								

	Week 2 (N=291)		Week 12 (N=237)		Week 26 (N=218)		Week 52 (N=201)	
	Hot Flashes		Hot Flashes		Hot Flashes		Hot Flashes	
	Yes (20%)	No (80%)	Yes (14%)	No (86%)	Yes (11%)	No (89%)	Yes (10%)	No (90%)
Yes	37 (22.4)	128 (77.6)	12 (10.5)	102 (89.5)	6 (6.5)	86 (93.5)	1 (6.3)	15 (93.8)
No	20 (16.5)	101 (83.5)	21 (17.2)	101 (82.8)	19 (15.2)	106 (84.8)	20 (10.9)	164 (89.1)
SSRI use [†]								
Yes	13 (24.1)	41 (75.9)	9 (17.0)	44 (83.0)	7 (14.6)	41 (85.4)	5 (10.0)	45 (90.0)
No	45 (19.0)	192 (81.0)	24 (13.0)	160 (87.0)	18 (10.6)	152 (89.4)	16 (10.6)	135 (89.4)

// Pre-pregnancy value;

[¶] Structured Interview Guide for the Hamilton Rating Scale for Depression-Atypical Depression Symptoms score;

[#] Breastfeeding status: 50% classified as yes, <50% classified as no

^{*} Significantly associated with hot flash status p<0.05;

[‡] Significantly varies by week p<0.05;

[‡] hot flash-by-week interaction p<0.05

Note: Descriptive statistics presented as mean ± standard deviation and n (%)

Table 3

Predictors of sleep-disturbing hot flashes during pregnancy

	OR	CI	P Value
Weeks gestation			0.02
20	--	--	Referent
30	1.89	1.12–3.20	0.02
36	1.94	1.13–3.35	0.02
Diagnosis			NS
Depression	0.81	0.38–1.73	
Mania	1.61	0.67–3.87	
Neither	--	--	Referent
Age	0.94	0.88–0.99	0.03
Education			0.02
College	--	--	Referent
<College	2.58	1.19–5.60	0.02
BMI (pre-pregnancy) [†]	1.05	1.01–1.10	0.03
Depressive symptoms [‡]	1.08	1.04–1.13	0.0001

[†] per unit increase in BMI;

[‡] per unit increase in Structured Interview Guide for the Hamilton Rating Scale for Depression-Atypical Depression Symptoms score

Table 4

Predictors of sleep-disturbing hot flashes postpartum

	OR	CI	P Value
Weeks postpartum			0.02
2	--	--	Referent
12	0.65	0.33–1.28	0.21
26	0.41	0.19–0.85	0.02
52	0.30	0.13–0.68	0.004
Diagnosis			NS
Depression	0.69	0.30–1.59	
Mania	1.24	0.50–3.09	
Neither	--	--	Referent
Depressive symptoms [‡]	1.19	1.14–1.25	<0.0001

[‡] per unit increase in Structured Interview Guide for the Hamilton Rating Scale for Depression-Atypical Depression Symptoms score