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Variation in symptoms of depression and anxiety in midlife women by menopausal status



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ABSTRACT

Objectives: To examine the association between menopausal status and the risk of symptoms of depression and anxiety in a community-based sample of Australian midlife women.

Study design: Female participants (mean age 50.6 ± 1.5) who were premenopausal (n = 237), perimenopausal (n = 249) or naturally postmenopausal (n = 225) were drawn from the Personality and Total Health (PATH) Through Life Project, a longitudinal study.

Main outcome measures: Symptoms of depression and anxiety were measured using the Goldberg Depression Scale and Goldberg Anxiety Scale. Generalised linear regression models with a negative binomial log link were used.

Results: Relative to premenopause and after adjusting for all relevant covariates, being perimenopausal was associated with increased risk of greater symptoms of depression (incidence rate ratio [IRR] = 1.29, p = 0.001), while being postmenopausal was associated with increased risk of greater symptoms of anxiety (IRR = 1.15, p = 0.041). Being perimenopausal or postmenopausal was associated with an increased risk of greater symptoms of depression (IRR = 1.35, p = 0.008; IRR = 1.31, p = 0.029) and anxiety (IRR = 1.22, p = 0.030; IRR = 1.32, p = 0.006) in women without a history of probable major depressive disorder or generalised anxiety disorder. Risk of symptoms did not differ with menopausal status in women with this history.

Conclusions: Menopausal status is associated with the risk of symptoms of depression and anxiety. There is a greater likelihood of increased symptoms of depression during perimenopause and symptoms of anxiety during postmenopause. In women without a history of depression or anxiety, the perimenopause and postmenopausal stages are associated with increased risk of greater symptoms of anxiety and depression relative to premenopause.

1. Introduction

Fluctuations in mood have been observed during periods of hormonal change, particularly surrounding events in the female life course such as puberty, the perinatal period, and the menopause transition (MT) [1–3]. There has been substantial research interest in the association between depression and menopausal status, while symptoms of anxiety have not been widely examined. The female reproductive life course can be classified into three broad stages: the reproductive period or premenopause; MT or perimenopause; and the postmenopause which follows the final menstrual period [4]. The endocrinological and physiological changes that begin in the early MT and continue during early postmenopause result in a changed hormonal environment that remains for the duration of the female lifespan [5], yet the immediate

consequences and longer term effects of these changes on psychological functioning remains unclear.

Research examining the association between menopausal status and symptoms of depression has yielded conflicting results. In recent years, several large community-based studies have identified associations between the MT and both an increase in symptoms of depression [6–9], and increased risk of major depressive episode [7,10,11]. However, others argue that symptoms of depression during this period may be a result of sociodemographic factors, life stress, and declining physical health [12–15]. Questions remain surrounding the contradictory findings and factors that may increase vulnerability to depression during midlife. Symptoms consistent with anxiety are reported by women during midlife [16], yet there has been considerably less attention dedicated to the study of anxiety and menopausal status. Of these

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limited studies, some have identified an increase in symptoms of anxiety during perimenopause [17,18]. One longitudinal study identified that transition to the MT was associated with heightened levels of anxiety in women without a history of anxiety during premenopause [19]. Of the anxiety symptoms examined, evidence suggests that panic attacks may be more common during postmenopause [20]. In one study, symptoms of anxiety were identified as a risk factor for distressing vasomotor symptoms such as hot flashes [21]. However, in a meta-analysis of nine studies investigating anxiety and the MT, the authors concluded that levels of anxiety remained low, but also acknowledged that many of the included studies failed to use validated psychometric instruments to measure anxiety [22]. The association between symptoms of anxiety and stage of menopause remains unclear, with a lack of research using validated measures of anxiety [22] and few studies examining anxiety during postmenopause relative to other stages.

Research that attempts to examine menopausal status and mental health is complicated by methodological challenges and inconsistencies in the measurement of reproductive stage and psychological symptoms. Further, the applicability of findings beyond the population studied and issues of issues of temporality continue to present challenges. To build upon existing research and address gaps in current findings, we examined a sample of Australian women in midlife who were premenopausal, perimenopausal, or naturally postmenopausal to determine whether menopausal status was associated with risk of symptoms consistent with depression and anxiety. We also examined the role of a past history of these symptoms on the severity of symptoms experienced during the MT and postmenopause. We expected that risk of symptoms of depression would be greater in perimenopause, and symptoms of anxiety greater in the perimenopause and postmenopause when compared to premenopause, and that participants with a history of depression or anxiety would be at increased risk of psychological symptoms during the MT and postmenopause.

2. Methods

2.1. Sample and study design

This study utilised data from the Personality and Total Health (PATH) Through Life Project, a longitudinal study of depression, anxiety, substance use and cognitive ability throughout the adult life span, described further in Anstey et al. [23]. The PATH study involves participants in three age-based cohorts, who were randomly selected from the community and interviewed at 4-year intervals. This study uses data collected at waves 1–3. Female participants from the PATH midlife cohort (n=1337), aged 40–44 years at study enrolment, were included in the current study if they met additional study criteria.

Participants were excluded from the analytic sample if they were not considered premenopausal at wave 1; if the cause of menopause was not determinable; or if data were incomplete for the main variables of interest. Ethical approval for PATH was obtained from the Human Research Ethics Committee at the Australian National University, and participants provided written informed consent. Descriptive statistics for the final sample (n = 711) are presented in Table 1.

2.2. Measures

2.2.1. Menopausal status

Menopausal status was assessed through questionnaire items that were self-completed by participants at study waves 1–3. Participants who self-reported hysterectomy or oophorectomy, current hormone therapy or hormonal contraceptive use, and those for whom menopause stage was otherwise indeterminable at wave 3 were excluded. Participants were categorised into one of three stages: premenopause (no change in frequency of menstruation); perimenopause (decreased predictability of menstrual periods) and postmenopause (menstruation ceased entirely). See Supplementary material S1 for additional details.

2.2.2. Depression and anxiety

The Goldberg Depression Scale (GDS) and Goldberg Anxiety Scale (GAS) at wave 3 were used as outcome variables, and each scale provided a count of symptoms consistent with depression and anxiety [24]. The GDS and GAS were originally developed for use as a screening measures for depression and anxiety in community-based populations. They each consist of a total of nine items, and require respondents to provide a "Yes" or "No" response to the presence of a given symptom during the past month [24]. The GDS and GAS demonstrated good criterion validity for depressive disorders and generalised anxiety disorder (GAD) against the World Mental Health Composite International Diagnostic Interview [25]. The GDS and GAS administered at wave 1 was used as a measure of past history of symptoms of depression and anxiety. The Composite International Diagnostic Interview Short Form (CIDI-SF) major depressive disorder (MDD) and GAD modules [26] were administered to PATH participants at wave 1, and outcomes were used to determine history of depression and anxiety in study 3 and 4. See Supplementary material S2 for additional details.

2.2.3. Covariates

Covariates were selected based on a review of the literature and identification of factors associated with poorer mental health outcomes. We adjusted for age and total education in years. Wave 3 self-reported financial difficulty, employment status, self-reported physical health, smoking status, number of life events during the 6 months prior to interview and current use of antidepressant or anxiolytic medication served as additional covariates. Further details about the definitions and measurement of covariates can be found in Supplementary material S2.

2.3. Statistical analyses

Regression analyses were selected to test the hypothesis that menopause stage was related to increased symptoms of depression and anxiety in midlife women after controlling for relevant covariates. The GDS and GAS served as dependent variables. A generalised linear regression model with a negative binomial log link was selected, as the dependent variables were counts, they were non-normally distributed and exhibited positive skew and over-dispersion [27]. The results refer to Incidence Rate Ratio's (IRR), interpreted as the risk of an increase by one unit on the outcome (symptoms of depression or anxiety), as a function of one unit increase in the predictor variable (menopause stage) relative to a reference category (premenopause). In study 1, where the GDS was the dependent variable and study 2, where the GAS was the dependent variable, the same analytic strategy was applied. Menopause stage served as the independent variable. All models were adjusted for age and total education in years. Model 2 included selfreported health, financial difficulty, employment status, smoking status, number of life events and use of antidepressant medication (study 1) or anxiolytic medication (study 2). Model 3 added GDS at wave 1 (study 1) or GAS at wave 1 (study 2). Pairwise comparisons were used to compare symptoms by menopause stage.

In study 3 and study 4, symptoms of depression and anxiety by menopause stage were re-examined with participants grouped based on probable caseness of MDD or GAD based on CIDI-SF scores at wave 1. Study 3 and 4 followed the same analytic strategy applied in study 1 and 2, with GDS (study 3) and GAS (study 4) as the dependent variables and menopause stage as the independent variable. All models adjusted for age and education, with the covariates self-reported health, current financial difficulty, employment status, smoking status, number of life events and antidepressant medication use (study 3) or anxiolytic medication use (study 4) entered into the model together.

The level of significance was set at p < 0.05. Statistical analysis was performed using IBM SPSS version 23.0.207.

Table 1Descriptive characteristics by wave 3 menopausal status.

Variable	Menopausal stage							
	Premenopause (n = 237)	Perimenopause (n = 249)	Postmenopause (n = 225)					
Sociodemographics								
Age current (mean, years)	49.98	50.52	51.29					
Employment current status (%)								
Full time	64.56	62.25	62.22					
Part time	27.85	29.31	24.44					
Unemployed, seeking employment	2.11	0.40	2.67					
Not in labour force	5.49	8.30	10.67					
Financial difficulty (%)								
No	83.97	84.34	81.78					
Sometimes	12.66	10.84	15.11					
Often	3.38	4.82	3.11					
Education (mean, years)	15.09	14.84	14.78					
Health and lifestyle factors								
Number of life events wave 3 (mean, number)	1.46	1.43	1.42					
Self rated physical health	50.76	50.23	50.19					
Use of antidepressants wave 3 (%)	9.28	10.84	13.78					
Use of anxiolytics wave 3 (%)	6.33	7.63	8.00					
Smoking status								
Never	56.54	51.41	62.22					
Past	32.90	36.95	21.78					
Current	10.55	11.65	16.00					
Parous wave 3 (%)	83.54	83.53	86.22					
Mental health								
Wave 1 Goldberg Anxiety Scale (mode)	3.00	1.00	0.00					
Wave 1 Goldberg Depression Scale (mode)	0.00	0.00	0.00					
Wave 3 Goldberg Anxiety Scale(mode)	1.00	4.00	0.00					
Wave 3 Goldberg Depression Scale (mode)	0.00	1.00	0.00					

3. Results

3.1. Study 1: depression and menopause stage

Following adjustment for age and education in model 1, being perimenopausal was associated with a 32% increased risk of higher symptoms of depression compared to being premenopausal. After the addition of all relevant covariates, the result remained significant with perimenopause associated with a 29% increased risk of higher symptoms (Table 2). Covariates that were significant in the final model included self-rated health (IRR = 0.97, p < 0.001), smoking status (IRR = 1.14, p = 0.004), life events (IRR = 1.06, p = 0.001), current antidepressant use (IRR = 1.46, p < 0.001) and GDS at wave 1

(IRR = 1.15, p < 0.001). Being postmenopausal was associated with a 22% increase in risk of symptoms in model 2 when adjusting for demographic, health and lifestyle factors but this result became non-significant (p > 0.05) in the final model when past depression was included. Follow-up pairwise comparisons revealed perimenopausal women had a greater number of symptoms of depression (M = 2.16) compared to premenopausal women (M = 1.67, p = 0.004). The differences in symptoms between premenopausal and postmenopausal (M = 1.92) women were non-significant (p > 0.05).

3.2. Study 2: anxiety and menopause stage

Being postmenopausal was associated with a 24% increased risk of

 Table 2

 Associations between number of depressive symptoms and menopausal status.

Measure	Model 1			Model 2			Model 3		
	Incidence rate ratio	95% CI	p	Incidence rate ratio	95% CI	p	Incidence rate ratio	95% CI	p
Menopausal status									
Postmenopause ^a	1.27	1.02 - 1.56	0.029	1.22	1.02 - 1.47	0.032	1.15	0.97 - 1.37	0.112
Perimenopause ^a	1.32	1.08-1.60	0.006	1.32	1.11-1.56	0.001	1.29	1.10-1.52	0.001
Age	0.96	0.91-1.02	0.177	0.98	0.93-1.03	0.400	0.98	0.94-1.03	0.517
Education	0.94	0.91-0.98	0.001	0.97	0.94-1.00	0.058	0.99	0.96 - 1.02	0.393
Physical health				0.96	0.96-0.97	0.000	0.97	0.97-0.98	0.000
Life events				1.08	1.04-1.12	0.009	1.06	1.02-1.10	0.001
Smoking status				1.15	1.05 - 1.27	0.004	1.14	1.04-1.25	0.004
Employment				0.93	0.88-0.98	0.010	0.97	0.92 - 1.02	0.202
Financial difficulty				0.93	0.81 - 1.07	0.285	0.97	0.85 - 1.10	0.662
Antidepressant user				1.68	1.39-2.04	0.000	1.46	1.22 - 1.75	0.000
Wave 1 Goldberg Depression Scale							1.15	1.11-1.18	0.000

Dependent Variable: Goldberg Depression Scale wave 3.

Model: (Intercept), Menopausal status, age, years of education physical health, life events, smoking status, employment status, financial difficulty, use of antidepressants, baseline Goldberg Depression Scale score.

^a Reference category is premenopause.

 Table 3

 Associations between number of anxiety symptoms and menopausal status.

Measure Model	Model 1			Model 2			Model 3		
	IRR	95% CI	p	IRR	95% CI	p	IRR	95% CI	p
Menopausal status									
Postmenopause ^a	1.24	1.05-1.46	0.013	1.22	1.05-1.41	0.008	1.15	1.01-1.31	0.041
Perimenopause ^a	1.16	1.00-1.36	0.055	1.16	1.01-1.33	0.037	1.11	0.99-1.26	0.084
Age	0.97	0.93-1.01	0.143	0.99	0.95-1.03	0.575	1.00	0.96-1.03	0.800
Education	0.97	0.95 - 1.00	0.066	0.99	0.97 - 1.02	0.476	1.00	0.97 - 1.02	0.702
Physical health				0.97	0.96-0.98	0.000	0.98	0.98-0.99	0.000
Smoking status				1.09	1.01-1.18	0.030	1.07	1.00-1.15	0.052
Life events				1.08	1.05-1.12	0.000	1.06	1.04-1.09	0.000
Employment status				0.97	0.93-1.01	0.160	0.99	0.95-1.03	0.515
Financial difficulty				0.97	0.86-1.09	0.586	1.02	0.92 - 1.12	0.749
Anxiolytic use				1.49	1.23-1.80	0.000	1.32	1.12-1.56	0.001
Wave 1 Goldberg Anxiety Scale							1.13	1.11-1.16	0.000

Dependent Variable: Goldberg Anxiety Scale wave 3.

Model: (Intercept), Menopausal status, age, years of education, physical health, employment status, smoking status, life events, financial difficulty, use of antidepressants, baseline Goldberg Anxiety Scale score.

greater symptoms of anxiety compared to being premenopausal (IRR = 1.24, p=0.013) after adjusting for age and education (model 1). A significant association remained between being postmenopausal and increased risk of symptoms of anxiety when all relevant sociodemographic, lifestyle and health covariates and past anxiety were added in the final model (model 3), revealing a 15% increased risk of greater symptoms in postmenopause relative to premenopause (Table 3). Covariates that were significant in the final model included self-rated health (IRR = 0.98, p < 0.001), life events (IRR = 1.06, p < 0.001), current anxiolytic use (IRR = 1.32, p < 0.001) and GAS at wave 1 (IRR = 1.13, p < 0.001). Follow-up pairwise comparisons did not detect statistically significant differences between symptoms of anxiety and stage of menopause after adjusting for all covariates.

3.3. Study 3: depression, menopause stage and history of symptoms

In women without probable MDD or GAD at wave 1 based on CIDI-SF, being perimenopausal was associated with a 35% increased risk of higher symptoms of depression relative to being premenopausal (IRR = 1.35, p = 0.008) and postmenopause was associated with a 31% increased risk of higher symptoms of depression compared to being premenopausal (IRR = 1.31, p = 0.029; Table 4). There was no significant association between menopause stage and symptoms of

Table 4
Association between number of symptoms of depressionand menopausal status by probable caseness based on CIDI-SF at wave 1.

Measure	Not probable ($n = 510$)			Proba	Probable (n = 201)			
	IRR	95% CI	p	IRR	95% CI	p		
Menopause status								
Postmenopause ^a	1.31	1.03-1.67	0.029	1.06	0.83 - 1.36	0.638		
Perimenopause ^a	1.35	1.08 - 1.68	0.008	1.25	0.98 - 1.58	0.069		
Age	0.99	0.93 - 1.05	0.761	0.96	0.90-1.03	0.242		
Education	0.97	0.93 - 1.01	0.189	0.97	0.93 - 1.01	0.164		
Physical health	0.96	0.95-0.97	0.000	0.97	0.96-0.98	0.000		
Smoking status	1.20	1.05-1.37	0.007	1.04	0.92 - 1.18	0.489		
Life events	1.07	1.01-1.13	0.021	1.06	1.02 - 1.11	0.008		
Employment	0.95	0.88 - 1.02	0.187	0.94	0.87 - 1.01	0.077		
Financial difficulty	0.81	0.67-0.98	0.034	1.13	0.93 - 1.34	0.179		
Antidepressant medication use	1.59	1.13-2.22	0.007	1.42	1.15–1.76	0.001		

Dependent Variable: Goldberg Depression Scale wave 3.

Model: (Intercept), Menopausal status, age, years of education, physical health, smoking status, life events, employment, financial difficulty, use of antidepressant medication.

depression in participants with a probable CIDI-SF diagnosis at wave 1.

3.4. Study 4: anxiety, menopause stage and history of symptoms

Being postmenopausal was associated with a 32% increased risk of higher symptoms of anxiety (IRR = 1.32, p=0.006) and being perimenopausal associated with a 22% increased risk of higher symptoms of anxiety (IRR = 1.22, p=0.030) compared to being premenopausal in participants without a probable MDD or GAD at wave 1, after adjusting for all relevant covariates (Table 5). For participants with a probable history of MDD or GAD at wave 1, there was no significant association between menopause stage and symptoms of anxiety.

4. Discussion

Changes in the hormonal environment during the female life course have long been associated with the presence of psychological symptoms [28]. In recent years, research has attempted to further clarify the role of menopausal status on the development of depression during midlife. Anxiety and anxiety disorders have not received equal attention, despite the frequency with which symptoms of anxiety appear during midlife and their effects on functioning. This study aimed to determine whether menopausal status was related to the severity of both

Table 5
Association between number of symptoms of anxiety and menopausal status by probable caseness based on CIDI-SF at wave 1.

Measure	Not probable ($n = 510$)			Probable ($n = 201$)			
	IRR	95% CI	p	IRR	95% CI	p	
Menopausal status							
Postmenopause ^a	1.32	1.08 - 1.60	0.006	1.01	0.84 - 1.21	0.921	
Perimenopause ^a	1.22	1.02 - 1.46	0.030	1.00	0.84-1.19	0.972	
Age	0.98	0.93 - 1.03	0.501	0.99	0.94-1.05	0.795	
Education	0.99	0.95 - 1.02	0.520	0.99	0.96 - 1.03	0.744	
Physical health	0.97	0.96-0.98	0.000	0.98	0.98-0.99	0.000	
Smoking status	1.10	0.99 - 1.23	0.083	1.02	0.94 - 1.12	0.601	
Life events	1.09	1.04-1.14	0.001	1.04	1.01-1.08	0.012	
Employment	0.96	0.90-1.02	0.196	1.00	0.95 - 1.05	0.949	
Financial difficulty	1.01	0.86-1.20	0.866	0.93	0.82 - 1.06	0.287	
Anxiolytic medication use	1.66	1.21-2.29	0.002	1.22	1.01–1.47	0.041	

Dependent Variable: Goldberg Anxiety Scale wave 3.

Model: (Intercept), Menopausal status, age, years of education, physical health, smoking status, life events, employment, financial difficulty, use of anxiolytic medication.

^a Reference category is premenopause.

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symptoms of depression and symptoms of anxiety, in a large community-based sample of midlife women who identified as premenopausal, perimenopausal or naturally postmenopausal. We also questioned whether a history of depression and anxiety was associated with increased risk of symptoms during the MT and postmenopause, with the aim of identifying factors affecting vulnerability to psychological distress in midlife women.

We found increased likelihood of symptoms of depression during perimenopause compared to premenopause, independent of the effects of a host of socio-demographic, lifestyle and health factors. These findings corroborate previous research that has identified an increase in depressive symptoms during perimenopause [6,7,9]. Symptoms in the postmenopause were lower than those observed in perimenopause, but were elevated above that seen in premenopause. These results are also consistent with earlier studies whereby symptoms of depression may be greater in postmenopause relative to premenopause [6,8,10]. Our results related to risk of anxiety and menopausal status revealed an increased likelihood of symptoms of anxiety in postmenopause relative to premenopause, although this increased risk during perimenopause was only identified prior to adjustment for past anxiety. While there have been relatively few studies of anxiety and menopausal status, our findings support previous studies which have identified an increase in symptoms of anxiety during perimenopause and postmenopause relative to premenopause [17,18]. Our results indicate that there may be patterns of psychological symptoms consistent with depression and anxiety that present differently by menopausal status.

The results of this study revealed that absence of depression and anxiety during premenopause may not predict an absence of symptoms during the MT and postmenopause. Women in our study who had a greater burden of symptoms at study entry, consistent with probable MDD or GAD, did not experience a significant increases in the risk of symptoms during the MT and postmenopause as expected. Rather, symptoms appeared to remain elevated at each menopausal stage, even after adjustment for factors that increase the risk of such symptoms, such as poorer physical health, smoking and the experience of stressful life events. Hence, women without significant history of symptoms of depression and anxiety in midlife who may be vulnerable to the development of psychological as they advance in menopause stage.

These findings have implications for midlife women who traverse menopause and health practitioners alike. Menopause is a normal biological process and an inevitable part of ageing. We report on symptoms alone, and while our findings do not report on prevelance of depressive or anxiety disorders during the MT or postmenopause, they add to growing evidence that patterns of psychological symptoms consistent with depression and anxiety vary by menopausal status and past history. Even though these changes in symptoms may not necessitate intervention, it should be acknowledged that changes in symptoms of depression and anxiety from that previously experienced have the potential to result in distress and impairment in functioning even if they do not warrant diagnoses. For this reason, attention to these changes may be important for health care practitioners, particularly in women without a history of these symptoms. In addition, the experience of psychological symptoms during the hormonally turbulent MT and postmenopause in women without a prior history may support the proposed existence of a reproductive related subtype of depression [29]. Further, the presence of symptoms of anxiety during the MT have been associated with vasomotor symptoms [21] and anxiety may increase the severity of vasomotor symptoms which contribute to significant distress during the MT [11,30]. Increased awareness about the psychological symptoms that may occur during the MT and postmenopause may improve outcomes for women during this period and increase the likelihood of effective and timely intervention.

Our sample consisted of community-based premenopausal, perimenopausal and naturally postmenopausal women and the findings of this study contributes to greater understanding of symptoms of depression and anxiety and menopausal status. We included validated

measures of symptoms of both depression and anxiety, which builds upon existing findings of symptoms of depression and adds to the literature on anxiety. Finally, our study had the ability to adjust for past mental health in addition to several socio-demographic, health and lifestyle factors.

These findings should be interpreted with known study limitations in mind. While the determination of menopause stage was guided by established criteria for the stages of natural menopause based on menstrual cycle changes [4], our data lacked the required specificity to categorize early and late perimenopause. The use of the GDS and GAS permits us to report on symptoms of depression and anxiety, but does not allow us to accurately identify psychological disorders. We only included women who reported natural menopause in the current study. and our results may not apply to women who experience menopause due to surgical intervention or other causes. Finally, our sample consisted overwhelmingly of Caucasian women, and it is unknown whether our findings apply to more diverse populations. The role of anxiety during the MT and postmenopause could be further explored in future studies and may be best addressed using longitudinal methods. Based on our findings, additional investigation of anxiety during the MT and postmenopause is warranted to identify risk factors for the development of symptoms of anxiety and depression midlife women.

5. Conclusion

This study has shown that symptoms of depression and anxiety vary in premenopausal, perimenopausal and postmenopausal women. We found that midlife women who are perimenopausal were more likely to experience increased symptoms of depression, and women who were postmenopausal were more likely to experience symptoms of anxiety relative to premenopause. Menopausal status was associated with psychological symptoms in women without a history of probable MDD or GAD, whereby being perimenopausal or postmenopausal was associated with increased risk of symptoms of depression and anxiety. In women with a probable history of MDD or GAD, menopausal status was not associated with this risk. Clinically, it is worth considering menopausal status in addition to individual history and established risk factors during the assessment and treatment of women in midlife who report psychological symptoms.

Contributors

Stephanie Mulhall contributed to study design, statistical analysis, and writing and revision of the manuscript.

Ross Andel contributed to study design, provided oversight for the statistical analysis, provided methodological input and contributed to the revision of the manuscript.

Kaarin J. Anstey contributed to data acquisition and study design, provided methodological input, and contributed to the revision of the manuscript.

All authors saw and approved the final manuscript.

Conflict of interest

The authors declare that they have no conflicts of interest.

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Ethical approval

The study protocol was approved by the Ethics Committee of the Australian National University, Canberra, ACT, Australia. Participants provided informed consent.

Provenance and peer review

This article has undergone peer review.

Research data (data sharing and collaboration)

There are no linked research data sets for this paper. PATH data are available on application to the PATH Governance Committee.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.maturitas.2017.11.005.

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