



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 self-reported 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.

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