HHS Public Access

Author manuscript

Obstet Gynecol Clin North Am. Author manuscript; available in PMC 2019 December 01.

Published in final edited form as:

Obstet Gynecol Clin North Am. 2018 December ; 45(4): 663–678. doi:10.1016/j.ogc.2018.07.007.

Depression During and After the Perimenopause: Impact of Hormones, Genetics, and Environmental Determinants of Disease

Joyce T. Bromberger[1,2] and **C. Neill Epperson**[3,4,5]

[1] Department of Epidemiology, University of Pittsburgh, Pittsburgh, PA

[2] Department of Psychiatry, University of Pittsburgh, Pittsburgh, PA

[3] Department of Psychiatry, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA

[4]Department of Obstetrics and Gynecology, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA

[5]Penn PROMOTES Research on Sex and Gender in Health, University of Pennsylvania, Philadelphia, PA

Synopsis:

Vulnerability to depression is increased across the menopause transition and in the early years after the final menstrual period. Clinicians should systematically screen women in this age group, and if depressive symptoms or disorder are present, treatment for depression should be initiated. Potential treatments include antidepressants for moderate to severe symptoms, psychotherapy to target psychological and interpersonal factors, and hormone therapy for women with first onset MDD or elevated depressive symptoms and at low risk for adverse effects. Behavioral interventions can improve physical activity and sleep patterns.

Keywords

Depression; Perimenopause; Hormones; Genetics; Environmental Determinants

Introduction

Epidemiologic research indicates that roughly 1 in 5 women will experience an episode of major depressive disorder (MDD) at some point in their lifetime.[1] Importantly, for some

Corresponding Author: Joyce T. Bromberger, Sterling Plaza, 201 North Craig Street, Suite 200, Pittsburgh, PA 15213, brombergerjt@upmc.edu.

Disclosures: Dr. Epperson consults to Sage Therapeutics and Shire Pharmaceuticals, and has investments in Pfizer, Merck, Johnson and Johnson, Abbott and Abbvie.

females, depression can present or worsen during periods of dynamic hormonal flux such as the premenstruum, peripartum, and the perimenopause.[2;3] Longitudinal research of women from the pre- to post-menopause stages of reproductive life, indicates that some women demonstrate a greater sensitivity to gonadal steroid shifts with respect to risk for negative mood symptoms such that a history of severe premenstrual mood symptoms is associated with increased risk for perimenopause onset or relapse of MDD.[4] The focus of this article is on the period of a woman's life when her reproductive system and its endocrine activity are changing and in transition (perimenopause) to a relatively hormonally quiescent stage (postmenopause). We will discuss the evidence that reproductive aging is associated with increased risk for depression as well as the varied endocrine, genetic, behavioral and social factors that may explain the association.

Defining Depression

Depression is a generic term used by the media, the general public and health care professionals to refer to negative mood symptoms that range in severity from unhappy psychological states to major depressive disorder (MDD). MDD is characterized in the Diagnostic Statistical Manual of Mental Disorders, fifth edition (DSM-5), by a range of mood, cognitive and behavioral symptoms that lead to clinically meaningful distress or functional impairment.[5] The various symptoms and behaviors included in the DSM-5 diagnosis for major and minor depressive disorder are included in Table 1. The term, "depression" can also refer to a cluster of negative mood and behavioral symptoms that do not meet diagnostic criteria for MDD, but may be associated with impaired functioning or distress and is likely to be more consistent with the diagnosis of minor depressive disorder.[6] Clinical (major and minor) depression and depressive symptoms are assessed in multiple settings, including primary care, gynecologic, and psychiatric. Depressive symptoms are typically assessed with self-report scales, of which there are many [e.g., Center for Epidemiological Studies of Depression (CES-D);[7] Beck Depression Inventory (BDI)[8] to name a few]. Self-report scales are useful to assess the number and severity of current symptoms and to identify individuals who should undergo additional screening, but are not diagnostic of major or minor depressive disorder. A standardized structured or semi-structured interview conducted by a trained clinician is the gold-standard for DSM-5 differential diagnosis of depressive disorders that include minor depression, dysthymia, premenstrual dysphoric disorder, or bipolar disorder-depressive episode. Clinicians may also utilize standard questionnaires such as the PRIME-MD, both clinician[9] and patient administered[10] and the Patient's Health Questionnaire (PHQ, 2-item for screening, and 9-item for diagnosis).[11] Most epidemiologic studies focusing on depression during the perimenopause rely on standardized patient-rated questionnaires to determine presence and duration of various depressive symptoms to quantify severity of symptoms and not a formal psychiatric evaluation or standardized interview to assess clinical depression. Therefore, we utilize here the term "depression" or "MDD" to connote a clinical condition that is evidenced by a standardized interview or the PRIME-MD or PHQ-9, which research has demonstrated to be consistent with a "probable diagnosis" of MDD. The term "depressive symptoms" will refer only to symptom levels or syndromes for which diagnosis of MDD or minor depression is doubtful or not confirmed.

Women interface with their healthcare providers relatively often during their reproductive years, prefer to be treated for depression in the primary care setting, and should be screened for MDD and for elevated depressive symptoms. Indeed, the U.S. Preventive Services Task Force recommends that all individuals are screened for depression at every contact with their healthcare provider.[12] Identifying a first episode of depression is critical, as the risk for recurrent episodes and chronicity of symptoms increases with failure to adequately treat patients with MDD. Fifty to 75% of individuals have recurring episodes of MDD.[13;14] MDD and depressive symptoms are about twice as common among women as men,[1] highlighting it as an important public health problem that significantly contributes to a bias in disease burden for women.

Depression and the Menopause Transition

Epidemiology

For many decades, there has been an ongoing debate about whether the menopause transition and/or postmenopause is associated with an increased risk for depressive symptoms or disorder. Though some studies failed to find a relationship between depression or depressive symptoms risk and the menopause transition,[15;16] two well-designed longitudinal studies of clinical depression found a 2 to 5-fold increased risk for MDD during the peri- versus late premenopause.[4;17–20] The Study of Women's Health Across the Nation (SWAN),[17;18] utilized a standardized semi-structured interview (Structured Clinical Interview for DSM-IV (SCID) and the Penn Ovarian Aging Study (POAS)[4;19;20] used standardized questionnaires (e.g. PRIME-MD and/or PHQ-9) and rating scales scores demonstrating sufficient severity (e.g. CES-D ⩾25), to confirm probable MDD. A similar increased risk for depressive symptoms was observed in other large, longitudinal studies (e.g., Harvard study of Mid-life Mood and Cycles,[21] the Australian Longitudinal Study of Women's Health (ASWH),[22] and the Seattle Midlife Women's Health Study;[23]. In addition to carefully characterizing the level of depressive symptom severity, each of these longitudinal studies utilized menstrual diaries and/or hormone levels to confirm menopause stage during which such symptoms were observed. Based on this literature, we conclude that there is a subset of women who are vulnerable to depressive disorder or symptoms during the menopause transition and early postmenopause. Importantly, the risk for depression appears to decline two to four years after the final menstrual period, particularly for those women whose only episode of depression occurred during the perimenopause[17;24] indicating that the increase in risk for depression and depressive symptoms during the MT is not due to aging itself.

Psychosocial and Health Related Factors

Current research is focused on elucidating why some women are more vulnerable to depression and depressive symptoms during the perimenopause, a time of changing and unpredictable patterns of gonadal steroid levels and menstrual cycles. A common hypothesis is that endocrine changes driving the menopause transition and affecting numerous tissues and biological systems including those in the brain are primarily responsible for unmasking the risk for depression symptoms or disorder in susceptible women. Nevertheless, there are

numerous and varied other domains and factors that are associated with depressive disorder and symptoms in general and during the perimenopause (Table 2) and (Figure 1).

Demographic Characteristics—Studies have shown that being unmarried (e.g., divorced, single, widowed), having a high school education or less and experiencing financial hardships are major risk factors for depressive *symptoms* during the menopause transition.[24–27] Results for race/ethnic differences in associations with depression symptoms are mixed and most observed differences for black and white women are no longer significant when adjusted for socio- demographic and health factors such as education, medical conditions, current significant stressors, and financial strain.[28–30]

Psychological Characteristics—Personality traits are predispositions that reflect cognitive, affective, or behavioral tendencies that are relatively stable across time and situations. While there are a greater number of such traits, only a small number have been examined in the context of depressive symptoms during midlife, *instrumentality (task/action oriented), pessimism, trait anxiety, and rumination. Middle-aged women characterized by being highly* action oriented showed less of an increase in depressive symptoms over three years than women less instrumental, after controlling for potential confounders, in one longitudinal study.[31] Studies of midlife women have also suggested that trait anxiety/ neuroticism (a tendency to experience chronic negative emotions), rumination/self-consciousness, and pessimism are significantly associated with risk for MDD and/or depressive symptoms.[18;32;33] It is also the case that negative attitudes toward menopause and/or aging are conceptually related to neuroticism and pessimism and predict depressive, anxious and negative mood in midlife women.[26;34–36]

Social factors—Similar to other times in life, the quality of one's social environment can impact risk for depression and depressive symptoms during menopause.[26] Social risk factors include acute and chronic stressors, daily hassles, lack of environmental resources and poor social relationships.[34,37–39] Midlife women with depression report higher prevalence of interpersonal problems, major events happening to significant others, and financial difficulties, compared to their non-depressed counterparts.[40] Stressful events have been associated with depressive symptoms in peri- compared to premenopausal women.[21] Among perimenopausal women, there were a greater number of adverse events in the 6 months before clinical depression occurrence than in the same period of time in non-depressed women.[41] Though vasomotor symptom severity is often correlated with depressive symptoms, they are not predictive,[42] and adverse life events are a more significant risk factor for MDD among perimenopausal women.[17] Hence, the fluctuating hormonal milieu of perimenopause may reduce the threshold for depression in the presence of adverse life events,[21;43–45] perhaps due to hormonal effects on neurotransmitters and brain regions implicated in the regulation of mood, cognition and the stress response.[46–48]

Adequate social support can buffer the individual from the adverse effects of stressful life events and daily hassles. There are different types of support, instrumental (e.g., help with chores), structural/social network (e.g., number of close friends or relatives, organization memberships) and emotional (e.g., someone to confide in or talk to). The most salient type of social support, is emotional support. Research has shown that an adequate number and

quality of social relationships can protect perimenopausal women from depression and depressive symptoms. For example, the Melbourne Women's Health Study[35] found that the magnitude of negative mood reported across the menopause transition was associated with the woman's negative feelings for her partner or lack of a partner entirely. Similarly, in the SWAN cohort, having low social support, marital dissatisfaction, and few close family members and friends was significantly associated with high depressive symptoms and MDD even after adjusting for multiple confounders (stressful events and negative attitudes toward aging and menopause). [18;34]

Psychosocial Stress and Adversity—Child adversity includes, but is not limited to abuse/neglect, family problems, and low childhood SES, poverty and unsafe environments. These and other significantly early life stressors or traumatic events can have enduring effects on stress-sensitive biological systems as well as behaviors that are detrimental to mental and physical health,[44;49;50] Childhood adversity is associated with increased lifetime risk for MDD as well as new onset MDD and depressive symptoms during the perimenopause.[45;51–53] Cumulative burden of depressive symptoms over 15 years has been shown to be greater for middle-aged women who grew up impoverished and had parents with low educational attainment versus those with parents of low educational attainment only.[51] Five adult factors (financial strain, lower education, low social support, low social function, and high bodily pain) jointly attenuated the association, suggesting a potential pathway between early adversity and midlife depressive symptom burden.[51]

Health-related factors—Depression and depressive symptoms are associated with suboptimal health behaviors, including smoking, inactivity, and sleep problems during midlife.[25;54;55] Prospective studies of middle-aged women indicate that physical activity and depression and depressive symptoms are inversely associated.[56–58] The SWAN[57] and the ASWH[58] reported that the 'dose' of moderate intensity physical activity that is consistent with public health guidelines is protective for depressed mood. Sleep difficulties are more frequently reported during perimenopause (50%) than premenopause (30%).[59] Although sleep disturbance is one of the cardinal symptoms of depression, the relationship between the two is bidirectional.[60] There is some evidence that sleep disturbance predicts subsequent depression[61] and a more severe depression course. In midlife women, those who reported sleep problems at study entry were 8 times more likely to experience a persistent or recurrent pattern of major depression over 13 years, independent of lifetime depression history and other covariates, than a single episode, minor depression, or no depression.[62] Additionally, in a clinical study, improvement in perceived sleep quality was associated with improvement in depressive symptoms among women with depression during the menopause transition.[63]

Poor self-reported physical health and functioning are associated with depressive symptoms in midlife women.[18;64] Depression often is associated with medical illnesses and risk factors, including subclinical cardiovascular conditions such as coronary and aortic calcification[65] and carotid atherosclerosis[66] as well as physical functioning.[67] While it is difficult to disentangle the direction of the relationship between depression and decline in physical functioning, evidence supports a reciprocal relationship in older populations.[68]

Depressive symptoms are also correlated with somatic symptoms in peri- and postmenopausal women in numerous cross-sectional studies[69–71] including dizziness, headaches, tiredness, aches and stiff joints, and urinary incontinence. While some studies find VMS are correlated with depressive symptoms or disorder,[72] others do not[17] or they note that the onset of depressive symptoms precedes the onset of VMS when they co-occur.[42] In SWAN, stressful life events were a stronger predictor of subsequent major depression than were VMS.[17]

Biological Factors

Similar to psychosocial and health related factors, the biological factors contributing to risk and resilience for depression during the menopause transition are complex and inter-related. For example, genetic vulnerability may be observed solely in the context of having experienced childhood adversity or significant stressful events during adulthood.[73;74] Research focusing on this gene by environment (G x E) interaction has rarely considered the potential for sex differences, despite the female bias for affective disorders, sex differences in response to early life stress, and the potential for sex to modify risk associated with specific genetic polymorphisms.[44] Perhaps for some women, the risk associated with this G x E interaction is sufficient to result in an episode of MDD in the absence of hormonal flux/reproductive transitions. For others, the erratic fluctuations of gonadal steroids during the perimenopause may be necessary to unmask risk for MDD either alone or in concert with stress history and genetics for a gene x environment x sex hormone interaction.[45]

Genes, Environment and Race/Ethnicity—The heritability of MDD is approximately 35% to 40%.[75;76] As with MDD occurring in the general population, there is some evidence that multiple “hits”, genetic (G) risk and environmental (E) factors such as childhood adversity and/or significant current stressors (E), are required in order to unmask risk for MDD during the perimenopause. Not surprisingly, genetic targets for investigation related to perimenopause or mid-life onset of depression are those related to estrogen receptors and steroid metabolizing enzymes in addition to estradiol’s downstream targets such as the serotonin (5-HT) transporter (5-HTT), post-synaptic 5-HT type 2 receptor density, and tryptophan hydroxylase (TH), monoamine oxidase A (MAO-A) and catechol-methyl transferase (COMT) gene expression.[77;78] TH is the rate limiting enzyme for the conversion of tryptophan to serotonin, while COMT and MAO-A are the primary enzymes responsible for synaptic amine degradation. Overall, estradiol appears to promote increased neurotransmitter synthesis and/or decrease degradation, essentially prolonging synaptic neurotransmitter levels.[46]

Though a recent review of the literature provides strong support for a G x E with respect to depression in the general population and a functional polymorphism in the SCL6A4 gene,74 the impact of sex and/or reproductive status (pre vs peri vs postmenopause) on this genetic polymorphism, which modulates the transcription and efficiency of the 5-HTT, has not been fully explored. The one study that examined polymorphisms in this gene, as well as the gene encoding MAO-A, and risk for depression among menopausal women failed to find an association between genotype and depression risk.[79] Whether the findings would have been

similar had the investigators focused specifically on depression onset during the perimenopause is not known.

As the genomic activity of estradiol is mediated through ER-α and ER-β, polymorphisms in the ER1 and ER2 genes could have a significant impact on receptor transcription and binding efficacy. Moreover, the antidepressant effects of estradiol are thought to be mediated primarily through ER-β. Several polymorphisms in ER1 and ER2 (which encode ER-α and ER-β, respectively) have been studied in relation to risk for late-life depression among 3525 women who would have been postmenopausal at the time of depression onset. Presence of the A allele for ER2 rs1256049 polymorphism was associated with onset of late-life depression, but only in women not currently using hormone therapy (HT), suggesting a protective effect of HT even in the face of a potential genetic risk factor.[80] Similarly, in a study of unmedicated reproductive-aged women (ages 18–39 years) and "menopausal" women (ages 40–60 years) experiencing their first episode of MDD and with a minimum score of 21 (at least moderate severity) on the Hamilton Depression Rating Scale (HAM-D), a genetic polymorphism in the gene encoding ER-β distinguished those with and without MDD regardless of reproductive stage. However, when lifetime adverse life event scores were considered, a G x E interaction was observed for both the ER2 polymorphisms studied (rs1256049 and rs4986938),[81] but only in the menopausal group. These data are interesting in light of additional findings from the POAS that childhood adversity was associated with a two- to three-fold increased risk for lifetime depression as well as *new onset* depression during the menopause transition.[82] Together these data support the need to consider a G x E x H (hormones) for depression during the menopause transition.

Findings from the POAS and SWAN implicate not only genetic variations in steroid metabolizing enyzmes in risk for perimenopausal depression, but highlight the potential modifying effect of race/ethnicity.[78;83] In the POAS, which included a community cohort of women [50% African American (AA), 50% European American (EA)] assessed yearly from pre to post menopause over 14 years, interactions between the cytochrome p450 enzymes CYP1B1*3 and CYP1B1*4 and menopause stage were observed for depressive symptoms among AA women only. CYP1B1s, which are highly expressed in estrogen target tissue, are responsible for the hydroxylation of estradiol. This process creates 4- hydroxyestradiol, which generates free radicals that could negatively affect target tissues.[84] Outside of altering local estradiol levels, the mechanism by which of CYP1B1s could impact depression during the perimenopause is unknown. In contrast, the sulfotransferase SULT1A1*3, which converts estradiol to the biologically inactive estradiol sulfate, was associated with a decreased risk for depressive symptoms, but increased risk of hot flashes among EA females. This disconnect between depressive symptoms and VMS is interesting, given that depressive symptoms are often (41% in the POAS cohort), but not always, comorbid with severe VMS.[42] No significant relationship between depression, menopause stage and genes encoding catechol-O-methyltransferase (COMT), CYP19, CYP1B1, CYP1A2, CYP1A1, or CYP3A4 were found for the entire group or by race.[78]

Similarly, a SWAN sub-study demonstrated a relationship between estrogen-metabolizing enzymes and depression risk which differed by race. Though the sample size was large (n=1538), menopause status was not considered with respect to depression onset (i.e.,

women may have also experienced MDD during the premenopause). In contrast to the POAS, SWAN found that EAs with the CYP1A1 rs2606345 CC and AC genotypes had two-fold greater odds of having depressive symptoms than those homozygous for the A allele. This relationship between the CC genotype was even greater for AA women (ten-fold). Among Japanese women, those homozygous for the T allele in the SNP CYP19 rs936306 were nearly five times as likely to have depressive symptoms as those with CC genotype. For Chinese women, the TT genotype at the SNP rs615942 for the 17 hydroxysteroid dehydrogenase gene was associated with a seven to eleven-fold increase risk.[83]

Finally, genetic analyses from the Seattle Midlife Women's Health Study focused on the estrogen synthesis pathway, specifically CYYP19 and 17-HSD, but this time in relationship to severity of symptom clusters identified through a latent class analysis of typical perimenopausal symptoms.[85] Though hot flash severity served as the basis for these clusters, depressed mood was included. Investigators found that a 17-beta hydroxysteroid dehydrogenase gene polymorphism was associated with the high-severity group, which included women with high-severity hot flashes and moderate sleep, mood, cognitive and pain symptoms. Again, unlike the POAS, analyses conducted in the Seattle Midlife Study did not consider menopause stage with respect to depression onset in their analyses and clustering of symptoms limits interpretation of their findings with respect to the genetics of perimenopause depression.

Gonadal Steroid Levels and Fluctuations—The fact that the years leading up to the final menstrual period are characterized by enhanced depression risk compared to subsequent years,[24] particularly among women with only perimenopausal onset of MDD, implicates dynamic hormonal changes in endogenous reproductive steroids versus absolute hypogonadism in this heightened risk. Given the robust impact of estradiol on brain neurochemistry, structure and function,[46] it isn't surprising that investigators have examined the timing of onset of menopause, rapidity of progression through menopause, the degree of hormonal fluctuations and absolute levels of gonadal steroids in the pathophysiology of perimenopause depression. Reproductive steroids [estradiol, progesterone, testosterone and dihydroepiandrosterone sulfate (DHEA-S)] levels at discrete time points or across the menopause transition are associated with depressive symptoms in some,[37;86–90] but not all studies.[23;91] Directionality of this relationship also varies by study, hormone and sample population. Increase in follicle-stimulating hormone and the variability of estradiol across the menopause transition, particularly in relationship to her own mean fluctuations, were significantly associated with greater risk for incident perimenopausal depression after controlling for smoking status, body mass index, poor sleep, hot flashes, and history of premenstrual syndrome.[19] Likewise, postmenopausal women with a decline in estradiol levels over a 2-year follow-up period were three times as likely to experience depressive symptoms, suggesting that changes in estradiol levels even after the final menstrual period (FMP) can impact depression risk.[91] Finally, studies including a recent meta-analysis indicates that a longer reproductive period, defined as later age at the time of final menstrual period, or greater number of years between menarche and onset of the menopause transition was associated with reduced risk for mid-life depression. [92;93]

Clinical Studies of Estradiol Treatment—Two double-blind, placebo-controlled studies indicate that conventional HT estradiol doses are more effective than placebo in reducing depressive symptoms among women who presented with perimenopausal MDD.[94;95] In a similar randomized clinical trial in postmenopausal women, estradiol did not differ in effectiveness from placebo.[96] Moreover, a recent study in which euthymic perimenopausal women randomized to receive estradiol (0.1 mg/d) plus intermittent progesterone (200 mg/d for 12 days every 3 months) versus those randomized to placebo were less likely to have potentially clinically significant depressive symptoms at any time during the 12-month assessment period. [97] On average, Center for Epidemiological Studies - Depression (CES-D) scores were higher in the placebo versus estradiol group across the study. When considering menopause stage, the positive effect of the hormone regimen on mood was limited to those in the early menopause transition versus those in the late perimenopause or early postmenopause stages. These findings support the notion of a "window of opportunity" during which women are more likely to be responsive to the anti-depressant effects of estradiol.[98]

Clinical Implications

This review highlights the importance of clinical screening for depression among middle-aged women as risk for MDD and depressive symptoms are increased during the MT even among those without a personal history of depression. Multiple factors contribute to risk for depression. Social factors play a critical role in depression onset and persistence. As mid-life women are often in transition with respect to interpersonal relationships, adequacy of social support, and current stressors, gynecologists treating menopausal women should periodically assess current stressors, as well as quality of their patients' intimate relationships and friendships. Current stressors among mid-life women often include caring for aging parents at the same time that women are managing their children's transitions to adulthood, stressful job changes, and conflict with spouse/partner. Given the association of lifetime traumas or childhood adversity with depression, clinicians may want to screen for these as well.

There are numerous screening instruments for clinicians to use in the routine assessment of depression symptoms and their severity. While self-rated scales are not diagnostic for MDD or minor depressive disorder, they can give the clinician an understanding of the range of symptoms and their individual severity. For example, the CES-D can be used to measure both key symptoms of MDD (anhedonia and low mood) as well as symptoms of anxiety and sleep disturbance which can also impair quality of life. Women scoring 16 or greater on the CES-D should be evaluated by their clinician for potential treatment in the primary care setting and/or referral to specialty behavioral health.

Though genetic polymorphisms and reproductive hormone fluctuations play a role in the manifestation of risk for MDD during the perimenopause, the measurement of these genetic differences is not yet recommended. Future research is needed to confirm the relationship between genotype and risk for depression during periods of dynamic hormonal flux such as the perimenopause.

Estradiol treatment was shown to be more effective than placebo for perimenopausal women meeting criteria for MDD.[95] The impact of estradiol treatment on depression appeared to be independent of the hormone's effect on vasomotor symptoms and sleep.

For menopausal women who experienced premenopausal episodes of MDD requiring psychiatric treatment, moderate-severe symptoms for the first time during the perimenopause or those with suicidal thinking, the standard of care would be treatment with antidepressants (assuming no history of bipolar disorder or current hypomania) and referral to a behavioral health specialist if one is available. Antidepressants may be started in the primary care setting in uncomplicated cases when the diagnosis is clear and there is no suicidal thinking. However, follow-up should occur within 1–2 weeks to assess for side effects and potential dose titration.

Conclusions

Depressive symptoms and diagnosis are common during the menopause transition and early postmenopause. Multiple psychosocial and biological factors are involved. Evaluation for depression and treatment may be conducted in the primary care practice and includes consideration of hormone therapy and antidepressants, alone or in combination, and cognitive behavioral therapy.

Acknowledgements:

This chapter has been written with financial support for Dr. Epperson's effort from the NIH Office of Research on Women's Health (P50 MH099910) and NIMH (P50 MH099910. And with financial support for Dr.Bromberger's effort from the NIA (AG012546)

Reference List

(1). Kessler RC, McGonagle KA, Zhao S et al. Lifetime and 12-month prevalence of DSM-III-R psychiatric disorders in the United States. Arch Gen Psychiatry 1994;51:8–19. [PubMed: 8279933]

(2). Hantsoo L, Epperson CN. Premenstrual Dysphoric Disorder: Epidemiology and Treatment. Curr Psychiatry Rep 2015;17:87. [PubMed: 26377947]

(3). Santoro N, Epperson CN, Mathews SB. Menopausal Symptoms and Their Management. Endocrinol Metab Clin North Am 2015;44:497–515. [PubMed: 26316239]

(4). Freeman EW, Sammel MD, Liu L, Gracia CR, Nelson DB, Hollander L. Hormones and menopausal status as predictors of depression in women in transition to menopause. Arch Gen Psychiatry 2004;61:62–70. [PubMed: 14706945]

(5). American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 5 ed 2013.

(6). Ayuso-Mateos JL, Nuevo R, Verdes E, Naidoo N, Chatterji S. From depressive symptoms to depressive disorders: the relevance of thresholds. Br J Psychiatry 2010;196:365–371. [PubMed: 20435961]

(7). Radloff LS. The CES-D Scale: A self-report depression scale for research in the general population. Applied Psychological Measurement 1977;1:385–401.

(8). Beck AT, Beamesderfer A. Assessment of depression: The depression inventory In: Pichot P, ed. Psychological measurements in psychopharmacology. (Vol. 7). Basel: Karger Press; 1974;151–169.

(9). Spitzer RL, Williams JB, Kroenke K, Hornyak R, McMurray J. Validity and utility of the PRIME-MD patient health questionnaire in assessment of 3000 obstetric-gynecologic patients: the

PRIME-MD Patient Health Questionnaire Obstetrics-Gynecology Study. Am J Obstet Gynecol 2000;183:759–769. [PubMed: 10992206]

(10). Spitzer RL, Kroenke K, Williams JB. Validation and utility of a self-report version of PRIME-MD: the PHQ primary care study. Primary Care Evaluation of Mental Disorders. Patient Health Questionnaire. JAMA 1999;282:1737–1744. [PubMed: 10568646]

(11). Moriarty AS, Gilbody S, McMillan D, Manea L. Screening and case finding for major depressive disorder using the Patient Health Questionnaire (PHQ-9): a meta-analysis. Gen Hosp Psychiatry 2015;37:567–576. [PubMed: 26195347]

(12). Siu AL, Bibbins-Domingo K, Grossman DC et al. Screening for Depression in Adults: US Preventive Services Task Force Recommendation Statement. JAMA 2016;315:380–387. [PubMed: 26813211]

(13). Hardeveld F, Spijker J, De GR, Nolen WA, Beekman AT. Prevalence and predictors of recurrence of major depressive disorder in the adult population. Acta Psychiatr Scand 2010;122:184–191. [PubMed: 20003092]

(14). Kessler RC. The effects of stressful life events on depression. Annu Rev Psychol 1997;48:191–214. [PubMed: 9046559]

(15). Rossler W, Ajdacic-Gross V, Riecher-Rossler A, Angst J, Hengartner MP. Does menopausal transition really influence mental health? Findings from the prospective long-term Zurich study. World Psychiatry 2016;15:146–154. [PubMed: 27265705]

(16). Vesco KK, Haney EM, Humphrey L, Fu R, Nelson HD. Influence of menopause on mood: a systematic review of cohort studies. Climacteric 2007;10:448–465. [PubMed: 18049938]

(17). Bromberger JT, Kravitz HM, Chang YF, Cyranowski JM, Brown C, Matthews KA. Major depression during and after the menopausal transition: Study of Women's Health Across the Nation (SWAN). Psychol Med 2011;41:1879–1888. [PubMed: 21306662]

(18). Bromberger JT, Schott L, Kravitz HM, Joffe H. Risk factors for major depression during midlife among a community sample of women with and without prior major depression: are they the same or different? Psychol Med 2015;45:1653–1664. [PubMed: 25417760]

(19). Freeman EW, Sammel MD, Lin H, Nelson DB. Associations of hormones and menopausal status with depressed mood in women with no history of depression. Arch Gen Psychiatry 2006;63:375–382. [PubMed: 16585466]

(20). Freeman EW. Associations of depression with the transition to menopause. Menopause 2010;17:823–827. [PubMed: 20531231]

(21). Cohen LS, Soares CN, Vitonis AF, Otto MW, Harlow BL. Risk for new onset of depression during the menopausal transition: the Harvard study of moods and cycles. Arch Gen Psychiatry 2006;63:385–390. [PubMed: 16585467]

(22). Hickey M, Schoenaker DA, Joffe H, Mishra GD. Depressive symptoms across the menopause transition: findings from a large population-based cohort study. Menopause 2016;23:1287–1293. [PubMed: 27552471]

(23). Woods NF, Smith-Dijulio K, Percival DB, Tao EY, Mariella A, Mitchell S. Depressed mood during the menopausal transition and early postmenopause: observations from the Seattle Midlife Women's Health Study. Menopause 2008;15:223–232. [PubMed: 18176355]

(24). Freeman EW, Sammel MD, Boorman DW, Zhang R. Longitudinal pattern of depressive symptoms around natural menopause. JAMA Psychiatry 2014;71:36–43. [PubMed: 24227182]

(25). Bromberger JT, Assmann SF, Avis NE, Schocken M, Kravitz HM, Cordal A. Persistent mood symptoms in a multiethnic community cohort of pre- and perimenopausal women. Am J Epidemiol 2003;158:347–356. [PubMed: 12915500]

(26). Gibbs Z, Lee S, Kulkarni J. What factors determine whether a woman becomes depressed during the perimenopause? Arch Womens Ment Health 2012;15:323–332. [PubMed: 22932961]

(27). Harlow BL, Cohen LS, Otto MW, Spiegelman D, Cramer DW. Prevalence and predictors of depressive symptoms in older premenopausal women: the Harvard Study of Moods and Cycles. Arch Gen Psychiatry 1999;56:418–424. [PubMed: 10232296]

(28). Bromberger JT, Harlow S, Avis N, Kravitz HM, Cordal A. Racial/ethnic differences in the prevalence of depressive symptoms among middle-aged women: The Study of Women's Health Across the Nation (SWAN). Am J Public Health 2004;94:1378–1385. [PubMed: 15284047]

(29). Liang J, Xu X, Quinones AR, Bennett JM, Ye W. Multiple trajectories of depressive symptoms in middle and late life: racial/ethnic variations. Psychol Aging 2011;26:761–777. [PubMed: 21875216]

(30). Spence NJ, Adkins DE, Dupre ME. Racial differences in depression trajectories among older women: socioeconomic, family, and health influences. J Health Soc Behav 2011;52:444–459. [PubMed: 22021654]

(31). Bromberger JT, Matthews KA. A “feminine” model of vulnerability to depressive symptoms: a longitudinal investigation of middle-aged women. J Pers Soc Psychol 1996;70:591–598. [PubMed: 8851743]

(32). Bromberger JT, Matthews KA. A longitudinal study of the effects of pessimism, trait anxiety, and life stress on depressive symptoms in middle-aged women. Psychol Aging 1996;11:207–213. [PubMed: 8795049]

(33). Kuh D, Hardy R, Rodgers B, Wadsworth ME. Lifetime risk factors for women’s psychological distress in midlife. Soc Sci Med 2002;55:1957–1973. [PubMed: 12406464]

(34). Bromberger JT, Matthews KA, Schott LL et al. Depressive symptoms during the menopausal transition: the Study of Women’s Health Across the Nation (SWAN). J Affect Disord 2007;103:267–272. [PubMed: 17331589]

(35). Dennerstein L, Lehert P, Burger H, Dudley E. Mood and the menopausal transition. J Nerv Ment Dis 1999;187:685–691. [PubMed: 10579597]

(36). Ayers B, Forshaw M, Hunter MS. The impact of attitudes towards the menopause on women’s symptom experience: a systematic review. Maturitas 2010;65:28–36. [PubMed: 19954900]

(37). Bromberger JT, Schott LL, Kravitz HM et al. Longitudinal change in reproductive hormones and depressive symptoms across the menopausal transition: results from the Study of Women’s Health Across the Nation (SWAN). Arch Gen Psychiatry 2010;67:598–607. [PubMed: 20530009]

(38). Pimenta F, Leal I, Maroco J, Ramos C. Menopausal symptoms: do life events predict severity of symptoms in peri- and post-menopause? Maturitas 2012;72:324–331. [PubMed: 22607812]

(39). Woods NF, Mitchell ES. Pathways to depressed mood for midlife women: observations from the Seattle Midlife Women’s Health Study. Res Nurs Health 1997;20:119–129. [PubMed: 9100742]

(40). Bromberger JT, Kravitz HM, Matthews K, Youk A, Brown C, Feng W. Predictors of first lifetime episodes of major depression in midlife women. Psychol Med 2009;39:55–64. [PubMed: 18377672]

(41). Schmidt PJ, Murphy JH, Haq N, Rubinow DR, Danaceau MA. Stressful life events, personal losses, and perimenopause-related depression. Arch Womens Ment Health 2004;7:19–26. [PubMed: 14963729]

(42). Freeman EW, Sammel MD, Lin H. Temporal associations of hot flashes and depression in the transition to menopause. Menopause 2009;16:728–734. [PubMed: 19188849]

(43). Gordon JL, Rubinow DR, Eisenlohr-Moul TA, Leserman J, Girdler SS. Estradiol variability, stressful life events, and the emergence of depressive symptomatology during the menopausal transition. Menopause 2016;23:257–266. [PubMed: 26529616]

(44). Bale TL, Epperson CN. Sex differences and stress across the lifespan. Nat Neurosci 2015;18:1413–1420. [PubMed: 26404716]

(45). Epperson CN, Sammel MD, Bale TL et al. Adverse Childhood Experiences and Risk for First-Episode Major Depression During the Menopause Transition. J Clin Psychiatry 2017;78:e298–e307. [PubMed: 28394509]

(46). Shanmugan S, Epperson CN. Estrogen and the prefrontal cortex: towards a new understanding of estrogen’s effects on executive functions in the menopause transition. Hum Brain Mapp 2014;35:847–865. [PubMed: 23238908]

(47). Shanmugan S, Satterthwaite TD, Sammel MD et al. Impact of early life adversity and tryptophan depletion on functional connectivity in menopausal women: A double-blind, placebo-controlled crossover study. Psychoneuroendocrinology 2017;84:197–205. [PubMed: 28755550]

(48). Shanmugan S, Loughead J, Cao W et al. Impact of Tryptophan Depletion on Executive System Function during Menopause is Moderated by Childhood Adversity. Neuropsychopharmacology 2017;42:2398–2406. [PubMed: 28322235]

(49). Anda RF, Croft JB, Felitti VJ et al. Adverse childhood experiences and smoking during adolescence and adulthood. JAMA 1999;282:1652–1658. [PubMed: 10553792]

(50). Anda RF, Felitti VJ, Bremner JD et al. The enduring effects of abuse and related adverse experiences in childhood. A convergence of evidence from neurobiology and epidemiology. Eur Arch Psychiatry Clin Neurosci 2006;256:174–186. [PubMed: 16311898]

(51). Bromberger JT, Schott LL, Matthews KA, Kravitz HM, Harlow SD, Montez JK. Childhood socioeconomic circumstances and depressive symptom burden across 15 years of follow-up during midlife: Study of Women's Health Across the Nation (SWAN). Arch Womens Ment Health 2017;20:495–504. [PubMed: 28660469]

(52). Felitti VJ, Anda RF, Nordenberg D et al. Relationship of childhood abuse and household dysfunction to many of the leading causes of death in adults. The Adverse Childhood Experiences (ACS) Study. Am J Prev Med 1998;14:245–258. [PubMed: 9635069]

(53). Heim C, Binder EB. Current research trends in early life stress and depression: review of human studies on sensitive periods, gene-environment interactions, and epigenetics. Exp Neurol 2012;233:102–111. [PubMed: 22101006]

(54). Freeman EW, Sammel MD, Lin H, Gracia CR, Kapoor S. Symptoms in the menopausal transition: hormone and behavioral correlates. Obstet Gynecol 2008;111:127–136. [PubMed: 18165401]

(55). Gallicchio L, Schilling C, Miller SR, Zacur H, Flaws JA. Correlates of depressive symptoms among women undergoing the menopausal transition. J Psychosom Res 2007;63:263–268. [PubMed: 17719363]

(56). Brown WJ, Ford JH, Burton NW, Marshall AL, Dobson AJ. Prospective study of physical activity and depressive symptoms in middle-aged women. Am J Prev Med 2005;29:265–272. [PubMed: 16242588]

(57). Dugan SA, Bromberger JT, Segawa E, Avery E, Sternfeld B. Association between physical activity and depressive symptoms: midlife women in SWAN. Med Sci Sports Exerc 2015;47:335–342. [PubMed: 24914519]

(58). van Uffelen JG, van Gellecum YR, Burton NW, Peeters G, Heesch KC, Brown WJ. Sitting-time, physical activity, and depressive symptoms in mid-aged women. Am J Prev Med 2013;45:276–281. [PubMed: 23953353]

(59). Polo-Kantola P Sleep problems in midlife and beyond. Maturitas 2011;68:224–232. [PubMed: 21295422]

(60). Alvaro PK, Roberts RM, Harris JK. A Systematic Review Assessing Bidirectionality between Sleep Disturbances, Anxiety, and Depression. Sleep 2013;36:1059–1068. [PubMed: 23814343]

(61). Breslau N, Roth T, Rosenthal L, Andreski P. Sleep disturbance and psychiatric disorders: a longitudinal epidemiological study of young adults. Biol Psychiatry 1996;39:411–418. [PubMed: 8679786]

(62). Bromberger JT, Kravitz HM, Youk A, Schott LL, Joffe H. Patterns of depressive disorders across 13 years and their determinants among midlife women: SWAN mental health study. J Affect Disord 2016;206:31–40. [PubMed: 27455356]

(63). Joffe H, Crawford SL, Freeman MP et al. Independent Contributions of Nocturnal Hot Flashes and Sleep Disturbance to Depression in Estrogen-Deprived Women. J Clin Endocrinol Metab 2016;101:3847–3855. [PubMed: 27680875]

(64). Bauld R, Brown RF. Stress, psychological distress, psychosocial factors, menopause symptoms and physical health in women. Maturitas 2009;62:160–165. [PubMed: 19167176]

(65). Agatisa PK, Matthews KA, Bromberger JT, Edmundowicz D, Chang YF, Sutton-Tyrrell K. Coronary and aortic calcification in women with a history of major depression. Arch Intern Med 2005;165:1229–1236. [PubMed: 15956001]

(66). Jones DJ, Bromberger JT, Sutton-Tyrrell K, Matthews KA. Lifetime history of depression and carotid atherosclerosis in middle-aged women. Arch Gen Psychiatry 2003;60:153–160. [PubMed: 12578432]

(67). Tomey K, Sowers MR, Harlow S, Jannausch M, Zheng H, Bromberger J. Physical functioning among mid-life women: associations with trajectory of depressive symptoms. Soc Sci Med 2010;71:1259–1267. [PubMed: 20692082]

(68). Ormel J, Rijsdijk FV, Sullivan M, van SE, Kempen GI. Temporal and reciprocal relationship between IADL/ADL disability and depressive symptoms in late life. J Gerontol B Psychol Sci Soc Sci 2002;57:338–347.

(69). Terauchi M, Hiramitsu S, Akiyoshi M et al. Associations among depression, anxiety and somatic symptoms in peri- and postmenopausal women. J Obstet Gynaecol Res 2013;39:1007–1013. [PubMed: 23379427]

(70). Wang HL, Booth-LaForce C, Tang SM, Wu WR, Chen CH. Depressive symptoms in Taiwanese women during the peri- and post-menopause years: associations with demographic, health, and psychosocial characteristics. Maturitas 2013;75:355–360. [PubMed: 23726260]

(71). Waetjen LE, Liao S, Johnson WO et al. Factors associated with prevalent and incident urinary incontinence in a cohort of midlife women: a longitudinal analysis of data: study of women's health across the nation. Am J Epidemiol 2007;165:309–318. [PubMed: 17132698]

(72). Joffe H, Hall JE, Soares CN et al. Vasomotor symptoms are associated with depression in perimenopausal women seeking primary care. Menopause 2002;9:392–398. [PubMed: 12439097]

(73). Caspi A, Sugden K, Moffitt TE et al. Influence of life stress on depression: moderation by a polymorphism in the 5-HTT gene. Science 2003;301:386–389. [PubMed: 12869766]

(74). Sharpley CF, Palanisamy SK, Glyde NS, Dillingham PW, Agnew LL. An update on the interaction between the serotonin transporter promoter variant (5-HTTLPR), stress and depression, plus an exploration of non-confirming findings. Behav Brain Res 2014;273:89–105. [PubMed: 25078292]

(75). Otte C, Gold SM, Penninx BW et al. Major depressive disorder. Nat Rev Dis Primers 2016;2:16065. [PubMed: 27629598]

(76). Sullivan PF, Neale MC, Kendler KS. Genetic epidemiology of major depression: review and meta analysis. Am J Psychiatry 2000;157:1552–1562. [PubMed: 11007705]

(77). Kugaya A, Epperson CN, Zoghbi S et al. Increase in prefrontal cortex serotonin 2A receptors following estrogen treatment in postmenopausal women. Am J Psychiatry 2003;160:1522–1524. [PubMed: 12900319]

(78). Rebbeck TR, Su HI, Sammel MD et al. Effect of hormone metabolism genotypes on steroid hormone levels and menopausal symptoms in a prospective population-based cohort of women experiencing the menopausal transition. Menopause 2010;17:1026–1034. [PubMed: 20505544]

(79). Grochans E, Jurczak A, Szkup M et al. Evaluation of the relationship between 5-HTT and MAO gene polymorphisms, mood and level of anxiety among postmenopausal women. Int J Environ Res Public Health 2014;12:268–281. [PubMed: 25547397]

(80). Ryan J, Scali J, Carriere I et al. Oestrogen receptor polymorphisms and late-life depression. Br J Psychiatry 2011;199:126–131. [PubMed: 21804148]

(81). Zhang J, Chen L, Ma J et al. Interaction of estrogen receptor beta and negative life events in susceptibility to major depressive disorder in a Chinese Han female population. J Affect Disord 2017;208:628–633. [PubMed: 27814959]

(82). Epperson CN, Shanmugan S, Kim DR et al. New onset executive function difficulties at menopause: a possible role for lisdexamfetamine. Psychopharmacology (Berl) 2015;232:3091–3100. [PubMed: 26063677]

(83). Kravitz HM, Janssen I, Lotrich FE, Kado DM, Bromberger JT. Sex steroid hormone gene polymorphisms and depressive symptoms in women at midlife. Am J Med 2006;119:S87–S93.

(84). Tsuchiya Y, Nakajima M, Yokoi T. Cytochrome P450-mediated metabolism of estrogens and its regulation in human. Cancer Lett 2005;227:115–124. [PubMed: 16112414]

(85). Woods NF, Cray LA, Mitchell ES, Farrin F, Herting J. Polymorphisms in Estrogen Synthesis Genes and Symptom Clusters During the Menopausal Transition and Early Postmenopause: Observations From the Seattle Midlife Women's Health Study. Biol Res Nurs 2018;1099800417753536.

(86). Colangelo LA, Ouyang P, Golden SH et al. Do sex hormones or hormone therapy modify the relation of n-3 fatty acids with incident depressive symptoms in postmenopausal women? The MESA Study. Psychoneuroendocrinology 2017;75:26–35. [PubMed: 27768981]

(87). Milman LW, Sammel MD, Barnhart KT, Freeman EW, Dokras A. Higher serum total testosterone levels correlate with increased risk of depressive symptoms in Caucasian women through the entire menopausal transition. Psychoneuroendocrinology 2015;62:107–113. [PubMed: 26280374]

(88). Morrison MF, Ten HT, Freeman EW, Sammel MD, Grisso JA. DHEA-S levels and depressive symptoms in a cohort of African American and Caucasian women in the late reproductive years. Biol Psychiatry 2001;50:705–711. [PubMed: 11704078]

(89). Santoro N, Torrens J, Crawford S et al. Correlates of circulating androgens in mid-life women: the study of women's health across the nation. J Clin Endocrinol Metab 2005;90:4836–4845. [PubMed: 15840738]

(90). Schmidt PJ, Murphy JH, Haq N, Danaceau MA, St CL. Basal plasma hormone levels in depressed perimenopausal women. Psychoneuroendocrinology 2002;27:907–920. [PubMed: 12383452]

(91). Ryan J, Burger HG, Szoeke C et al. A prospective study of the association between endogenous hormones and depressive symptoms in postmenopausal women. Menopause 2009;16:509–517. [PubMed: 19169164]

(92). Marsh WK, Bromberger JT, Crawford SL et al. Lifelong estradiol exposure and risk of depressive symptoms during the transition to menopause and postmenopause. Menopause 2017;24:1351–1359. [PubMed: 28719421]

(93). Georgakis MK, Thomopoulos TP, Diamantaras AA et al. Association of Age at Menopause and Duration of Reproductive Period With Depression After Menopause: A Systematic Review and Meta-analysis. JAMA Psychiatry 2016;73:139–149. [PubMed: 26747373]

(94). Schmidt PJ, Nieman L, Danaceau MA et al. Estrogen replacement in perimenopause-related depression: a preliminary report. Am J Obstet Gynecol 2000;183:414–420. [PubMed: 10942479]

(95). Soares CN, Almeida OP, Joffe H, Cohen LS. Efficacy of estradiol for the treatment of depressive disorders in perimenopausal women: a double-blind, randomized, placebo-controlled trial. Arch Gen Psychiatry 2001;58:529–534. [PubMed: 11386980]

(96). Morrison MF, Kallan MJ, Ten HT, Katz I, Tweedy K, Battistini M. Lack of efficacy of estradiol for depression in postmenopausal women: a randomized, controlled trial. Biol Psychiatry 2004;55:406–412. [PubMed: 14960294]

(97). Gordon JL, Rubinow DR, Eisenlohr-Moul TA, Xia K, Schmidt PJ, Girdler SS. Efficacy of Transdermal Estradiol and Micronized Progesterone in the Prevention of Depressive Symptoms in the Menopause Transition: A Randomized Clinical Trial. JAMA Psychiatry 2018;75:149–157. [PubMed: 29322164]

(98). Soares CN, Maki PM. Menopausal transition, mood, and cognition: an integrated view to close the gaps. Menopause 2010;17:812–814. [PubMed: 20616667]

Key Points:

- Longitudinal studies, conducted across the world and in diverse populations, confirm that women are 2–5 times more likely to experience a depressive disorder during the peri versus the late premenopausal years.
- Screening for depressive symptoms or disorder in the primary care setting is recommended and can be accomplished easily with standard patient-rated scales.
- Treatment for depression or depressive symptoms during the peri and early postmenopause includes use of standard antidepressants, hormone therapy, and behavioral modifications to sleep patterns and exercise.
- As current and early life stressors/adversity are often contributing factors, many women may benefit from psychotherapy or cognitive behavioral or trauma-focused therapy.

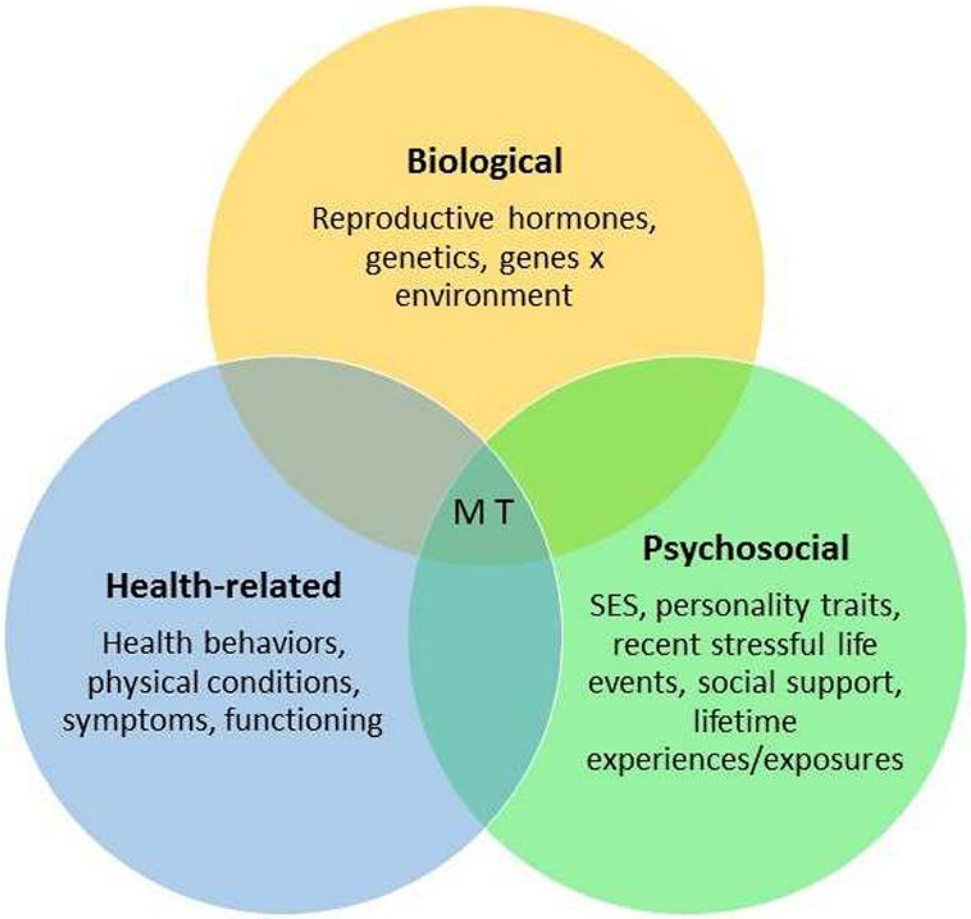

Figure 1:
Intersection of multiple risk factors for depression during the menopause transition (MT).

Table 1:

Major versus Minor Depressive Disorder

CHARACTERISTICS	MAJOR	MINOR
Symptoms		
Depressed mood (e.g., sad, hopeless)	X	X
Decreased interest or pleasure	X	X
Weight change (>5% of body weight/month) or change in appetite	+/−	+/−
Sleep disturbance (insomnia/hypersomnia)	+/−	+/−
Fatigue	+/−	+/−
Feelings of worthlessness or excessive guilt	+/−	+/−
Difficulty concentrating	+/−	+/−
Psychomotor agitation or slowing	+/−	+/−
Recurrent thoughts of death	+/−	+/−
Number of Symptoms	5 or more	2–4
	Most days for at least 2 weeks	Most days for at least 2 weeks
Significant distress or impairment in function	X	X
Not attributable to physiologic effect of a substance, medication or general medical condition	X	X
Does not occur exclusively during a psychotic disorder	X	X

Major and minor depression both require one of the two hallmark symptoms (*italicized font*) of depressed mood or decreased interest or pleasure in all, or almost all, activities. For both diagnoses, symptoms must be present most of the days during a two week period, cause clinically meaningful distress or impairment in social, occupational or other areas of function, and not be solely attributable to another disorder, medical condition or substance. The other symptoms are listed at +/− as they do not have to be present, though 5 symptoms are required for Major Depressive Disorder, while only 2–4 symptoms are required for Minor Depressive Disorder.

Table 2

: PSYCHOSOCIAL AND HEALTH-RELATED RISK FACTORS FOR DEPRESSION AND/OR DEPRESSION SYMPTOMS DURING THE MENOPAUSE TRANSITION

CATEGORIES OF RISK	DOMAINS	SPECIFIC RISK FACTOR
Demographic	Race/ethnicity; Income; Education; Marital status	Minority status Low Income Low education attainment Unmarried, divorced, widowed
Psychological	Personality traits; Attitudes toward menopause, aging	Trait anxiety Pessimism Rumination
Social/environmental	Adverse life events; Chronic adverse conditions; Social relationships	Childhood and lifetime adversity, trauma Current stressful situations Poor social supports
Health-related	Health behaviors; Chronic conditions; Physical symptoms; Functioning	Smoking, Physical inactivity, Sleep disturbance or disorders Lifetime psychiatric disorder(s) Co-morbid medical conditions Chronic pain Vasomotor symptoms Limitations in functioning due to physical or emotional problems