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Research Article

Depression During the Menopausal Transition: An Integrated Biopsychosocial Framework for Understanding Its Multifactorial Determinants

“Beyond Hormones: Unravelling the Interconnected Pathways of Biological Change, Emotional Vulnerability, Psychological Adaptation, Social Stress, and Individual Experience Across the Menopausal Journey”

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Abstract

Background: The menopausal transition represents a complex biological and psychosocial phase of midlife. Although menopause is a physiological process, the transition is accompanied by fluctuating reproductive hormones, vasomotor symptoms, sleep disturbance, changes in physical health, alterations in social roles, and psychological challenges. Increasing evidence suggests that some women may experience heightened vulnerability to depressive symptoms during perimenopause. However, depression during this period cannot be adequately explained by hormonal changes alone.

Objective: This review aims to examine depression during the menopausal transition through an integrated biopsychosocial framework, with particular emphasis on biological, psychological, and social determinants and their potential interactions.

Methods: An integrative narrative review of published literature concerning menopause, perimenopause, depression, reproductive hormones, vasomotor symptoms, sleep disturbance, psychosocial stressors, and biopsychosocial determinants was undertaken. Evidence from longitudinal cohort studies, systematic reviews, meta-analyses, clinical guidelines, and relevant narrative reviews was synthesized conceptually.

Results: Evidence indicates that depressive symptoms may increase during the menopausal transition, particularly among susceptible subgroups. Biological contributors include reproductive hormone fluctuation, altered neuroendocrine signalling, vasomotor symptoms, sleep disruption, and associated physical morbidity. Psychological determinants include previous depression, anxiety, perceived loss of control, negative attitudes toward ageing and menopause, body-image concerns, and difficulties adapting to midlife changes. Social determinants include relationship difficulties, caregiving responsibilities, occupational stress, financial insecurity, adverse life events, reduced social support, and changing family roles. These factors may interact synergistically rather than operate independently.

Conclusion: Depression during the menopausal transition should be conceptualized as a multifactorial phenomenon arising from interactions among biological vulnerability, psychological processes, and social context. A biopsychosocial framework provides a clinically meaningful model for comprehensive assessment, risk stratification, prevention, and individualized management. Future

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research should employ longitudinal designs and multidimensional assessment models capable of examining interactions among endocrine, psychological, behavioural, and social variables.

KEYWORDS: menopause transition; perimenopause; depression; depressive symptoms; biopsychosocial model; reproductive hormones; psychosocial stress; women's mental health; midlife women.

1. INTRODUCTION

The menopausal transition is a dynamic period characterised by progressive changes in ovarian function, menstrual cyclicity, reproductive hormone concentrations, and eventually cessation of menstruation. Although menopause itself is a normal physiological event, the transition to menopause may coincide with substantial biological, psychological, interpersonal, occupational, and social changes. Consequently, the experience of menopause varies considerably between individuals.

Depressive symptoms are among the psychological manifestations reported during the menopausal transition. Importantly, the relationship between menopause and depression is neither universal nor adequately explained by chronological ageing. Contemporary evidence indicates that the menopausal transition may constitute a period of increased vulnerability for depressive symptoms in susceptible women, particularly during perimenopause. A 2024 systematic review and meta-analysis of prospective cohort studies reported significantly greater odds of depressive symptoms or diagnoses among perimenopausal compared with premenopausal women, although increased risk was not consistently demonstrated in postmenopausal women.

Earlier longitudinal investigations also contributed substantially to understanding this relationship. The Harvard Study of Moods and Cycles reported that women entering perimenopause without a previous history of depression were approximately twice as likely to develop significant depressive symptoms as women who remained premenopausal. Similarly, the Study of Women's Health Across the Nation (SWAN) demonstrated an association between menopausal-stage progression and clinically relevant depressive symptoms.

Nevertheless, menopause should not be regarded as a singular causal factor. The current literature increasingly supports a model in which hormonal changes interact with previous

psychiatric vulnerability, menopausal symptoms, sleep disturbance, life stress, interpersonal circumstances, health behaviours, and broader socioeconomic conditions.

This conceptual shift provides the rationale for applying a **biopsychosocial model** to depression during the menopausal transition.

2. Conceptual Basis of the Biopsychosocial Model

The biopsychosocial model emphasizes that health and illness arise through dynamic interactions among biological processes, psychological states, and social/environmental circumstances.

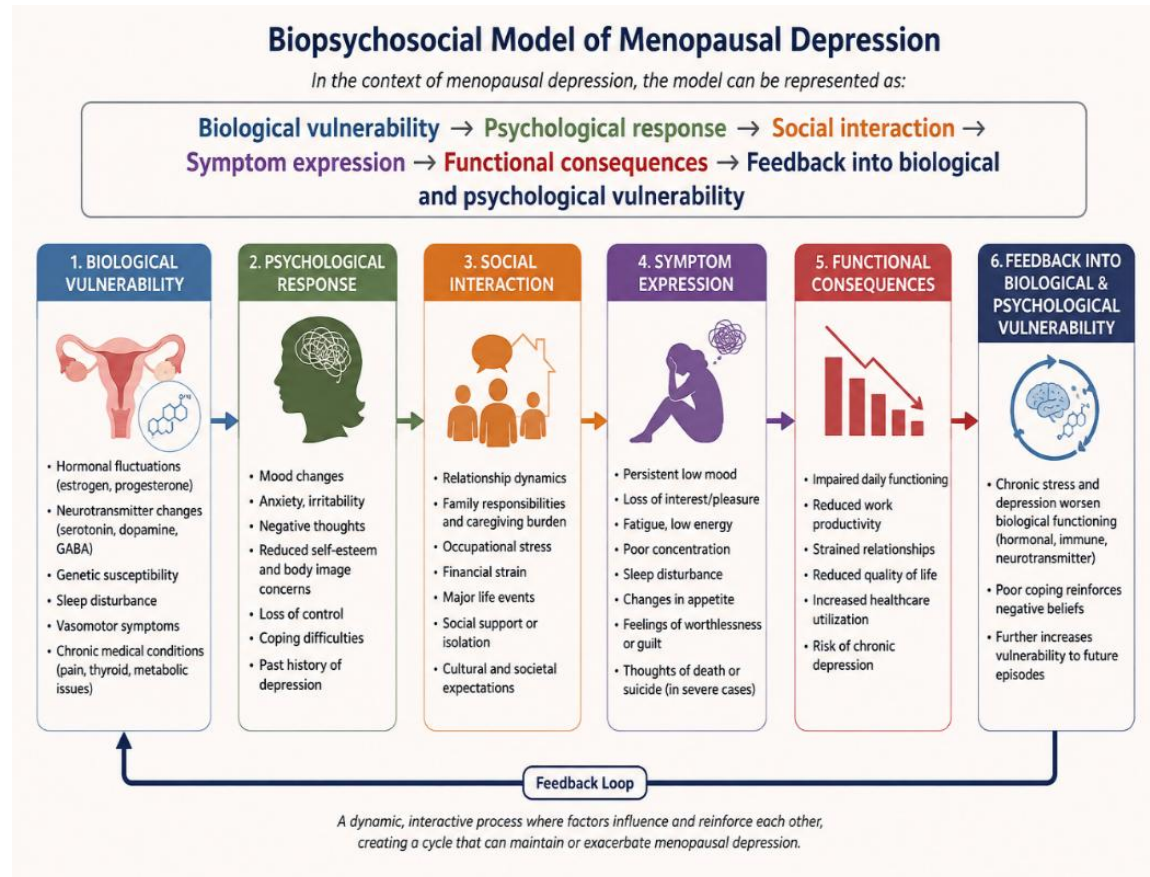
In the context of menopausal depression, the model can be represented as:

Biological vulnerability → Psychological response → Social interaction → Symptom expression → Functional consequences → Feedback into biological and psychological vulnerability

The model does not assume that every woman experiencing hormonal changes will develop depression. Instead, it proposes that biological transition may interact with pre-existing susceptibility and environmental stressors to influence the probability, severity, and persistence of depressive symptoms.

This perspective is particularly relevant because menopause occurs within the broader context of midlife. Women may simultaneously experience changing family responsibilities, occupational demands, relationship transitions, caregiving for ageing parents, changing socioeconomic circumstances, altered body image, and concerns regarding ageing and health.

Therefore, depression during menopause is better understood as an interactional phenomenon rather than a purely endocrine disorder.



3. Biological Determinants

3.1 Reproductive Hormonal Fluctuation

The menopausal transition is characterized by substantial changes in ovarian function, including fluctuations in estradiol and progressive changes in follicle-stimulating hormone. The endocrine environment is dynamic rather than simply representing a gradual reduction in estrogen.

Reproductive hormones influence several neural systems involved in mood regulation. Estrogen interacts with serotonergic, noradrenergic, dopaminergic, and other neurobiological pathways associated with emotional regulation. Consequently, rapid hormonal fluctuation may be more relevant to mood vulnerability in susceptible women than the absolute postmenopausal hormone concentration alone.

Evidence from longitudinal studies suggests that reproductive hormonal changes are associated with depressive symptoms in some women, although measured hormone concentrations account for only part of the variability in mood outcomes.

Thus, an endocrine explanation is biologically plausible but insufficient as a comprehensive model.

3.2 Vasomotor Symptoms

Hot flashes and night sweats are among the most characteristic symptoms of the menopausal transition. They may contribute indirectly to psychological morbidity through sleep disruption, fatigue, irritability, reduced concentration, and impaired quality of life.

The relationship between vasomotor symptoms and depression appears clinically important. Earlier research identified vasomotor symptoms as a potential predictor of depressive symptoms, while more recent reviews suggest that women with severe or sleep-disrupting vasomotor symptoms may represent a particularly vulnerable subgroup.

Consequently, vasomotor symptoms should not merely be regarded as isolated physical complaints; their psychological and behavioural consequences should also be assessed.

3.3 Sleep Disturbance

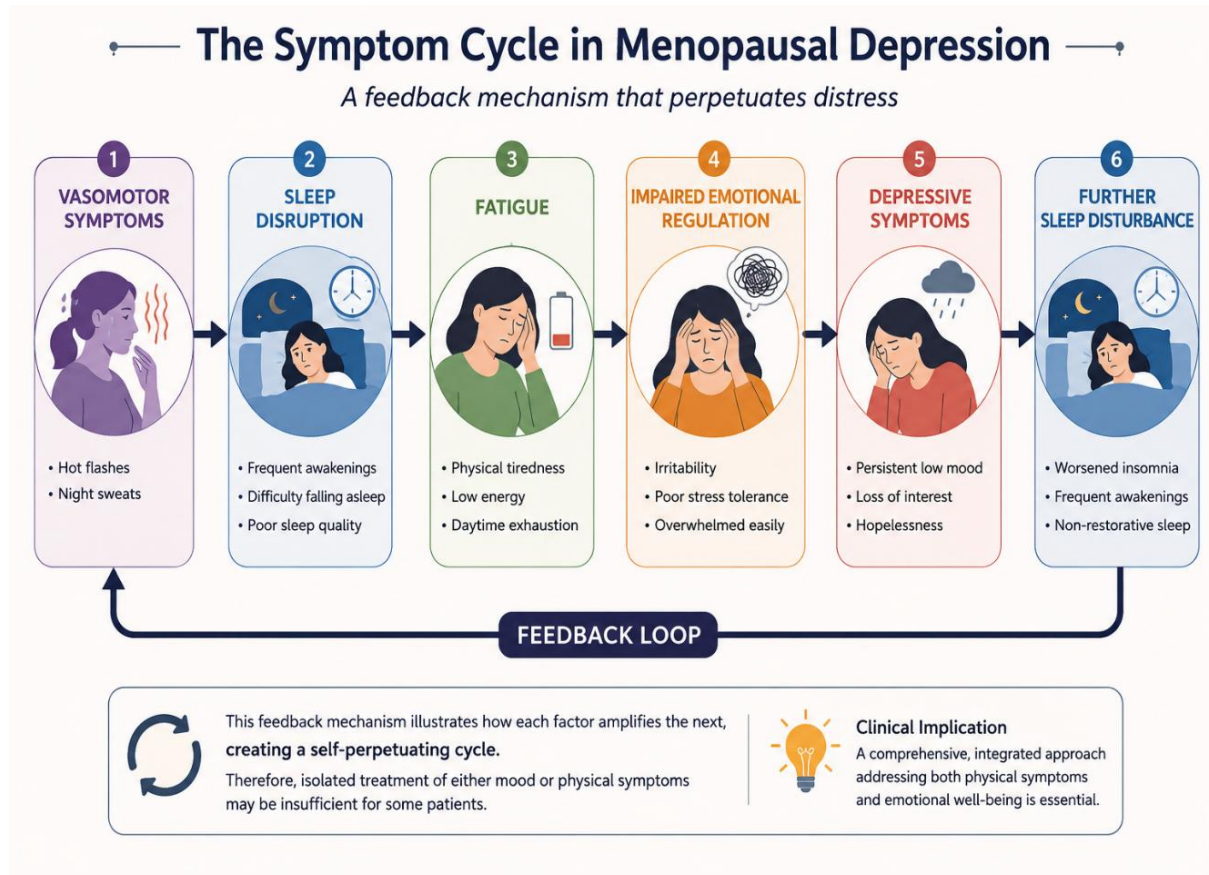
Sleep disturbance is an important intermediary between menopause and depression.

Night sweats, hot flashes, insomnia, sleep fragmentation, anxiety, and changing sleep patterns can produce cumulative fatigue and impaired emotional regulation. Conversely, depression itself may worsen sleep, generating a bidirectional relationship.

The resulting cycle may be conceptualized as:

**Vasomotor symptoms → sleep disruption → fatigue →
impaired emotional regulation → depressive symptoms →
further sleep disturbance**

This feedback mechanism illustrates why isolated treatment of either mood or physical symptoms may be insufficient for some patients.



3.4 Physical Health and Comorbidity

Midlife is also associated with increasing prevalence of chronic health conditions. Pain, obesity, diabetes, cardiovascular risk factors, thyroid dysfunction, and other chronic diseases may influence psychological well-being and functional status.

A 2024 systematic review and meta-analysis involving more than 385,000 postmenopausal women found substantial prevalence of depression and identified chronic disease, menopausal symptoms, previous mental illness, and other demographic and reproductive factors among variables associated with depression.

The presence of multimorbidity may therefore increase biological and psychological burden simultaneously.

4. Psychological Determinants

4.1 Previous History of Depression

Previous depression represents one of the most consistently recognized predictors of depressive episodes during the menopausal transition.

The 2019 guidelines developed by the North American Menopause Society and the National Network of Depression Centers emphasized that many midlife women experiencing a major depressive episode during perimenopause have experienced depression previously.

A history of depression related to reproductive hormonal changes—such as premenstrual mood disturbance or postpartum depression—may indicate particular sensitivity to reproductive endocrine fluctuations.

4.2 Anxiety and Emotional Vulnerability

Depression and anxiety frequently coexist. Anxiety concerning ageing, health, family responsibilities, changing relationships, sexuality, or occupational circumstances may amplify emotional vulnerability.

Persistent anxiety can contribute to insomnia, cognitive preoccupation, fatigue, and reduced coping capacity. These processes may subsequently intensify depressive symptoms.

Therefore, assessment of depression during menopause should include relevant anxiety symptoms rather than treating depressive symptoms in isolation.

4.3 Attitudes Toward Menopause and Ageing

Individual interpretation of menopause may influence psychological outcomes.

Women who perceive menopause as a natural developmental transition may respond differently from those who associate it predominantly with loss of femininity, attractiveness, fertility, social value, or physical capability.

Negative attitudes toward menopause and ageing have been identified among psychosocial factors associated with depressive symptoms.

This suggests that the meaning attributed to menopause may be as clinically relevant as the physiological transition itself.

4.4 Body Image and Self-Identity

Changes in body composition, weight, skin, hair, sexuality, and physical appearance may affect self-perception.

For some women, these changes may challenge established identities and contribute to reduced self-esteem. The psychological impact is likely to depend on cultural expectations, interpersonal relationships, previous body-image concerns, and individual coping mechanisms.

A biopsychosocial model therefore recognizes body image as an interface between biological change and psychological/social interpretation.

5. Social Determinants

5.1 Adverse Life Events

Midlife may involve multiple simultaneous life transitions. These can include bereavement, marital conflict, separation, divorce, unemployment, retirement, financial difficulty, relocation, illness within the family, and other stressful circumstances.

Evidence indicates that adverse life events can substantially modify the risk of depressive symptoms during the menopausal transition. The Harvard Study of Moods and Cycles demonstrated the importance of negative life events in the relationship between perimenopause and depression.

Thus, menopause-related biological vulnerability may become clinically important particularly when combined with psychosocial stress.

5.2 Family and Caregiving Responsibilities

Women in midlife may simultaneously provide support to children, partners, parents, or other family members.

The combination of caregiving demands and occupational responsibilities may produce chronic stress and limited opportunities for self-care. Such circumstances may contribute to emotional exhaustion, sleep disturbance, and depressive symptoms.

Social support may therefore function as a potentially protective factor, whereas isolation and inadequate support may increase vulnerability.

5.3 Occupational and Economic Stress

Employment conditions, financial insecurity, workplace discrimination, reduced productivity, and concerns regarding career progression may influence mental health.

The socioeconomic environment can also determine access to healthcare, psychological services, nutritious food, physical activity opportunities, and social resources.

Consequently, social determinants may indirectly influence biological and psychological pathways rather than simply acting as external stressors.

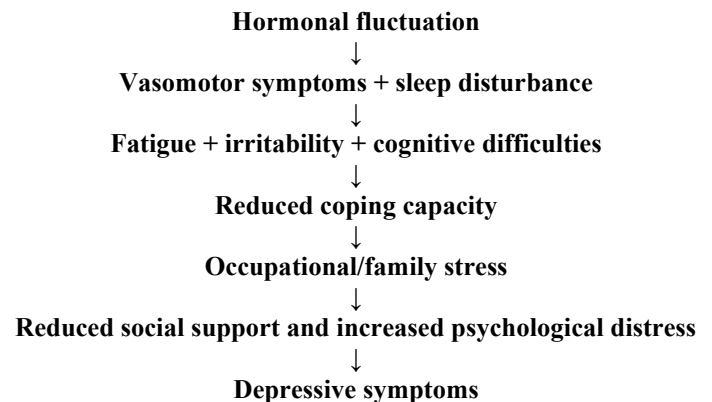
6. Interaction Between Biological, Psychological, and Social Factors

The central strength of the biopsychosocial model lies in its recognition of **interaction**.

For example, a woman experiencing fluctuating reproductive hormones may develop hot flashes and disturbed sleep. Sleep deprivation may produce fatigue and irritability. These symptoms may reduce work performance and increase interpersonal conflict. Relationship difficulties may then

intensify emotional distress, while persistent stress may further impair sleep.

The resulting pathway can be represented as:



This model also explains why women exposed to similar biological changes may have markedly different psychological outcomes.

7. Evidence Supporting the Biopsychosocial Framework

Contemporary evidence provides support for a multifactorial model rather than a single-factor hormonal explanation.

A 2022 study examining biopsychosocial risk factors in women undergoing the menopausal transition found relationships between depressive symptom severity and menopausal symptoms, reproductive endocrine variables, age, and other characteristics. Particularly strong associations were observed between menopausal symptom burden and depression severity.

A systematic review published in 2023 similarly concluded that depression and anxiety are common during the menopausal period, with prior depression and vasomotor symptoms contributing to risk.

More recently, a 2024 systematic review and meta-analysis found that perimenopausal women had significantly greater odds of depressive symptoms or depressive diagnoses compared with premenopausal women, although this increased risk was not demonstrated consistently after menopause.

At the same time, a 2024 clinical review emphasized that evidence does not establish a universal increase in depression across all women undergoing menopause. Instead, vulnerability appears concentrated in subgroups characterized by severe vasomotor symptoms, sleep disturbance, prolonged transition, reproductive hormone dynamics, and psychosocial stress.

This distinction is important. The biopsychosocial model should therefore be interpreted as a **vulnerability-interaction model**, not as evidence that menopause inevitably causes depression.

8. Clinical Assessment Through a Biopsychosocial Lens

A comprehensive assessment should extend beyond asking whether a patient has depressive symptoms.

Biological domain

- Menstrual and menopausal status
- Duration of menopausal transition

- Vasomotor symptoms
- Sleep quality
- Reproductive and endocrine history
- Chronic medical conditions
- Medication history
- Pain and physical symptoms
- Lifestyle and physical activity

Psychological domain

- Depressed mood
- Anhedonia
- Anxiety
- Irritability
- Cognitive complaints
- Previous depressive episodes
- Previous reproductive-related mood disorders
- Self-esteem and body image
- Coping mechanisms
- Perception of menopause and ageing

Social domain

- Marital/relationship circumstances
- Family responsibilities
- Caregiving burden
- Occupational stress
- Financial circumstances
- Social support
- Major life events
- Cultural expectations
- Access to healthcare

This approach can identify modifiable contributors and clinically relevant vulnerabilities that may otherwise remain unrecognized.

9. Screening and Differential Considerations

Depressive symptoms during menopause may overlap with common menopausal complaints such as fatigue, insomnia, poor concentration, reduced energy, and sexual dysfunction. Therefore, clinicians should avoid automatically attributing all psychological symptoms to menopause.

Validated depression screening instruments may assist identification of clinically significant symptoms, but positive screening should be followed by appropriate clinical assessment.

Particular attention should be paid to:

- persistent depressed mood;
- loss of interest or pleasure;
- hopelessness;
- significant functional impairment;
- recurrent depressive episodes;
- severe anxiety;
- suicidal ideation or self-harm thoughts.

Menopausal symptoms and depressive disorders may coexist, and the presence of one should not obscure recognition of the other.

10. Management Implications

A biopsychosocial formulation naturally leads to an individualized management strategy.

10.1 Biological interventions

Management of significant menopausal symptoms may improve overall quality of life and may indirectly benefit psychological well-being.

Current evidence-based menopause guidance supports several approaches for vasomotor symptoms, including hormone therapy in appropriately selected women and evidence-based nonhormonal options when hormone therapy is unsuitable or undesired.

However, treatment decisions should be individualized according to age, time since menopause, symptoms, medical history, contraindications, preferences, and risk-benefit considerations.

10.2 Psychological interventions

Psychological interventions may include:

- cognitive-behavioural therapy;
- supportive psychotherapy;
- psychoeducation;
- stress-management strategies;
- behavioural interventions for sleep;
- interventions targeting maladaptive beliefs and negative interpretations of menopause.

The 2019 perimenopausal depression guidelines emphasize assessment and treatment of depression using established approaches while considering the specific menopausal context.

10.3 Social and Lifestyle Interventions

Lifestyle and social interventions may include:

- regular physical activity;
- improved sleep routines;
- healthy dietary patterns;
- reduction of tobacco and excessive alcohol exposure;
- strengthening social networks;
- addressing occupational stress;
- family counselling where appropriate;
- improving access to community and healthcare resources.

These interventions should not be presented as substitutes for treatment of major depressive disorder when formal treatment is indicated. Rather, they form part of a broader comprehensive care model.

11. Implications for Research

The biopsychosocial model provides several opportunities for future research.

First, longitudinal studies should evaluate women before, during, and after the menopausal transition rather than relying exclusively on cross-sectional comparisons.

Second, studies should distinguish between:

- depressive symptoms;
- clinically diagnosed major depressive disorder;
- anxiety;
- menopause-specific symptoms; and

- psychological distress.

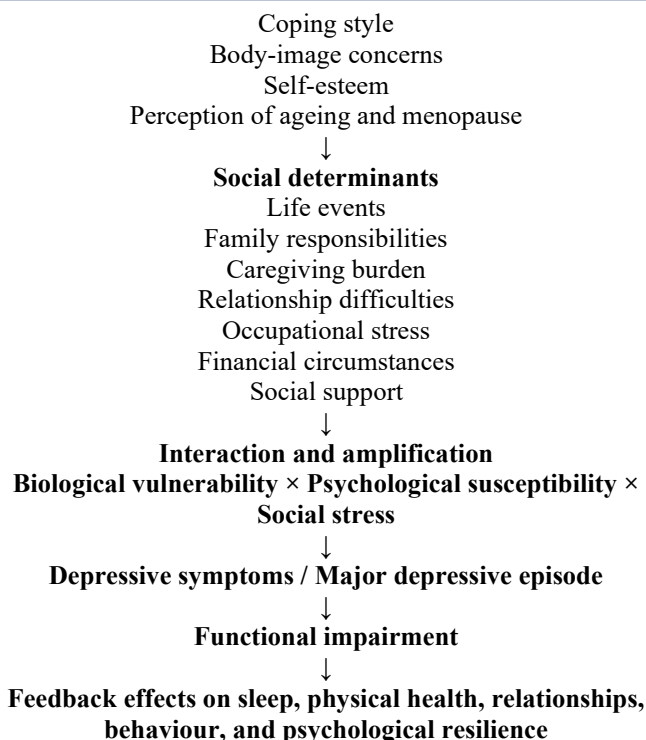
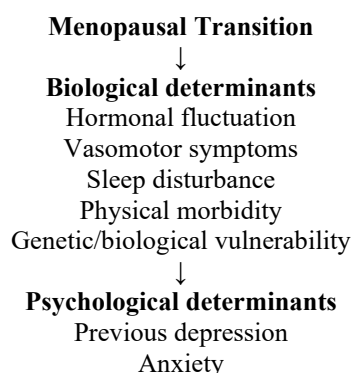
Third, future research should investigate interactions among reproductive hormone dynamics, sleep, vasomotor symptoms, previous depression, stressful life events, and social support.

Fourth, culturally diverse populations should be included. Experiences of menopause are shaped by social expectations, family structures, healthcare access, occupation, socioeconomic status, and cultural interpretations.

Finally, future studies should move beyond identifying isolated risk factors toward development of multidimensional predictive models capable of identifying women at higher risk before severe depression develops.

12. Proposed Integrated Biopsychosocial Framework

Based on the literature reviewed, the following conceptual framework may be proposed:



This framework emphasizes that no single domain should be considered sufficient to explain the clinical presentation.

Materia Medica Differential for Menopausal Depression

Remedy	Characteristic mental picture	Menopausal/physical indications	Key differentiating features
Lachesis mutus	Intense, talkative, suspicious, jealous; emotional intensity; depression with irritability	Hot flushes, especially around menopause; headaches; sleep disturbance; menstrual suppression/irregularity	Worse after sleep; intolerance of tight clothing around neck/waist; symptoms often left-sided; loquacity
Sepia officinalis	Indifference to loved ones; irritability; aversion to family; emotional exhaustion; feeling overwhelmed	Hot flushes, night sweats, pelvic bearing-down sensation, hormonal changes	“Don't care” state + exhaustion + irritability; better from vigorous exercise
Cimicifuga racemosa	Depression with anxiety, fear, gloom, emotional instability; dark thoughts	Menstrual irregularity, muscular pains, headaches, menopausal symptoms	Marked mental gloom with muscular/neck/back symptoms; changing, contradictory mental states
Pulsatilla nigricans	Weepy, emotional, dependent, seeks consolation; mood changes	Irregular menstrual history, hot flushes, digestive complaints	Weeps easily, wants company and consolation; changeable symptoms; generally better in open air
Natrum muriaticum	Silent grief, withdrawal, brooding, sensitivity to criticism; difficulty expressing emotions	Menstrual irregularity, headaches, weakness, sleep disturbance	Wants to be alone; consolation aggravates; dwells on past disappointments/grief
Ignatia amara	Acute grief, emotional contradiction, sighing, mood fluctuations	Menstrual irregularity, headaches, spasmodic symptoms, sleep disturbance	Paradoxical/contradictory symptoms; grief-related picture; frequent sighing
Aurum metallicum	Profound hopelessness, self-reproach, worthlessness; strong sense of failure	Menopausal depression with marked exhaustion and cardiovascular complaints	Very deep depressive state; feelings of failure/worthlessness; suicidal ideation requires urgent conventional assessment
Kali carbonicum	Anxiety, insecurity, irritability, excessive responsibility; fearfulness	Climacteric complaints, weakness, backache, sleep disturbance	Anxious, rigid, duty-oriented personality; marked weakness and back symptoms
Sanguinaria canadensis	Irritability, anxiety, mental fatigue	Climacteric hot flushes, headaches, burning sensations	Prominent right-sided headaches/hot flush pattern; characteristic physical concomitants
Glonoinum	Confusion, irritability, emotional instability	Sudden intense hot flushes, throbbing headaches, vascular symptoms	Sudden congestive/vascular episodes; sensation of heat and pulsation

Causticum	Sadness, anxiety, insecurity; emotional response to prolonged stress	Menopausal weakness, rheumatic complaints, sleep disturbance	Chronic stress + exhaustion + marked physical complaints; tendency toward stiffness/contractures
Graphites	Depressed, indecisive, anxious; sensitive and withdrawn	Menopausal symptoms with weight/metabolic and skin complaints	Depression associated with characteristic skin symptoms and constitutional features

High-yield differentiation

Lachesis → “I am intensely emotional, irritable and cannot tolerate restriction.”

Sepia → “I am exhausted and emotionally indifferent—even toward my family.”

Cimicifuga → “My mind is gloomy, anxious and constantly changing.”

Natrum mur → “I suffer silently and don't want consolation.”

Pulsatilla → “I feel emotional and need someone to comfort me.”

Ignatia → “My emotions are contradictory and linked with grief.”

Aurum → “I feel worthless, hopeless and have failed.”

Kali carb → “I am anxious, insecure and burdened by responsibilities.”

Biopsychosocial Materia Medica Mapping

For your particular research article, I think this is more innovative than a conventional remedy list:

1. Biological dimension

Menopausal transition → **hormonal fluctuation** → **vasomotor symptoms** → **sleep disturbance**

Possible traditional Materia Medica correlations:

Lachesis • Sepia • Sanguinaria • Glonoinum • Cimicifuga

2. Psychological dimension

Hormonal/physical burden → **anxiety** → **irritability** → **emotional dysregulation** → **depressive symptoms**

Possible differentials:

Cimicifuga • Sepia • Ignatia • Natrum muriaticum • Aurum metallicum

3. Social dimension

Family responsibility → **caregiving burden** → **occupational stress** → **relationship difficulties** → **emotional exhaustion**

Possible differentials:

Sepia • Kali carbonicum • Causticum • Aurum metallicum

4. Grief / emotional trauma pathway

Loss / disappointment → **internalization** → **withdrawal** → **depressive state**

Possible differentials:

Natrum muriaticum • Ignatia • Aurum metallicum

5. Dependency / need for emotional support

Loneliness → **need for reassurance** → **emotional instability**

Possible differential:

Pulsatilla

13. DISCUSSION

The relationship between menopause and depression has historically been debated. Early explanations frequently emphasized hormonal depletion, whereas psychosocial approaches emphasized life circumstances and cultural interpretations. Current evidence supports a more nuanced position.

The menopausal transition may represent a period of biological sensitivity, but biological sensitivity does not inevitably produce depression. Rather, depressive vulnerability appears to emerge when endocrine changes interact with individual psychological susceptibility and environmental stressors.

This interpretation is consistent with prospective research showing increased depressive vulnerability during perimenopause while also demonstrating substantial heterogeneity among women.

The distinction between menopause as a biological transition and depression as a clinical disorder is particularly important. Menopause is universal among women who reach the relevant stage of reproductive ageing, whereas major depressive disorder is not. Therefore, causal assumptions based solely on temporal association are inappropriate.

The biopsychosocial model provides a clinically useful bridge between these perspectives. It accommodates endocrine mechanisms without reducing psychological suffering to hormonal deficiency. It also recognizes that psychosocial stress cannot be separated completely from biological processes.

For example, sleep disturbance may originate from vasomotor symptoms but subsequently become a psychological and behavioural problem. Similarly, financial stress may initially be social but can produce neuroendocrine stress responses, sleep disturbance, anxiety, and depressive symptoms.

Thus, the boundaries between biological, psychological, and social determinants are permeable and interactive.

14. Limitations

This article is an integrative narrative review rather than a systematic review with a registered protocol. Therefore, the literature synthesis may be influenced by selection of relevant publications.

The available evidence is also heterogeneous. Studies differ in their definitions of menopause stages, methods of assessing depression, populations studied, follow-up duration, and measurement of reproductive hormones. The 2024 meta-analysis specifically noted methodological heterogeneity across studies.

Furthermore, associations between menopause-related symptoms and depression do not necessarily establish causality. Future systematic reviews and prospective studies should employ standardized definitions and validated instruments and should investigate interactions between biological, psychological, and social determinants.

15. CONCLUSION

Depression during the menopausal transition represents a complex and heterogeneous clinical phenomenon. Current evidence supports the view that perimenopause may constitute a period of increased vulnerability to depressive symptoms in some women, but menopause should not be regarded as a universal or singular cause of depression.

An integrated biopsychosocial framework provides a more comprehensive explanation by recognizing the interaction of reproductive endocrine changes, vasomotor symptoms, sleep disturbance, physical health, previous psychiatric vulnerability, coping processes, life events, relationships, occupational circumstances, socioeconomic conditions, and social support.

The central clinical implication is that the woman, rather than menopause alone, should remain the unit of assessment.

Accordingly, evaluation should integrate biological history, psychological characteristics, symptom burden, functional status, and social context. Such an approach may improve early identification of vulnerable women and support individualized prevention and management strategies.

Future research should focus on longitudinal, culturally diverse, multidimensional models capable of identifying how biological transitions interact with psychological and social determinants to influence the onset, severity, and persistence of depression during midlife.

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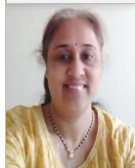
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