



Four Years of Menopausal Symptoms Treated as Anxiety: A Narrative Review of Diagnostic Overlap and the Quality of the Supporting Evidence

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Abstract

Fatigue, poor concentration, disturbed sleep, irritability and low mood in a woman in her forties will satisfy the criteria for a depressive or anxiety disorder. They are also the commonest features of the menopausal transition. The two descriptions are not distinguishable on symptoms alone, which is the whole difficulty.

Objectives: To review the published evidence on the overlap between menopausal symptoms and common mental disorder: how far the diagnostic criteria coincide, what is known about misattribution, what treatment response shows, and how good the supporting evidence actually is.

Material and Methods: Narrative review of clinic cohorts, audits, prescribing data, society guidance and industry-sponsored surveys indexed in PubMed and the major obstetric, primary care and psychiatric journals. No new patient data were generated; every estimate quoted is one published by the original investigators, and the sponsorship of each source is stated.

Results: In a cohort of 978 women attending a menopause clinic, the five most prevalent symptoms were fatigue (96 per cent), memory problems (93 per cent), difficulty concentrating (91 per cent), irritability (90 per cent) and feeling tense or nervous (90 per cent); hot flushes and night sweats ranked 18th and 14th. Seven of the eight items on the PHQ-8 depression scale may be produced by the menopausal transition. In an audit of women diagnosed with depression at a tertiary centre, 78 per cent had significant perimenopausal symptoms that had been overlooked, 82 per cent were treated with antidepressants, and 45 per cent reported satisfactory symptom management.

Conclusion: The overlap is genuine and clinically important. The evidence describing it is unusually weak: single-clinic cohorts without control groups, an audit in one hospital, and surveys funded by companies selling hormone therapy. Both statements need to be made together, because the strength of the argument does not match the strength of the data.

Abbreviations: CBT – Cognitive Behavioural Therapy, HRT – Hormone Replacement Therapy, MENQOL – Menopause-Specific Quality of Life questionnaire, PHQ-8 – Patient Health Questionnaire 8-item, SSRI – Selective Serotonin Reuptake Inhibitor, VMS – Vasomotor Symptoms.

Keywords: Perimenopause; Diagnostic Overlap; Depression; Misattribution; Evidence Quality

Introduction

The menopausal transition is defined by changing ovarian function and is accompanied by vasomotor, psychological, cognitive, genitourinary and musculoskeletal symptoms that may begin years before the final menstrual period [1,2]. Its duration is variable and often underestimated, with vasomotor symptoms persisting a median of several years in longitudinal cohorts [3].

Depressive symptoms are more common during the perimenopause than before it, with reported risk in the region of one and a half to two times the premenopausal rate, and the increase is most marked in women without a prior psychiatric history [4,5,6]. That association is well established and is not in dispute.

What is in dispute is attribution in the individual case. A woman presenting with fatigue, poor sleep, low mood and difficulty concentrating meets criteria for a depressive disorder and also describes a typical perimenopausal presentation [7,8]. This review examines the overlap, and is deliberately explicit about the quality of the evidence, which is weaker than the confidence with which the topic is usually discussed.

Material and Methods

Search strategy: PubMed and the archives of the major obstetric, primary care, psychiatric and menopause journals were searched for studies of symptom overlap and misattribution in the menopausal transition. Search terms combined perimenopause and menopause with depression, anxiety, misdiagnosis, antidepressant, PHQ-9 and quality of life. Reference lists of society guidance [9,10] were screened by hand for primary sources.

Eligibility: Studies were included if they quantified symptom prevalence in defined menopausal populations, examined the relationship between menopausal status and mood disorder, or reported prescribing or diagnostic patterns. Non-peer-reviewed surveys are included where they are the only available data on a question, and are identified as such throughout.

Data extraction and handling: Design, sample size, recruitment setting, funding source and the reported estimate were extracted as published. The recruitment setting and funding source are reported alongside every figure, because much of the available data comes from specialist clinics treating self-selected patients or from surveys commissioned by manufacturers, and both selection and sponsorship bear directly on interpretation. No pooling or re-analysis was performed. Figures 1 to 4 and Tables 1 and 2 reproduce published values only. This is a narrative synthesis and was not registered as a systematic review.

Results

What the symptoms actually are: A survey of 978 consecutive new patients at a specialist menopause clinic, using a modified Greene Climacteric Symptom Questionnaire [24], found the five most prevalent symptoms to be feeling tired or lacking in energy (96 per cent), memory problems (93 per cent), difficulty concentrating (91 per cent), irritability (90 per cent) and feeling tense or nervous (90 per cent) (Figure 1) [11]. Hot flushes and night sweats ranked 18th and 14th in that cohort. Every one of the top five is also a feature of common mental disorder.

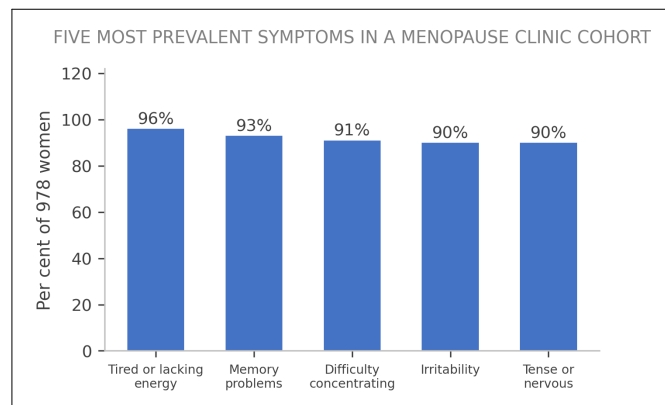


Figure 1: Five most prevalent symptoms in a specialist menopause clinic cohort [11]

The scales cannot separate them: Seven of the eight items on the PHQ-8 depression scale, including sleep disturbance, appetite change, fatigue, poor concentration and mood disturbance, may be produced by the menopausal transition rather than by a depressive disorder (Figure 3) [7,12]. A screening instrument built from those items cannot distinguish the two conditions, and will return a positive result in a symptomatic perimenopausal woman who has no depressive illness.

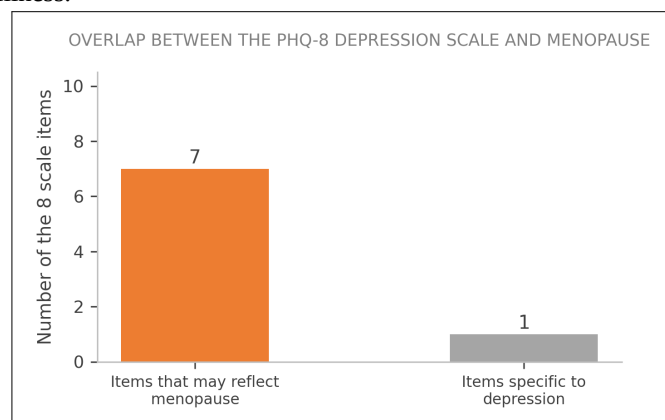


Figure 3: Overlap between items on the PHQ-8 depression scale and features of the menopausal transition [7,12]

What that produces in practice: A focused audit at a tertiary centre retrospectively screened women who had been diagnosed with depression. Seventy-eight per cent had significant perimenopausal symptoms on the Greene Climacteric

Scale that had been overlooked at the time of diagnosis, and 65 per cent showed a substantial quality-of-life impact attributable to menopausal symptoms on MENQOL [25]. Treatment was predominantly pharmacological, with 82 per cent receiving antidepressants, 8 per cent psychological therapy and 10 per cent lifestyle or non-hormonal advice. Only 45 per cent reported satisfactory symptom management (Figure 2) [13].

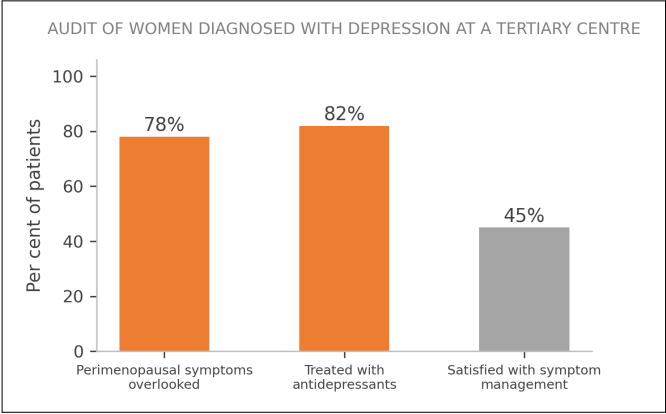


Figure 2: Findings from an audit of women diagnosed with depression at a tertiary centre [13]

Prescribing context: Antidepressant use in national survey data is highest among women aged 60 and over at 24.3 per cent, followed by women aged 40 to 59 at 20.1 per cent [12,14]. That distribution is consistent with a diagnostic overlap and is equally consistent with a genuinely higher prevalence of depressive illness in midlife women; it does not by itself establish misattribution.

What treatment response suggests: In the menopause clinic cohort, all 978 patients were started on hormone therapy and a third additionally on transdermal testosterone. At three months every symptom score had improved: profound low mood improved most, by 69 per cent, followed by attacks of anxiety and panic at 61 per cent (Figure 4) [11]. No patient discontinued treatment during the study period. Non-hormonal options also have evidence, with cognitive behavioural therapy reducing the frequency and severity of vasomotor symptoms and improving mood and anxiety [15,16,34]. Randomised evidence for hormonal treatment of mood exists and is more informative than uncontrolled cohorts, including trials of estradiol withdrawal, of transdermal estradiol for prevention of depressive symptoms, and of estradiol in perimenopausal depression [21,22,23].

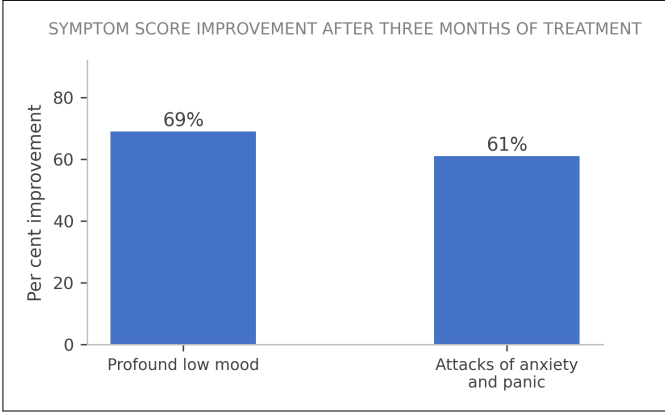


Figure 4: Improvement in mood symptom scores after three months of treatment in a single-arm clinic cohort [11]

Source	Design and funding	Principal reported finding
Newson Health cohort [11]	978 patients, single specialist clinic, single-arm	Fatigue 96%, memory 93%; mood scores improved on treatment
Tertiary centre audit [13]	Retrospective audit, women diagnosed with depression	78% had overlooked perimenopausal symptoms; 82% on antidepressants
PHQ-8 overlap analysis [7,12]	Commentary on scale content	Seven of eight items may reflect menopause
National survey data [14]	Population prescribing survey	Antidepressant use 20.1% at 40-59, 24.3% at 60+
Industry-sponsored survey [17]	Consumer survey funded by a hormone company	About 40% of respondents felt misdiagnosed
Bromberger et al. [4,5]	SWAN longitudinal cohort	Depressive symptoms more likely during perimenopause
NICE guideline [9]	National guidance	Advises against routinely offering SSRIs as first-line for low mood

Table 1: Principal sources reviewed, with design, funding and the finding as reported

The industry-sponsored data: Much of the material circulating on this topic comes from surveys commissioned by companies that sell hormone therapy. One such survey reported that about 40 per cent of women seeking care for perimenopausal symptoms felt misdiagnosed, with more than half treated for anxiety, depression, panic attacks or mood swings, and 33 per cent specifically for anxiety [17,18]. These figures are widely quoted. They come from a self-selected consumer sample, were not peer reviewed, and were produced by a party with a direct commercial interest in the conclusion. That does not make them wrong, and it does mean they cannot carry the weight often placed on them.

What guidance says: National guidance advises that menopause be diagnosed clinically in women over 45 with typical symptoms, without laboratory testing, and specifically advises against routinely offering selective serotonin reuptake inhibitors as first-line treatment for low mood arising as part of the menopause [9,10,19]. That recommendation exists precisely because the substitution described here was recognised as common [28,29].

Claim	Evidence status	Basis
Symptoms overlap substantially	Well supported	Seven of eight PHQ-8 items; clinic symptom profile [7,11]
Depressive symptoms rise in perimenopause	Well supported	Longitudinal cohort data [4,5,6]
Misattribution is common	Weakly supported	One single-centre audit; industry surveys [13,17]
Antidepressants are over-prescribed here	Not established	Prescribing data are consistent with either account [12,14]
Hormone therapy improves mood symptoms	Supported but uncontrolled	Single-arm clinic cohort, no comparator [11]
CBT helps vasomotor and mood symptoms	Supported	Randomised evidence exists [15,16]

Table 2: Claims made about menopause and mood, and the current evidential status of each

Discussion

Two things are true at once here, and reviews of this topic tend to assert the first while omitting the second.

The first is that the diagnostic overlap is real and consequential. Seven of the eight items on a widely used depression screening scale can be produced by the menopausal transition [7,12]. In a clinic population, fatigue, memory problems and poor concentration were more prevalent than hot flushes [11]. A woman presenting with those symptoms to a general practice with a ten-minute appointment will meet criteria for depression, and nothing in the consultation will necessarily prompt anyone to ask about her cycle. Guidance advises against routinely offering an SSRI for low mood arising as part of the menopause, which is an unusual thing for a national body to say unless the practice was widespread [9].

The second is that the evidence establishing how often this happens is poor. The audit reporting that 78 per cent of women diagnosed with depression had overlooked perimenopausal symptoms is a single retrospective screen at one hospital [13]. The 978 patient cohort is a single specialist clinic, self-referred, in which all patients received hormone therapy and there was no comparison group, so the reported symptom improvements cannot be separated from regression to the mean, from expectation, or from the effect of finally being taken seriously [11]. The most widely circulated figure, that around 40 per cent of women felt misdiagnosed, comes from a consumer survey commissioned by a hormone therapy company [17]. Naming that is not cynicism; it is the same standard this review would apply to a drug trial.

There is also a risk in the corrective that deserves stating. If every midlife presentation of low mood is reattributed to hormones, women with depressive illness will have effective treatment withheld, and depression in midlife carries real mortality. The overlap runs in both directions. The clinically defensible position is not that anxiety in a woman of 47 is probably menopause, but that menstrual history belongs in the

assessment, that the two can coexist, and that a partial response to an antidepressant should prompt the question rather than a dose increase [8,20,35]. Cognitive and mood changes across the transition have been characterised prospectively [30,31,32].

What is genuinely missing is a properly controlled study: women presenting to primary care with new midlife mood symptoms, systematically assessed for menopausal status, randomised or at minimum prospectively followed by treatment received. Nothing of that design appears in this literature, which is why a topic with a strong prior and a large affected population still rests on audits and surveys.

Study limitations

The limitations belong to the underlying literature and are unusually severe. The largest symptom cohort is single-clinic, self-selected and single-arm, with all patients treated and no control group [11]. The audit reporting overlooked symptoms is retrospective, from one centre, with outcomes assessed by follow-up interview [13]. Widely quoted misdiagnosis figures derive from a non-peer-reviewed consumer survey funded by a manufacturer of hormone therapy [17,18]. Prescribing data are cross-sectional and cannot distinguish over-diagnosis of depression from genuinely higher prevalence [14]. Menopausal status is often self-reported and staging criteria vary between studies [1,3,33]. Symptom interference with work and relationships is documented but rarely used as an outcome [26,27,33]. No study identified assessed diagnostic accuracy prospectively against a reference standard. And the literature is dominated by high-income settings and by women who reached a specialist service, who are by definition not those whose symptoms were never investigated [11,13].

Conclusion

A woman treated for four years for anxiety whose symptoms were menopausal is a recognisable clinical story, and the reason it is recognisable is that the two conditions share almost all of their presenting features: seven of the eight items on a standard depression scale can be produced by the menopausal transition. Asking about the menstrual cycle in a midlife woman presenting with mood symptoms costs one question and is plainly good practice. What cannot honestly be claimed is precision about how often the substitution occurs, because the numbers in circulation come from one hospital audit, one uncontrolled clinic cohort and a survey paid for by a company selling the alternative treatment. The clinical point stands on its own; it does not need the statistics it is usually given.

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Conflict of Interest

The authors declare no competing interests.

Ethics Statement

This article reviews previously published studies only. No new patient data were collected and no participants were recruited, so ethical approval was not required.

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