



Review article

Menopause and multiple sclerosis: A scoping review of symptoms, disease course, and lived experience

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ABSTRACT

Menopause influences disease activity in women with multiple sclerosis. This scoping review mapped current evidence on menopause in women with multiple sclerosis across symptom, disease, biological, and lived experience domains. This review followed Preferred Reporting Items for Systematic Reviews and Meta-Analyses and was preregistered on Open Science Framework (DOI [10.17605/OSF.IO/H8QBM](https://doi.org/10.17605/OSF.IO/H8QBM)). PubMed/MEDLINE, Embase, Web of Science, Scopus, CINAHL, and PsycINFO were searched for studies between January 1, 2018, and April 29, 2025. Two reviewers independently screened records with third-party adjudication. Eligible studies included women with multiple sclerosis (peri-, menopausal, or postmenopausal) and examined menopause-related outcomes. Data were synthesized descriptively across four domains: symptomatology, disease course, biological mechanisms, and quantitative patient perspectives. Of 7862 records, 19 studies were included, of which 18 were observational (cross-sectional, retrospective, longitudinal) and one a feasibility trial of menopausal hormone therapy. Menopause definitions varied (≥ 12 months amenorrhea, self-reported, biological, or analytic/time-varying). Most participants had relapsing-remitting multiple sclerosis with mild to moderate disability. Relapse activity declined after menopause, whereas indices of neurodegeneration and functional decline worsened. Symptoms often intensified and overlapped with aging. No studies captured patient perspectives using qualitative or mixed-method designs and relied solely on patient-reported outcomes. Evidence suggests menopause may accelerate multiple sclerosis progression, with reduced inflammation but greater neurodegeneration and symptom burden. Research is constrained by heterogeneity in accounting for age, inconsistent menopause definitions, and lack of qualitative studies. Clinicians should recognize overlapping menopausal and multiple sclerosis symptoms to inform individualized care. Future priorities include standardized menopause definitions and age-specific analytic frameworks in future mechanistic and qualitative MS research.

Abbreviations

CIS clinically isolated syndrome

EDDS Expanded Disability Status Scale
FMP final menstrual period
HRT hormone replacement therapy

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MRI	magnetic resonance imaging
MS	multiple sclerosis
MSFC	Multiple Sclerosis Functional Composite
PPMS	primary progressive multiple sclerosis
PRISMA-ScR	Preferred Reporting Items for Systematic Reviews and Meta-Analysis, Scoping Review
PROs	patient-reported outcomes
QOL	quality of life
RRMS	relapse-remitting MS
sNfL	serum neurofilament light chain
SPMS	secondary progressive multiple sclerosis

1. Introduction

Multiple sclerosis (MS) is a chronic, immune-mediated, neurodegenerative disease of the central nervous system that affects approximately one million adults in the United States (U.S), with women comprising nearly two-thirds of cases [1,2]. Although MS typically begins in early adulthood, most women live with the disease for decades and inevitably experience menopause during its course. An estimated one-third of women with MS are currently peri- or postmenopausal [3,4], a proportion expected to grow as the MS population continues to age. Menopause is characterized by a decline in estrogen and other hormonal changes that affect immune regulation, vascular health, and neurological function [5,6]. Importantly, MS severity and progression are strongly influenced by chronological age, independent of disease duration, with advancing age associated with reduced inflammatory activity, but greater neurodegeneration and disability accumulation [7,8]. Because the menopausal transition typically occurs during midlife, a period when MS often shifts from a relapsing to a more progressive disease course, disentangling the effects of reproductive aging from those of chronological aging is methodologically challenging. The intersection of MS-related neuroinflammation, reproductive aging, and chronological aging raises important but insufficiently studied questions about how these processes may interact or overlap. Despite its relevance, menopause remains insufficiently addressed in MS research and clinical guidelines [9].

Existing studies examined menopause in relation to patient-reported, clinical, and biological outcomes, yet findings remain inconsistent. Some studies suggest that disability progression accelerates following menopause [3,10,11], but others report no significant change [4,12]. A subset of studies identify menopause as a potential inflection point for neuronal injury, reflected in worsening Multiple Sclerosis Functional Composite (MSFC) scores and elevated serum neurofilament light chain (sNfL) concentrations [7,11]; however, others observe no postmenopausal symptom worsening or associations with progression [13,14]. Proposed mechanisms include the loss of neuroprotective estrogen effects, age-related immunosenescence, and cumulative neurodegeneration [5,6,8,9].

Although the literature examining biological and clinical correlates of menopause in MS is expanding, far fewer studies have explored how women experience this transition in daily life. Only one study examined the patient perspectives of menopausal women with MS [15], and no reviews have synthesized these perspectives. Prior syntheses focused narrowly on topics such as hormone replacement therapy (HRT) or reproductive history [3,5,16], without encompassing broader health experiences. These gaps highlight the need for a scoping review to map how menopause has been studied in women with MS across clinical, biological, and experiential domains. Scoping reviews chart the extent, range, and nature of existing evidence, identify conceptual and methodological gaps, and inform future systematic or mechanistic research [17]. This review sought to map and synthesize evidence on menopause and MS and explored two main questions: (1) How does menopause affect MS-related symptoms, disease course, and mechanisms? and (2) To what extent have qualitative or mixed-methods studies examined quantitative patient perspectives of women with MS during menopause?

2. Methods

This scoping review followed the PRISMA-ScR guidelines [18] (Supplementary file A). It was guided by the Population, Concept, Context framework and the Joanna Briggs Institute methodology for scoping reviews [19]. The protocol was preregistered on OSF (ID: DOI [10.17605/OSF.IO/H8QBM](https://doi.org/10.17605/OSF.IO/H8QBM)).

2.1. Identification of relevant literature

Comprehensive searches were conducted in six databases (PubMed/MEDLINE, Embase, Web of Science, Scopus, CINAHL, and PsycINFO). The search strategy, developed by a multidisciplinary team of neurologists, researchers, and women with MS, was implemented by two reviewers (DM & VF). Searches combined controlled vocabulary and free-text keywords for *multiple sclerosis*, *menopause*, *perimenopause*, and *postmenopause*, with related outcomes (Supplementary File B). Peer-reviewed articles published in English between January 1, 2018, and April 29, 2025, were included to map contemporary evidence on reproductive transitions in menopausal women with MS. This time frame captured research emerging after key foundational studies that first characterized menopausal transitions in MS [15,20–22]. While these earlier reports provided initial insights into symptom changes and hormonal influences, no reviews synthesized evidence across physiological, psychosocial, and experiential domains or incorporated post-2018 advances in diagnostics, disease-modifying therapies, and patient-centered outcomes.

2.2. Identifying relevant studies

Eligible studies included adult women (≥ 18 years) with diagnosed MS of any subtype (clinically isolated syndrome, radiologically isolated syndrome, relapsing-remitting MS [RRMS], primary progressive MS [PPMS], or secondary progressive MS [SPMS]), who were perimenopausal, menopausal, or postmenopausal. Studies were included if they examined at least one menopause-related concept, including (1) physiological, psychological, or neurodegenerative changes such as fatigue, cognition, biomarkers, disability progression, or quality of life (QOL), and/or (2) experiential aspects of menopause (e.g., symptom perceptions, coping, or healthcare interactions). Eligible designs encompassed quantitative, qualitative, and mixed-methods observational formats. At least one menopause-specific variable or measure (e.g., hormonal or immune markers, relapse rate, Expanded Disability Status Scale [EDSS], or a qualitative construct) was required.

Exclusion criteria were: (1) animal studies, (2) male-only samples, (3) premenopausal women only, (4) menopause without MS, (5) MS without menopause as an explicit focus, or (6) intervention trials where menopause-related data could not be disaggregated. Non-peer-reviewed materials and non-English publications without translation were excluded.

2.3. Study selection

Titles and abstracts were screened independently by two reviewers (DM & VF) in Covidence, with conflicts resolved by a third review (RM). The same process was applied to full-text review.

2.4. Data extraction

Data were extracted independently by at least two reviewers (SB, CR, VF, AS, JH, DM, NB, and YH), with adjudication by a third (RM) when discrepancies occurred. A structured template guided charting of study features, including identifiers, country, design, sample, menopausal definition, outcomes, and key findings (Supplementary File C). In addition, we mapped how studies considered chronological (e.g., descriptive reporting, age-restricted or age-matched designs,

multivariable adjustment, or longitudinal age-adjusted modeling), with further categorization based on whether menopause-related associations were reported and whether such associations persisted after accounting for chronological age and/or disease duration or were mixed or outcome-specific.

2.5. Synthesis and presentation of results

Data were synthesized descriptively and narratively. Quantitative data were summarized as frequencies, proportions, or ranges, and qualitative observations were organized thematically. Studies were grouped into four domains: (1) symptomatology, (2) disease course and activity, (3) physiological and biological mechanisms, and (4) quantitative patient perspectives. No formal quality appraisal was conducted, consistent with scoping review methodology [23].

3. Results

3.1. Results of search

Database searches across platforms yielded 7862 records. Following title, abstract, and full-text screening, 19 were included (Fig. 1).

3.2. Study characteristics

Nineteen studies published between 2018 and 2025 were mapped (Table 1). The evidence was dominated by observational designs ($n = 18$, 94.7%) [4,7,8,10,11,14,24–35]: cross-sectional surveys ($n = 6$, 32%) [8,26,28,29,31,32], retrospective or case-control studies ($n = 4$, 21%) [4,10,27,34], and nine (47%) prospective or longitudinal cohorts [7,11,14,24,25,30,31,33,35]. One Phase Ib/IIa randomized trial tested menopausal hormone therapy [36]. Studies were frequently conducted in the U.S and Spain.

Across the 19 included studies, approaches to handling chronological age varied substantially and clustered into several methodological strategies. Six studies relied primarily on descriptive age reporting or age-restricted samples without analytic adjustment ($n = 6$, 31.6%) [26–30,32]. Four studies used design-based controls with age-matched cohorts or controls ($n = 4$, 21.1%) [31,34–36]. Seven studies implemented statistical adjustment for age using multivariable regression, Cox survival, or longitudinal mixed-effects models ($n = 7$, 36.8%) [4,8,10,14,24,25,33], and two longitudinal studies applied age-adjusted segmented mixed-effects models to examine within-person inflection points at menopause onset with functional and biomarker outcomes ($n = 2$, 10.5%) [7,11].

Definitions of menopause varied widely. Three categories emerged: (1) Chronological definitions (≥ 12 months of amenorrhea following the final menstrual period [FMP]) [10,27,28,35], (2) Self-reported or biologically informed definitions based on cessation of menses [30] or post-FMP timing [29], and (3) Analytic definitions modeling menopause as a time-varying covariate or reproductive-stage category [4,7,11,24,33,34]. Several studies included surgical menopause following oophorectomy or gonadotoxic therapy [4,7,14,27,33,35], whereas others restricted to natural menopause [10].

3.3. Study populations

Samples ranged between 59 and 1117 women (median = 127), and participant ages ranged between 18 and 81 years. Age at menopause ranged between 30 and 60 years. Most samples were primarily women with RRMS [7,8,10,24,27,29,31,36]. Across reporting studies, disability levels were mild to moderate: the lowest median baseline EDSS was 2.0 [24], the most common median was 2.5 [4,7], and the highest mean was 3.4 [8]. Reported EDSS values at menopause ranged between 1.4 and 3.4. Disability data were not consistently reported in six studies [25,26,28,30–32], and only three studies reported race or ethnicity

[7,29,36]. Six studies included women with surgical or therapy-induced menopause [4,7,14,27,33,35], limiting comparisons with natural menopause, whereas one study explicitly excluded such participants [10].

3.4. Study outcomes

Nine studies (47%) examined symptomatology including fatigue, mood, cognition, vasomotor symptoms, bladder issues, QOL, and sleep disruption (Table 2) [7,25,26,28–31,35,36] and frequently reported menopause-associated symptom changes, although most findings were derived from studies relying on descriptive age reporting or design-based age control. Twelve studies (63%) focused on disease course and activity including relapse rate, disability progression, and functional decline (Table 3) [4,7,8,10,11,14,24,25,27,33–35]. Within this domain, studies that adjusted for chronological age and/or disease duration more often reported no independent association between menopause and disability trajectories, whereas menopause-associated effects were more commonly observed in studies using functional or biomarker outcomes. Seven studies (37%) explored physiological and biological mechanisms, such as hormonal changes, neurodegenerations, and MRI indicators in relation to menopause and MS (Table 4) [7,8,11,25,27,30,35], with several reporting menopause-associated neurodegenerative changes even after accounting for age. Notably, none of the studies employed qualitative or mixed-methods approaches designs. Instead, five studies (26%) relied exclusively on quantitative patient-reported outcomes (PROs) for symptoms and QOL [26,28,29,31,32].

3.5. Study concepts

The included studies mapped overlapping domains at the intersection of menopause and MS disease activity. Several studies examined both disability progression and neurodegenerative markers [8,10,25,30,35], or linked functional assessments with neuronal injury biomarkers [7,11]. Some studies focused on single domains, such as disability [14,24], or symptom-symptom patterns [29]. Those addressing the patient perspective of menopausal women with MS did so through quantitative survey instruments assessing symptom attribution and QOL [26,28,31,32]. No studies captured quantitative patient perspectives of menopause in MS directly through qualitative inquiry.

Additional concepts emerged around reproductive history, hormonal and treatment variables, and lifestyle factors. These included the role of parity and pregnancy in menopause and MS [4,10,32,34], and treatment considerations, such as disease-modifying therapy exposure as a covariate in studies evaluating hormonal therapy [36], and patient-reported treatment decisions such as breastfeeding cessation due to medication [32]. Smoking was linked with greater disability progression [10], and HRT use correlated with higher physical activity [26]. Some studies noted diagnostic time effects, such as longer intervals from symptom onset to MS diagnosis among postmenopausal women [33], and associations between premature menopause and earlier progression to SPMS [34].

4. Discussion

This scoping review addressed two key questions: (1) How does menopause affect MS-related symptoms, disease course, and mechanisms? and (2) To what extent have qualitative or mixed-methods studies examined the quantitative patient perspectives of women with MS during menopause? The evidence, derived largely from quantitative studies, indicates that menopause may mark an inflection point for functional decline within the MS trajectory; however, its association with broader disability progression remains uncertain. Although the second question sought to synthesize qualitative or mixed-methods evidence on patient perspective, specifically lived experience, recent literature provided little to address it. No MS studies were designed to

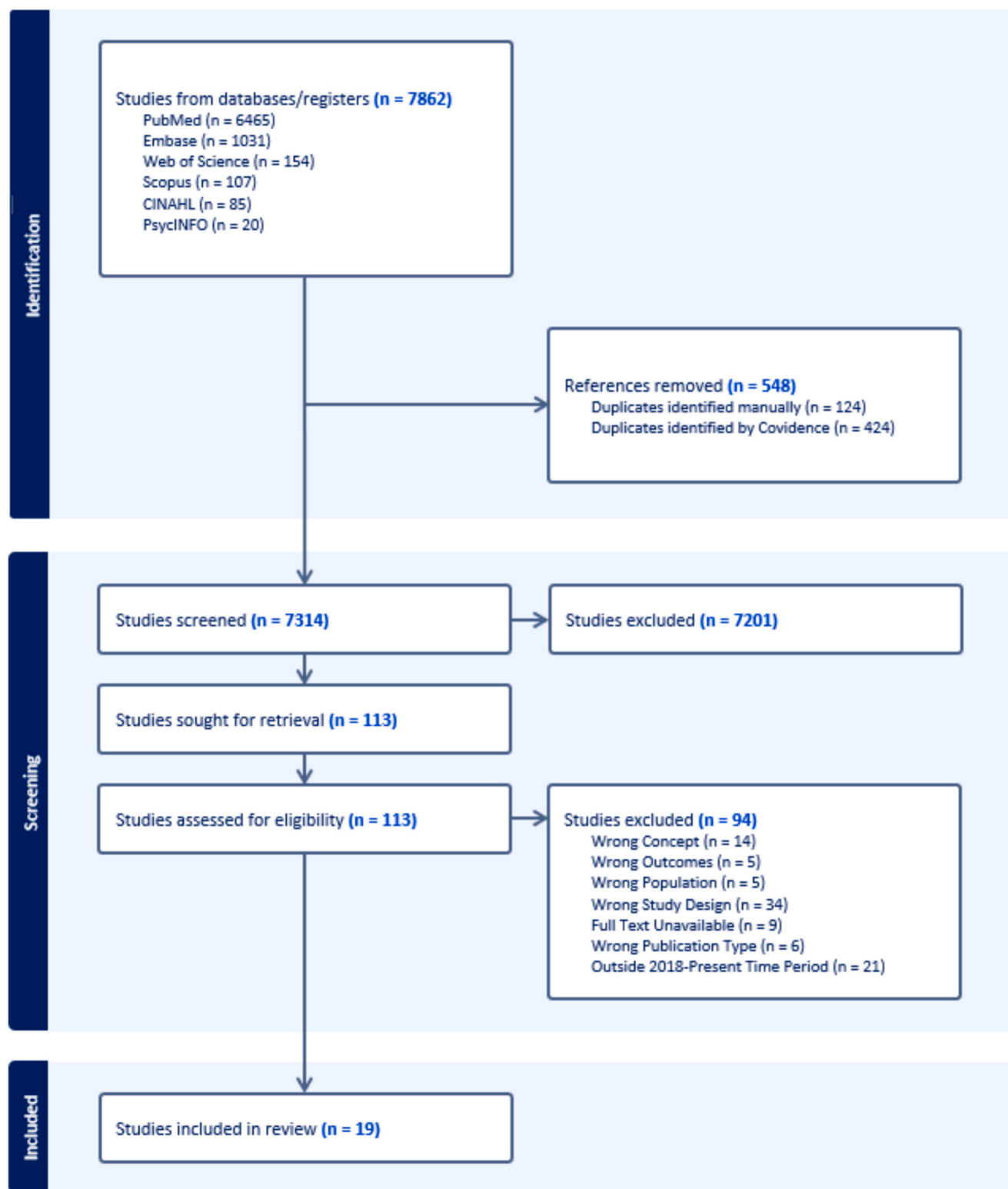


Fig. 1. PRISMA-ScR Flow Diagram of Study Selection

Flow diagram depicting the identification, screening, and inclusion process for studies examining menopause in women with multiple sclerosis. Database searches across six platforms yielded 7862 records. After removal of 548 duplicates, 7314 records were screened, with 113 full texts assessed for eligibility. Nineteen studies met inclusion criteria and were included in the review.

Abbreviations: MS, multiple sclerosis; PRISMA-ScR, Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews.

Table 1
Characteristics of included studies and their participants.

Study	Country	Study Design	Sample Size (N)	Mean Age (yrs $\pm$ SD)	Race/Ethnicity	MS Type (n)	Disease Duration (mean yrs)	Approach to Chronological Age*	Menopause Definition	Aim/Purpose
Baroncini et al., 2019	Italy	Retrospective cohort	148 WwMS	At menopause: 50.3 $\pm$ 3.8	NR	Primarily RRMS (5% SPMS at start)	Since menopause: 14.9 $\pm$ 8.1	Age-adjusted multivariable model interaction analysis	FMP followed by 12 consecutive months of amenorrhea	To understand the impact of natural menopause on the course of MS, investigating inflammatory and progressive aspects of MS
Bove et al., 2022	United States	RCT (Phase Ib/IIa, double-blind)	24 enrolled, 21 completed	51.2 $\pm$ 3.6 total	88% White 4% Black, 4% NH or other PI, 4% NR	22 RRMS; 2 SPMS	Median = 10	Age-restricted cohort with age-matched control design	Perimenopause: STRAW+10 criteria (amenorrhea $\geq$ 6 months, or irregular cycles with symptoms, or LMP within 2 years)	Evaluate feasibility, tolerability and symptom response of Duavee® in MW
Bridge et al., 2024	Australia	Prospective cohort	1117 in final analysis	Median at menopause 48.8 (IQR 44.7–52.0)	NR	CIS & relapse onset MS	NR	Age-adjusted multivariable Cox model analysis	Treated as time-varying covariate	To assess whether the onset of menopause influences risk of MS disability progression
Ianniello et al., 2024	Italy	Prospective cohort	21 completed both timepoints	At baseline Menop+: 51.1; Menop-: 50.4	NR	Implied RRMS or similar relapse onset MS	Menop+: 18.4; Menop-: 15.4	Age-restricted sample with descriptive reporting and age-adjusted multivariable regression analysis	Not defined	To assess whether menopause is a critical phase for disability progression and brain atrophy in WwMS, considering lifetime estrogen exposure
Johnson et al., 2025	United States	Cross-sectional survey	380 WwMS	Total: 55 $\pm$ 9 At menopause: 50 $\pm$ 4	NR	Subtypes NR	At MS diagnosis: 37 $\pm$ 9	Descriptive age reporting only	Not defined	To characterize the impact of menopause on disease symptoms, physical functions, and IADLs in WwMS
Ladeira et al., 2018	Portugal	Retrospective cohort	37 WwMS	At menopause: 50	NR	28 RRMS; 2 PPMS; 7 SPMS	14.0 $\pm$ 8.64	Age-restricted cohort with descriptive age reporting	FMP + 12 months amenorrhea; surgical: date of procedure	To evaluate impact of menopause in MS course, including disease activity and disability progression
Lorefice et al., 2023	Italy	Cross-sectional survey	147: 84 MW, 63 non-MW	MW: 52.6 $\pm$ 3.2; Non-MW: 46.1 $\pm$ 3.1)	NR	RRMS	MW: 18.2 $\pm$ 8.7; Non-MW: 15.5 $\pm$ 6.3	Age-restricted sample with descriptive reporting and age-adjusted multivariable regression analysis	FMP + 12 months in association of neurovegetative menopausal symptoms	To evaluate possible impact of menopausal transition on clinical activity and MRI outcomes
Madueno et al., 2023	Spain	Cross-sectional survey	106 responses	At menopause: 49.4	NR	NR	NR	Descriptive age reporting only	12 months amenorrhea	To determine the age of onset of

(continued on next page)

Table 1 (continued)

Study	Country	Study Design	Sample Size (N)	Mean Age (yrs $\pm$ SD)	Race/Ethnicity	MS Type (n)	Disease Duration (mean yrs)	Approach to Chronological Age*	Menopause Definition	Aim/Purpose
Morales-Rodriguez et al., 2023	United States	Cross-sectional survey	59 WwMS	Total: 51.8 $\pm$ 3.4	92% NH White, 3% H/L, 3% Black, 2% PI	94.9% RRMS	11.3 $\pm$ 7.6	Descriptive age reporting only	Amenorrhea for $\geq$ 6 months or LMP within 2 years; Post menopause: 12 months amenorrhea	menopause in patients diagnosed with MS and its impact on mood, cognitive and urinary symptoms To explore associations between mental health, sleep, and QOL metrics, and VMSs in ambulatory MW
Nylander et al., 2023	United States	Prospective cohort	177	Median age at menopause: 52 (IQR = 5)	NR	NR	NR	Age-restricted cohort with descriptive reporting	Natural menopause defined by participant-reported cessation of menses	To analyze change in MRI volumetric measures and cognitive performance after menopause in a longitudinal cohort of WwMS
Oreja-Guevara et al., 2024	Spain	Prospective cohort	112 MS; 112 non-MS	MS: 53	NR	RRMS	NR	Age-restricted cohort with age-matched control	N/A (inclusion criteria required having been in menopause for up to 5 years)	To understand impact of menopause on QOL in MS patients for optimizing management and care strategies
Otero-Romero et al., 2022	Spain	Prospective cohort	496 (74 became MW)	At menopause: 47.2 $\pm$ 5.6	NR	CIS & Relapse onset MS	MW: 13.3 $\pm$ 4.4; Non-MW: 9.1 $\pm$ 5.4	Age at disease onset accounted for in matched longitudinal analysis	Natural menopause: LMP + 12 months amenorrhea; surgical menopause included	To evaluate effect of menopause on disability accumulation in women followed from onset of CIS
Perillan et al., 2024	Spain	Cross-sectional survey	214 WwMS	At survey end: 41.8, At diagnosis: 32.1; At menopause: 47.5	NR	NR	9.8	Descriptive age reporting only	NR	To explore the reproductive factors in an MS-diagnosed population and to identify ways to support patients and their decision-making process
Silverman et al., 2023	United States	Prospective cohort	186 WwMS	Median at natural menopause: 52 (IQR = 5)	NR	NR	Median = 15 (IQR = 13)	Age included as covariate in age-adjusted segmented linear mixed-effects models	NR	To evaluate the effect of menopause on functional outcomes and disease biomarkers in a longitudinal cohort of WwMS
Silverman et al., 2025	United States	Prospective cohort	184 Menop+	63 $\pm$ 8	83% NH White	69% RRMS 31% Other	Median = 24	Age included as covariate in age-adjusted segmented linear mixed-effects models	12 months amenorrhea	To assess the trajectory of functional outcomes and disease biomarkers in

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Table 1 (continued)

Study	Country	Study Design	Sample Size (N)	Mean Age (yrs $\pm$ SD)	Race/Ethnicity	MS Type (n)	Disease Duration (mean yrs)	Approach to Chronological Age*	Menopause Definition	Aim/Purpose
Simonsen et al., 2023	Norway	Prospective, Retrospective cohort	559 became MW	59.7 $\pm$ 7.9	NR	NR	NR (median EDSS at menopause = 2.5)	(including age-adjusted sNfL) Age-adjusted multivariable regression analysis	NR	WwMS before and after menopause To determine the association between menopause and MS onset, diagnosis and disease course
Simonsen et al., 2025	Norway	Retrospective cohort	559 WwMS	W = 60.6 $\pm$ 7.9	NR	RRMS; SPMS; PPMS	18.3 $\pm$ 8.5	Age-adjusted linear mixed-effects longitudinal analysis	12 months amenorrhea	To determine the association between menopause and MS disease course
Zeydan et al., 2020	United States	Cross-sectional, case-control	137 Menop+	51.0 $\pm$ 3.0	NR	Women: 92% RRMS 8% SPMS	Women: 21.0 $\pm$ 8.6	Age-matched, case-control design with age included in multivariable regression analysis	12 months amenorrhea or no menses due to surgery/therapy	To investigate if reproductive history including onset of menarche, number of pregnancies, age/type of menopause are associated with an earlier onset of the progressive phase in WwMS
Zeydan et al., 2025	United States	Prospective cohort	173, 100 WwMS	NR	NR	69% RRMS 32% PPMS & SPMS	Women: 9.2	Age- and sex-matched controls with age included in multivariable mixed-effects models	12 months amenorrhea without any intervention/lack of menses after intervention	Investigate the impact of sex and menopause status on spinal cord atrophy

Notes: NR: not reported; MS: multiple sclerosis; WwMS: women with multiple sclerosis; PwMS: people with multiple sclerosis; MW: menopausal women; non-MW: non-menopausal women; Menop+: postmenopausal women; Menop-: non-postmenopausal women; NH White: non-Hispanic White; NH or other PI: Native Hawaiian or other Pacific Islander; H/L: Hispanic/Latino; RRMS: relapsing-remitting multiple sclerosis; SPMS: secondary progressive multiple sclerosis; PPMS: primary progressive multiple sclerosis; CIS: clinically isolated syndrome; RCT: randomized controlled trial; FMP: final menstrual period; LMP: last menstrual period; IQR: interquartile range; yrs.: years; SD: standard deviation; sNfL: serum neurofilament light chain; QOL: quality of life; IADLs: instrumental activities of daily living; MRI: magnetic resonance imaging; HRT: hormone replacement therapy; VMS: vasomotor symptoms; NR: not reported; STRAW+10: Stages of Reproductive Aging Workshop +10 criteria. *Categories reflect increasing levels of methodological control for chronological age, ranging from descriptive reporting to longitudinal and segmented age-adjusted modeling; labels are based on author-reported analytic approaches and do not imply adequacy of adjustment.

capture perspectives of menopausal women with MS directly. Most studies focused on symptomatology and disease activity, and none incorporated patient perspectives. This imbalance highlights a critical gap, as despite substantial advances in biological research, psychosocial and experiential dimensions of menopause in MS remain markedly underexplored relative to the number of women with MS who experience this transition.

Variability in findings across studies appears closely linked to how chronological age and disease duration were handled methodologically and analytically. Studies relying on descriptive age reporting or design-based age control more frequently reported menopause-associated changes in symptoms or disease activity, whereas studies incorporating multivariable adjustment or longitudinal age-adjusted modeling more often reported attenuation or loss of menopause-related effects on disability trajectories. In contrast, studies using sensitive functional and biomarker outcomes within age-adjusted longitudinal frameworks

identified menopause as a potential inflection point independent of chronological aging. These patterns suggest that heterogeneity in age-handling approaches contributes to inconsistencies in the literature [4,7,10,11,14], and that observed menopause-related effects may reflect differences in analytic sensitivity rather than true biological inconsistency.

An additional source of heterogeneity across studies was the lack of standardized definitions and staging of menopause. Studies varied widely in how menopausal status was operationalized, including self-reported final menstrual period, age-based proxies, symptom-based classification, or reproductive history, limiting comparability across outcomes. This methodological variability constrains causal inference and reduces statistical robustness, particularly when attempting to isolate menopause-specific effects from chronological aging and disease duration. For instance, studies using age-based or self-reported menopausal status reported inconsistent associations between menopause and

Table 2
Studies exploring symptomology outcomes.

Study	Symptom(s) of Interest	Outcome Measure(s)	Approach to Chronological Age	Main Findings
Studies reporting menopause-associated symptom changes				
Bove et al., 2022	VMS, sleep quality, QOL, cognition and physical function, neuropsychological impairment	HFRDIS, ISI, PSQI, MSQOL54, SDMT, LNS, T25FW, MSNQ, MSRS	Age-matched design	Treatment (Duavee®) improved menopausal symptoms (HFRDIS, insomnia severity and sleep quality), and most measures of MS-related function and QOL (SDMT, MSNQ, MSQOL mental and physical
Johnson et al., 2025	VMS, sleep quality, cognition, urinary/fecal, fatigue, muscle weakness, and IADLs	Self-reported survey on MS symptoms, menopause symptoms, and changes in physical functions/IADLs	Descriptive age reporting only	94% experienced menopause symptoms (Hot flashes 73%, night sweats/sleep problems 63%). Menopause exacerbated MS symptoms: cognitive difficulty (66%), urinary incontinence (60%), and fatigue (51%), most common IADL to worsen was climbing stairs (50%)
Madueno et al., 2023	Mood, cognitive, and urinary	Self-reported online questionnaire	Descriptive age reporting only	Participants reported: hot flashes (54%), urinary issues (78%), mood changes (51%), anxiety (48%), apathy (21%); cognitive decline (50%)
Morales-Rodriguez et al., 2023	Mental health, sleep, VMS, QOL, and physical function	SF-36, PSQI, ISI, CES—D, HFRDIS, T25FW, SDMT	Descriptive age reporting only	Mental health moderately correlated with better sleep and mood; relationship between VMS frequency and general mental health was mediated by PSQI; worse sleep was correlated with higher VMS
Oreja-Guevara et al., 2024	QOL, VMS, mood	Cervantes-SF Scale	Age-matched design	Most frequent menopausal symptoms: urination (86%), skin changes (74%), memory loss (71%), back pain (70%), weight gain (50%), hot flushes (37%), night sweats (31%), and increased facial hair (25%)
Silverman et al., 2025	Cognition and physical function	PASAT, 9HPT, T25FW, MSSS	Age-adjusted segmented mixed-effects models	Significant worsening in T25W ($p = 0.0043$); nonsignificant trend in PASAT ($p = 0.45$) and 9HPT ($p = 0.09$), no significant change in MSSS
Zeydan et al., 2025	Cognition and physical function	PASAT, 9HPT, T25FW	Age- and sex-matched design with age-adjusted models	Smaller upper spinal cord area correlated with worse 9HPT scores ($p = 0.005$), and primary driven by postmenopausal women ($p = 0.014$); No other significant subgroup analyses or correlations with PASAT or T25FW
Studies reporting no or limited menopause-associated symptom changes				
Ianniello et al., 2024	Cognition function	PASAT, SDMT	Age-restricted sample; age adjusted in multivariable models	Menop- had lower PASAT ($p = 0.004$) and SDMT ($p = 0.029$) compared to Menop+; no significant changes in neuropsychological tests
Nylander et al., 2023	Cognition	PASAT, SDMT	Age-restricted sample	No significant changes observed in PASAT and SDMT post-menopause

Notes: VMS: vasomotor symptoms; QOL: quality of life; HFRDIS: Hot Flash Related Diary Weekly Interference Scale; ISI: Insomnia Severity Index; PSQI: Pittsburgh Sleep Quality Index; MSQOL54: MS Quality of Life 54; SDMT: Symbol Digit Modalities Test; 9HPT: 9-Hole Peg Test; LNS: Letter Number Sequencing; T25FW: Timed 25-Foot Walk; PASAT: Paced Auditory Serial Addition Test; MSNQ: MS Neuropsychological Questionnaire; MSRS: MS Rating Scale; Menop+: postmenopausal women; Menop-: non-postmenopausal women; IADLs: instrumental activities of daily living; SF-36: 36-Item Short-Form Survey; CES—D: Center for Epidemiologist Studies – Depression Scale; Cervantes-SF: Cervantes Short-Form Scale; MSSS: MS Severity Scale. Studies are grouped by whether menopause-associated symptom changes were reported. Age-handling categories reflect author-reported analytic approaches and do not imply adequacy of adjustment.

disability or symptom trajectories [10,26,28], whereas studies employing longitudinal or biological definitions more consistently identified menopause as an inflection point for functional or biomarkers outcomes independent of age [7,11]. Thus, adoption of standardized reproductive aging frameworks (e.g., STRAW+10) in future MS research would enhance consistency and improve interpretability across studies, as well as strengthen the capacity to detect menopause-related biological and clinical effects.

We observed convergent patterns clarify mechanisms linking menopause to MS progression. Inflammatory activity, reflected by reduced relapse rates, consistently declined after menopause [4,8,10,27]. However, neurodegeneration and functional decline, including disability progression and brain and spinal cord atrophy, tended to accelerate during this same period [11,25,30,35]. These patterns suggest a decoupling of inflammatory and degenerative processes, similar to the broader transition observed in progressive MS [37]. Menopause may represent a biological and hormonal inflection point that accelerates this shift. Our synthesis describing increased sNfL levels, worsening MSFC scores, and heightened symptoms of fatigue, cognitive decline, urinary dysfunction, and musculoskeletal weakness supports this interpretation [7,11,26,28].

Across the nine studies examining symptomatology, menopause emerged as a multidimensional amplifier of symptom burden in women with MS. Menopausal and MS-related symptoms frequently overlapped across fatigue, mood, cognition, vasomotor symptoms, and sleep

[26,28,29,31,36]. This convergence suggests shared neuroendocrine and neuroinflammatory pathways and complicates attribution of symptom changes solely to disease activity. For example, associations between sleep disturbance, mood, and QOL [29] imply hormonal fluctuations contribute to the emotional and cognitive domains commonly affected in MS. Studies linking higher overall symptom burden with poorer physical function highlight potential feedback loops between physiological stress, behavioral fatigue, and diminished mobility [26]. This overlap has critical implications, as menopause-related changes may obscure disease progression and hinder targeted management. However, few studies have developed conceptual frameworks or clinical markers distinguishing neuroendocrine from inflammatory drivers of symptom change. The resulting diagnostic ambiguity risks undertreatment of menopause-specific concerns or inappropriate escalation of MS therapies.

Menopause consistently marked a shift in the biological and clinical course of MS. Relapse rates declined [4,8,10,27], yet disability accumulation often accelerated, suggesting a progression toward neurodegeneration [7,10,11,30]. Longitudinal biomarker and imaging data support this interpretation, as postmenopausal women exhibited rising sNfL concentrations, worsening MSFC, and accelerated gray matter and spinal cord atrophy [7,11,24,35]. Notably, these changes persisted independent of age [30], indicating hormonal decline may act as a catalyst for degeneration. MRI studies demonstrated accelerated whole-brain atrophy independent of age and disease duration [25,30], and cervical

Table 3
Studies exploring disease course and activity outcomes.

Study	Purpose/Aim	Outcome Measure(s)	Approach to Chronological Age	Main Findings
Studies reporting menopause-associated changes in disease course or activity				
Baroncini et al., 2019	Understand impact of natural menopause on inflammatory and MS progression	EDSS; ARR	Age adjusted in multivariable models	ARR ↓ postmenopause (0.21 to 0.13 ($p = 0.005$)); EDSS ↑ 0.4 to 0.2 ($p = 0.014$) → suggests potential transition to more progressive course
Ladeira et al., 2018	Evaluate impact of menopausal transition on MS course	ARR; EDSS pts./year; EDSS progression events (6-month confirmed EDSS progression ≥ 0.5 pts)	Age-restricted cohort with descriptive age reporting	ARR ↓: 0.37 ± 0.35 (pre) → 0.08 ± 0.18 (post), $p < 0.001$; EDSS rate: 0.13 ± 0.24 (pre) → 0.13 ± 0.18 (post), $p = 0.935$; EDSS events: 37.8% (pre) → 48.6% (post), $p = 0.424$; Trends consistent without DMT changes or comorbidities
Lorefice et al., 2023	Investigate role of menopause in influencing MS from clinical and neuroradiological perspectives	ARR	Age-restricted sample with age-adjusted multivariable models	MW had ↓ disease activity vs. non-MW (↓ ARR (0.29 vs. 0.52; $p < 0.01$), independent of age
Silverman et al., 2023	Evaluate effect of menopause on functional outcomes and disease biomarkers WwMS	MSFC	Age-adjusted segmented mixed-effects models	After menopause → inflection point in functional decline (MSFC ↑ slope: 0.074; $p = 0.014$); → suggests functional loss
Silverman et al., 2025	Assess functional outcomes and disease biomarkers before and after menopause; evaluate menopause and CNS injury	MSFC (25FWT, 9HPT, PASAT); EDSS	Age-adjusted segmented mixed-effects models	↓ MSFC after menopause ($p = 0.0163$); ↑ EDSS score more rapidly before menopause, with a slight deceleration in worsening after menopause ($p = 0.0200$)
Zeydan et al., 2025	Assess how sex and menopause affect spinal cord atrophy in PwMS, focusing on upper cervical SC as a biomarker of progressive MS	Clinical: MSFC (25FWT, 9HPT, PASAT), EDSS (≥ 6), MS type/duration, menopause status/age	Age- and sex-matched design with age-adjusted models	↓ MSFC scores (-0.26 vs. 0.28 ; $p = 0.012$) → consistent with menopause-related inflection in disease progression
Studies reporting no independent association after age and/or disease duration adjustment				
Bridge et al., 2024	Assess whether onset of menopause influences risk of disability progression	CDP; conversion to SPMS	Age adjusted in multivariable models	Menopause is not significantly independent predictor of CDP or SPMS when adjusted for confounders (aHR 1.11, $p = 0.5$, aHR 1.09, $p = 0.7$)
Otero-Romero et al., 2022	Evaluate the effect of menopause on disability accumulation / prognosis in WwMS and CIS followed from MS onset	EDSS trajectories	Age-adjusted longitudinal models	When age and disease duration were controlled in matched analysis, menopause did not independently impact disability progression ($p = 0.321$); no statistically significant inflection point in EDSS progression was found before vs. after menopause
Simonsen et al., 2025	Determine the association between menopause and MS disease course	EDSS and ARR analyzed ± 5 yrs. around menopause	Age-adjusted longitudinal models	ARR significantly ↓ postmenopause; EDSS progression showed no significant change after menopause. WwMS' EDSS progressed slower than men with MS after menopause ($p = 0.032$)
Studies reporting mixed or outcome-specific associations				
Ianniello et al., 2024	Assess whether menopause affects disability progression and brain atrophy	EDSS; cognition (SDMT, PASAT)	Age-restricted sample with age-adjusted multivariable models	No differences in EDSS or cognitive tests
Simonsen et al., 2023	Determine the association between menopause and MS onset, diagnosis, and disease course	Age at menopause; time from MS onset to diagnosis; associations (age of menopause and age of MS onset; age of menopause and age of MS diagnosis); ARR; EDSS	Age adjusted in multivariable models	No association was found between age of menopause and age of MS onset. Time from onset to diagnosis was significantly longer in patients diagnosed with MS after menopause (8.8 years vs 5.5 years, $p < 0.001$)
Zeydan et al., 2020	Examine whether premature menopause and/or low parity results in earlier onset of progressive MS, using a combined survey and case-control design	Reproductive factors: menarche age, parity, menopause type/age (≤ 45 vs. > 45); MS outcomes: age at RRMS onset, age at progression, EDSS 6, time to progression	Age-matched design with age-adjusted models	WwMS had ↓ pregnancies ($p < 0.001$) and ↑ non-natural menopause (40.7% vs. 30.1%; $p = 0.030$); natural menopause age was similar (50 vs. 51 yrs.; $p = 0.476$), while non-natural menopause occurred later in MS (44.5 vs. 39 yrs.; $p = 0.009$), with reproductive factors associated with the timing of progressive MS onset, but menopause itself did not uniformly alter disease course metrics.

Notes: MS: multiple sclerosis; ARR: annualized relapse rate; CDP: confirmed disability progression; SPMS: secondary progressive multiple sclerosis; EDSS: expanded disability status scale; aHR: adjusted Hazard Ratio; pts.: points; MSFC: multiple sclerosis functional composite; 25FWT: 25-ft walk test; 9HPT: 9-hole peg test; PASAT: paced auditory serial addition test; SDMT: symbol digit modalities test; WwMS: women with multiple sclerosis; MW: menopausal women; non-MW: non-menopausal women; SC: spinal cord; PwMS: person with MS. Studies are grouped by direction and persistence of menopause-related associations after accounting for age and/or disease duration; grouping does not imply study quality.

spinal cord atrophy progressed more steeply after menopause [35]. Elevated FSH and reduced estrogen were associated with greater brain atrophy and cognitive decline, suggesting that dysregulated neuroendocrine signaling accelerates neuronal loss [25]. Together, these observations suggest that menopause may accelerate the transition from inflammatory to neurodegenerative dominance, likely arising from the

combined effects of estrogen loss, immunosenescence, and impaired neuroprotection. Estrogen exerts anti-inflammatory and neurotrophic effects in both central and peripheral tissues, and its decline increases susceptibility to axonal injury. Earlier menarche, premature menopause, and lower parity were linked with earlier progression and shorter RRMS [34]. Concurrent immune exhaustion may limit repair capacity and

Table 4
Studies exploring physiological and biological outcomes.

Study	Marker Studied	Measure/ Method	Approach to Chronological Age	Main Findings
Studies reporting menopause-associated biological or neurodegenerative changes				
Ianniello et al., 2024	Brain Atrophy, T2-Lesion Load, Hormones	MRI (PBVC, GM/ thalamic fraction, T2 lesion load), FSH levels	Age-restricted sample with age-adjusted multivariable models	Menop+ ↑ PBVC loss ($p = 0.029$) and ↑ FSH levels compared to Menop- → suggests menopause may accelerate brain atrophy
Lorefice et al., 2023	Brain Volume/ Atrophy	MRI (WB, WM, GM, and cGM)	Age-restricted sample with age-adjusted multivariable models	↓ MRI activity (13.1% vs. 20.6%; $p = 0.03$); but ↑ cGM atrophy (578.1 vs. 596.9 mL; $p < 0.01$); Menopausal status independently associated with ↓ disease activity ($p = 0.001$) and cGM loss ($p = 0.002$) → suggests menopause may selectively accelerate GM loss
Nylander et al., 2023	Brain Volume/ Atrophy	MRI (Rate of GM volume loss slope)	Age-restricted sample	Menop+ had ↑ GM atrophy ($p = 0.039$), independent of age, disease duration, and DMT; No changes in WB, or WM → suggests menopause has selective GM loss
Silverman et al., 2023	Neuronal Injury Biomarker	sNfL	Age-adjusted segmented mixed-effects models	↑ Neuronal injury (sNfL slope = 0.81; $p = 0.017$), providing objective biomarker evidence of menopause-associated neurodegeneration
Silverman et al., 2025	Neuronal Injury Biomarker, T2- Lesion Load	sNfL (age-adjusted and z-scored), T2 Lesion Volume	Age-adjusted segmented mixed-effects models	↑ sNfL after menopause ($p = 0.019$)
Zeydan et al., 2025	Spinal Cord Atrophy	UCCbrain (C1-C2) derived from brain MRI	Age- and sex-matched design with age-adjusted models	Menop+ had ↓ UCCbrain vs premenopausal women (49.4 vs. 52.9 mm ² ; $p < 0.001$), ↑ progressive MS common in Menop+ vs premenopausal women (45.6% vs. 7.0%; $p < 0.001$) → consistent with menopause contributing to spinal cord atrophy
Studies reporting no or limited menopause-associated biological changes				
Ladeira et al., 2018	T2 lesion volume	MRI	Age-restricted cohort with descriptive age reporting	↓ New T2 and gadolinium-enhancing lesions (non-significant) → suggests no disease progress after menopause

Notes: MRI: magnetic resonance imaging; PBVC: percent brain volume change; FSH: follicular stimulating hormone; Menop+: postmenopausal women; Menop-: non-postmenopausal women; WB: whole brain, WM: white matter; GM: gray matter; cGM: cortical gray matter; sNfL: serum neurofilament light chain; UCCbrain: upper cervical spinal cord area of brain. Studies are grouped by whether menopause-associated biological or neurodegenerative changes were reported. Findings reflect author-reported results and analytic approaches and do not imply causal inference or study quality.

exacerbate degeneration even without new lesions. These processes may explain continued progression despite fewer relapses.

Few studies distinguished between natural and induced menopause [7,27,34,35], despite emerging evidence that the abrupt estrogen withdrawal associated with surgical menopause may exert distinct neurodegenerative implications in MS [7]. In contrast, several studies focused exclusively on natural menopause to avoid this confounding and acknowledged the absence of induced menopause analyses as a limitation [4,8,10,14,36]. This distinction is clinically relevant because surgical menopause often occurs at a younger age than natural menopause and appears more prevalent among women with MS. For example, the median age of natural menopause was approximately 50 years compared with 45 years for surgical menopause [7], and non-natural menopause was significantly more common in women with MS (40.7%) than in healthy controls (30.1%) [34]. This is particularly relevant in MS, where neurodegeneration may be sensitive to both hormonal timing and rate of decline.

Contextual factors such as reproductive history, hormonal timing, and lifestyle also influence trajectories. Higher parity, a marker of estrogen exposure, was associated with delayed MS progression, whereas early menarche and premature menopause predicted earlier onset [34]. Evidence on behavioral modifiers is preliminary, as smoking was linked with worsened postmenopausal disability [10], and HRT use correlated with greater physical activity [26], suggesting interplay between behavioral and endocrine resilience. Menopause represents a vulnerable window for subtle neurodegeneration, thus relying on inflammatory markers could underestimate disease activity. Integrating hormonal status, reproductive history, and lifestyle factors into longitudinal monitoring may enable earlier identification of progression and tailored management strategies for women with MS during and after menopause.

Parallel evidence from non-MS populations corroborates these patterns. Menopause in the general population is associated with cortical thinning, reduced gray matter volume and cognitive slowing [38,39]. However, these effects appear amplified in MS, likely due to the additive impact of pre-existing demyelination and neuroinflammation. Thus, menopause represents not only a normative neuroendocrine milestone, but a synergistic stressor that accelerates pre-established CNS injury. Hormonal status may also shape diagnostic pathways, as women diagnosed after menopause experienced longer delays to diagnosis [33], suggesting that symptom overlap between menopause and MS may obscure recognition of disease onset in midlife. These observations indicate that estrogen decline functions both as a biological catalyst of neurodegeneration and as a contextual modifier of disease recognition and progression. Though this synthesis aligns with prior models of estrogen's neuroprotective role [5,6], evidence regarding its direct effect on disability accumulation remains inconclusive [12,16], and more studies integrating hormonal, neuroimaging, and immunological markers are needed to confirm this.

Since the completion of this review's search period, longitudinal evidence from the MS Base Registry indicated that menopause was not independently associated with confirmed disability progression or transition to SPMS after adjusting for age, disease duration, and treatment exposure [40]. This suggests that reproductive aging may interact with disease mechanisms and aging processes, but menopause itself may not represent a discrete inflection point for worsening disability.

No studies explicitly employed qualitative or mixed-methods designs to examine lived experience of menopausal women with MS. Instead, a

few studies quantified PROs without exploring perspectives or meaning through qualitative methodologies [26,28,29,31,32]. These surveys suggested that menopause may intensify physical, cognitive, and psychosocial challenges, yet 67% of women did not discuss these concerns with a healthcare provider [26]. Sleep disturbance was identified as a mediator linking vasomotor symptoms and mood [29], and urinary and cognitive complaints were often attributed to menopause rather than MS, though few women received targeted treatment [28]. Other studies reported mixed QOL outcomes with worse mood and aging scores, but somewhat improved vasomotor outcomes, and highlighted reproductive decisions, such as discontinuing breastfeeding due to medication concerns [31,32]. Although these PROs offer limited insight, they underscore a substantial gap in qualitative evidence regarding how women experience, interpret, and manage menopause in the context of MS. This absence constrains understanding of experiential processes, such as identity redefinition, coping strategies, and patient-provider communication, that influence treatment decision-making and symptom management.

Prior reviews of menopause and MS have focused largely on disease-related disability, symptom management, and pharmacologic or behavioral intervention for disease management [22,41–43], but none have incorporated lived experiences or psychosocial dimensions. This scoping review extends prior syntheses by mapping menopause as a potential inflection point in the MS trajectory and emphasizing the near-total absence of evidence on how women with MS experience this transition. Our synthesis demonstrates that menopause not only compounds existing MS symptom burden, but also intensifies diagnostic and therapeutic ambiguity, making it difficult for women and clinicians to disentangle hormonal from disease-related changes. Our results align and expand upon a broader shift in menopause research that increasingly values mixed-methods and qualitative inquiry to capture women's lived experiences, psychosocial adjustment, and care expectations in women without MS [44–46]. Extending this paradigm to women with MS is essential to bridge biological mechanisms with lived experience and inform more holistic menopause-specific MS care.

This review's strengths include comprehensive search coverage and inclusion of both clinical and experiential outcomes. Limitations reflect those of the underlying literature, as definitions of menopause varied, outcome measures were heterogeneous, and disability reporting was inconsistent. Few studies included diverse populations, and none provided in-depth qualitative data. Additional measurement gaps, such as non-standardized menopause staging, limited hormone assays, and inconsistent disability and MRI reporting, further complicate cross-study synthesis and causal inference. Additionally, one study published after our search period was not formally included [40]. Consistent with scoping review methodology [23], formal quality appraisal was not conducted; thus, results should be interpreted as mapping the breadth of available evidence rather than providing quantitative effect sizes.

5. Conclusion

Menopause represents a potential inflection point in MS disease expression and lived experience; thus, clinicians should monitor women with MS closely during the menopausal transition and attend to both inflammatory disease activity and subtle indicators of disability progression. Evidence remains limited by heterogeneity in accounting for age and inconsistent definitions of menopause, minimal use of sensitive hormonal or neuroimaging biomarkers, and scarce attention to modifiable lifestyle factors (e.g., exercise, diet, and other health-promoting behaviors). There is broad evidence for the beneficial impact of exercise on MS outcomes [47], and future studies may investigate whether acute and chronic exercise interventions could help women with MS manage symptom burden and potentially slow neurodegenerative changes in perimenopause or during menopause. Lifestyle changes integrated into menopausal MS care could support both biological and psychosocial resilience. Future research should prioritize longitudinal

and interventional designs with hormonal, lifestyle, and psychosocial measures to inform tailored therapeutic strategies.

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Contributors

Dawn Morgan contributed to conceptualization, investigation, data acquisition, review and editing, and project administration.

Victoria Aviado Flores contributed to conceptualization, methodology, investigation, data acquisition, data analysis and interpretation, resources, visualization, original draft preparation, and project administration.

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All authors saw and approved the final version and no other person made a substantial contribution to the paper.

Ethical statement

This study is a scoping review of published literature and did not involve human participants or animals. Ethical approval and informed consent were therefore not required. The review followed established methodological guidance (PRISMA-ScR and Joanna Briggs Institute) and was preregistered on the Open Science Framework (DOI: [10.17605/OSF.IO/H8QBM](https://doi.org/10.17605/OSF.IO/H8QBM)).

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Data availability statement

The data supporting the findings of this study are available from the

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References

- [1] F. Murgia, F. Giagnoni, L. Lorefice, P. Caria, T. Dettori, M.N. D'Alterio, et al., Sex Hormones as Key Modulators of the Immune Response in Multiple Sclerosis: A Review, *Biomedicines* 10 (12) (2022 Dec 1) 3107.
- [2] M.T. Wallin, W.J. Culpepper, J.D. Campbell, L.M. Nelson, A. Langer-Gould, R. A. Marrie, et al., The prevalence of MS in the United States: A population-based estimate using health claims data, *Neurology* 92 (10) (2019 Mar 5) e1029–e1040.
- [3] R. Bove, T. Chitnis, M. Houtchens, Menopause in multiple sclerosis: therapeutic considerations, *J. Neurol.* 261 (7) (2014 July) 1257–1268.
- [4] C.S. Simonsen, H.Ø. Flemmen, L. Broch, H. Myklebust, P. Berg-Hansen, C. Brunborg, et al., The influence of menopause on multiple sclerosis, *Eur. J. Neurol.* 32 (1) (2025 Jan) e16566.
- [5] F. Bridge, H. Butzkueven, A. Van der Walt, V.G. Jokubaitis, The impact of menopause on multiple sclerosis, *Autoimmun. Rev.* 22 (8) (2023 Aug) 103363.
- [6] M.S. Christianson, V.A. Mensah, W. Shen, Multiple sclerosis at menopause: Potential neuroprotective effects of estrogen, *Maturitas* 80 (2) (2015 Feb) 133–139.
- [7] H.E. Silverman, A. Bostrom, A.N. Nylander, A. Akula, A.A. Lazar, R. Gomez, et al., Association of Menopause with Functional Outcomes and Disease Biomarkers in Women with Multiple Sclerosis, *Neurology* 104 (2) (2025 Jan 28) e210228.
- [8] L. Lorefice, M.N. D'Alterio, D. Firinu, G. Fenu, E. Cocco, Impact of Menopause in Patients with Multiple Sclerosis: Current Perspectives, *Int. J. Women's Health* 15 (2023) 103–109.
- [9] R. Bove, A. Okai, M. Houtchens, B. Elias-Hamp, A. Lugaresi, K. Hellwig, et al., Effects of Menopause in Women With Multiple Sclerosis: An Evidence-Based Review, *Front. Neurol.* 12 (2021) 554375.
- [10] D. Baroncini, P.O. Annovazzi, N. De Rossi, G. Mallucci, V. Torri Clerici, S. Tonietti, et al., Impact of natural menopause on multiple sclerosis: a multicentre study, *J. Neurol. Neurosurg. Psychiatry* 90 (11) (2019) 1201–1206. Nov.
- [11] H. Silverman, A. Bostrom, A. Lazar, R. Gomez, A. Santaniello, A. Renschen, et al., Accelerated worsening in serum neurofilament light chain levels and multiple sclerosis functional composite in women with MS after menopause (S9.009), *Neurology* 100 (17_supplement 2) (2023) 3364.
- [12] V. Karageorgiou, I. Lambrinou, D.G. Goulis, Menopause in women with multiple sclerosis: A systematic review, *Maturitas* 135 (2020) 68–73. May.
- [13] P. Holmqvist, M. Wallberg, M. Hammar, A.M. Landtblom, J. Brynhildsen, Symptoms of multiple sclerosis in women in relation to sex steroid exposure, *Maturitas* 54 (2) (2006 May 20) 149–153.
- [14] S. Otero-Romero, L. Midaglia, P. Carbonell-Mirabent, M. Zuluaga, I. Galán, J. Río, et al., Menopause does not modify disability trajectories in a longitudinal cohort of women with clinically isolated syndrome and multiple sclerosis followed from disease onset, *Eur. J. Neurol.* 29 (4) (2022 Apr) 1075–1081.
- [15] R. Bove, T. Vaughan, T. Chitnis, P. Wicks, P.L. De Jager, Women's experiences of menopause in an online MS cohort: A case series, *Mult. Scler. Relat. Disord.* 9 (2016) 56–59. Sept.
- [16] L. Midaglia, S. Otero, F. Baró, X. Montalbán, M. Tintoré, Menopause and multiple sclerosis: Influence on prognosis and role of disease-modifying drugs and hormonal replacement therapy, *Mult Scler Houndmills Basingstoke Engl.* 28 (2) (2022 Feb) 173–182.
- [17] Z. Munn, D. Pollock, H. Khalil, L. Alexander, P. McInerney, C.M. Godfrey, et al., What are scoping reviews? Providing a formal definition of scoping reviews as a type of evidence synthesis, *JBIM Evid Synth.* 20 (4) (2022 Apr) 950.
- [18] A.C. Tricco, E. Lillie, W. Zarin, K.K. O'Brien, H. Colquhoun, D. Levac, et al., PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation, *Ann. Intern. Med.* 169 (7) (2018 Oct 2) 467–473.
- [19] H. Arksey, L. O'Malley, Scoping studies: towards a methodological framework, *Int. J. Soc. Res. Methodol.* 8 (1) (2005 Feb 1) 19–32.
- [20] R. Bove, B.C. Healy, E. Secor, T. Vaughan, B. Katic, T. Chitnis, et al., Patients report worse MS symptoms after menopause: Findings from an online cohort, *Mult. Scler. Relat. Disord.* 4 (1) (2015 Jan 1) 18–24.
- [21] M. Kaisey, N. Scotte, B. Giesser, Multiple sclerosis management and reproductive changes: A guide for general neurologists, *Neurol Clin Pract.* 8 (2) (2018 Apr) 142–147.
- [22] K. Rankin, R. Bove, Caring for Women with Multiple Sclerosis Across the Lifespan, *Curr. Neurol. Neurosci. Rep.* 18 (7) (2018 May 23) 36.
- [23] M.D.J. Peters, C. Marnie, A.C. Tricco, D. Pollock, Z. Munn, L. Alexander, et al., Updated methodological guidance for the conduct of scoping reviews, *JBIM Evid Synth.* 18 (10) (2020 Oct) 2119–2126.
- [24] F. Bridge, P. Sanfilippo, O. Skibina, A.L. Nguyen, T. Kalincik, K. Buzzard, et al., Driving forces: Investigating Menopause's Influence on MS Disability Progression, In *Multiple Sclerosis Journal* 30 (2024) (3S) 125–680, p. P091/464.
- [25] A. Ianniello, C. Piervincenzi, L. De Giglio, I. Ferrante, F. Satriano, R. Nistri, et al., The impact of menopausal status on disease progression, retinal and brain atrophy in patients with multiple sclerosis, *Multiple Sclerosis Journal* 30 (S3) (2024) 125–680, p. P726/631.
- [26] K. Johnson, L. DuBose, A. Shah, B. Fling, The impact of menopause in women with multiple sclerosis: a survey study, In *Multiple Sclerosis and Related Disorders* (2025) 106480.
- [27] F. Ladeira, M. Salavisa, A. Caetano, R. Barbosa, F. Sá, A.S. Correia, The Influence of Menopause in Multiple Sclerosis Course: A Longitudinal Cohort Study, *Eur. Neurol.* 80 (3–4) (2018) 223–227.
- [28] S.E. Madueno, S. Banda Ramirez, J. Dotor Garcia-Soto, Insenser M. Ben-Yelun, Menopause in Multiple Sclerosis: listening to women's voices. The importance of women's health throughout life 29, 2023, pp. (3S) 650–1044, p. P1118/444.
- [29] D. Morales-Rodriguez, A. Anderson, A. Nylander, S. Hsu, J. Singh, W. Rowles, et al., Well-being at midlife: Correlates of mental health in ambulatory menopausal women with multiple sclerosis, *Mult Scler Houndmills Basingstoke Engl.* 29 (11–12) (2023 Oct) 1493–1502.
- [30] A. Nylander, H.E. Silverman, A. Akula, A. Bostrom, A.A. Lazar, R. Gomez, et al., Accelerated rate of grey matter brain atrophy after menopause in a longitudinal cohort of women with MS, In *Medical Publishers*, 2023 p. O175/2286.
- [31] C. Oreja-Guevara, J. Moarquez-Rodriguez, L. García-Vasco, I. Gómez-Estévez, E. Alba-Suárez, 1. Impact of menopause on quality of life in multiple sclerosis patients, *Mult Scler Relat Disord.* 92 (2024) 105951.
- [32] C. Perillan, A. Coto, J. Argüelles, P. Nuñez, Study of the impact of multiple sclerosis on the reproductive life of Spanish women: An online survey, *Mult. Scler. Relat. Disord.* 90 (2024 Oct) 105789.
- [33] C. Simonsen, H. Oyen Flemmen, L. Broch, H. Myklebust, P. Berg-Hansen, C. Brunborg, et al., The association between menopause and multiple sclerosis in a Norwegian MS cohort, Sage, In London, England, 2023, pp. 724–725.
- [34] B. Zeydan, E.J. Atkinson, D.M. Weis, C.Y. Smith, L. Gazzuola Rocca, W.A. Rocca, et al., Reproductive history and progressive multiple sclerosis risk in women, *Brain Commun.* 2(2):fcaa185 (2020).
- [35] B. Zeydan, J. Son, N. Neyal, C.G. Schwarz, E.J. Atkinson, H.A. Morrison, et al., Upper cervical spinal cord atrophy in MS: Sex, menopause, and neurodegeneration, *Mult Scler Houndmills Basingstoke Engl.* 31 (3) (2025 Mar) 278–289.
- [36] R. Bove, A. Anderson, W. Rowles, K.A. Rankin, N.K. Hills, M. Carleton, et al., A hormonal therapy for menopausal women with MS: A phase Ib/IIa randomized controlled trial, *Mult. Scler. Relat. Disord.* 1 (61) (2022 May) 103747.
- [37] J.M. Frischer, S. Bramow, A. Dal-Bianco, C.F. Lucchinetti, H. Rauschka, M. Schmidbauer, et al., The relation between inflammation and neurodegeneration in multiple sclerosis brains, *Brain J. Neurol.* 132 (Pt 5) (2009 May) 1175–1189.
- [38] C.A. Metcalf, K.A. Duffy, C.E. Page, A.M. Novick, Cognitive Problems in Perimenopause: A Review of Recent Evidence, *Curr. Psychiatry Rep.* 25 (10) (2023 Oct) 501–511.
- [39] L. Mosconi, V. Berti, J. Dyke, E. Schelbaum, S. Jett, L. Loughlin, et al., Menopause impacts human brain structure, connectivity, energy metabolism, and amyloid-beta deposition, *Sci. Rep.* 9 (11) (2021 June) 10867.
- [40] F. Bridge, P.G. Sanfilippo, C. Zhu, O. Skibina, A.L. Nguyen, T. Kalincik, et al., Menopause impact on multiple sclerosis disability progression, *JAMA Neurol.* (2025) e253538.
- [41] R. Bove, T. Chitnis, M. Houtchens, Menopause in multiple sclerosis: therapeutic considerations, *J. Neurol.* 261 (7) (2014 July) 1257–1268.
- [42] L. Ross, H.S. Ng, J. O'Mahony, M.P. Amato, J.A. Cohen, M.P. Harnegie, et al., Women's health in multiple sclerosis: a scoping review, *Front Neurol.* [Internet] (2022) [cited 2025 Sept 23];12. Available from: <https://www.frontiersin.org/journals/neurology/articles/10.3389/fneur.2021.812147/full>.
- [43] Z. Shahraki, M. Rastkar, E. Rastkar, M. Mohammadifar, A. Mohamadi, M. Ghajrzadeh, Impact of menopause on relapse rate and disability level in patients with multiple sclerosis (MS): a systematic review and meta-analysis, *BMC Neurol.* 4 (23) (2023 Sept) 316.
- [44] N. Marvi, S. Mollazadeh, F. Erfanian Arghavanian, A. Atashi, T. Khadivzadeh, Designing, validation and evaluation of the expert system of "Healthy Menopause" and assessing its effect on the management of menopause symptoms: an exploratory mixed method study protocol, *Reprod. Health* 21 (1) (2024 Jan 20) 9.
- [45] O. Hendriks, J.C. McIntyre, A.K. Rose, C. Crockett, L. Newson, P. Saini, The mental health challenges, especially suicidality, experienced by women during perimenopause and menopause: A qualitative study, *Women's Health (Lond. Engl.)* 21 (2025) 17455057251338941.
- [46] K. Wood, S. McCarthy, H. Pitt, M. Randle, S.L. Thomas, Women's experiences and expectations during the menopause transition: a systematic qualitative narrative review, *Health Promot. Int.* 17;40(1):daaf005 (2025 Jan).
- [47] R.W. Motl, L.A. Pilutti, The benefits of exercise training in multiple sclerosis, *Nat. Rev. Neurol.* 8 (9) (2012 Sept) 487–497.