Understanding the Impact and Burden of Menopause on Multiple Sclerosis Through a Targeted Literature Review

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OBJECTIVE

To evaluate published literature on menopause and MS related to the impact of menopause on MS disease trajectory, the burden of menopause in women with MS, and the impact of menopause on use of MS DMTs.

KEY TAKEAWAYS

Menopause compounds disease burden with increased cognitive dysfunction, fatigue, mood disturbance, sleep disruption and urinary symptoms that reduce quality of life, as well as a shift from inflammatory relapse activity to progressive neurodegeneration.

Despite current clinical disability measures inadequately measuring postmenopausal disease burden, high-efficacy DMTs have been shown to be protective against disease sequelae in this patient population.

A critical evidence gap exists regarding the impact of menopause on DMT use and effectiveness, despite evidence that treatment changes often occur during this transition.

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BACKGROUND

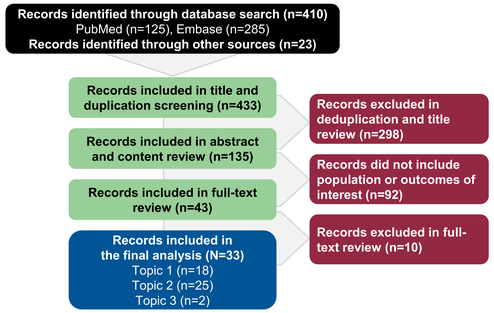
- Multiple sclerosis (MS) disproportionately affects women, with approximately 75% of patients being female and an estimated 30% of the MS population currently peri- or post-menopausal, making menopause increasingly relevant to MS management[1,2]
- Female sex hormones influence immune activity and neuroprotection;[3] therefore, the hormonal decline during menopause may represent a biological inflection point in the MS disease course
- Menopause has been hypothesized to coincide with a shift in MS phenotype characterized by reduced inflammatory relapse activity but increasing neurodegeneration and disability progression[4,5]
- However, the relationship between menopause and MS remains poorly understood, with limited evidence on its impact on disease trajectory, symptom burden and disease-modifying therapy (DMT) use, representing an important evidence gap[6-8]

METHODS

- A targeted literature review was conducted to evaluate the relationship between menopause and MS, focusing on three predefined topics:
  1. Burden of menopause in women with MS
  2. Influence of menopause on MS disease progression
  3. Impact of menopause on MS DMT use
- Searches were performed in PubMed, Embase, Cochrane Library and Google Scholar, as well as AAN and ACTRIMS/ECTRIMS conference databases, using combinations of menopause and MS-related search terms appearing in titles or abstracts
- Searches included records from database inception through December 2025
- Studies were eligible if they evaluated women with MS undergoing the menopausal transition and reported qualitative or quantitative clinical outcomes related to disease progression, symptom burden or treatment patterns; there were no criteria for interventions, comparators or treatment settings

RESULTS

A Total of 433 Records Were Screened, Including 410 (95%) from Database search and 23 (5%) from Other Sources



Distribution of Studies by Topic (N=33)

Study	Topic 1: burden	Topic 2: relapse activity	Topic 2: clinical disability	Topic 2: biomarkers & imaging	Topic 3: DMT use
Baroncini et al. 2019					
Bove et al. 2013					
Bove et al. 2014					
Bove et al. 2016					
Bove et al. 2016					
Bove et al. 2021					
Bridge et al. 2025					
Elias-Hamp et al. 2017					
Graves et al. 2018					
Holmqvist et al. 2006					
Johnson et al. 2025					
Karageorgiou et al. 2020					
Ladeira et al. 2018					
Lohner et al. 2022					
Lorefice et al. 2023					
Madueno et al. 2023					
Nylander et al. 2023					
Nylander et al. 2025					
Oreja-Guevara et al. 2020					
Oreja-Guevara et al. 2024					
Otero-Romero et al. 2020					
Pilotto et al. 2022					
Rojas et al. 2016					
Rubin et al. 2012					
Sepulveda et al. 2015					
Shahraki et al. 2023					
Sheehan et al. 2023					
Silverman et al. 2025					
Simonsen et al. 2024					
Singh et al. 2021					
Smith & Studd 1992					
Zeydan et al. 2020					
Zeydan et al. 2025					

Topic 1: Burden of Menopause in Women With MS

18 studies evaluated symptom burden and QoL, primarily through patient surveys, qualitative interviews and patient-reported outcomes:

Cognitive tests largely showed no statistically significant inflection around menopause despite the large volume of qualitative data[9-13]

HOWEVER

40%-70% **of women reported worsening symptom burden and QoL during the menopausal transition[9-13]**

Cognitive and Psychological Symptoms[15-17]

≈87% **of women with MS reported cognitive changes, often associated with frustration and concerns about work performance**

Mood disturbances, including anxiety, depression, and emotional distress, were frequently reported and associated with poorer psychological quality-of-life scores

Physical and Functional Burden[8,10,18-20]

94% **of women experienced menopausal symptoms accompanied by incontinence (60%), muscle weakness (56%) and limitations to IADLs (50%)[19]**

Studies also reported worsening urinary dysfunction, sexual dysfunction, muscle weakness and limitations in daily activities

Fatigue, Sleep and Vasomotor Symptoms[21-24]

59% **of perimenopausal women felt that menopausal fatigue impacted MS symptoms, particularly related to hot flashes/night sweats[22]**

Vasomotor symptoms may act as thermal triggers for MS pseudo-exacerbations, contributing to worsening fatigue, sleep disruption and cognitive decline

Topic 2: Influence of Menopause in MS Disease Progression

25 studies evaluated the influence of menopause on MS disease progression across three domains:

Relapse Activity[9,20,26-31] 8/25 studies (32%)

Most studies reported a decrease in ARR after menopause

Some analyses found that the reduction was not statistically significant after adjustment for age and disease characteristics

Decline in relapse activity is likely age related rather than solely hormone driven, as similar reductions occur in both men and women with MS during mid-life

Clinical Disability[9-11,13,19,21,23,25,26,28,31-34,40] 15/25 studies (60%)

Evidence on disability progression was mixed: Some longitudinal studies suggest acceleration after menopause, and some large registries reported little change in EDSS trajectories. **These differences across studies may reflect methodological heterogeneity, including limitations of EDSS, which may underestimate disability progression by not fully capturing cognitive or upper limb impairment**

Biomarkers and Neuroimaging[9,12,13,27-29,35-40] 12/25 studies (48%)

Biomarker and imaging studies consistently demonstrated increased neurodegenerative activity after menopause, including increased serum neurofilament light chain levels and accelerated gray matter and spinal cord atrophy. These findings may provide biological context for reported cognitive worsening (Topic 1), given the known associations between gray matter atrophy, neuroaxonal injury and cognitive decline in MS

Topic 3: Impact of Menopause on MS DMT Use

Only 2 studies evaluated the impact of menopause on women's use of DMTs for their MS[31,32]

A substantial proportion of women modify DMT regimens around the time of menopause, including starting, stopping or switching therapies

Exposure to high-efficacy DMTs during the menopausal transition may be protective against MS disability progression[32]

LIMITATIONS

- It is difficult to distinguish the biological effects of menopause from those of aging and mid-life physiological changes from MS progression
- Many studies relied on self-reported menopause onset rather than objective biomarkers (eg, anti-Müllerian hormone), which may introduce misclassification bias
- Some analyses did not adequately control for key variables such as body mass index, disease duration, or treatment exposure[5]
- The EDSS, which is heavily weighted toward ambulation, was commonly used and may not capture cognitive dysfunction, fatigue, and upper-limb impairment reported during the menopausal transition

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ABBREVIATIONS

AAN, American Academy of Neurology; **ACTRIMS,** Americas Committee for Research and Treatment in Multiple Sclerosis; **DMT,** disease-modifying therapy; **ECTRIMS,** European Committee for Research and Treatment in Multiple Sclerosis; **EDSS,** Expanded Disability Status Scale; **MS,** multiple sclerosis; **QoL**, quality of life.

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DISCLOSURES

D. Jain, A. Ravelo, I. Abioye and **E.D. Pineda** are employees of Genentech, Inc., and shareholders of F. Hoffmann-La Roche Ltd.

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