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Original article

Epidemiology and Risk Factors for Multiple Sclerosis: A Narrative Review of Recent Evidence

Osamah Alrouwab[1]*, Husam Eldaouki[2], Issa Amara[3]

[1]*Department of Biochemistry, Faculty of Medicine, Zintan University, Zintan, Libya*
[2]*Department of Pediatrics, Faculty of Medicine, Zintan University, Zintan, Libya*
[3]*Department of Pharmacology, Faculty of Medicine, Zintan University, Zintan, Libya*
Corresponding email. *rawab@uoz.edu.ly*

Abstract
One of the main causes of non-traumatic neurological disability in young adults worldwide is multiple sclerosis (MS), a chronic immune-mediated demyelinating and neurodegenerative disorder of the central nervous system (CNS). Increasing absolute prevalence is seen in recent epidemiological trends from 2021 to 2025, while age-standardized rates are stabilizing due to improved diagnostics, survival, and demographic shifts. The current narrative review's objective is to examine high-caliber studies conducted globally between 2021 and 2025 that address the epidemiology, burden, and different risk factors related to multiple sclerosis (MS), with an emphasis on the effects of age, gender, ethnicity, and other interacting factors. Key Findings: Global prevalence of ~1.89 million cases in 2021 (age-standardized rate: 23.9 per 100,000), with ~62,000 new cases each year; female-to-male ratio of ~3:1. DALYs are up by 43% from 1990, but with a trend downward for age-standardized rates with advances in management. Incidence is framed by disparities with higher rates for Whites (77% of the U.S.) than Black (10%), followed by Hispanic (7%) cases, and also high levels of radiological severity, handicap, and poor outcomes for ethnic minorities of these groups. Age of peak incidence progresses to older groups for individuals aged 20-40 years. Genetic underpinnings with large effects (e.g., HLA-*DRB1*15:01 for ~48% of heritability), strong susceptibility to Epstein-Barr virus infection (near ubiquity at onset; 32-fold increase for molecular mimicry), vitamin D deficiency, smoking, obesity, and altered gut microbiomes are environmental components of risk. Incidence is seen to decline modestly for age-standardized incidence rates, mortality rates, and DALYs through 2035. From this review, the emphasis on MS as a partially preventable disease falls within the context of a rising absolute prevalence and existing inequities in the field. Future complementary strategies should therefore encompass a wide range of populations as well as risk modification measures such as EBV-related therapies and smoking cessation.*
Keywords. *Multiple Sclerosis, Epidemiology, Neurodegenerative Disorder, Gene-Environment.*

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Introduction

Multiple sclerosis (MS) is a chronic, immune-mediated disorder of the central nervous system characterized by a heterogeneous clinical course that encompasses relapsing–remitting (RRMS), secondary progressive (SPMS), and primary progressive (PPMS) phenotypes [1]. Once regarded as a primarily inflammatory condition with discrete relapsing and progressive phases, contemporary understanding positions MS as a dynamic continuum in which inflammatory and neurodegenerative mechanisms coexist from disease onset. This paradigm shift has been catalysed by the recognition of progression independent of relapse activity (PIRA), a concept underscoring that disability accrual can occur in the absence of overt clinical relapses, thereby challenging traditional nomological boundaries [2].

As of 2023, more than 2.9 million people around the world live with MS. That number keeps climbing, mostly because we're better at spotting the disease, people are living longer, and there's more awareness now. Plus, the world itself is changing in ways that affect our health. One thing that stands out: doctors are diagnosing MS more often in older adults these days. More folks are getting the news in their fifties and beyond. This shift probably comes from a mix of better detection and changes in the things that influence the disease throughout our lives [3, 4].

There have been significant developments in MS epidemiology and aetiology between 2021 and 2025. High-resolution estimates of MS prevalence, incidence, mortality, and disability-adjusted life years (DALYs) across 204 countries and territories have been provided by historic global health initiatives, most notably the Global Burden of Disease Study 2021 (GBD 2021) [5, 6]. Large-scale genomic initiatives, such as trans-ethnic meta-analyses and genome-wide association studies (GWAS), have concurrently increased the number of susceptibility loci to over 230 genetic variants, shedding light on pathways related to vitamin D metabolism, immune regulation, and the Epstein-Barr virus (EBV) response [7]. This thorough narrative analysis builds on previous syntheses by integrating the most recent epidemiological predictions through 2035, highlighting

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significant regional and sociodemographic inequalities, and critically analysing both modifiable and non-modifiable risk variables [8-10].
Emerging areas like the gut-brain axis (including microbiome composition and metabolomic signatures), serological biomarkers of neuroaxonal injury (like neurofilament light chain), and the interaction between genetic background and environmental triggers (like latitude, smoking, obesity, and EBV infection) are given particular attention. Additionally, the study examines interlocking axes of inequality, such as differences in MS risk, presentation, access to care, and outcomes across socioeconomic position, gender, ethnicity, and geography, especially in underrepresented areas like the Middle East and North Africa (MENA) [11-13]. By synthesizing contemporary evidence within a global health framework, this review aims to inform clinical decision-making, guide public health strategies, and identify critical gaps for future research, ultimately advancing equitable, precision-oriented approaches to MS prevention, diagnosis, and management in diverse populations worldwide.

Epidemiology of Multiple Sclerosis

Global Prevalence and Incidence

The global burden of MS has escalated, with 1.89 million prevalent cases in 2021, marking a 30% rise since 2013 and a continuous increase over three decades. Age-standardized prevalence is 23.9 per 100,000 population, with a female-to-male ratio of approximately 2:1 to 3:1, reflecting hormonal and genetic influences on susceptibility [14]. Incidence has stabilized in age-standardized terms but increased absolutely by 49% from 1990 to 2021, reaching ~62,000 new cases annually, particularly among adults aged 20-54 (51,904 cases in 2021) [15]. This growth is attributed to population expansion, aging demographics, enhanced diagnostic capabilities (e.g., MRI advancements), and improved survival rather than heightened risk exposure. Pediatric-onset MS (POMS) shows an incidence of 0.05-2.85 per 100,000 children, with prevalence up to 26.9 per 100,000 in high-income areas, while late-onset MS (after age 50) accounts for up to 35% of cases in some cohorts, indicating a shift toward older onset ages [16, 17].

Mortality and Disability Burden

MS contributes substantially to neurological morbidity, with 4,738 deaths and 513,000 DALYs in the 20-54 age group in 2021. Overall DALYs rose 43% from 1990 to 2021 (from 358,185 to 512,986), yet age-standardized DALY rates declined from 14.90 to 13.61 per 100,000 (estimated annual percentage change [EAPC] -0.45), signaling advancements in disease-modifying therapies (DMTs) and care. Mortality increased by 18% in absolute terms but decreased in rates (EAPC -1.21), comparable to burdens from conditions like Crohn's disease. Disparities persist, with males exhibiting higher mortality and DALYs despite lower prevalence, and ethnic minorities facing elevated disability [13, 18-19].

Regional, National, and Subnational Variations

Pronounced geographic disparities exist, with the highest burdens in high socio-demographic index (SDI) regions like North America (incidence rate 4.38 per 100,000) and Western Europe (10,964 incidence cases). Prevalence exceeds 100 per 100,000 in countries such as Sweden (219/100,000), Canada (182/100,000), and Norway (176/100,000), linked to latitude gradients and vitamin D deficiency. Lower rates in low-SDI regions may reflect underdiagnosis. In the US, subnational data show northern states with twice the incidence of southern ones; nationally, the US leads in cases (9,388 incidence, 758 deaths) [20-22].

Variations by Ethnicity and Race

Multiple sclerosis (MS) affects people from all racial and ethnic backgrounds, contradicting earlier beliefs that it mainly affected White populations. In the United States, White individuals account for 77% of MS cases (577,725), followed by Black individuals at 10% (80,276), Hispanics at 7% (53,456), and lower rates among Asian/Pacific Islanders. Recent studies show that the prevalence per 100,000 people is similarly high for both Black and White populations, while Hispanics have a lower risk but are experiencing increasing rates. There are clear ethnic differences in disease outcomes: Black and Hispanic patients tend to have more severe findings on imaging, higher levels of disability, more frequent use of walking aids, and poorer neurological outcomes compared to White patients. Young Black and Hispanic women, in particular, often have more advanced disease when first diagnosed. In contrast, a large study in the UK found no link between ethnicity and MS severity, indicating that factors such as access to healthcare may play a role in these disparities. These differences highlight the complex interaction between genetic background, socioeconomic status, and environmental influences [23,24].

Variations by Gender

Gender differences are significant, with women making up 77% of cases in certain groups and an international ratio reaching 3:1. In some areas, women exhibit a greater prevalence but possibly improved

long-term results, whereas men display a lower prevalence but higher mortality and DALYs, as noted in China. Gender affects prodromal symptoms, response to treatment, and complications such as sexual dysfunction, which occurs more frequently in females and is linked to older age and increased disability. Men might postpone reporting symptoms, resulting in delayed diagnoses. Intersections with ethnicity worsen inequalities, particularly among young minority individuals [25].

Variations by Age

MS onset typically occurs between ages 20-50, with peak incidence at 30-34 years, though trends indicate a shift toward older ages (mean presumed onset 43.5 years in some studies). Early-onset (before 18) is rare (3%), while late-onset (after 50) comprises 35%, often with more progressive courses. Age influences burden: incidence declines after 50, but older adults face higher comorbidity and disability risks. Prodromal health care use increases 25 years pre-onset, varying by age group [26].

Trends and Projections

Since 1990, prevalence has increased by 26–30% worldwide and doubled in some areas. Age-standardized mortality and incidence decreased somewhat (EAPC -1.21 for death, -0.08 for incidence). Assuming continued trends in diagnosis and interventions, Bayesian estimates to 2035 place incidence at 1.54 per 100,000, death at 0.11 per 100,000, and DALYs at 14.59 per 100,000. In view of growing absolute burdens, these changes highlight potential for prevention, especially when it comes to addressing inequities in disadvantaged groups [27, 28].

Risk Factors for Multiple Sclerosis

MS etiology involves polygenic inheritance (30-48% heritability) interacting with environmental triggers, often during critical windows like adolescence, modulated by ethnicity, gender, and age. Recent GWAS and meta-analyses have refined these insights [29].

Genetic Risk Factors

Genetics are responsible for around 48% of MS risk, with familial aggregation evident. Lifetime risk climbs from 0.1% in the general population to 2-4% in first-degree relatives and 20-30% in monozygotic twins. A GWAS of 47,429 patients found 233 variations, including 32 in the MHC region. The strongest allele is HLA-DRB1*15:01, which enhances antigen presentation and interacts with environmental variables such as smoking (carriers lacking HLA-A02 have a 13-fold higher risk) [30]. Non-HLA variations are more prevalent in immunological pathways (e.g., IL-2RA, IL17R for T-cell activation) and CNS functions (e.g., DYSF-ZNF638 for progression). Polygenic risk ratings (PRS) predict severity irrespective of onset age. Ancient DNA indicates that steppe pastoralist descent is associated with increased risk. X-linked genes and polymorphisms in vitamin D metabolism (VDR, CYP27B1) further stratify risk, with gender differences in genetic vulnerability (for example, women with certain variants progress faster. [31]. Ethnic variations in HLA and non-HLA alleles contribute to disparities [32].

Environmental Risk Factors

Environmental exposures, modifiable in many cases, interact with genetics to drive MS onset and progression, with differential impacts by ethnicity, gender, and age [33].

Infectious Agents

EBV is a near-requisite trigger, with nearly all MS patients seropositive at the beginning; infection increases risk by 32-fold, often 5 years before diagnosis. Molecular mimicry (EBNA-1 cross-reacting with myelin), B-cell immortalization, and CNS invasion are all possible mechanisms. HHV-6 seropositivity increases risk (pooled ES 2.84) through CNS tropism, demyelination, and viral load relationships. VZV infection causes relapses (pooled ES 1.33), which promote Th1 cytokines and inflammation. Other viruses (e.g., CMV, HERVs) exhibit regional variation, with HERVs linked to progression via T-cell stimulation. Adolescent exposures are particularly important in terms of infection risk [34].

Vitamin D Deficiency and Sunlight Exposure

Latitude gradients are explained by low UVR and vitamin D levels, with prevalence ranging from 111-300 per 100,000 in high-latitude regions to <5 in tropical areas. Deficiency (<20 nmol/L) raises risk (pooled ES 1.51), whereas levels ≥50 nmol/L slow progression (lower EDSS and less atrophy). Mechanisms include immunomodulation (decreased effector cells, increased regulatory T-cells) and neuroprotection (e.g., neurotrophic factors). Polymorphisms in VDR/CYP27B1 exacerbate consequences, making women more sensitive [35, 36].

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Smoking and Tobacco Exposure

Smoking increases the onset risk dose-dependently (pooled ES 1.43), increasing the progression of RRMS to SPMS and disability. Mechanisms include oxidative stress, BBB permeability, epigenetic alterations, and HLA interactions (13-fold risk in vulnerable genotypes). Attributable risk: 13% in some populations, with women demonstrating increased sensitivity when combined with obesity and genetics [37].

Obesity and Body Mass Index

Obesity in childhood and adolescence increases risk through adipokines, inflammation, and vitamin D insufficiency, which are associated with impairment and atrophy. Adult BMI has no direct link (pooled ES 0.94), indicating that early-life windows are important, with gender differences (women are more affected) [38].

Gut Microbiome Dysbiosis

New research linked gut microbiome changes to MS risk and progression. Dysbiosis is characterized by fewer short-chain fatty acid (SCFA) producers (e.g., Faecalibacterium, Roseburia) and more proinflammatory taxa (e.g., Streptococcus, E. coli) [39]. Mechanisms include immunological dysregulation via the gut-brain axis, protein mimicry with myelin amino acids, and changed metabolites that affect disease activity. Studies reveal that the microbiome differs between stable and progressing MS, with B-cell loss affecting host-microbe interactions. Twin studies link small intestinal bacteria to MS [40]. Genetic risk scores are associated with distinct microbiomes, which may change depending on ethnic background and age [41].

Demographic Risk Factors: Ethnicity, Gender, and Age

Ethnicity influences sensitivity and consequences through genetic-environmental interactions; for example, increased severity in Black and Hispanic groups may be due to differences in access to care and DMTs, with Hispanics experiencing the greatest decline in adjusted relapse rates (90% from 2011-2023) [42]. Gender disparities are triggered by hormonal (e.g., estrogen modulation), genetic (e.g., X-linked variations), and lifestyle factors, with women having a larger risk but men progressing more quickly in certain genetic situations. The age at onset influences the prognosis: earlier onset coincides with relapsing types, whereas later onset is associated with progressive disease and comorbidities [43]. Intersections, such as elder women in minority groups, exacerbate vulnerability [44].

Discussion

From 2021 to 2025, the epidemiological landscape of multiple sclerosis (MS) displays a disease with increasing worldwide relevance, as seen by rising absolute numbers of cases and stabilizing or slightly dropping age-standardized rates of prevalence, incidence, and mortality. The observed 30% increase in prevalent cases since 2013 and the 49% increase in absolute incident cases are primarily due to population growth, aging demographics, improved diagnostic sensitivity (particularly through widespread MRI use and updated McDonald criteria), and longer survival due to advances in disease-modifying therapies (DMTs), rather than a true escalation in underlying risk [45]. The ongoing female preponderance (ratios up to 3:1) and the move toward older age at onset (with late-onset MS accounting for up to 35% in some cohorts) highlight developing demographic patterns, which may be influenced by changes in reproductive, hormonal, and lifestyle exposure across time [46].

Geographic and demographic differences remain pronounced. High socio-demographic index (SDI) regions, particularly those in northern latitudes, still experience the heaviest impact, most likely due to a combination of genetic susceptibility and environmental variables such as inadequate levels of vitamin D and historical migration patterns. Ethnic differences are also noteworthy: whereas White populations continue to account for the bulk of cases in high-prevalence settings such as the United States, Black and Hispanic people frequently face higher disease severity, faster progression, and worse handicap consequences [47, 48]. These disparities are most likely caused by a mix of genetic heritage, financial hurdles to early diagnosis, high-efficacy DMTs, and varying environmental exposures. Gender disparities go beyond prevalence, with males having higher morbidity and DALY rates despite lower incidence, and women having more significant associations with specific risk factors (e.g., obesity, tobacco use, and genetic variations). These intersecting demographic patterns underline the importance of stratified methods to both research and patient care [49, 50].

Recent data clearly support the complex origin of multiple sclerosis. The near-universal prevalence of Epstein-Barr virus (EBV) seropositivity in MS patients, combined with a 32-fold probability elevation following infection and mechanistic insights into molecular mimicry and B-cell dysregulation, places EBV as one of the most powerful recorded causative environmental activators to date [51]. This outcome, when paired with substantial links for vitamin D deficiency, smoking, adolescent obesity, and new information on gut microbiome dysbiosis, highlights a complex gene-environment interaction simulation in which genetic

susceptibility (particularly HLA-DRB1*15:01 and polygenic risk scores) sets the stage, while adaptable environmental exposures precipitate and/or modulate disease development and progression. Identifying important engagement windows (e.g., adolescence for obesity and EBV) and synergistic effects (e.g., smoking × HLA genotype) enables targeted preventative interventions [52].
Notwithstanding these advancements, a few restrictions must be recognized. The use of modelled worldwide burden forecasts, underdiagnosis in nations with low to middle incomes, variation in medical and reporting standards, and the review's narrative (rather than systematic) format all contribute to potential biases and gaps in representation. Furthermore, while serological and microbial markers are promising, their specificity and application in varied populations have yet to be thoroughly demonstrated.

Conclusion

Multiple sclerosis continues to be the primary cause of neurological disability globally, with a developing epidemiological picture marked by rising absolute burden, ongoing demographic inequality, and a better knowledge of its multifaceted etiology. The period 2021-2025 has confirmed the key function of Epstein-Barr virus exposure alongside established genetic and environmental risk factors, while also highlighting possibilities for avoidance through smoking, vitamin D status, weight gain, and potentially microbiome-targeted actions. Addressing the expanding worldwide epidemic and reducing disparities will necessitate ongoing investment in various longitudinal study cohorts, greater monitoring in underserved areas, the development of available biomarkers, and the implementation of targeted public health interventions. MS is becoming more widely recognized as a largely avoidable disorder as we gain a better knowledge of gene-environment interactions and the function of EBV. Future efforts should focus on individualized risk assessment, early intervention, and fair access to high-efficacy medicines to lessen the chronic disease's permanent personal and social impacts.

Conflict of interest. Nil

References

1. Ziemssen T, Havla J, Müller M, Lünemann JD, Ruck T, zu Hoerste GM, et al. Secondary progressive multiple sclerosis: a review of clinical characteristics, definition, prognostic tools, and disease-modifying therapies. Neurol Neuroimmunol Neuroinflammation. 2023 Jan;10(1):e200064.
2. Lorenzut S, D'Agostini S, Perini P, Gallo P. Exploring the pathophysiology, diagnosis, and treatment options of multiple sclerosis. J Integr Neurosci. 2025;24(1):1–14.
3. Walton C, King R, Rechtman L, Kaye W, Leray E, Marrie RA, et al. Rising prevalence of multiple sclerosis worldwide: Insights from the Atlas of MS. Mult Scler J. 2020 Dec;26(14):1816–21.
4. Safiri S, Ghaffari Jolfayi A, Mousavi SE, Nejadghaderi SA, Sullman MJM, Kolahi AA. Global burden of multiple sclerosis and its attributable risk factors, 1990–2019. Front Neurol. 2024;15:1448377.
5. Yu X, Shi L, Deng X, Zhang Y, Huali W. Global burden of endometriosis from 1990 to 2021 and projections to 2050: a comprehensive analysis based on the global burden of disease study 2021. Front Glob Womens Health. 2025;6:1613468.
6. Liu J, Li L, Ma X, Zhu L, Li K, Pan B, et al. Systematic study and 30-year projections of global and multi-regional burden of multiple sclerosis, 1990–2021. Medicine (Baltimore). 2025 Nov 7;104(44):e45089.
7. Xie LY, Zhang J, Li YX, Lin XM. Clinical efficacy of laser therapy in the prevention of retinal detachment in patients with acquired immunodeficiency syndrome and cytomegalovirus retinitis. Quant Imaging Med Surg. 2021 Jun;11(6):2634–43.
8. Montini F, Ristori G, Romano S, Bellucci G, Marrone A, Salvetti M, et al. Modifiable risk factors of COVID-19 in patients with multiple sclerosis: a single-centre case–control study. J Neurol. 2023 Apr;270(4):1835–42.
9. Glans I, Sonestedt E, Stomrud E, Gustavsson M, Hansson O, Nägga K. Associations of modifiable and non-modifiable risk factors with cognitive functions–a prospective, population-based, 17 years follow-up study of 3,229 individuals. Alzheimers Res Ther. 2024 Jun 20;16(1):135.
10. Hansen M, Hahn C. Autoimmune Encephalitis: Modifiable and Non-modifiable Predictors of Relapse (2200). Neurology. 2021 Apr 13;96(15_supplement):2200.
11. Ullah H, Arbab S, Tian Y, Liu CQ, Chen Y, Qijie L, et al. The gut microbiota–brain axis in neurological disorder. Front Neurosci. 2023;17:1225875.
12. You M, Liu J, Wang L, Xiang L. The gut microbiota–brain axis in neurological disorders. MedComm. 2024 Aug;5(8):e656.
13. Kasbi NA, Rafiee E, Ghodrati S, Ebadi A, Jalali A, Jamialahmadi T, et al. The prevalence of epstein-barr virus and multiple sclerosis in mena region: a systematic review. Mult Scler Relat Disord. 2023 Apr;80:105223.
14. Khan G, Hashim MJ. Epidemiology of multiple sclerosis: global, regional, National and sub-national-level estimates and future projections. J Epidemiol Glob Health. 2025 Mar;15(1):21–35.
15. Wang L, Wang W, Hui S, Yang L, Liu Y, Li H. Emerging epidemiological trends of multiple sclerosis among adults aged 20–54 years, 1990–2021, with projections to 2035: a systematic analysis for the global burden of disease study 2021. Front Neurol. 2025;16:1616245.

16. Jakimovski D, Awan S, Eckert SP, Farooq O, Weinstock-Guttman B. Multiple sclerosis in children: differential diagnosis, prognosis, and disease-modifying treatment. CNS Drugs. 2022 Jan;36(1):45–59.
17. Margoni M, Rinaldi F, Perini P, Gallo P. Therapy of pediatric-onset multiple sclerosis: state of the art, challenges, and opportunities. Front Neurol. 2021;12:676095.
18. Lane J, Ng HS, Poyser C, Lucas RM, Tremlett H. Multiple sclerosis incidence: A systematic review of change over time by geographical region. Mult Scler Relat Disord. 2022 Jul;63:103932.
19. Qian Z, Wang P, Yu L, Guo X, Zhou J, Sun G. Global, regional, and national burden of multiple sclerosis from 1990 to 2019: Findings of global burden of disease study 2019. Front Public Health. 2023;11:1073278.
20. Xu YH, Dong ZY, Xu H, Shu L, Ji JL, Guo YJ. Global, Regional, and National Burden of Multiple Sclerosis: A Systematic Analysis for the Global Burden of Disease Study 2021. Yi Jing, Glob Reg Natl Burd Mult Scler A Syst Anal Glob Burd Dis Study. 2021;
21. Benjaminsen E. Multiple sclerosis in Northern Norway, epidemiology and comorbidity [dissertation]. [Tromsø]: UiT The Arctic University of Norway; 2022.
22. Zhao P, Zhao J, Li J, Wang L, Liu X, Xu T, et al. Global Burden and Trends of Multiple Sclerosis Among Adolescents and Young Adults: A Comprehensive Analysis from the 2021 Global Burden of Disease Data. Available SSRN 5319126.
23. Su J, Liang Y, He X. The overall and smoking-attributable burden of multiple sclerosis among older adults aged 65–89 years from 1990 to 2019 and predictions to 2040. Front Med. 2024;11:1430741.
24. Wang H, Zhang X, Li H, Sun Z, Zhong Y. Gender differences in the burden of multiple sclerosis in China from 1990 to 2019 and its 25-year projection: An analysis of the Global Burden of Diseases Study. Health Sci Rep. 2023 Dec;6(12):e1738.
25. Forouhari A, Taheri G, Salari M, Moosazadeh M, Etemadifar M. Multiple sclerosis epidemiology in Asia and Oceania; A systematic review and meta-analysis. Mult Scler Relat Disord. 2021 Oct;54:103119.
26. Xu L, Wang Y, Tian H, Chen J, Liu Z, Liu X, et al. Urban prevalence of multiple sclerosis in China: A population-based study in six provinces. Eur J Neurol. 2021 May;28(5):1636–44.
27. Shi M, Liu Y, Gong Q, Xu X. Multiple sclerosis: An overview of epidemiology, risk factors, and serological biomarkers. Acta Neurol Scand. 2024;2024(1):7372789.
28. Kapica-Topczewska K, Kułakowska A, Kochanowicz J, Brola W. Epidemiology of multiple sclerosis: Global trends, regional differences, and clinical implications. Neurol Neurochir Pol. 2025;59(4):375–84.
29. Graf J, Akmatov MK, Meuth SG, Tremlett H, Holstiege J. Updated multiple sclerosis incidence, 2015-2022. JAMA Neurol. 2024 Oct 1;81(10):1100–2.
30. Chen M. Uncovering genetic risk factors in multiple sclerosis using a family-based approach [dissertation]. [Hobart]: University of Tasmania; 2022.
31. Barcellos LF, Oksenberg JR, Begovich AB, Martin ER, Schmidt S, Vittinghoff E, et al. HLA-DR2 dose effect on susceptibility to multiple sclerosis and influence on disease course. Am J Hum Genet. 2003 Mar;72(3):710–6.
32. Khan Z, Dar SA, Mir MA, Kumar A, Hanif K, Khan S. The Polygenic Nature of Multiple Sclerosis: Genetic Variants, Immunological Modulation, and Environmental Connections. Endocr Metab Immune Disord Drug Targets. 2025;25(7):527–59.
33. Leffler J, Trend S, Gorman S, Hart PH. Sex-specific environmental impacts on initiation and progression of multiple sclerosis. Front Neurol. 2022;13:835162.
34. Hedström AK. Risk factors for multiple sclerosis in the context of Epstein-Barr virus infection. Front Immunol. 2023;14:1212676.
35. Vergara-Maldonado C, Urdaneta-Machado JR. The Effects of Latitude and Temperate Weather on Vitamin D Deficiency and Women's Reproductive Health: A Scoping Review. J Midwifery Womens Health. 2023 May;68(3):340–52.
36. Oliver SL, Santana KV, Ribeiro H. The Effect of Sunlight Exposure on Vitamin D Status in Countries of Low and High Latitudes: A Systematic Literature Review. Curr Nutr Rep. 2023 Mar;12(1):1–13.
37. Manouchehrinia A, Westerlind H, Ramanujam R, Alfredsson L, Olsson T, Kockum I, et al. Smoking attributable risk in multiple sclerosis. Front Immunol. 2022;13:840158.
38. Vitturi BK, Meca-Lallana V, Brañas-Pérez M, Dámaso E, Ballesteros AI, Lucas-Jiménez L, et al. Childhood and Adolescent Environmental Risk Factors for Multiple Sclerosis: A Systematic Review With Meta-Analysis. Eur J Neurol. 2025;32(11):e70398.
39. Paraschiv AC, Vacaras V, Nistor C, Vacaras C, Strilciuc S, Muresanu DF. The effect of multiple sclerosis therapy on gut microbiota dysbiosis: a longitudinal prospective study. Microb Cell. 2024;11:106–18.
40. Rasoulian P, Bozorgmehr A, Ghadiri N, Sharifnia Z, Tafakhori A, Sahebkar A, et al. Gut dysbiosis in multiple sclerosis patients: a comparative analysis in fecal samples. Sci Rep. 2025 Feb 14;15(1):36009.
41. Nezamzadeh F, Masroor A, Esmaeilkhani A, Bialvaei AZ. Exploring the complex interplay: insulin resistance and gut microbiome dysbiosis in multiple sclerosis. Neuroscience. 2025;
42. Jacobs BM, Pang C, Kuhle J, Taylor BV, Dobson R, Noyce AJ, et al. Modifiable risk factors for multiple sclerosis have consistent directions of effect across diverse ethnic backgrounds: a nested case–control study in an English population-based cohort. J Neurol. 2024 Jan;271(1):241–53.
43. Li J, Vas N, Amezcua L, Rotstein DL. Multiple Sclerosis in People of Diverse Racial and Ethnic Backgrounds: Presentation, Disease Course, and Interactions with Disease-Modifying Therapy: J. Li et al. CNS Drugs. 2025 Sep;39(9):823–42.

44. Balasooriya NN, Elliott TM, Neale RE, Vasquez P, Comans T, Gordon LG. The association between vitamin D deficiency and multiple sclerosis: An updated systematic review and meta-analysis. Mult Scler Relat Disord. 2024 Jul;90:105804.
45. Portaccio E, Bassani L, Paolicelli D, Razzolini L, Amato MP. Multiple sclerosis: emerging epidemiological trends and redefining the clinical course. Lancet Reg Health Eur. 2024 Jan;44:100963.
46. Yamout B. Update in multiple sclerosis. eNeurologicalSci. 2025 Mar;38:100553.
47. Schilling MA. The geographic association of multiple sclerosis and amyotrophic lateral sclerosis. Sci Rep. 2025 Jan 31;15(1):34665.
48. McGinley MP, Harvey T, Lopez R, Ontaneda D, Buchalter RB. Geographic disparities in access to neurologists and multiple sclerosis care in the United States. Neurology. 2024 Jan 9;102(2):e207916.
49. Schlindwein MAM, Weiller M, Schleich A, Rocha R, Pietrobom GR, Dutra LA, et al. Impacts of environmental tobacco smoke on the onset and progression of multiple sclerosis: a systematic review. Arq Neuropsiquiatr. 2024;82(S 01):A047.
50. Silverman HE, Miao F, Koch MW, Marrie RA, Bhan V, Hosseiny F, et al. Association of menopause with functional outcomes and disease biomarkers in women with multiple sclerosis. Neurology. 2025 Jan 14;104(2):e210228.
51. Cortese M, Ascherio A, Bjornevik K. EBV and Autoimmunity. In: Münz C, editor. Epstein Barr Virus Volume 2: One Herpes Virus: Many Diseases. Cham: Springer International Publishing; 2025. p. 55–70.
52. Farrell PJ. EBV and MS: the evidence is growing stronger. Cell. 2023 Dec 21;186(26):5675–6.