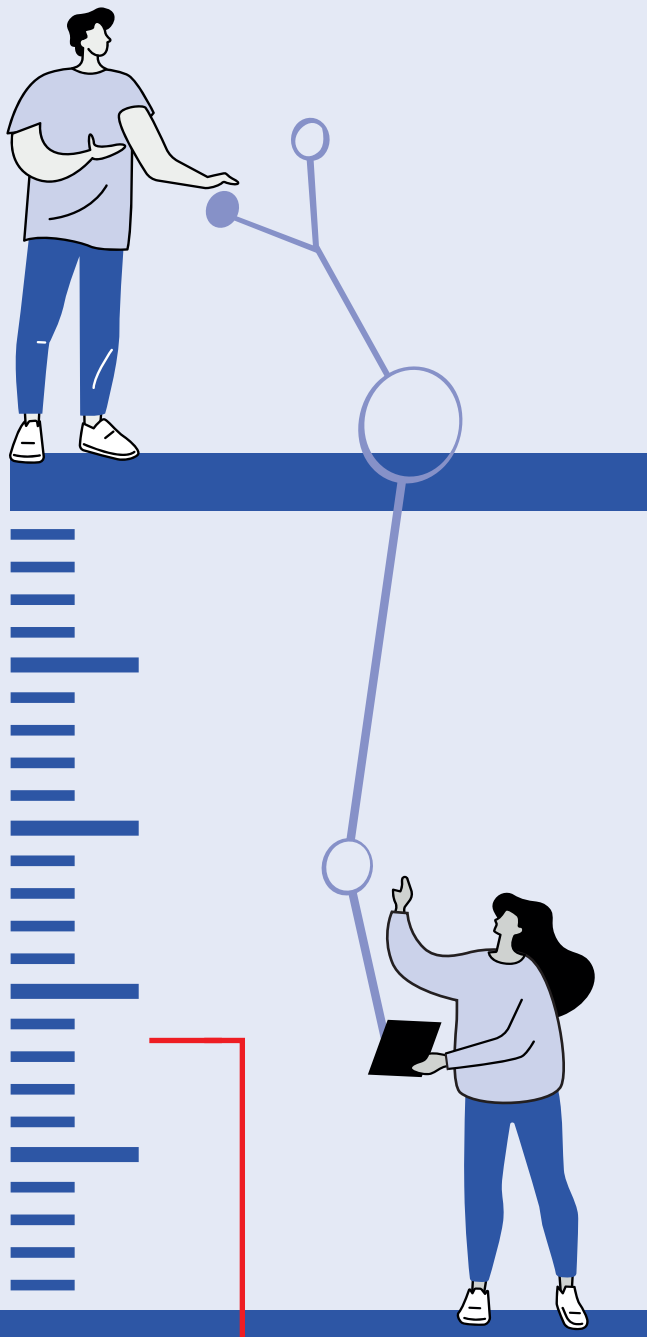


ECONOMIST IMPACT

Measuring what matters

Bridging the gap between disability impact and economic burden in multiple sclerosis

Supported by sanofi

Contents

Executive summary

The accumulation of disability in multiple sclerosis (MS) is a major driver of both individual and societal costs, which increase substantially as the disease progresses. However, it is likely that the true economic burden is being underestimated, largely because current approaches to measuring disability fail to reflect the full complexity of living with MS. By focusing narrowly on physical impairment and overlooking the often invisible yet debilitating symptoms experienced by people living with MS, existing frameworks misrepresent the real impact of the condition. This disconnect affects not only clinical care, but also decisions around resource allocation, health policy and long-term service planning. Our multi-method research—spanning a literature review, burden of disease analysis and consultation with MS experts—highlights critical gaps in how disability is currently assessed, offering evidence that these limitations obscure our understanding of the actual scale and cost of MS.

Key findings

The economic burden of MS is substantial, with annual costs exceeding per capita GDP in each of the modelled countries

The economic burden of MS is substantial. In 2025, the average annual costs (irrespective of severity) ranged from US$57,140 to US$145,857 in the UK and the US respectively. Stratifying by disability severity, in Germany, Italy, Sweden and the UK the annual economic burden among people with severe disability is over twice as high as for those with mild disability. In every country studied, the annual cost of MS-related disability exceeds per capita gross domestic product (GDP)—evidence that MS poses a major societal and economic challenge.

As MS progresses, the composition of costs shifts dramatically. For people with mild disability, the largest share of costs comes from direct healthcare spending, particularly drugs and inpatient care. However, with advancing disease, indirect costs—including lost productivity and informal caregiving—overtake direct healthcare expenditures as the principal driver of economic burden. Direct non-healthcare expenses also climb sharply with worsening disability, from just

1% of total costs in those with mild impairment to nearly 25% among those with severe disability. These include home adaptations, mobility support and vehicle modifications, reflecting how disease progression amplifies the financial impact far beyond the healthcare system.

There is a disconnect between patient experience and assessment of MS in clinical practice

Our research reveals a profound mismatch between the symptoms experienced by people with MS and the clinical focus of neurologists. Across nearly all cases, the proportion of patients reporting symptoms far exceeds the proportion of neurologists routinely assessing for them. For example, while the Impact of Multiple Sclerosis Symptoms (IMSS) survey of more than 17,000 people with MS, conducted by the European Multiple Sclerosis Platform, found that 94% of respondents experience fatigue, our survey revealed that only 53% of neurologists routinely assess fatigue levels in clinical practice. This gap exposes a critical disconnect between patient needs and clinical priorities. The findings are consistent with surveys across North America and Europe showing that healthcare professionals tend to rely on motor and sensory impairments to trigger disability assessments, while people with MS report fatigue and cognitive challenges as the most disabling.[1] By relying on a narrow, mobility-focused lens, many clinicians overlook symptoms that drive poor quality of life and contribute to hidden disability. The consequences are significant. This misalignment leaves people with MS under-supported and inappropriately managed, with repercussions extending beyond the individual to their families, workplaces and society.[2]

There is an urgent need to rethink how symptoms are assessed, shifting towards person-centred approaches that reflect the lived realities of people with MS. Redesigning clinical care to systematically capture a broader and more nuanced set of symptoms—particularly in progressive forms of the disease—will be essential to improving outcomes and reducing the wider social and economic burden.

The majority of neurologists believe a more comprehensive approach is needed to assess disability among people with MS

Neurologists recognise an urgent need to improve how disability is measured in people with MS, particularly in ways that translate directly into clinical practice. With consultation time under constant pressure, simplification ranks among their top three priorities for improving assessment. At the same time, surveyed neurologists—here and in other studies—agree that the current standard, the Expanded Disability Status Scale (EDSS), is too limited on its own.[1] They emphasise the need to augment the EDSS with tools that enable more holistic evaluation, better reflecting the complexity of MS and the full spectrum of disability experienced by people living with the condition.

Person-centred care means one size does not need to fit all

Disability is a complex, multidimensional concept, with clinical manifestations varying both between individuals and within the same person over time. As such, a single outcome measure, or even a simple suite of them, is unlikely to ever fully capture the complete picture of a person's condition. Instead, a more personalised approach is needed, one that aligns the assessment of disability with its specific purpose. This will enable a move away from a one-size-fits-all model towards a person-centred approach. This means selecting or developing tools that are fit-for-purpose rather than attempting to force a single metric to serve multiple, sometimes conflicting, objectives. This philosophy is crucial for both personalised medicine, which requires nuanced

data to tailor interventions, and for a palliative care approach, which shifts the focus from a single measure of disability to a holistic understanding of a person's overall wellbeing. By being more intentional about measurement strategies, health services can ensure that they truly reflect the unique and evolving needs of each individual living with MS.

Technology holds promise, but strong supporting systems are needed to progress

New technologies, from wearable sensors to mobile applications, offer exciting potential to capture a more nuanced and continuous picture of disability. Although these tools can generate a wealth of objective data, their integration into clinical practice and research is a complex process. A strategic approach to implementation, alongside the necessary supporting frameworks, is necessary to ensure that these technologies can be used to make meaningful improvements in patient care. Without a concerted effort to validate, standardise and integrate this new information with existing data streams, there is a risk of increased complexity and fragmentation.

Change is slow, despite significant work across existing initiatives—the momentum needs to be regained

Meaningful change in disability measurement requires careful orchestration of multiple stakeholders while maintaining the continuity necessary for ongoing patient care and research progress. To move beyond the rhetoric, all stakeholders must recognise—and reinvigorate where necessary—the considerable and broad efforts that are underway. Some degree of fragmentation is inevitable, yet coordination and strategic alignment are essential to accelerate progress and avoid duplication of effort.

About this report

Measuring what matters: bridging the gap between disability impact and economic burden in multiple sclerosis is a multi-method research project that addresses a fundamental challenge in multiple sclerosis (MS) care: how health services identify, quantify and respond to disability. Our findings draw from a multi-method assessment: a literature review; interviews with 15 clinicians, researchers, people with MS and policymakers; a quantitative analysis of MS disability burden across seven countries (France, Germany, Italy, Spain, Sweden, the UK and the US); and a survey of 850 neurologists. Our quantification of disability costs expands beyond traditional burden-of-illness studies by incorporating disability-related pension expenditure, productivity losses (unemployment, presenteeism, absenteeism and earning capacity), diagnostic and prodromal costs, and an attempt at a more comprehensive assessment of the economic impact of disability.

Advances in diagnosis, treatment and management mean that today's MS landscape bears little resemblance to that of past decades. Early diagnosis and intervention with disease-modifying therapies have transformed outcomes for many. Yet despite these advances, MS remains incurable, and disabilities continue to compound over time for people living with the condition, creating cascading challenges in every aspect of their lives.

Many of the most debilitating symptoms of MS—cognitive impairment, fatigue, sexual dysfunction and mood changes—remain largely invisible to standard assessment tools yet profoundly shape the daily realities of people living with the condition. This invisibility is not inherent to the symptoms themselves but reflects the limitations of current measurement approaches and of our conversations with people with MS.

Our goal with this paper is to contribute to the growing consensus among clinicians, researchers, people with MS and their advocates calling for reform in how disability is assessed in MS. What is measured shapes what is managed. By evolving the assessment landscape to better reflect the daily reality of living with MS, Economist Impact hopes to help bridge the gap between clinical metrics and lived experience, ultimately ensuring that invisible symptoms are no longer unmeasured and unaddressed.

A note on terminology: we recognise the evolving and sensitive nature of language used to refer to individuals with chronic health conditions. To ensure clarity and respect, this report primarily

refers to affected individuals as "people living with MS". We use "patients" when describing direct clinical care experiences or the therapeutic relationship between individuals and their physicians, and "participants" when referring to individuals in research studies.

The following experts provided their time and insights to this research through interviews. We thank them for their contributions:

- **Kate Durack**, MSIN Director of Communication and Patient Focus, Multiple Sclerosis Association of America, and person with MS, United States
- **Anthony Feinstein**, Professor of Psychiatry, University of Toronto, Canada
- **Peter Feys**, Professor in Rehabilitation Sciences and Physiotherapy, Rehabilitation Research Centre (REVAL), Rehabilitation Sciences, Hasselt University, Belgium
- **Jan Hillert**, Senior Professor in Neurology, Karolinska Institutet, Sweden
- **Jeremy Hobart**, Consultant Neurologist, University Hospitals Plymouth; Professor, Plymouth University Peninsula Schools of Medicine and Dentistry, United Kingdom
- **Elisabeth Kasilingam**, Chief Executive Officer, European Multiple Sclerosis Platform; Vice-President, European Patients' Forum
- **Eva Månsson Lexell**, Registered Occupational Therapist, Associate Professor and Senior Lecturer, Department of Health Sciences, Lund University, Sweden
- **Lydia Makaroff**, Chief Executive, Multiple Sclerosis International Federation
- **José Manuel García-Domínguez**, Neurologist, Hospital General Universitario Gregorio Marañón, Spain
- **Gianvito Martino**, Neurologist and Scientific Director of IRCCS, San Raffaele Hospital; Full Professor of Applied Biology and Vice-Rector for Research and the Third Mission, Vita-Salute San Raffaele University, Italy
- **Jérôme De Sèze**, Professor of Neurology and Head of the Department of Neuroimmunology, Strasbourg University Hospital, France
- **Bari Talente**, Executive Vice President, Advocacy & Healthcare Access, National MS Society, United States
- **Herbert Temmes**, Federal Managing Director, German Multiple Sclerosis Society Federal Association, Germany
- **Raymond Voltz**, Director of the Centre for Palliative Medicine, University Hospital Cologne, Germany
- **Anita Williams**, person living with MS, United States

We would also like to thank the 850 neurologists who provided responses to our survey.

This research was commissioned by Sanofi, but independently conducted by Economist Impact. This programme was led by Amanda Stucke. The research was led by Gerard Dunleavy and Alicia White, with inputs from Emily Tiemann, Jason Yin and Radha Raghupathy. The economic analysis was led by Triangulate Health Ltd, in collaboration with Economist Impact. The neurologists' survey was led by Georgina Lovati. This report was written by Ceilidh Stapelkamp, and edited by Paul Tucker and Gerard Dunleavy.

Economist Impact bears sole responsibility for the content of this report. The findings and views expressed in the report do not necessarily reflect the views of the sponsor or the experts who kindly gave their time to advise us.

Background

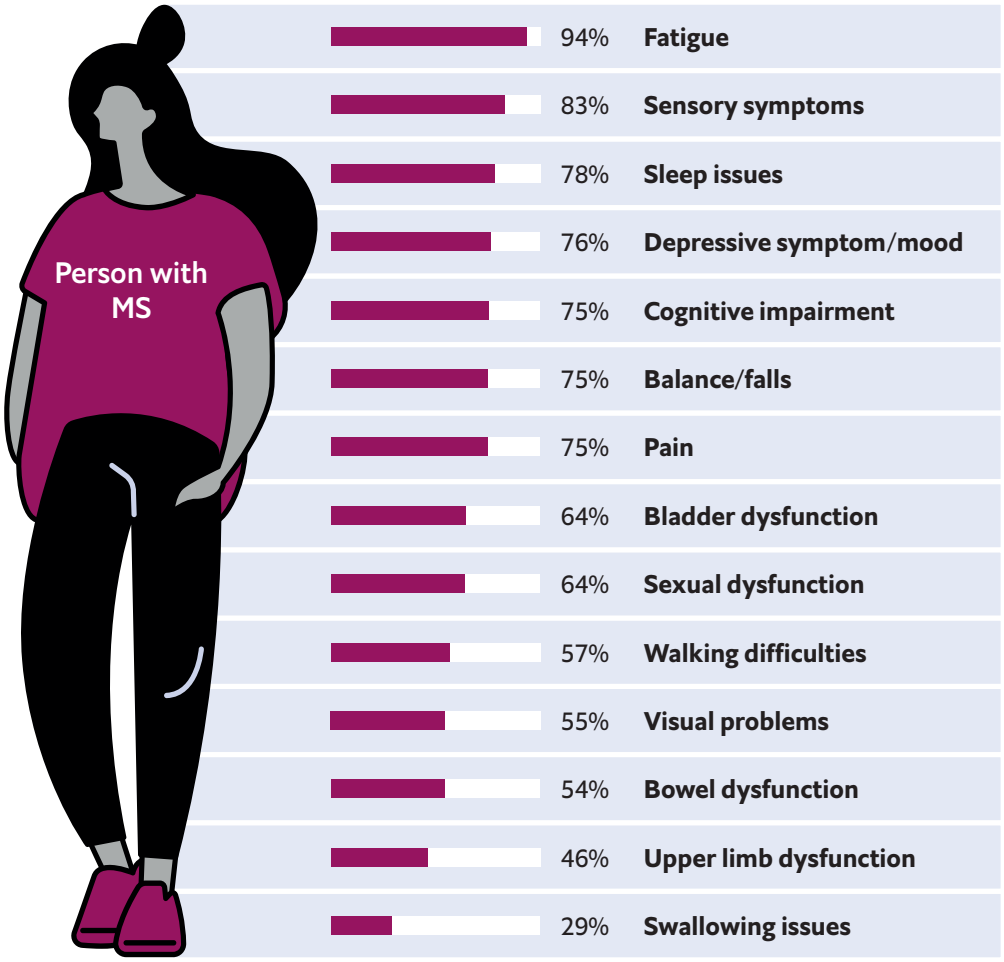
Multiple sclerosis (MS) is a long-lasting (chronic) condition that causes the body's own immune system to attack the protective sheath around the nerves, affecting the brain and spinal cord. The flow of information is then interrupted as the nerves lose their ability to efficiently conduct electrical impulses to and from the brain. This can have many consequences, and the specific symptoms depend on where the inflammation and damage have happened or is happening at any one time.

Traditionally, MS has been classified according to its clinical presentation: relapsing-remitting MS (RRMS) – which is the most common diagnosis[3] – secondary progressive MS (SPMS), and primary progressive MS (PPMS). However, growing insights into the underlying disease biology suggest that these categories do not fully capture the complexity of MS pathophysiology.

Increasingly, MS is recognised as being driven by two interrelated processes – acute and chronic neuroinflammation. Acute neuroinflammation, more prominent in the earlier stages, manifests clinically as relapses and radiologically as MRI lesions. Over time, the disease evolves towards a predominantly progressive biology, characterised by gradual and cumulative disability. Notably, evidence indicates that neuroaxonal damage and subtle progression begin even during the relapsing-onset phase.

MS is a life-long and life-limiting condition, and people living with MS have multidimensional problems and needs that can last for many years. Pain, fatigue and movement and vision problems are common, as are weakness and coordination issues, and trouble with mood, memory and cognition. The recent Impact of Multiple Sclerosis Symptoms (IMSS) survey (IMSS), a study of more than 17,000 people living with MS across 22 countries, confirms just how frequent and impactful the symptoms can be. People living with MS live with multiple, concurrent symptoms, some experiencing up to 14 symptoms at the same time.[2] "Invisible" or "silent" symptoms—fatigue, sensory symptoms, sleep issues and depression, among others—are among the most common (Figure 1). Continuous fatigue was reported in as many as 40% of people.[2]

Figure 1: MS symptoms and prevalence



Source for patient-reported symptoms (sum of responses for France, Germany, Italy and Spain): European Multiple Sclerosis Platform's (EMSP) Impact of Multiple Sclerosis Symptoms (IMSS) survey.[2]

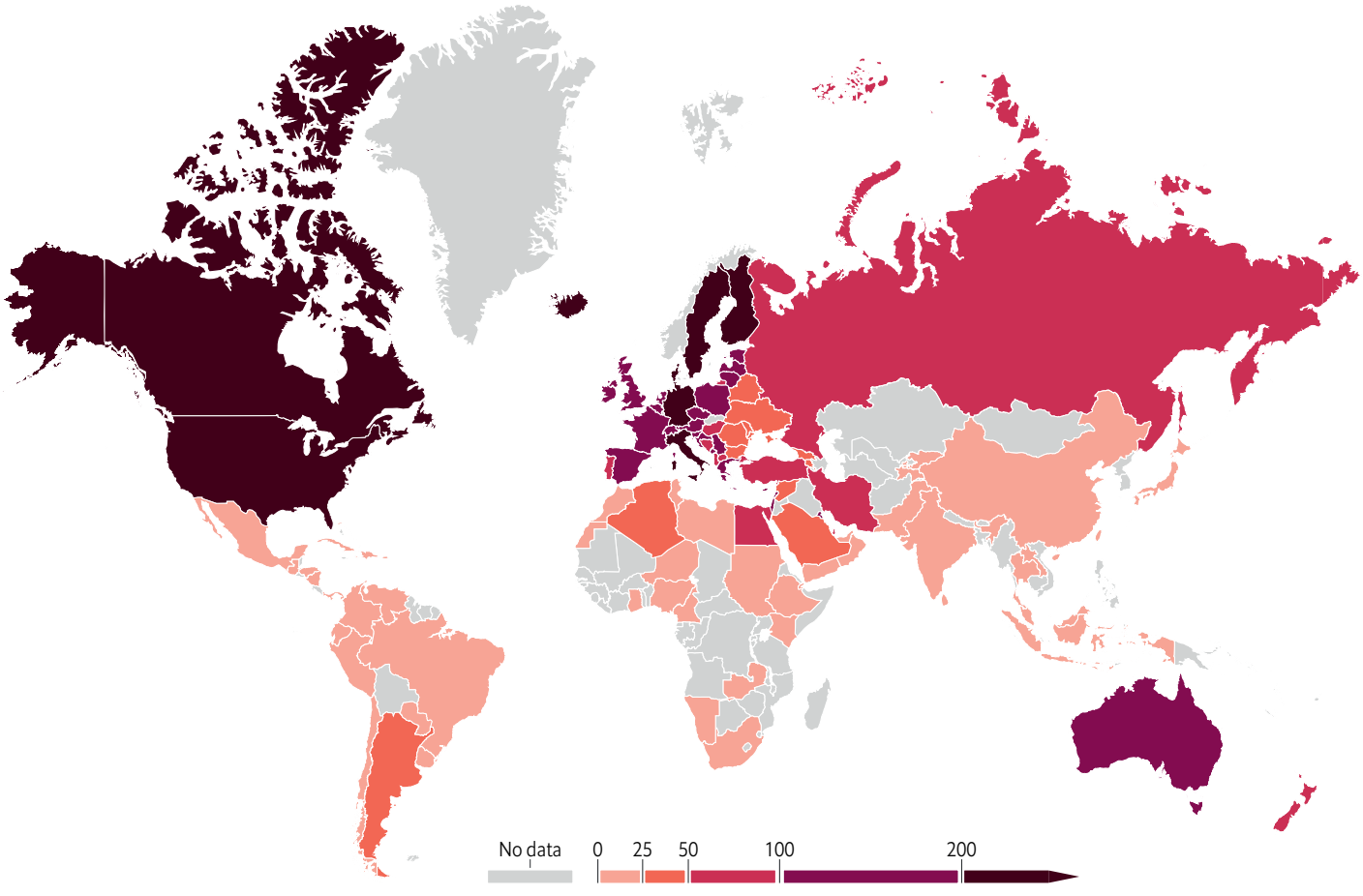
Cognitive impairment, fatigue and depression significantly impact quality of life and are common in the early disease stages.[4] For example, symptoms of cognitive impairment are present in 30-45% of people with relapsing-remitting MS and up to 75% of people with secondary progressive disease.[5] These many and varied neurological symptoms cascade throughout an individual's life. Cognitive difficulties, unpredictable fatigue and invisible pain can quickly lead to financial instability, social isolation and family stress.

The consequences extend well beyond the individual. Unfortunately, these symptoms are often overlooked—not only because they are subjective and hard to measure reliably, but also because they simply are not given the attention they deserve. This neglect is particularly troubling given that these symptoms often prove more disabling to a person's daily life than the more visible motor impairments that traditionally receive clinical focus.

The global picture

The epidemiology of MS is well described. Approximately 3m people worldwide are affected by the disease.[6,7] People of Northern European descent and white people have a higher risk of developing MS, and the lowest prevalence is found in countries near the equator (Figure 2).[6,8] The global average prevalence (2020) is 36 per 100,000 ranging from 5 per 100,000 in the Western Pacific region to 133 per 100,000 in Europe.[7] This is equivalent to 1 person in 3,000 living with MS.

Figure 2: Number of people with MS per 100,000 people



Source: The Multiple Sclerosis International Federation.[5]

Although global prevalence is increasing, the consensus is that this is most likely due to earlier and improved diagnosis, population growth, and longer survival, rather than real increases in risk.[7,9] This thesis is confirmed by data that show declines in the overall rate of new MS cases, suggesting movement towards improved awareness and diagnosis.[6,10] However, the burden is still high—someone is diagnosed with MS somewhere in the world every 5 minutes (pooled average incidence rate of 2.1 per 100,000 population).[7]

A broad range of both genetic and environmental factors increase MS risk, but overall it isn't clear why one person develops the disease and another does not.[8] There is a marked gender disparity: two to three times more women are living with MS than men.[6,9] The condition can manifest at any age, yet 90% of diagnoses occur in individuals aged 18-50 years. These are peak productive years during which most people are building a career, raising a family or actively contributing to society in other ways. Consequently, MS profoundly impacts individuals, their families and society, and is a significant, and growing, global public health issue.[11,12]

Evolving disease landscape and understanding

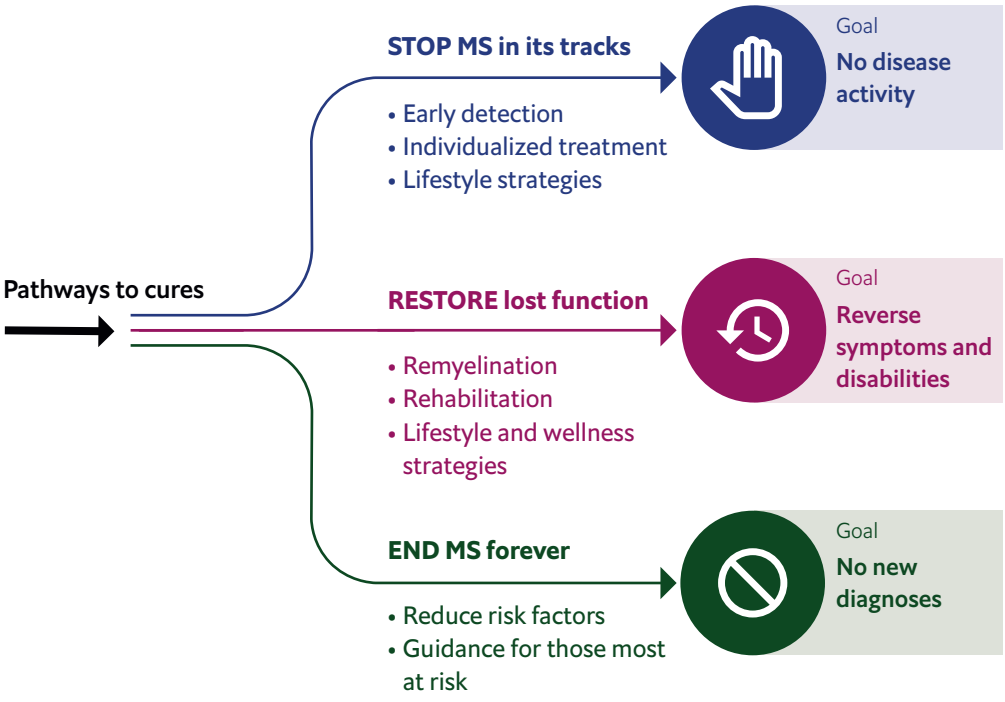
Over the past few decades, the landscape of MS has transformed alongside a growing understanding of the disease's underlying pathology. Significant advancements in the diagnosis, treatment, management and understanding of MS have improved outcomes in the short term. The following are some of the most notable advances that have reshaped patient care in recent decades:

- The McDonald criteria for MS diagnosis—introduced in 2001—integrated clinical, MRI and spinal fluid analyses, enabling earlier detection and establishing a standardised approach. Revisions made in 2024 retain the core framework but broaden the diagnostic pathways, supporting more timely and accurate diagnosis.[13]
- A rapid expansion in the number of available disease-modifying treatments has provided an array of options for patients since the 1990s.
- An increasing understanding of disease pathology has shifted treatment goals from managing relapses to actively preventing disease activity, minimising the accumulation of disability and improving long-term outcomes.

MS is a well-researched disease. One study estimates the value of MS research funded between 2021 and 2023 (by governments and non-profits) at nearly €1.5bn (US$1.74bn) across more than 2,300 active projects.[14] The International Progressive MS Alliance (a global partnership uniting MS advocacy groups, scientific researchers, healthcare providers, pharmaceutical and corporate partners, charitable foundations, and individuals affected by progressive MS) will alone have committed €60m by the end of 2025 towards multiple research initiatives consistent with its strategic priorities. The global collaboration and momentum are coalescing around a singular, ambitious goal—an MS 'cure'. The Pathways to Cure initiative is a global research roadmap with three distinct pathways: stopping the disease, restoring function and ending MS through prevention (Figure 3).[15,16]

Figure 3: Pathways to Cures Roadmap—the global plan to 'stop MS in its tracks'

More than 30 global MS advocacy and professional organisations have committed to a global research strategy to cure MS. The Pathways to Cures Roadmap sets out the guiding principles to describe gaps in understanding, milestones and research priorities. Its specific goals are to (1) promote research in scientific areas with great potential to reveal insights leading to cures and (2) inspire greater coordination of global resources that accelerate scientific progress. There are three pathways through which this can be achieved: (1) The Stop pathway is focused on achieving a state of no new disease activity or CNS injury, (2) the Restore pathway aims to reverse symptoms and recover neurological function, and (3) the End pathway strives to prevent incident cases of MS.[2]



Source: Adapted from Bebo Jr et al.[15]

MS is increasingly managed as a chronic, lifelong condition. This shifts the public health challenge towards providing long-term support and rehabilitation so that people living with MS can function and maintain their independence. The scientific discourse is continuing to evolve too. Subtle, difficult-to-detect deterioration is now acknowledged in recent literature with concepts such as "PIRA" (progression independent of relapse activity), "unrecognised progression" and "smouldering pathological processes" beginning to gain ground as more becomes known about disease pathology.[17]

Amid this significant activity and increasing knowledge, the true measure of progress is whether healthcare systems effectively apply these advancements to improve the day-to-day care and quality of life for people living with MS. Significant, insidious worsening can begin early in the disease journey, and it is currently going unnoticed by conventional metrics.

Significant needs remain

Globally, inequities in service provision, early diagnosis and access to disease-modifying treatments (DMTs) persist, impacting people living with MS significantly. A European survey revealed that although seven in ten people living with MS are currently using DMTs, most faced waits exceeding a year to start treatment.[2] The MS Barometer survey conducted by the European Multiple Sclerosis Platform (EMSP), which covers 35 European countries, highlights critical gaps in healthcare and social support, with only 48% of people living with MS having access to physical rehabilitation and even fewer receiving cognitive, psychological or occupational support.[18] Notably, no country reported rehabilitation access of more than 50% among people living with MS, and workforce imbalances across Europe challenge the delivery of optimal multidisciplinary care.[18] The estimated case load per core MS specialist (neurologist or MS nurse) is variable across the seven countries of interest in our study (Table 1).

Caseloads per neurologist and MS nurse vary widely among countries, influencing the quality and accessibility of care. Many people living with MS express dissatisfaction, citing lack of essential services such as physiotherapy and psychological support, with one-third of UK respondents reporting unmet needs for daily living support.[19] Symptomatic care is less prioritised than DMTs at governmental levels, reflected in lower availability and reimbursement. This failure to address the multifaceted symptoms of MS underscores systemic barriers—from limited measurement tools and clinical time constraints to an entrenched medical model—that overlook the full burden of disability.[18]

Table 1: Estimated case load—people living with MS (PwMS) per neurologist and MS nurse[20]

	PwMS/ neurologist	PwMS/ MS nurse
France	333	416
Germany	504	315
Italy	182	364
Sweden	543	362
Spain	275	275
United Kingdom	153	379
United States	153	416

Through this report, Economist Impact seeks to develop a better understanding of disability in MS and the potential reasons for the blind spots in clinical practice. We gathered experts' views through interviews and a structured survey of 850 neurologists. We also quantified the burden of MS across seven countries (France, Germany, Italy, Sweden, Spain, the UK and the US), taking a broad approach to the inclusion of disability-related expenditure. Our approach aggregates specific, individual-level factors—including out-of-pocket expenses and caregiver costs—to provide a more comprehensive understanding of the extensive economic burden across multiple systems.

BRIEF OVERVIEW OF THE RESEARCH PROCESS

There were four stages to our research:

- **Stage 1:** An in-depth literature review.
- **Stage 2:** Establishment of the healthcare professional perspective through interviews with 15 MS experts.
- **Stage 3:** Profiling the disability measurement landscape through a survey of 850 neurologists. The full list of survey questions and response options is detailed in Appendix B.
- **Stage 4:** Quantitative analysis of MS disease and disability burden across seven countries. The methods for the economic analysis are described in Appendix A.

Consequences and impact of MS disability

Growing MS burden despite meaningful progress

MS is a substantial public health issue, particularly in high-income regions such as North America and Western Europe, where its prevalence is highest.[21] In 2016, MS ranked 14th in a global study of age-standardised DALY* rates for all neurological disorders by region, contributing significantly to years lived with disability and years of life lost due to premature mortality.[22]

The landscape of MS is changing. Recent assessments of long-term data find that while the total burden—the absolute number of DALYs attributable to MS—is increasing, there is a reduction in the DALY rate.[9,21,23] The DALY rate is a measure of the number of years of healthy life that a community loses due to disease or premature death (usually expressed per 100,000 people). The improvement in the DALY rate may reflect how therapeutic and management advancements are translating into tangible reductions in overall disease burden. However, the pattern is far from consistent across regions, and MS remains a significant contributor to the burden of neurological disease[9,21,23] Of most relevance to this analysis, morbidity—years lived in disability—makes a larger contribution to overall disease burden than years of life lost.[24,25] This is important because, given the limited lens through which disability in MS is being defined, we may only be capturing a fraction of morbidity's true impact and risk significantly underestimating the full consequences of the condition.

Given the limited lens through which disability in MS is being defined, we may only be capturing a fraction of morbidity's true impact and risk significantly underestimating the full consequences of the condition.

* A disability-adjusted life year (DALY) is a measure based on years of life lost from premature death and years of life lived in less than full health. A disability-adjusted life year (DALY) is a measure based on years of life lost from premature death and years of life lived in less than full health.

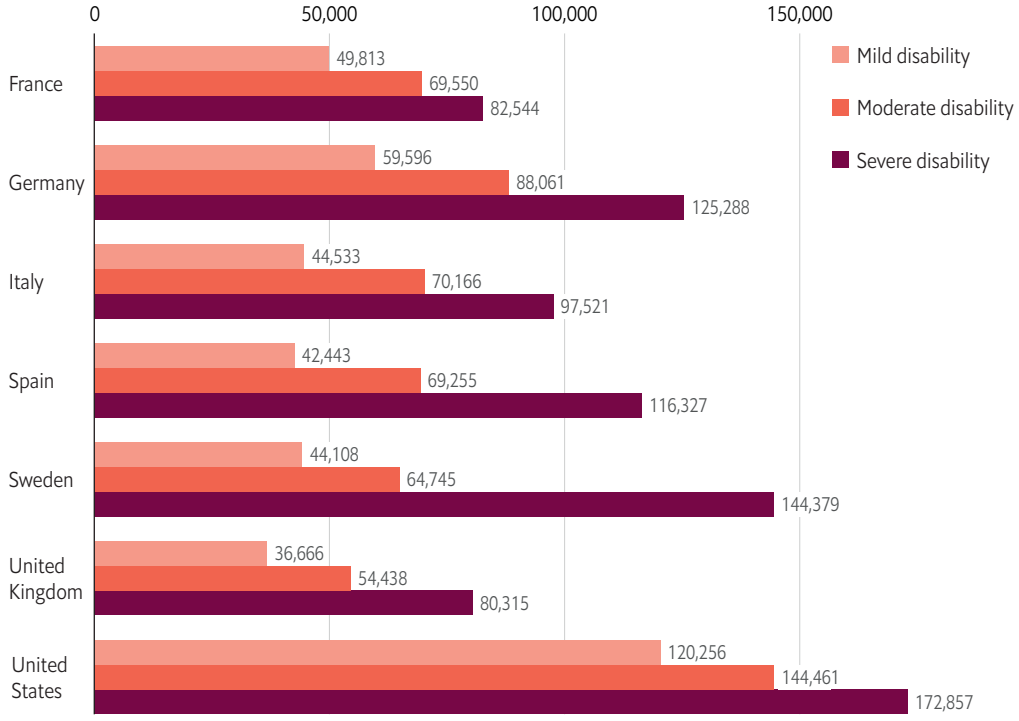
A broader perspective on economic burden

Most burden of illness studies in MS include direct healthcare expenses, such as DMTs, outpatient care, hospitalisations and pharmacy use. However, fewer report costs related to primary or community services, diagnosis, end-of-life care, and rehabilitation services. When it comes to indirect costs, absenteeism is frequently described, while income loss, presenteeism, disability allowances or illness benefits, and childcare expenses, are mentioned far less often. This indicates a gap in understanding the full economic impact of MS. Our burden of illness modelling attempted to close this gap by including prodromal and diagnostic costs, productivity losses (unemployment, presenteeism, absenteeism and earning capacity), and disability insurance (see Appendix A). In this section, we discuss the results of this economic analysis, grouping the findings by key themes across and within the countries of interest.

The annual economic burden of MS exceeds per capita GDP

The economic burden of MS is substantial. In 2025, the average annual costs (irrespective of severity) were US$57,140 in the UK and US$145,857 in the US. When stratifying by disability severity, the annual economic burden for people living with MS with severe disability in Germany, Italy, Sweden and the UK is more than twice the burden for those with mild disability (see Figure 4). The annual economic burden of MS-related disability exceeds per capita GDP in each of the modelled countries.[26]

Figure 4: Annual economic burden by disability severity level (per person with MS, US$)

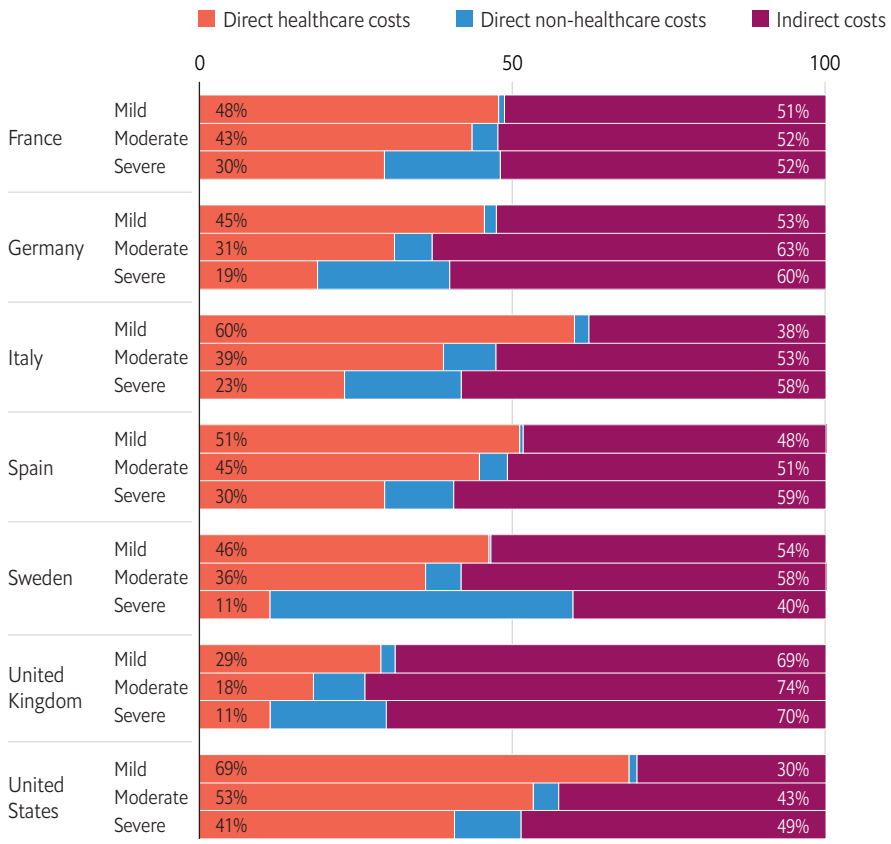


Source: Economist Impact.

Non-healthcare costs dominate as disability becomes more severe

Across all countries, there is a consistent shift in the composition of MS-related costs as disability worsens (Figure 5). For people living with MS with mild disability, direct healthcare costs—mainly drug expenses and inpatient care—represent the largest share of the economic burden in the majority of countries. However, as MS advances the cost profile shifts significantly, with indirect costs such as lost productivity and informal caregiving becoming the dominant expense. In addition, direct non-healthcare costs—such as home and vehicle modifications—increase substantially, growing from an average of just 1% of total costs in people living with MS with mild disability to nearly 25% in those with severe disability. This evolving cost distribution underscores how advancing disability broadens the financial impact far beyond healthcare alone.

Figure 5: Proportion of direct and indirect costs as a % of total costs (per person with MS, by disability severity level)

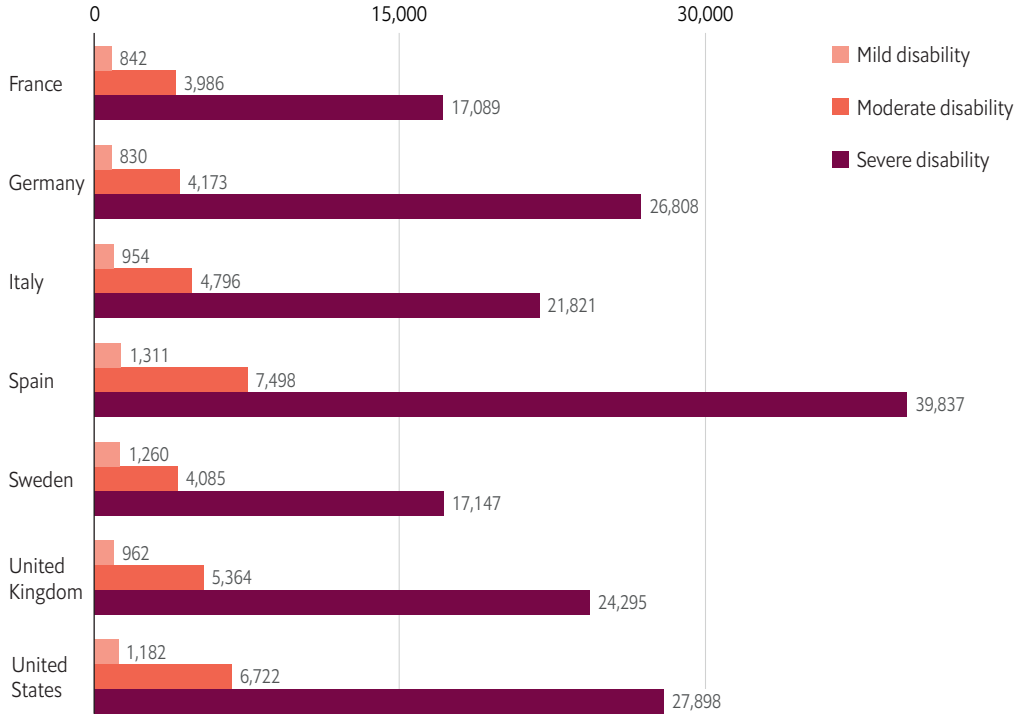


Source: Economist Impact.

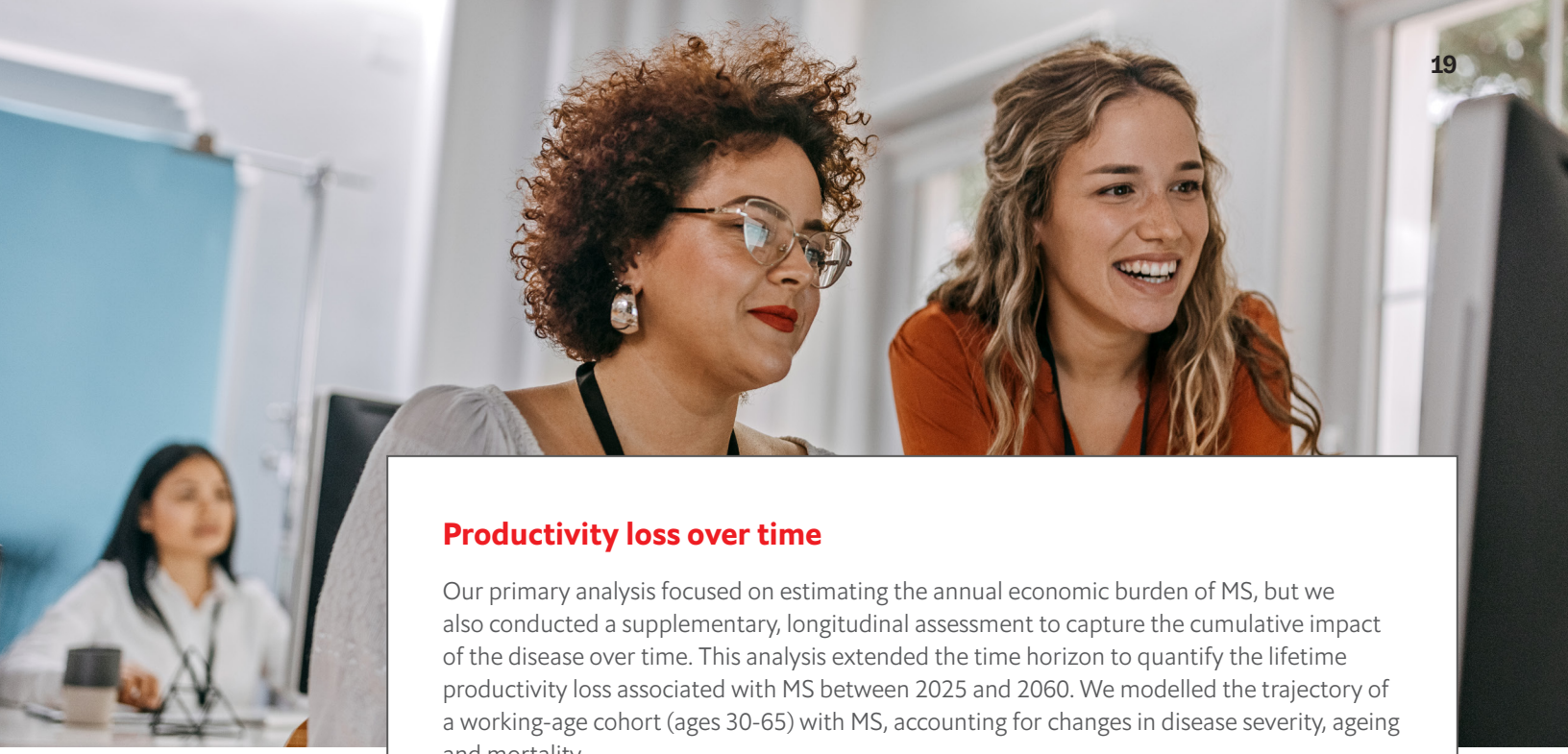
The burden on caregivers is substantial, but often overlooked

Neurologists estimate that approximately 82% of people living with MS with severe disability require support from an informal caregiver, typically an unpaid family member, highlighting the substantial caregiving demands associated with advanced disease. Caregiving for people living with MS often involves assisting with daily tasks such as dressing and bathing, as well as mobility support, like transferring from a bed to a wheelchair. Caregivers also manage medication schedules, accompany patients to medical appointments, help with household tasks like cooking and cleaning, and provide emotional support to address the psychological challenges of living with MS. Even among those with mild disability, about 1 in 5 (21%) need informal care. Our burden of illness analysis reveals that time spent caregiving leads to significant productivity losses for caregivers (Figure 6). Importantly, caregiver-related costs escalate alongside disease severity, underscoring the growing social and economic impact of MS progression on both patients and their families.

Figure 6: Annual economic burden in terms of productivity losses for caregivers (per person with MS, by disability severity level, US$)



Source: Economist Impact.



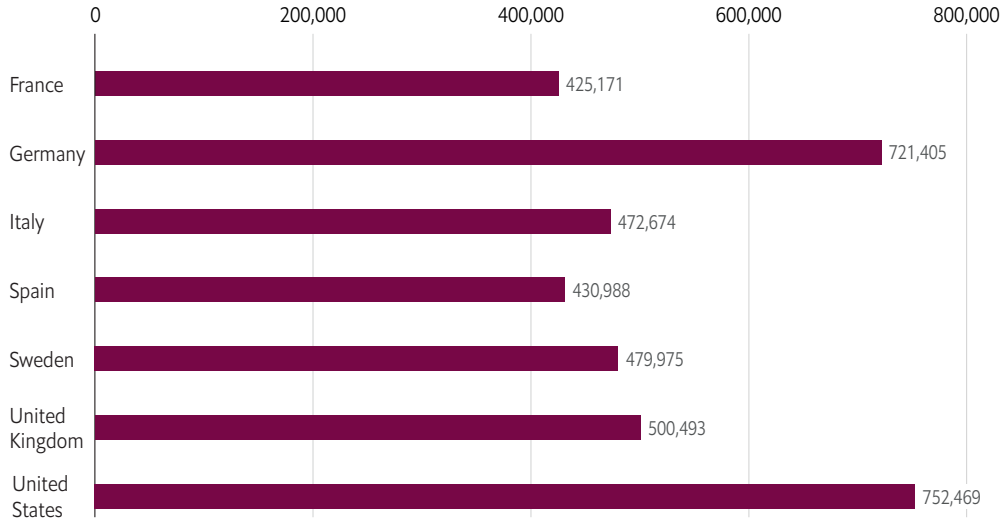
Productivity loss over time

Our primary analysis focused on estimating the annual economic burden of MS, but we also conducted a supplementary, longitudinal assessment to capture the cumulative impact of the disease over time. This analysis extended the time horizon to quantify the lifetime productivity loss associated with MS between 2025 and 2060. We modelled the trajectory of a working-age cohort (ages 30-65) with MS, accounting for changes in disease severity, ageing and mortality.

By integrating these dynamic population movements with cost estimates stratified by disability level, we calculated the total indirect costs linked to productivity loss over a lifetime. Our projections reveal a significant economic toll: the average lifetime productivity loss for an individual developing MS at age 30 ranges from US$425,171 in France to US$752,469 in the US.

These findings highlight the substantial and enduring impact of MS on workforce participation and economic productivity. The scale of the lifetime productivity loss not only underscores the personal and societal burden of MS; it also reinforces the critical importance of timely intervention, comprehensive care, and effective policy solutions aimed at preserving workforce engagement and supporting those affected throughout their working years.

Figure 7: Productivity loss between the age of 30-65 years (per person with MS, US$)

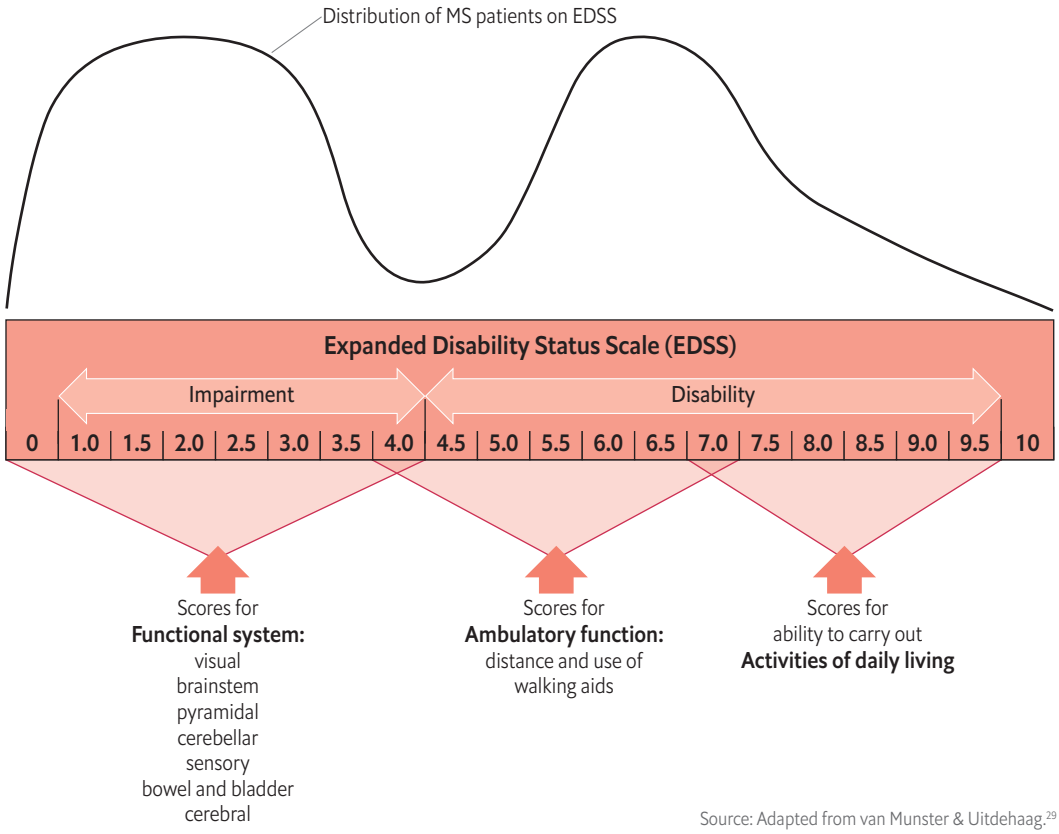


Source: Economist Impact.

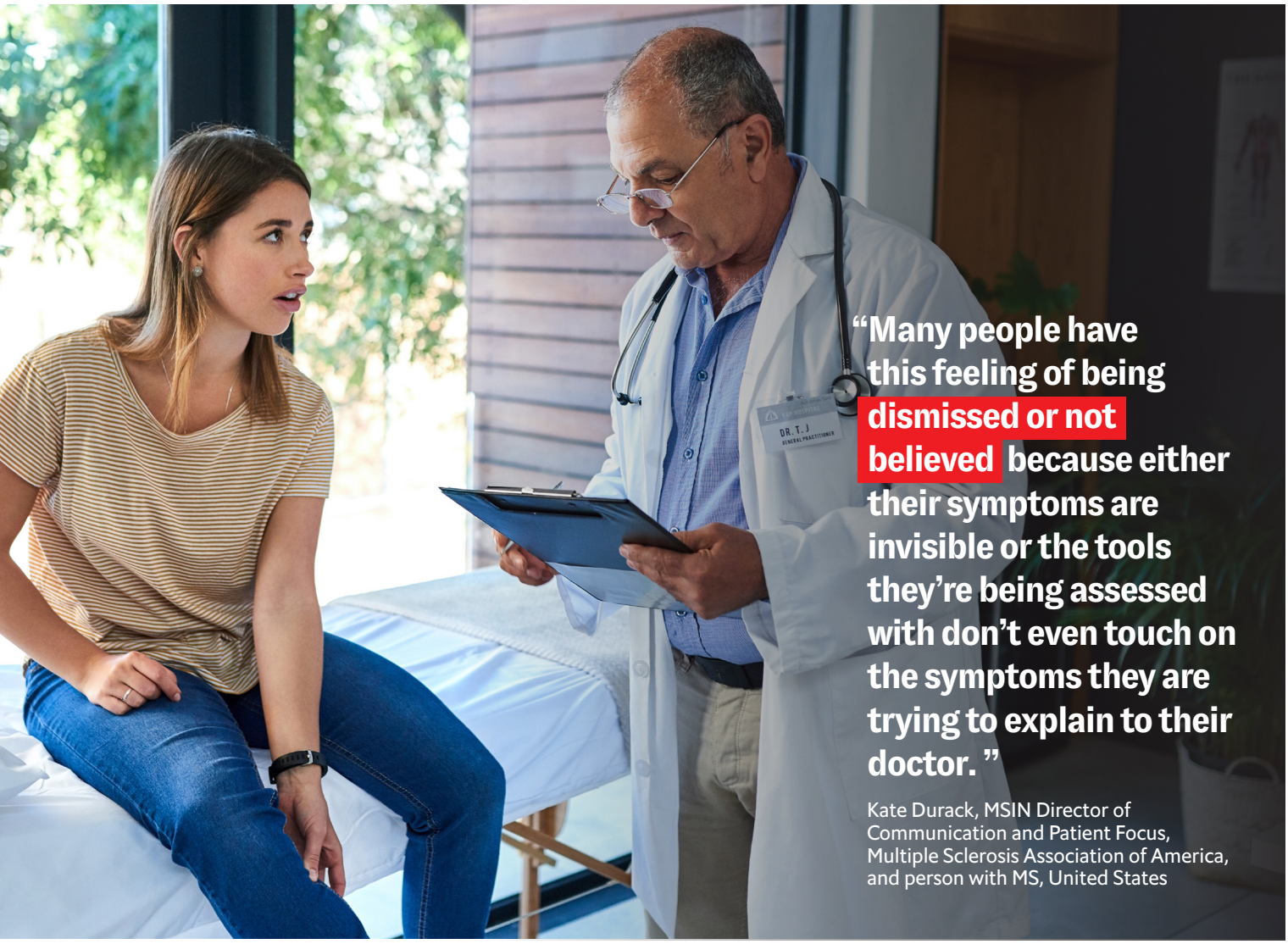
Commonly used disability scales do not provide holistic assessments and lack sensitivity

The Expanded Disability Status Scale (EDSS) remains the most widely used measure for assessing disability in MS research and clinical practice worldwide.[27] Originally developed by neurologist John Kurtzke in 1983 to evaluate neurological impairment across eight functional systems, the EDSS provides a standardised framework for stratifying disease severity, ranging from 0 (no disability) to 10 (death due to MS).[28] Traditionally focused on physical disability—particularly ambulatory function—it correlates disability severity with treatment and care costs. However, growing evidence highlights significant blind spots: the EDSS overlooks cognitive, emotional and social aspects of MS, and its scoring is nonlinear, with reduced sensitivity at higher disability levels.[27,29-33] Kate Durack, the MSIN director of communication and patient focus of the Multiple Sclerosis Association of America, who lives with MS, voices a common frustration: "Many people have this feeling of being dismissed or not believed because either their symptoms are invisible or the tools they're being assessed with don't even touch on the symptoms they are trying to explain to their doctor." Lydia Makaroff, CEO of the Multiple Sclerosis International Federation, underscores the challenge, noting that invisible symptoms like fatigue, cognitive fog and stress "are very difficult to measure … and there's a lack of consensus even on how to measure disability."

Figure 8: Factors determining EDSS score and distribution of scores [33]



Source: Adapted from van Munster & Uitdehaag.[29]



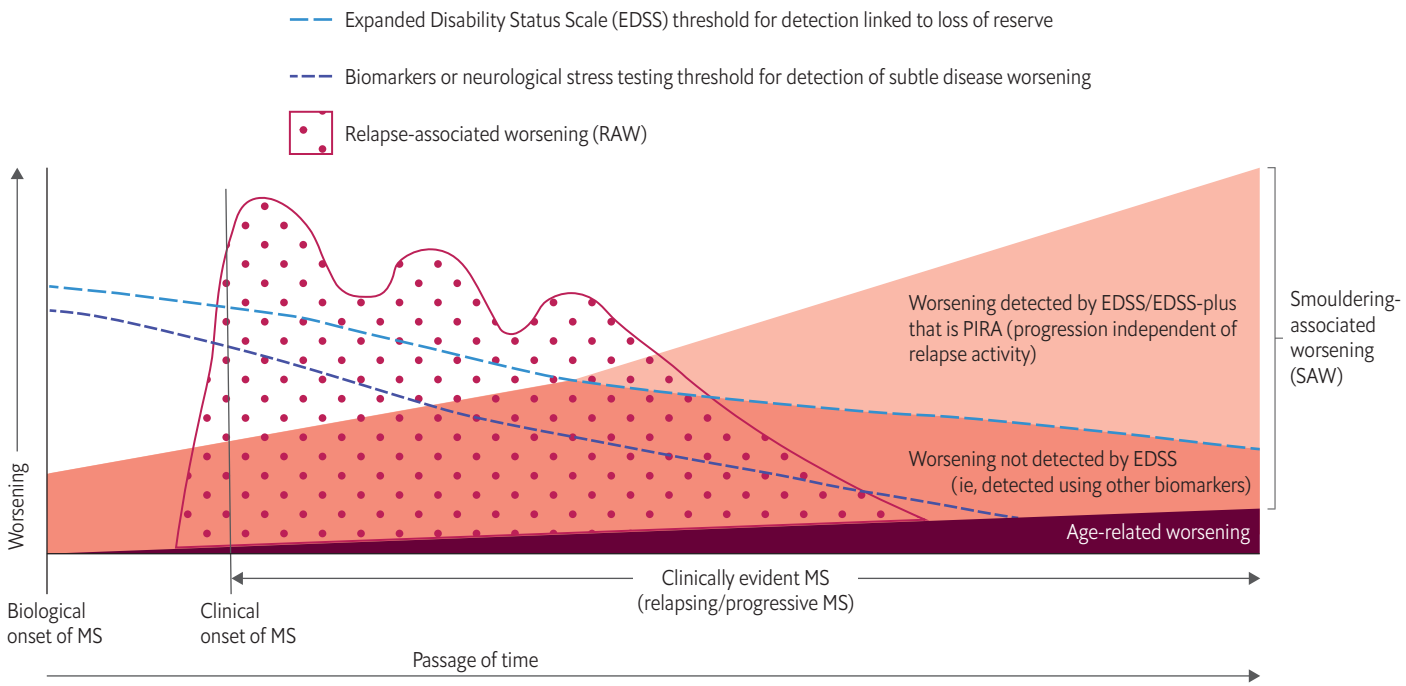
Although the EDSS may still serve as a useful communication tool among clinicians—“If I’m meeting someone with an EDSS of 6, I know what to expect in my practice,” explains Jeremy Hobart, a consultant neurologist at University Hospitals Plymouth in the UK—it is less effective for tracking gradual disability progression characteristic of progressive MS.[34,35,36] “We need to use assessments that also measure daily tasks and the activities that you engage in during a whole day,” says Eva Månsson Lexell, a registered occupational therapist and associate professor in the Department of Health Sciences at Lund University, Sweden. This approach provides a broader and more patient-centred view of disability. The expanding understanding of MS necessitates revisiting how disability is measured to ensure assessments capture the full lived experience and inform better care and research.

The contemporary discourse around smouldering-associated worsening (SAW) in MS brings the

issue to the foreground. SAW is an umbrella term to describe worsening that occurs outside of the acute neuroinflammation that can lead to relapses and/or MRI lesions, where functional change can occur due to a wide range of often subtle worsening symptoms, "a relentless accumulation" primarily driven by ***chronic*** neuroinflammation.[17]

Scalfari et al's (2024) depiction of the accumulation of disability in MS highlights that a more granular assessment is needed to capture subtle and often invisible aspects of disability that aren't picked up by the EDSS (Figure 9).[17] Researchers and clinicians have the option of a variety of alternative instruments that may offer a more complete perspective, particularly when used in combination (Table 2). "In the last years, we've been developing several other ways of measuring disability, and if you put all of those measures together, you can have a quite decent figure of the real situation," says Gianvito Martino, a neurologist and Scientific Director of IRCCS San Raffaele, a university hospital in Italy. "There are a lot of them. It seems that a combination of all of them could be a reliable way of measuring real disability." For example, a composite endpoint EDSS-Plus (EDSS + T25FW + 9HPT[†]), for example, has been shown to be better than EDSS alone for detecting disease progression in secondary progressive MS.[17,37] Is it time to move beyond the EDSS?[38]

Figure 9: Domains of disability accumulation in MS



Source: Adapted from Scalfari et al.[17]

[†] T25FW, Timed 25-foot Walk; 9HPT, Nine Hole Peg Test

Table 2: Other MS disability assessment instruments

Expanded Disability Status Scale-Plus (EDSS-Plus)[37]	An enhanced version of the traditional EDSS that incorporates additional data, such as walking speed and cognitive function
Patient Reported Expanded Disability Status Scale (PR-EDSS)[39]	A patient-reported version of the EDSS that allows individuals to self-assess their level of disability, offering a patient's perspective on their functional status
Overall Disability Response Score (ODRS)[40]	A composite endpoint including EDSS, Timed 25-foot Walk and 9-Hole Peg Test
Multiple Sclerosis Functional Composite (MSFC)[41]	A multidimensional assessment tool that measures three key areas of function: walking speed (Timed 25-Foot Walk), arm and hand function (9-Hole Peg Test), and cognitive processing speed (either with Paced Auditory Serial Addition Test or Symbol Digit Modalities Test)
Multiple Sclerosis Clinical Outcome Assessment (MSCOA)[42]	A collection of four performance-based measures (Timed 25-Foot Walk, 9-Hole Peg Test, Low Contrast Letter Acuity and Symbol Digit Modalities Test)
Multiple Sclerosis Performance Test (MSPT)[43]	An iPad-based battery of tests designed to measure aspects of physical and cognitive function, including walking, dexterity and cognition
Multiple Sclerosis Severity Score (MSSS)[44]	A measure that adjusts a person's EDSS score based on the duration of their disease
Patient Determined Disease Steps (PDDS) scale[45]	A patient-reported scale allowing a person to describe their level of disability by choosing from 12 distinct steps
WHO Disability Assessment Schedule 2.0 (WHODAS 2.0)	A generic tool assessing functioning across six domains of life (understanding and communicating, getting around, self-care, getting along with people, life activities, and participation in society), providing a global measure that is not specific to MS

The true burden of MS is not fully captured

Our understanding of the economic and humanistic burden of disability in MS comes from burden of illness studies, such as the one we conducted above. The clinical relevance and well-established severity cut-offs of the EDSS do provide a way to stratify study participants.

Unfortunately, due to the perpetuation of the EDSS's limitations in existing research, it is likely that cost drivers and relevant expenses are inadvertently excluded. People living with MS with significant cognitive impairment, severe fatigue or sexual dysfunction may have low EDSS scores despite experiencing substantial functional limitations. When researchers conceptualise disability primarily through the EDSS lens, they may be less likely to calculate burden inclusive of costs associated with cognitive rehabilitation, fatigue management interventions, workplace accommodations for invisible symptoms or mental health services. This narrow framing of what constitutes "disability-related costs" can lead to systematic underestimation of economic burden, as expenses tied to non-motor disabilities may be overlooked entirely.

There are alternative ways to stratify for disability. For example, Wasem et al (2024) were able to assign costs to each 1-scale-step worsening on

several complementary disability scales—SDMT, MFIS-5, 9HPT, and T25FW.[‡,46] Given that in some cases these instruments have shown advantages over EDSS, there is value in refining the standard approaches.

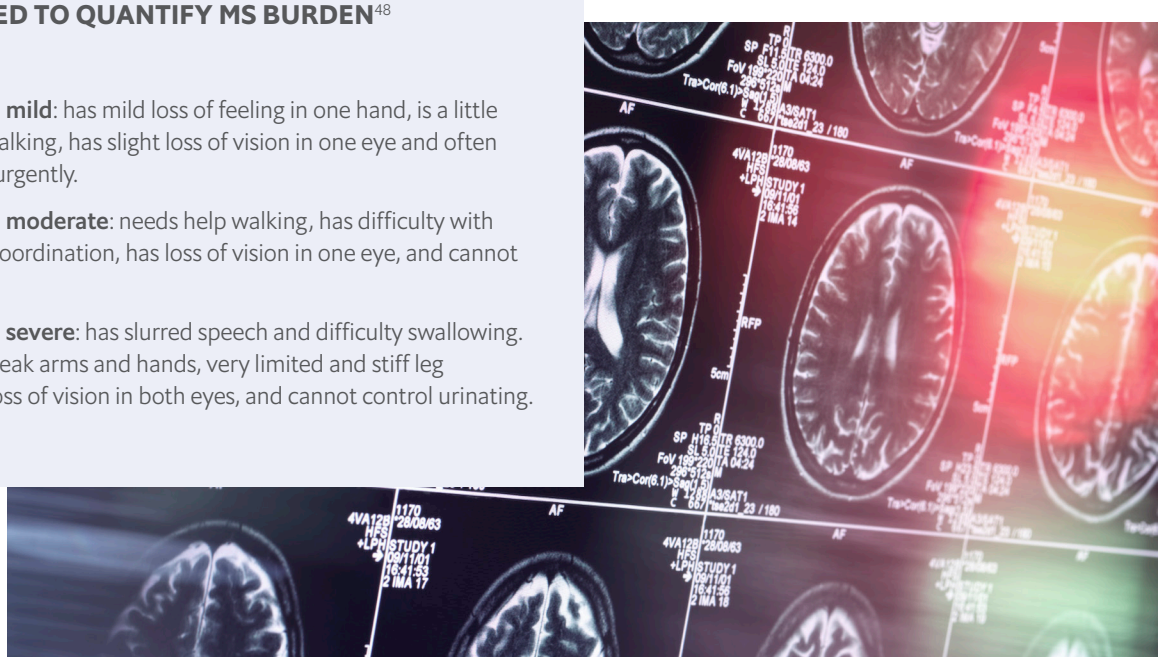
The Global Burden of Disease (GBD) study's approach to quantifying MS disability also reveals limitations in how neurological impairment is conceptualised and measured. To calculate years lived with disability (a component of the DALY estimate), the GBD needs an understanding of how society 'values' different states of health. It achieves this by conducting large-scale surveys where respondents compare a brief, lay description of symptoms and functional consequences with other versions.[47] These descriptions of MS severity and the way they are ranked, aim to capture societal preferences, but their scope is remarkably narrow.

The GBD descriptions focus predominantly on visible, physical manifestations, omitting cognitive impairment, fatigue, pain, depression and other invisible symptoms that can profoundly impact quality of life and functional capacity. By reducing the complex, heterogeneous experience of MS disability to these simplistic physical descriptors, the GBD methodology may also be systematically underestimating the true burden of the disease.

This overly narrow lens is not confined to cost-of-illness studies. It is a critical consideration for all stakeholders in MS care and research. The assessment of disability is a foundational component of routine clinical practice, informing treatment decisions, monitoring disease progression and shaping the patient's own understanding of their condition. It is therefore relevant to explore how different definitions and measurement tools are applied and interpreted, and the extent to which they succeed or fail at capturing the full, multifaceted reality of living with MS.

THE GBD'S THREE-TIER CLASSIFICATION OF MS DISABILITY USED TO QUANTIFY MS BURDEN[48]

- Multiple sclerosis, **mild**: has mild loss of feeling in one hand, is a little unsteady while walking, has slight loss of vision in one eye and often needs to urinate urgently.
- Multiple sclerosis, **moderate**: needs help walking, has difficulty with writing and arm coordination, has loss of vision in one eye, and cannot control urinating.
- Multiple sclerosis, **severe**: has slurred speech and difficulty swallowing. The person has weak arms and hands, very limited and stiff leg movement, has loss of vision in both eyes, and cannot control urinating.

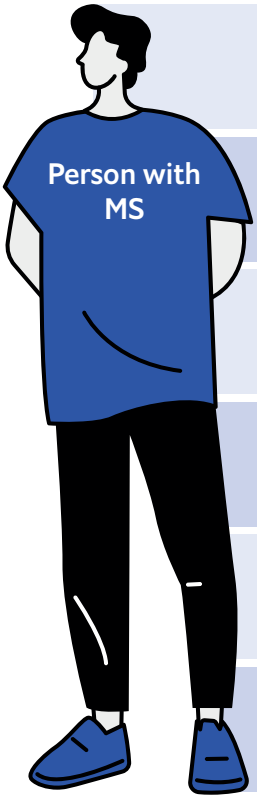


‡ SDMT, Symbol Digit Modalities Test; MFIS-5, 5-item Modified Fatigue Impact Scale

Varied perspectives on what to measure and why

Disability or disease severity require measuring for a range of different reasons. A physician needs to track their patient's health and monitor disease progression, while a payer may use such measurements to decide if they will reimburse a treatment. Meanwhile, researchers need a standard measure across time, geographies and studies to compare treatments with one another and to monitor shifts in disease course. Governments and other organisations may use a measure of disability to determine who gets disability benefits or access to other critical support. This interconnected web of different purposes (Figure 10) makes the simplicity of a single, objective tool very appealing. Yet disability is a complex and multidimensional concept, not a simple, single parameter. Its various facets—physical, cognitive and psychosocial—rarely progress in a uniform manner and often have highly subjective consequences for individuals. Daily symptoms are not even predictable for the people experiencing them. "I don't know that there's a tool that is comprehensive enough to reflect the wide range of experiences among people living with MS," says Ms Durack. "It's unclear how to capture how fickle MS can be."

Figure 10: The many stakeholders and reasons to understand and measure disability



Doctor	Assessments should reflect lived experience, functional independence, response to treatment and quality of life-priorities that matter most to individuals
Regulators and payer	Tools should allow fair decision-making about treatment benefit, access and reimbursement
Social / community services	Services need a measure of a person's individualised needs to tailor their interventions
Researcher	Need to ensure stratification of populations, comparability, benchmarking, efficacy, and generalisability of data
Policymaker	Need to determine disease burden, epidemiology and broad needs to shape health policy
Patient advocacy	Advocates need to understand the full spectrum of needs for a person with MS so their advocacy can be comprehensive

Source: Economist Impact.

The clinical course of MS is highly variable and there is no uniform concept of disability. Disability often accumulates slowly and over time, and it may be difficult to parse the effects of the disease and the effects of treatment, for example. The extent to which individual symptoms are contributing to overall disability is unclear, and many symptoms have no objective measure, such as fatigue and pain. This variability and subjectivity present a key challenge to measurement with which existing approaches in research and clinical practice struggle, relying instead on what is most objective and easily observed, such as physical mobility. This leaves a significant portion of the lived reality of MS uncaptured and unacknowledged, creating a gap between the daily struggles of people living with MS and what is 'visible' to their healthcare and support systems.

"The best tool we can use is our ears, to listen to a person with MS. It is critical to discuss and understand how the condition truly impacts their daily life."

Jérôme De Sèze, professor of neurology and head of neuroimmunology, University Hospital of Strasbourg.

The real-world clinical experience

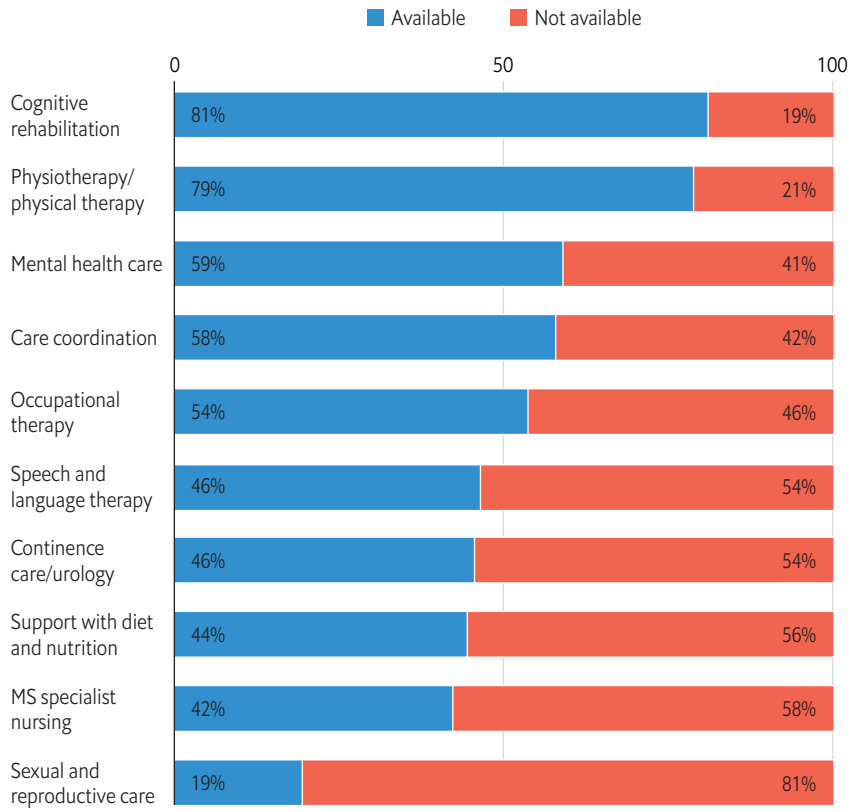
Our survey of 850 neurologists across multiple countries captures the real-world perspective. The aim was to bridge the gap between theoretical discussions of challenges in disability measurement and the practical realities faced by clinicians in their daily management of people living with MS. The findings offer key insights into current clinical practice and attitudes and are grouped by theme.

There are significant gaps in support from multidisciplinary teams

There are significant gaps in access to multidisciplinary care and effective care coordination for people living with MS across different countries, creating major barriers to managing the complex disabilities associated with the disease. Anita Williams, a person living with MS in the US highlights the challenge of a holistic approach if MDTs are lacking in key areas. "I feel like, as an MS patient, there is not the holistic approach," she says. "A lot of what I'm hearing from the MS healthcare community is that we want to treat the whole patient, but in many cases I'm not seeing this whole-patient approach."

Many people living with MS face fragmented care pathways with limited access not only to DMTs but also to essential support services including rehabilitation, psychological care, continence management and assistance with daily living. Moreover, only 19% of multidisciplinary MS care teams provide access to sexual and reproductive health services, despite many people living with MS being diagnosed during their prime reproductive years (Figure 11). Jan Hillert, senior professor in Neurology at Karolinska Institutet in Sweden, further underscores these systemic shortcomings. "When progression becomes more evident, there are lots of things that we don't do as well as we should," he says. "MS affects so many different bodily functions; we need a network of clinicians and nurses, physiotherapists, occupational therapists, counsellors, psychologists etc., and that kind of service is not as developed as it should be." Addressing these persistent gaps is crucial for delivering truly patient-centred, holistic care that improves outcomes and quality of life.

Figure 11: Overall access to multidisciplinary services (all countries combined)



Source: Economist Impact.

Many of the most impactful symptoms are not being routinely assessed

People living with MS experience a broad spectrum of symptoms, ranging from fatigue, pain and mobility difficulties to vision, cognitive and emotional challenges. These symptoms differ in severity and progression between individuals. Estimates suggest that people living with MS experience an average of 14 symptoms,[2] yet many of the most impactful symptoms in daily life are not routinely assessed (Figure 12).

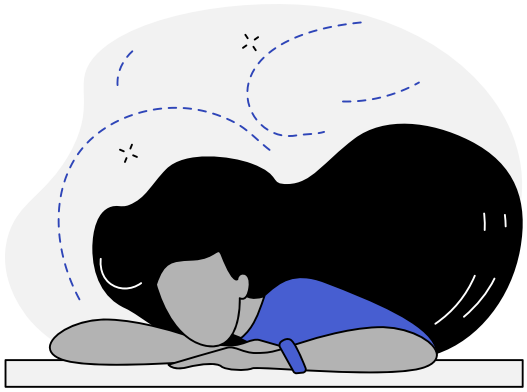
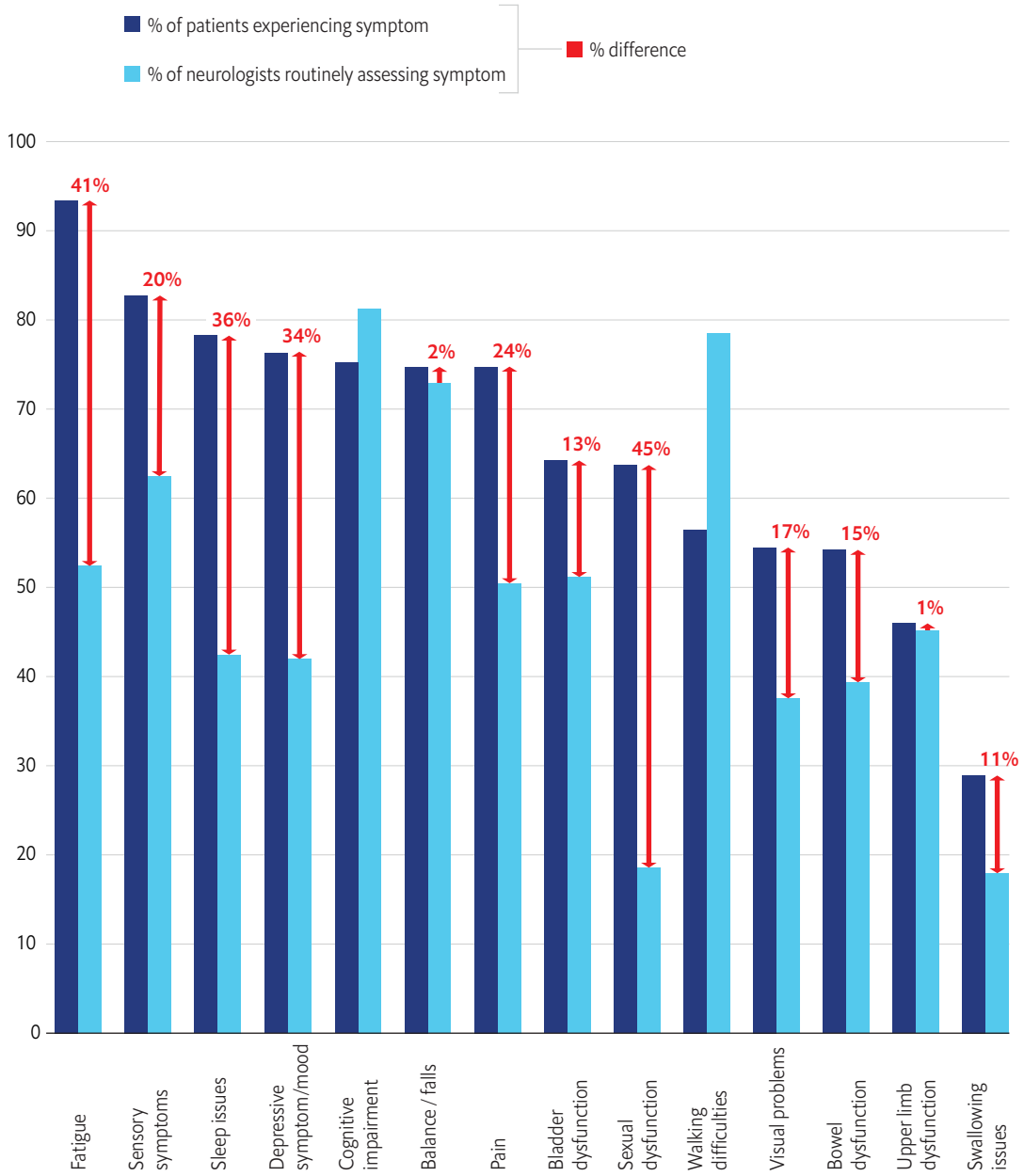


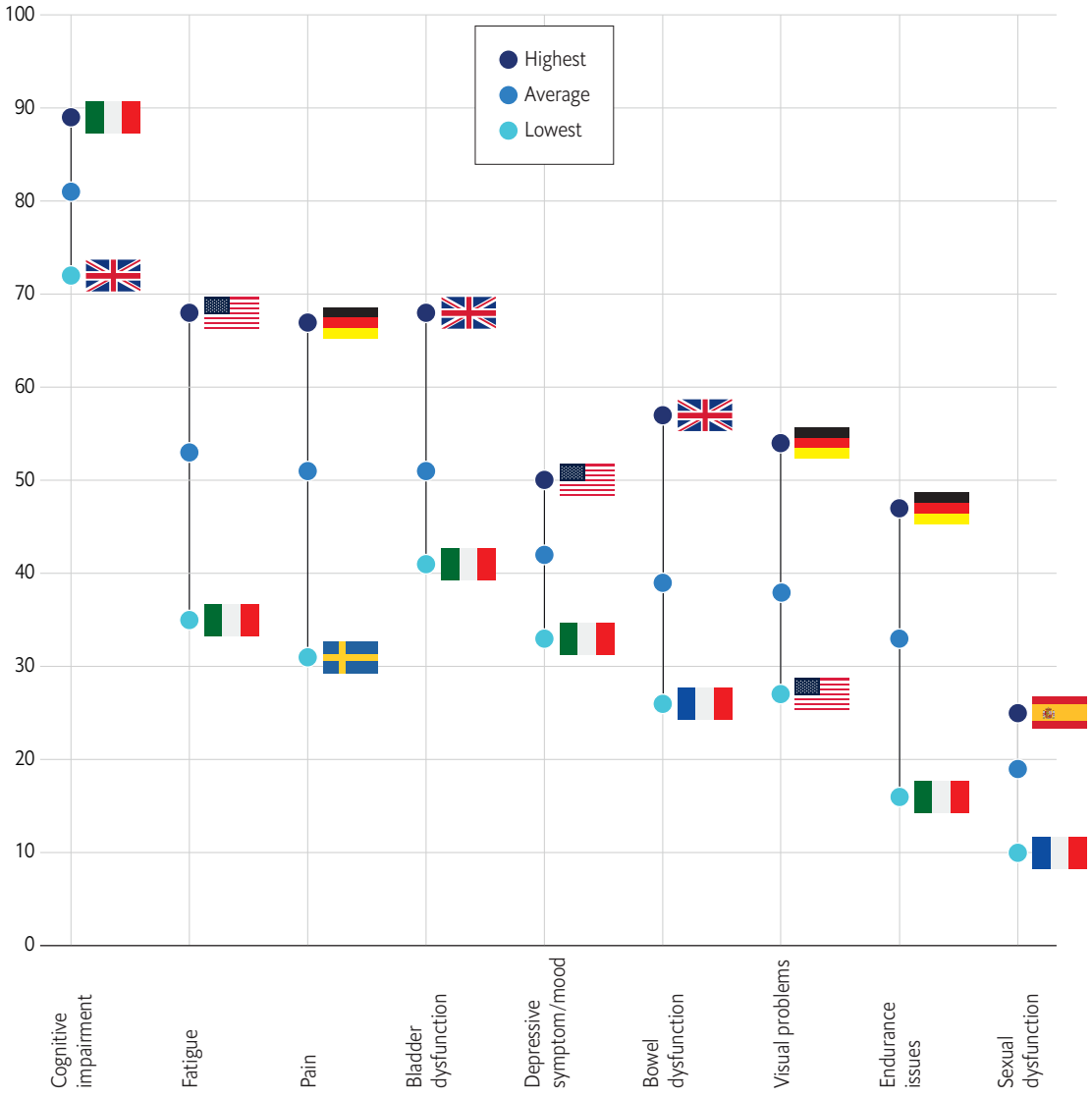
Figure 12: Patients' experience and symptoms of MS versus what clinicians are assessing



Source for neurologist assessments: Economist Impact.
Source for patient-reported symptoms (sum of responses for France, Germany, Italy and Spain): EMSP. Impact of Multiple Sclerosis Symptoms (IMSS): Europe results. 2025. European Multiple Sclerosis Platform.

Routine assessment of MS symptoms varies significantly across countries, reflecting differences in healthcare practices and resources. For example, neurologists in Italy report the least routine assessment for four key MS symptoms—fatigue, bladder dysfunction, depressive symptoms and endurance issues—among the nine symptoms presented, indicating gaps in symptom monitoring.

Figure 13: The routine assessment of MS symptoms across countries, %

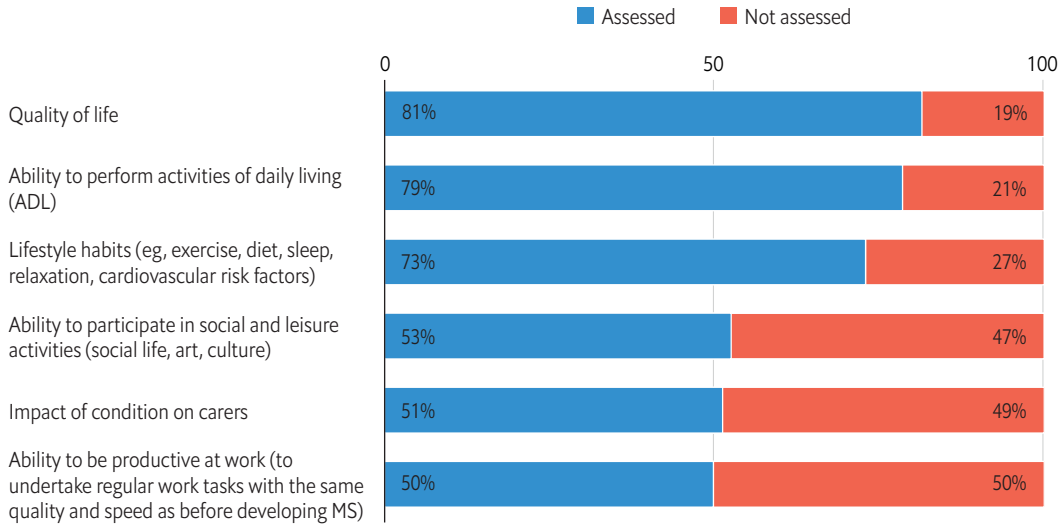


Source: Economist Impact.

Gaps in assessment increase the burden on patients and caregivers

Multidisciplinary teams for people living with MS often do not consistently assess the impact of the disease on patients' emotional and social lives, occupational functioning, or caregivers. Such gaps contribute to missed opportunities for timely interventions, leaving critical symptoms and challenges unaddressed, potentially worsening patients' quality of life and increasing caregiver burden.

Figure 14: Routine assessment of the impact of MS (all countries combined)



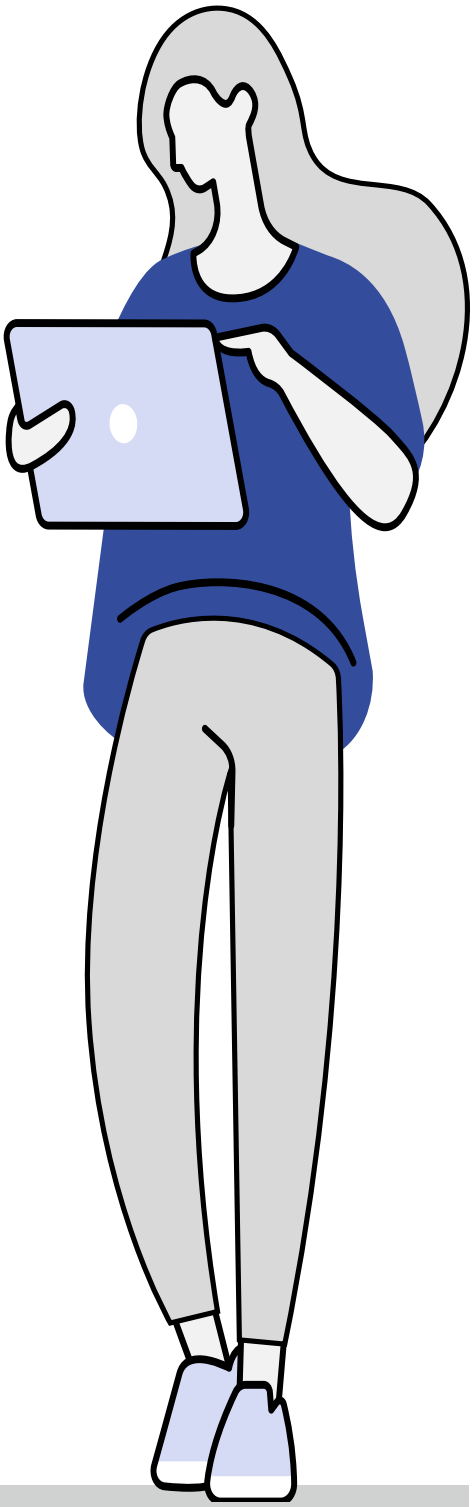
Source: Economist Impact.

The limitations of the EDSS lead to relatively infrequent use across countries

Although the EDSS remains the most commonly used tool overall, it is routinely used by only half (51%) of neurologists on average, with utilisation ranging from 36% in Germany to 69% in Sweden. Other frequently used tools include the Multiple Sclerosis Performance Test (MSPT), used by 39% of neurologists, and the Multiple Sclerosis Functional Composite (MSFC), used by 31%. Performance-based assessments, such as the Timed 25-Foot Walk (used by 75% of neurologists) and the Nine-Hole Peg Test (56%), are more commonly adopted, yet the Low-Contrast Letter Acuity test is used by just 20%.

Although all neurologists report incorporating at least one patient-reported outcome measure (PROM), uptake again varies. The Multiple Sclerosis Impact Scale (MSIS-29) is the most widely used PROM (68%), reflecting recognition of the importance of measuring patient perspectives. However, limited and inconsistent use of such standardised measures raises concerns about the accuracy and comparability of symptom data in routine practice. Without structured, repeatable assessments, subtle but clinically meaningful changes may go undetected, reducing opportunities for timely treatment adjustments or referral to multidisciplinary teams.

The misalignment between reported symptom assessment and tool use further underscores these challenges. For instance, although 81% of neurologists report assessing cognition, only 68% use MSIS-29, the main instrument that evaluates non-mobility symptoms. This suggests reliance on informal or ad hoc methods rather than validated tools, potentially reducing the reliability of data for both clinical management and research. Inconsistent measurement not only hampers longitudinal tracking of patients but also complicates communication among healthcare providers, ultimately limiting the delivery of coordinated, person-centred care.



Most neurologists report that a more comprehensive approach is needed to measure MS-associated disability

Our survey data suggests a strong consensus that existing measures of disability in MS are falling short of clinical needs. The field is at a critical juncture, where traditional approaches are increasingly viewed as inadequate. The specific barriers that neurologists describe are shown in Figure 15. The overarching direction suggests that neurologists see the solutions in integrated, efficient and holistic disability monitoring that does not overwhelm clinical workflows. There is a clear trajectory towards streamlined, technology-enabled approaches, which makes sense in the context of the systemic challenges that clinicians describe.

Figure 15: Barriers and solutions to disability comprehensive measurement

Lack of resources and measurement accuracy are the main barriers to more comprehensive assessment of MS disability

Around half of neurologists surveyed report the following barriers when assessing disability in routine clinical practice:

- Insufficient time during appointments to administer standardised measures of disability: **56%**
- Lack of staff/resources to support comprehensive assessments: **52%**
- Concerns about existing measures' ability to detect disability progression: **49%**
- Difficulty integrating measures into workflow or electronic health records: **49%**

There is an urgent need to improve disability measurement in ways that change the practice in neurology

72% of neurologists report that a more comprehensive approach is needed to measure disability in MS.

Neurologists ranked the following as the top three potential improvements to disability assessments among people with MS:

1. Simplify disability assessment tools so that they can be completed easily by a clinician in a short period of time
2. Develop automated templates to input data that estimate disability scores and can be linked to electronic health records
3. Augment the EDSS with supplementary assessments (eg, related to cognitive function and upper-limb function) to provide a more holistic assessment

Source: Economist Impact.

Evolving disability measures

"There is a whole new outlook with this disease. They talk about the 'new MS', MS in the age of disease modifying therapies. The advances have been enormous."

Anthony Feinstein, Professor of Psychiatry, University of Toronto, Canada

Measuring what matters for the 'new MS'

Our research highlights a persistent challenge in MS care: the need for improved disability measures that capture the complex interaction of physical, cognitive and psychosocial factors affecting people living with MS. Despite longstanding criticism since the 1990s, the EDSS remains deeply entrenched in clinical practice and research, focusing narrowly on physical disability and largely neglecting many invisible symptoms and patient experiences.[49] The resulting overreliance on outdated scales and a narrow perception of the daily experience of people living with MS is out of step with our improved understanding of the condition and the advances being made in other spheres. Alternative, more comprehensive approaches to disability assessment are emerging. However, their integration into clinical practice, trials and policy frameworks has been gradual and inconsistent. Reform is imperative because our current understanding of disability is gatekeeping access to comprehensive and holistic treatment, clinical trials, social welfare, and disability support.[2]

National guidelines and policies increasingly recognise the perspective of people living with MS as central to their health journey. A remaining issue is the lack of awareness among MS patients themselves of the impact of certain symptoms, particularly fatigue. Many people living with MS, even after years of suffering, may not realise which of their symptoms are directly connected to the condition. This lack of understanding prevents them from seeking help. "The list of symptoms is quite wide," says Elisabeth Kasilingam, CEO of the European Multiple Sclerosis Platform. "It includes so many things that people with MS don't think about. When you're newly affected … you don't necessarily relate one symptom to the condition, and that makes it even more tricky to understand and to make sure we address all the needs of the people. So we need to raise awareness about those symptoms; it's not just pain and the most obvious [symptoms]—there are many more, and people need to understand … so that they can talk about this with their healthcare professional. So having

a checklist, working with the checklist, will help [patients and healthcare professionals] to really understand the disease and … connect the dots."

The clinical conversations and methods used to collect symptom data must be truly fit for purpose; otherwise, there is a risk of silencing those at the heart of care. "[The perception is] there's nothing [to be done] so at a certain point I just stop talking about it," says Ms Durack. Ms Williams shares similar frustrations: "I don't fit into the standard patient [archetype] … I am continually updating my neurologist about the problems I'm having [and] there's really nothing that they can do. I don't feel like they're actually measuring. It's just me saying, 'Oh, you know, it hurts; it's getting worse.'"

Change may be even more difficult in research where there are different objectives and motivators. Researchers strive to minimise bias, often in the controlled environment of randomised controlled trials. They use highly standardised protocols to focus on objective, quantifiable outcomes. Detecting population-level differences between intervention and control groups is not necessarily served by focusing on individual-level experiences. The bridge between research and clinical practice is in complementing, not replacing, EDSS. This allows for new research to preserve comparability with historical data while also attempting to capture the nuanced, lived experience of disability.

The research discourse is shifting away from how to manage relapses towards how therapies can affect progression. Some groups attribute the high failure rate in clinical trials in the neurosciences to methodological aspects of clinical trials, including the selection of outcomes and endpoints.[50] Supplementing traditional measures of disability with other functional scores improves detection of progression. This means that research and developments in MS care are incentivised to move in that direction.

Change in research will be slow but the adoption of different outcomes will gradually allow for meaningful comparisons across different trials. Targeting specific functional domains—particularly those less well measured—with validated instruments will also help trials to detect clinically meaningful endpoints for people living with MS, potentially leading to innovation in MS interventions.

The role of regulators

The regulatory role is pivotal. Both the European Medicines Agency (EMA) and the US Food and Drug Administration (FDA) recommend a patient-centric approach to trial design and scrutinise, rightly so, the outcomes that are used by trials to assess and claim benefit.[51,52] They each have formal processes to 'endorse' outcome measures, although these are not obligatory.

The Multiple Sclerosis Outcome Assessments Consortium (MSOAC), an MS Working Group of the Critical Path Institute has been engaging for years with the FDA, seeking endorsement for more comprehensive disability measurement in MS.[42,53] The MSOAC initially signalled intent to the FDA Clinical Outcome Assessment qualification programme in 2013, 2017 and 2019 for programmes relating to SDMT, physical function and fatigue PROs respectively. The final FDA qualification determinations have yet to be made; however, evidence generation is underway to meet the rigorous requirements of the processes.[54] Specifically, two short-form Patient-Reported Outcomes Measurement Information System (PROMIS) instruments are being progressed—one for fatigue and one assessing physical functioning more completely than the EDSS does.[55]

The MSOAC's proposal to the EMA for the qualification of performance measures of ambulation, dexterity, vision and cognition (T25FW, 9HPT, LCLA and SDMT respectively) as outcomes was only partially successful. The application was seeking an endorsement of the battery of these four tests to serve as primary, co-primary or secondary endpoints. In 2020, the EMA's Committee for Medicinal Products for Human Use ruled that these measures (either as a battery of tests or independently) could "not be used as primary outcomes in the absence of a functional measure such as EDSS". The committee did accept that the T25FW and 9HPT could be included in a composite primary endpoint combined with a functional endpoint (such as the EDSS); the use of the tests as secondary endpoints is accepted.[56]

The "composite confirmed disability worsening/progression" (cCDW/cCDP) endpoint combines the EDSS with performance tests of ambulation and dexterity (T25FWT and 9HPT).[31] A recent post-hoc analyses of clinical trials including more than 5,000 people living with MS supports the use of this composite as a primary endpoint and establishes the predictive validity and clinical relevance of performance-test worsening.[31] These instruments have been used together before as the EDSS-Plus.[17,37] It is unclear how long it may take for this suite of tools to be more commonly used in trials than the EDSS alone, or to find their way into routine clinical conversations. Unfortunately, although an improvement on using only the EDSS, this composite does not include measures in some of the key domains of worsening that have the greatest impact on people living with MS, which we have discussed extensively in this report. Nevertheless, the regulator's endorsement is an important step forward in diversifying the accepted view of MS disability, and it may be just the impetus that researchers require.

As cumbersome as the processes may be, a regulator-endorsed outcome provides researchers with validated tools that have undergone rigorous scientific review. Once qualified, the measures can be used with greater regulatory confidence and efficiency. Of note, the EDSS has not undergone the same level of scrutiny as many of these newer instruments are expected to, and is the de facto standard disability measure only through decades of use in clinical trials.

Today's technology and monitoring

Mobile and wearable technologies offer promising avenues for collecting relevant disability information in MS through more frequent, sometimes continuous, monitoring. This approach has the potential to overcome limitations of traditional assessments like the EDSS, which capture only brief snapshots during annual or biannual visits. However, a 2021 review of 119 digital technology studies in MS revealed that over 75% focused solely on motor function, with only 15% addressing cognition, indicating gaps in the scope of current digital assessments.[57] In our survey, around 40% of neurologists ranked technology-based solutions—such as automated data extraction and patient self-monitoring—as top methods to improve disability assessments, though barriers including limited staff, resources and clinic time remain significant. "Disability assessment now is very time consuming in our clinics, and it is increasingly more difficult to do all the tests in the same visit for a patient," says José Manuel García-Domínguez, a neurologist at the Hospital General Universitario Gregorio Marañón in Spain, emphasising the need for concise, time-efficient MS assessment toolkits.

Several mobile apps, such as MSCopilot and Floodlight Open, enable people living with MS to self-assess walking, dexterity, cognition and vision remotely, with some data-sharing capabilities for clinicians.[58] For example, Floodlight Open combines active smartphone sensor tests with passive data collection to monitor mood, cognition, motor function and gait, showing reliable concordance with clinical tests.[59] However, patient engagement and retention remain challenges.[60,61]

"I think wearables have a role [in remote monitoring of disability], but they're quite complicated because there's lots of variability," says Prof Hobart. "But it would make sense that continuous monitoring provides you with good quality data to look at trends and changes." Meanwhile, Dr García-Domínguez points to the challenges of integrating such technologies. "We are trying now to implement some wearables," he says. "But it's very difficult to analyse all the data … we're in a very early phase for wearables."

Overall, wearables and digital health tools hold significant promise to capture more relevant and regular data on disability impact, but full adoption requires overcoming hurdles linked to data management, healthcare capacity and patient engagement. These technologies remain nascent but represent a growing opportunity to enhance MS care and monitoring.

Big data networks and registries

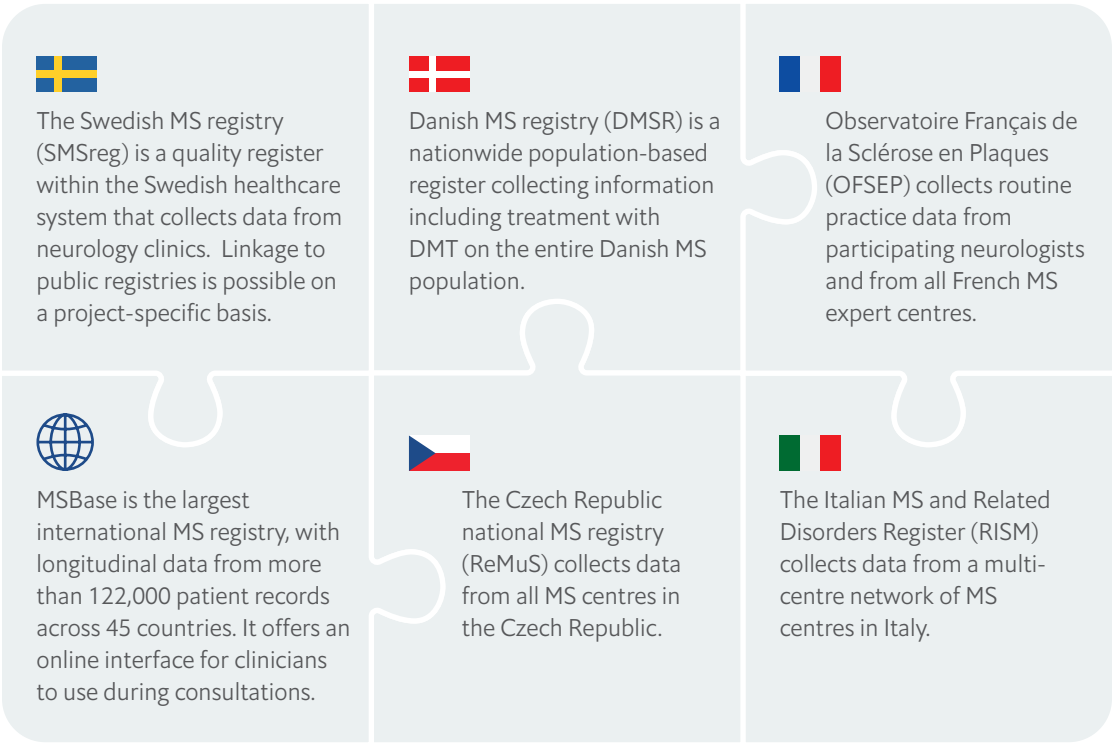
All countries in this study maintain MS registries at national or local levels, which are increasingly recognised as critical for collecting national data on patients and care, potentially enhancing clinical practice data quality. "It is absolutely necessary to have an MS registry," says Herbert Temmes, federal managing director of the German Multiple Sclerosis Society. "The registry in Germany gives us an overview of DMT use, symptom change and improvement. We are in discussion about adding PROs for fatigue and depression." The MS Data Alliance's Core Dataset initiative offers one of the most advanced guidelines, recommending a core set of 44 variables that include all common and 'invisible' MS symptoms such as fatigue, depression and cognitive issues, alongside various disability

measures beyond the traditional EDSS, including T25FW, 9HPT, SDMT and PDDS, promoting comprehensive disability assessment.[62] Although not going so far as to recommend which instruments registries should use, the guidance on including these data in national registries is encouraging.

Prof Hillert highlights the value of registries in standardising measurements, "if you go back a number of years, there were no databases in the world that would collect something such as the EDSS. The only context in which that would happen would be for clinical trials." The Swedish MS Registry, which covers 85% of people diagnosed with MS in the country, further integrates PROs and scales for depression and anxiety, although their consistent use is hindered by barriers such as clinician time constraints, limited understanding of PRO value and insufficient training.[63]

Work remains to standardise what data are collected, to harmonise systems within and across geographies, and to increase coverage. There could be efficiencies in big-data collectives and partnerships between registries, such as the Big Multiple Sclerosis Data Network, a collective of the national MS registries of the Czech Republic, Denmark, France, Italy and Sweden, as well as the international MSBase (Figure 16). There are over 350,000 people living with MS in the database.

Figure 16: The Big Multiple Sclerosis Data Network



Source: Economist Impact.

Overall, though, registry coverage remains limited—only an estimated 35% of people living with MS across Europe are recorded in national MS disease registries.[18] In addition, existing registries do not necessarily collect information on the breadth of disability symptoms; personal and basic disease data are the most collected categories of variables, whereas data on fatigue and cognition are the least collected in MS registries/cohorts.[64] There is significant room for improvement. More standardised and complete data collection would enhance the ability of registries to provide meaningful data, share it across borders and increase analytical power through using combined data sets.

Registries are potentially powerful instruments of change, particularly where there is momentum to use them—mandated or otherwise. As real-world data collection systems, they can bridge the gaps between existing clinical approaches and more appropriate definitions of disability that are consistent with the holistic impact of MS.

Ensuring management follows measurement

Rehabilitation and barriers

Multidisciplinary care is essential for managing MS; however, access and care provision is often limited and inconsistent. Experts note that people living with MS and their families frequently need to actively seek out rehabilitation, peer support and psychological services, as these supports are rarely offered proactively during appointments and are more commonly provided by charities than national healthcare systems. This results in regional disparities—for example, in Spain, only large referral centres typically offer such multidisciplinary care, while in the US, comprehensive MS centres are rare and mostly limited to major metropolitan academic institutions, creating fragmented care experiences and MS neurology 'deserts' in underserved areas. "Assessment and measurement have changed in the last ten years", says Peter Feys, professor of rehabilitation sciences and physiotherapy in the Rehabilitation Research Centre (REVAL) of Hasselt University in Belgium. "People realise that we need a battery of questionnaires and tests to address invisible symptoms such as cognition and fatigue," he adds, but these comprehensive evaluations are often confined to specialised centres, highlighting ongoing gaps even in well-resourced settings.

An assessment of interventions for MS symptoms is beyond the scope of this research; however, a review of reviews summarises the wide range of interventions that are backed by high quality evidence.[65] Multidisciplinary rehabilitation, physiotherapy and exercise improve physical functioning, and CBT/MBSR is effective for cognitive functioning.[65] Meanwhile, multidisciplinary rehabilitation, including cognitive rehabilitation can treat MS related cognitive decline at low cost.[66,67] "Brain-healthy" and "metabolically healthy" lifestyles are also important therapeutic strategies, as they aid in

preserving the neurological system's capacity to buffer against normal ageing and damage caused by disease.[68]

Historically, rehabilitation has received less attention and investment than other healthcare interventions, despite the fact that an estimated 1 in 3 people globally have a health condition that would benefit from it.[69] For MS at least, there may have been a perception that a focus on functional improvement is not as essential as directly treating the underlying disease.

"Rehabilitation has been neglected for years because people thought it was not worthwhile—because they frankly didn't believe in it."

Gianvito Martino, Neurologist and Scientific Director of IRCCS, San Raffaele Hospital; Full Professor of Applied Biology and Vice-Rector for Research and the Third Mission, Vita-Salute San Raffaele University, Italy

For people living with MS, rehabilitation is particularly complex, as the disease changes over time and affects many aspects of life.[70] Cognitive dysfunction and fatigue, two of the most common symptoms, are multidimensional and sometimes interrelated.[2] Cognitive problems in people living with MS can increase with age and disease severity. It is often difficult to untangle cause and effect, as treatments, symptomatic relief and comorbidities, including anxiety and depression, can also lead to these sequelae.[71] Differentiating cognitive impairment due to MS from other age-related diseases can also be particularly challenging.

A lack of understanding, funding and/or resources may also explain why services lag in providing the full spectrum of effective and necessary interventions, leaving people with severe MS particularly vulnerable since few medical treatments exist as disability advances. As a result, people living with MS suffer and are dissatisfied with certain aspects of their care.[2] One of the experts we interviewed believed that these lags in services are somewhat inevitable, reflecting on the fact that only when DMTs became available did significant improvements in general MS care occur. Should there ever be approved, reimbursed treatments for progressive MS, healthcare services would need to adapt to the numbers who would receive these, and the supporting services would inevitably improve. "We would have to reinforce MS care significantly," says Prof Hillert.

Barriers to service implementation are multifaceted and vary by country and healthcare system. For instance, as Dr Martino explains, "In Italy, the healthcare system allows you a few hours per week and a few weeks per year of rehabilitation, which is absolutely nothing—we know you should do at least two hours per day … But since there is less business behind neuro-rehabilitation, people are not interested. The market is not willing to promote rehabilitation as a way to treat patients, because there's no way of making money through rehabilitation."

Globally, there is increasing recognition of these challenges. A WHO resolution from 2023, "Strengthening rehabilitation in health systems," provides an international roadmap to drive improvements.[72] National and professional guidelines in each of the study countries support multidisciplinary care and use of DMTs, but clear protocols for monitoring symptom progression and managing most MS symptoms remain elusive.

MS nurses play a crucial role as key workers and healthcare navigators, often forming the primary point of contact for patients from pre-diagnosis through to long-term follow-up. "[MS nurses] take care of many symptoms, and they identify disability accrual earlier than sometimes we do as neurologists, because they have more of a relationship with our patients—they have a really open relationship," says Dr García-Domínguez. Nurses' responsibilities include explaining

treatment options, helping patients to navigate the healthcare system, managing symptoms, answering questions about side effects and referring to support services. However, despite their pivotal role in ongoing care, MS nurses remain underutilised and are often limited to specialised centres, suggesting significant potential to strengthen this vital resource.

Improvements in managing MS symptoms do not always require large-scale reforms or heavy financial investments. "They don't require grand solutions," says Ms Kasilingam. "Small adjustments in the workplace, for example, or in the support that you receive in your housing, could be enough." By focusing on the roles and interactions of healthcare providers and other key stakeholders involved in a person's functioning (see Figure 10), incremental but meaningful progress can be made to enhance care quality.

Personalised medicine and the ethos of palliative care

Understanding the experience and needs of individuals with MS is crucial to ensure patient-centric management. People living with MS need holistic care and a multidisciplinary approach. The conventional focus on DMTs and relapse prevention means that healthcare services fall short in addressing the full spectrum of needs of people living with MS.[2]

Personalised medicine is a priority of the European Commission's agenda, and policies exist at national and central levels to increase engagement of people living with MS in research to "promote the paradigm shift toward predictive, preventive and personalised medicine".[73,74] Brain health and preservation of cognitive function are named by those living with MS as priority treatment goals, followed by prevention of disability related to walking, strength and vision.[75,76]

Palliative care, the person and family-centred approach to services that concentrates on relieving health-related suffering, is underutilised across neurological conditions.[77] It has a significant role across the many dimensions of disability in MS. Specific areas of support include communication, education and advice, symptom management, occupational support, family support, spiritual wellbeing, and help with planning for the future— all of which are relevant to people living with MS throughout their lives.[77,78] In both the literature and discussion with the experts we interviewed, we heard a strong call for closer collaboration between neurologists and palliative teams.[77,79] "These two worlds still have to grow together," says Raymond Voltz, director of the Centre for Palliative Medicine, University Hospital Cologne in Germany. "It's not routine for neurologists to think about palliative care support for our patients. [Meanwhile,] traditional palliative care services may not be prepared to care for a person with MS."

Palliative care is proposed to help people with advanced MS who have complex and varying bio-psychosocial needs and few treatment options. The European Academy of Neurology provides a guideline on palliative care for people with severe, progressive MS.[67] Recommendations are comprehensive and evidence-based, and include the complex and deeply sensitive issue of assisted suicide.[67]

Since palliation includes symptomatic treatment, it can be initiated at any stage of disease to complement standard care and address complex needs, including those of carers and relatives.[77,80] Unfortunately, palliative care is not an area that all neurologists are comfortable with, and integration into neurological services is new.[81] It is still most closely associated with end-of-life care, and most people living with MS do not get the support that they need.[77] In the 2020 edition of the EMSP's MS Barometer study, access to early palliative care was clearly identified as a gap across a number of European countries: only ten of the 35 participating countries offered early palliative care for people living with MS.[18] Misconceptions may explain the lack of broader acceptance. Whatever the reasons, better collaboration between neurology and palliative care services will improve quality of life for people with serious illness and their families by addressing their multidimensional suffering.[77]

In summary, meaningful change in disability measurement requires careful orchestration across multiple stakeholders while maintaining the continuity necessary for ongoing patient care and research progress. Substantial efforts are being made to move the field forward. Given the considerable breadth of effort, some degree of fragmentation is inevitable, yet coordination and strategic alignment across these initiatives are essential to accelerate progress and avoid duplication of effort.

Table 3: Key initiatives include:

The World Health Organization (WHO) Intersectoral global action plan on epilepsy and other neurological disorders 2022-2031 (IGAP)	At the 75th World Health Assembly (in 2022), member states adopted a global action plan on epilepsy and other neurological conditions, a "comprehensive, coordinated and integrated public health response over a ten-year timeframe" (2022-2031). The WHO's recently published Global Status Report on Neurology (2025) established baseline data on brain health and neurological disorders and identifies significant gaps and barriers in global capacity to respond to neurological disorders.[82] It offers evidence-based recommendations to accelerate progress, ensure that people with neurological conditions are at the centre of action, and align efforts globally toward the IGAP targets by 2031.
The Multiple Sclerosis Outcome Assessments Consortium (MSOAC), of the Critical Path Institute	The MSOAC provides a standardised, anonymised database of placebo arm data from MS clinical trials, including diverse clinical, functional and patient-reported outcome measures. The platform facilitates comprehensive research by aggregating and harmonising data to improve disability assessment and accelerate drug development in MS. There are other key initiatives under the CPI umbrella, including the Multiple Sclerosis Working Group's efforts to achieve regulator-endorsed outcome measures for fatigue and upper-limb mobility (shortcomings of the EDSS).[55]
The Global PROMS Initiative (https://proms-initiative.org/)	The Global Patient-Reported Outcomes for MS Initiative has an ambitious mission.[74] It brings together the global MS community, people living with MS, healthcare workers and researchers, the healthcare industry, and more, with the goal of ensuring the informed and quality participation of people living with MS in the decision-making processes of research and healthcare. The initiative is a unique collaboration, aiming to reach consensus on a set of standardised patient-reported outcomes to be used in therapy development and healthcare.[74]
The Progressive MS Alliance Principles of Patient Engagement in MS Research.	The Progressive MS Alliance is a global collaboration of MS organisations, researchers, healthcare professionals, industry partners and people affected by progressive MS that is dedicated to accelerating the development of effective treatments. Its mission is to improve the quality of life for those living with progressive MS through funding transformational research, promoting innovation and integrating diverse expertise. By fostering global partnerships and supporting pioneering studies, the Alliance aims to identify, prevent and reverse disease progression; accelerate clinical trials; and improve patient wellbeing.
SOS MS consensus group	The SOS MS consensus group developed the internationally accepted, patient-relevant Standard Outcome Set for Multiple Sclerosis, focused on improving value-based MS care.[83] The group's approach combined systematic literature review, patient focus groups and a multidisciplinary expert panel to reach consensus on outcomes that matter most to people living with MS. The resulting set comprises 14 outcomes spanning disease activity, symptoms, functional status and quality of life, with each outcome linked to a specific measurement protocol for benchmarking and clinical practice.

Source: Economist Impact.

Conclusion

The evidence is clear: the economic burden of MS is substantial and increases as disability becomes more severe. Our modelling confirms that costs shift considerably from direct healthcare expenses in early disease to indirect and social costs in advanced stages. This reflects both the currently available treatments and how the needs of people living with MS change as their disease progresses.

Beyond the economics, MS serves as a powerful case study for the broader issue of disability. It is a complex, heterogeneous disease that demands a shift from traditional medical models towards more comprehensive, person-centred approaches. Challenges faced by people living with MS are reflective of struggles across various chronic conditions, providing a crucial lens through which initiatives like the UN Convention on the Rights of Persons with Disabilities and the EU Disability Strategy should be applied.

Traditionally, population health has been measured through mortality (who dies and when) and morbidity (who gets sick and how often). Although these remain foundational indicators, they present an incomplete picture of wellbeing, especially for chronic, debilitating conditions like MS. The evolving understanding of health increasingly recognises functioning as the essential third pillar, capturing the 'lived health' of individuals and their ability to participate in life.[84] Functioning encapsulates what clinical metrics often miss: the ability to work, maintain relationships, pursue passions and live independently. Our report suggests an urgent need to improve assessment of these aspects, in both clinical and research contexts. Despite an exhaustive discourse about its limitations, the EDSS is still the most utilised instrument in our survey, albeit by only one in two neurologists. Most surveyed neurologists acknowledge the need for more holistic ways to measure disability, using simple tools that can be completed in a short time. This aligns with a repeated and decades-long call for evolution in disability measurement.

A global web of interrelated actions and initiatives on disability measurement stretches back for decades. Rather than duplicating efforts, strategic coordination is needed to identify gaps where additional work is most needed, leverage existing validated instruments and datasets, and ensure interoperability between emerging measurement systems.

The practical constraints are real. They include physician time and resource, regulatory processes and timelines, healthcare system capacity for change, technology infrastructure limitations, and the need to maintain continuity with historical data for longitudinal research. But today, more than ever before, the opportunity exists to leverage emerging technologies to improve and standardise the collection of information on real-world functioning of people living with MS. Doctors, researchers, patient advocacy groups and people living with MS themselves acknowledge and are asking for a move beyond medicalised models towards a personalised medicine agenda that recognises each individual's unique needs, goals and definition of wellness. The path forward requires unprecedented coordination and collaboration. Success will require pragmatic sequencing of improvements that can be implemented within existing clinical workflows while building towards more transformative long-term changes in the conceptualisation and measurement of disability in MS.

Success will require pragmatic sequencing of improvements that can be implemented within existing clinical workflows while building towards more transformative long-term changes in the conceptualisation and measurement of disability in MS.

Economist Impact

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Appendix A: Methodology for economic analysis

Overview of the methodology

The economic model aimed to calculate the economic impact of MS associated disability in the following seven countries: France, Germany, Italy, Spain, Sweden, the UK, and the US. To do this, a combination of literature review, data collection, stakeholder engagement, and economic impact modelling were employed.

The methodology consisted of three phases:

Phase 1: Model framework development

A model framework was developed, based on initial findings from available literature describing the natural history of MS, MS clinical pathways, and economic evaluation of the impact of MS. Survey and interview questions were then designed, drawing on recognised gaps in the literature and knowledge of parameters commonly underrepresented in previous economic evaluations of MS, to address these data gaps.

Phase 2: Identification of individual model parameters

A parameter sheet was created in excel, which aims to guide data collection according to the model framework, for each country studied. Data was collected from published literature and stakeholder engagement using surveys and interviews with neurologists conducted by the Economist Impact team. An initial methods brief was developed summarising the overall approach to the project.

Phase 3: Model development and results

An economic model was developed using Microsoft Excel, presenting the economic impact of MS by annual current costs per patient across Expanded Disability Status Scale (EDSS) groups (Mild: EDSS 0 to 3.5; Moderate: EDSS 4 - 6.5; and Severe: EDSS 7 - 9.5) and total societal burden stratified by EDSS group.

Initial findings from the literature

A literature search was conducted in Medline, Embase, and the grey literature, focusing on studies quantifying the cost of managing adult MS patients in France, Germany, Italy, Spain, Sweden, the UK, and the US to obtain country-specific data. Both direct and indirect costs related to MS management were considered. The main outcomes studied were the economic impact of MS per case and nationally, the impact of MS disability levels, and the costs incurred by each disability level.

Seven of the most relevant studies are described in Table 1.

Table 1: Country-specific studies retrieved from the literature search

Country	Year	Author/s	Title
France	2017	Lebrun-Frenay et al[1]	New insights into the burden and costs of multiple sclerosis in Europe: Results for France
Germany	2017	Flachenecker et al[2]	New insights into the burden and costs of multiple sclerosis in Europe: Results for Germany
Italy	2022	Battaglia et al[3]	Patients with multiple sclerosis: a burden and cost of illness study
Spain	2017	Celia Oreja-Guevara[4]	New insights into the burden and costs of multiple sclerosis in Europe: Results for Spain
Sweden	2017	Brundin et al[5]	New insights into the burden and costs of multiple sclerosis in Europe: Results for Sweden
UK	2017	Thompson et al[6]	New insights into the burden and costs of multiple sclerosis in Europe: Results for the United Kingdom
US	2022	Bebo et al[7]	The Economic Burden of Multiple Sclerosis in the United States: Estimate of Direct and Indirect Costs

Across the literature, direct costs associated with multiple sclerosis are more frequently studied than indirect costs. Within these direct costs, hospitalisations, inpatient care, medications, and outpatient services are the most commonly reported components. In contrast, there is far less information reported on the costs related to primary or community services, rehabilitation, and the use of emergency services. When it comes to indirect costs, absenteeism is the most frequently discussed aspect in the research. Other important indirect costs, such as income loss, disability allowances or illness benefits, and childcare expenses, are mentioned far less often, indicating a gap in the current understanding of the full economic impact of multiple sclerosis. Further targeted literature searches were conducted to support data collection.

Modelling

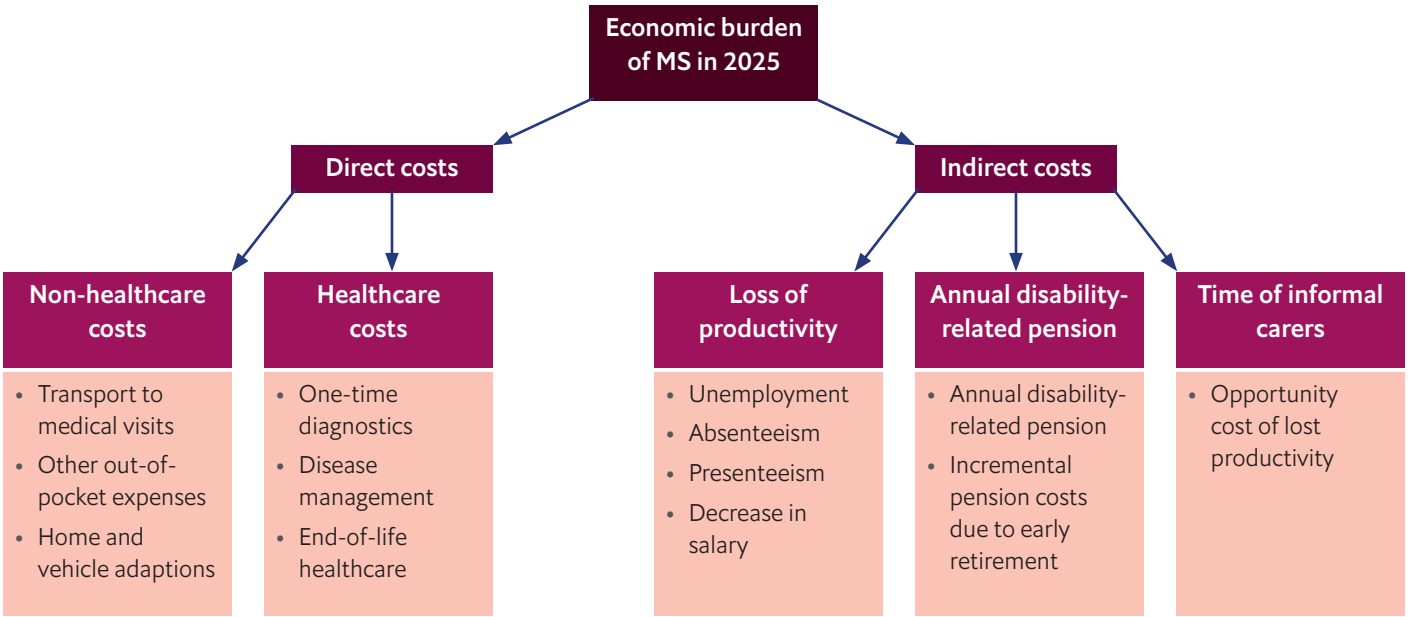
The cost of illness analysis estimated the societal burden of Multiple Sclerosis (MS) across seven countries—France, Germany, Italy, Spain, Sweden, the United Kingdom, and the United States—for the year 2025. Employing a societal perspective, the analysis captured both direct and indirect costs associated with MS, non-healthcare costs, productivity losses, and informal care. A bottom-up approach was implemented, estimating costs on a per patient-year basis for each cost component. Subsequently, country-specific prevalence rates were applied to these per patient-year costs to estimate the total societal cost burden of MS in each country. Data sources include epidemiological, clinical, and economic datasets relevant to each country to ensure robust, context-specific estimates. All data collected was dated year 2025, or the latest available year. For years earlier than 2025, the data was inflated to show 2025 values.

The economic impact was expressed in USD and presented as the following outcomes:

- Annual current costs per patient across EDSS groups (Mild: EDSS 0 to 3.5; Moderate: EDSS 4 - 6.5; and Severe: EDSS 7 - 9.5)
- Total societal burden stratified by EDSS group.

Both direct and indirect costs were gathered from available databases, peer-reviewed literature, and stakeholder engagement through interviews and surveys with key experts. An abbreviated model framework is illustrated in Figure 1, and the complete model framework can be found in Annexe A.

Figure 1: Modelling Framework



Source: Economist Impact.

Data collection

Epidemiological parameters

Overall disease prevalence, incidence, and mortality data will be collected for this study. Epidemiological data will be retrieved from available databases such as the Institute for Heath Metrics and Evaluation's Global Burden of Disease (GBD) database.[8]

GBD incidence data on MS severity across both sexes and all ages were used. EDSS groupings in Table 2 show the severity level distribution against the EDSS score.

Disability-related parameters

The EDSS, also known as the Kurtzke scale, is a commonly used measure to track MS progression.[9] The scale measures disability and mobility across 10 levels, with lower scores representing lower levels of disability. Existing studies tend to use EDSS scores to group disability levels into mild, moderate and severe disease. While there is some variability in the EDSS cut-offs for mild, moderate and severe disability, they are generally defined as EDSS values of 1-3.5, 4-6.5 and 7-9.5 for mild, moderate and severe disability, respectively.[10] The EDSS scale is summarised and grouped into GBD severity categories in Table 2 and were applied to this analysis.

To estimate the economic impact of MS per patient across EDSS groups, country-specific data was gathered from published literature, surveys and interviews.

Table 2: EDSS Scoring and GBD database grouping

GBD database groupings	EDSS score	Disability	Symptoms
Asymptomatic	**0**	None	No symptoms
Mild **EDSS: 1 - 3.5**	**1**	None	Minimal symptoms in one functional system
	1.5	None	Minimal symptoms in more than one functional system.
	2	Minimal (single system)	Minimal disability in a single functional system.
	2.5	Mild (single system) or Minimal (two systems)	Mild disability in one system or minimal disability in two functional systems.
	3	Some (single system) or Mild (3-4 systems)	Some disability in a single system or mild disability in three to four systems.
	3.5	Moderate (single system) or Some (several)	Moderate disability in a single system and some disability in several others.

GBD database groupings	EDSS score	Disability	Symptoms
Moderate **EDSS 4 - 6.5**	**4**	Significant	Self-sufficient and functional for half a day
	4.5	Significant	Active most of the day and able to walk continuously unassisted for 300 meters
	5	Significant	Disability affects full daily activities and able to walk continuously unassisted for 200 meters
	5.5	Significant	Disability affects full daily activities and able to walk continuously unassisted for 100 meters
	6	Significant	Requires a cane or crutch to ambulate 100 meters
	6.5	Significant	Requires two canes or crutches to ambulate 20 meters
Severe **EDSS 7 - 9.5**	**7**	Severe	Unable to ambulate more than 5 meters even with assistance. Able to get in and out of a wheelchair unassisted.
	7.5	Severe	Unable to ambulate more than a few steps. Needs assistance getting in and out of a wheelchair.
	8	Severe	Wheelchair-bound, sitting, or always lying down but able to use arms efficiently and do most things
	8.5	Severe	Mostly in bed but has some use of arms and do some things independently
	9	Severe	In bed always but able to talk and eat independently
	9.5	Severe	In bed always and depends on others for care. Unable to effectively talk or swallow
Death	**10**	Death	Death

The EDSS assesses 8 functional systems:

1. pyramidal (P) - muscle weakness or difficulty moving limbs;
2. cerebellar (C11) - ataxia, loss of balance, coordination or tremor;
3. brainstem (BS) - problems with speech, swallowing and nystagmus;
4. sensory (S) - numbness or loss of sensations;
5. bowel and bladder function (BB);
6. visual function (V) - problems with sight;
7. cerebral functions (Cb) - problems with thinking and memory;
8. other (O) - any other neurologic findings attributed to MS.

Direct cost inputs

Direct costs were reported as the average annual resources required per patient and the unit cost of each resource were expressed in 2025 US dollars. Country-specific direct cost data were collected where possible (Table 3). Direct costs incorporated cost variability using ranges where feasible to account for uncertainty. Central, minimum, and maximum costs were extracted to identify the most reliable data input.

Healthcare costs

The following healthcare costs listed in Table 3 were gathered for the study. One-time diagnostic costs were only be applied to incident cases, while end-of-life costs was applied only to deaths. Disease management costs were applied to all prevalent cases. All resource inputs were adjusted by utilisation rates. The end-of-life costs focussed on the 5-day period before patient death within the hospital setting. A percentage of patients who died in the hospital was used. Stratification by EDSS category was applied to disease management costs. This is because the greatest differences in costs were expected to appear in the management of MS as it progressed between mild, moderate and severe stages.

Table 3: Healthcare costs

Cost	Inclusions
One-time diagnostic	• Consultations • Tests (laboratory work, imaging)
Disease management	• Medicines (disease modifying therapies, symptomatic medication) • Hospitalisations (Inpatient care per day admissions) • Healthcare consultations • Tests (routine laboratory work, imaging)
End-of-life	• Hospital ward stays (for the last five days prior death)

Non-healthcare costs

Under direct costs, the analysis included non-healthcare costs to account for the additional expenses MS patients incur as their disability level worsens. These included mobility and home adaptations, and other expenses summarised in Table 4.

These costs were applied to all prevalent cases, adjusted by utilisation rates. Annual resources needed per patient, resource utilisation rate, and cost per unit in 2025 US dollars were collected. When possible, the minimum and maximum range values were also collected. Stratification by EDSS level was applied to all non-healthcare costs since these expenses are related to the disability level of an MS patient.

Table 4: Non-healthcare costs

Cost	Inclusions
Transportation	• Transportation to medical visits
Adaptations/ Modifications	• Home adaptations (includes ramps, grab bars, and other accessibility modifications)
Mobility	• Vehicle modifications
Other expenses	• Equipment and devices aiding mobility

Indirect cost inputs

Indirect costs were categorised into three principal domains: productivity losses, annual disability-related pension expenditures, and the valuation of informal caregiver time (Table 5).

To estimate the economic value of informal caregiving, various methods have been proposed and applied in previous research. The proxy good method estimates the value of informal care using the market wage of a comparable formal service, assuming the existence of a close substitute, such as home-based nursing care. This study adopts the proxy good method, using the average hourly wage of workers in health-related social assistance as a proxy for the shadow price of informal care.[11]

This study did not include longitudinal projections of future income losses, but a cross-sectional analysis estimating salary reductions attributable to MS was presented. The following indirect costs were derived from a primary survey of 850 healthcare practitioners across seven countries (France, Germany, Italy, France, Spain, Sweden, the UK and the US): unemployment rate due to MS by EDSS level, total days per year lost (Absenteeism) by EDSS level, and percentage of patients requiring informal caregiving by EDSS level.

Indirect costs were then modelled for prevalent cases in 2025, with stratification by EDSS level to capture variations in disease severity.

Table 5: Indirect costs

Domain	Cost	Inclusions
Productivity losses	**Unemployment**	• Percentage of patients below retirement age currently unemployed due to MS • Productivity losses due to early retirement
	Salary decreases	• Decrease in annual salaries due to MS
	Absenteeism	• Work absenteeism in days per year
	Presenteeism	• Time with reduced productivity on days worked
Annual disability-related pension expenditures	**Retirement**	• Annual disability-related pension paid to patients retiring prematurely due to MS
Informal caregiver time	**Caregiving**	• Informal caregiver hours in hours per week • Percentage of patient requiring informal caregiving

Assumptions

Country-specific assumptions were implemented to reflect nuances in both direct and indirect costs. The following assumptions were used to supplement gaps in data points necessary to complete the model. Assumptions were specific to each for country. To ensure comparability, all cost variables were standardised. For sources that added more variables under direct or indirect costs, individual variables not pertinent to the study were removed. Details of the country-specific assumptions are found in Annexe B.

Table 6: Summary of standardised variables for modelling

Cost category	Standardised variables
Direct healthcare costs	• Medicines (DMTs, symptomatic medication) • Inpatient care/day admissions • Consultations • Diagnostic tests
Direct non-healthcare costs	• Home and vehicle adaptations • Investments in equipment and devices to aid patients' mobility • Other expenses (Community services) • Transportation
Indirect costs	• Caregivers' indirect costs ◦ Informal caregiving • Patients' indirect costs ◦ Absenteeism ◦ Presenteeism ◦ Productivity loss due to early retirement ◦ Productivity loss due to unemployment ◦ Decrease in income relative to the period prior to illness onset • Disability insurance due to early retirement

Supplementary analysis: Individual lifetime productivity loss

An expected value model was used to estimate the lifetime indirect cost for a representative working-age individual diagnosed with MS at age 30 and followed until age 65. The analysis captures the cumulative productivity loss associated with disease progression across EDSS levels, assuming the person survives the entire period (ie, mortality is excluded).

At each yearly cycle ***t***, the probability of being in each EDSS category—mild, moderate, or severe—is calculated using transition probabilities from Walz et al., which describe the likelihood of progressing from one EDSS state to another.[12] These probabilities determine the expected distribution of disease severity over time, rather than simulating individual patient pathways.

The expected annual cost in year ***t*** is computed as the weighted sum of costs across EDSS states, where the weights correspond to the probability of being in each state:

$$E(C_t) = Sum[(P_{t,s}) * C_{EDSS(s)}]$$

where $P_{t,s}$ is the expected probability of being in severity state s (mild, moderate, severe) at year ***t***, and $C_{EDSS(s)}$ is the per-person annual productivity loss cost associated with that state. The only costs included are productivity loss due to absenteeism, unemployment and early retirement.

The total expected lifetime cost from age 30 to 65 is then obtained by summing the discounted annual expected costs ($E(C_t)$ factoring in discount rate) over all 35 years. Annual discount rate is assumed to be 3% in line with other health economic studies.

The final results reflect the expected economic burden of an average 30 year old conditional on the disease progression rates.

Key assumptions

The model assumes (1) no mortality across years, since it is an estimate of lifetime cost until retirement; and (2) fixed indirect costs per EDSS level, with exception of discount rate. These simplifications enable a simple estimation of long-term cost dynamics while maintaining alignment with available epidemiological and economic data.

Outcomes

Cost estimates were expressed in 2025 US dollars and reported as mean annual per-patient costs stratified by EDSS categories. In addition to these stratified estimates, the study estimated the aggregate economic burden of MS across all EDSS groups, capturing the total societal impact.

Uncertainty

Uncertainty in model inputs were addressed deterministically by applying value ranges (minimum and maximum) around central point estimates for each parameter. Minimum and maximum values were retrieved from literature for costs at the patient level. Minimum and maximum prevalence, incidence, and mortality rates reported by GBD were considered for minimum and maximum values at the national level.

For patient-level cost outcomes, uncertainty reflected variability in resource utilisation patterns and unit cost data. For aggregate-level outcomes—such as total societal burden—uncertainty will additionally incorporate variability in key epidemiological parameters, including prevalence, incidence, and mortality, as reported by the GBD study.

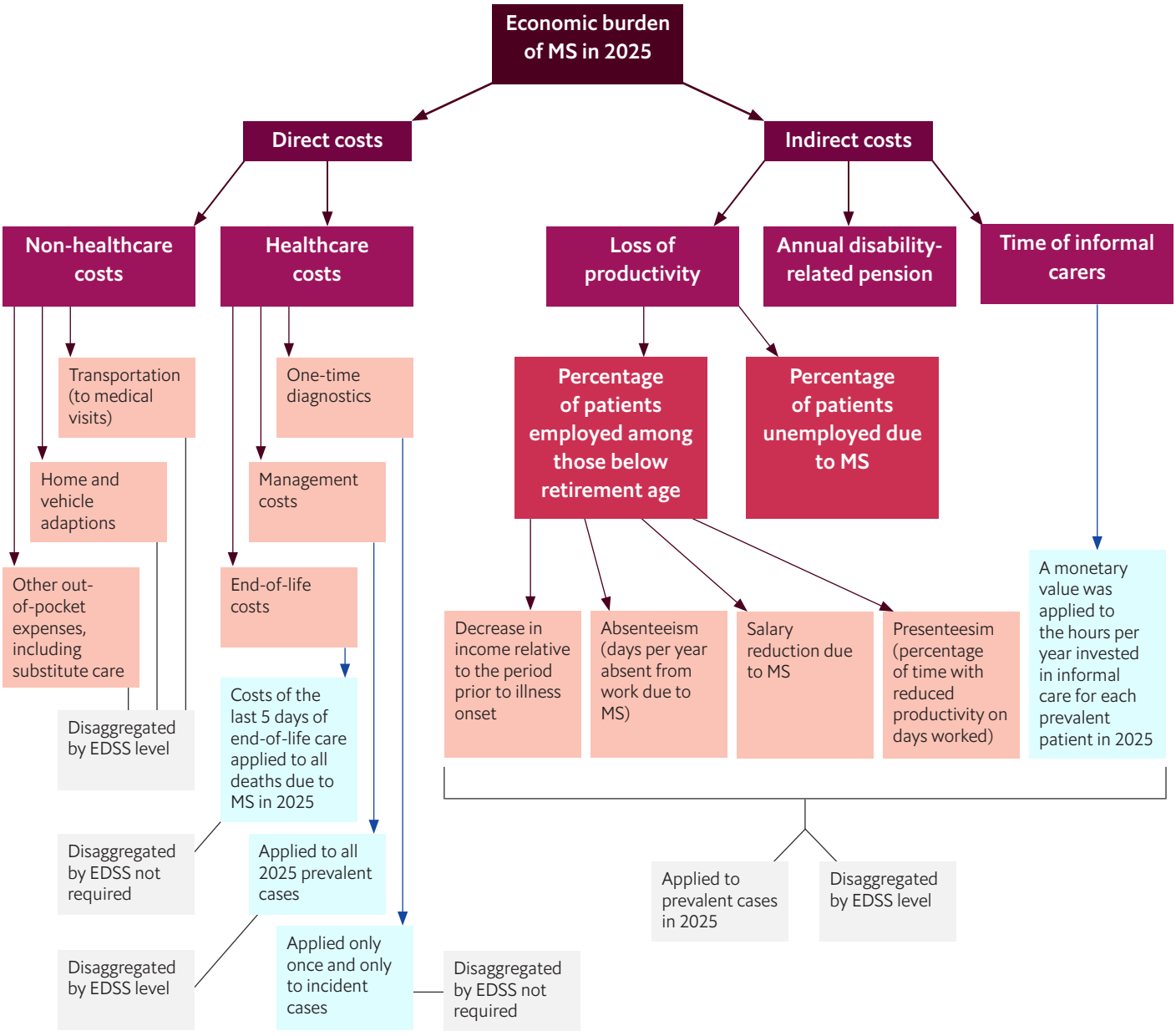
Handling missing data

To ensure completeness and comparability across countries, a structured approach will be applied to address data gaps. When country-specific data is not available, informed assumptions and extrapolation techniques will be employed to maintain consistency in the analysis.

In the case of missing data on healthcare resource utilisation for a given country, the analysis will assume utilisation patterns equivalent to those observed in another study country where contextually comparable or, where appropriate, in a high-income country (HIC) outside the study scope as appropriate. The choice of proxy country will be based on similarities in healthcare system structure, clinical practice, and economic context.

Similarly, for missing unit cost inputs, available cost data from another study country will be used and adjusted to the target setting. Such adjustments will be conducted using standardised methods such as purchasing power parity (PPP) conversion factors or scaling based on per capita health expenditure, to account for cross-country differences in healthcare prices and economic capacity.

Annexe A: Model framework



Source: Economist Impact.

Annexe B: Assumptions (by country)

United Kingdom

Direct healthcare costs

EDSS level	Inclusions	Main source	Assumption/s
0-3.5	Medicines, inpatient care/day admissions, consultations, and tests.	• Thompson et al, 2017	Table 4 from Thompson et al. was used.
4-6.5	Medicines, inpatient care/day admissions, consultations, and tests.	• Thompson et al, 2017	Table 4 from Thompson et al. was used.
7-9.5	Medicines, inpatient care/day admissions, consultations, and tests.	• Thompson et al, 2017	Table 4 from Thompson et al. was used.

Other direct costs

EDSS level	Inclusions	Main source	Assumption/s
0-3.5	Home and vehicle adaptations + Investments in equipment and devices to aid patients' mobility + Other expenses (Community services) + Transportation.	• Thompson et al, 2017	Table 4 from Thompson et al. was used.

United Kingdom

Other direct costs (continued)

EDSS level	Inclusions	Main source	Assumption/s
4-6.5	Home and vehicle adaptations + Investments in equipment and devices to aid patients' mobility + Other expenses (Community services) + Transportation.	• Thompson et al, 2017	Table 4 from Thompson et al. was used.
7-9.5	Home and vehicle adaptations + Investments in equipment and devices to aid patients' mobility + Other expenses (Community services) + Transportation.	• Thompson et al, 2017	Table 4 from Thompson et al. was used.

Indirect costs

EDSS level	Inclusions	Main source	Assumption/s
0-3.5	Caregivers' indirect costs - Informal caregiving.	• Thompson et al, 2017 • Survey • Skills for care, 2024	To estimate this value, the following were used: the percentage of patients requiring an informal caregiver for this EDSS category (on average), the total average number of hours per week of informal care needed for this EDSS category, and the average hourly wage of workers in health-related social assistance in the country as a proxy for the shadow price of informal care.
4-6.5	Caregivers' indirect costs - Informal caregiving.	• Thompson et al, 2017 • Survey • Skills for care, 2024	To estimate this value, the following were used: the percentage of patients requiring an informal caregiver for this EDSS category (on average), the total average number of hours per week of informal care needed for this EDSS category, and the average hourly wage of workers in health-related social assistance in the country as a proxy for the shadow price of informal care.
7-9.5	Caregivers' indirect costs - Informal caregiving.	• Thompson et al, 2017 • Survey • Skills for care, 2024	To estimate this value, the following were used: the percentage of patients requiring an informal caregiver for this EDSS category (on average), the total average number of hours per week of informal care needed for this EDSS category, and the average hourly wage of workers in health-related social assistance in the country as a proxy for the shadow price of informal care.

United Kingdom

Indirect costs (continued)

EDSS level	Inclusions	Main source	Assumption/s
0-3.5	Patients' indirect costs - Absenteeism.	• Survey • ILOSTAT • Thompson et al, 2017	The value for the average number of hours per week of absenteeism per patient was obtained from the survey conducted. This value was applied to the average salary of individuals with disabilities in the UK to estimate the annual productivity loss. This was also adjusted by the percentage of MS patients currently employed in this EDSS category. Given the lack of wage data for patients with MS, the average annual salary of individuals with disabilities for the UK was considered.
4-6.5	Patients' indirect costs - Absenteeism.	• Survey • ILOSTAT • Thompson et al, 2017	The value for the average number of hours per week of absenteeism per patient was obtained from the survey conducted. This value was applied to the average salary of individuals with disabilities in the UK to estimate the annual productivity loss. This was also adjusted by the percentage of MS patients currently employed in this EDSS category. Given the lack of wage data for patients with MS, the average annual salary of individuals with disabilities for the UK was considered.
7-9.5	Patients' indirect costs - Absenteeism.	• Survey • ILOSTAT • Thompson et al, 2017	The value for the average number of hours per week of absenteeism per patient was obtained from the survey conducted. This value was applied to the average salary of individuals with disabilities in the UK to estimate the annual productivity loss. This was also adjusted by the percentage of MS patients currently employed in this EDSS category. Given the lack of wage data for patients with MS, the average annual salary of individuals with disabilities for the UK was considered.
0-3.5	Patients' indirect costs - Presenteeism.	• Bebo et al, 2022	Given the lack of information on reduced working hours, the data provided by Bebo et al. was used, where the estimated annual burden per average MS patient due to presenteeism and absenteeism was reported. That ratio (economic burden due to presenteeism/absenteeism) was obtained and used to estimate the economic burden of presenteeism by multiplying it by the calculated absenteeism value for each EDSS group.
4-6.5	Patients' indirect costs - Presenteeism.	• Bebo et al, 2022	Given the lack of information on reduced working hours, the data provided by Bebo et al. was used, where the estimated annual burden per average MS patient due to presenteeism and absenteeism was reported. That ratio (economic burden due to presenteeism/absenteeism) was obtained and used to estimate the economic burden of presenteeism by multiplying it by the calculated absenteeism value for each EDSS group.
7-9.5	Patients' indirect costs - Presenteeism.	• Bebo et al, 2022	Given the lack of information on reduced working hours, the data provided by Bebo et al. was used, where the estimated annual burden per average MS patient due to presenteeism and absenteeism was reported. That ratio (economic burden due to presenteeism/absenteeism) was obtained and used to estimate the economic burden of presenteeism by multiplying it by the calculated absenteeism value for each EDSS group.

United Kingdom

Indirect costs (continued)

EDSS level	Inclusions	Main source	Assumption/s
0-3.5	Patients' indirect costs - Productivity loss due to early retirement.	• Thompson et al, 2017	To estimate the productivity loss due to premature retirement, the prevalence of premature retirement for each EDSS group was obtained and multiplied by the annual average salary.
4-6.5	Patients' indirect costs - Productivity loss due to early retirement.	• Thompson et al, 2017	To estimate the productivity loss due to premature retirement, the prevalence of premature retirement for each EDSS group was obtained and multiplied by the annual average salary.
7-9.5	Patients' indirect costs - Productivity loss due to early retirement.	• Thompson et al, 2017	To estimate the productivity loss due to premature retirement, the prevalence of premature retirement for each EDSS group was obtained and multiplied by the annual average salary.
0-3.5	Disability Insurance due to early retirement.	• Thompson et al, 2017 • UK Department for Work & Pensions, 2024	To estimate Disability Insurance costs due to early retirement caused by multiple sclerosis (MS), the prevalence of premature retirement for each EDSS group was obtained and multiplied by the average annual Disability Insurance benefit in the UK.
4-6.5	Disability Insurance due to early retirement.	• Thompson et al, 2017 • UK Department for Work & Pensions, 2024	To estimate Disability Insurance costs due to early retirement caused by multiple sclerosis (MS), the prevalence of premature retirement for each EDSS group was obtained and multiplied by the average annual Disability Insurance benefit in the UK.
7-9.5	Disability Insurance due to early retirement.	• Thompson et al, 2017 • UK Department for Work & Pensions, 2024	To estimate Disability Insurance costs due to early retirement caused by multiple sclerosis (MS), the prevalence of premature retirement for each EDSS group was obtained and multiplied by the average annual Disability Insurance benefit in the UK.
0-3.5	Patients' indirect costs - Productivity loss due to unemployment.	• ILOSTAT • OECD 2024 • Thompson et al, 2017	To estimate the productivity loss due to unemployment caused by multiple sclerosis (MS), we used the unemployment rate stratified by EDSS groups. This rate was adjusted for the proportion of the MS population within working age, the general unemployment rate in the country, and the percentage of MS patients in early retirement, which was subtracted to avoid double counting. The national average wage was used to calculate the monetary value of productivity loss. As a conservative approach, the proportion of patients within the EDSS 0–3.5 category deemed asymptomatic according to GBD criteria was excluded from the analysis, under the assumption that this subset was not unemployed as a consequence of their disease.

United Kingdom

Indirect costs (continued)

EDSS level	Inclusions	Main source	Assumption/s
4-6.5	Patients' indirect costs - Productivity loss due to unemployment.	• ILOSTAT • OECD 2024 • Thompson et al, 2017	To estimate the productivity loss due to unemployment caused by multiple sclerosis (MS), we used the unemployment rate stratified by EDSS groups. This rate was adjusted for the proportion of the MS population within working age, the general unemployment rate in the country, and the percentage of MS patients in early retirement, which was subtracted to avoid double counting. The national average wage was used to calculate the monetary value of productivity loss. As a conservative approach, the proportion of patients within the EDSS 0–3.5 category deemed asymptomatic according to GBD criteria was excluded from the analysis, under the assumption that this subset was not unemployed as a consequence of their disease.
7-9.5	Patients' indirect costs - Productivity loss due to unemployment.	• ILOSTAT • OECD 2024 • Thompson et al, 2017	To estimate the productivity loss due to unemployment caused by multiple sclerosis (MS), we used the unemployment rate stratified by EDSS groups. This rate was adjusted for the proportion of the MS population within working age, the general unemployment rate in the country, and the percentage of MS patients in early retirement, which was subtracted to avoid double counting. The national average wage was used to calculate the monetary value of productivity loss. As a conservative approach, the proportion of patients within the EDSS 0–3.5 category deemed asymptomatic according to GBD criteria was excluded from the analysis, under the assumption that this subset was not unemployed as a consequence of their disease.
0-3.5	Patients' indirect costs - Productivity loss caused by a decrease in salary.	• ILOSTAT	For those currently employed, the salary reduction due to disability (assumed to be caused by MS) was calculated. This calculation applied the annual difference reported by the ILO for the country, comparing the average salary to the average salary for individuals with disabilities in the country.
4-6.5	Patients' indirect costs - Productivity loss caused by a decrease in salary.	• ILOSTAT	For those currently employed, the salary reduction due to disability (assumed to be caused by MS) was calculated. This calculation applied the annual difference reported by the ILO for the country, comparing the average salary to the average salary for individuals with disabilities in the country.
7-9.5	Patients' indirect costs - Productivity loss caused by a decrease in salary.	• ILOSTAT	For those currently employed, the salary reduction due to disability (assumed to be caused by MS) was calculated. This calculation applied the annual difference reported by the ILO for the country, comparing the average salary to the average salary for individuals with disabilities in the country.
NA	One-Time Diagnostic Costs: Primary care visit, Neurology consultation, Blood test, Lumbar puncture, MRI.	• Thompson et al, 2017	Given the lack of information for this parameter, the annual per-patient value reported by Thompson et al. (2017) was used, as a proxy, for the following items: tests and consultations (Table 4). As a conservative approach, data reported for the EDSS 0–3.5 group were used and assumed for each average patient at the time of diagnosis.

United States

Direct healthcare costs

EDSS level	Inclusions	Main source	Assumption/s
0-3.5	Medicines, inpatient care/day admissions, consultations, and tests.	• Bebo et al, 2022	It is assumed that the value reported by Bebo B. et al. represents, on average, patients with an EDSS between 0-3.5.
4-6.5	Medicines, inpatient care/day admissions, consultations, and tests.	• Bebo et al, 2022 • Thompson et al, 2017	The expected differences in direct healthcare costs for higher EDSS groups were derived as ratios relative to the cost of the lowest EDSS group, based on the findings reported by Alan Thompson et al. for the UK.
7-9.5	Medicines, inpatient care/day admissions, consultations, and tests.	• Bebo et al, 2022 • Thompson et al, 2017	The expected differences in direct healthcare costs for higher EDSS groups were derived as ratios relative to the cost of the lowest EDSS group, based on the findings reported by Alan Thompson et al. for the UK.

Other direct costs

EDSS level	Inclusions	Main source	Assumption/s
0-3.5	Home and vehicle adaptations + Investments in equipment and devices to aid patients' mobility + Other expenses (Community services) + Transportation.	• Bebo et al, 2022	It is assumed that the value reported by Bebo B. et al. represents, on average, patients with an EDSS between 0-3.5.
4-6.5	Home and vehicle adaptations + Investments in equipment and devices to aid patients' mobility + Other expenses (Community services) + Transportation.	• Bebo et al, 2022 • Thompson et al, 2017	It was calculated assuming incremental increases according to the EDSS score, reflecting the relative differences across increasing EDSS groups as reported by Alan Thompson et al. for the UK.

United States

Other direct costs (continued)

EDSS level	Inclusions	Main source	Assumption/s
7-9.5	Home and vehicle adaptations + Investments in equipment and devices to aid patients' mobility + Other expenses (Community services) + Transportation.	• Bebo et al, 2022 • Thompson et al, 2017	It was calculated assuming incremental increases according to the EDSS score, reflecting the relative differences across increasing EDSS groups as reported by Alan Thompson et al. for the UK.

Indirect costs

EDSS level	Inclusions	Main source	Assumption/s
0-3.5	Caregivers' indirect costs - Informal caregiving.	• Thompson et al, 2017 • Survey • Health Care and Social Assistance: NAICS 62 : U.S. Bureau of Labor Statistics	To estimate this value, the following inputs were used: the percentage of patients requiring an informal caregiver for this EDSS category (in the absence of US-specific data, this value was taken from Thompson et al., reported for the United Kingdom); the total average number of hours per week of informal care required for this EDSS category (also sourced from Thompson et al. due to the lack of US-specific estimates); and the average hourly wage of workers in health-related social assistance in the US, used as a proxy for the shadow price of informal care.
4-6.5	Caregivers' indirect costs - Informal caregiving.	• Thompson et al, 2017 • Survey • Health Care and Social Assistance: NAICS 62 : U.S. Bureau of Labor Statistics	To estimate this value, the following inputs were used: the percentage of patients requiring an informal caregiver for this EDSS category (in the absence of US-specific data, this value was taken from Thompson et al., reported for the United Kingdom); the total average number of hours per week of informal care required for this EDSS category (also sourced from Thompson et al. due to the lack of US-specific estimates); and the average hourly wage of workers in health-related social assistance in the US, used as a proxy for the shadow price of informal care.
7-9.5	Caregivers' indirect costs - Informal caregiving.	• Thompson et al, 2017 • Survey • Health Care and Social Assistance: NAICS 62 : U.S. Bureau of Labor Statistics	To estimate this value, the following inputs were used: the percentage of patients requiring an informal caregiver for this EDSS category (in the absence of US-specific data, this value was taken from Thompson et al., reported for the United Kingdom); the total average number of hours per week of informal care required for this EDSS category (also sourced from Thompson et al. due to the lack of US-specific estimates); and the average hourly wage of workers in health-related social assistance in the US, used as a proxy for the shadow price of informal care.

United States

Indirect costs (continued)

EDSS level	Inclusions	Main source	Assumption/s
0-3.5	Patients' indirect costs - Absenteeism.	• Survey • ILOSTAT	The value for the average number of hours per week of absenteeism per patient was obtained from the survey conducted. This value was applied to the average salary of individuals with disabilities in the US to estimate the annual productivity loss. This was also adjusted by the percentage of MS patients currently employed in this EDSS category. Given the lack of wage data for patients with MS, the average annual salary of individuals with disabilities for the US was considered.
4-6.5	Patients' indirect costs - Absenteeism.	• Survey • ILOSTAT	The value for the average number of hours per week of absenteeism per patient was obtained from the survey conducted. This value was applied to the average salary of individuals with disabilities in the US to estimate the annual productivity loss. This was also adjusted by the percentage of MS patients currently employed in this EDSS category. Given the lack of wage data for patients with MS, the average annual salary of individuals with disabilities for the US was considered.
7-9.5	Patients' indirect costs - Absenteeism.	• Survey • ILOSTAT	The value for the average number of hours per week of absenteeism per patient was obtained from the survey conducted. This value was applied to the average salary of individuals with disabilities in the US to estimate the annual productivity loss. This was also adjusted by the percentage of MS patients currently employed in this EDSS category. Given the lack of wage data for patients with MS, the average annual salary of individuals with disabilities for the US was considered.
0-3.5	Patients' indirect costs - Presenteeism.	• Bebo et al, 2022	Given the lack of information on reduced working hours, the data provided by Bebo et al. was used, where the estimated annual burden per average MS patient due to presenteeism and absenteeism was reported. That ratio (economic burden due to presenteeism/absenteeism) was obtained and used to estimate the economic burden of presenteeism by multiplying it by the calculated absenteeism value for each EDSS group.
4-6.5	Patients' indirect costs - Presenteeism.	• Bebo et al, 2022	Given the lack of information on reduced working hours, the data provided by Bebo et al. was used, where the estimated annual burden per average MS patient due to presenteeism and absenteeism was reported. That ratio (economic burden due to presenteeism/absenteeism) was obtained and used to estimate the economic burden of presenteeism by multiplying it by the calculated absenteeism value for each EDSS group.
7-9.5	Patients' indirect costs - Presenteeism.	• Bebo et al, 2022	Given the lack of information on reduced working hours, the data provided by Bebo et al. was used, where the estimated annual burden per average MS patient due to presenteeism and absenteeism was reported. That ratio (economic burden due to presenteeism/absenteeism) was obtained and used to estimate the economic burden of presenteeism by multiplying it by the calculated absenteeism value for each EDSS group.

United States

Indirect costs (continued)

EDSS level	Inclusions	Main source	Assumption/s
0-3.5	Patients' indirect costs - Productivity loss due to early retirement.	• Vitturi et al, 2022	To estimate the productivity loss due to premature retirement, the prevalence of premature retirement for each EDSS group was obtained and multiplied by the annual average salary.
4-6.5	Patients' indirect costs - Productivity loss due to early retirement.	• Vitturi et al, 2022	To estimate the productivity loss due to premature retirement, the prevalence of premature retirement for each EDSS group was obtained and multiplied by the annual average salary.
7-9.5	Patients' indirect costs - Productivity loss due to early retirement.	• Vitturi et al, 2022	To estimate the productivity loss due to premature retirement, the prevalence of premature retirement for each EDSS group was obtained and multiplied by the annual average salary.
0-3.5	Disability Insurance due to early retirement.	• Vitturi et al, 2022 • Social Security US (Monthly Statistical Snapshot, July 2025)	To estimate Disability Insurance costs due to early retirement caused by multiple sclerosis (MS), the prevalence of premature retirement for each EDSS group was obtained and multiplied by the average annual Disability Insurance benefit in the US.
4-6.5	Disability Insurance due to early retirement.	• Vitturi et al, 2022 • Social Security US (Monthly Statistical Snapshot, July 2025)	To estimate Disability Insurance costs due to early retirement caused by multiple sclerosis (MS), the prevalence of premature retirement for each EDSS group was obtained and multiplied by the average annual Disability Insurance benefit in the US.
7-9.5	Disability Insurance due to early retirement.	• Vitturi et al, 2022 • Social Security US (Monthly Statistical Snapshot, July 2025)	To estimate Disability Insurance costs due to early retirement caused by multiple sclerosis (MS), the prevalence of premature retirement for each EDSS group was obtained and multiplied by the average annual Disability Insurance benefit in the US.
0-3.5	Patients' indirect costs - Productivity loss due to unemployment.	• Ponzio et al, 2023 • ILOSTAT • OECD 2024	Calculation based on Figure 3 of Ponzio et al. To estimate the productivity loss due to unemployment caused by multiple sclerosis (MS), we used the unemployment rate stratified by EDSS groups. This rate was adjusted for the proportion of the MS population within working age (according to GBD), the general unemployment rate in the country, and the percentage of MS patients in early retirement, which was subtracted to avoid double counting. The national average wage was used to calculate the monetary value of productivity loss. As a conservative approach, the proportion of patients within the EDSS 0–3.5 category deemed asymptomatic according to GBD criteria was excluded from the analysis, under the assumption that this subset was not unemployed as a consequence of their disease.

United States

Indirect costs (continued)

EDSS level	Inclusions	Main source	Assumption/s
4-6.5	Patients' indirect costs - Productivity loss due to unemployment.	• Ponzio et al, 2023 • ILOSTAT • OECD 2024	Calculation based on Figure 3 of Ponzio et al. To estimate the productivity loss due to unemployment caused by multiple sclerosis (MS), we used the unemployment rate stratified by EDSS groups. This rate was adjusted for the proportion of the MS population within working age (according to GBD), the general unemployment rate in the country, and the percentage of MS patients in early retirement, which was subtracted to avoid double counting. The national average wage was used to calculate the monetary value of productivity loss. As a conservative approach, the proportion of patients within the EDSS 0–3.5 category deemed asymptomatic according to GBD criteria was excluded from the analysis, under the assumption that this subset was not unemployed as a consequence of their disease.
7-9.5	Patients' indirect costs - Productivity loss due to unemployment.	• Ponzio et al, 2023 • ILOSTAT • OECD 2024	Calculation based on Figure 3 of Ponzio et al. To estimate the productivity loss due to unemployment caused by multiple sclerosis (MS), we used the unemployment rate stratified by EDSS groups. This rate was adjusted for the proportion of the MS population within working age (according to GBD), the general unemployment rate in the country, and the percentage of MS patients in early retirement, which was subtracted to avoid double counting. The national average wage was used to calculate the monetary value of productivity loss. As a conservative approach, the proportion of patients within the EDSS 0–3.5 category deemed asymptomatic according to GBD criteria was excluded from the analysis, under the assumption that this subset was not unemployed as a consequence of their disease.
0-3.5	Patients' indirect costs - Productivity loss caused by a decrease in salary.	• ILOSTAT	Calculation based on information reported by the ILO regarding average salaries for the general population and average salaries for individuals with disabilities
4-6.5	Patients' indirect costs - Productivity loss caused by a decrease in salary.	• ILOSTAT	Calculation based on information reported by the ILO regarding average salaries for the general population and average salaries for individuals with disabilities
7-9.5	Patients' indirect costs - Productivity loss caused by a decrease in salary.	• ILOSTAT	Calculation based on information reported by the ILO regarding average salaries for the general population and average salaries for individuals with disabilities

United States

Additional costs related to diagnosis (Incident cases)

EDSS level	Inclusions	Main source	Assumption/s
NA	One-Time Diagnostic Costs: Primary care visit, Neurology consultation, Blood test, Lumbar puncture, MRI.	• Jiang et al, 2023 • Sidecare Health cost calculator	A conservative assumption was made of only two visits with a general practitioner, two visits with a neurologist, two blood tests, one lumbar puncture, and one MRI of both the brain and spinal cord.

Germany

Direct medical costs

EDSS level	Inclusions	Main source	Assumption/s
0-3.5	Medicines, inpatient care/day admissions, consultations, and tests.	• Flachenecker et al, 2017	Flachenecker et al. was used for the central values.
4-6.5	Medicines, inpatient care/day admissions, consultations, and tests.	• Flachenecker et al, 2017	Flachenecker et al. was used for the central values.
7-9.5	Medicines, inpatient care/day admissions, consultations, and tests.	• Flachenecker et al, 2017	Flachenecker et al. was used for the central values.

Other direct costs

EDSS level	Inclusions	Main source	Assumption/s
0-3.5	Home and vehicle adaptations + Investments in equipment and devices to aid patients' mobility + Other expenses (Community services) + Transportation.	• Flachenecker et al, 2017 • Dillon et al, 2023 • Battaglia et al, 2022	Home and vehicle adaptations + Investments in equipment and devices to aid patients' mobility + Other expenses (Community services) + Transportation (for transportation costs, and due to the lack of information for the country, the percentage of transportation costs out of total non-healthcare direct costs for each EDSS group was taken from Battaglia et al. 2022.
4-6.5	Home and vehicle adaptations + Investments in equipment and devices to aid patients' mobility + Other expenses (Community services) + Transportation.	• Flachenecker et al, 2017 • Dillon et al, 2023	Home and vehicle adaptations + Investments in equipment and devices to aid patients' mobility + Other expenses (Community services) + Transportation (for transportation costs, and due to the lack of information for the country, the percentage of transportation costs out of total non-healthcare direct costs for each EDSS group was taken from Battaglia et al. 2022.

Germany

Other direct costs (continued)

EDSS level	Inclusions	Main source	Assumption/s
7-9.5	Home and vehicle adaptations + Investments in equipment and devices to aid patients' mobility + Other expenses (Community services) + Transportation.	• Flachenecker et al, 2017 • Dillon et al, 2023 • Battaglia et al, 2022	Home and vehicle adaptations + Investments in equipment and devices to aid patients' mobility + Other expenses (Community services) + Transportation (for transportation costs, and due to the lack of information for the country, the percentage of transportation costs out of total non-healthcare direct costs for each EDSS group was taken from Battaglia et al. 2022.

Indirect costs

EDSS level	Inclusions	Main source	Assumption/s
0-3.5	Caregivers' indirect costs - Informal caregiving.	• Flachenecker et al, 2017 • Survey • Federal Government of Germany, "Mindestlohn in der Altenpflege." Bundesregierung – Aktuelles, 2025	To estimate this value, the following were used: the percentage of patients requiring an informal caregiver for this EDSS category (on average), the total average number of hours per week of informal care needed for this EDSS category, and the average hourly wage of workers in health-related social assistance in Italy as a proxy for the shadow price of informal care.
4-6.5	Caregivers' indirect costs - Informal caregiving.	• Flachenecker et al, 2017 • Survey • Federal Government of Germany, "Mindestlohn in der Altenpflege." Bundesregierung – Aktuelles, 2025	To estimate this value, the following were used: the percentage of patients requiring an informal caregiver for this EDSS category (on average), the total average number of hours per week of informal care needed for this EDSS category, and the average hourly wage of workers in health-related social assistance in Italy as a proxy for the shadow price of informal care.

Germany

Indirect costs (continued)

EDSS level	Inclusions	Main source	Assumption/s
7-9.5	Caregivers' indirect costs - Informal caregiving.	• Flachenecker et al, 2017 • Survey • Federal Government of Germany, "Mindestlohn in der Altenpflege." Bundesregierung – Aktuelles, 2025	To estimate this value, the following were used: the percentage of patients requiring an informal caregiver for this EDSS category (on average), the total average number of hours per week of informal care needed for this EDSS category, and the average hourly wage of workers in health-related social assistance in Italy as a proxy for the shadow price of informal care.
0-3.5	Patients' indirect costs - Absenteeism.	• Flachenecker et al, 2017	The value for the average number of hours per week of absenteeism per patient was obtained from the survey conducted. This value was applied to the average salary of individuals with disabilities in the Germany to estimate the annual productivity loss. This was also adjusted by the percentage of MS patients currently employed in this EDSS category. Given the lack of wage data for patients with MS, the average annual salary of individuals with disabilities for Germany was considered.
4-6.5	Patients' indirect costs - Absenteeism.	• Flachenecker et al, 2017	The value for the average number of hours per week of absenteeism per patient was obtained from the survey conducted. This value was applied to the average salary of individuals with disabilities in the Germany to estimate the annual productivity loss. This was also adjusted by the percentage of MS patients currently employed in this EDSS category. Given the lack of wage data for patients with MS, the average annual salary of individuals with disabilities for Germany was considered.
7-9.5	Patients' indirect costs - Absenteeism.	• Flachenecker et al, 2017	The value for the average number of hours per week of absenteeism per patient was obtained from the survey conducted. This value was applied to the average salary of individuals with disabilities in the Germany to estimate the annual productivity loss. This was also adjusted by the percentage of MS patients currently employed in this EDSS category. Given the lack of wage data for patients with MS, the average annual salary of individuals with disabilities for Germany was considered.
0-3.5	Patients' indirect costs - Presenteeism.	• Bebo et al, 2022	Given the lack of information on reduced working hours, the data provided by Bebo et al. was used, where the estimated annual burden per average MS patient due to presenteeism and absenteeism was reported. That ratio (economic burden due to presenteeism/absenteeism) was obtained and used to estimate the economic burden of presenteeism by multiplying it by the calculated absenteeism value for each EDSS group.

Germany

Indirect costs (continued)

EDSS level	Inclusions	Main source	Assumption/s
4-6.5	Patients' indirect costs - Presenteeism.	• Bebo et al, 2022	Given the lack of information on reduced working hours, the data provided by Bebo et al. was used, where the estimated annual burden per average MS patient due to presenteeism and absenteeism was reported. That ratio (economic burden due to presenteeism/absenteeism) was obtained and used to estimate the economic burden of presenteeism by multiplying it by the calculated absenteeism value for each EDSS group.
7-9.5	Patients' indirect costs - Presenteeism.	• Bebo et al, 2022	Given the lack of information on reduced working hours, the data provided by Bebo et al. was used, where the estimated annual burden per average MS patient due to presenteeism and absenteeism was reported. That ratio (economic burden due to presenteeism/absenteeism) was obtained and used to estimate the economic burden of presenteeism by multiplying it by the calculated absenteeism value for each EDSS group.
0-3.5	Patients' indirect costs - Productivity loss due to early retirement.	• Flachenecker et al, 2017 • ILOSTAT	To estimate the productivity loss due to premature retirement, the prevalence of premature retirement for each EDSS group was obtained and multiplied by the annual average salary.
4-6.5	Patients' indirect costs - Productivity loss due to early retirement.	• Flachenecker et al, 2017 • ILOSTAT	To estimate the productivity loss due to premature retirement, the prevalence of premature retirement for each EDSS group was obtained and multiplied by the annual average salary.
7-9.5	Patients' indirect costs - Productivity loss due to early retirement.	• Flachenecker et al, 2017 • ILOSTAT	To estimate the productivity loss due to premature retirement, the prevalence of premature retirement for each EDSS group was obtained and multiplied by the annual average salary.
0-3.5	Disability Insurance due to early retirement.	• Flachenecker et al, 2017 • Institut Arbeit und Qualifikation, Universität Duisburg-Essen, 2023	To estimate Disability Insurance costs due to early retirement caused by multiple sclerosis (MS), the prevalence of premature retirement for each EDSS group was obtained and multiplied by the average annual Disability Insurance benefit in the country
4-6.5	Disability Insurance due to early retirement.	• Flachenecker et al, 2017 • Institut Arbeit und Qualifikation, Universität Duisburg-Essen, 2023	To estimate Disability Insurance costs due to early retirement caused by multiple sclerosis (MS), the prevalence of premature retirement for each EDSS group was obtained and multiplied by the average annual Disability Insurance benefit in the country

Germany

Indirect costs (continued)

EDSS level	Inclusions	Main source	Assumption/s
7-9.5	Disability Insurance due to early retirement.	• Flachenecker et al, 2017 • Institut Arbeit und Qualifikation, Universität Duisburg-Essen, 2023	To estimate Disability Insurance costs due to early retirement caused by multiple sclerosis (MS), the prevalence of premature retirement for each EDSS group was obtained and multiplied by the average annual Disability Insurance benefit in the country
0-3.5	Patients' indirect costs - Productivity loss due to unemployment.	• ILOSTAT • Flachenecker et al.,2017 • OECD 2024	To estimate the productivity loss due to unemployment caused by multiple sclerosis (MS), we used the unemployment rate stratified by EDSS groups. This rate was adjusted for the proportion of the MS population within working age, the general unemployment rate in the country, and the percentage of MS patients in early retirement, which was subtracted to avoid double counting. The national average wage was used to calculate the monetary value of productivity loss.
4-6.5	Patients' indirect costs - Productivity loss due to unemployment.	• ILOSTAT • Flachenecker et al.,2017 • OECD 2024	To estimate the productivity loss due to unemployment caused by multiple sclerosis (MS), we used the unemployment rate stratified by EDSS groups. This rate was adjusted for the proportion of the MS population within working age, the general unemployment rate in the country, and the percentage of MS patients in early retirement, which was subtracted to avoid double counting. The national average wage was used to calculate the monetary value of productivity loss.
7-9.5	Patients' indirect costs - Productivity loss due to unemployment.	• ILOSTAT • Flachenecker et al.,2017 • OECD 2024	To estimate the productivity loss due to unemployment caused by multiple sclerosis (MS), we used the unemployment rate stratified by EDSS groups. This rate was adjusted for the proportion of the MS population within working age, the general unemployment rate in the country, and the percentage of MS patients in early retirement, which was subtracted to avoid double counting. The national average wage was used to calculate the monetary value of productivity loss.
0-3.5	Patients' indirect costs - Productivity loss caused by a decrease in salary.	• ILOSTAT	For those currently employed, the salary reduction due to disability (assumed to be caused by MS) was calculated. This calculation applied the annual difference reported by the ILO for the country, comparing the average salary to the average salary for individuals with disabilities in the country.
4-6.5	Patients' indirect costs - Productivity loss caused by a decrease in salary.	• ILOSTAT	For those currently employed, the salary reduction due to disability (assumed to be caused by MS) was calculated. This calculation applied the annual difference reported by the ILO for the country, comparing the average salary to the average salary for individuals with disabilities in the country.

Germany

Indirect costs (continued)

EDSS level	Inclusions	Main source	Assumption/s
7-9.5	Patients' indirect costs - Productivity loss caused by a decrease in salary.	• ILOSTAT	For those currently employed, the salary reduction due to disability (assumed to be caused by MS) was calculated. This calculation applied the annual difference reported by the ILO for the country, comparing the average salary to the average salary for individuals with disabilities in the country.

Additional costs related to diagnosis (Incident cases)

EDSS level	Inclusions	Main source	Assumption/s
NA	One-Time Diagnostic Costs: Primary care visit, Neurology consultation, Blood test, Lumbar puncture, MRI.	• Dillon et al, 2023	Given the lack of information for this parameter, the annual per-patient value reported by Dillon et al. (2023) was used, as a proxy, for the following items: tests and consultations (Table 3). As a conservative approach, data reported for the EDSS 0–3.5 group were used and assumed for each average patient at the time of diagnosis

Italy

Direct medical costs

EDSS level	Inclusions	Main source	Assumption/s
0-3.5	Medicines, inpatient care/day admissions, consultations, and tests.	• Battaglia et al, 2022	Battaglia et al. for central values.
4-6.5	Medicines, inpatient care/day admissions, consultations, and tests.	• Battaglia et al, 2022	Battaglia et al. for central values.
7-9.5	Medicines, inpatient care/day admissions, consultations, and tests.	• Battaglia et al, 2022	Battaglia et al. for central values.

Other direct costs

EDSS level	Inclusions	Main source	Assumption/s
0-3.5	Home and vehicle adaptations + Investments in equipment and devices to aid patients' mobility + Other expenses (Community services) + Transportation.	• Battaglia et al, 2022	Battaglia et al. for central values.
4-6.5	Home and vehicle adaptations + Investments in equipment and devices to aid patients' mobility + Other expenses (Community services) + Transportation.	• Battaglia et al, 2022	Battaglia et al. for central values.

Italy

Other direct costs (continued)

EDSS level	Inclusions	Main source	Assumption/s
7-9.5	Home and vehicle adaptations + Investments in equipment and devices to aid patients' mobility + Other expenses (Community services) + Transportation.	• Battaglia et al, 2022	Battaglia et al. for central values.

Indirect costs

EDSS level	Inclusions	Main source	Assumption/s
0-3.5	Caregivers' indirect costs - Informal caregiving.	• Battaglia et al, 2022 • Survey	To estimate this value, the following were used: the percentage of patients requiring an informal caregiver for this EDSS category (on average), the total average number of hours per week of informal care needed for this EDSS category, and the average hourly wage of workers in health-related social assistance in Italy as a proxy for the shadow price of informal care. Supplementary Table 2 was used from Battaglia et al.
4-6.5	Caregivers' indirect costs - Informal caregiving.	• Battaglia et al, 2022 • Survey	To estimate this value, the following were used: the percentage of patients requiring an informal caregiver for this EDSS category (on average), the total average number of hours per week of informal care needed for this EDSS category, and the average hourly wage of workers in health-related social assistance in Italy as a proxy for the shadow price of informal care. Supplementary Table 2 was used from Battaglia et al.
7-9.5	Caregivers' indirect costs - Informal caregiving.	• Battaglia et al, 2022 • Survey	To estimate this value, the following were used: the percentage of patients requiring an informal caregiver for this EDSS category (on average), the total average number of hours per week of informal care needed for this EDSS category, and the average hourly wage of workers in health-related social assistance in Italy as a proxy for the shadow price of informal care. Supplementary Table 2 was used from Battaglia et al.
0-3.5	Patients' indirect costs - Absenteeism.	• Battaglia et al, 2022 • Survey	The value for the average number of hours per week of absenteeism per patient was obtained from the survey conducted. This value was applied to the average salary of individuals with disabilities in Italy to estimate the annual productivity loss. This was also adjusted by the percentage of MS patients currently employed in this EDSS category. Given the lack of wage data for patients with MS, the average annual salary of individuals with disabilities for Italy was considered.

Italy

Indirect costs (continued)

EDSS level	Inclusions	Main source	Assumption/s
4-6.5	Patients' indirect costs - Absenteeism.	• Battaglia et al, 2022 • Survey	The value for the average number of hours per week of absenteeism per patient was obtained from the survey conducted. This value was applied to the average salary of individuals with disabilities in Italy to estimate the annual productivity loss. This was also adjusted by the percentage of MS patients currently employed in this EDSS category. Given the lack of wage data for patients with MS, the average annual salary of individuals with disabilities for Italy was considered.
7-9.5	Patients' indirect costs - Absenteeism.	• Battaglia et al, 2022 • Survey	The value for the average number of hours per week of absenteeism per patient was obtained from the survey conducted. This value was applied to the average salary of individuals with disabilities in Italy to estimate the annual productivity loss. This was also adjusted by the percentage of MS patients currently employed in this EDSS category. Given the lack of wage data for patients with MS, the average annual salary of individuals with disabilities for Italy was considered.
0-3.5	Patients' indirect costs - Presenteeism.	• Bebo et al, 2022	Given the lack of information on reduced working hours, the data provided by Bebo et al. was used, where the estimated annual burden per average MS patient due to presenteeism and absenteeism was reported. That ratio (economic burden due to presenteeism/absenteeism) was obtained and used to estimate the economic burden of presenteeism by multiplying it by the calculated absenteeism value for each EDSS group.
4-6.5	Patients' indirect costs - Presenteeism.	• Bebo et al, 2022	Given the lack of information on reduced working hours, the data provided by Bebo et al. was used, where the estimated annual burden per average MS patient due to presenteeism and absenteeism was reported. That ratio (economic burden due to presenteeism/absenteeism) was obtained and used to estimate the economic burden of presenteeism by multiplying it by the calculated absenteeism value for each EDSS group.
7-9.5	Patients' indirect costs - Presenteeism.	• Bebo et al, 2022	Given the lack of information on reduced working hours, the data provided by Bebo et al. was used, where the estimated annual burden per average MS patient due to presenteeism and absenteeism was reported. That ratio (economic burden due to presenteeism/absenteeism) was obtained and used to estimate the economic burden of presenteeism by multiplying it by the calculated absenteeism value for each EDSS group.
0-3.5	Patients' indirect costs - Productivity loss due to early retirement.	• Battaglia et al, 2022 • ILOSTAT	To estimate the productivity loss due to premature retirement, the prevalence of premature retirement for each EDSS group was obtained and multiplied by the annual average salary.

Italy

Indirect costs (continued)

EDSS level	Inclusions	Main source	Assumption/s
4-6.5	Patients' indirect costs - Productivity loss due to early retirement.	• Battaglia et al, 2022 • ILOSTAT	To estimate the productivity loss due to premature retirement, the prevalence of premature retirement for each EDSS group was obtained and multiplied by the annual average salary.
7-9.5	Patients' indirect costs - Productivity loss due to early retirement.	• Battaglia et al, 2022 • ILOSTAT	To estimate the productivity loss due to premature retirement, the prevalence of premature retirement for each EDSS group was obtained and multiplied by the annual average salary.
0-3.5	Disability Insurance due to early retirement.	• Battaglia et al, 2022 • Instituto Nazional Previdenza Sociale	To estimate Disability Insurance costs due to early retirement caused by multiple sclerosis (MS), the prevalence of premature retirement for each EDSS group was obtained and multiplied by the average annual Disability Insurance benefit in the country.
4-6.5	Disability Insurance due to early retirement.	• Battaglia et al, 2022 • Instituto Nazional Previdenza Sociale	To estimate Disability Insurance costs due to early retirement caused by multiple sclerosis (MS), the prevalence of premature retirement for each EDSS group was obtained and multiplied by the average annual Disability Insurance benefit in the country.
7-9.5	Disability Insurance due to early retirement.	• Battaglia et al, 2022 • Instituto Nazional Previdenza Sociale	To estimate Disability Insurance costs due to early retirement caused by multiple sclerosis (MS), the prevalence of premature retirement for each EDSS group was obtained and multiplied by the average annual Disability Insurance benefit in the country.
0-3.5	Patients' indirect costs - Productivity loss due to unemployment.	• Ponzio et al, 2024 • ILOSTAT • OECD 2024	To estimate the productivity loss due to unemployment caused by multiple sclerosis (MS), we used the unemployment rate stratified by EDSS groups. This rate was adjusted for the proportion of the MS population within working age, the general unemployment rate in the country, and the percentage of MS patients in early retirement, which was subtracted to avoid double counting. The national average wage was used to calculate the monetary value of productivity loss. As a conservative approach, the proportion of patients within the EDSS 0–3.5 category deemed asymptomatic according to GBD criteria was excluded from the analysis, under the assumption that this subset was not unemployed as a consequence of their disease.

Italy

Indirect costs (continued)

EDSS level	Inclusions	Main source	Assumption/s
4-6.5	Patients' indirect costs - Productivity loss due to unemployment.	• Ponzio et al, 2024 • ILOSTAT • OECD 2024	To estimate the productivity loss due to unemployment caused by multiple sclerosis (MS), we used the unemployment rate stratified by EDSS groups. This rate was adjusted for the proportion of the MS population within working age, the general unemployment rate in the country, and the percentage of MS patients in early retirement, which was subtracted to avoid double counting. The national average wage was used to calculate the monetary value of productivity loss. As a conservative approach, the proportion of patients within the EDSS 0–3.5 category deemed asymptomatic according to GBD criteria was excluded from the analysis, under the assumption that this subset was not unemployed as a consequence of their disease.
7-9.5	Patients' indirect costs - Productivity loss due to unemployment.	• Ponzio et al, 2024 • ILOSTAT • OECD 2024	To estimate the productivity loss due to unemployment caused by multiple sclerosis (MS), we used the unemployment rate stratified by EDSS groups. This rate was adjusted for the proportion of the MS population within working age, the general unemployment rate in the country, and the percentage of MS patients in early retirement, which was subtracted to avoid double counting. The national average wage was used to calculate the monetary value of productivity loss. As a conservative approach, the proportion of patients within the EDSS 0–3.5 category deemed asymptomatic according to GBD criteria was excluded from the analysis, under the assumption that this subset was not unemployed as a consequence of their disease.
0-3.5	Patients' indirect costs - Productivity loss caused by a decrease in salary.	• ILOSTAT	For those currently employed, the salary reduction due to disability (assumed to be caused by MS) was calculated. This calculation applied the annual difference reported by the ILO for the country, comparing the average salary to the average salary for individuals with disabilities in the country.
4-6.5	Patients' indirect costs - Productivity loss caused by a decrease in salary.	• ILOSTAT	For those currently employed, the salary reduction due to disability (assumed to be caused by MS) was calculated. This calculation applied the annual difference reported by the ILO for the country, comparing the average salary to the average salary for individuals with disabilities in the country.
7-9.5	Patients' indirect costs - Productivity loss caused by a decrease in salary.	• ILOSTAT	For those currently employed, the salary reduction due to disability (assumed to be caused by MS) was calculated. This calculation applied the annual difference reported by the ILO for the country, comparing the average salary to the average salary for individuals with disabilities in the country.

Italy

Additional costs related to diagnosis (Incident cases)

EDSS level	Inclusions	Main source	Assumption/s
NA	One-Time Diagnostic Costs: Primary care visit, Neurology consultation, Blood test, Lumbar puncture, MRI.	• Ponzio et al, 2025	Given the lack of information for this parameter, the annual per-patient value reported by Ponzio et al. (2025) was used, as a proxy, for the following items: tests and specialist visit (Table 3). As a conservative approach, data reported for the EDSS 0–3.5 group were used and assumed for each average patient at the time of diagnosis.

Sweden

Direct medical costs

EDSS level	Inclusions	Main source	Assumption/s
0-3.5	Medicines, inpatient care/day admissions, consultations, and tests.	• Brundin et al, 2017 • Socialstyrelsen, 2022	Table 4 from Brundin et al. was used.
4-6.5	Medicines, inpatient care/day admissions, consultations, and tests.	• Brundin et al, 2017 • Socialstyrelsen, 2022	Table 4 from Brundin et al. was used.
7-9.5	Medicines, inpatient care/day admissions, consultations, and tests.	• Brundin et al, 2017 • Socialstyrelsen, 2022	Table 4 from Brundin et al. was used.

Other direct costs

EDSS level	Inclusions	Main source	Assumption/s
0-3.5	Home and vehicle adaptations + Investments in equipment and devices to aid patients' mobility + Other expenses (Community services) + Transportation.	• Brundin et al, 2017	Table 3 from Brundin et al. was used.
4-6.5	Home and vehicle adaptations + Investments in equipment and devices to aid patients' mobility + Other expenses (Community services) + Transportation.	• Brundin et al, 2017	Table 3 from Brundin et al. was used.

Sweden

Other direct costs (continued)			
EDSS level	**Inclusions**	**Main source**	**Assumption/s**
7-9.5	Home and vehicle adaptations + Investments in equipment and devices to aid patients' mobility + Other expenses (Community services) + Transportation.	• Brundin et al, 2017	Table 3 from Brundin et al. was used.

Indirect costs			
EDSS level	**Inclusions**	**Main source**	**Assumption/s**
0-3.5	Caregivers' indirect costs - Informal caregiving.	• Brundin et al, 2017 • Survey • Statistics Sweden, 2024	To estimate this value, the following were used: the percentage of patients requiring an informal caregiver for this EDSS category (on average), the total average number of hours per week of informal care needed for this EDSS category, and the average hourly wage of workers in health-related social assistance in Italy as a proxy for the shadow price of informal care.
4-6.5	Caregivers' indirect costs - Informal caregiving.	• Brundin et al, 2017 • Survey • Statistics Sweden, 2024	To estimate this value, the following were used: the percentage of patients requiring an informal caregiver for this EDSS category (on average), the total average number of hours per week of informal care needed for this EDSS category, and the average hourly wage of workers in health-related social assistance in Italy as a proxy for the shadow price of informal care.
7-9.5	Caregivers' indirect costs - Informal caregiving.	• Brundin et al, 2017 • Survey • Statistics Sweden, 2024	To estimate this value, the following were used: the percentage of patients requiring an informal caregiver for this EDSS category (on average), the total average number of hours per week of informal care needed for this EDSS category, and the average hourly wage of workers in health-related social assistance in Italy as a proxy for the shadow price of informal care.
0-3.5	Patients' indirect costs – Absenteeism.	• Brundin et al, 2017 • Survey • ILOSTAT	The value for the average number of hours per week of absenteeism per patient was obtained from the survey conducted. This value was applied to the average salary of individuals with disabilities in the country to estimate the annual productivity loss. This was also adjusted by the percentage of MS patients currently employed in this EDSS category. Given the lack of wage data for patients with MS, the average annual salary of individuals with disabilities was considered.

Sweden

Indirect costs (continued)

EDSS level	Inclusions	Main source	Assumption/s
4-6.5	Patients' indirect costs – Absenteeism.	• Brundin et al, 2017 • Survey • ILOSTAT	The value for the average number of hours per week of absenteeism per patient was obtained from the survey conducted. This value was applied to the average salary of individuals with disabilities in the country to estimate the annual productivity loss. This was also adjusted by the percentage of MS patients currently employed in this EDSS category. Given the lack of wage data for patients with MS, the average annual salary of individuals with disabilities was considered.
7-9.5	Patients' indirect costs - Absenteeism.	• Brundin et al, 2017 • Survey • ILOSTAT	The value for the average number of hours per week of absenteeism per patient was obtained from the survey conducted. This value was applied to the average salary of individuals with disabilities in the country to estimate the annual productivity loss. This was also adjusted by the percentage of MS patients currently employed in this EDSS category. Given the lack of wage data for patients with MS, the average annual salary of individuals with disabilities was considered.
0-3.5	Patients' indirect costs - Presenteeism.	• Bebo et al, 2022 • ILOSTAT	Given the lack of information on reduced working hours, the data provided by Bebo et al. was used, where the estimated annual burden per average MS patient due to presenteeism and absenteeism was reported. That ratio (economic burden due to presenteeism/absenteeism) was obtained and used to estimate the economic burden of presenteeism by multiplying it by the calculated absenteeism value for each EDSS group.
4-6.5	Patients' indirect costs - Presenteeism.	• Bebo et al, 2022 • ILOSTAT	Given the lack of information on reduced working hours, the data provided by Bebo et al. was used, where the estimated annual burden per average MS patient due to presenteeism and absenteeism was reported. That ratio (economic burden due to presenteeism/absenteeism) was obtained and used to estimate the economic burden of presenteeism by multiplying it by the calculated absenteeism value for each EDSS group.
7-9.5	Patients' indirect costs - Presenteeism.	• Bebo et al, 2022 • ILOSTAT	Given the lack of information on reduced working hours, the data provided by Bebo et al. was used, where the estimated annual burden per average MS patient due to presenteeism and absenteeism was reported. That ratio (economic burden due to presenteeism/absenteeism) was obtained and used to estimate the economic burden of presenteeism by multiplying it by the calculated absenteeism value for each EDSS group.
0-3.5	Patients' indirect costs - Productivity loss due to early retirement.	• ILOSTAT	To estimate the productivity loss due to premature retirement, the prevalence of premature retirement for each EDSS group was obtained and multiplied by the annual average salary.

Sweden

Indirect costs (continued)

EDSS level	Inclusions	Main source	Assumption/s
4-6.5	Patients' indirect costs - Productivity loss due to early retirement.	• ILOSTAT	To estimate the productivity loss due to premature retirement, the prevalence of premature retirement for each EDSS group was obtained and multiplied by the annual average salary.
7-9.5	Patients' indirect costs - Productivity loss due to early retirement.	• ILOSTAT	To estimate the productivity loss due to premature retirement, the prevalence of premature retirement for each EDSS group was obtained and multiplied by the annual average salary.
0-3.5	Disability Insurance due to early retirement.	• Försäkringskassan, 2025 • Brundin et al, 2017	To estimate Disability Insurance costs due to early retirement caused by multiple sclerosis (MS), the prevalence of premature retirement for each EDSS group was obtained and multiplied by the average annual Disability Insurance benefit in the UK.
4-6.5	Disability Insurance due to early retirement.	• Försäkringskassan, 2025 • Brundin et al, 2017	To estimate Disability Insurance costs due to early retirement caused by multiple sclerosis (MS), the prevalence of premature retirement for each EDSS group was obtained and multiplied by the average annual Disability Insurance benefit in the UK.
7-9.5	Disability Insurance due to early retirement.	• Försäkringskassan, 2025 • Brundin et al, 2017	To estimate Disability Insurance costs due to early retirement caused by multiple sclerosis (MS), the prevalence of premature retirement for each EDSS group was obtained and multiplied by the average annual Disability Insurance benefit in the UK.
0-3.5	Patients' indirect costs - Productivity loss due to unemployment.	• ILOSTAT • OECD 2024	To estimate the productivity loss due to unemployment caused by multiple sclerosis (MS), we used the unemployment rate stratified by EDSS groups. This rate was adjusted for the proportion of the MS population within working age, the general unemployment rate in the country, and the percentage of MS patients in early retirement, which was subtracted to avoid double counting. The national average wage was used to calculate the monetary value of productivity loss.
4-6.5	Patients' indirect costs - Productivity loss due to unemployment.	• ILOSTAT • OECD 2024	To estimate the productivity loss due to unemployment caused by multiple sclerosis (MS), we used the unemployment rate stratified by EDSS groups. This rate was adjusted for the proportion of the MS population within working age, the general unemployment rate in the country, and the percentage of MS patients in early retirement, which was subtracted to avoid double counting. The national average wage was used to calculate the monetary value of productivity loss.

Sweden

Indirect costs (continued)			
EDSS level	**Inclusions**	**Main source**	**Assumption/s**
7-9.5	Patients' indirect costs - Productivity loss due to unemployment.	• ILOSTAT • OECD 2024	To estimate the productivity loss due to unemployment caused by multiple sclerosis (MS), we used the unemployment rate stratified by EDSS groups. This rate was adjusted for the proportion of the MS population within working age, the general unemployment rate in the country, and the percentage of MS patients in early retirement, which was subtracted to avoid double counting. The national average wage was used to calculate the monetary value of productivity loss.
0-3.5	Patients' indirect costs - Productivity loss caused by a decrease in salary.	• Brundin et al, 2017 • ILOSTAT	For those currently employed, the salary reduction due to disability (assumed to be caused by MS) was calculated. This calculation applied the annual difference reported by the ILO for the country, comparing the average salary to the average salary for individuals with disabilities in the country.
4-6.5	Patients' indirect costs - Productivity loss caused by a decrease in salary.	• Brundin et al, 2017 • ILOSTAT	For those currently employed, the salary reduction due to disability (assumed to be caused by MS) was calculated. This calculation applied the annual difference reported by the ILO for the country, comparing the average salary to the average salary for individuals with disabilities in the country.
7-9.5	Patients' indirect costs - Productivity loss caused by a decrease in salary.	• Brundin et al, 2017 • ILOSTAT	For those currently employed, the salary reduction due to disability (assumed to be caused by MS) was calculated. This calculation applied the annual difference reported by the ILO for the country, comparing the average salary to the average salary for individuals with disabilities in the country.

Additional costs related to diagnosis (Incident cases)			
EDSS level	**Inclusions**	**Main source**	**Assumption/s**
NA	One-Time Diagnostic Costs: Primary care visit, Neurology consultation, Blood test, Lumbar puncture, MRI.	• Socialstyrelsen, 2022 • Södra Sjukvårdsregionen, 2025 • Region Skåne, Prislistor bild- och funktionsmedicin, 2025	Central values were used.

France

Direct medical costs

EDSS level	Inclusions	Main source	Assumption/s
0-3.5	Medicines (DMTs), inpatient care/ day admissions, consultations, test and other medications.	• Lebrun-Frenay et al, 2017	Central value was from Lebrun-Frenay et al.
4-6.5	Medicines, inpatient care/day admissions, consultations, and tests.	• Lebrun-Frenay et al, 2017	Central value was from Lebrun-Frenay et al.
7-9.5	Medicines, inpatient care/day admissions, consultations, and tests.	• Lebrun-Frenay et al, 2017	Central value was from Lebrun-Frenay et al.

Other direct costs

EDSS level	Inclusions	Main source	Assumption/s
0-3.5	Home and vehicle adaptations + Investments in equipment and devices to aid patients' mobility + Other expenses (Community services) + Transportation.	• Lebrun-Frenay et al, 2017	Table 4 was used for data.
4-6.5	Home and vehicle adaptations + Investments in equipment and devices to aid patients' mobility + Other expenses (Community services) + Transportation.	• Lebrun-Frenay et al, 2017	Table 4 was used for data.

France

Other direct costs (continued)

EDSS level	Inclusions	Main source	Assumption/s
7-9.5	Home and vehicle adaptations + Investments in equipment and devices to aid patients' mobility + Other expenses (Community services) + Transportation.	• Lebrun-Frenay et al, 2017	Table 4 was used for data.

Indirect costs

EDSS level	Inclusions	Main source	Assumption/s
0-3.5	Caregivers' indirect costs - Informal caregiving.	• Lebrun-Frenay et al, 2017 • Survey • Direction de l'information légale et administrative) "Paie du salarié à domicile employé par un particulier," 2025	To estimate this value, the following were used: the percentage of patients requiring an informal caregiver for this EDSS category (on average), the total average number of hours per week of informal care needed for this EDSS category, and the average hourly wage of workers in health-related social assistance in the country as a proxy for the shadow price of informal care.
4-6.5	Caregivers' indirect costs - Informal caregiving.	• Lebrun-Frenay et al, 2017 • Survey • Direction de l'information légale et administrative) "Paie du salarié à domicile employé par un particulier," 2025	To estimate this value, the following were used: the percentage of patients requiring an informal caregiver for this EDSS category (on average), the total average number of hours per week of informal care needed for this EDSS category, and the average hourly wage of workers in health-related social assistance in the country as a proxy for the shadow price of informal care.

France

Indirect costs (continued)

EDSS level	Inclusions	Main source	Assumption/s
7-9.5	Caregivers' indirect costs - Informal caregiving.	• Lebrun-Frenay et al, 2017 • Survey • Direction de l'information légale et administrative) "Paie du salarié à domicile employé par un particulier," 2025	To estimate this value, the following were used: the percentage of patients requiring an informal caregiver for this EDSS category (on average), the total average number of hours per week of informal care needed for this EDSS category, and the average hourly wage of workers in health-related social assistance in the country as a proxy for the shadow price of informal care.
0-3.5	Patients' indirect costs - Absenteeism.	• Lebrun-Frenay et al, 2017 • Survey	The value for the average number of hours per week of absenteeism per patient was obtained from the survey conducted. This value was applied to the average salary of individuals with disabilities in the country to estimate the annual productivity loss. This was also adjusted by the percentage of MS patients currently employed in this EDSS category. Given the lack of wage data for patients with MS, the average annual salary of individuals with disabilities was considered.
4-6.5	Patients' indirect costs - Absenteeism.	• Lebrun-Frenay et al, 2017 • Survey	The value for the average number of hours per week of absenteeism per patient was obtained from the survey conducted. This value was applied to the average salary of individuals with disabilities in the country to estimate the annual productivity loss. This was also adjusted by the percentage of MS patients currently employed in this EDSS category. Given the lack of wage data for patients with MS, the average annual salary of individuals with disabilities was considered.
7-9.5	Patients' indirect costs - Absenteeism.	• Lebrun-Frenay et al, 2017 • Survey	The value for the average number of hours per week of absenteeism per patient was obtained from the survey conducted. This value was applied to the average salary of individuals with disabilities in the country to estimate the annual productivity loss. This was also adjusted by the percentage of MS patients currently employed in this EDSS category. Given the lack of wage data for patients with MS, the average annual salary of individuals with disabilities was considered.
0-3.5	Patients' indirect costs - Presenteeism.	• Bebo et al, 2022	Given the lack of information on reduced working hours, the data provided by Bebo et al was used, where the estimated annual burden per average MS patient due to presenteeism and absenteeism was reported. That ratio (economic burden due to presenteeism/absenteeism) was obtained and used to estimate the economic burden of presenteeism by multiplying it by the calculated absenteeism value for each EDSS group

France

Indirect costs (continued)

EDSS level	Inclusions	Main source	Assumption/s
4-6.5	Patients' indirect costs - Presenteeism.	• Bebo et al, 2022	Given the lack of information on reduced working hours, the data provided by Bebo et al was used, where the estimated annual burden per average MS patient due to presenteeism and absenteeism was reported. That ratio (economic burden due to presenteeism/absenteeism) was obtained and used to estimate the economic burden of presenteeism by multiplying it by the calculated absenteeism value for each EDSS group
7-9.5	Patients' indirect costs - Presenteeism.	• Bebo et al, 2022	Given the lack of information on reduced working hours, the data provided by Bebo et al was used, where the estimated annual burden per average MS patient due to presenteeism and absenteeism was reported. That ratio (economic burden due to presenteeism/absenteeism) was obtained and used to estimate the economic burden of presenteeism by multiplying it by the calculated absenteeism value for each EDSS group.
0-3.5	Patients' indirect costs - Productivity loss due to early retirement.	• Lebrun-Frenay et al, 2017 • ILOSTAT	To estimate the productivity loss due to premature retirement, the prevalence of premature retirement for each EDSS group was obtained and multiplied by the annual average salary.
4-6.5	Patients' indirect costs - Productivity loss due to early retirement.	• Lebrun-Frenay et al, 2017 • ILOSTAT	To estimate the productivity loss due to premature retirement, the prevalence of premature retirement for each EDSS group was obtained and multiplied by the annual average salary.
7-9.5	Patients' indirect costs - Productivity loss due to early retirement.	• Lebrun-Frenay et al, 2017 • ILOSTAT	To estimate the productivity loss due to premature retirement, the prevalence of premature retirement for each EDSS group was obtained and multiplied by the annual average salary.
0-3.5	Disability Insurance due to early retirement.	• Direction de l'information légale et administrative (Premier ministre), 2025 • Lebrun-Frenay et al, 2017	To estimate Disability Insurance costs due to early retirement caused by multiple sclerosis (MS), the prevalence of premature retirement for each EDSS group was obtained and multiplied by the average annual Disability Insurance benefit in the country.
4-6.5	Disability Insurance due to early retirement.	• Direction de l'information légale et administrative (Premier ministre), 2025 • Lebrun-Frenay et al, 2017	To estimate Disability Insurance costs due to early retirement caused by multiple sclerosis (MS), the prevalence of premature retirement for each EDSS group was obtained and multiplied by the average annual Disability Insurance benefit in the country.

France

Indirect costs (continued)

EDSS level	Inclusions	Main source	Assumption/s
7-9.5	Disability Insurance due to early retirement.	• Direction de l'information légale et administrative (Premier ministre), 2025 • Lebrun-Frenay et al, 2017	To estimate Disability Insurance costs due to early retirement caused by multiple sclerosis (MS), the prevalence of premature retirement for each EDSS group was obtained and multiplied by the average annual Disability Insurance benefit in the country.
0-3.5	Patients' indirect costs - Productivity loss due to unemployment.	• OECD, 2024 • ILOSTAT	To estimate the productivity loss due to unemployment caused by multiple sclerosis (MS), we used the unemployment rate stratified by EDSS groups. This rate was adjusted for the proportion of the MS population within working age, the general unemployment rate in the country, and the percentage of MS patients in early retirement, which was subtracted to avoid double counting. The national average wage was used to calculate the monetary value of productivity loss. As a conservative approach, the proportion of patients within the EDSS 0–3.5 category deemed asymptomatic according to GBD criteria was excluded from the analysis, under the assumption that this subset was not unemployed as a consequence of their disease.
4-6.5	Patients' indirect costs - Productivity loss due to unemployment.	• OECD, 2024 • ILOSTAT	To estimate the productivity loss due to unemployment caused by multiple sclerosis (MS), we used the unemployment rate stratified by EDSS groups. This rate was adjusted for the proportion of the MS population within working age, the general unemployment rate in the country, and the percentage of MS patients in early retirement, which was subtracted to avoid double counting. The national average wage was used to calculate the monetary value of productivity loss. As a conservative approach, the proportion of patients within the EDSS 0–3.5 category deemed asymptomatic according to GBD criteria was excluded from the analysis, under the assumption that this subset was not unemployed as a consequence of their disease.
7-9.5	Patients' indirect costs - Productivity loss due to unemployment.	• OECD, 2024 • ILOSTAT	To estimate the productivity loss due to unemployment caused by multiple sclerosis (MS), we used the unemployment rate stratified by EDSS groups. This rate was adjusted for the proportion of the MS population within working age, the general unemployment rate in the country, and the percentage of MS patients in early retirement, which was subtracted to avoid double counting. The national average wage was used to calculate the monetary value of productivity loss. As a conservative approach, the proportion of patients within the EDSS 0–3.5 category deemed asymptomatic according to GBD criteria was excluded from the analysis, under the assumption that this subset was not unemployed as a consequence of their disease.

France

Indirect costs (continued)

EDSS level	Inclusions	Main source	Assumption/s
0-3.5	Patients' indirect costs - Productivity loss caused by a decrease in salary.	• Lebrun-Frenay et al, 2017 • ILOSTAT	For those currently employed, the salary reduction due to disability (assumed to be caused by MS) was calculated. This calculation applied the annual difference reported by the ILO for the country, comparing the average salary to the average salary for individuals with disabilities in the country.
4-6.5	Patients' indirect costs - Productivity loss caused by a decrease in salary.	• Lebrun-Frenay et al, 2017 • ILOSTAT	For those currently employed, the salary reduction due to disability (assumed to be caused by MS) was calculated. This calculation applied the annual difference reported by the ILO for the country, comparing the average salary to the average salary for individuals with disabilities in the country.
EDSS 7-9.5	Patients' indirect costs - Productivity loss caused by a decrease in salary.	• Lebrun-Frenay et al, 2017 • ILOSTAT	For those currently employed, the salary reduction due to disability (assumed to be caused by MS) was calculated. This calculation applied the annual difference reported by the ILO for the country, comparing the average salary to the average salary for individuals with disabilities in the country.

Additional costs related to diagnosis (Incident cases)

EDSS level	Inclusions	Main source	Assumption/s
NA	One-Time Diagnostic Costs: Primary care visit, Neurology consultation, Blood test, Lumbar puncture, MRI.	• Lebrun-Frenay et al, 2017	Given the lack of information for this parameter, the annual per-patient value reported by Christine Lebrun-Frenay. (2017) was used, as a proxy, for the following items: tests and consultations (Table 4). As a conservative approach, data reported for the EDSS 0–3.5 group were used and assumed for each average patient at the time of diagnosis.

Spain

Direct medical costs

EDSS level	Inclusions	Main source	Assumption/s
0-3.5	Medicines (DMTs), inpatient care/ day admissions, consultations, test and other medications.	• Oreja-Guevara et al, 2017	Table 4 from Oreja-Guevara was used for data.
4-6.5	Medicines (DMTs), inpatient care/ day admissions, consultations, test and other medications.	• Oreja-Guevara et al, 2017	Table 4 from Oreja-Guevara was used for data.
7-9.5	Medicines (DMTs), inpatient care/ day admissions, consultations, test and other medications.	• Oreja-Guevara et al, 2017	Table 4 from Oreja-Guevara was used for data.

Other direct costs

EDSS level	Inclusions	Main source	Assumption/s
0-3.5	Home and vehicle adaptations + Investments in equipment and devices to aid patients' mobility + Other expenses (Community services) + Transportation.	• Oreja-Guevara et al, 2017	Table 4 from Oreja-Guevara was used for data.
4-6.5	Home and vehicle adaptations + Investments in equipment and devices to aid patients' mobility + Other expenses (Community services) + Transportation.	• Oreja-Guevara et al, 2017	Table 4 from Oreja-Guevara was used for data.

Spain

Other direct costs (continued)

EDSS level	Inclusions	Main source	Assumption/s
7-9.5	Home and vehicle adaptations + Investments in equipment and devices to aid patients' mobility + Other expenses (Community services) + Transportation.	• Oreja-Guevara et al, 2017	Table 4 from Oreja-Guevara was used for data.

Indirect costs

EDSS level	Inclusions	Main source	Assumption/s
0-3.5	Caregivers' indirect costs - Informal caregiving.	• Oreja-Guevara et al, 2017 • Survey • Economic Research Institute	To estimate this value, the following were used: the percentage of patients requiring an informal caregiver for this EDSS category (on average), the total average number of hours per week of informal care needed for this EDSS category, and the average hourly wage of workers in health-related social assistance in the country as a proxy for the shadow price of informal care.
4-6.5	Caregivers' indirect costs - Informal caregiving.	• Oreja-Guevara et al, 2017 • Survey • Economic Research Institute	To estimate this value, the following were used: the percentage of patients requiring an informal caregiver for this EDSS category (on average), the total average number of hours per week of informal care needed for this EDSS category, and the average hourly wage of workers in health-related social assistance in the country as a proxy for the shadow price of informal care.
7-9.5	Caregivers' indirect costs - Informal caregiving.	• Oreja-Guevara et al, 2017 • Survey • Economic Research Institute	To estimate this value, the following were used: the percentage of patients requiring an informal caregiver for this EDSS category (on average), the total average number of hours per week of informal care needed for this EDSS category, and the average hourly wage of workers in health-related social assistance in the country as a proxy for the shadow price of informal care.
0-3.5	Patients' indirect costs - Absenteeism.	• Oreja-Guevara et al, 2017 • ILOSTAT • Survey	The value for the average number of hours per week of absenteeism per patient was obtained from the survey conducted. This value was applied to the average salary of individuals with disabilities in the country to estimate the annual productivity loss. This was also adjusted by the percentage of MS patients currently employed in this EDSS category. Given the lack of wage data for patients with MS, the average annual salary of individuals with disabilities was considered.

Spain

Indirect costs (continued)

EDSS level	Inclusions	Main source	Assumption/s
4-6.5	Patients' indirect costs - Absenteeism.	• Oreja-Guevara et al, 2017 • ILOSTAT • Survey	The value for the average number of hours per week of absenteeism per patient was obtained from the survey conducted. This value was applied to the average salary of individuals with disabilities in the country to estimate the annual productivity loss. This was also adjusted by the percentage of MS patients currently employed in this EDSS category. Given the lack of wage data for patients with MS, the average annual salary of individuals with disabilities was considered.
7-9.5	Patients' indirect costs - Absenteeism.	• Oreja-Guevara et al, 2017 • ILOSTAT • Survey	The value for the average number of hours per week of absenteeism per patient was obtained from the survey conducted. This value was applied to the average salary of individuals with disabilities in the country to estimate the annual productivity loss. This was also adjusted by the percentage of MS patients currently employed in this EDSS category. Given the lack of wage data for patients with MS, the average annual salary of individuals with disabilities was considered.
0-3.5	Patients' indirect costs - Presenteeism.	• Bebo et al, 2022 • Oreja-Guevara et al, 2017 • ILOSTAT • Survey	Given the lack of information on reduced working hours, the data provided by Bebo et al. was used, where the estimated annual burden per average MS patient due to presenteeism and absenteeism was reported. That ratio (economic burden due to presenteeism/absenteeism) was obtained and used to estimate the economic burden of presenteeism by multiplying it by the calculated absenteeism value for each EDSS group.
4-6.5	Patients' indirect costs - Presenteeism.	• Bebo et al, 2022 • Oreja-Guevara et al, 2017 • ILOSTAT • Survey	Given the lack of information on reduced working hours, the data provided by Bebo et al. was used, where the estimated annual burden per average MS patient due to presenteeism and absenteeism was reported. That ratio (economic burden due to presenteeism/absenteeism) was obtained and used to estimate the economic burden of presenteeism by multiplying it by the calculated absenteeism value for each EDSS group.
7-9.5	Patients' indirect costs - Presenteeism.	• Bebo et al, 2022 • Oreja-Guevara et al, 2017 • ILOSTAT • Survey	Given the lack of information on reduced working hours, the data provided by Bebo et al. was used, where the estimated annual burden per average MS patient due to presenteeism and absenteeism was reported. That ratio (economic burden due to presenteeism/absenteeism) was obtained and used to estimate the economic burden of presenteeism by multiplying it by the calculated absenteeism value for each EDSS group.
0-3.5	Patients' indirect costs - Productivity loss due to early retirement.	• Oreja-Guevara et al, 2017 • ILOSTAT	To estimate the productivity loss due to premature retirement, the prevalence of premature retirement for each EDSS group was obtained and multiplied by the annual average salary.

Spain

Indirect costs (continued)

EDSS level	Inclusions	Main source	Assumption/s
4-6.5	Patients' indirect costs - Productivity loss due to early retirement.	• Oreja-Guevara et al, 2017 • ILOSTAT	To estimate the productivity loss due to premature retirement, the prevalence of premature retirement for each EDSS group was obtained and multiplied by the annual average salary.
7-9.5	Patients' indirect costs - Productivity loss due to early retirement.	• Oreja-Guevara et al, 2017 • ILOSTAT	To estimate the productivity loss due to premature retirement, the prevalence of premature retirement for each EDSS group was obtained and multiplied by the annual average salary.
0-3.5	Disability Insurance due to early retirement.	• Oreja-Guevara et al, 2017 • Ministerio de Inclusión, Seguridad Social y Migraciones	To estimate Disability Insurance costs due to early retirement caused by multiple sclerosis (MS), the prevalence of premature retirement for each EDSS group was obtained and multiplied by the average annual Disability Insurance benefit in the country.
4-6.5	Disability Insurance due to early retirement.	• Oreja-Guevara et al, 2017 • Ministerio de Inclusión, Seguridad Social y Migraciones	To estimate Disability Insurance costs due to early retirement caused by multiple sclerosis (MS), the prevalence of premature retirement for each EDSS group was obtained and multiplied by the average annual Disability Insurance benefit in the country.
7-9.5	Disability Insurance due to early retirement.	• Oreja-Guevara et al, 2017 • Ministerio de Inclusión, Seguridad Social y Migraciones	To estimate Disability Insurance costs due to early retirement caused by multiple sclerosis (MS), the prevalence of premature retirement for each EDSS group was obtained and multiplied by the average annual Disability Insurance benefit in the country.
0-3.5	Patients' indirect costs - Productivity loss due to unemployment.	• Oreja-Guevara et al, 2017 • OECD, 2025 • ILOSTAT • GBD, 2025	To estimate the productivity loss due to unemployment caused by multiple sclerosis (MS), we used the unemployment rate stratified by EDSS groups. This rate was adjusted for the proportion of the MS population within working age, the general unemployment rate in the country, and the percentage of MS patients in early retirement, which was subtracted to avoid double counting. The national average wage was used to calculate the monetary value of productivity loss. As a conservative approach, the proportion of patients within the EDSS 0–3.5 category deemed asymptomatic according to GBD criteria was excluded from the analysis, under the assumption that this subset was not unemployed as a consequence of their disease.

Spain

Indirect costs (continued)

EDSS level	Inclusions	Main source	Assumption/s
4-6.5	Patients' indirect costs - Productivity loss due to unemployment.	• Oreja-Guevara et al, 2017 • OECD, 2025 • ILOSTAT	To estimate the productivity loss due to unemployment caused by multiple sclerosis (MS), we used the unemployment rate stratified by EDSS groups. This rate was adjusted for the proportion of the MS population within working age, the general unemployment rate in the country, and the percentage of MS patients in early retirement, which was subtracted to avoid double counting. The national average wage was used to calculate the monetary value of productivity loss.
7-9.5	Patients' indirect costs - Productivity loss due to unemployment.	• Oreja-Guevara et al, 2017 • OECD, 2025 • ILOSTAT	To estimate the productivity loss due to unemployment caused by multiple sclerosis (MS), we used the unemployment rate stratified by EDSS groups. This rate was adjusted for the proportion of the MS population within working age, the general unemployment rate in the country, and the percentage of MS patients in early retirement, which was subtracted to avoid double counting. The national average wage was used to calculate the monetary value of productivity loss.
0-3.5	Patients' indirect costs - Productivity loss caused by a decrease in salary.	• Oreja-Guevara et al, 2017 • ILOSTAT	For those currently employed, the salary reduction due to disability (assumed to be caused by MS) was calculated. This calculation applied the annual difference reported by the ILO for the country, comparing the average salary to the average salary for individuals with disabilities in the country.
4-6.5	Patients' indirect costs - Productivity loss caused by a decrease in salary.	• Oreja-Guevara et al, 2017 • ILOSTAT	For those currently employed, the salary reduction due to disability (assumed to be caused by MS) was calculated. This calculation applied the annual difference reported by the ILO for the country, comparing the average salary to the average salary for individuals with disabilities in the country.
7-9.5	Patients' indirect costs - Productivity loss caused by a decrease in salary.	• Oreja-Guevara et al, 2017 • ILOSTAT	For those currently employed, the salary reduction due to disability (assumed to be caused by MS) was calculated. This calculation applied the annual difference reported by the ILO for the country, comparing the average salary to the average salary for individuals with disabilities in the country.

Additional costs related to diagnosis (Incident cases)

EDSS level	Inclusions	Main source	Assumption/s
NA	One-Time Diagnostic Costs: Primary care visit, Neurology consultation, Blood test, Lumbar puncture, MRI.	• Oreja-Guevara et al, 2017	Given the lack of information for this parameter, the annual per-patient value reported by Oreja-Guevara et al 2017 was used, as a proxy, for the following items: tests and consultations (Table 4). As a conservative approach, data reported for the EDSS 0–3.5 group were used and assumed for each average patient at the time of diagnosis

Additional costs (cross-countries)

Additional costs due to death and premature death

EDSS level	Inclusions	Main source	Assumption/s
NA	Cost of hospitalisation per day (weighted average), length of stay in hospital (end-of life), percentage costs for primary hospitals (community) and tertiary hospitals (university).	• WHO CHOICE, 2010 • Murtonen et al, 2021	Direct costs due to death: end-of-life costs were applied, considering the percentage of individuals with MS who die in hospital. Indirect Costs (productivity loss) due to premature death were applied only to those deaths for patients under retirement age and adjusted by the unemployment rate in the country.

Additional indirect costs (absenteeism) incurred during the pre-diagnosis period

EDSS level	Inclusions	Main source	Assumption/s
0-3.5	Absenteeism during the pre-diagnosis period.	• Manouchehrinia et al, 2024	Assumptions were based on data reported for Sweden by Ali Manouchehrinia (2024), concerning incremental absenteeism costs relative to matched controls during the year preceding MS diagnosis. To prevent double counting, this incremental cost was applied exclusively to incident cases.
4-6.5	Absenteeism during the pre-diagnosis period.	• Manouchehrinia et al, 2024	Assumptions were based on data reported for Sweden by Ali Manouchehrinia (2024), concerning incremental absenteeism costs relative to matched controls during the year preceding MS diagnosis. To prevent double counting, this incremental cost was applied exclusively to incident cases.
7-9.5	Absenteeism during the pre-diagnosis period.	• Manouchehrinia et al, 2024	Assumptions were based on data reported for Sweden by Ali Manouchehrinia (2024), concerning incremental absenteeism costs relative to matched controls during the year preceding MS diagnosis. To prevent double counting, this incremental cost was applied exclusively to incident cases.

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Appendix B: Survey questions

1. Which of these areas of specialism are included/available within your multidisciplinary team caring for people with MS? (select all that apply)

- Physiotherapy/physical therapy
- Occupational therapy
- Speech and language therapy
- Mental health care
- Cognitive rehabilitation
- Sexual and reproductive care
- Continence care/urology
- Support with diet and nutrition
- MS specialist nursing
- Care coordination
- None of the above

2. Within your clinic, do you or another member of the multidisciplinary team routinely ask adult patients about the impact of MS on any of these? Select all that apply

- Their ability to do any paid work and remain in employment
- Their ability to be productive at work (to do their normal work tasks with the same quality and speed as they did before they developed MS)
- Their earning capacity (that is, whether they are still able to do the same or a similarly paid job as they did before they developed MS)
- Their ability to care for family members
- Their ability to perform activities of daily living (ADL)
- Their quality of life
- Their lifestyle habits (eg, exercise, diet, sleep, relaxation, cardiovascular risk factors)
- Their ability to participate in social and leisure activities (social life, art, culture)
- The impact of their condition is having on their carers
- None of the above

3. Which of the following symptoms and functional areas do you routinely assess (eg, every 6 months) among your adult patients with MS? (Select all that apply)

- Fatigue
- Endurance
- Depressive symptoms/mood
- Pain
- Bladder dysfunction
- Bowel dysfunction
- Cognition
- Walking ability and gait
- Balance/falls
- Upper limb function
- Visual function
- Sexual function
- Swallowing
- Sleep
- Sensory symptoms (eg, burning, tingling, pins and needles, sensitive skin or similar sensations)

4. Which of the following disability assessment tools do you or your multidisciplinary team routinely use (eg, every 6 months) in adult patients with MS? (Select all that apply)

- Expanded Disability Status Scale (EDSS)
- Expanded Disability Status Scale-Plus (EDSS-Plus)
- Patient Reported Expanded Disability Status Scale (PR-EDSS)
- Overall Disability Response Score (ODRS)
- Multiple Sclerosis Functional Composite (MSFC)
- Multiple Sclerosis Clinical Outcome Assessment (MSCOA)
- Multiple Sclerosis Performance Test (MSPT)
- Multiple Sclerosis Severity Score (MSSS)
- Patient Determined Disease Steps (PDDS) scale
- WHO Disability Assessment Schedule 2.0 (WHODAS 2.0)
- Other
- None of the above

5. Which of the following performance assessments do you or your multidisciplinary team routinely use in your practice (eg, every 6 months) when evaluating adult patients with MS? (Select all that apply)

- Timed 25-foot walk test (T25FWT)
- Nine-Hole Peg Test (9HPT/NHPT)
- Timed up and go test (TUG)
- Paced Auditory Serial Addition Test 3-second version (PASAT 3)
- Symbol Digit Modalities Test (SDMT)
- Low-contrast letter acuity test (LCLA)
- None of the above

6. Which of the following patient-reported outcome measures (PROMs) do you or your multidisciplinary team routinely use in your practice when assessing adult patients with MS? (Select all that apply)

- 9-item patient health questionnaire (PHQ-9)
- Multiple Sclerosis Impact Scale (MSIS-29)
- Modified Fatigue Impact Scale (MFIS)
- Visual analog scale (VAS) for pain
- 36-Item Short Form Health Survey (SF-36)
- MS Quality Of Life-54 item instrument (MSQoL-54)
- Neuro-QoL tool
- Other [ANCHOR]
- None of the above [ANCHOR-EXCLUSIVE]

7. To the best of your knowledge, what percentage of your MS patients within each of the following severity groups would you estimate are currently unemployed due to MS?

- Patients with mild disability (that is, patients with an EDSS score of 0-3.5) _____%
- Patients with moderate disability (that is, patients with an EDSS score: 4-6.5) _____%
- Patients with severe disability (that is, patients with an EDSS score: 7-9.5) _____%
- Don't know/not sure

8. To the best of your knowledge, how many days per year on average would you estimate that patients in each MS severity level group take a leave of absence from work due to MS-associated sick leave or medical appointments? (mild, moderate and severe)

- Patients with mild disability (EDSS score: 0 -3.5) _____days off work due to MS per year
- Patients with moderate disability (EDSS score: 4.5-6.5) _____ days off work due to MS per year
- Patients with severe disability (EDSS score: 7-9.5) _____ days off work due to MS per year
- Don't know/not sure

9. To the best of your knowledge, what percentage of MS patients in each severity level group do you estimate require support from an informal caregiver (unpaid support, usually from a family member)?

- Patients with mild disability (EDSS score: 0-3.5) _____%
- Patients with moderate disability (EDSS score: 4-6.5) _____%
- Patients with severe disability (EDSS score: 7-9.5) _____%
- Don't know/not sure

10. To what extent do you agree with the following statements:

Randomise	Strongly agree	Somewhat agree	Neither agree nor disagree	Somewhat disagree	Strongly disagree
Existing aggregated measures of disability are capable of detecting subtle changes in disability in patients with MS					
Using separate measures to assess individual functional areas (eg, walking ability, fatigue, cognition, bladder symptoms, mood etc.) is better for detecting subtle changes in disability progression than using aggregate measures of disability					
I feel confident that I can distinguish between temporary relapses and permanent disability progression during assessments					
A more comprehensive approach is needed to measure disability in MS					

11. Which of the following barriers do you encounter when using disability measures in routine clinical practice for MS patients? (Select all that apply)

- Insufficient time during appointments to administer standardised measures of disability
- Lack of staff/resources to support comprehensive assessments
- Limited reimbursement for comprehensive disability evaluations
- Inadequate training on using specific measurement tools
- Patient fatigue/cognitive limitations affecting assessment accuracy
- Difficulty integrating measures into workflow or electronic health records
- Concerns about existing measures' ability to detect disability progression
- Misalignment between assessments and what matters most to patients
- Other barrier(s)
- None of the above - I don't encounter any barriers

12. Which of the following do you believe would most improve assessments of disability in MS patients? (Rank top 3)

- Develop technology-based solutions to extract information from physician notes in the electronic medical record to calculate standardised disability scores
- Develop automated templates to input data that estimate disability scores and can be linked to the electronic medical record
- Augment the EDSS scale with supplementary assessments (eg, related to cognitive function and upper limb function) to provide a more holistic assessment
- Simplify disability assessment tools so that they can be completed easily by a clinician in a short period of time
- Provide reimbursement specifically for assessing disability scores
- Develop better patient self-monitoring and reporting options for disability
- Improve options for remote assessment of disability (eg, telemedicine)
- None of the above

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