Multiple sclerosis – the challenge of access to medicines

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Disclaimer

- I am a member of the South African National Essential List Committee and co-chair of its Expert Review Committee.
- However, I am speaking here today as an independent academic, not on behalf of any official body.

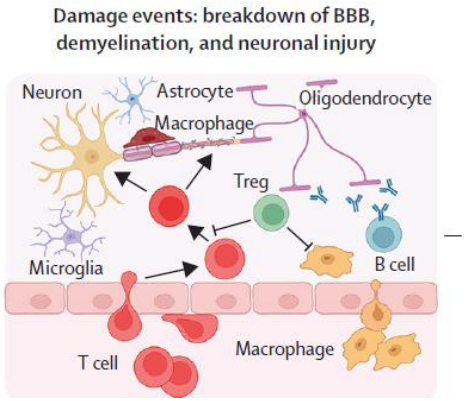
Outline

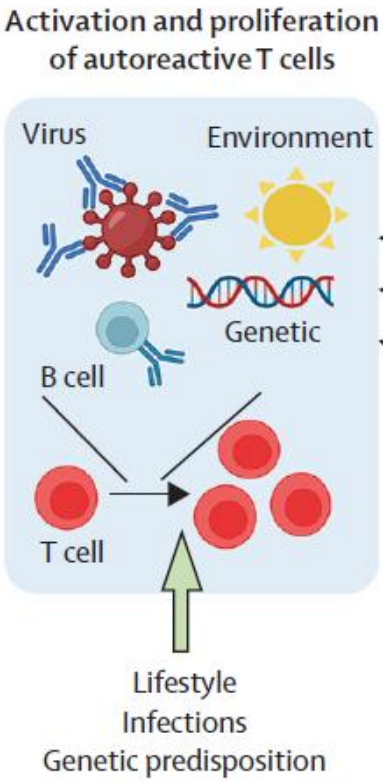
- Multiple sclerosis (MS) - background
- How many people are affected by multiple sclerosis in different parts of the world?
  - Access to diagnosis
  - Access to treatment
- Treatment options and access
  - WHO Model List of Essential Medicines
  - South African public sector EML

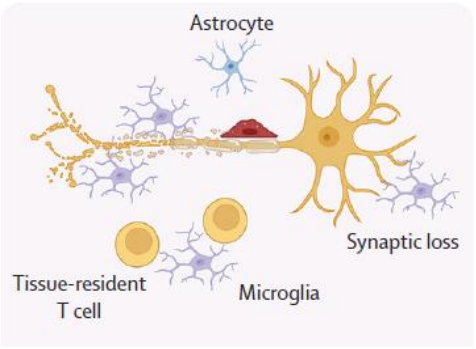
Multiple sclerosis (MS) - background

- MS is an **inflammatory disease** of the central nervous system (brain and spinal cord) which causes a loss of the fatty protective layer around nerves (the myelin sheath), resulting in damage.
- MS is one of the most common causes of disability in young adults, other than trauma.
- MS affects **2-3 times more females than males**.
- Most patients with MS are diagnosed as young adults (about 32 years of age), but MS is also being diagnosed now in more older adults (over 50 years of age).
- With treatment, more patients with MS are living longer, meaning that the total prevalence is increasing.
- Most people with MS present with a **relapsing–remitting** condition – acute episodes (relapses) separated by periods of stability (remissions).

“Acute” vs “smouldering” pathology







Lancet 2024; 403: 183–202
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November 7, 2023
https://doi.org/10.1016/S0140-6736(23)01473-3

How lifestyle and genetic factors influence either “acute” or “smouldering” pathology is poorly understood

ms international federation | Atlas of MS

Map view | Chart view | Factsheet

STATISTICS CATEGORY: Epidemiology

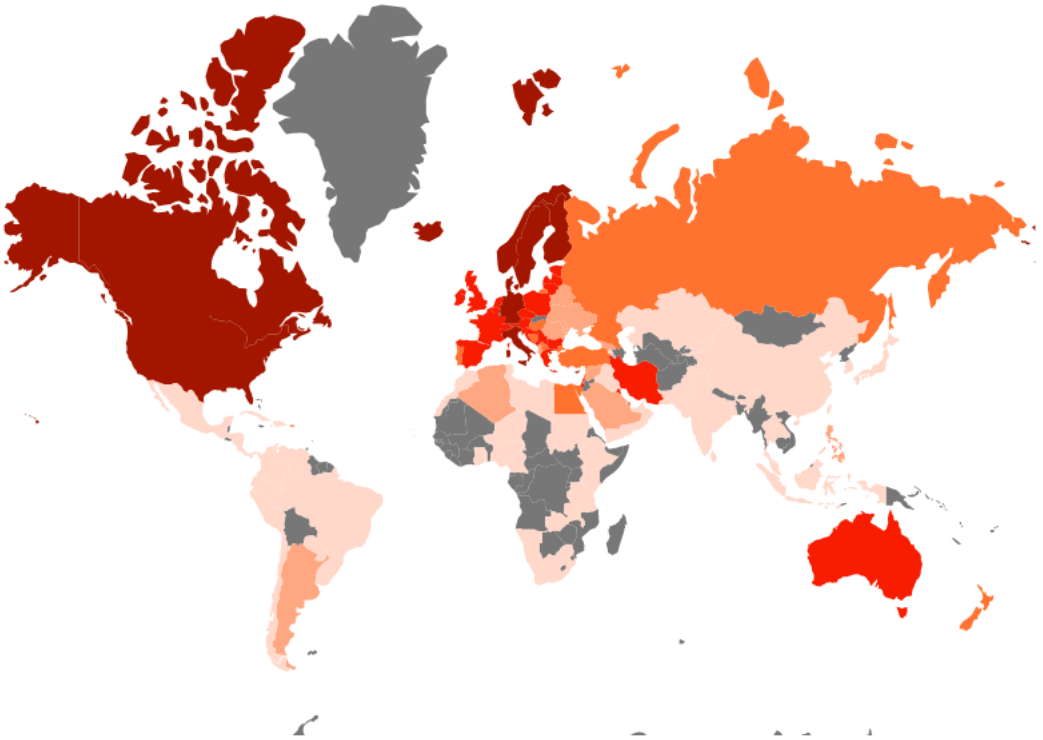
FIND STATISTICS FOR: Number of people with MS
Prevalence per 100,000 people

Use your cursor to hover over a country to reveal country information.

https://www.atlasofms.org/map/global/epidemiology/number-of-people-with-ms

Germany (83m pop):
280 000 MS patients;
prevalence 300 per
100 000 people

South Africa (64m pop):
4 685 MS patients;
prevalence 8 per
100 000 people



ms international federation | September 2020

Summary of key findings

https://www.msif.org/wp-content/uploads/2020/10/Atlas-3rd-Edition-Epidemiology-report-EN-updated-30-9-20.pdf

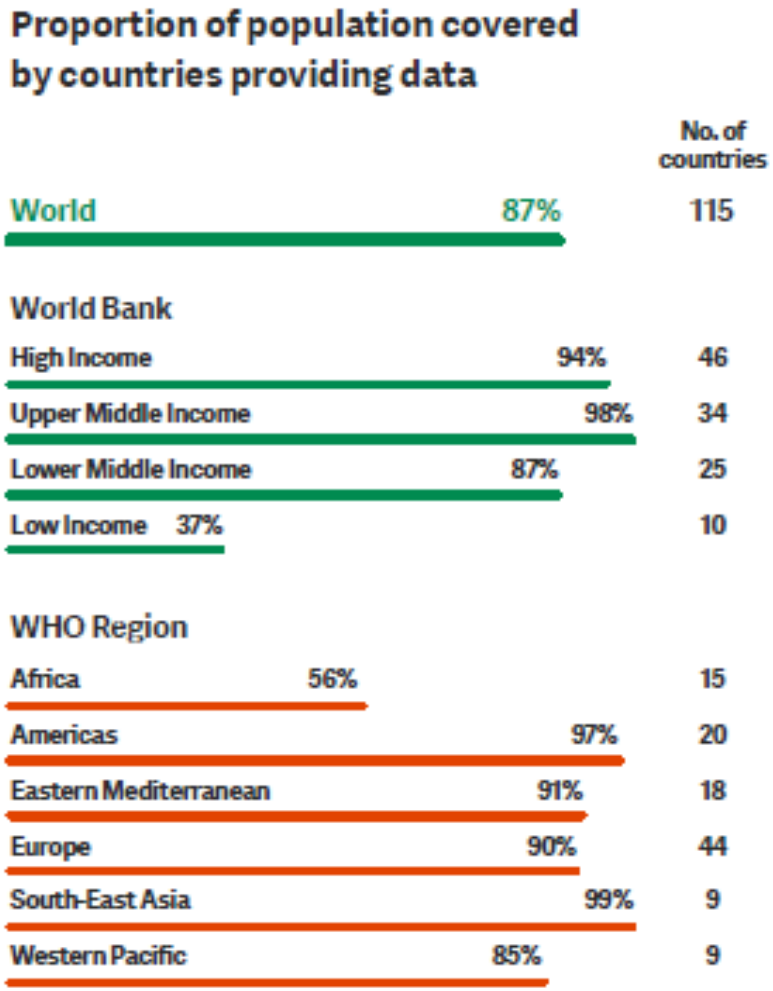
There are **2.8 million people** living with MS around the globe. This is our most accurate and up-to-date estimate of the number of people living with MS worldwide.

This equates to **1 in 3,000 people** in the world living with MS. In countries with the highest prevalence, as many as **1 in every 300** people have MS.

The estimated number of people with MS globally has **increased from 2.3 million** people in 2013.

Several factors are likely to be contributing to the increase, including: better counting methods nationally and globally as well as improved diagnosis, people with MS living longer and global population growth. However, from the data available we cannot rule out that there may also be some increase in the risk of developing MS.

Still a lack of data on low-income countries in Africa



Unanswered questions

- Is the difference in prevalence (e.g. between Germany and South Africa) due to:
  - real differences in risk (lifestyle, infections, genetic factors)
  - a lack of access to diagnosis and treatment in low- and middle-income countries (LMICs)?

From the Atlas reports

Diagnosing MS

An early diagnosis is vital to enable early treatment with disease modifying therapies that can minimise relapses and reduce future disability. Even if disease modifying therapies are not available, an early diagnosis is still crucial as it allows for lifestyle changes to help manage the disease and improve quality of life.

1

The majority (83%) of countries worldwide have barriers that prevent early diagnosis of MS. Globally the most commonly reported barrier is a lack of awareness of MS symptoms amongst the public and healthcare professionals. In low and lower middle income countries[1] other barriers are also common, including the availability of qualified healthcare professionals as well as the availability and cost of the diagnostic equipment and tests.

2

Use of the most recent criteria for diagnosing MS (McDonald 2017) correlates with country wealth. There is almost universal use (98%) in high income countries compared to less than half (40%) of low income countries using the criteria. The most common barrier cited for not using McDonald 2017 is a lack of awareness or training for neurologists.

ms international federation | April 2021

https://www.msif.org/wp-content/uploads/2021/05/Atlas-3rd-Edition-clinical-management-report-EN-5-5-21.pdf

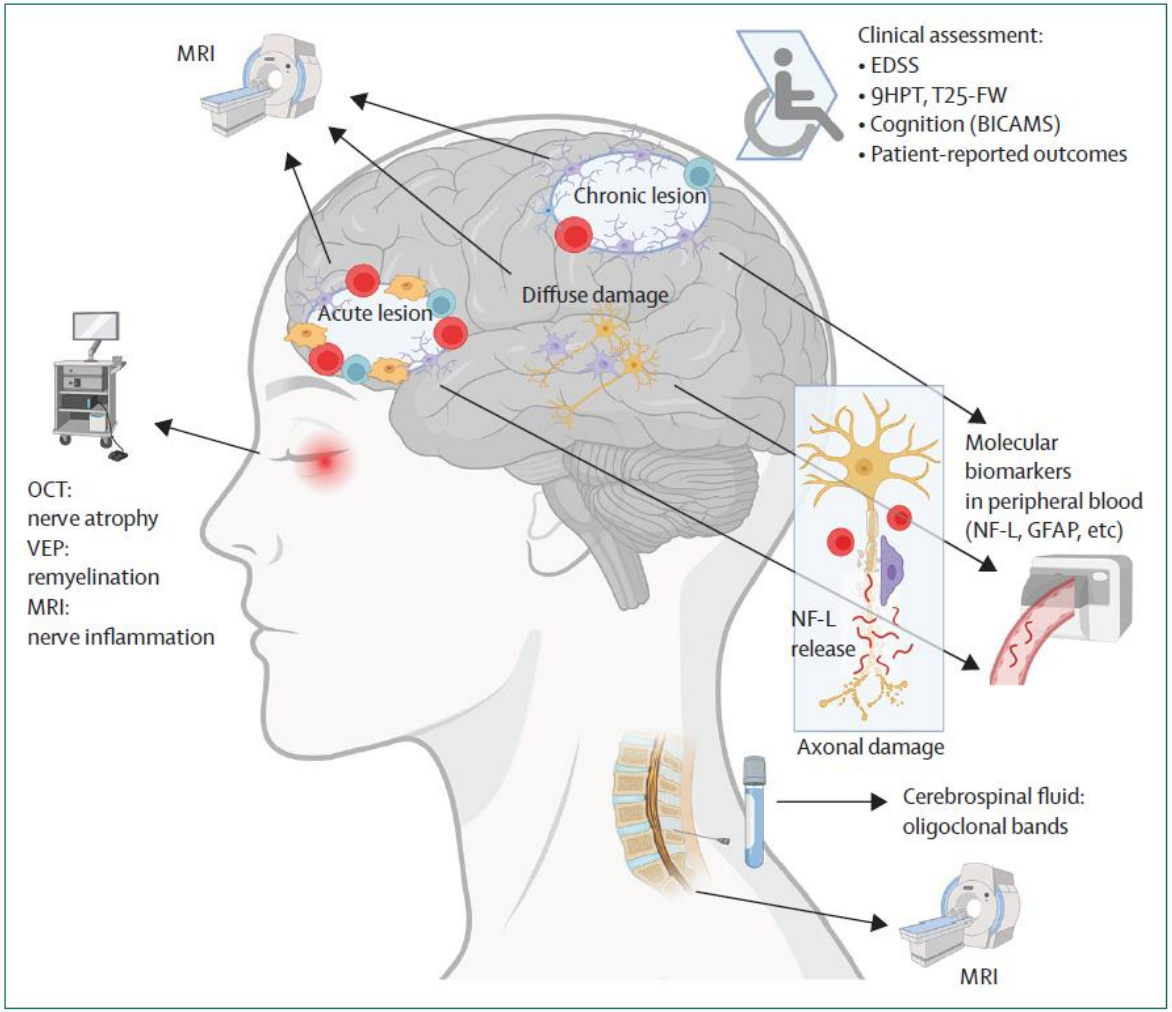


Figure 2: **Biomarkers in multiple sclerosis**
Pathological processes in multiple sclerosis can be assessed and quantified by different paraclinical biomarkers, including brain and spinal cord MRI, OCT, analysis of cerebrospinal fluid, and peripheral blood (via single molecule array). BICAMS=Brief International Cognitive Assessment for Multiple Sclerosis. EDSS=Expanded Disability Status Scale. OCT=optical coherence tomography. T25-FW=timed 25-foot walk. VEP=visual evoked potentials. 9HPT=nine-hole peg test. Figure created with BioRender.com.

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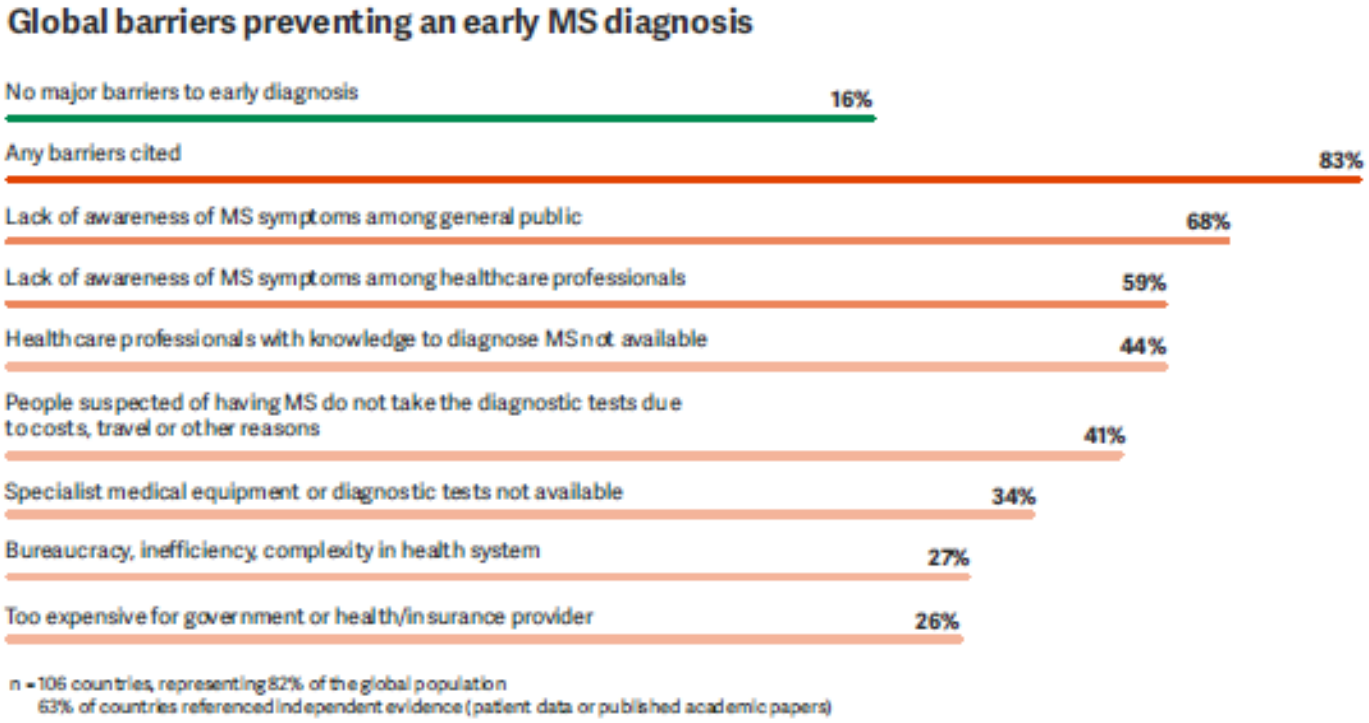
S0140-6736(23)01473-3

Access to sophisticated diagnostics tests, such as magnetic resonance imaging (MRI) scans, is limited in LMICs

From the Atlas report



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Current Practices, Challenges, and Future Directions in Multiple Sclerosis Management in Sub-Saharan Africa

Nicholas Aderinto, MD

ABSTRACT

Multiple sclerosis (MS) is a chronic, inflammatory, and neurodegenerative condition characterized by the immune system's attack on the myelin sheath, leading to neurological dysfunction. While the prevalence of MS in Africa remains lower than in other regions, it has been rising steadily in recent years, with unique challenges hindering its effective management. These challenges include limited health care resources, inadequate diagnostic tools, financial constraints on accessing disease-modifying therapies, and a lack of trained health care professionals (HCPs). Cultural stigma surrounding MS further complicates patient care and treatment adherence. However, ongoing efforts by patient organizations, international collaborations, and local HCPs are focused on raising awareness, enhancing diagnosis and treatment access, and training HCPs. Future directions include integrating MS into national health policies, expanding education and research initiatives, and improving patient support networks. These efforts are vital in addressing the growing burden of MS in Africa and ensuring equitable access to care.

Int J MS Care. 2025;27:T13-T16. doi:10.7224/1537-2073.2024-080

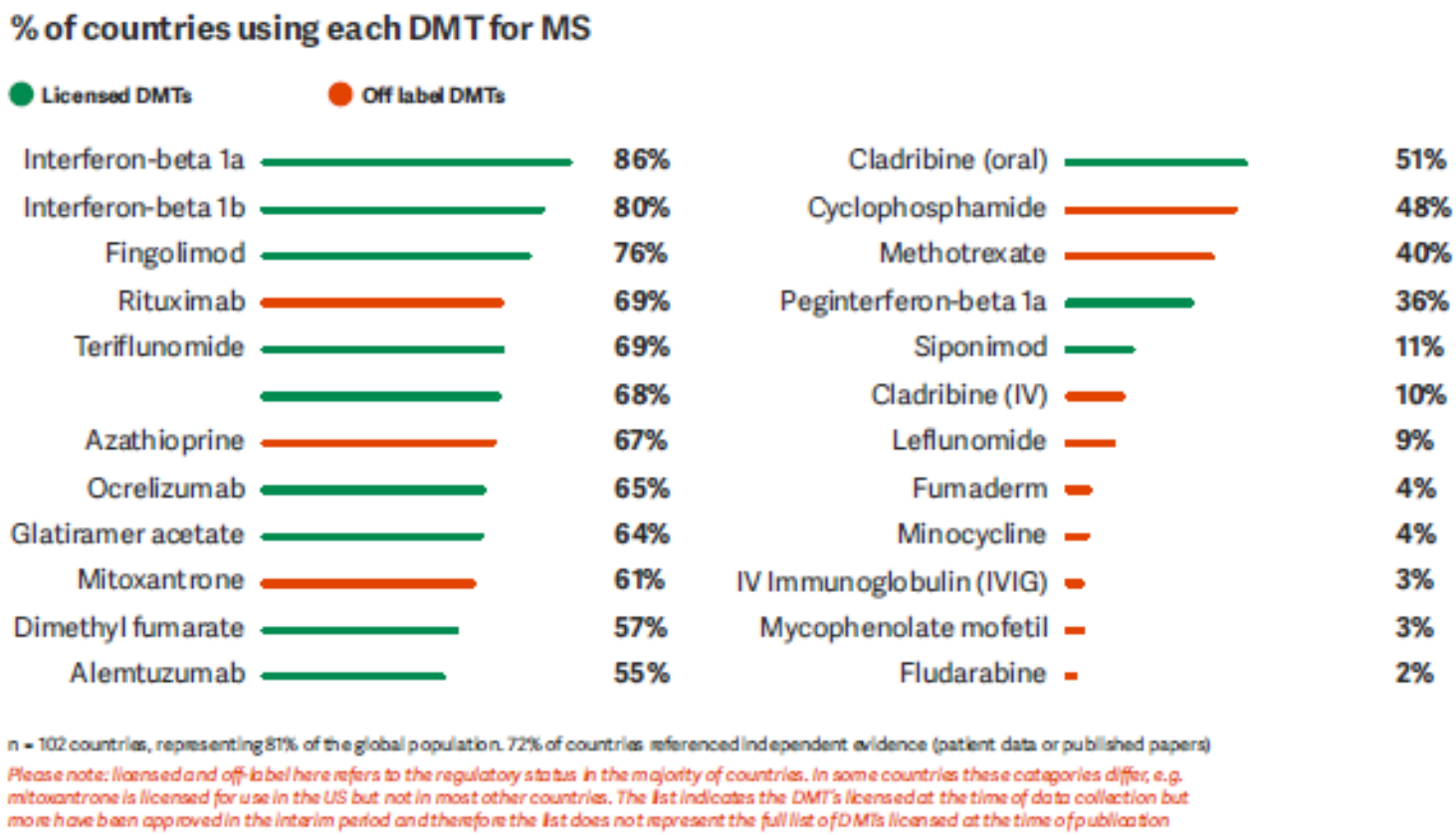
"Establishing more networks for patients and caregivers is essential to deliver holistic support to individuals in Africa who live with MS, as collaboration facilitates access to critical information, resources, and emotional support, all vital for enhancing patients' quality of life. **Support groups, patient advocacy organizations, and community outreach programs** empower individuals with MS and their families by creating supportive environments and studies have shown that community support enhances treatment adherence and well-being."

Disease modifying therapy (DMT)
(year of first approval)

- **Injectables**
  - Interferon beta-1b (1993)
  - Interferon beta-1a (1997)
  - Peg-interferon beta-1a (2014)
  - Glatiramer acetate (1996)
  - Ofatumamab (2020)
  - Mitoxantrone (2000)
  - Natalizumab (2004)
  - Alemtuzumab (2007)
  - Ocrelizumab (2017)
  - Ublituximab (2022)
- **Oral medication**
  - Fingolimod (2010)
  - Teriflunomide (2012)
  - Dimethyl fumarate (2013)
  - Cladribine (2019)
  - Siponimod (2019)
  - Diroximel fumarate (2019)
  - Monomethyl fumarate (2020)
  - Ozanimod (2020)
  - Ponesimod (2021)

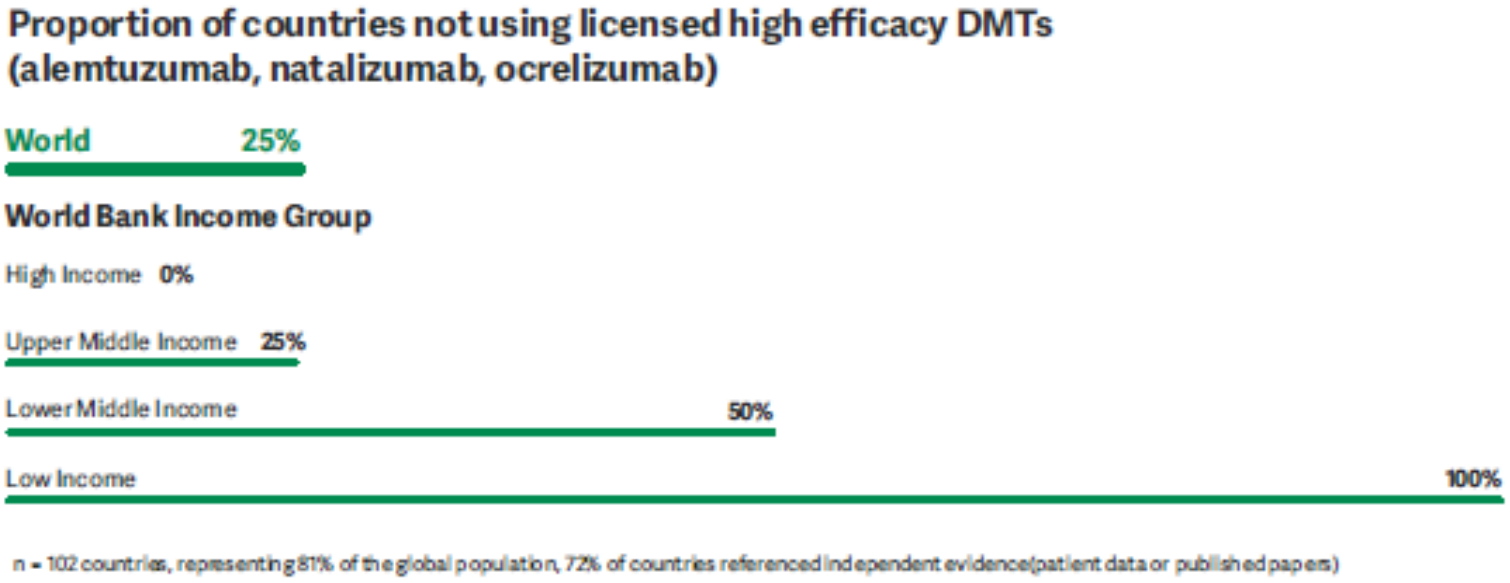
Observation: many options; some biologicals' many with similar side effects; trials of newer agents compared to standard of care rather than placebo; also others used off-label

From the Atlas reports



Another way to look at it …

High efficacy	Good efficacy	Moderate efficacy
Alemtuzumab	Cladribine (oral)	Glatiramer acetate
Natalizumab	Dimethyl fumarate	Interferon-beta 1a
Ocrelizumab	Fingolimod	Interferon-beta 1b
	Siponimod	Peginterferon-beta 1a
		Teriflunomide



Barriers to people with MS receiving DMTs by World Bank income level	High Income	Upper Middle Income	Lower Middle Income	Low Income
	n=44 countries (92% of the population)	n=29 countries (95% of the population)	n=23 countries (73% of the population)	n=10 countries (43% of the population)
No major barriers	**55%**	10%	4%	0%
Too expensive for the government, healthcare or insurance provider	18%	**69%**	**74%**	**70%**
People with MS do not take DMTs due to costs, side-effects or preference for other treatments/lifestyle measures	**23%**	52%	52%	40%
Healthcare professionals not readily available	18%	28%	39%	**70%**
Complete range of DMTs not available	14%	38%	52%	30%
Lack of awareness of DMTs amongst healthcare professionals	11%	34%	30%	**70%**
Equipment or tests to monitor treatments not available	2%	31%	57%	60%
DMTs only available in some areas of the country or certain hospitals	11%	34%	48%	30%
Bureaucracy, inefficiency or complexity in health system	**23%**	34%	22%	20%
DMTs not supplied to the country	5%	10%	35%	60%
DMTs frequently go out of stock or supply is irregular	0%	7%	26%	10%

*Shading indicates the barriers cited by 50% or more countries in each income category. Numbers in bold show the most common answers.

Discover Medicine

Review

High-dose vitamin D supplementation in multiple sclerosis: a systematic review of clinical effects and future directions

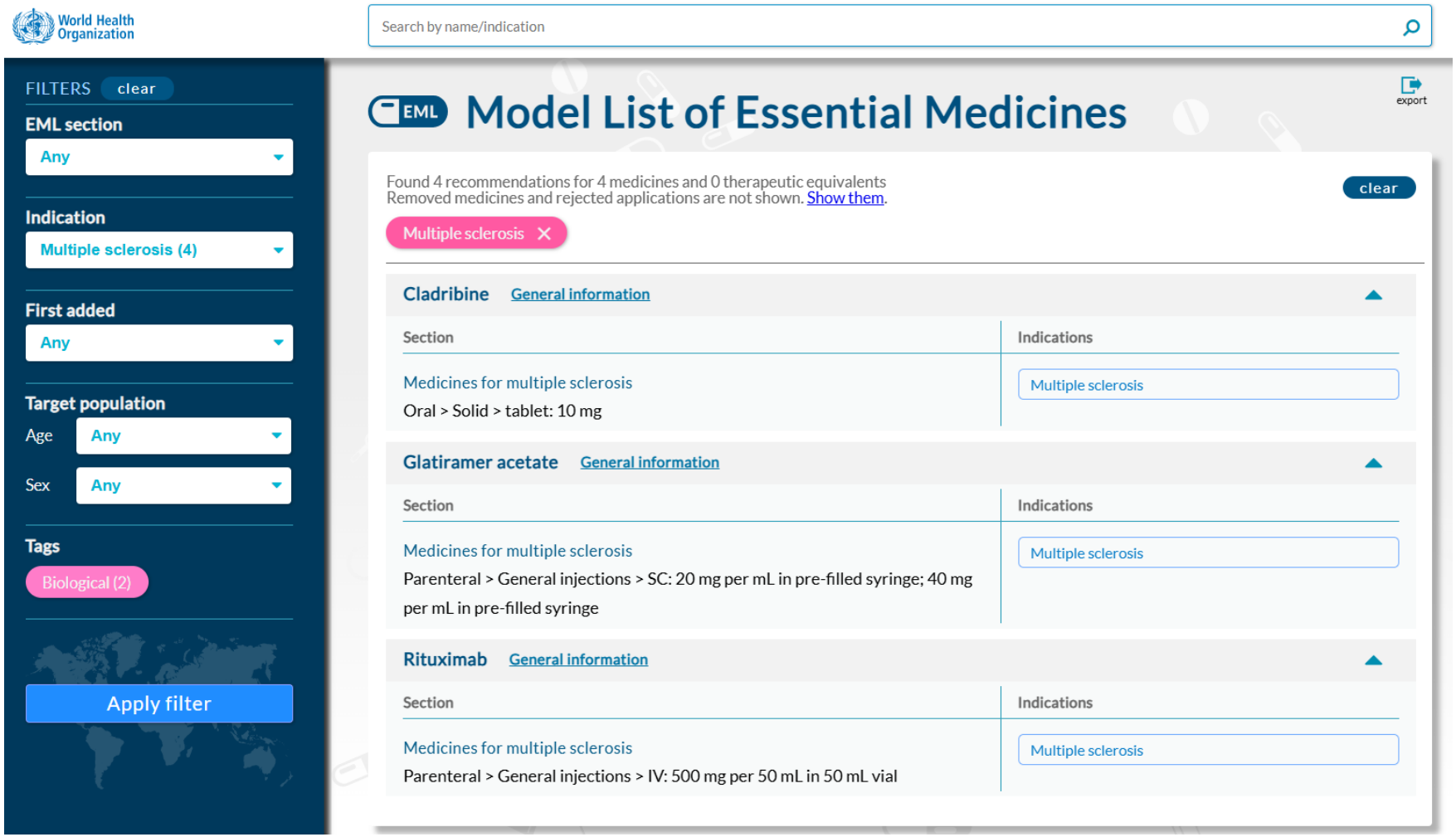
Nicholas Aderinto[1] · Gbolahan Olatunji[2] · Emmanuel Kokori[2] · Ikponmwosa Jude Ogieuhi[3] · Emmanuel Adetola Babalola[4] · Owolabi Samuel[5] · Israel Charles Abraham[2] · Julia Kwape Mimi[6] · Aminnah Oyesomi[7] · Yewande Abigail Adebayo[8] · Emmanuel Egbunu[9] · Akinmeji Ayodeji[10] · Oluwatobi Taiwo Omoworare[11]

Received: 20 May 2024 / Accepted: 10 July 2024
Published online: 17 July 2024

Abstract
Vitamin D deficiency is common in multiple sclerosis (MS) patients. This review explores the potential benefits and limitations of high-dose vitamin D supplementation in MS management. We reviewed relevant literature on the effects of high-dose vitamin D supplementation on relapse rates, disability progression, quality of life, and MRI markers of disease activity in MS patients. Additionally, we discussed the mechanisms by which vitamin D might influence MS, potential adverse effects, and future research directions. Studies suggest that high-dose vitamin D supplementation may reduce relapse rates and improve MRI markers of disease activity in MS. However, the evidence for its impact on disability progression and quality of life remains inconclusive. Vitamin D's immunomodulatory properties are well-documented, and its potential for neuroprotection and neurogenesis warrants further investigation. High-dose vitamin D supplementation holds promise as a complementary or disease-modifying therapy for MS. However, further robust research is required to solidify its role in clinical practice. Exploring vitamin D's multifaceted effects on the immune system, neuroprotection, and neurogenesis paves the way for novel therapeutic strategies to improve the lives of individuals with MS.

"A recent concern suggests that uncontrolled intake of ultra-high doses of vitamin D may mimic the progression of primary progressive MS, potentially causing a delay in diagnosis until the side effects become irreversible or even fatal".

WHO Model List of Essential Medicines



https://list.essentialmeds.org/

export

Ocrelizumab

REJECTED

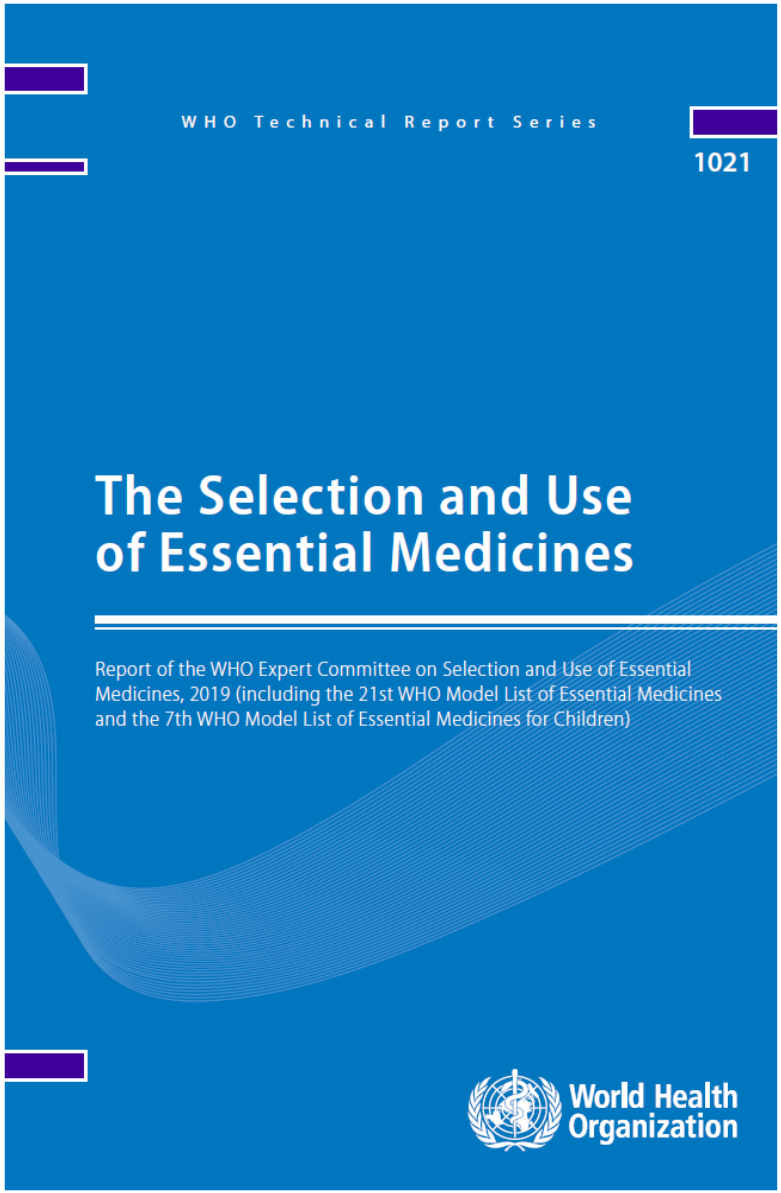
The Expert Committee, after evaluation, declines to list the medicine proposed in the application.
The Model List of Essential Medicines reports reasons that Committee Members have identified for denying listing.

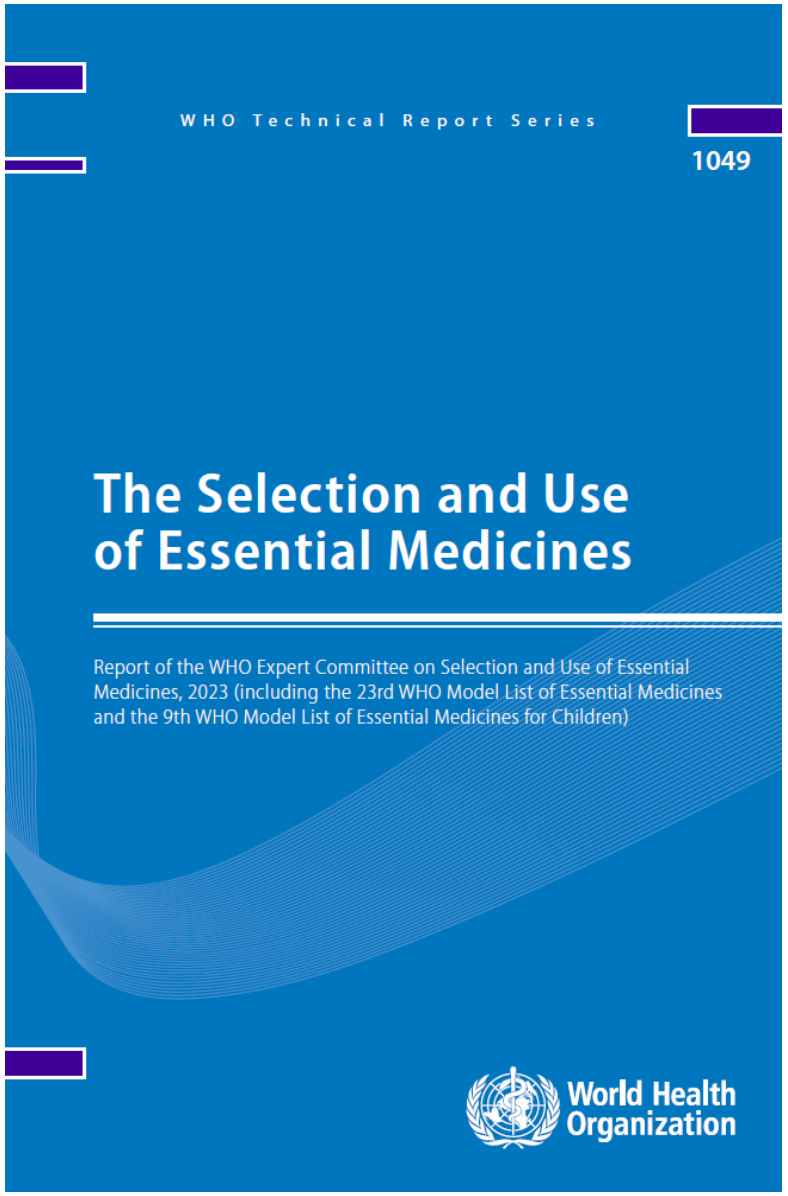
REJECTED

REJECTED

General description

INN	Ocrelizumab
ATC codes	L04AG08
Medicine type	Biological agent
EML status history	Application rejected in 2019 (TRS 1021) for Relapsing-remitting multiple sclerosis Application rejected in 2023 (TRS 1049) for Multiple sclerosis
Wikipedia	Ocrelizumab
DrugBank	Ocrelizumab


WHO Technical Report Series
1021
The Selection and Use of Essential Medicines
Report of the WHO Expert Committee on Selection and Use of Essential Medicines, 2019 (including the 21st WHO Model List of Essential Medicines and the 7th WHO Model List of Essential Medicines for Children)
World Health Organization


WHO Technical Report Series
1049
The Selection and Use of Essential Medicines
Report of the WHO Expert Committee on Selection and Use of Essential Medicines, 2023 (including the 23rd WHO Model List of Essential Medicines and the 9th WHO Model List of Essential Medicines for Children)
World Health Organization

WHO Expert Committee 2023

Medicines for multiple sclerosis: The Expert Committee recommended the inclusion of cladribine, glatiramer acetate and rituximab as individual medicines on the complementary list of the EML for the treatment of multiple sclerosis. The Committee did not recommend the inclusion of ocrelizumab for this indication, either as an individual medicine, or as a therapeutic alternative to rituximab under a square box listing.

…

The Committee acknowledged the benefits of ocrelizumab in the management of relapsing and primary progressive forms of multiple sclerosis. However, **there was no compelling evidence of its superiority over other alternatives, specifically rituximab**, which has the same target (CD20) and a similar peptide sequence, is widely used, **more affordable** and reimbursed for use in multiple sclerosis in several countries.

World Health Organization

Health Topics | Countries | Newsroom | Emergencies | Data

25th Expert Committee on Selection and Use of Essential Medicines

The meeting of the 25th WHO Expert Committee on the Selection and Use of Essential Medicines will be held at WHO Headquarters, Geneva, from **5 to 9 May 2025** to revise and update the WHO Model List of Essential Medicines (EML) and the WHO Model List of Essential Medicines for Children (EMLc).

No further applications for MS DMTs were submitted to this meeting

Standard Treatment Guidelines and Essential Medicines List for South Africa

Hospital Level, Adults
2019 Edition

health
Department:
Health
REPUBLIC OF SOUTH AFRICA

2030 NDP

14.10 MULTIPLE SCLEROSIS

G35

DESCRIPTION

A demyelinating disease of the central nervous system, characterised by relapsing and remitting episodes of unifocal or multifocal neurological dysfunction. Diagnosis is confirmed by imaging. The CSF may show oligoclonal bands and raised IgG index.
Recovery between acute flares of illness is common, although a general stepwise deterioration from baseline is usually found.
Consult with neurologist for diagnosis and treatment.

REFERRAL

All patients.

health
Department:
Health
REPUBLIC OF SOUTH AFRICA

National Essential Medicines List Committee (NEMLC)

TERTIARY AND QUATERNARY LEVEL ESSENTIAL MEDICINES LIST

Reviewed Items

OCTOBER 2024

L03AB07/ L03AB08	Interferon beta	Relapsing remitting multiple sclerosis	Approved
L04AA31	Teriflunomide	Relapsing remitting multiple sclerosis.	Approved Provided offered price is comparable or lower than beta interferon

Observation: limited options; both moderate efficacy choices; very price sensitive; some individual patient access to off-label medicines (rituximab)

Conclusions

- MS remains a challenging diagnosis, especially in countries with limited access to advanced technology.
- Despite many medicines approved by regulators, access to disease-modifying therapy (DMTs) remains limited, even in middle-income countries.
- Access to affordable biosimilars may offer new options.


THANK
YOU