

What is MS?

Dr Marco PISA Dr Emie PABEAU

Newly diagnosed information day 19th of May

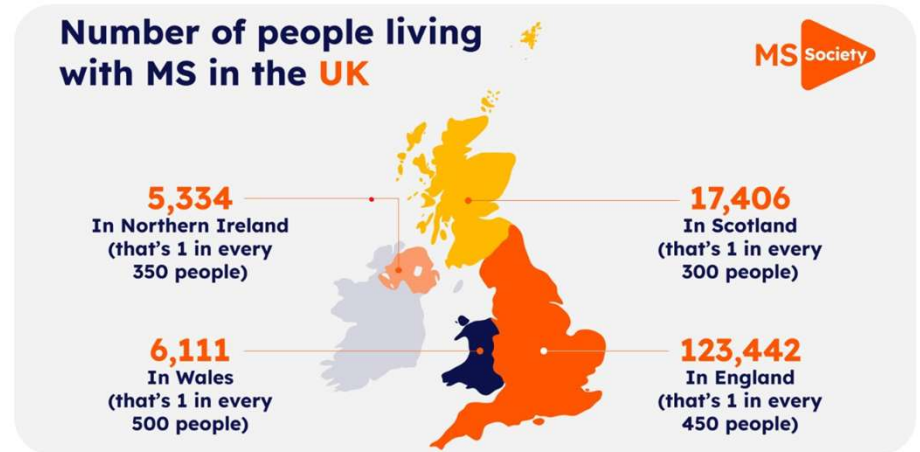
What is MS?



Chronic auto-immune disease that damages the myelin in the brain and spinal cord

Who gets MS?

Over 150 000 people in the UK
Population from Northern Europe

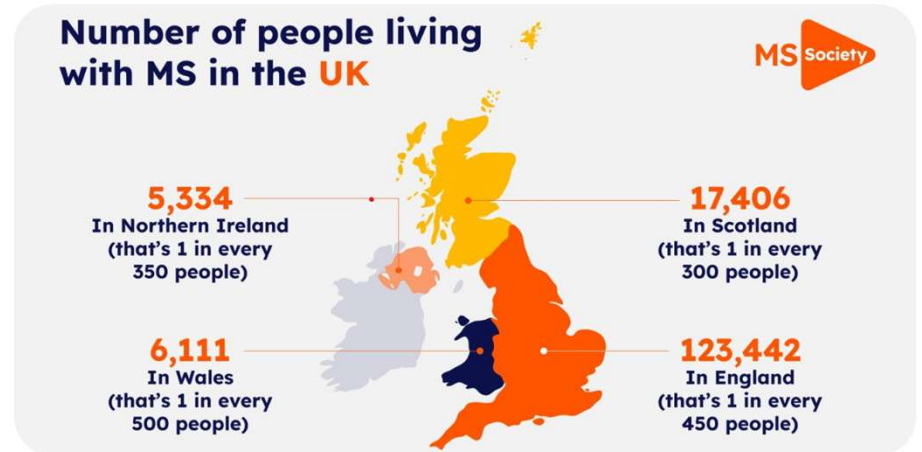


Who gets MS?

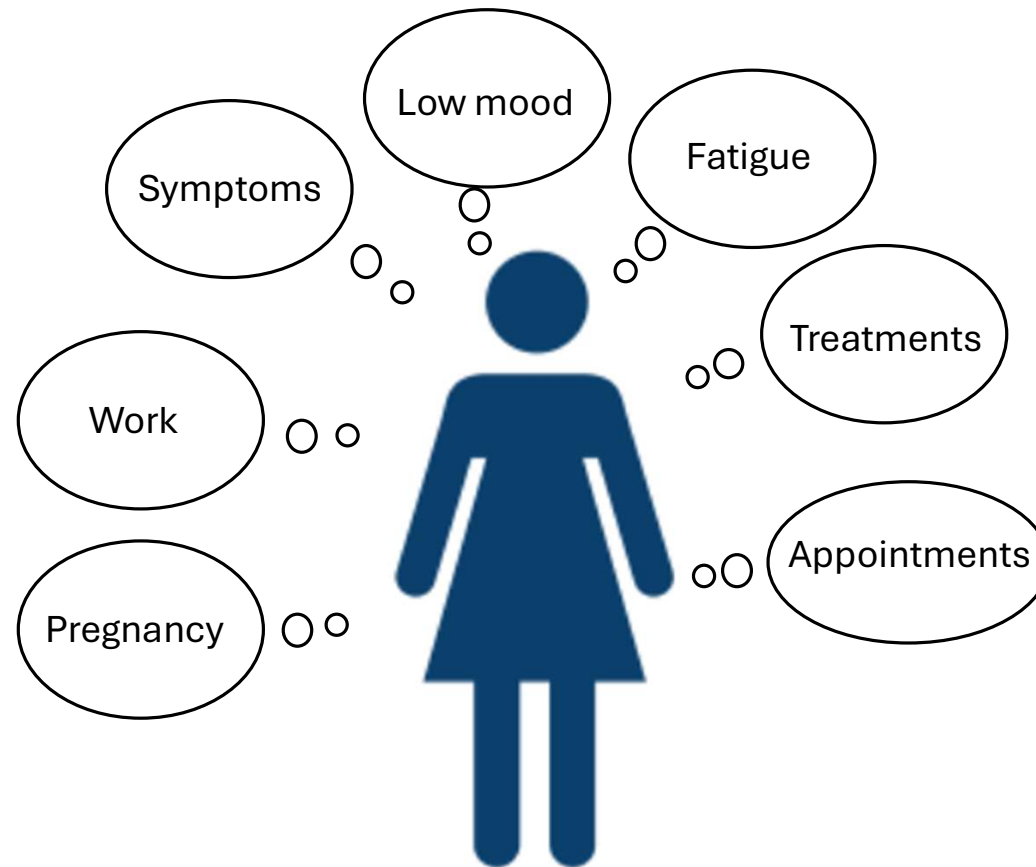
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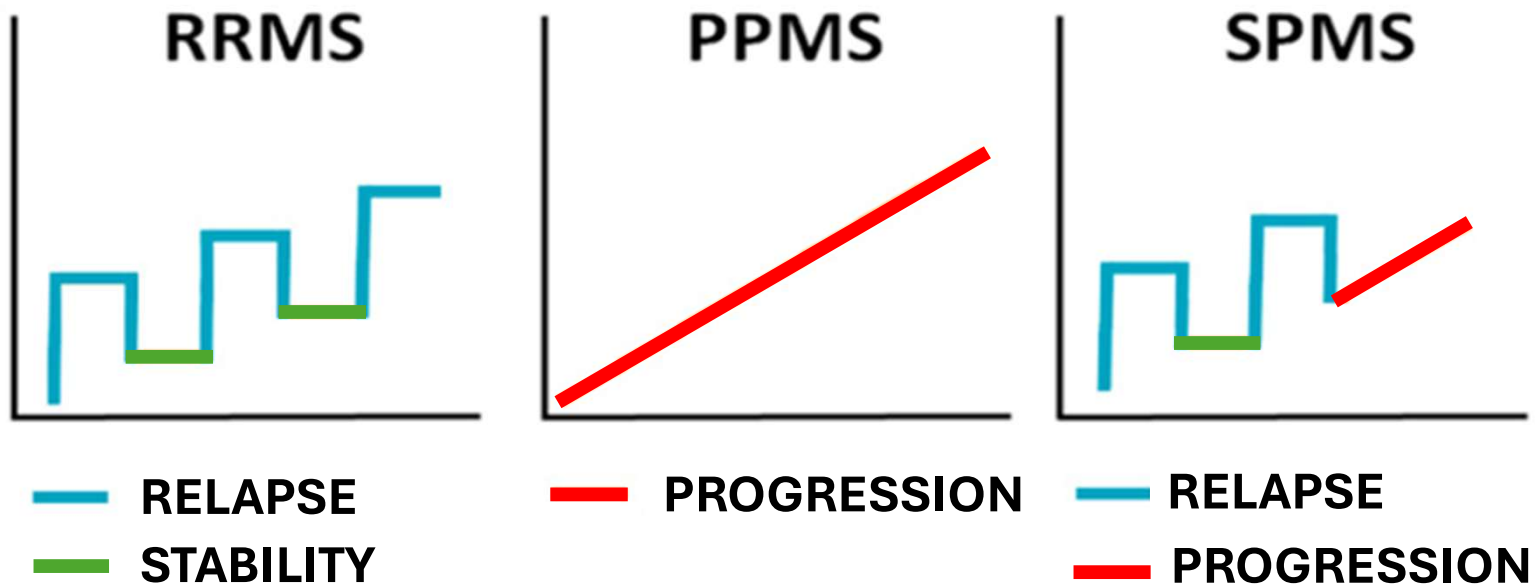
3 woman/1 man
Between 20 and 40 years old



How can MS impact my life?



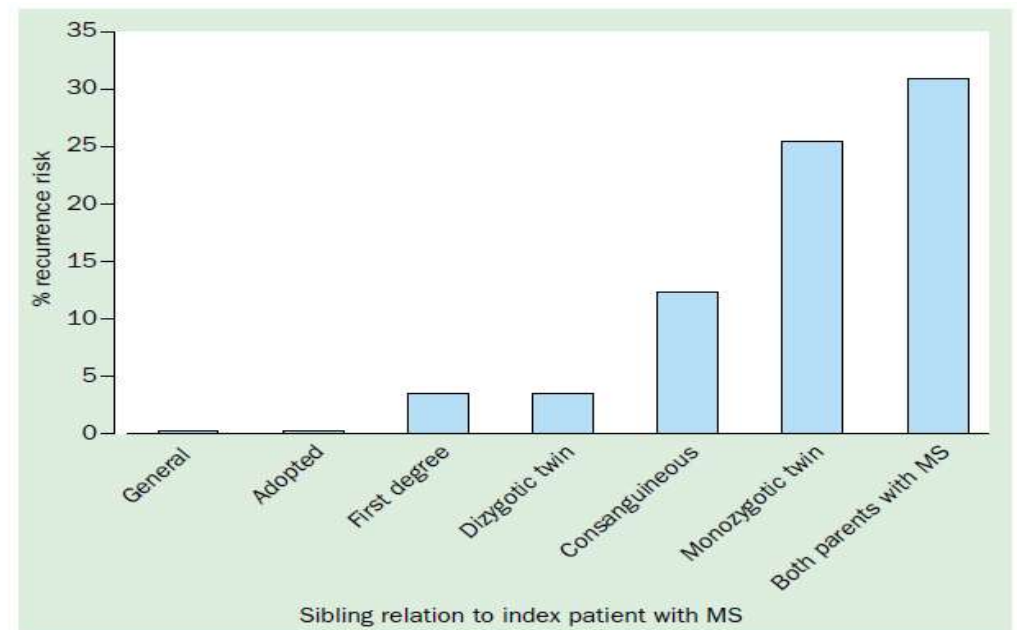
The “phases” and “types” of MS



What causes MS?

Genes:

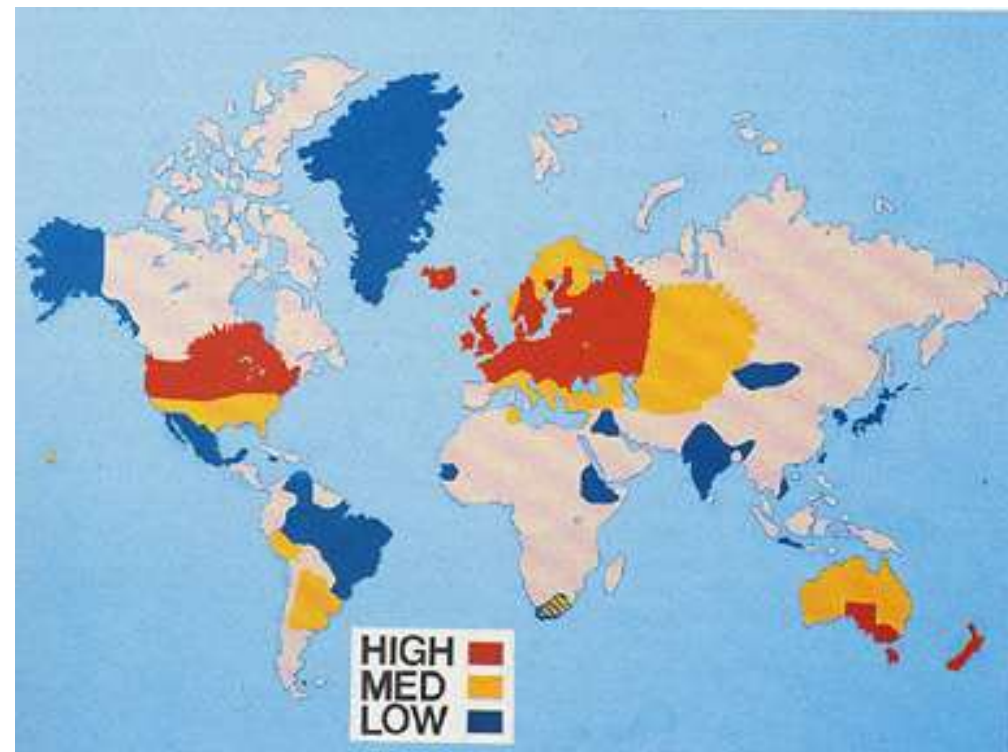
- Sex
- Family history
- Ethnicity



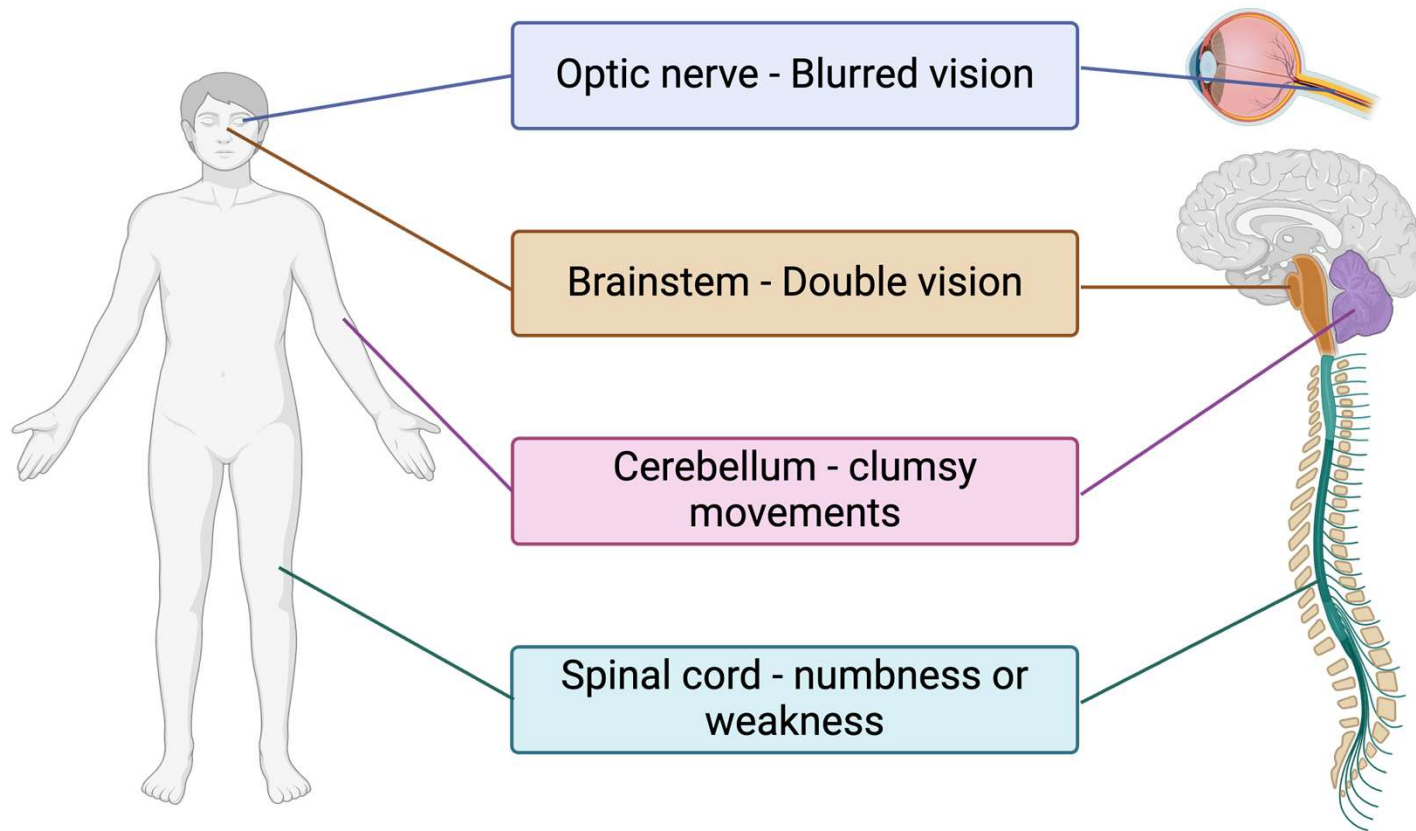
What causes MS?

Environment

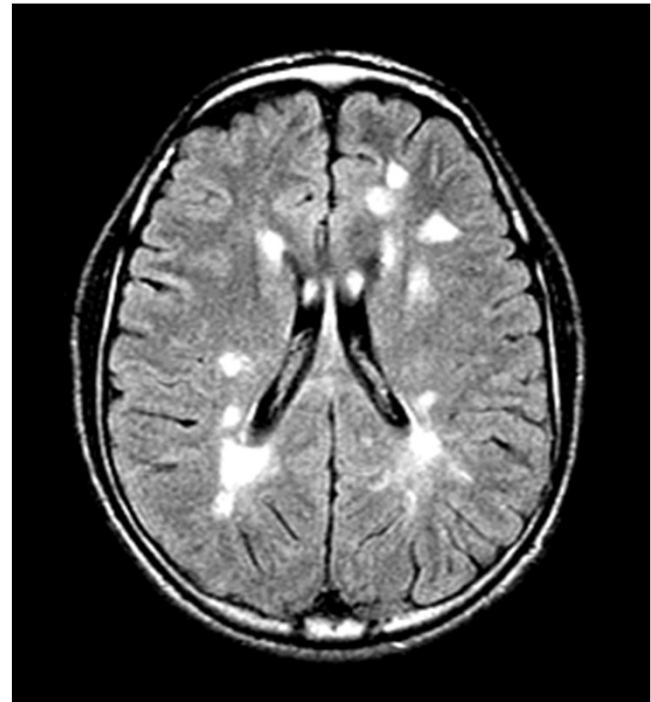
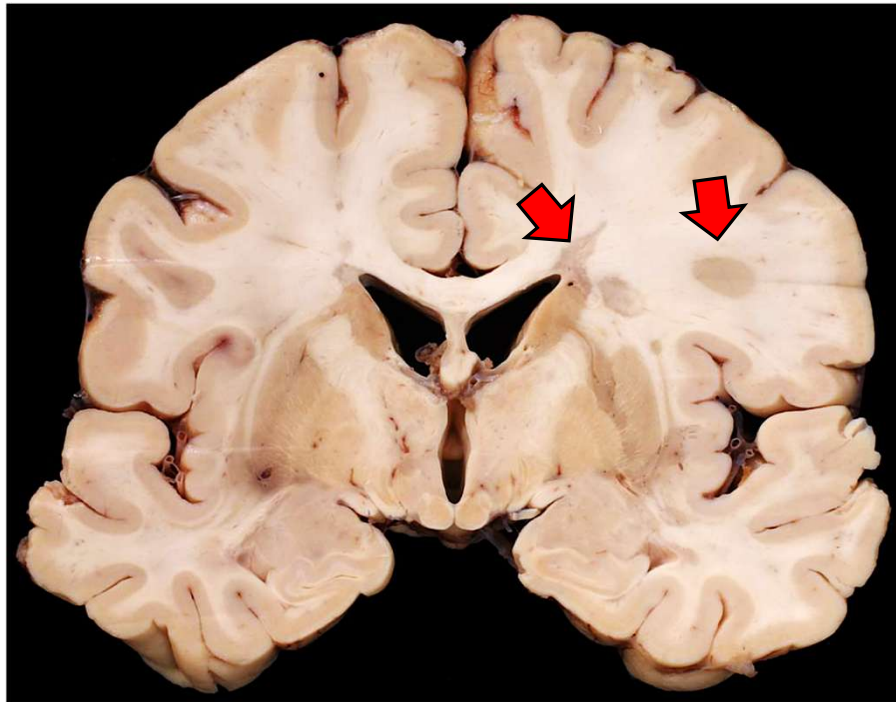
- EBV (glandular fever)!!
- Climate
- Vitamin D
- Smoking
- “The early hygiene hypothesis”



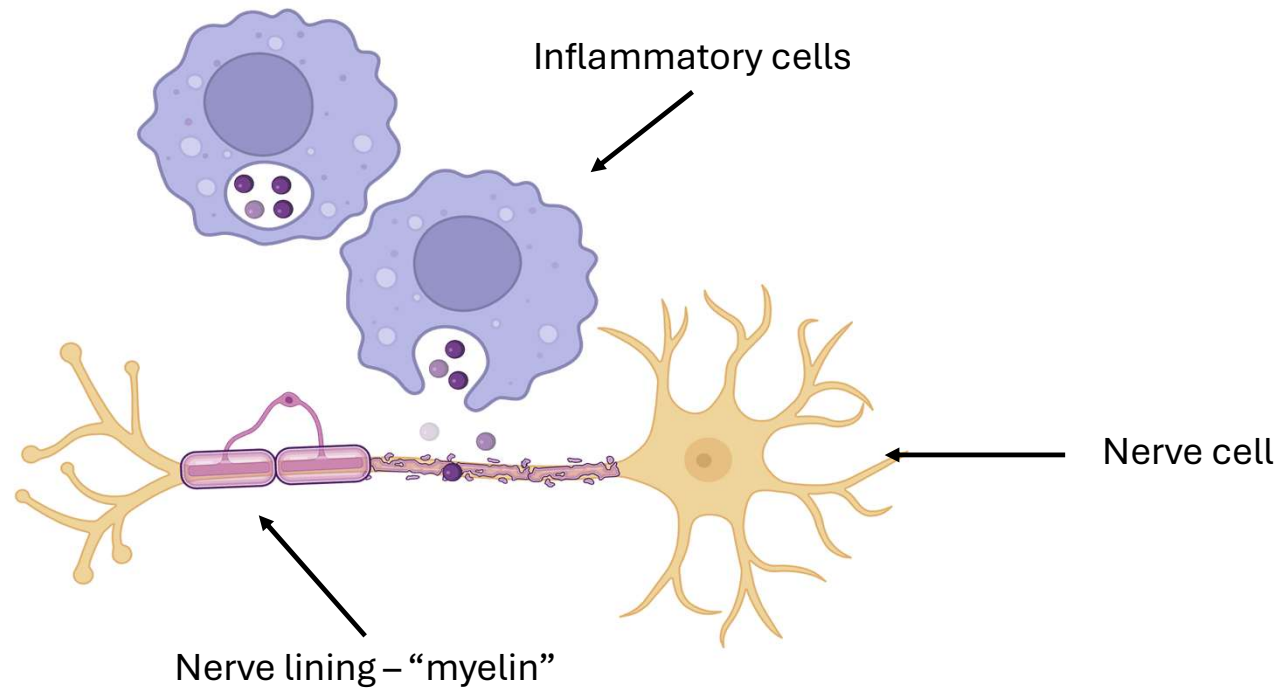
The “relapsing-remitting” phase: *Many different types of presentation*



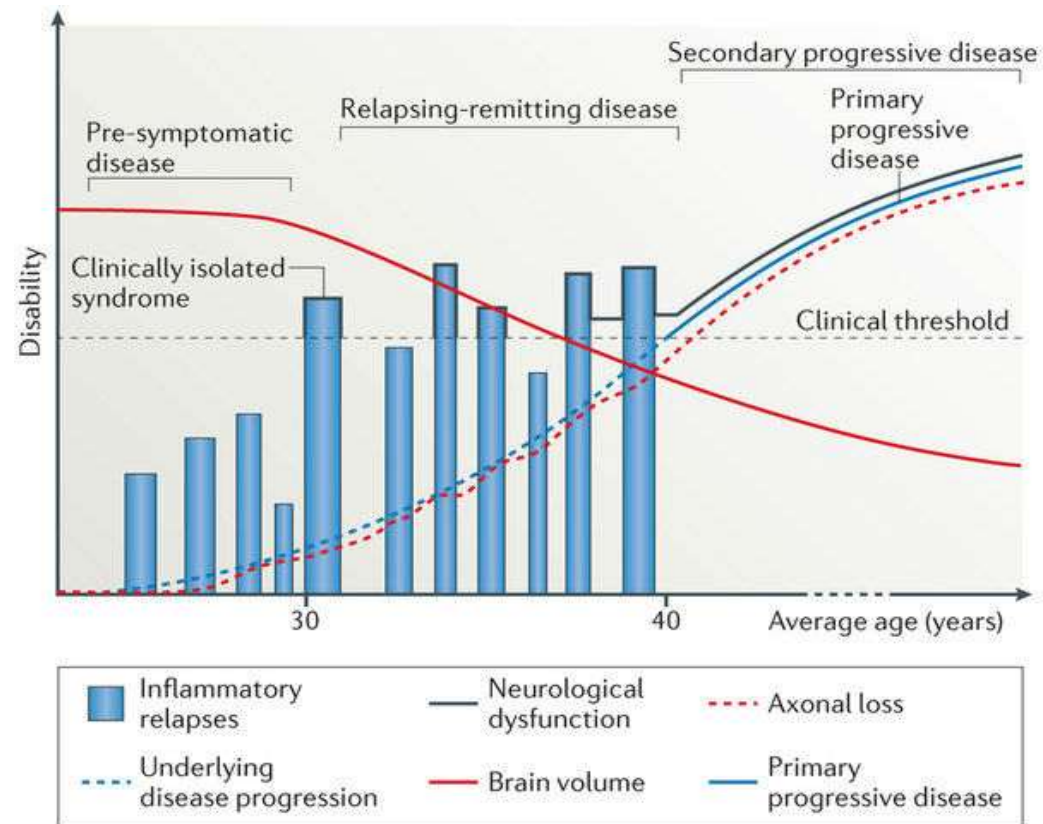
The “relapsing-remitting” phase:
...all explained by areas of inflammation called plaques



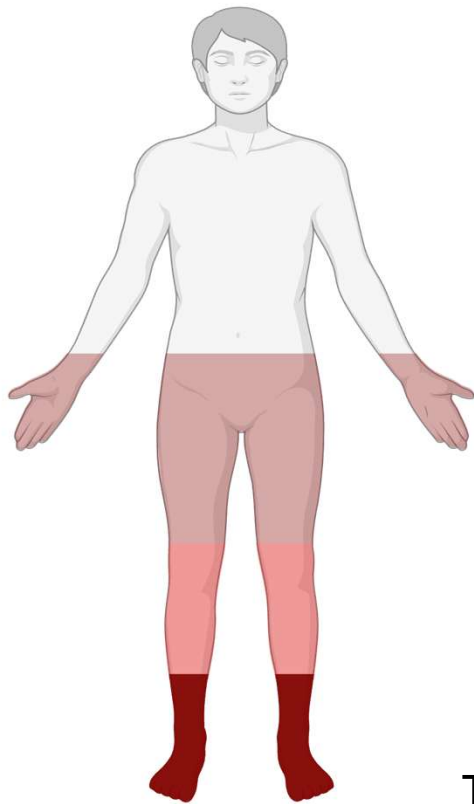
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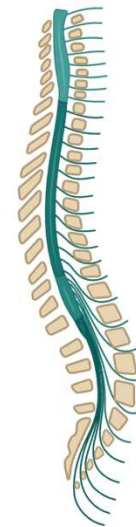
The history of MS



The “progressive” phase: *Commonly motor- and leg-predominant*



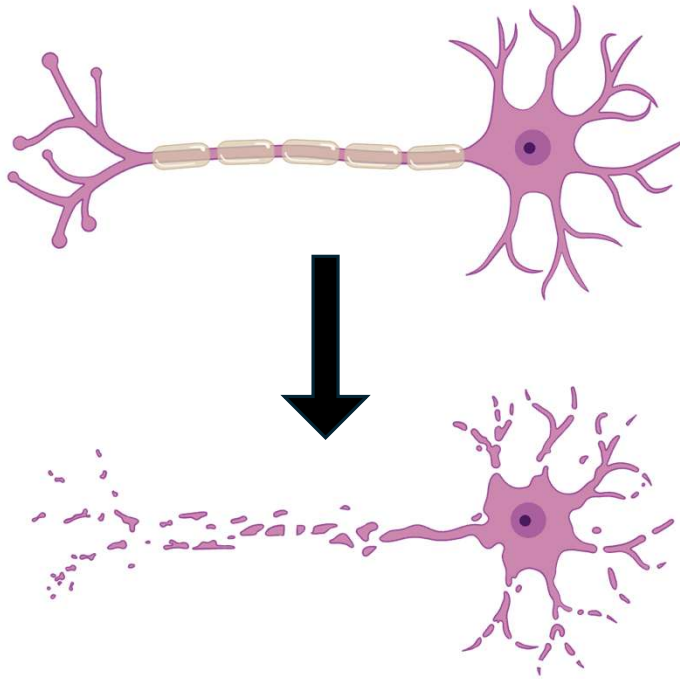
Motor symptoms
predominate



This is why we always ask walking
distance in clinic!

The “progressive” phase:

... many unknowns & possible causes, amongst which:



- New plaques **×**
- Inflammation in the lining of the brain **?**
- Ongoing inflammation in some plaques **?**
- Toxic factor in the fluid around the brain **?**

The “progressive” phase:

... many unknowns & possible causes, amongst which:

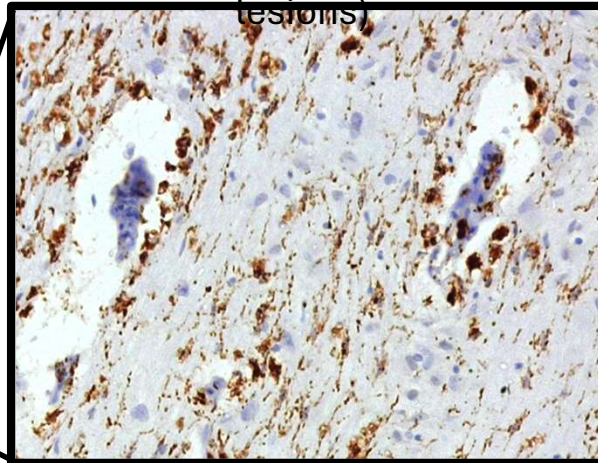
Plaque formation

(presence of MS lesions)



Inflammation

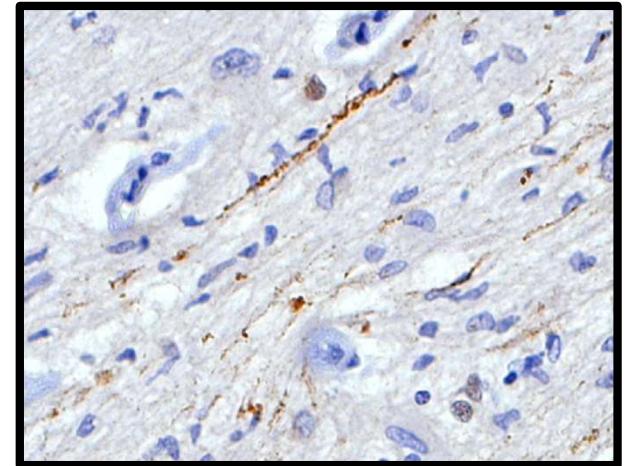
(both in and outside the lesions)



Inflammation is severe both in and outside the plaques

Axonal injury

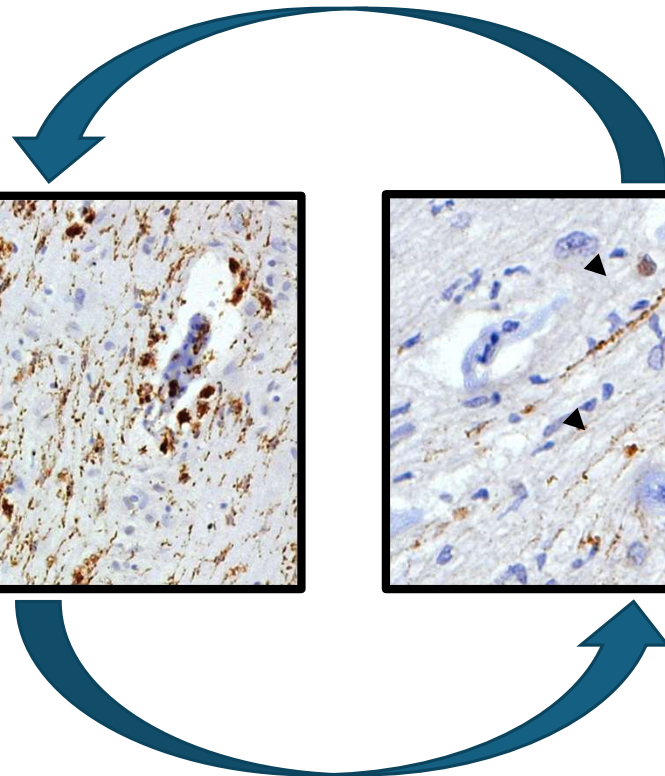
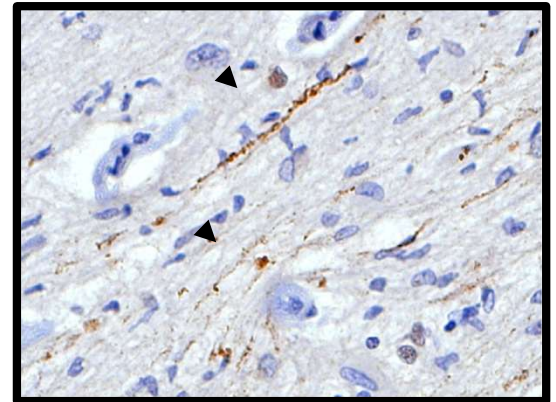
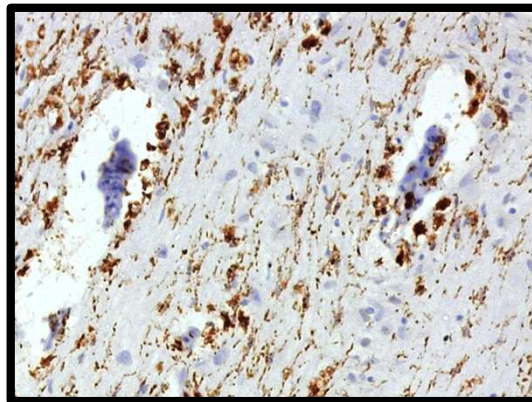
(damaged nerve fibres)



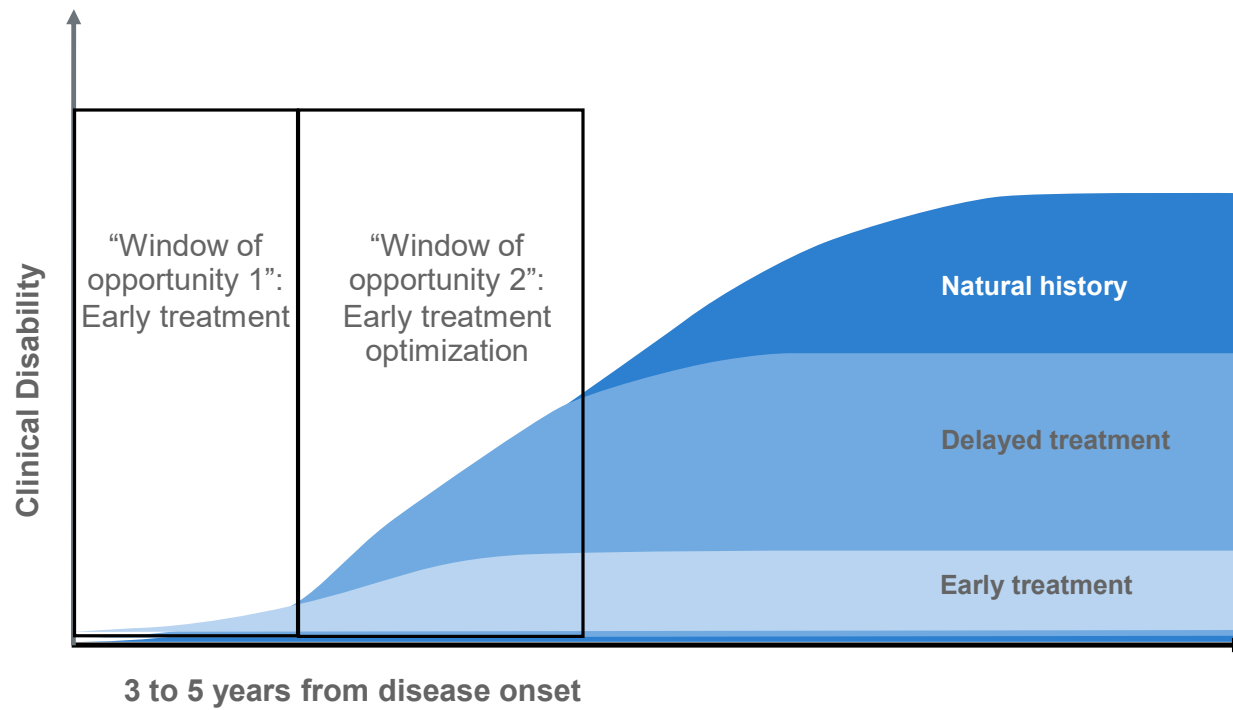
Damaged nerves are common in and outside the plaques

The “progressive” phase:

... many unknowns & possible causes, amongst which:



Can we stop MS?



Disease-modifying therapy



+ ofatumumab (Kesimpta), diroximel fumarate (Vumerity), ponesimod (Ponvory), siponimod.....

Disease-modifying therapy - updates

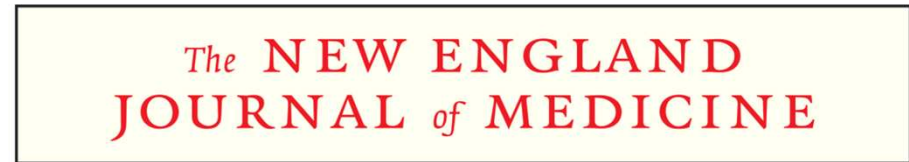
Bruton's tyrosine kinase (BTK) inhibitors

Tolebrutinib is a new drug treatment under investigation for secondary progressive and primary progressive multiple sclerosis (MS). It is taken as a tablet once daily.

Tolebrutinib for secondary progressive MS: [Licensing](#)



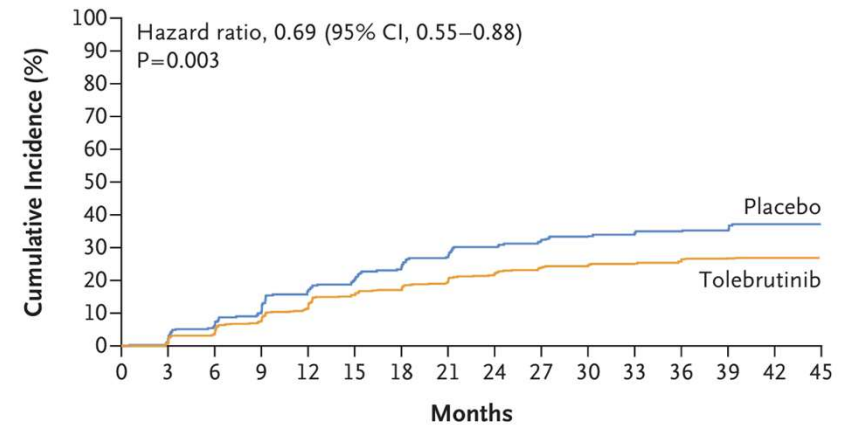
Tolebrutinib for primary progressive MS: [Phase III](#)



ESTABLISHED IN 1812 MAY 15/22, 2025 VOL. 392 NO. 19

Tolebrutinib in Nonrelapsing Secondary Progressive Multiple Sclerosis

A Confirmed Disability Progression Sustained for ≥6 Months



No. at Risk

Placebo	377	367	341	311	280	261	246	218	201	181	156	129	84	59	22	4
Tolebrutinib	754	726	696	646	604	561	535	486	455	418	349	278	203	141	67	16

(Fox, 2025)

How early and aggressively should we treat MS?

EARLIER DIAGNOSIS

Review > *Lancet Neurol.* 2025 Oct;24(10):850-865. doi: 10.1016/S1474-4422(25)00270-4.

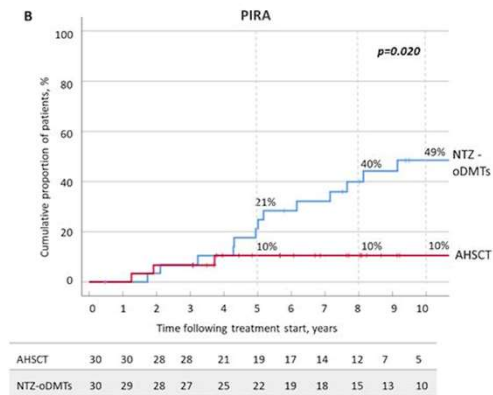
Diagnosis of multiple sclerosis: 2024 revisions of the McDonald criteria

- Recent revision of the diagnostic criteria for MS allows earlier diagnosis, even in patients who have not even developed symptoms!

Montalban et al, *Lancet Neurol* 2025

MORE AGGRESSIVE INDUCTION THERAPY

- Stem cell transplant (aHSCT) may be superior to other therapies in reducing neurodegeneration in MS
- StarMS trial (aHSCT vs high efficacy DMT) results awaited.



Mariottini, *JNNP* 2025; <https://www.isrctn.com/ISRCTNISRCTN88667898>

Can we prevent MS?

DETECTING PEOPLE AT RISK OF MS

Early treatment is effective in preventing disability in MS. Are there screening tests for people at risk of developing MS?

nature medicine

Article

<https://doi.org/10.1038/s41591-024-02938-3>

An autoantibody signature predictive for multiple sclerosis

Zamecnik et al, *Nat Med* 2024

A VACCINE FOR MS

REPORT

MULTIPLE SCLEROSIS

Longitudinal analysis reveals high prevalence of Epstein-Barr virus associated with multiple sclerosis

- 10 million young adults on active duty in US military, 955 developed MS
- MS only occurs after EBV exposure
- EBV is necessary to develop, but not sufficient (95% of the population is positive for it!)

Bjornevik et al, *Science* 2022

Several EBV vaccine candidates are in early-stage clinical trials

Is recovery possible? The failure of remyelination trials

Remyelination therapies have shown negative results in clinical trials, despite promising preclinical evidence:

- Disability in MS is driven mainly by loss of nerve fibres, not demyelination
- Remyelinated plaques remain vulnerable to new inflammation → success requires controlling inflammation

Agent	Trial Name	Outcome
Clemastine fumarate	ReBUILD (NCT02040298)	Positive – improved VEP latency (by 1.7msec)
Opicinumab (anti-LINGO-1)	RENEW / SYNERGY / AFFINITY	Negative – no consistent clinical benefit
Bexarotene (RXR agonist)	CCMR-One	Positive (biological signal) but limited by toxicity
High-dose biotin (MD1003)	MS-SPI / SPI2	Negative – no confirmed benefit in progressive MS
Simvastatin (cholesterol-lowering agent)	MS-STAT / MS-STAT2	Negative – no slowing of disability; ↑ lesion activity
Neural stem cell transplantation	STEMS (NCT03269071) & related phase I	Ongoing – early safety signals only
Clemastine + metformin	COMBAT-MS / other investigator-led	Ongoing – combination remyelination strategy

Important things patients CAN do:

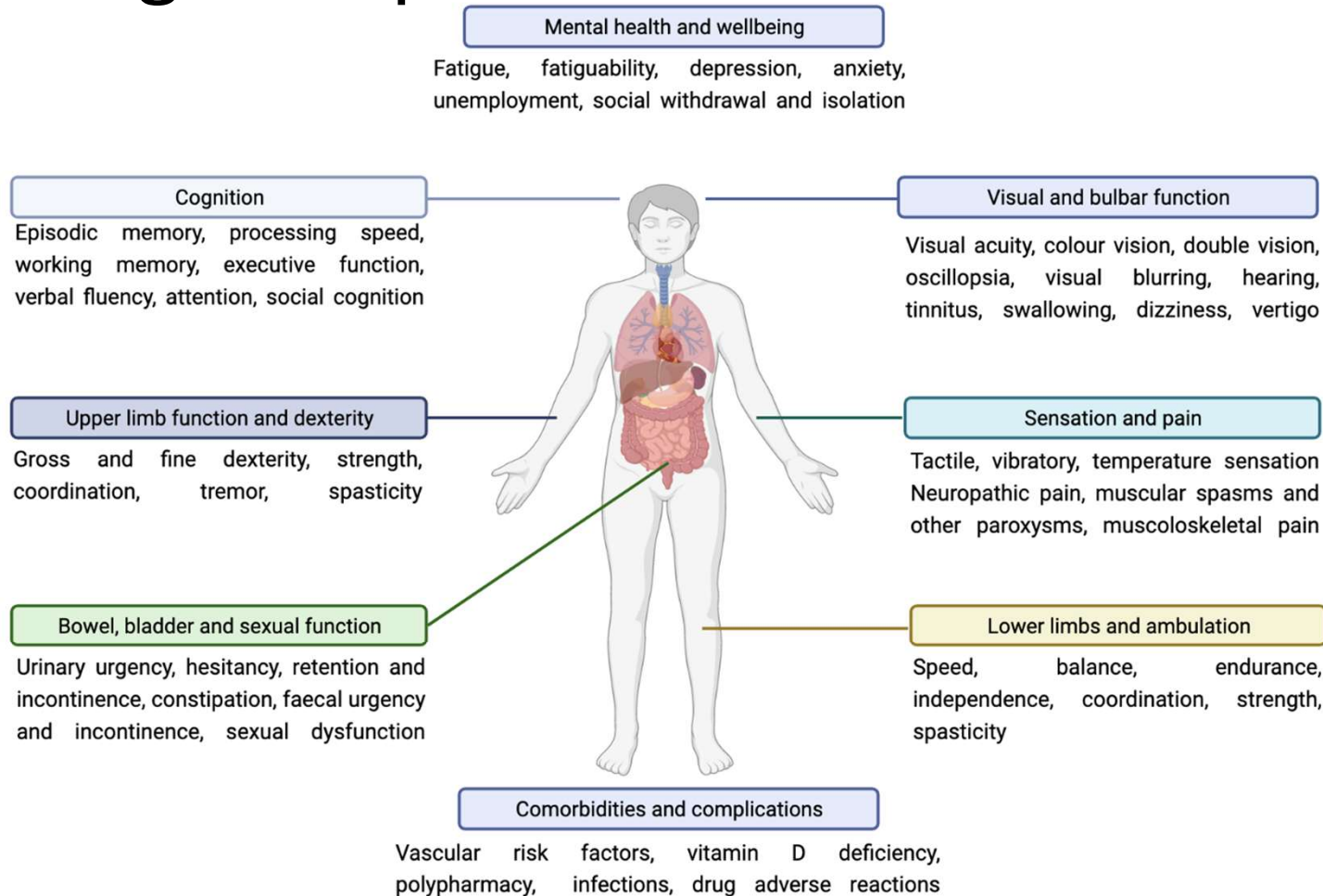
- Healthy (Mediterranean) diet
- Exercise, particularly cardio exercise
- Vitamin D 4,000 IU
- Controlling 'vascular risk factors':
 - STOP SMOKING
 - Blood pressure
 - Blood sugar
 - Cholesterol



Important things patients CAN do:

- Take treatment regularly (or let us know if you wish to stop it)
- Attend your bloods and MRI
- Let us know if you have new symptoms

Am I having a relapse?



Am I having a relapse?

If the person develops new symptoms or their existing symptoms get worse and last for more than 24 hours in the absence of infection or any other cause after a stable period of at least 1 month.

Assess and offer treatment for relapses of MS that affect the person's ability to perform their usual tasks, as early as possible and within 14 days of onset of symptoms. **[2014]**

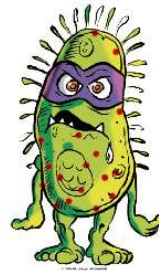
Offer treatment for relapse of MS with oral methylprednisolone 0.5 g daily for 5 days. **[2014]**

Multiple sclerosis in adults: management

NICE guideline [NG220] Published: 22 June 2022

Or a pseudo-relapse?

- Weather
- Infection
- Emotional stress
- Physical stress
- Fatigue



Who patients need to tell.....

- DVLA
- Insurers

Who patients might want to tell.....

- Employer (occupational health)