

Progression - what to do ?

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Acronyms used in this talk:

RRMS = Relapsing Remitting MS

SPMS = Secondary Progressive MS

PPMS = Primary Progressive MS

CIS= Clinically Isolated Syndrome

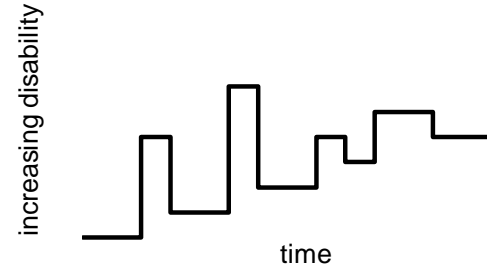
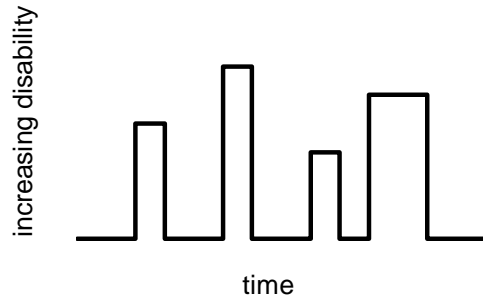
GD = gadolinium enhancing lesions

T2 lesions = T2 lesions on MRI scans

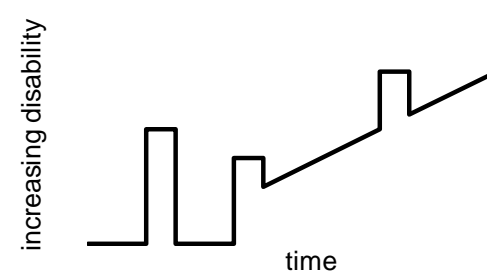
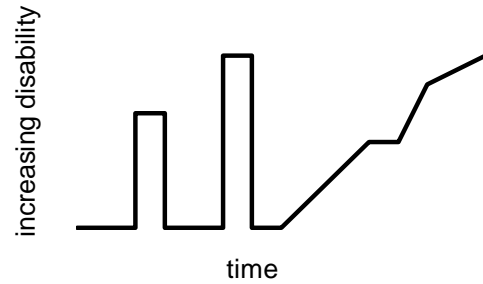
SAD = Sustained accumulation of disability

Clinical courses of MS

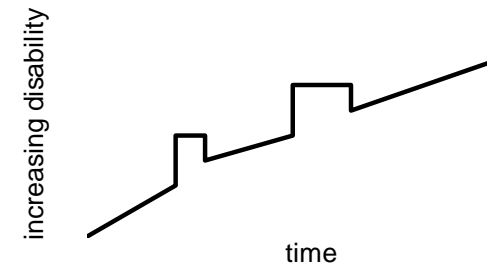
RRMS

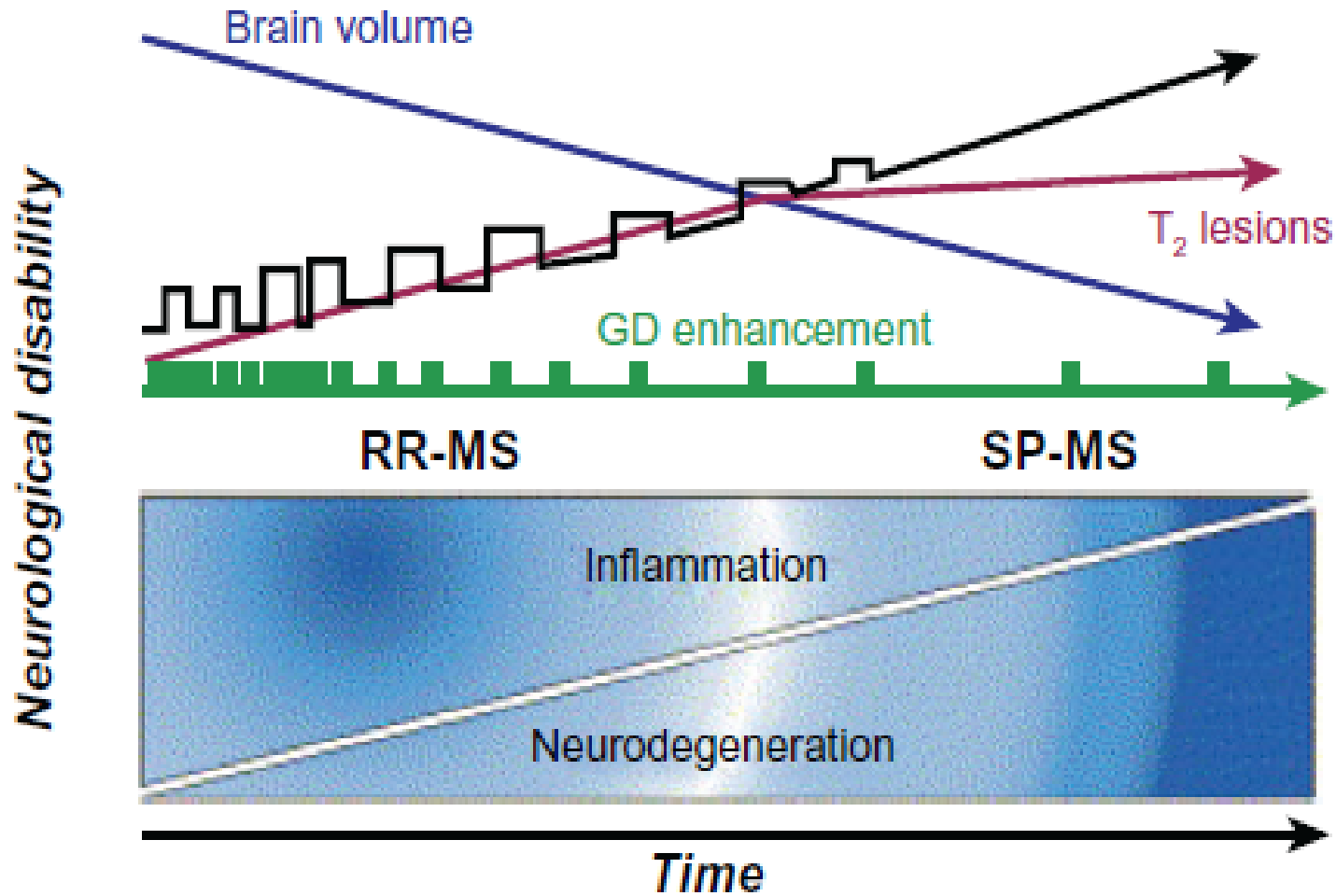


SPMS

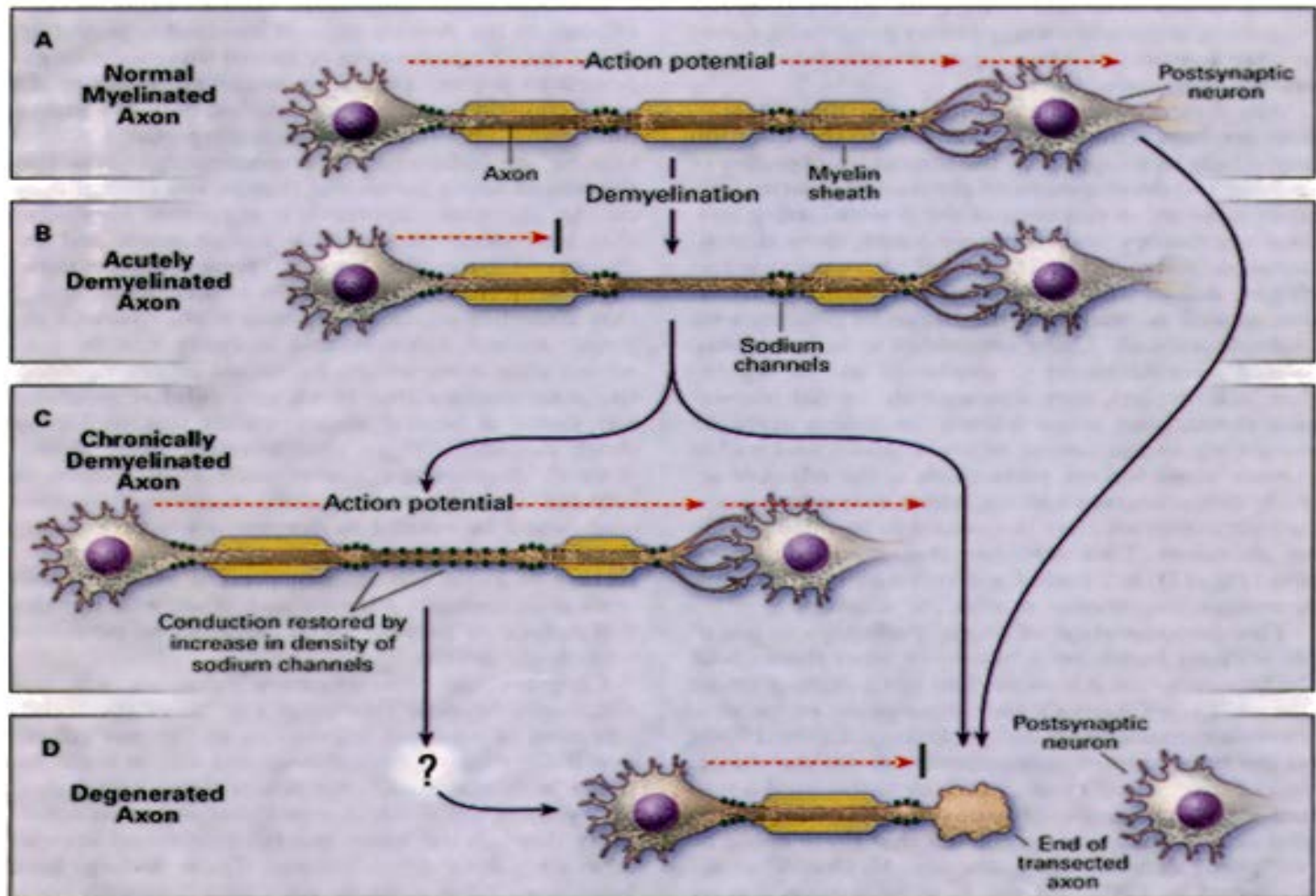


PPMS





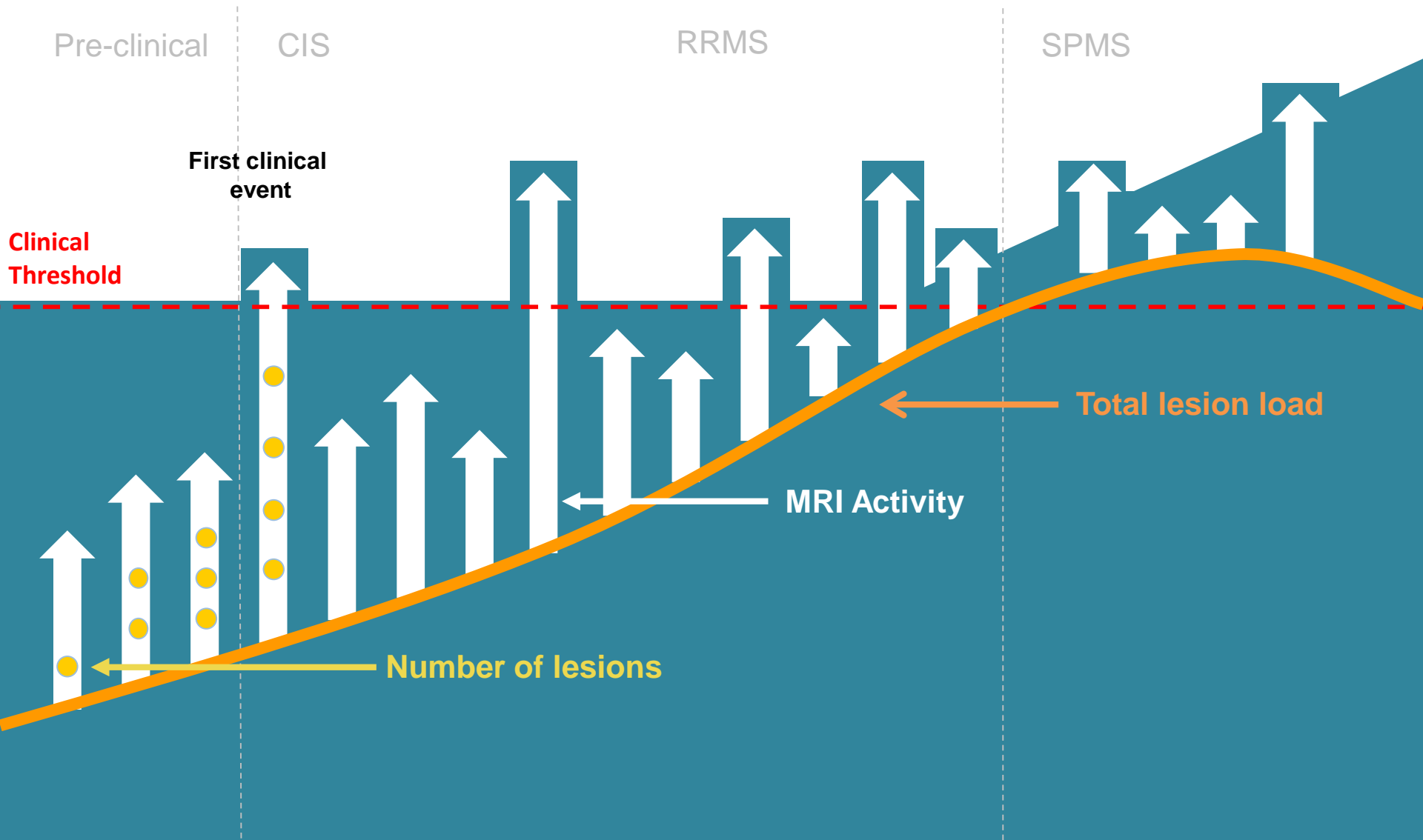
- RRMS: relapsing remitting multiple sclerosis; SPMS: secondary progressive multiple sclerosis
- Barten LJ et al Drug Des Devel Ther 2010;4:343-66



Demyelination and Axonal Degeneration in MS

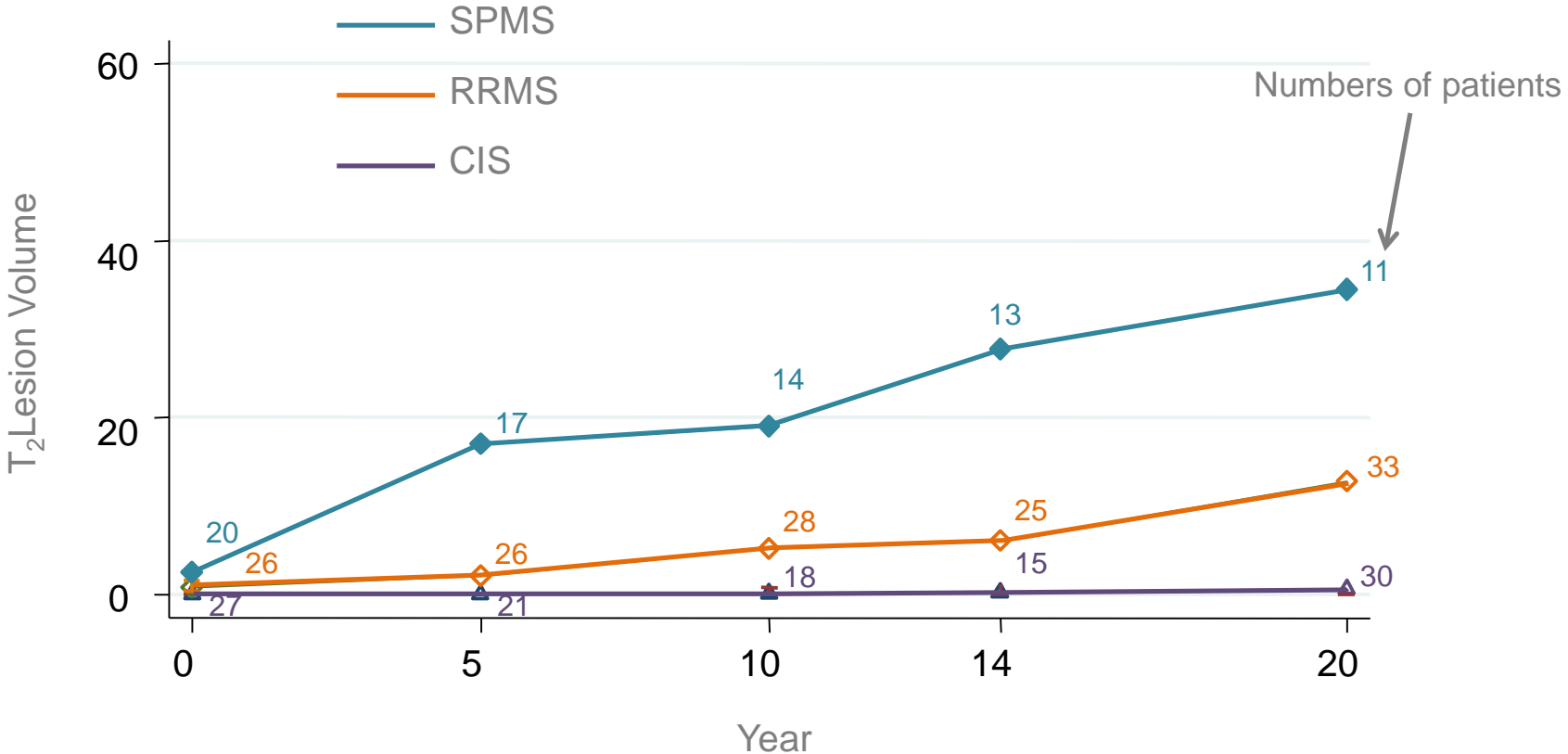
Waxman S. *NEJM* 338, 5, 323

The Evolution of MS



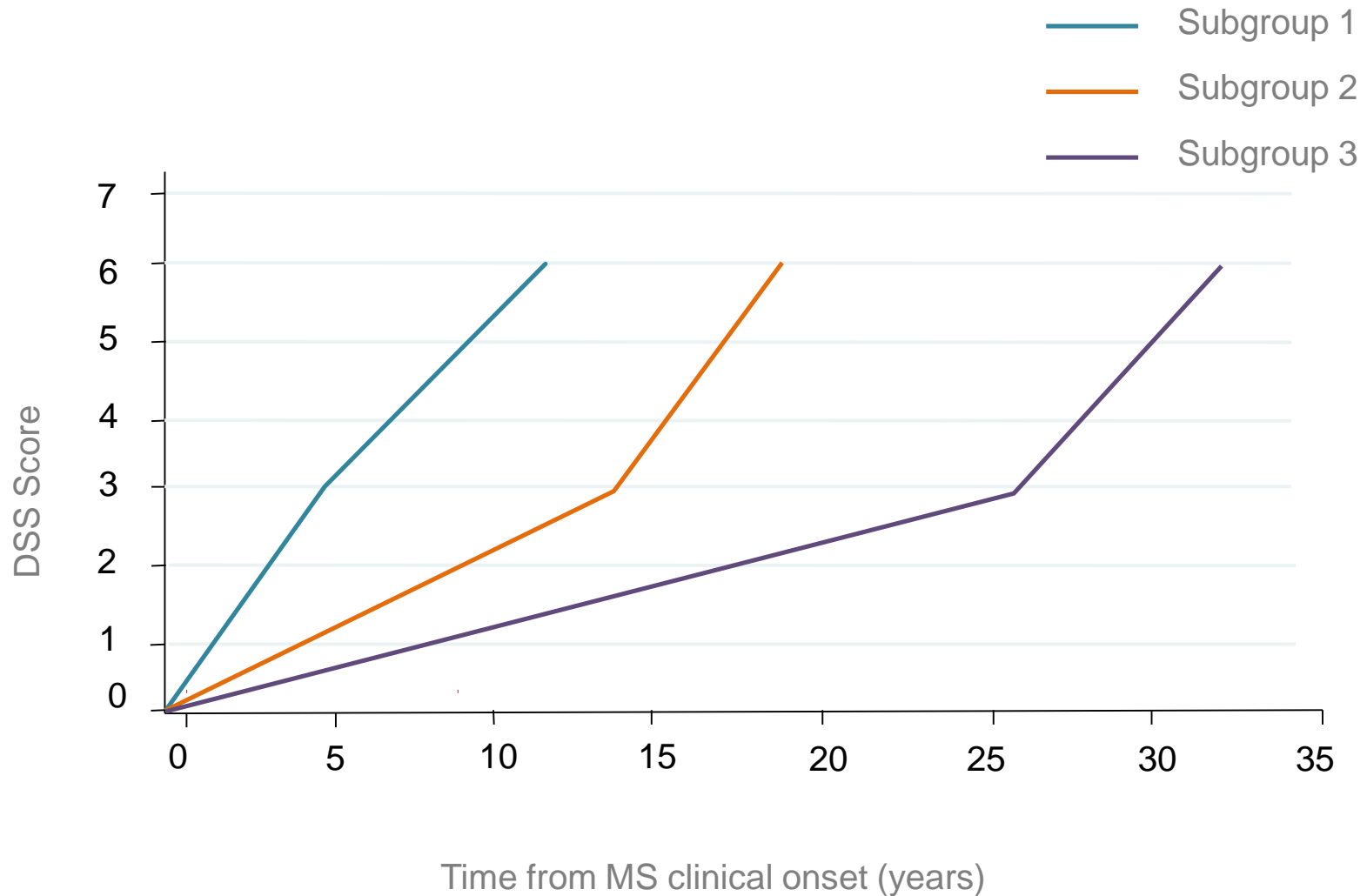
20-year follow-up Results: Serial median T2 Lesion Load (cm³)

Median T₂ lesion volume (cm³) over time for patient groups



Estimated rate of lesion growth in SPMS = 2.89 cm³/year
Estimated rate of lesion growth in RRMS = 0.80 cm³/year (p<0.001)

Is the rate of progression the same for all patients ?





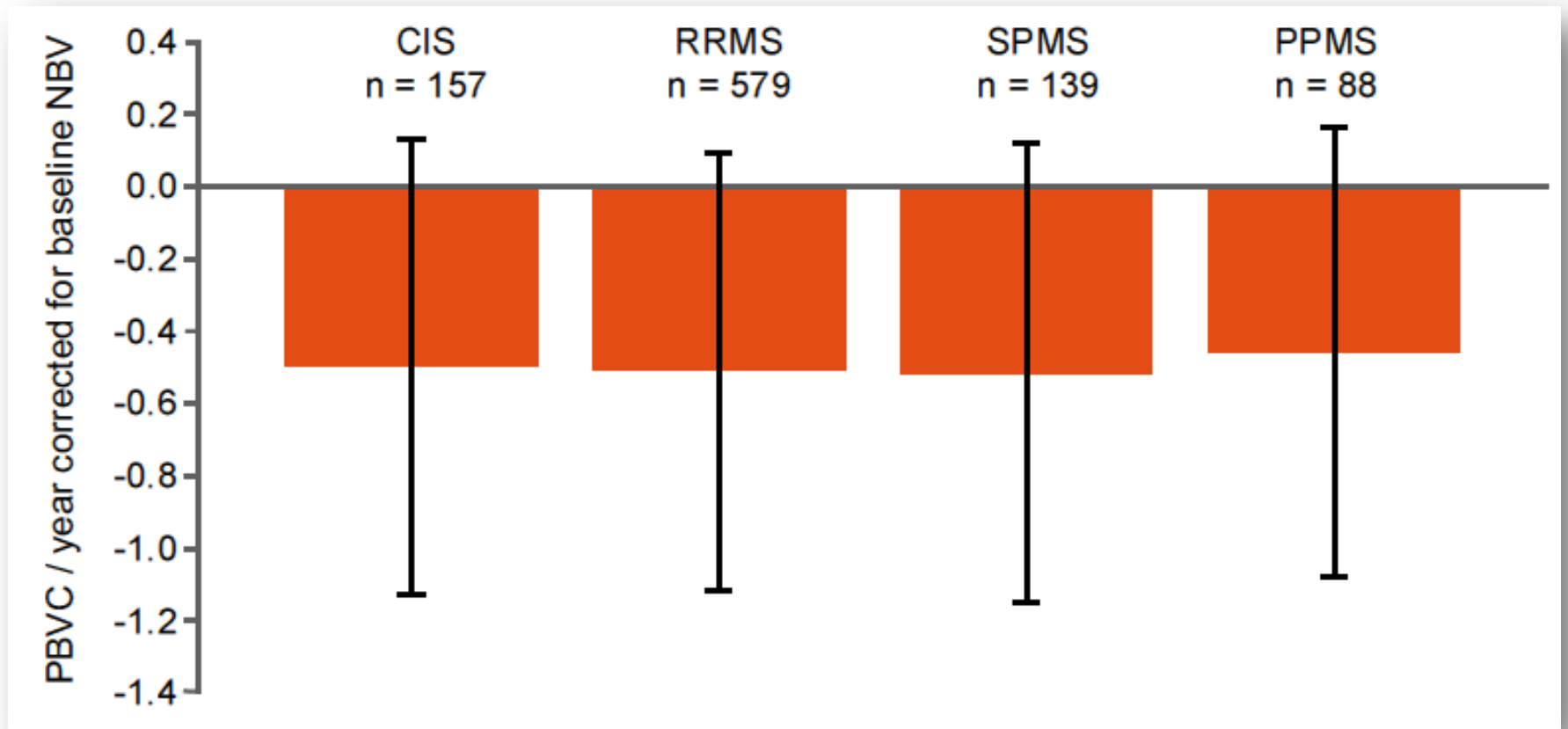
Control



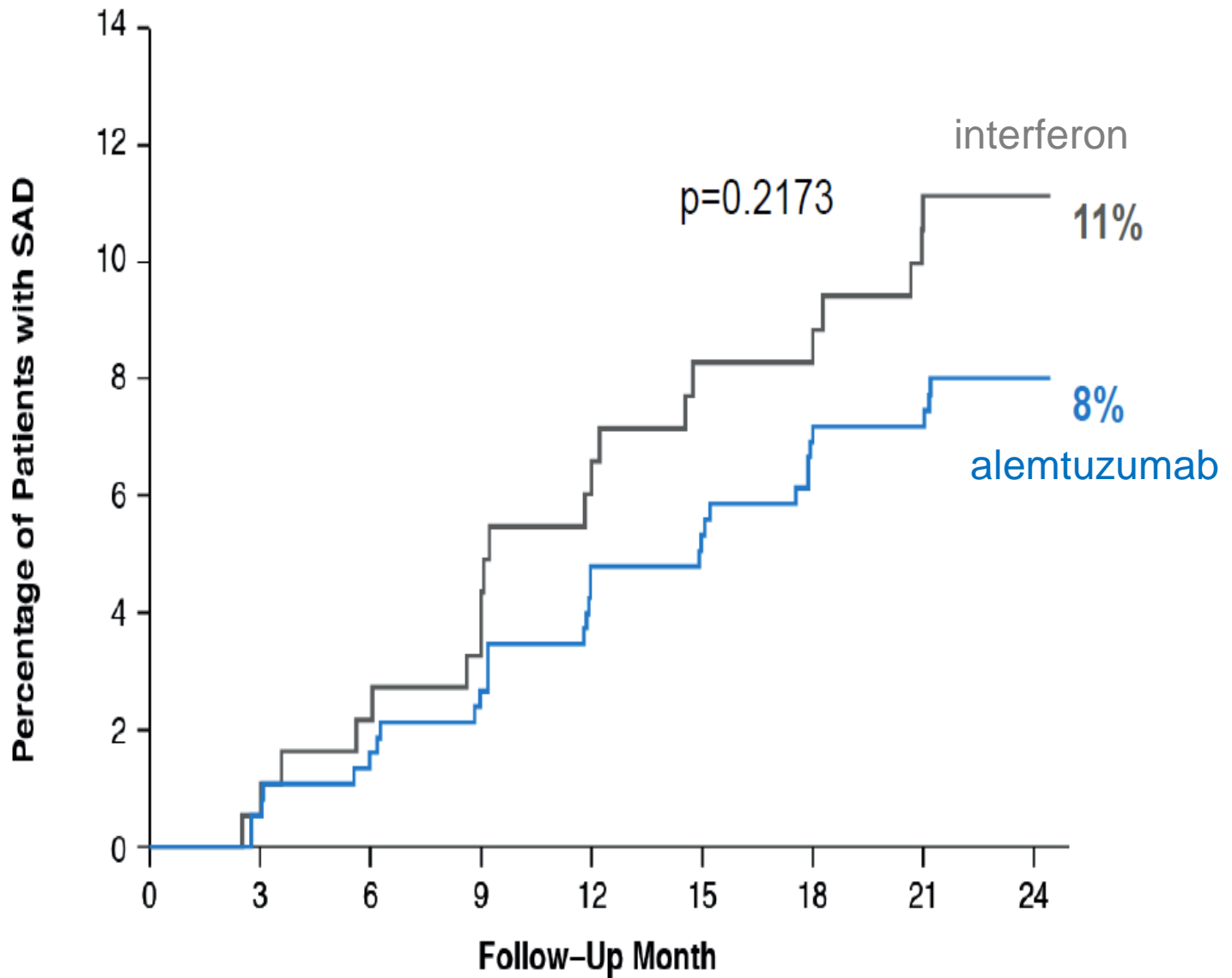
Multiple sclerosis

Brain atrophy occurs across all stages

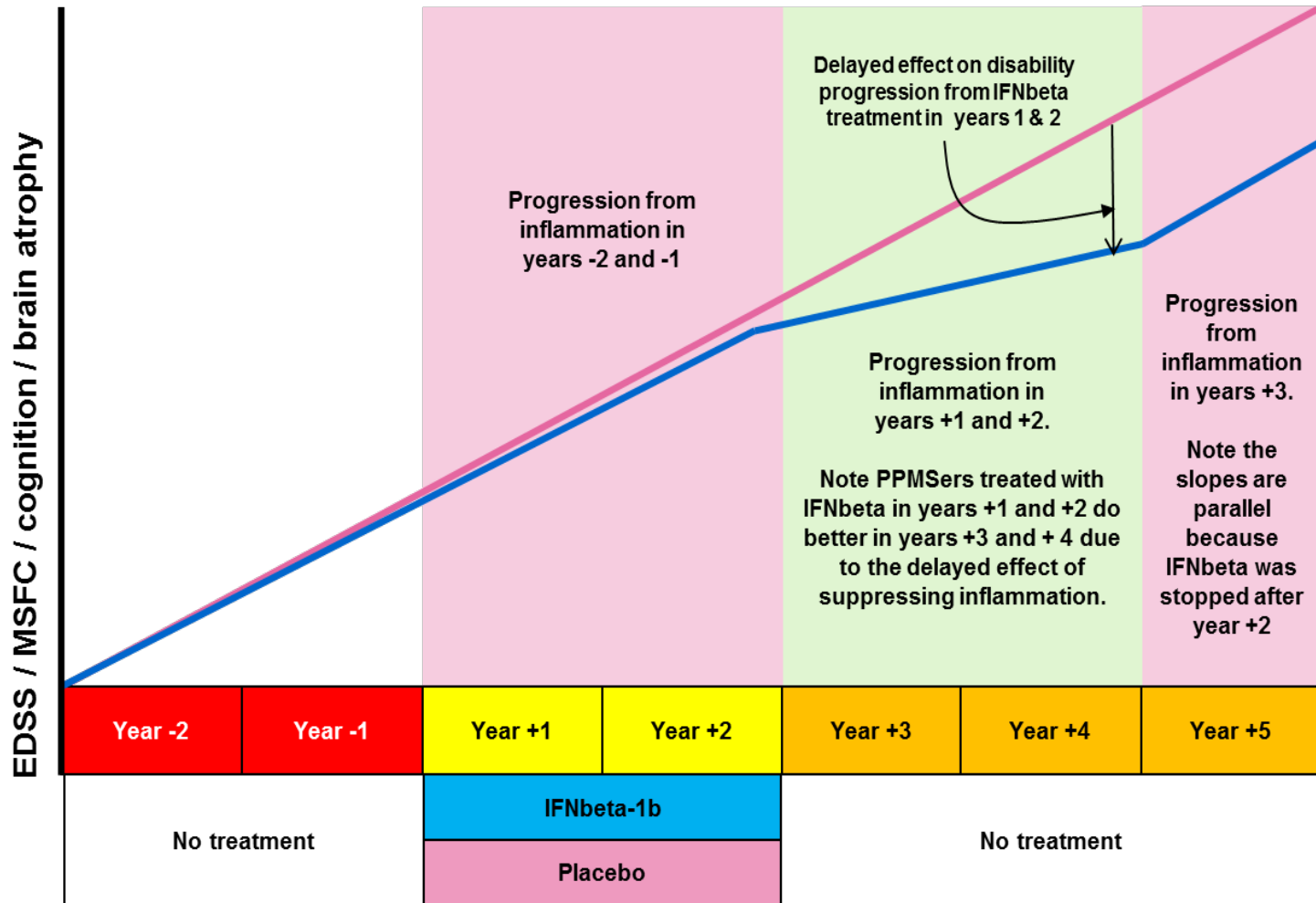
n = 963 pwMS



Time to 6-Month Sustained Accumulation of Disability (Co primary endpoint)



Therapeutic Lag



Tur et al. Interferon Beta-1b for the Treatment of Primary Progressive Multiple Sclerosis: Five-Year Clinical Trial Follow-up. Arch Neurol. 2011 Nov;68(11):1421-7.

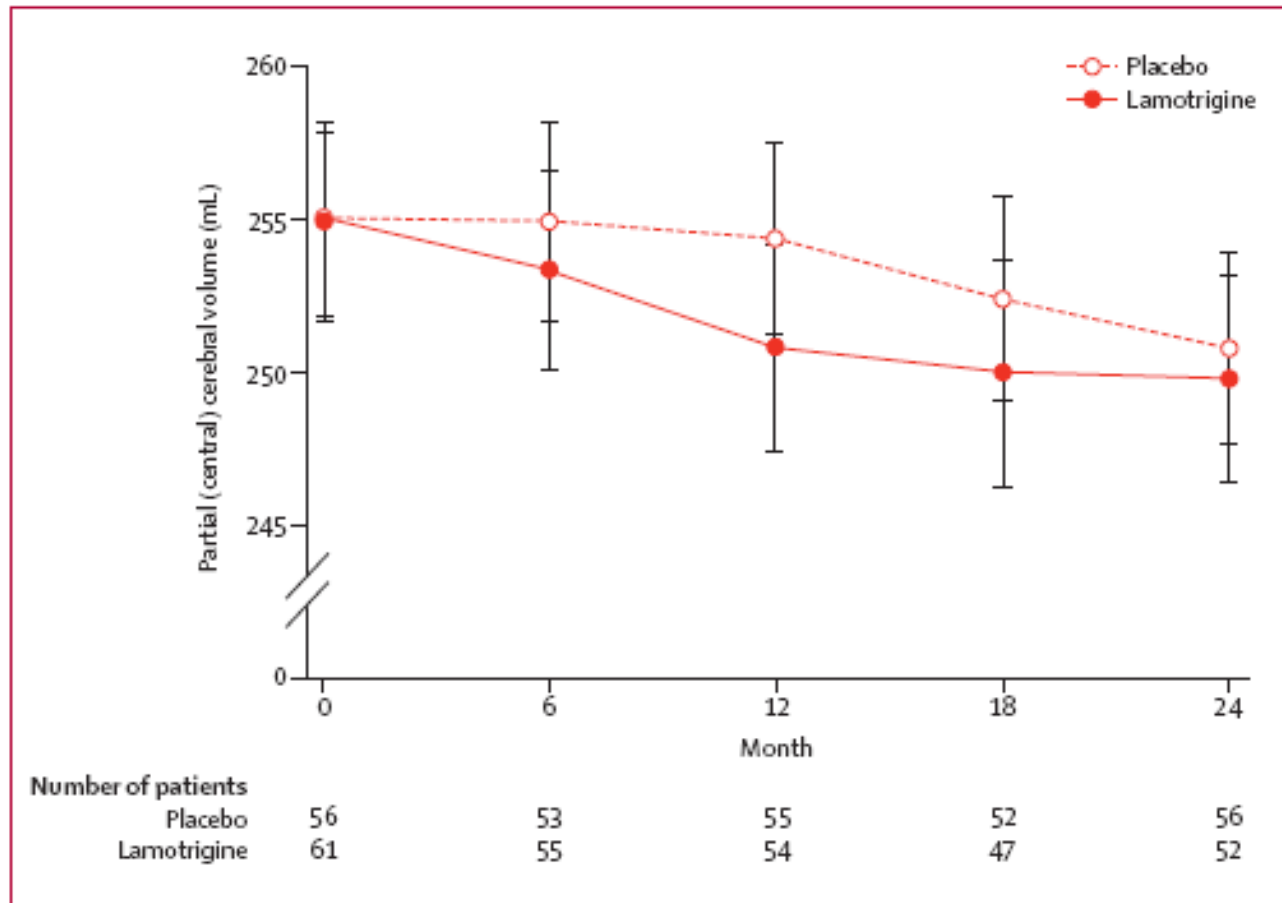
MS-STAT trial - High dose oral Simvastatin in Secondary Progressive Multiple Sclerosis in whole brain volume (%/year)

| | Mean (SD) placebo | Mean (SD) simvastatin | Difference in means (95% CI)* | p-value |
|---------------------------|------------------------------|----------------------------------|--|----------------|
| Change WBV (%/year) | 0.589 (0.528) | 0.298 (0.562) | -0.254 (-0.423 to -0.085) | 0.003 |
| Number patients evaluated | 64 | 66 | | |
| | | | | |

*Adjusting for minimisation variables and MRI site

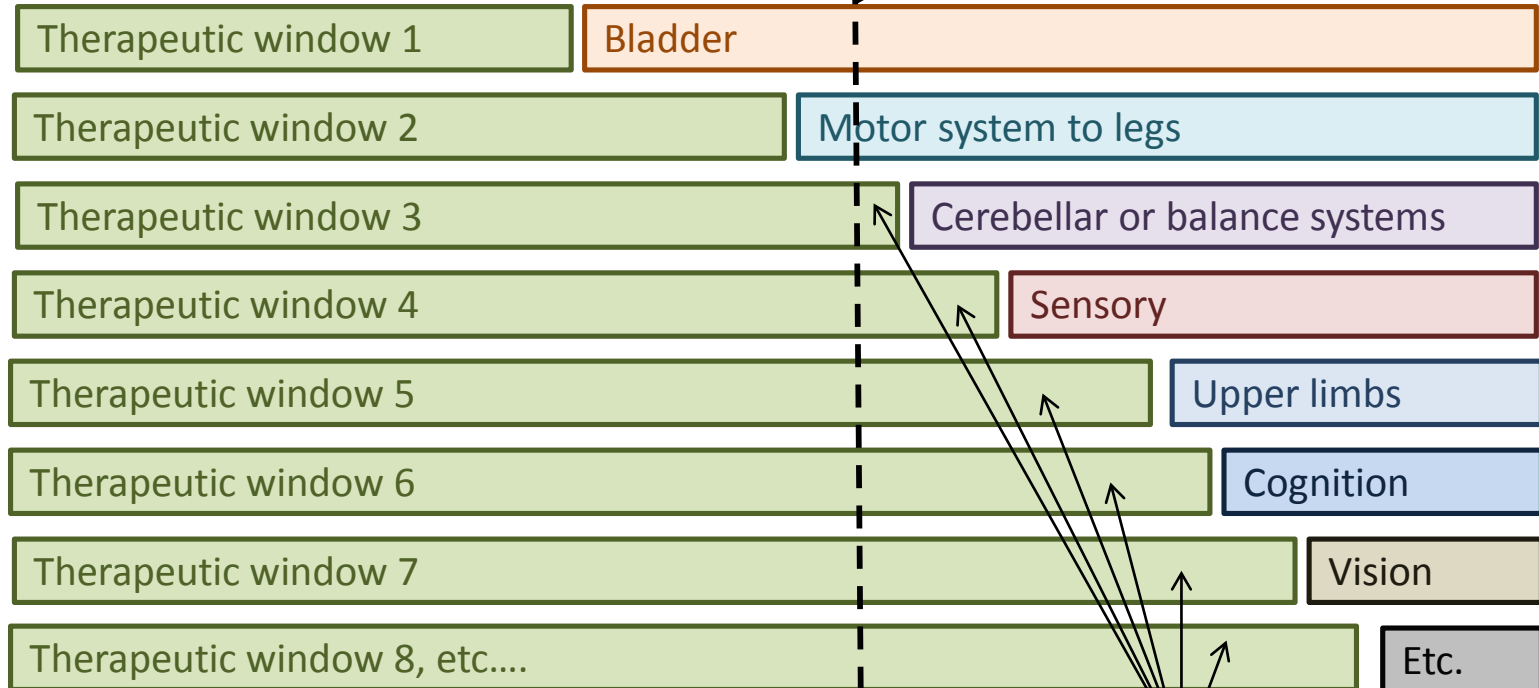
Lamotrigine for neuroprotection in secondary progressive multiple sclerosis: a randomised, double-blind, placebo-controlled, parallel-group trial

Raju Kapoor, Julian Furby, Thomas Hayton, Kenneth J Smith, Daniel R Altmann, Robert Brenner, Jeremy Chataway, Richard A C Hughes, David H Miller

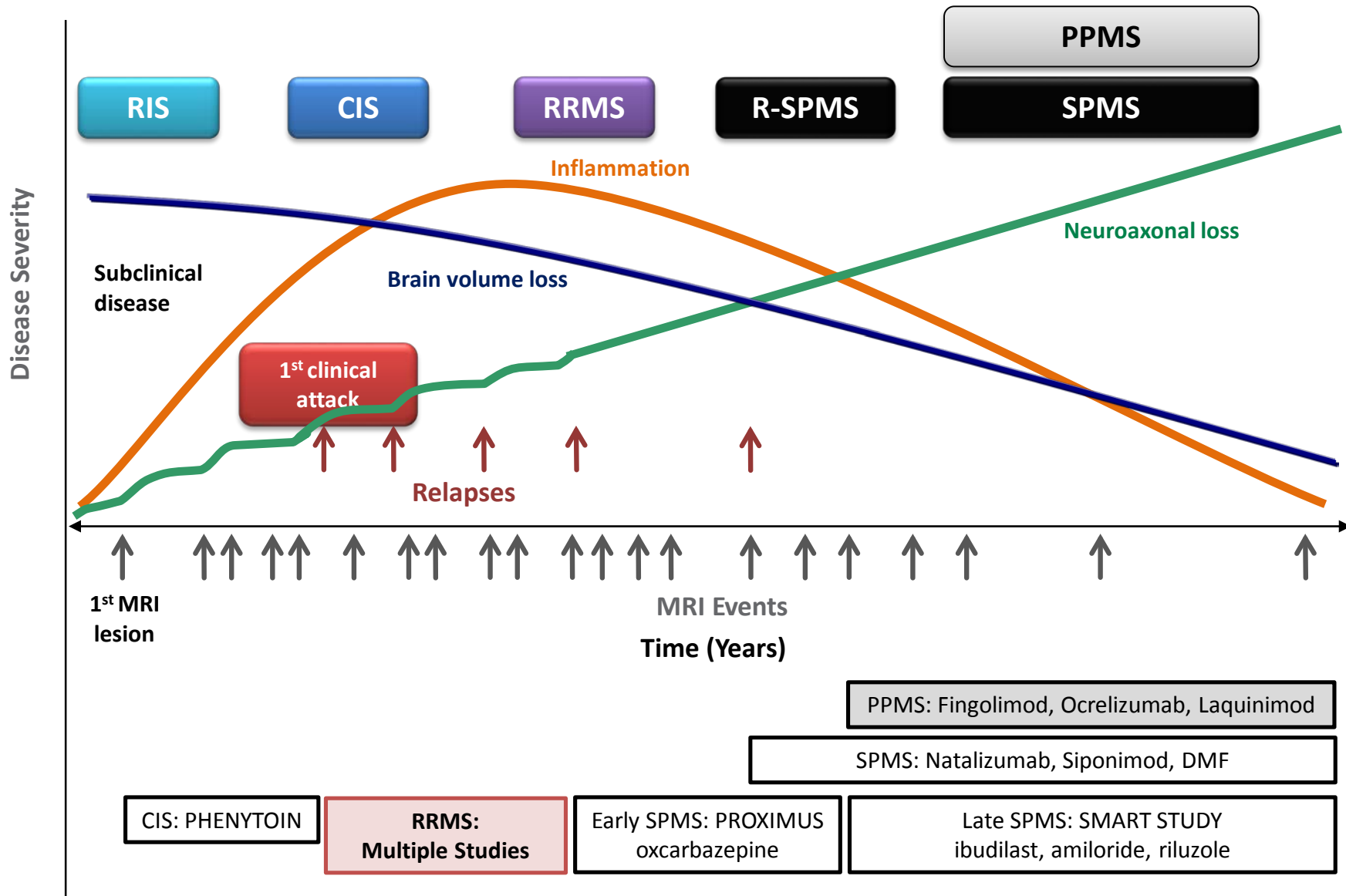


The Asynchronous Progressive MS hypothesis

Diagnosis of Progressive MS



Effective DMTs could still target the remaining windows of therapeutic opportunity for individual neurological systems



RIS = radiologically isolated syndrome; CIS = clinically isolated syndrome, RRMS = relapsing-remitting MS; R-SPMS = relapsing secondary progressive MS; SPMS = secondary progressive MS; PPMS = primary progressive MS



Thank You

Ben Turner

