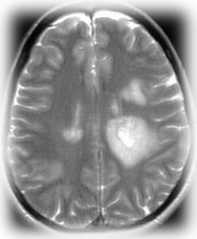
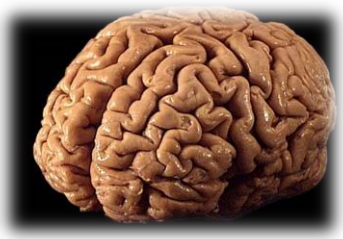
Why haven't we cured MS yet?

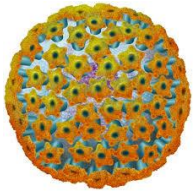
Gavin Giovannoni

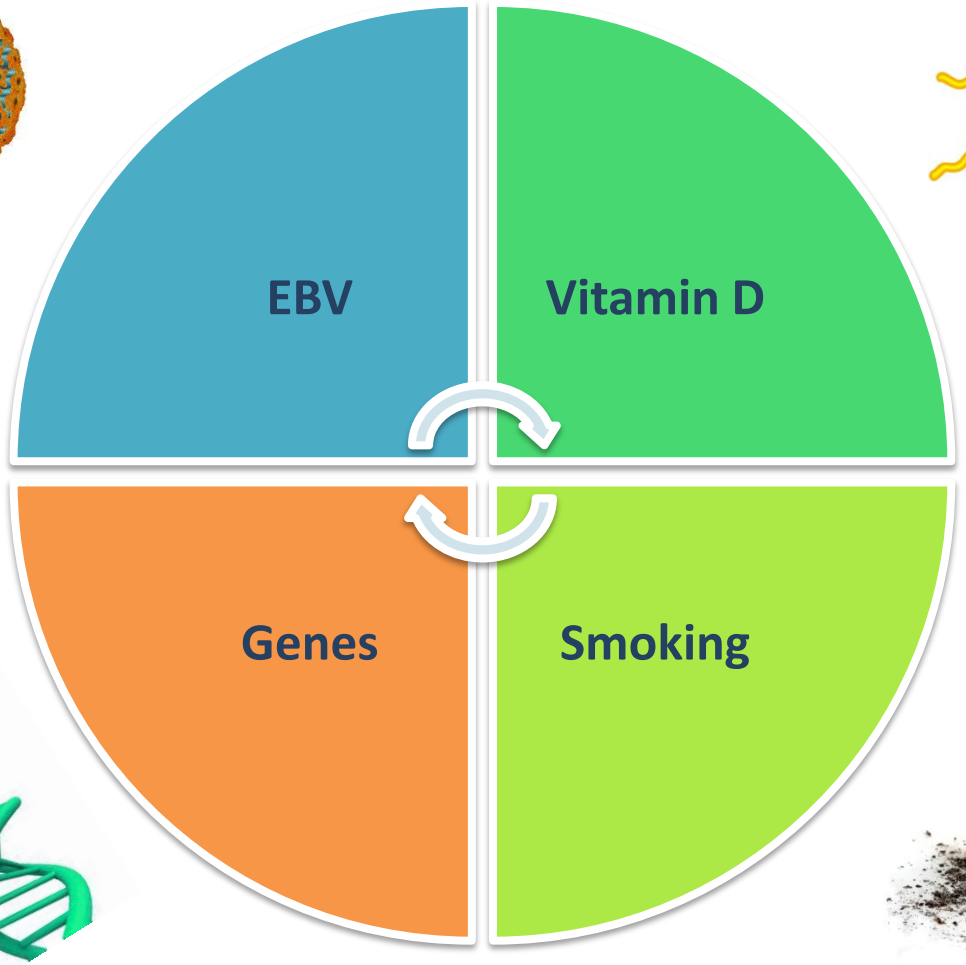
Barts and The London



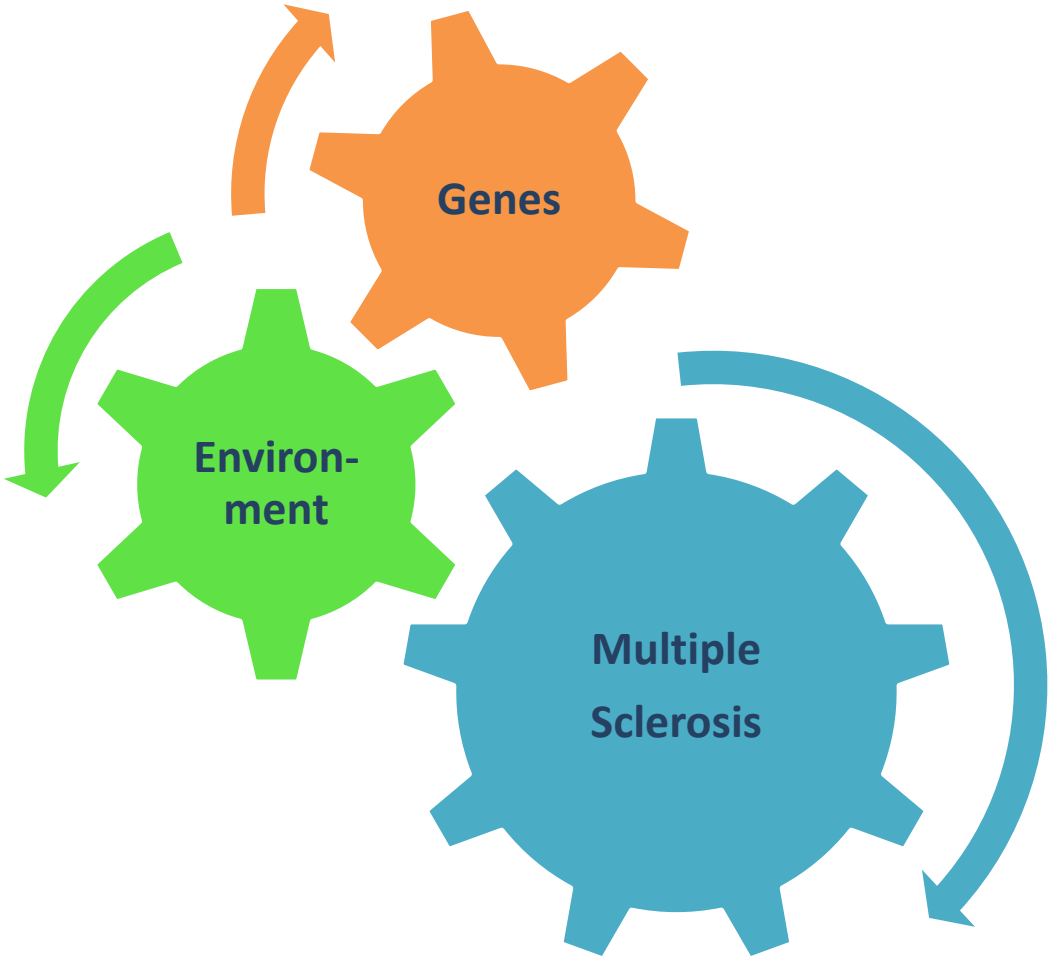


To cure MS do we need to know the cause?

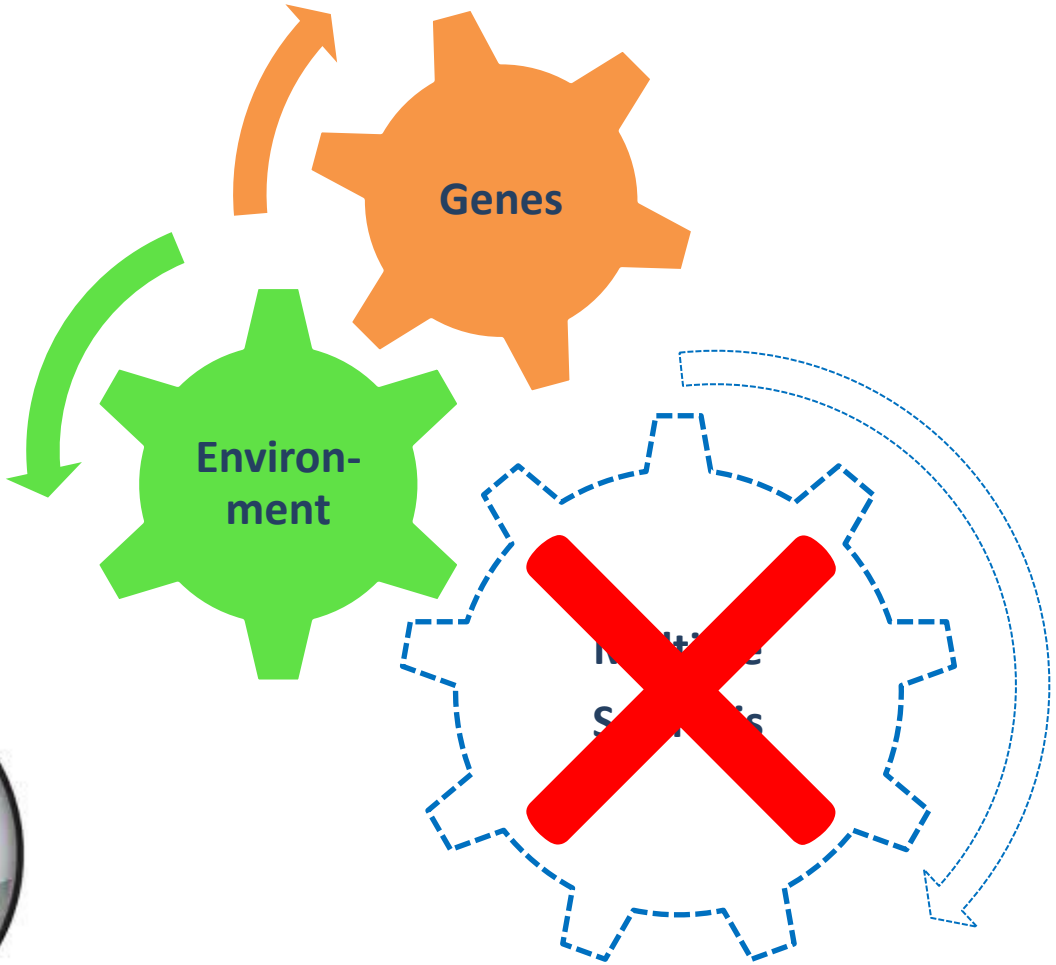




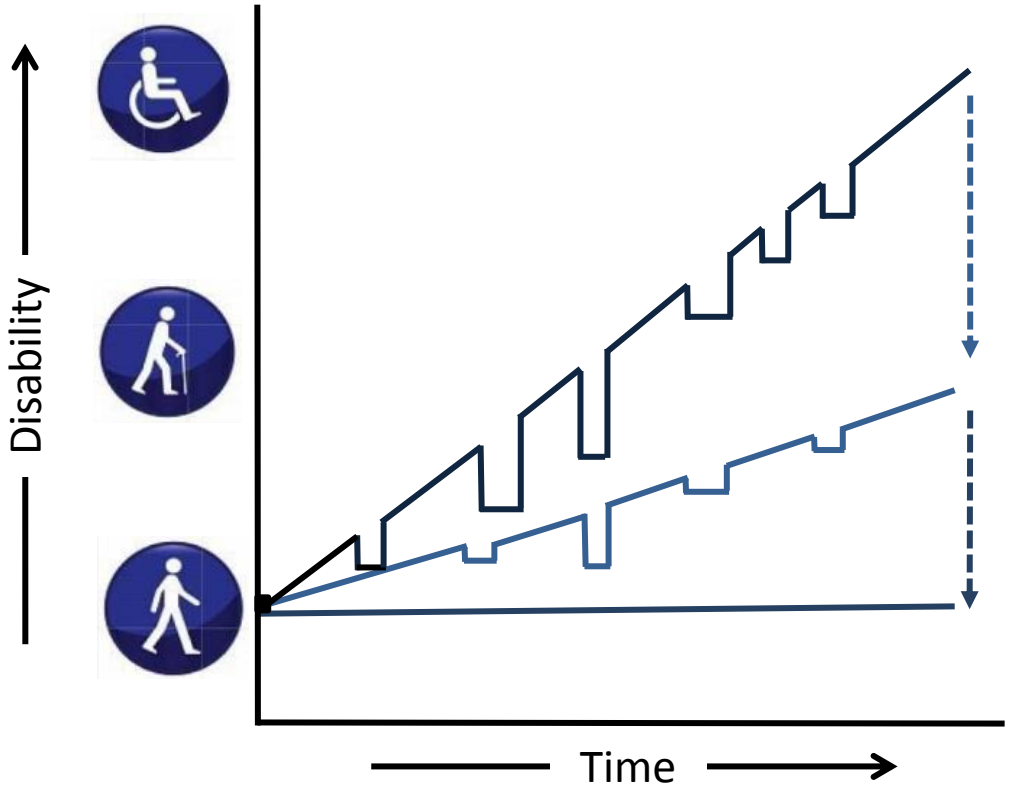
We work on the hypothesis that MS is an autoimmune disease.



The autoimmune hypothesis

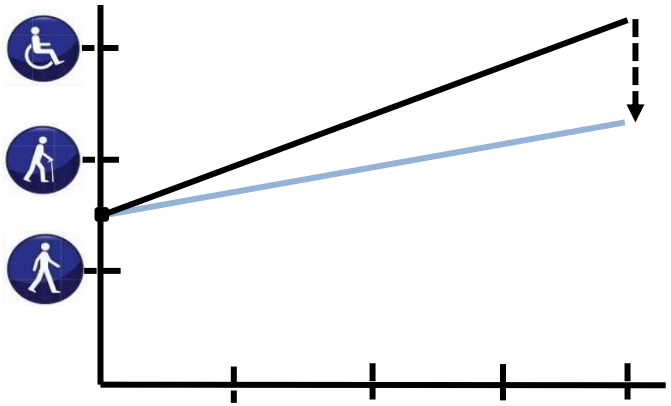


What does a cure mean?

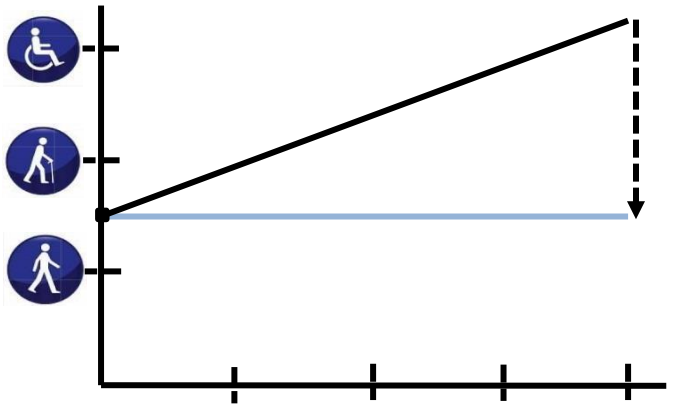


What does a cure mean?

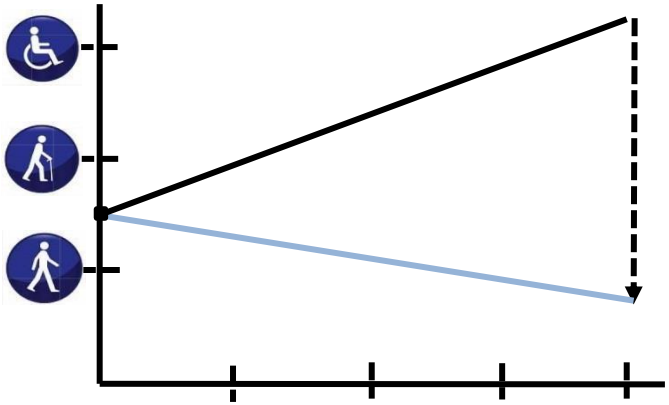
delayed worsening



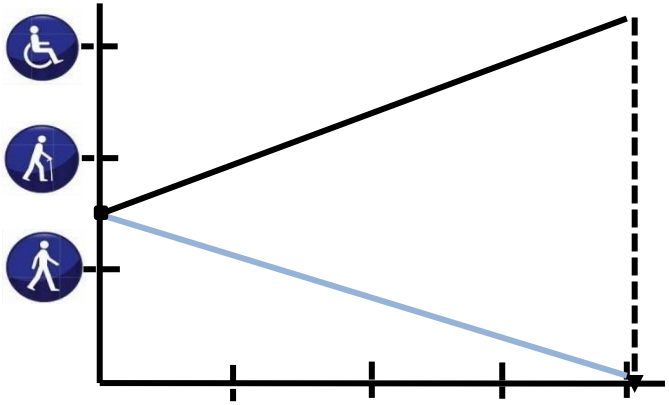
stabilised



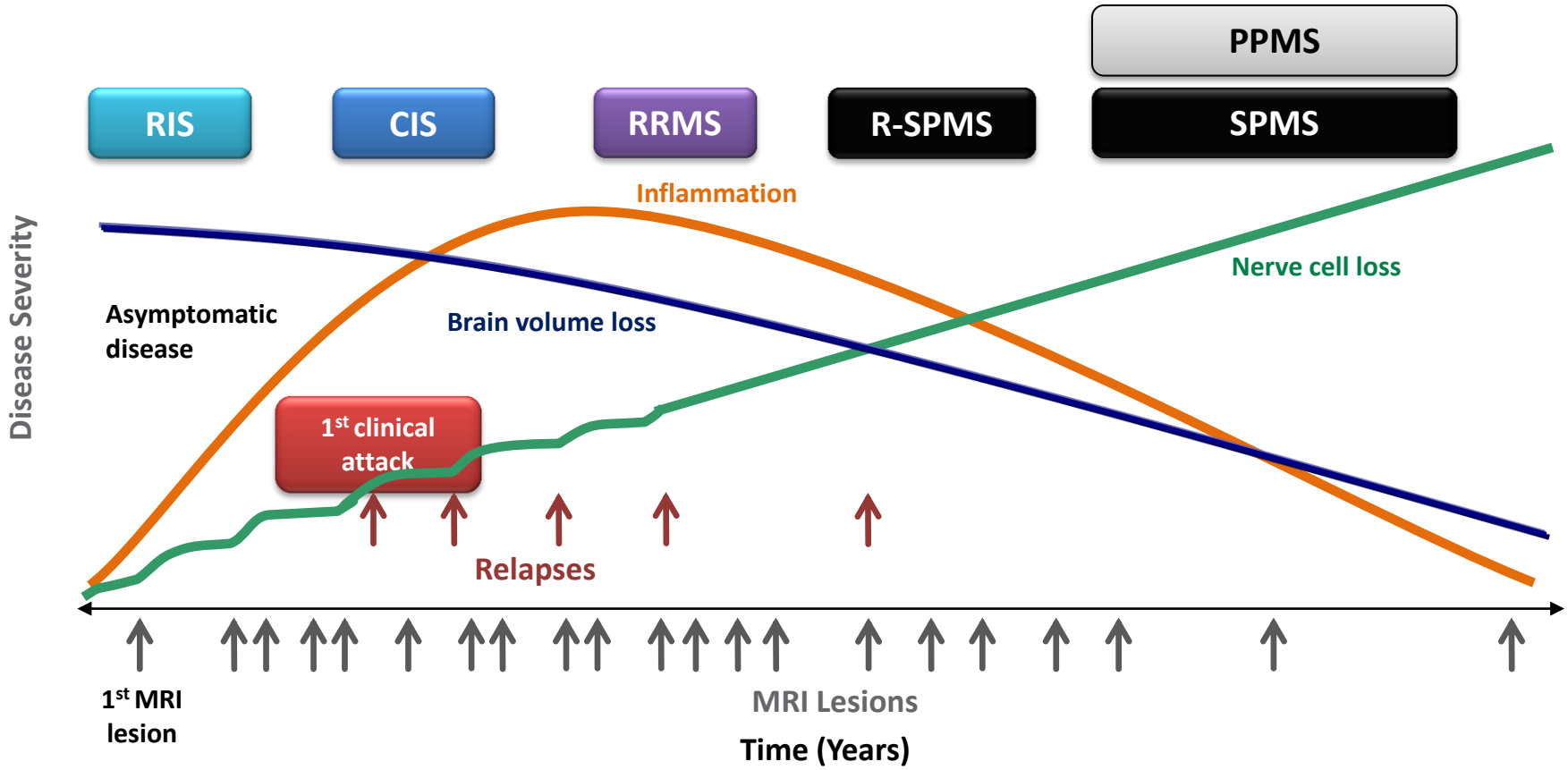
improved function



recovered function

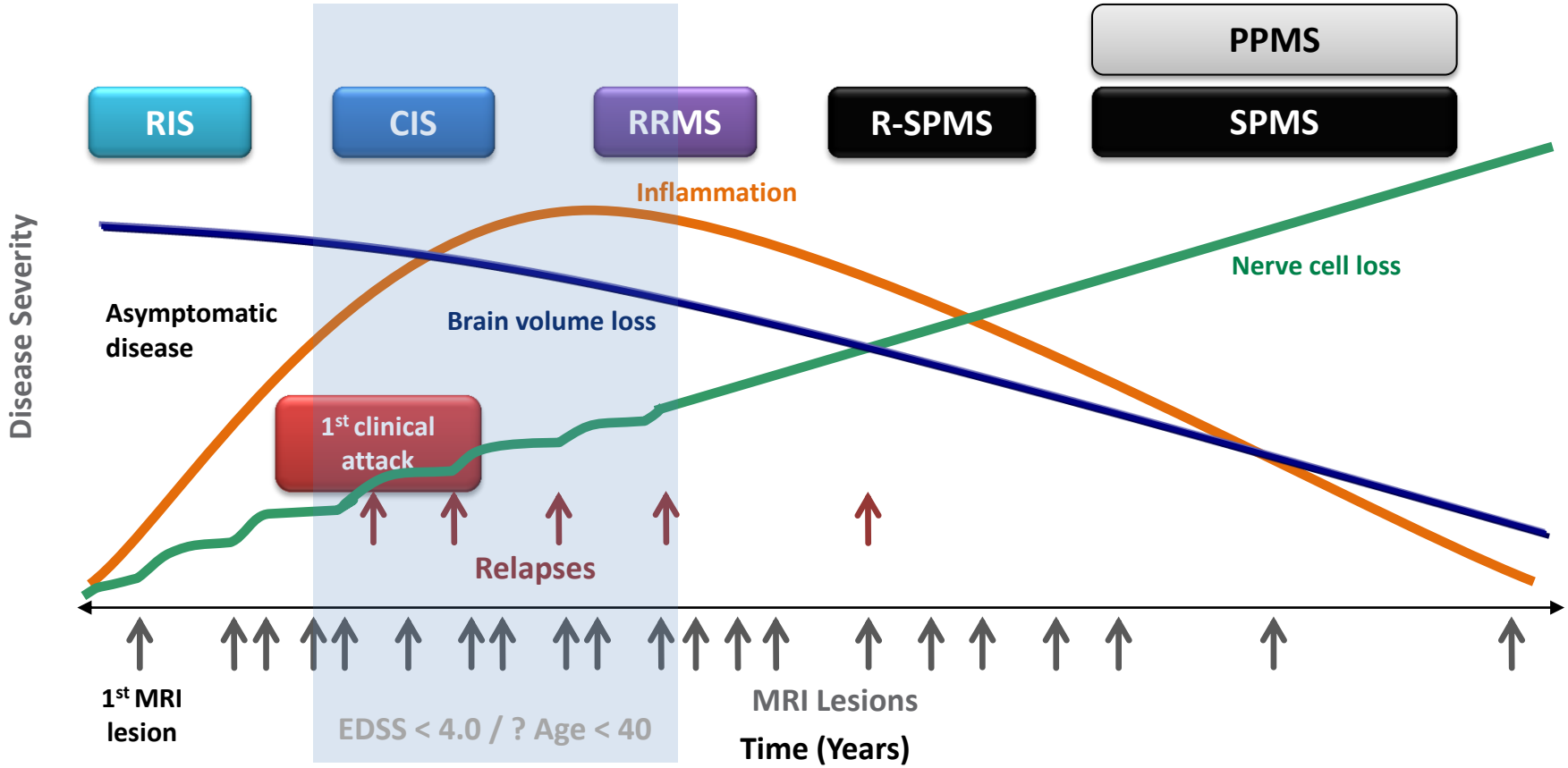


The therapeutic window for recovery



RIS = radiologically isolated syndrome (asymptomatic MS)
CIS = clinically isolated syndrome
RRMS = relapsing-remitting MS
R-SPMS = relapsing secondary progressive MS
SPMS = secondary progressive MS
PPMS = primary progressive MS

The therapeutic window for recovery



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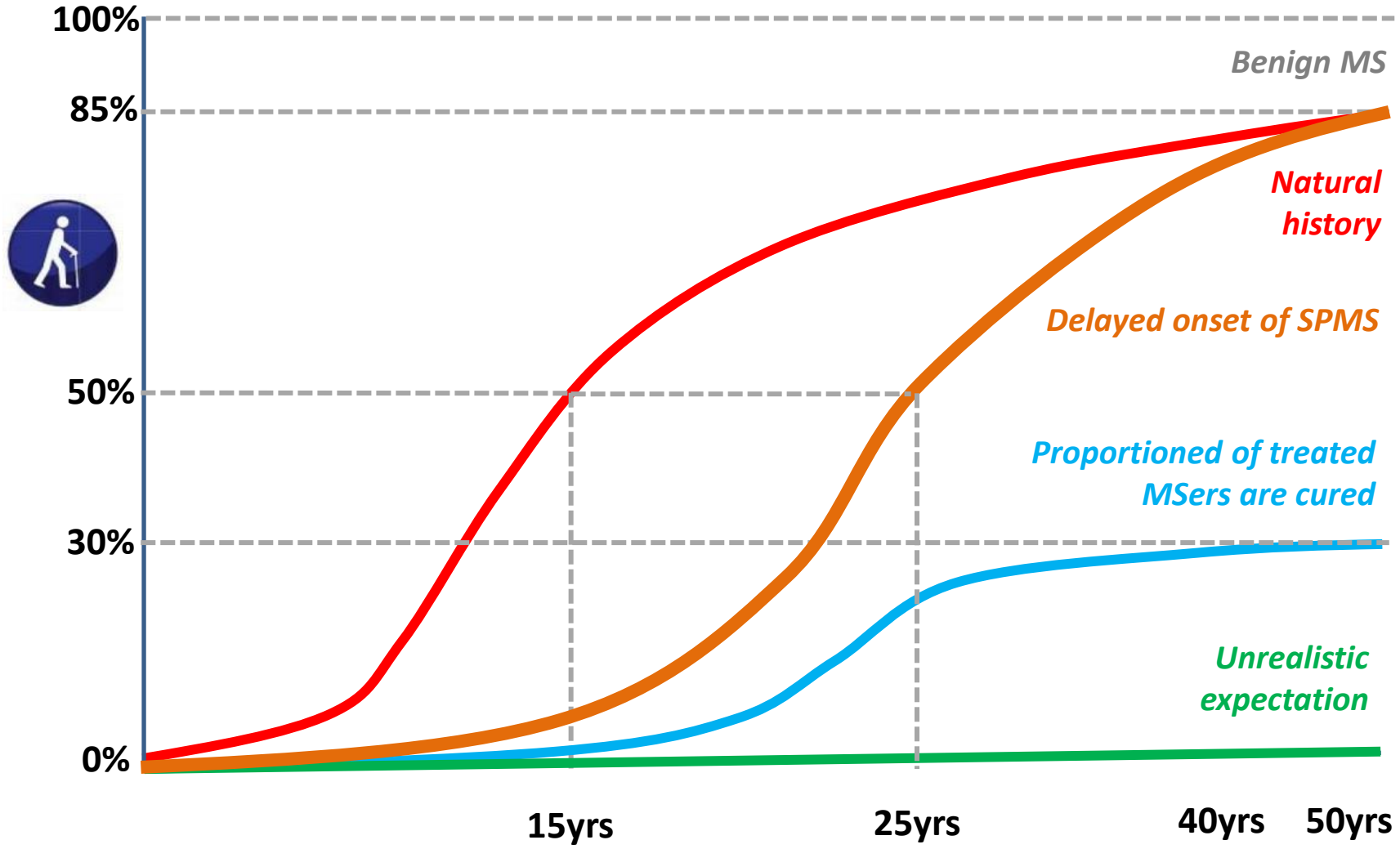
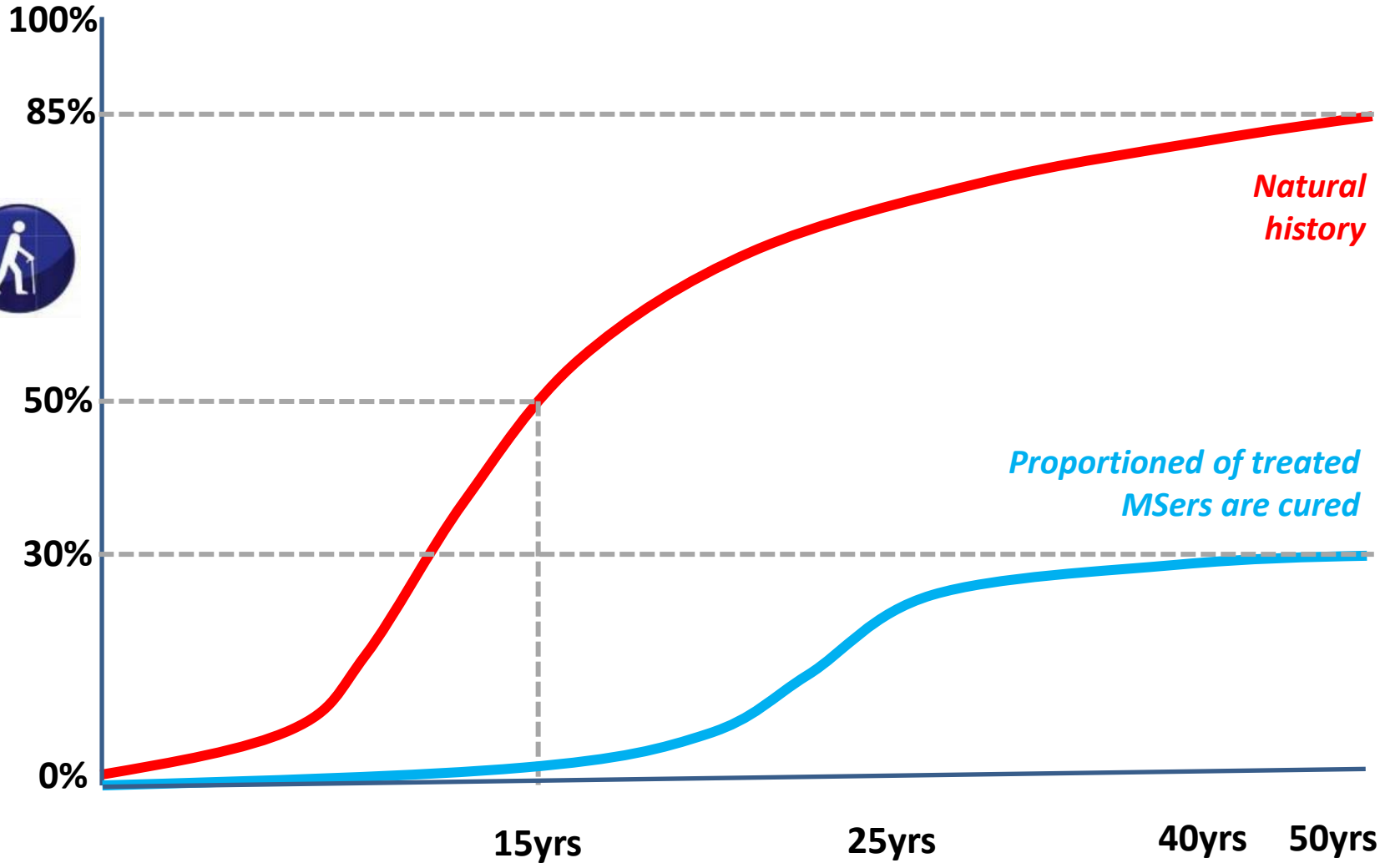
Survival Curves

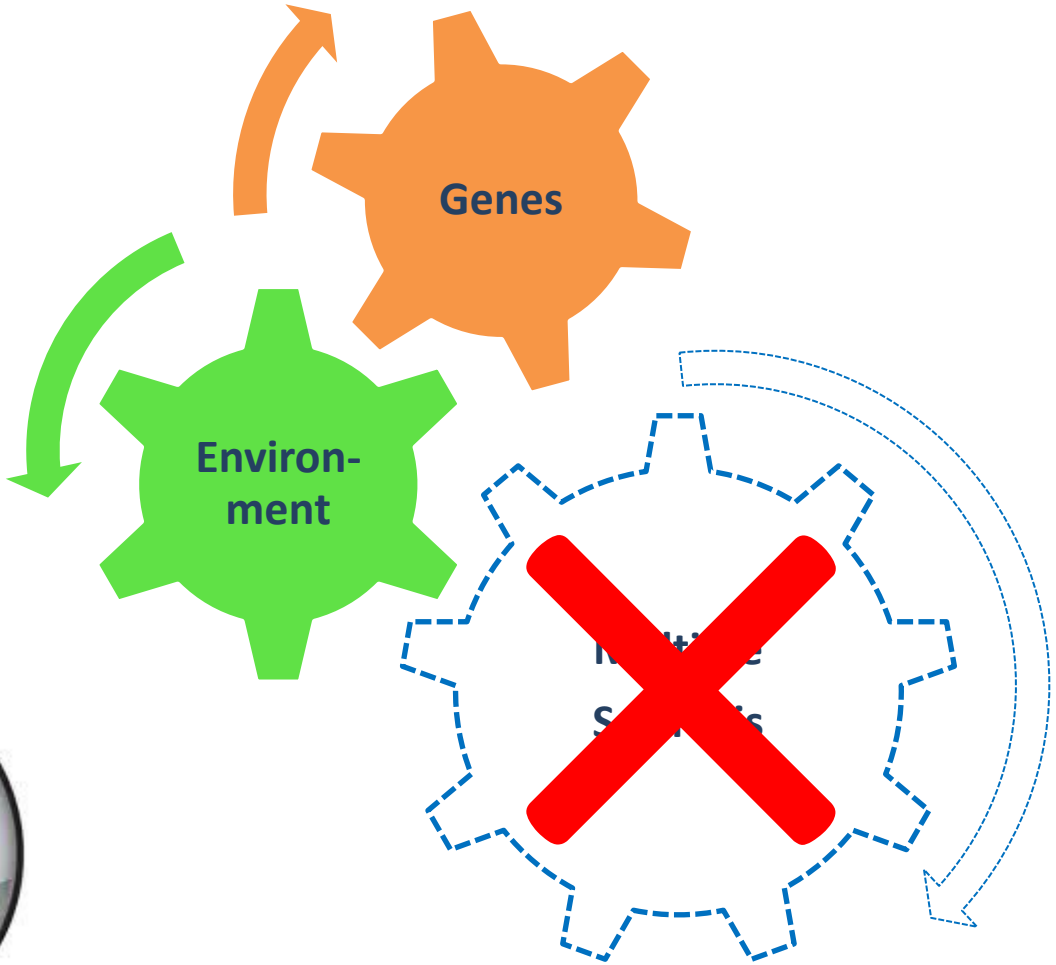


Defining a cure: a working definition

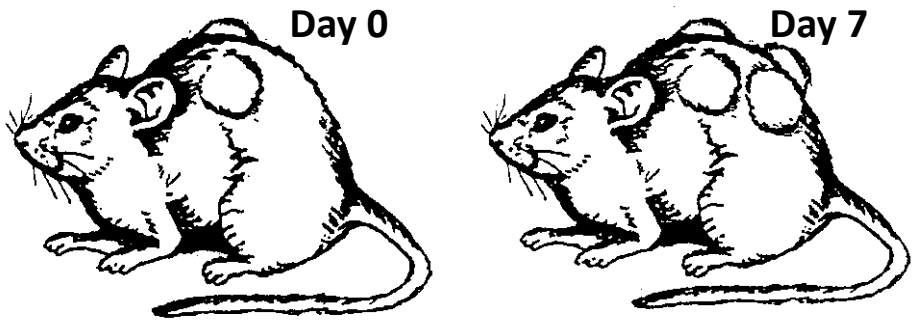


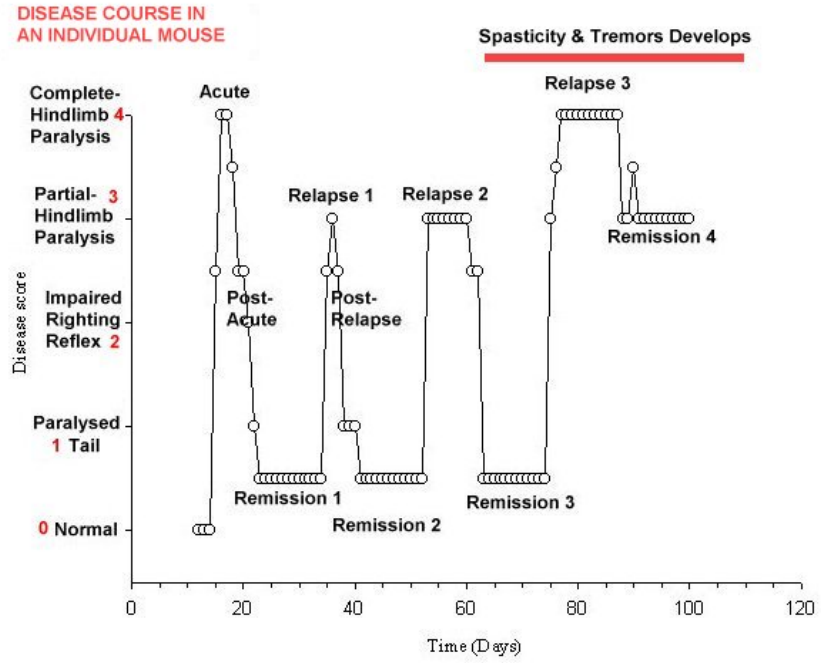
NEDA = no evident disease activity

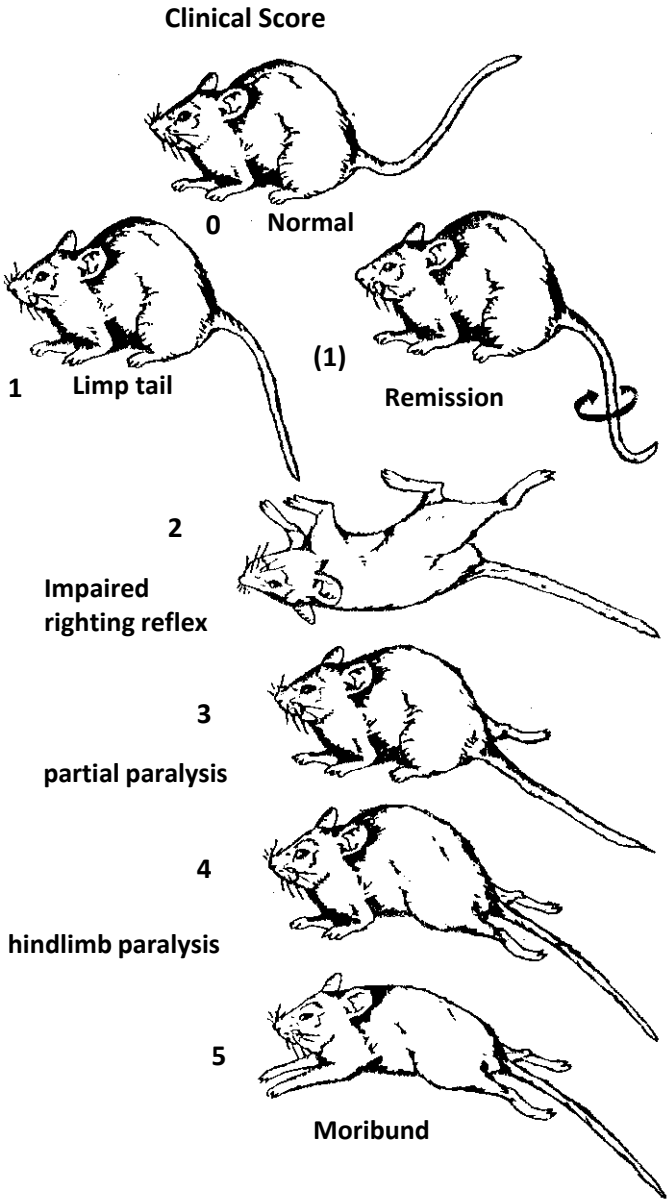
The autoimmune hypothesis



Professor Baker's Animal model of MS

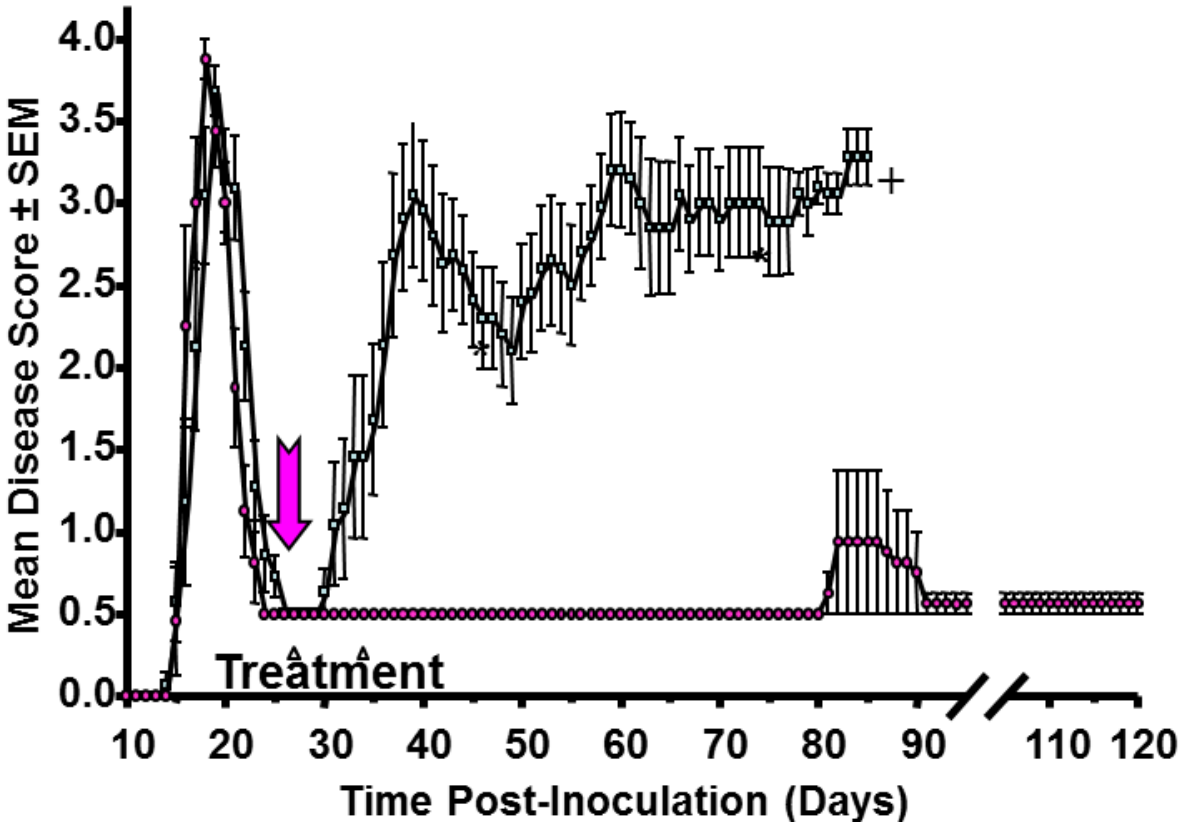




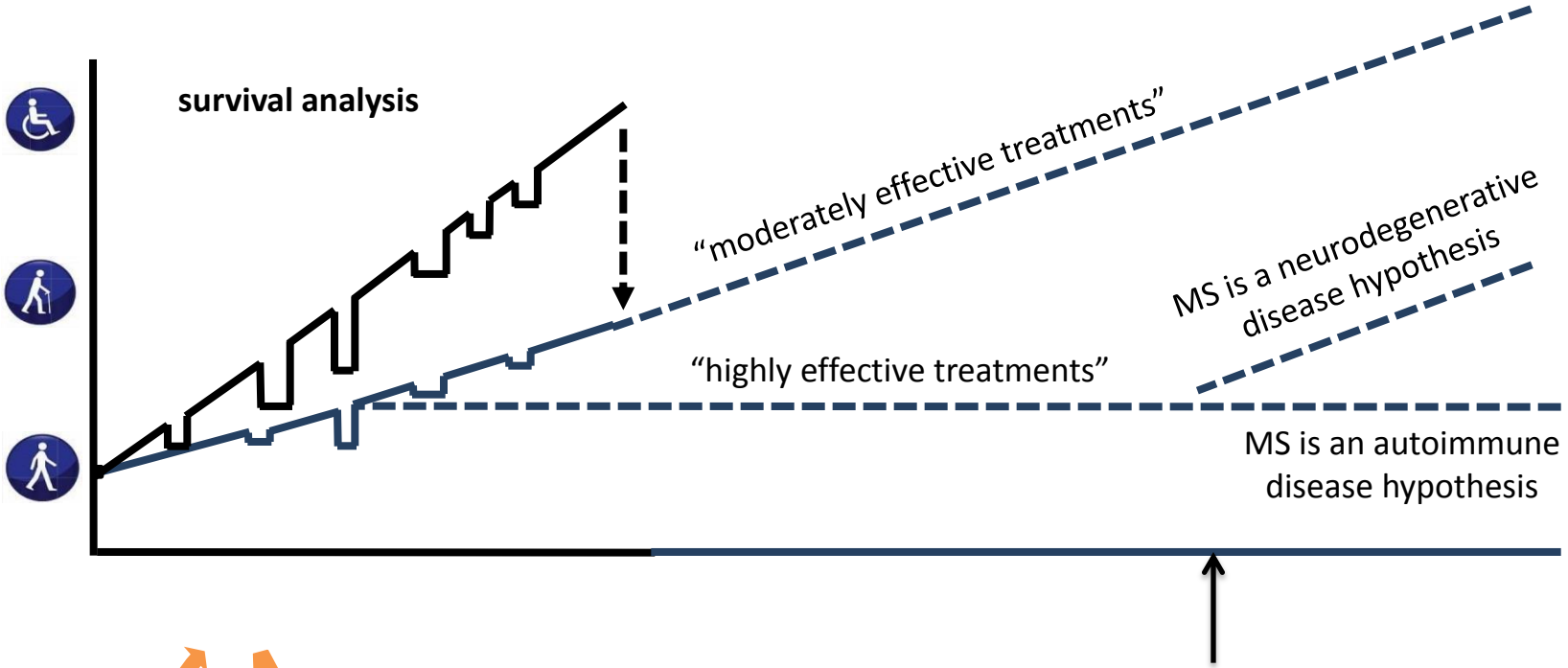


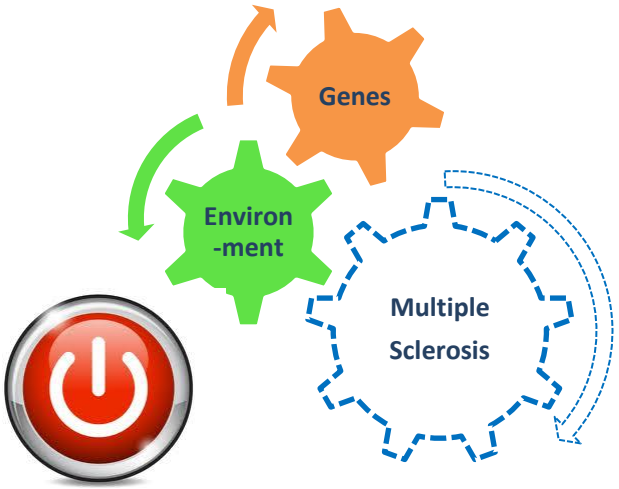
Slide courtesy David Baker

Curing animal MS

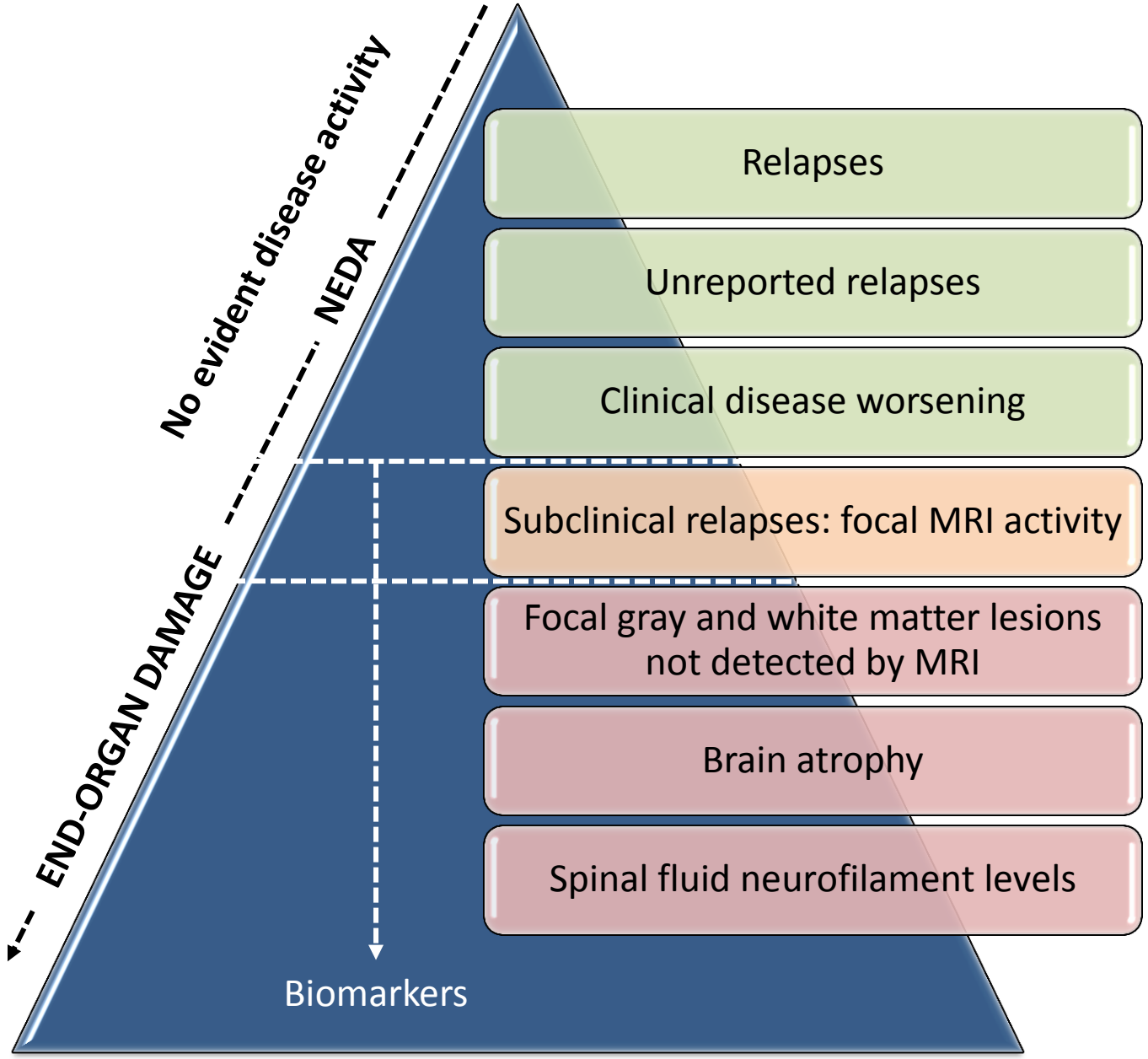


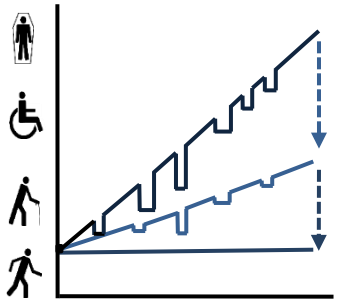
Can we repeat the animal experiment in MS?



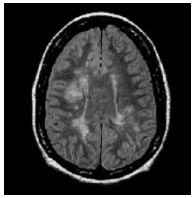


Moving the target: the MS Iceberg

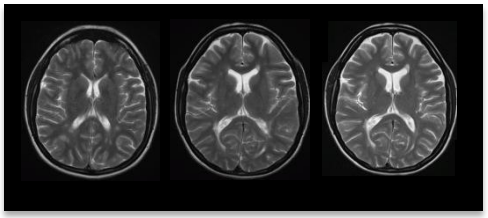




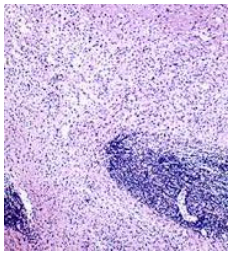
Clinical activity



Focal MRI activity



Hidden focal and diffuse MRI activity



Microscopic or biochemical pathology

Moving the target: end-organ damage

Control

Multiple sclerosis

NEDA

Treat-2-target

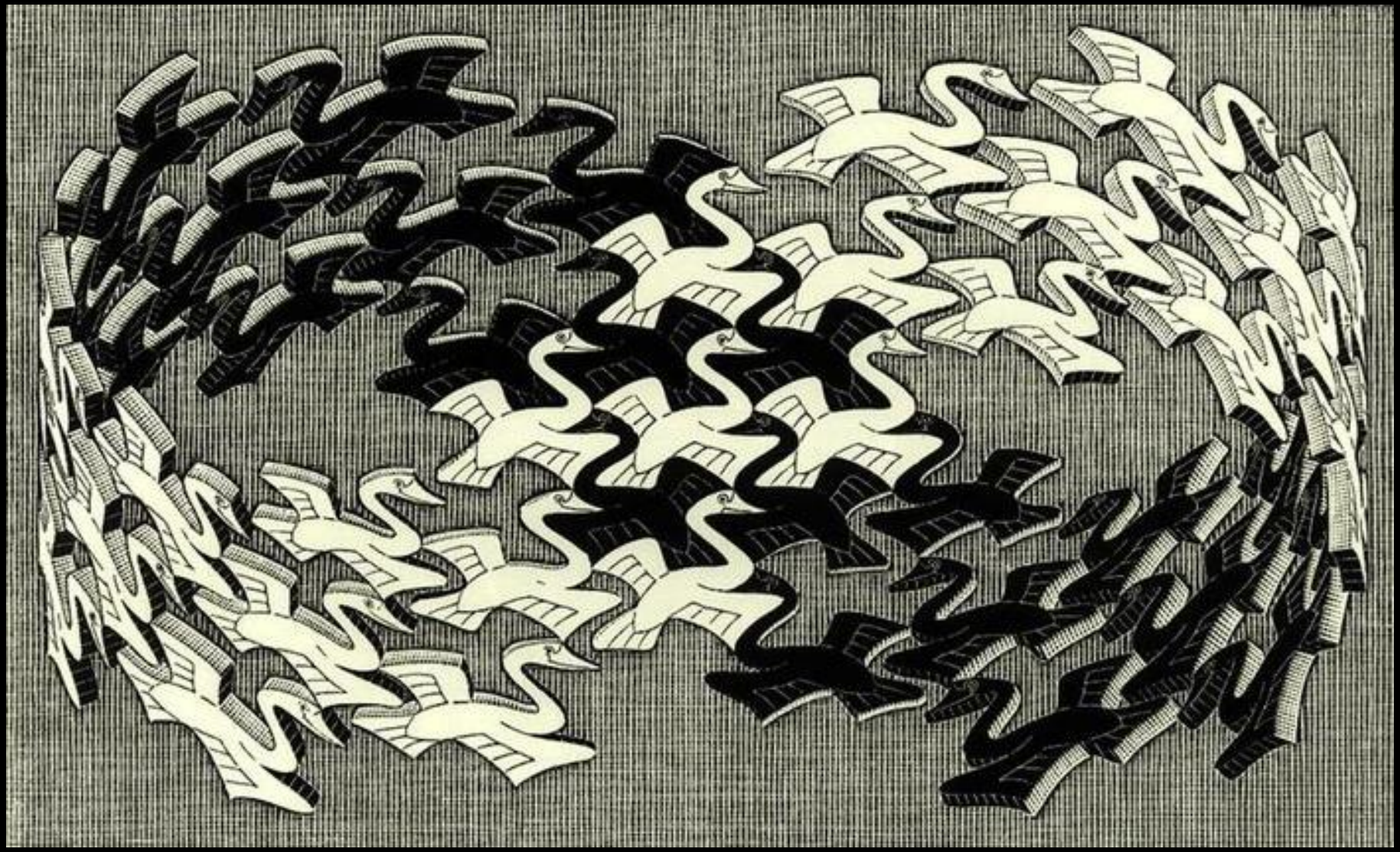
No evidence of disease activity defined as:[1,2]

- No relapses
- No sustained worsening of disability
- No MRI activity
  - No new or enlarging T2 lesions
  - No Gd-enhancing lesions

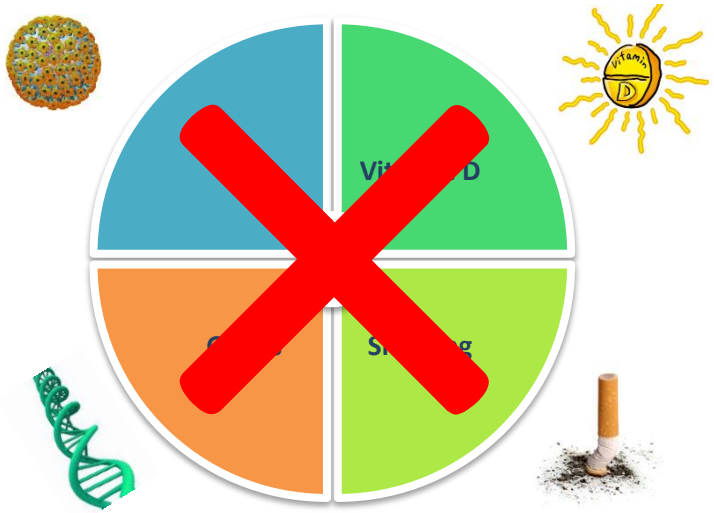
Brain volume loss should be included in our definition for NEDA

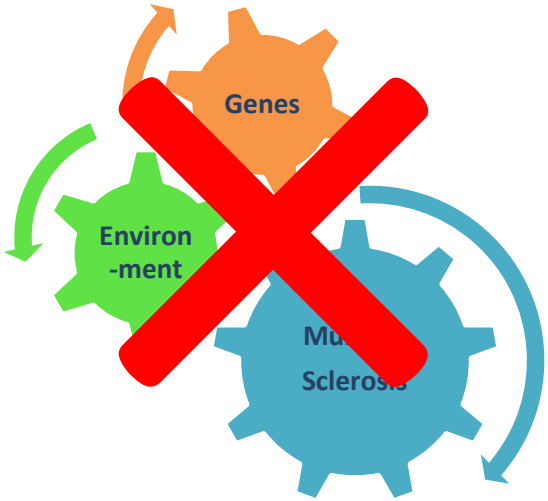
Gd, gadolinium.

1. Havrdova E, *et al*. *Lancet Neurol* 2009; 8:254–260; 2. Giovannoni G, *et al. Lancet Neurol* 2011; 10:329–337.



Have we got it wrong?





Is MS due to a virus?

Charcot Project

INSPIRE Trial (Raltegravir)

Etc. etc. etc.

Why haven’t we cured MS yet?

We may have, we need time to tell, or alternatively a **black swan** may fly in to the change the time-line.