

The importance of early intervention – clinician perspective

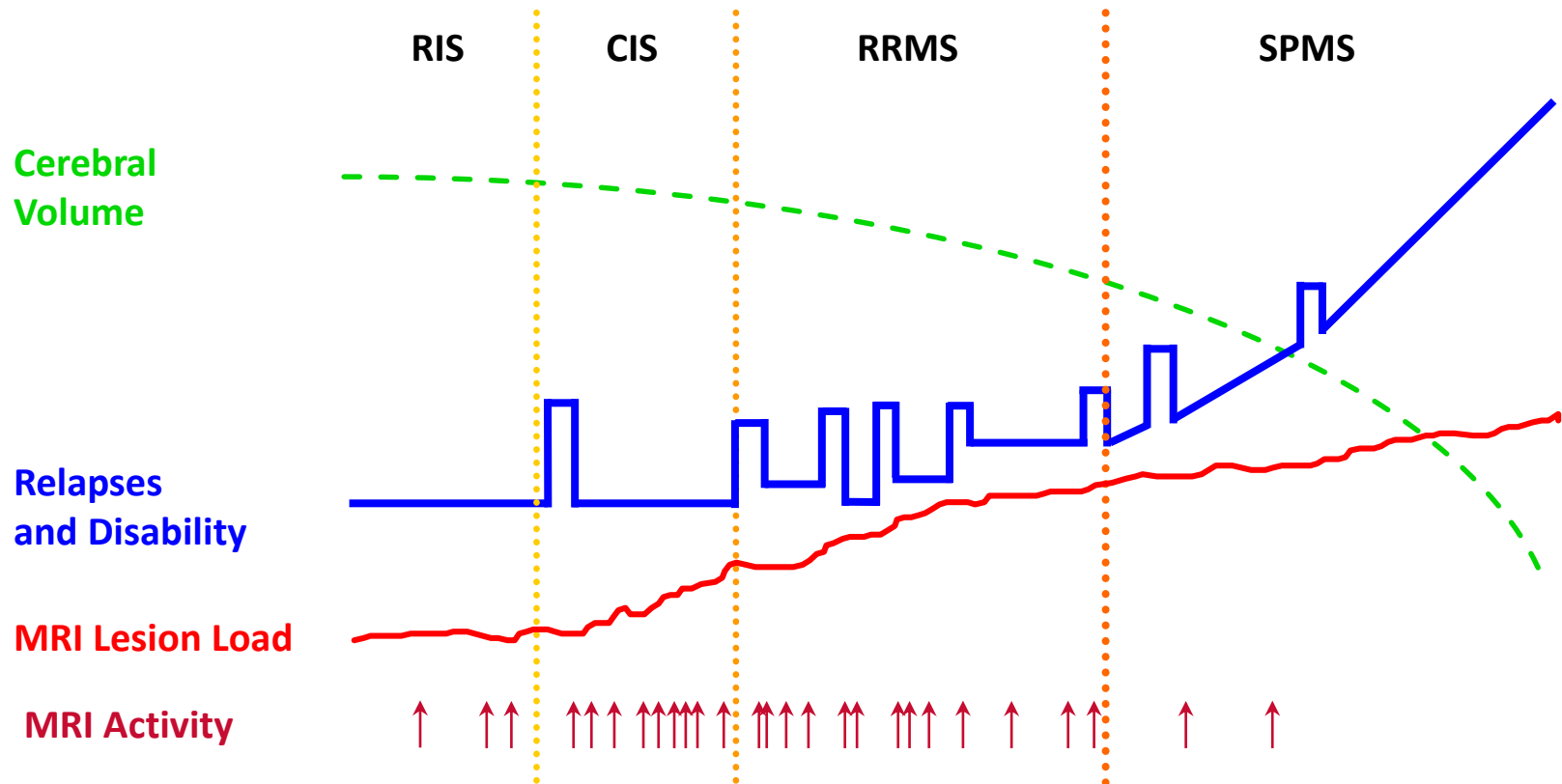
Øivind Grytten Torkildsen

«You can never diagnose MS too late»

Neuroradiologist from Norway, early 1990s

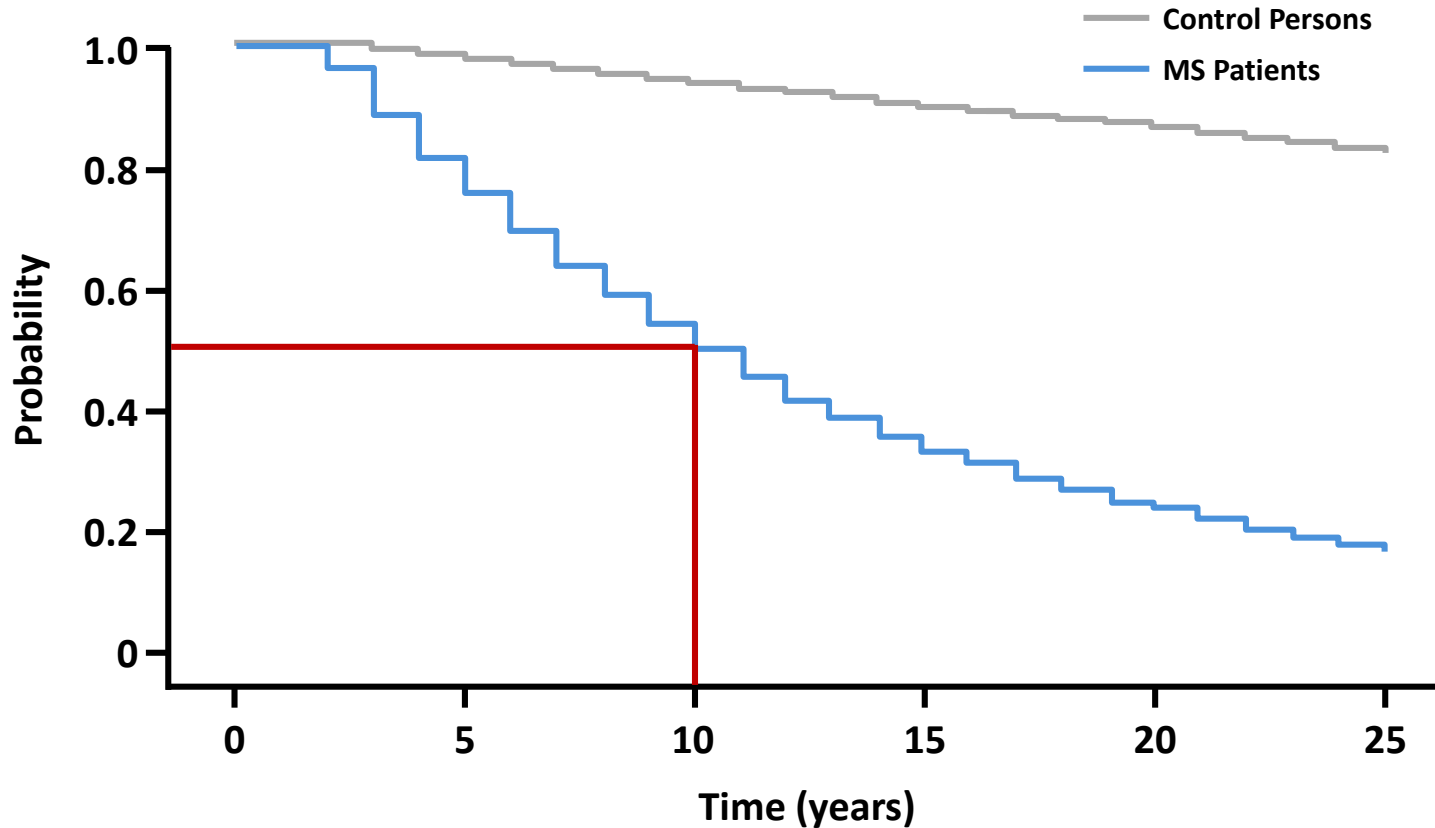
Prognosis in untreated MS

Early diagnosis

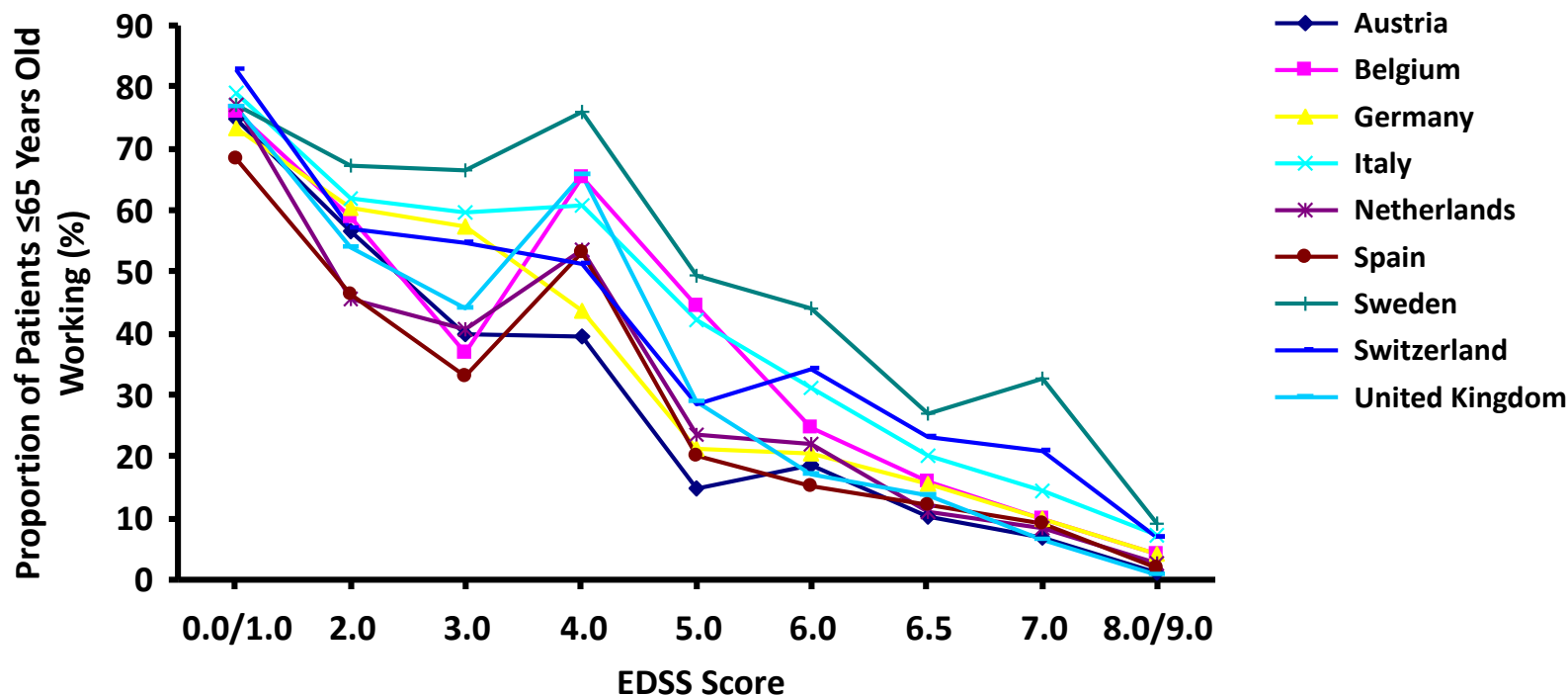


Employment in untreated MS

Probability of Remaining in Active Employment After Onset of MS

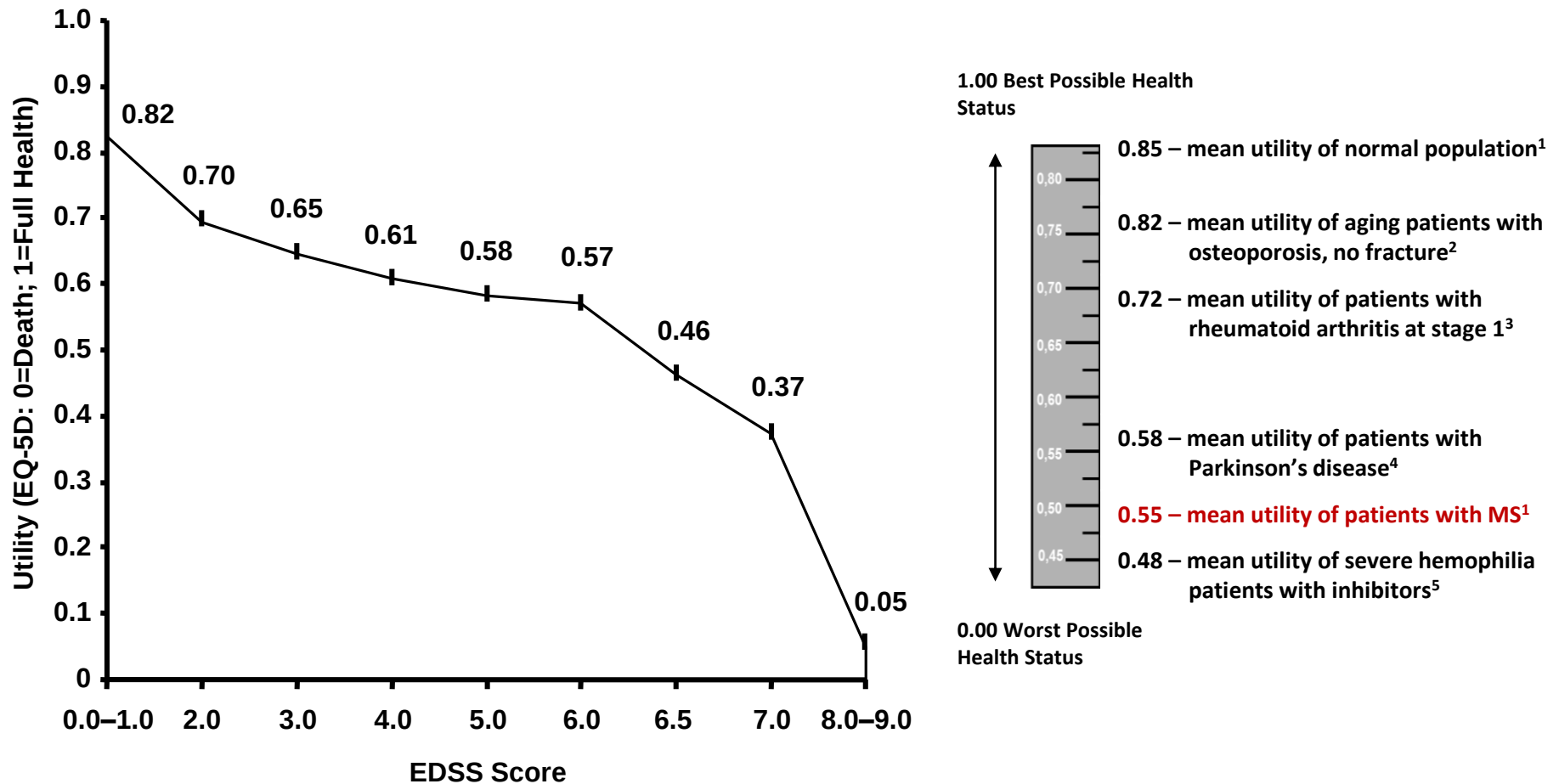


Employment Change with EDSS Score Increase

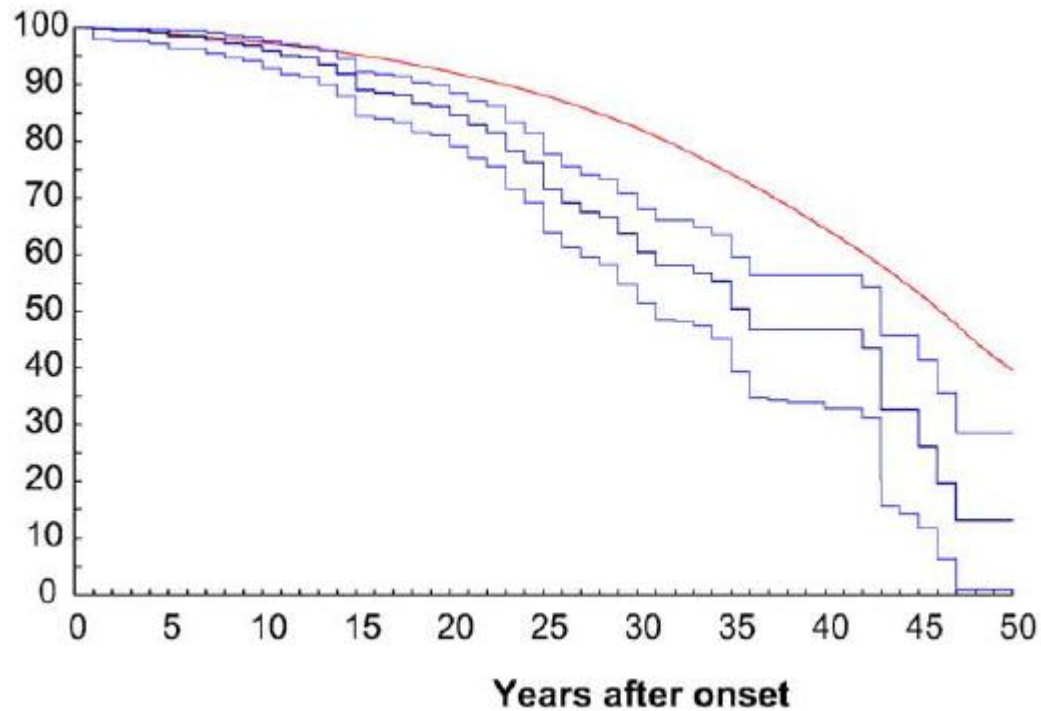


Adapted from Kobelt G et al. *J Neurol Neurosurg Psychiatry*. 2006;77:918-926.

Quality of life decreases with increasing EDSS-score



Survival in untreated MS



8 years decreased survival

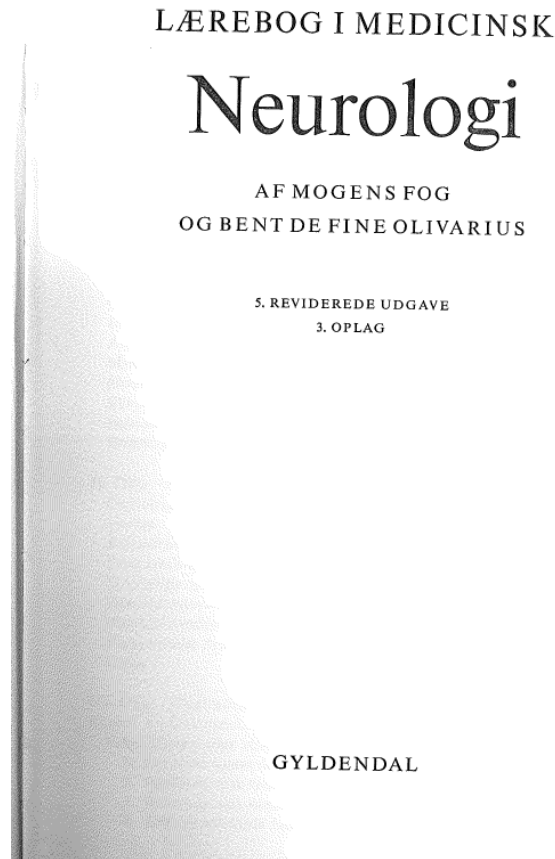
RESEARCH PAPER

Multiple Sclerosis 2008; 14: 1191–1198

**Survival and cause of death in multiple sclerosis:
results from a 50-year follow-up in Western Norway**

N Grytten Torkildsen^{1,2}, SA Lie³, JH Aarseth⁴, H Nyland⁵ and KM Myhr^{1,2}

In other words...

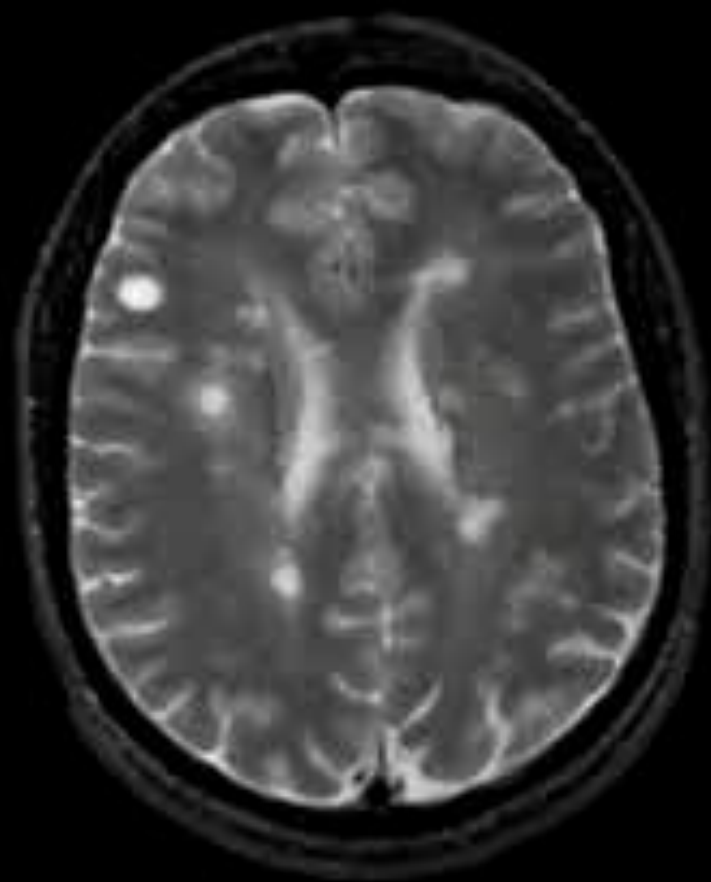


After 10 years:

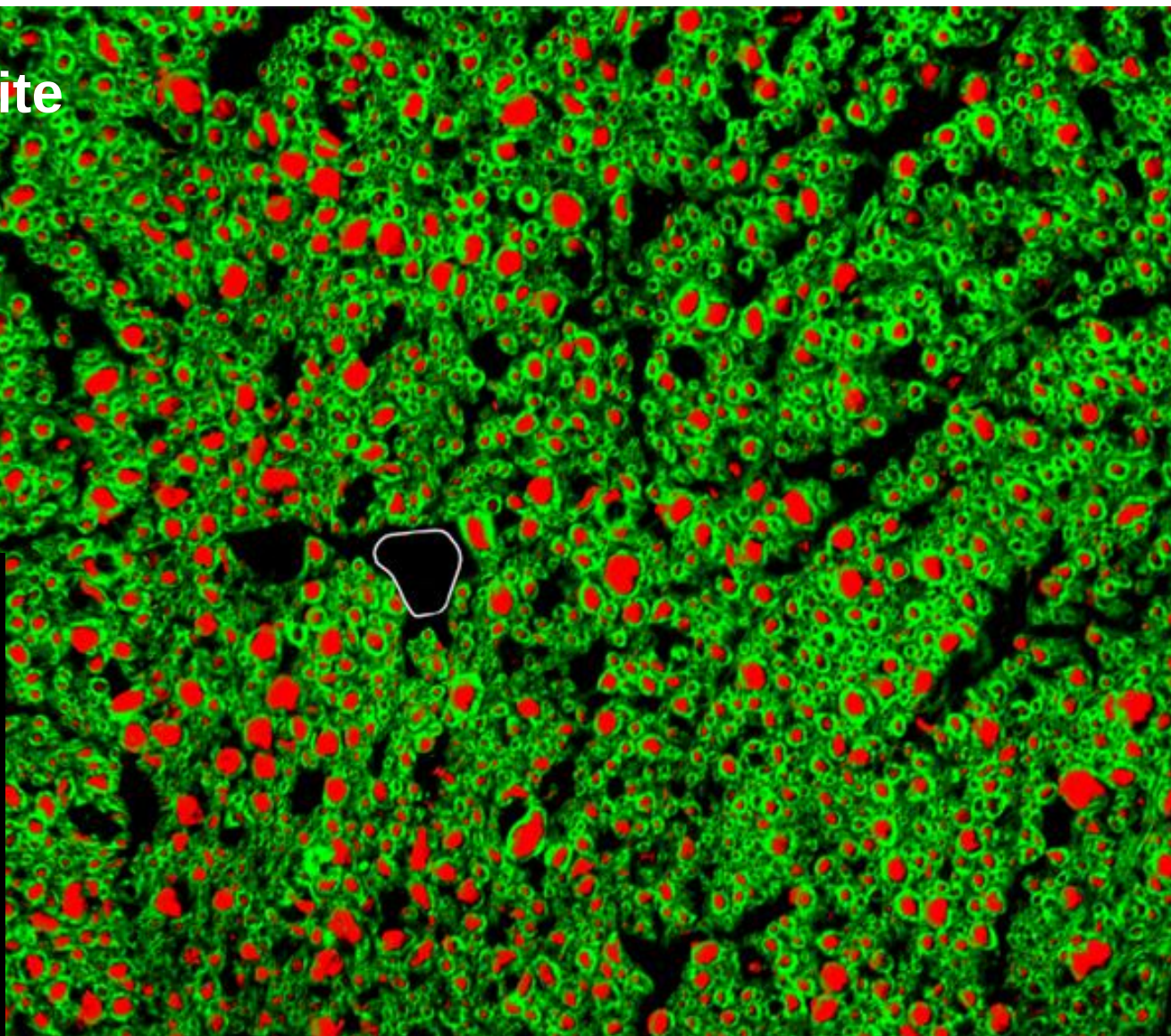
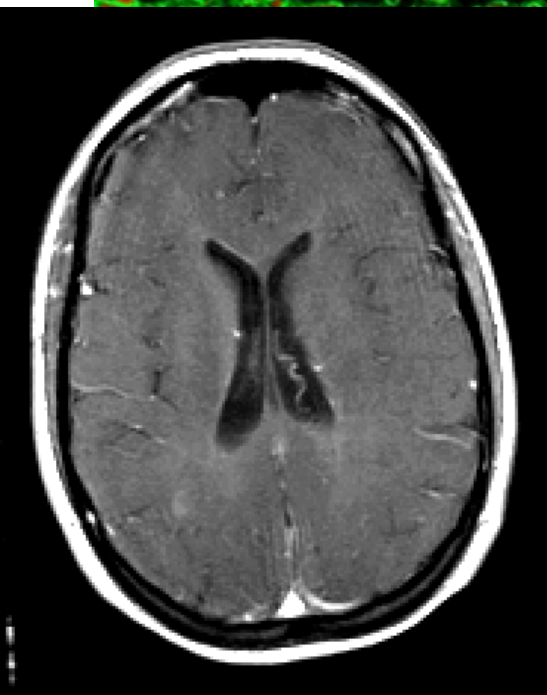
- $\frac{1}{4}$ of MS-patients have died from the disease
- $\frac{1}{4}$ are still employed
- $\frac{1}{2}$ are not employed, with different degrees of disability

What happens in MS

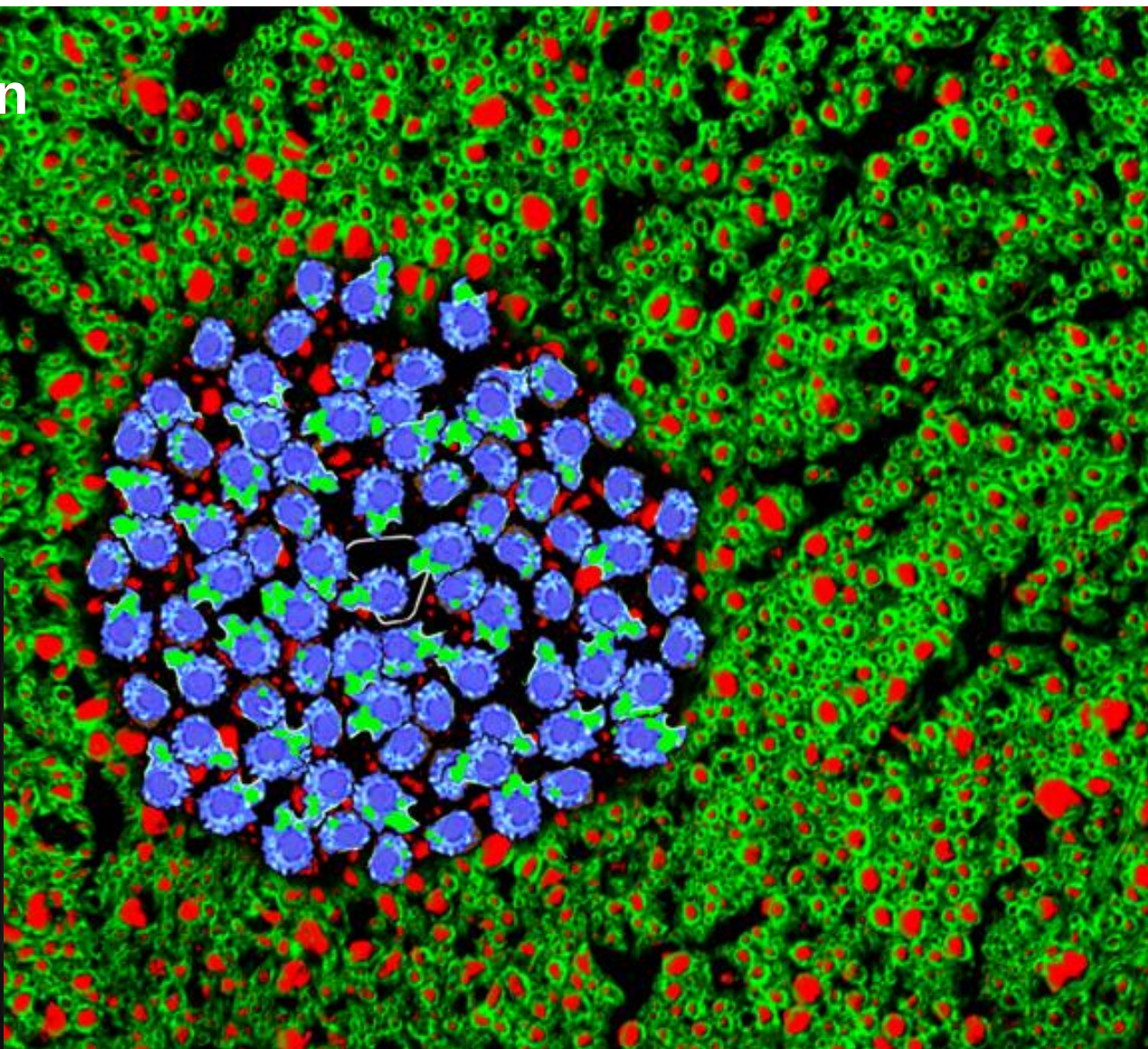
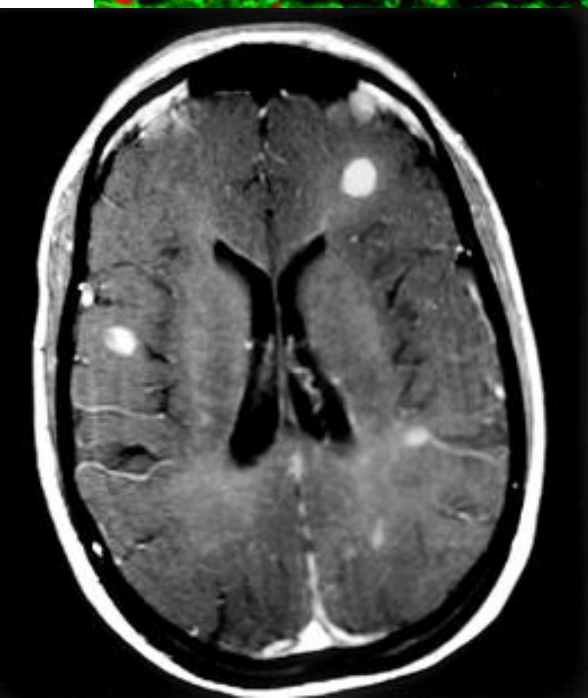
Acute damages



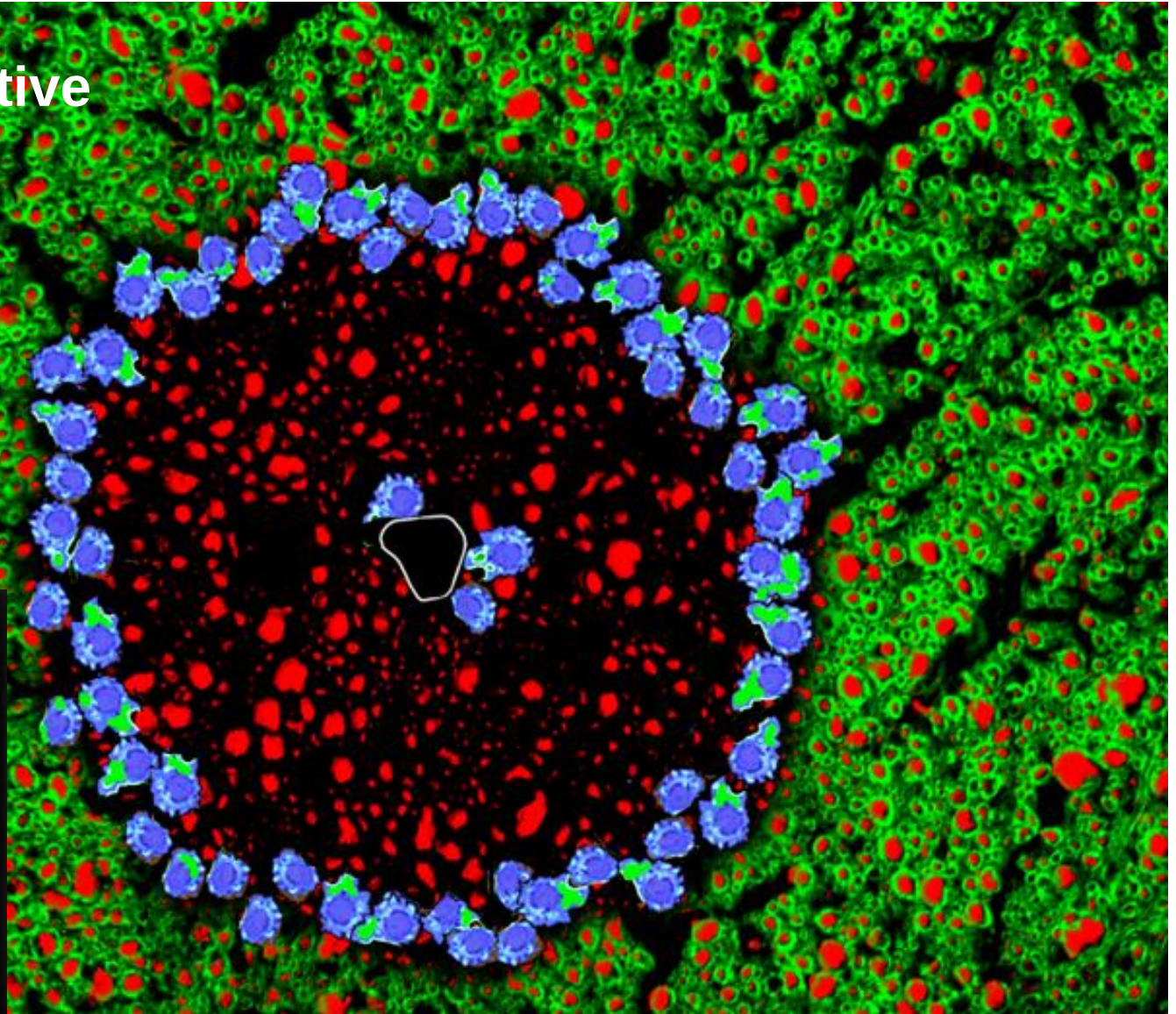
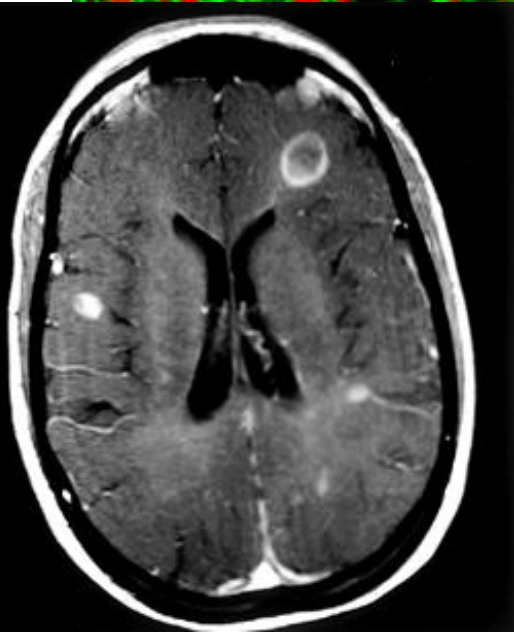
Normal White Matter



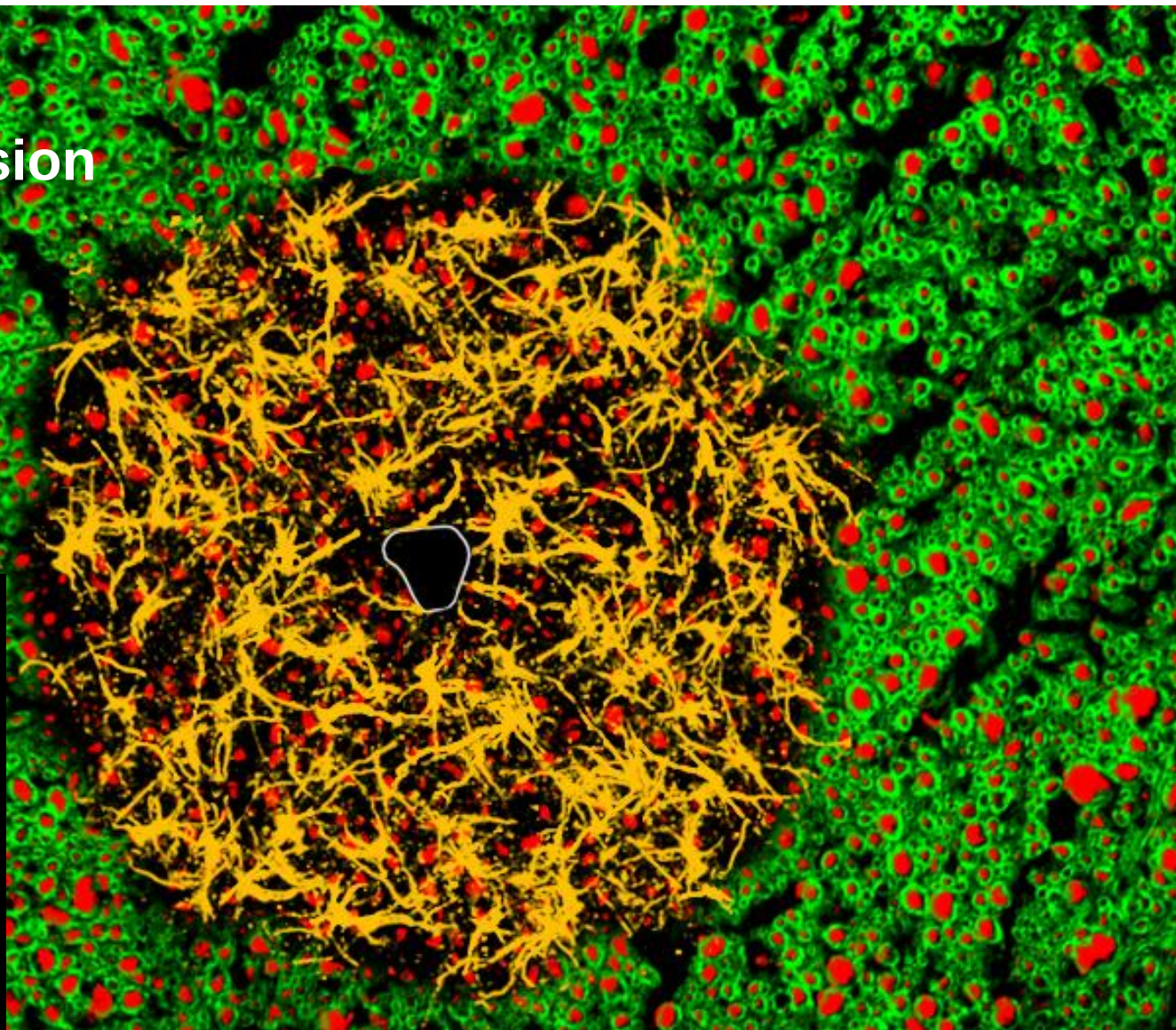
Active Lesion

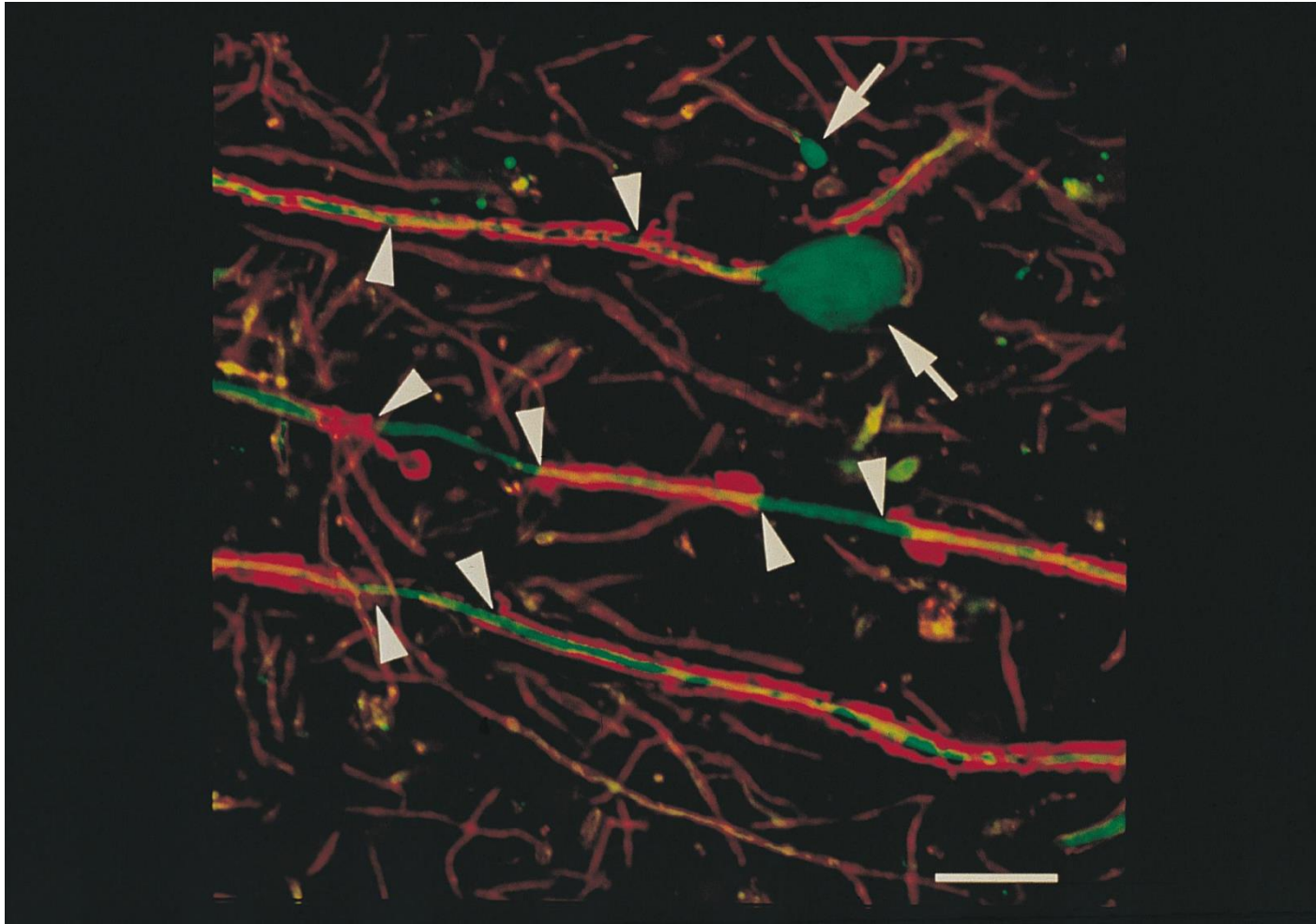


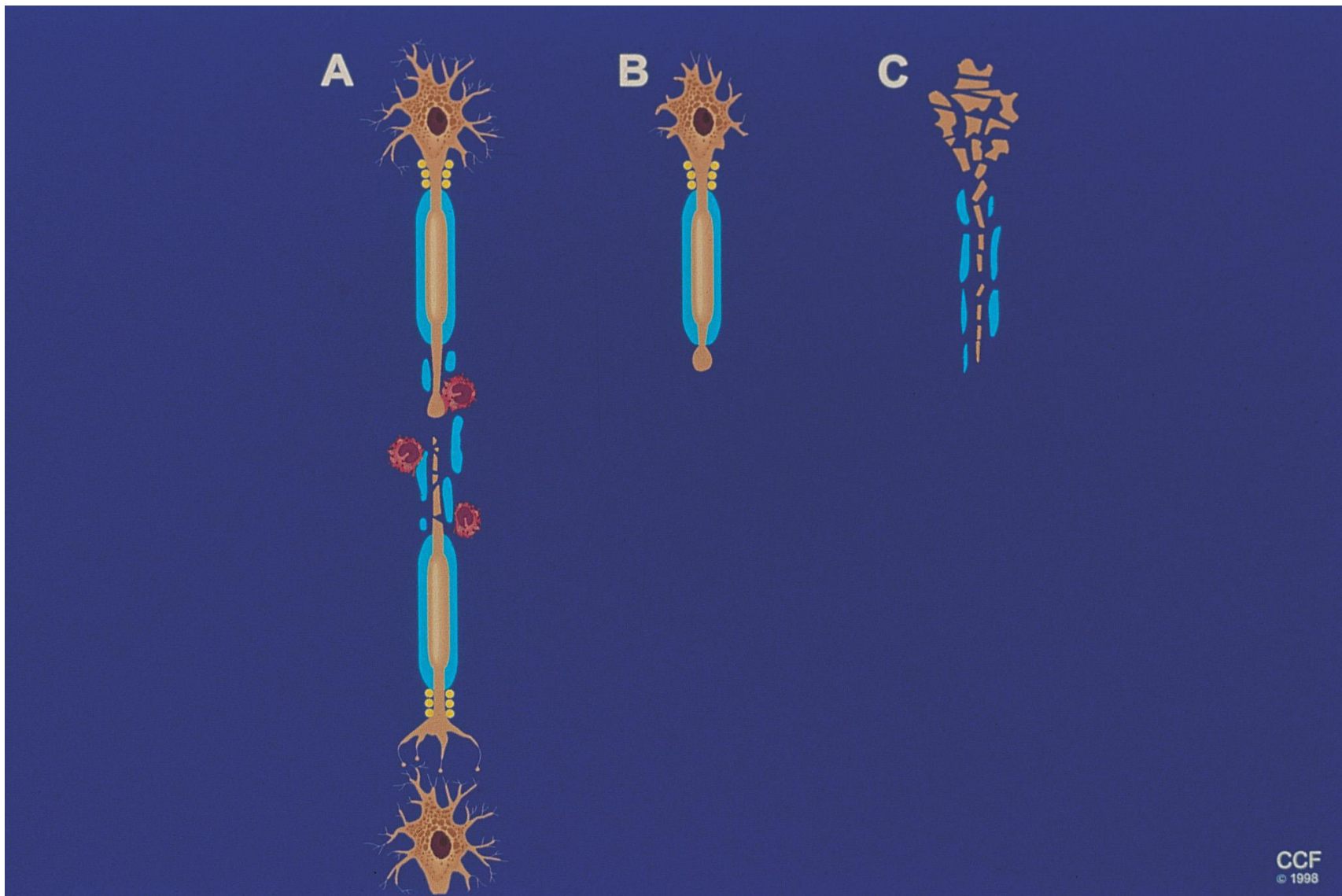
Chronic Active Lesion



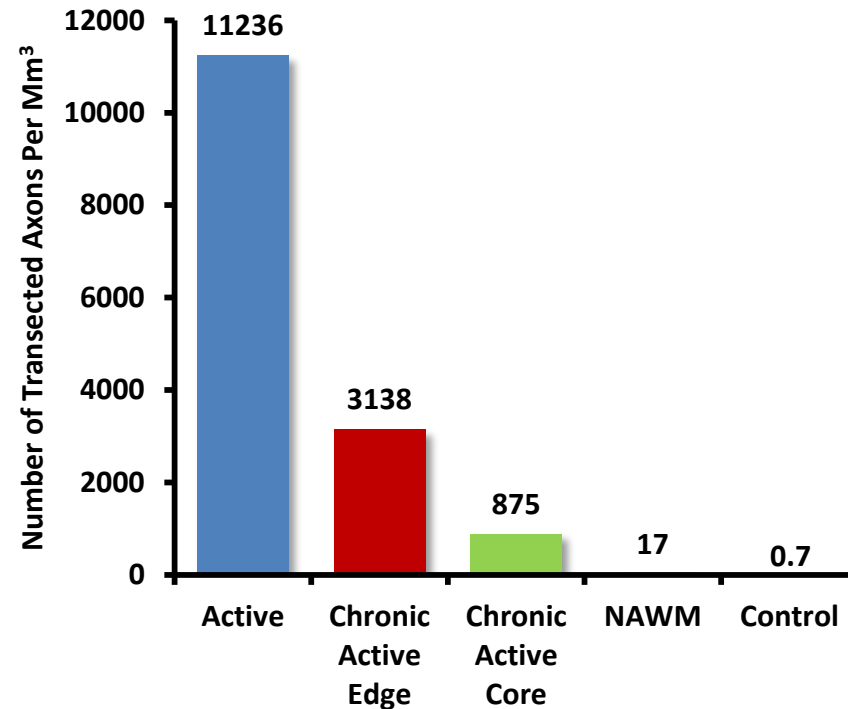
Chronic Inactive Lesion



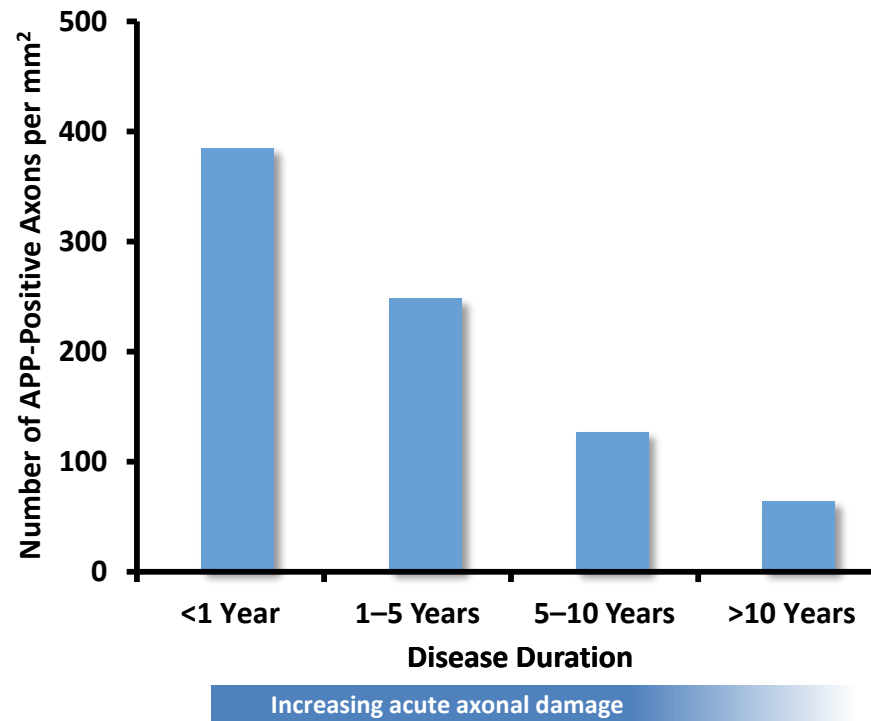


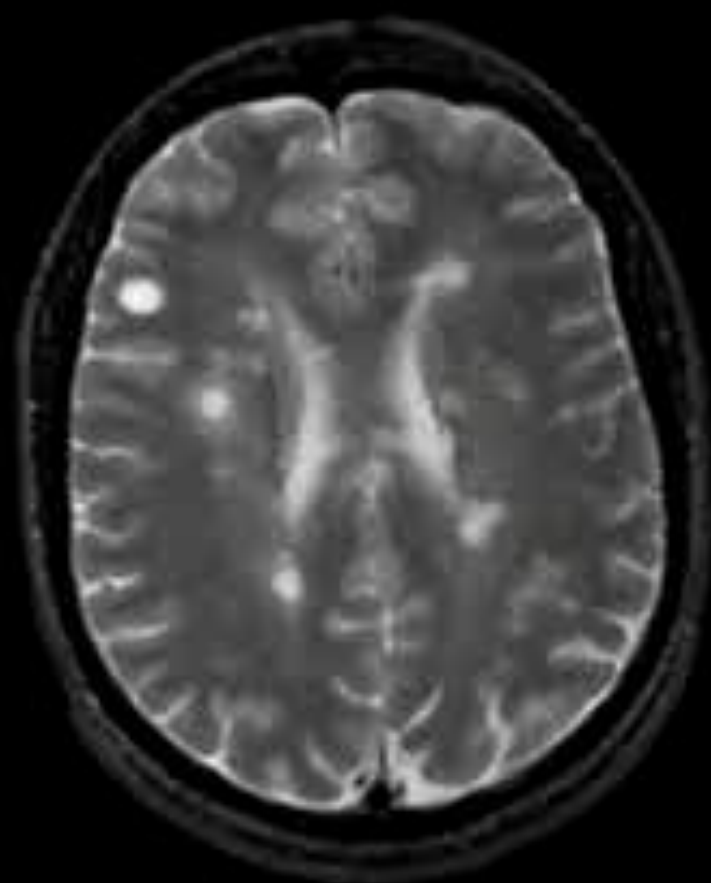


Transected axons in different MS-lesions



Number of damaged axons by disease duration

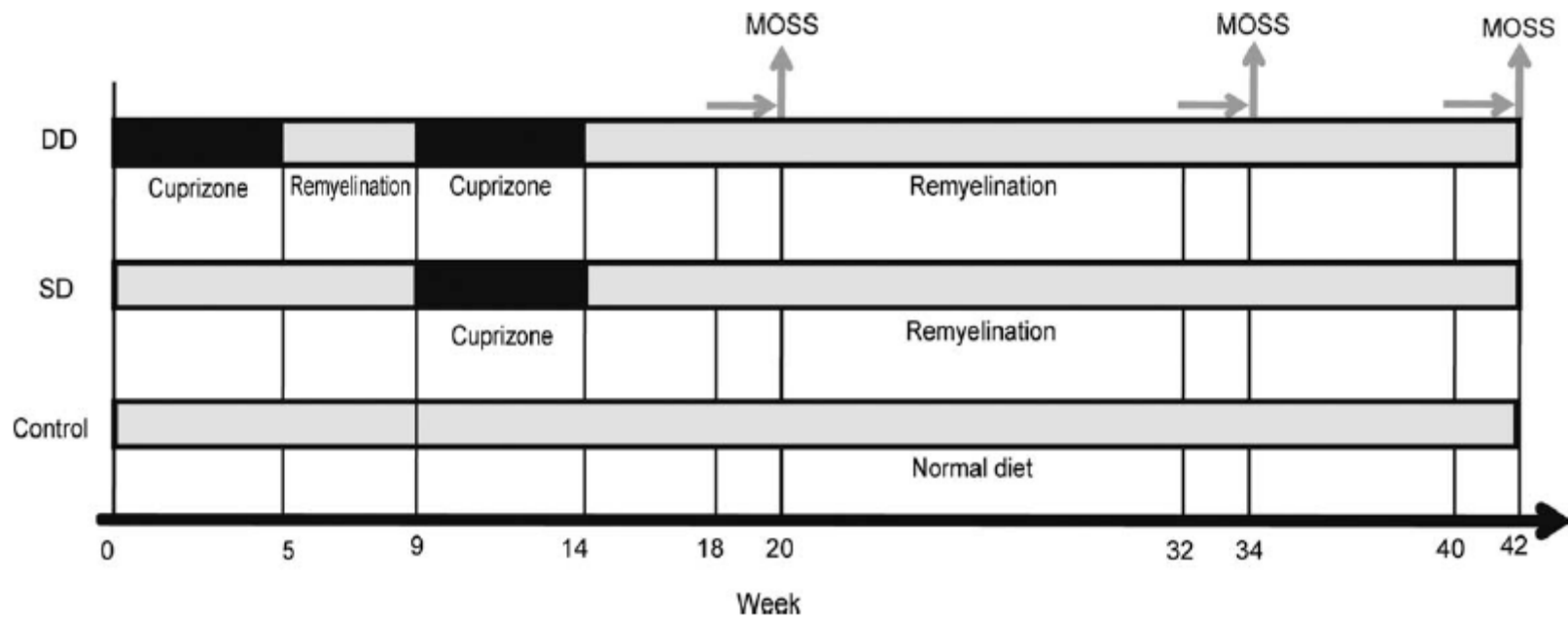


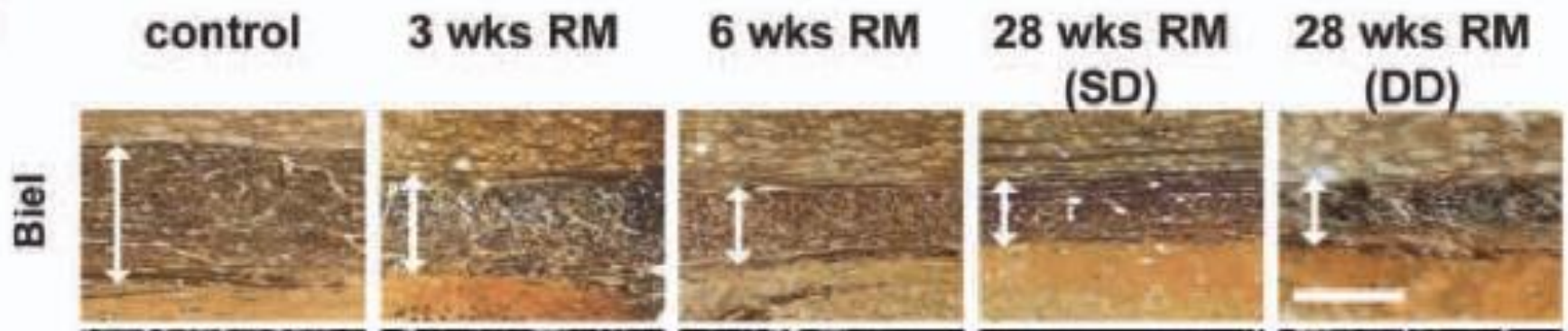
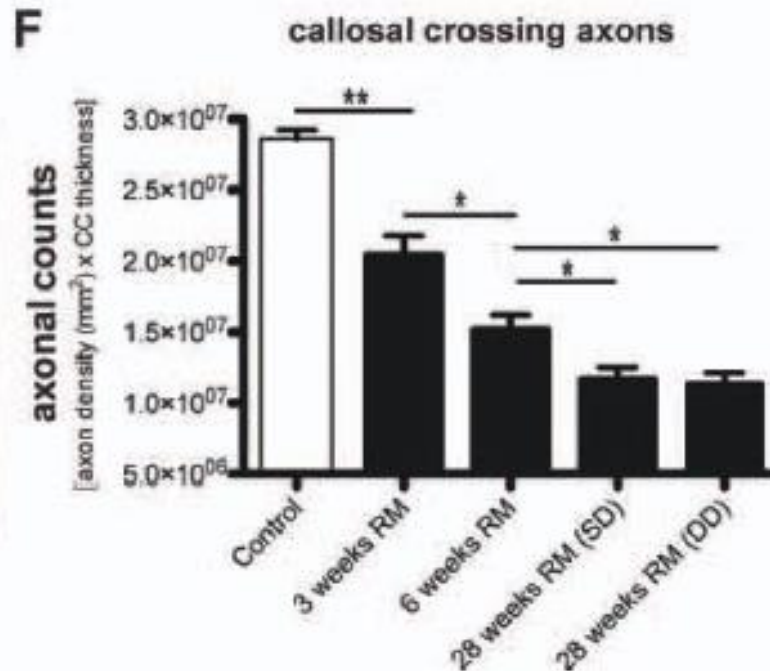


What happens in progressive MS?

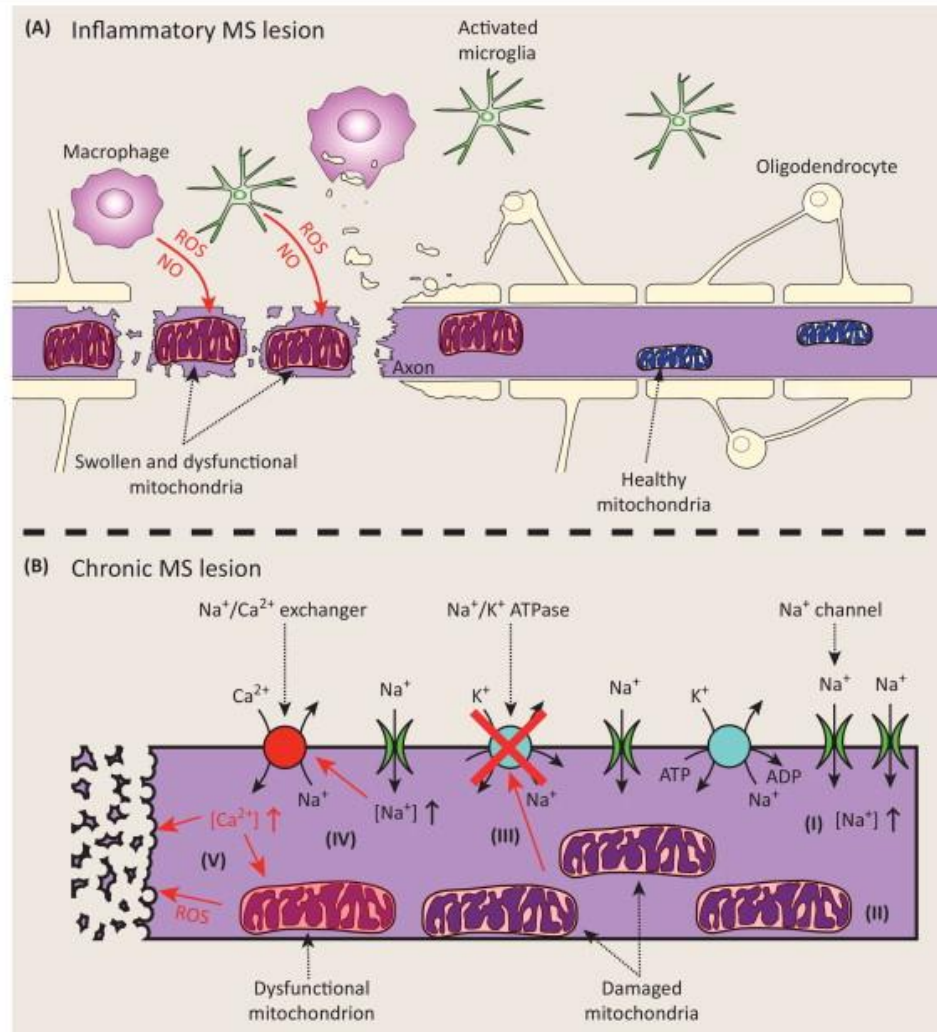
Late Motor Decline After Accomplished Remyelination: Impact for Progressive Multiple Sclerosis

Natalia Manrique-Hoyos, MSc,¹ Tanja Jürgens, MSc,^{2,3,4} Mads Grønberg, PhD,^{5,6}
Mario Kreutzfeldt, MSc,^{2,3,4} Mariann Schedensack,^{2,3} Tanja Kuhlmann, MD,⁷
Christina Schrick,^{2,3} Wolfgang Brück, MD,^{2,3} Henning Urlaub, PhD,⁶
Mikael Simons, MD,^{1,8} and Doron Merkler, MD^{2,3,4}





Mitochondrial damage?

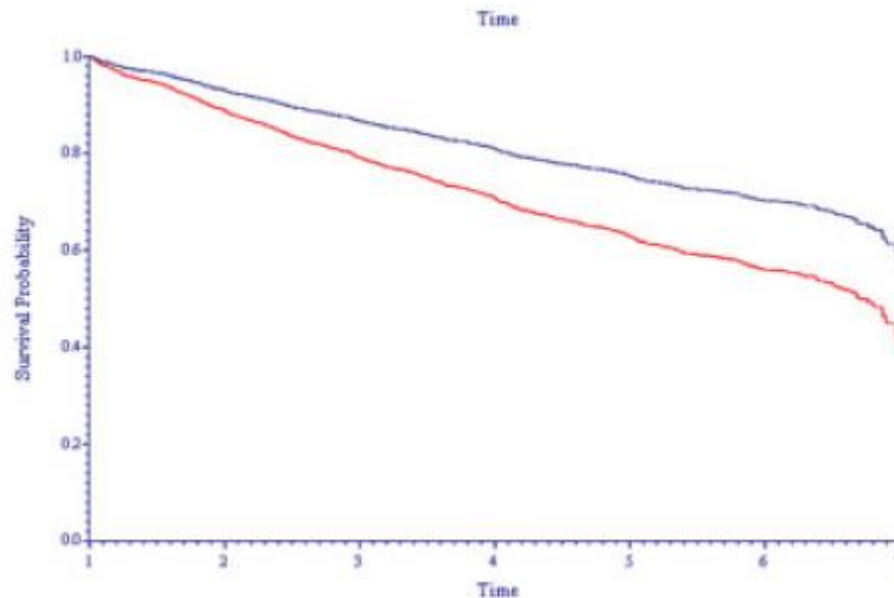


TRENDS in Molecular Medicine

Prognosis with treated MS

Real-Life Impact of Early Interferon β Therapy in Relapsing Multiple Sclerosis

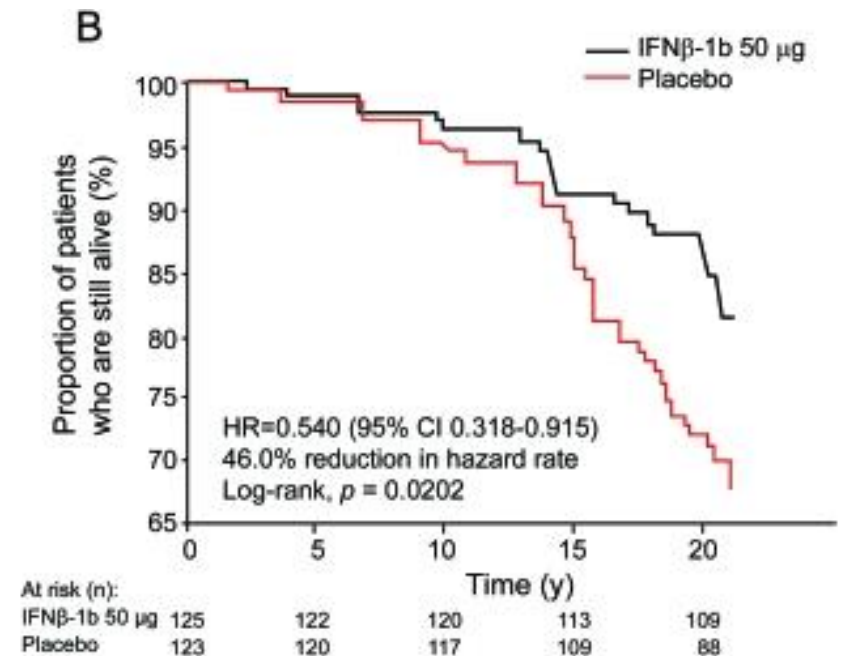
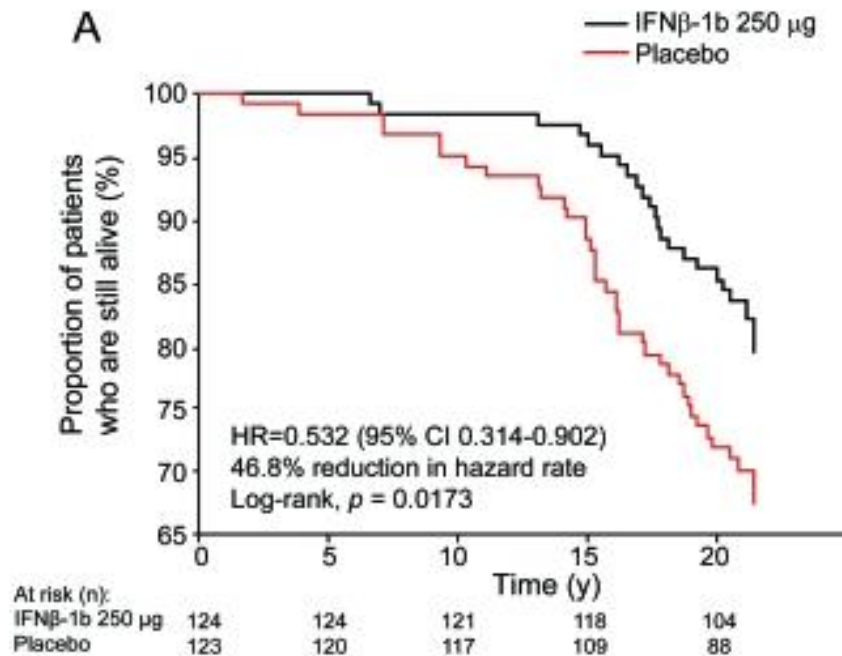
M. Trojano, MD,¹ F. Pellegrini, MDeStat,² D. Paolicelli, MD,¹ A. Fuiani, MD,¹ G.B. Zimatore, MD,¹ C. Tortorella, MD,¹ I.L. Simone, MD,¹ F. Patti, MD,³ A. Ghezzi, MD,⁴ V. Zipoli, MD,⁵ P. Rossi, MD,⁶ C. Pozzilli, MD,⁷ G. Salemi, MD,⁸ A. Lugaresi, MD,⁹ R. Bergamaschi, MD,¹⁰ E. Millefiorini, MD,¹¹ M. Clerico, MD,¹² G. Lus, MD,¹³ M. Vianello, MD,¹⁴ C. Avolio, MD,¹⁵ P. Cavalla, MD,¹⁶ V. Lepore, MD,² P. Livrea, MD,¹ G. Comi, MD,⁶ and M.P. Amato, MD⁵; for the Italian Multiple Sclerosis Database Network (MSDN) Group



Early treatment significantly reduced the risk of EDSS-progression

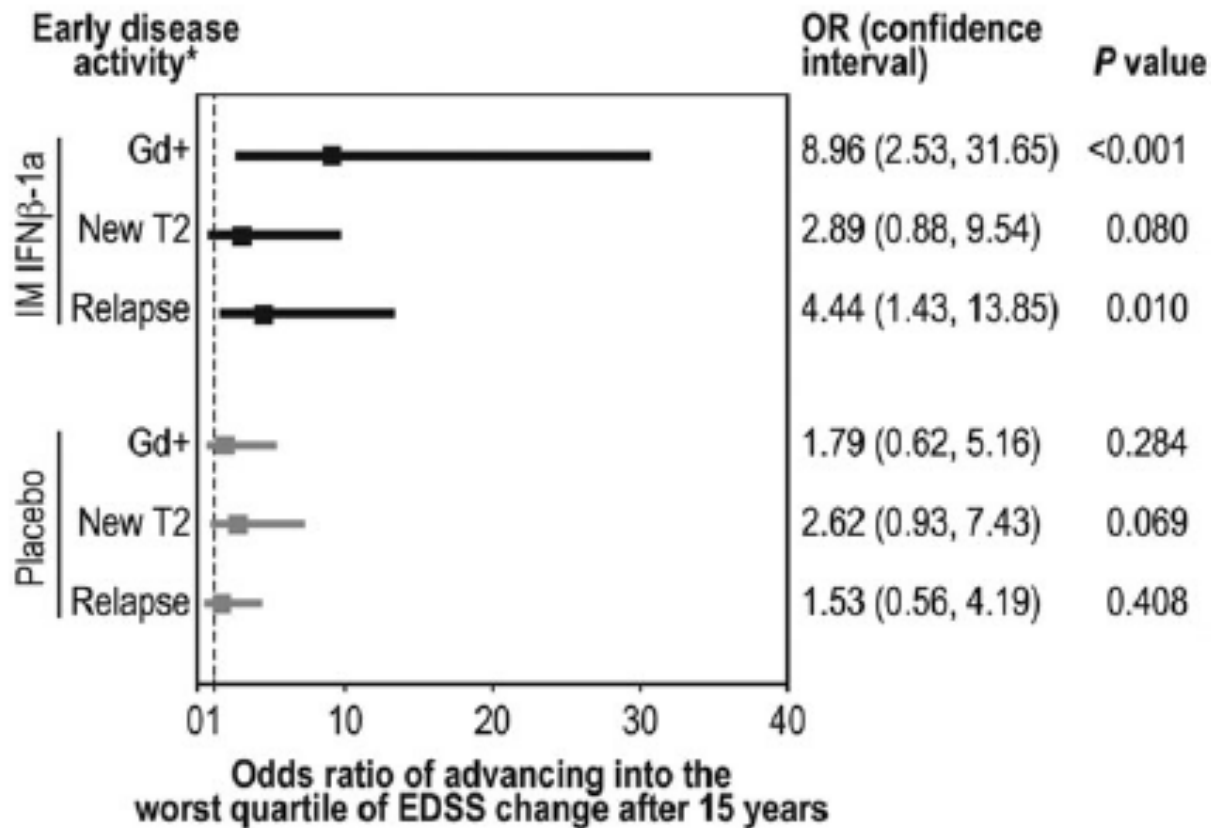
Survival in MS

A randomized cohort study 21 years after the start of the pivotal IFN β -1b trial

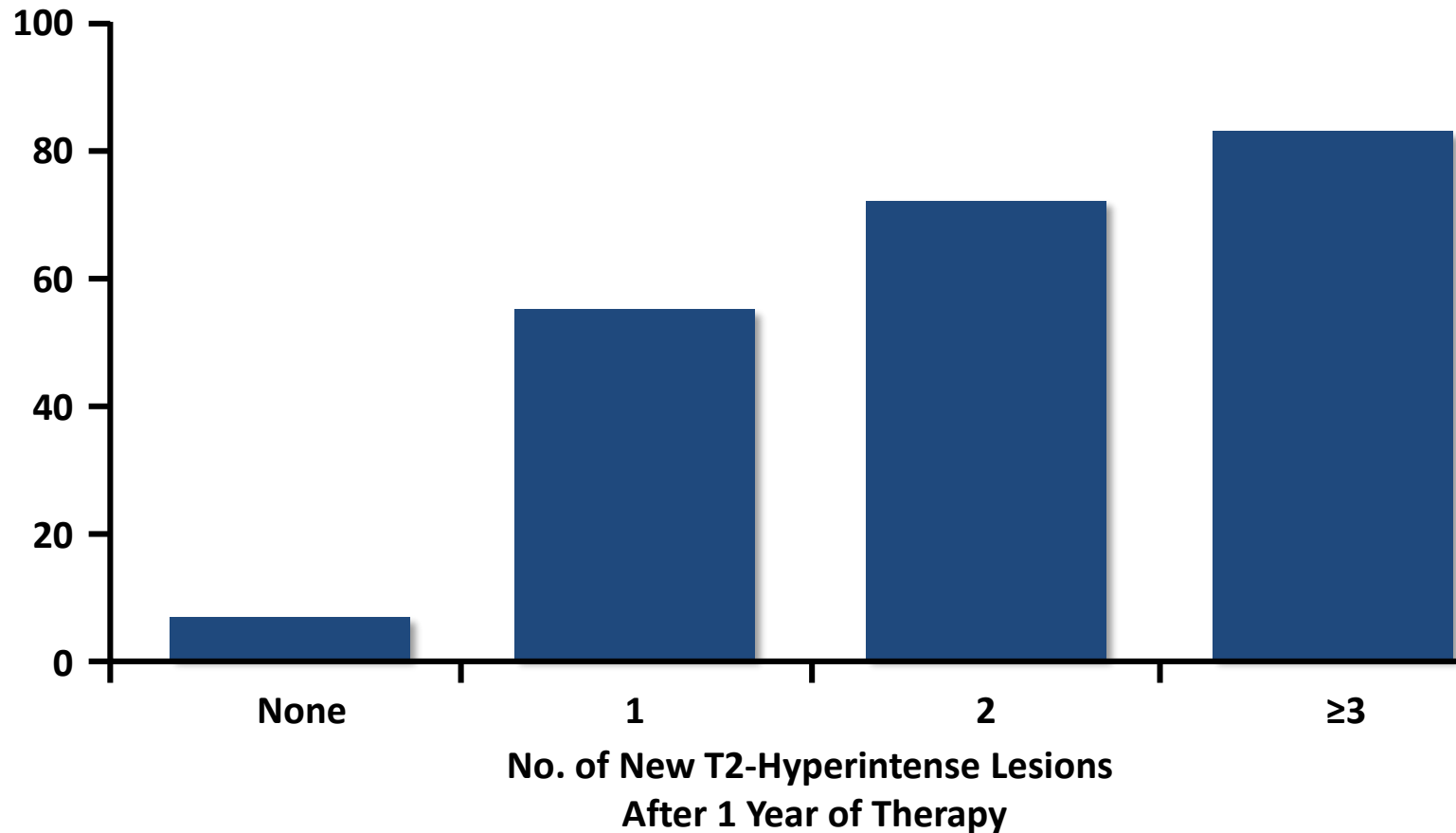


Predictors of Long-Term Outcome in Multiple Sclerosis Patients Treated with Interferon Beta

Robert A. Bermel, MD,¹ Xiaojun You, PhD,² Pamela Foulds, MD,² Robert Hyde, PhD,²
Jack H. Simon, MD,³ Elizabeth Fisher, PhD,⁴ and Richard A. Rudick, MD¹



New MRI-lesions during MS-treatment predict disability progression

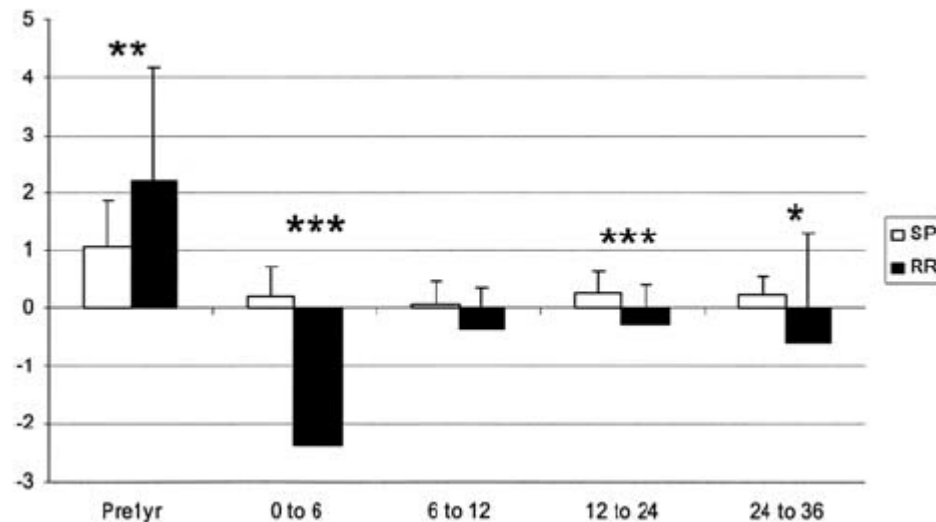


*Sustained disability progression was defined as a ≥ 1.0 -point increase in EDSS score confirmed at 6 months. Mean follow-up was 4.8 years.
Prosperini L et al. *Eur J Neurol.* 2009;16:1202-1209.

Alasdair J. Coles
Amanda Cox
Emmanuelle Le Page
Joanne Jones
S. Anand Trip
Jackie Deans
Shaun Seaman
David H. Miller
Geoff Hale
Herman Waldmann
D. Alastair Compston

The window of therapeutic opportunity in multiple sclerosis

Evidence from monoclonal antibody therapy



Summary

- Early treatment → most effective
- Disease activity during treatment → poorer prognosis

Goals of Therapy

Outcome Measures

Address Symptoms

Slow Disease Progression

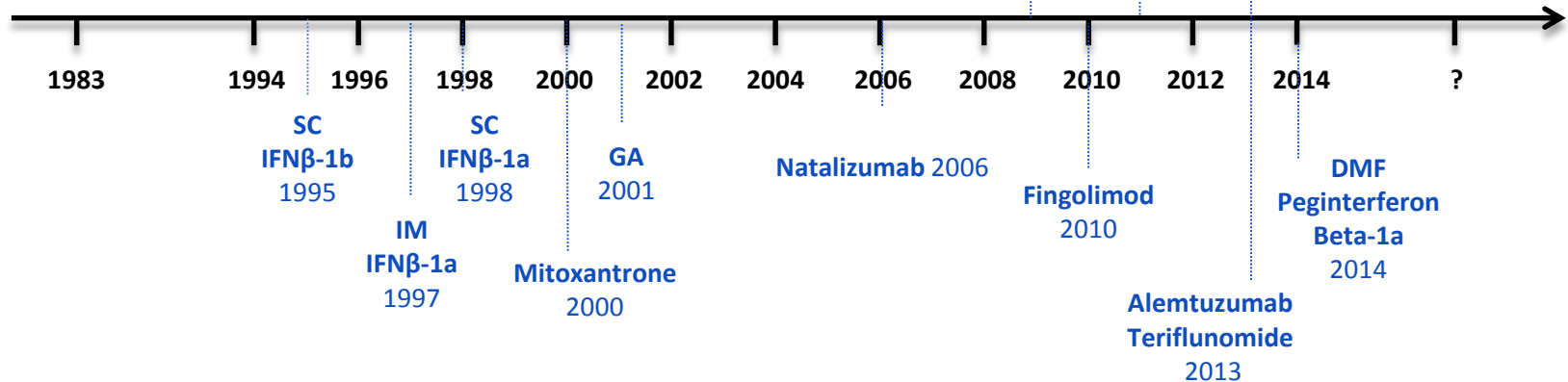
Stop Disease Progression

Repair

No Evidence of Disease Activity
(NEDA)⁶
2009

Sustained
improvement⁷
2011

Introduction of RRMS
Therapies in the EU



No Evidence of Disease Activity (NEDA)

Relapses

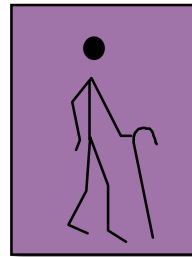
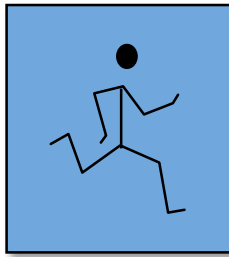
- No relapses



+

EDSS-progression

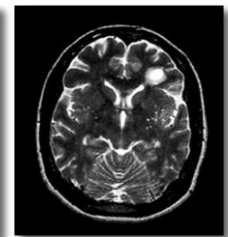
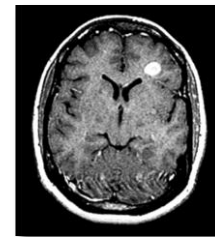
- No EDSS progression



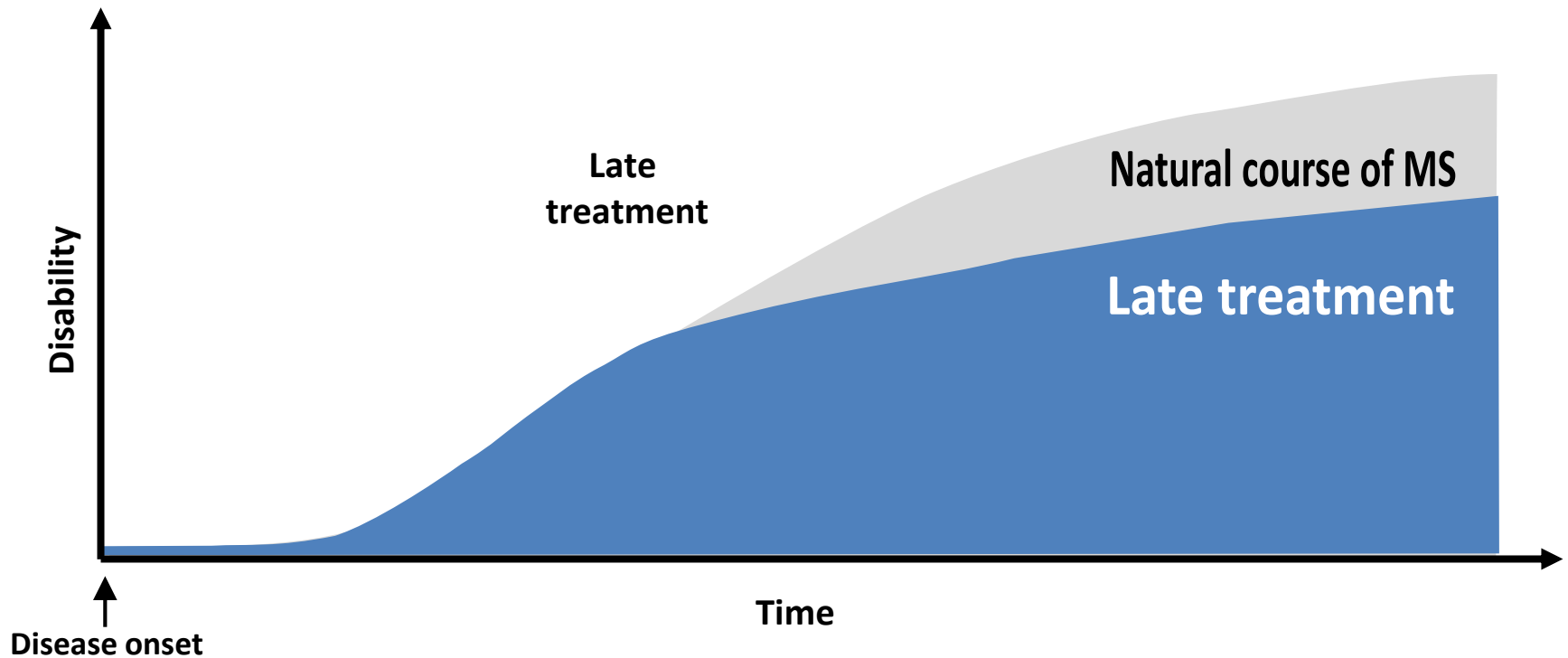
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MRI activity

- No new T2-lesions
- No new Gd+-lesions

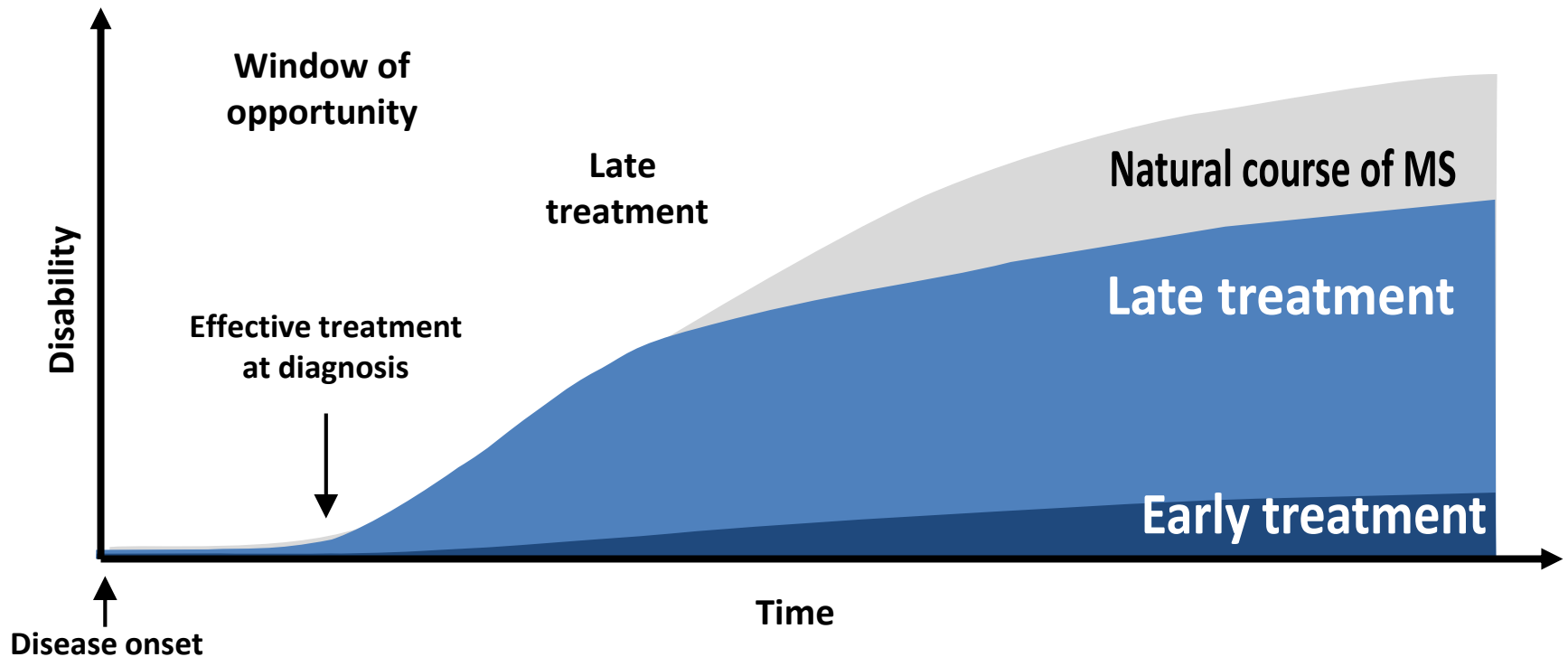


Early Treatment vs Later Treatment



Adapted from Miller JR. *J Manag Care Pharm.* 2004;10(suppl S-b):S4-S11.

Early Treatment vs Later Treatment



Adapted from Miller JR. *J Manag Care Pharm.* 2004;10(suppl S-b):S4-S11.

Summary

- MS is a serious disease, if untreated.
- Early and effective treatment can alter the prognosis.

"When you change the way you look at things,
the things you look at change."

Max Planck