Modern Management of Multiple Sclerosis

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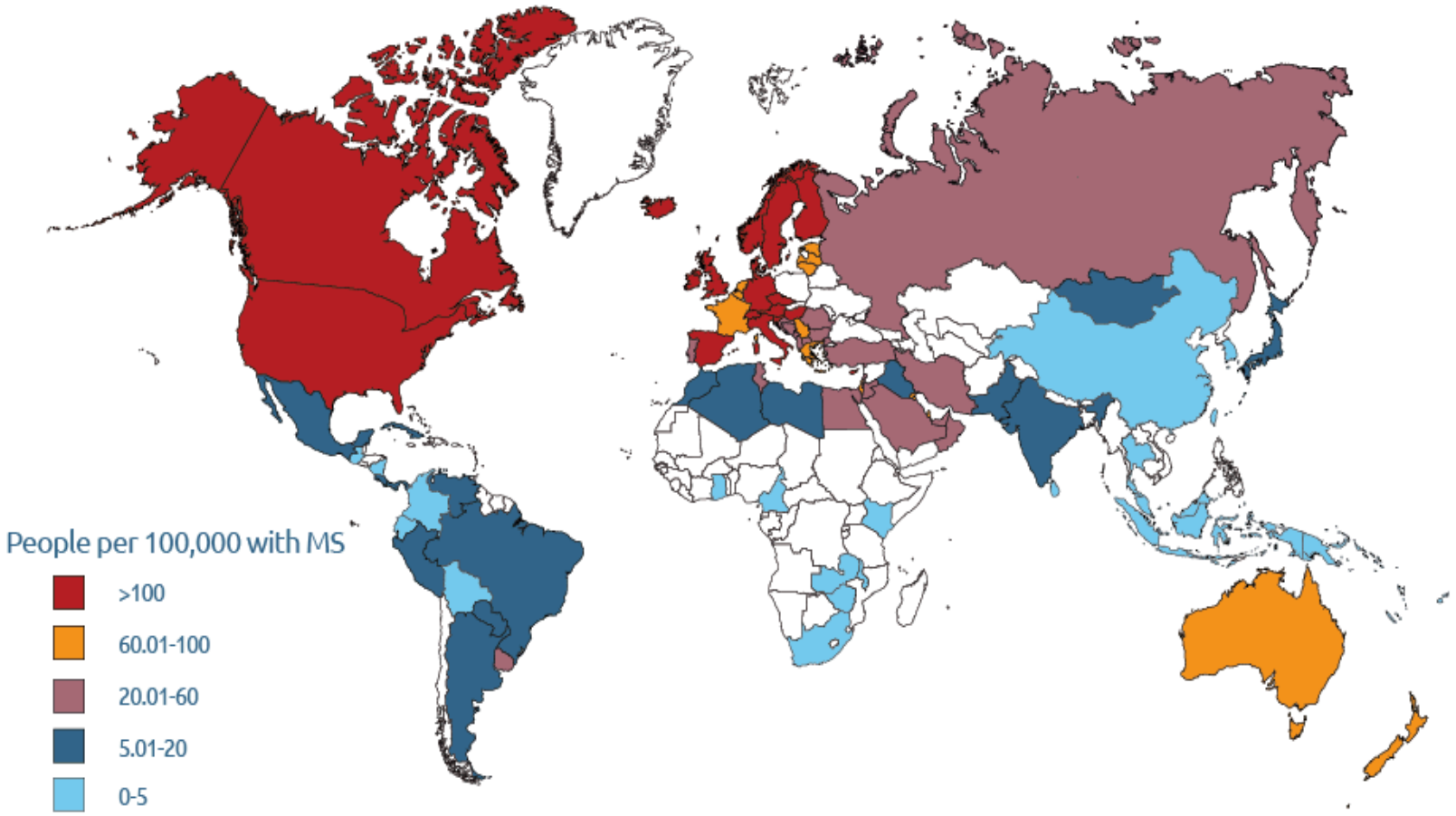
Faculty Disclosure

	No, nothing to disclose
√	Yes, please specify:

Company Name	*Honoraria/ Expenses*	*Consulting/ Advisory Board*	*Funded Research*	*Royalties/ Patent*	*Stock Options*	*Ownership/ Equity Position*	*Employee*	*Other (please specify)*
MedDay	X	X						
Biogen Idec (Optum Insight)	X	X						
Eisai	X	X						
Novartis	X	X						Lecturing
Teva	X							Lecturing
EXCEMED	X							Lecturing
SAGE Publications	X							Editor-in-Chief, Multiple Sclerosis Journal

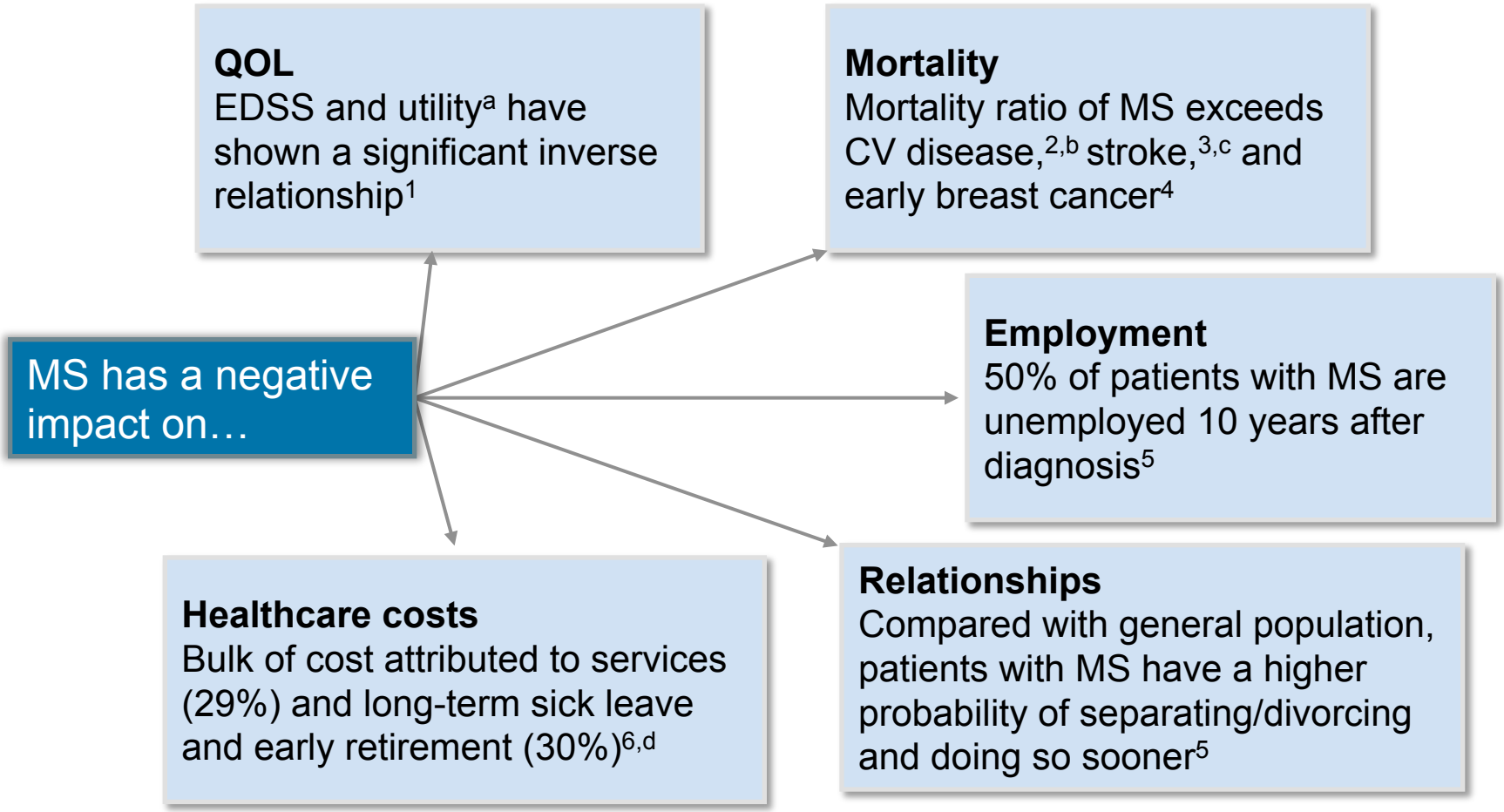
Prevalence of MS

2013 : 2.3 million



ms international federation

MS Is a Disabling Condition

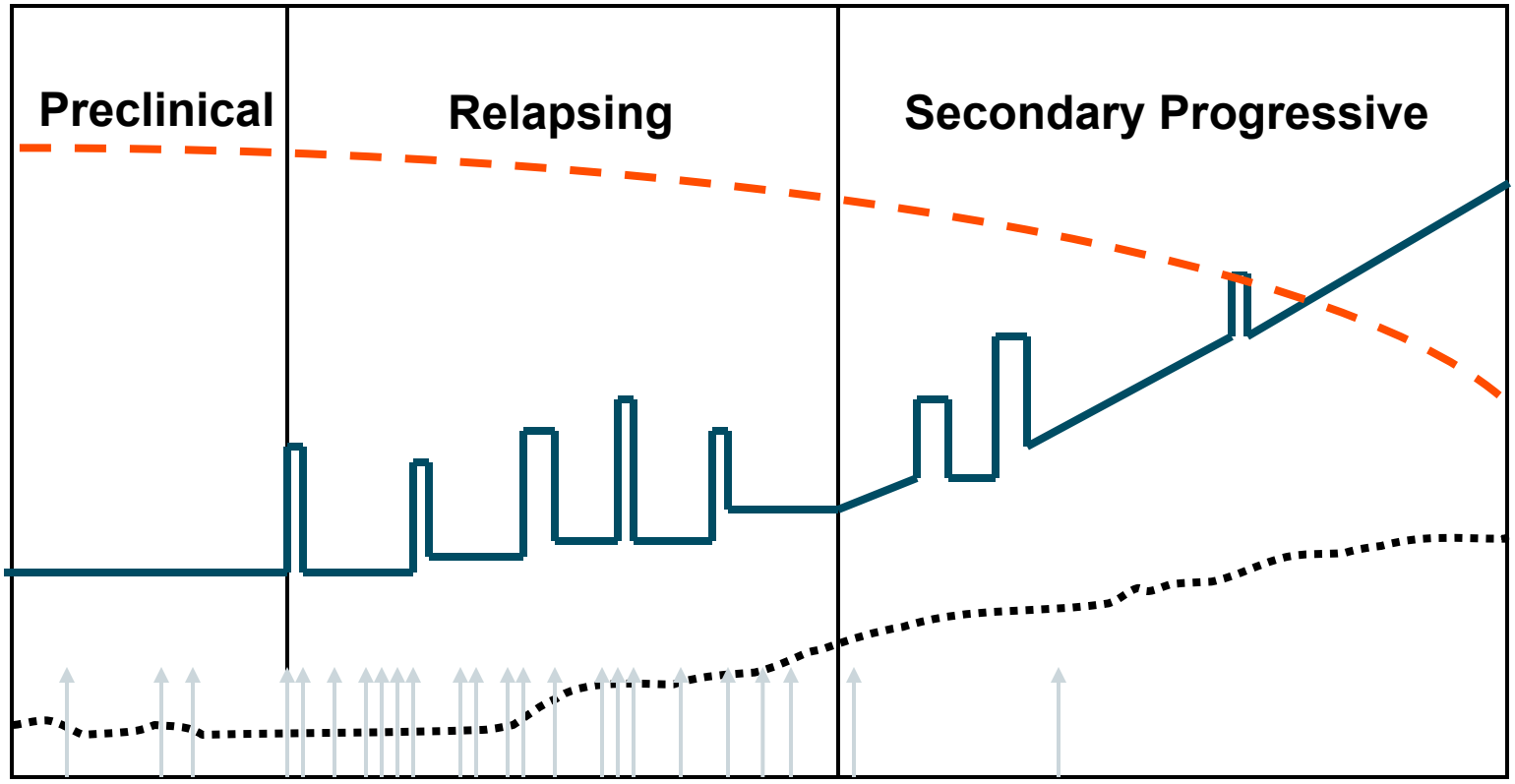


CV=cardiovascular; EQ-5D=EQ-5D=EuroQol 5-Dimension questionnaire.

1. Orme M et al. *Value Health*. 2007;10:54-60.
2. De Marco R et al. *Diabetes Care.* 1999;22:756-761.
3. Petty DW et al. *Mayo Clin Proc*. 2005;80:1001-1008.
4. Hooning MJ et a. *Int J Radiat Oncol Biol Phys.* 2006;64:1081-1091.
5. Pfleger CC et al. *Mult Scler*. 2010;16:121-126.
6. Berg J et al. *Eur J Health Econ*. 2006;7 (suppl 2):S75-S85.

a. Utility measures derived from EQ-5D
b. In patients with type 2 diabetes
c. In patients with valvular heart disease in Olmsted County, Minnesota
d. MS patients with EDSS ≥6.0

Natural History of MS



Recommended Diagnostic Criteria for Multiple Sclerosis: Guidelines from the International Panel on the Diagnosis of Multiple Sclerosis

W. Ian McDonald, FRCP,[1] Alistair Compston, FRCP,[2] Gilles Edan, MD,[3] Donald Goodkin,[4] Hans-Peter Hartung, MD,[5] Fred D. Lublin, MD,[6] Henry F. McFarland, MD,[7] Donald W. Paty, MD,[8] Chris H. Polman, MD,[9] Stephen C. Reingold, PhD,[10] Magnhild Sandberg-Wollheim, MD,[11] William Sibley, MD,[12] Alan Thompson, MD,[13] Stanley van den Noort, MD,[14] Brian Y. Weinshenker, MD,[15] and Jerry S. Wolinsky, MD[16]

Diagnostic Criteria for Multiple Sclerosis: 2005 Revisions to the "McDonald Criteria"

Chris H. Polman, MD, PhD,[1] Stephen C. Reingold, PhD,[2] Gilles Edan, MD,[3] Massimo Filippi, MD,[4] Hans-Peter Hartung, MD,[5] Ludwig Kappos, MD,[6] Fred D. Lublin, MD,[7] Luanne M. Metz, MD,[8] Henry F. McFarland, MD,[9] Paul W. O'Connor, MD,[10] Magnhild Sandberg-Wollheim, MD,[11] Alan J. Thompson, MD,[12] Brian G. Weinshenker, MD,[13] and Jerry S. Wolinsky, MD[14]

Diagnostic Criteria for Multiple Sclerosis: 2010 Revisions to the McDonald Criteria

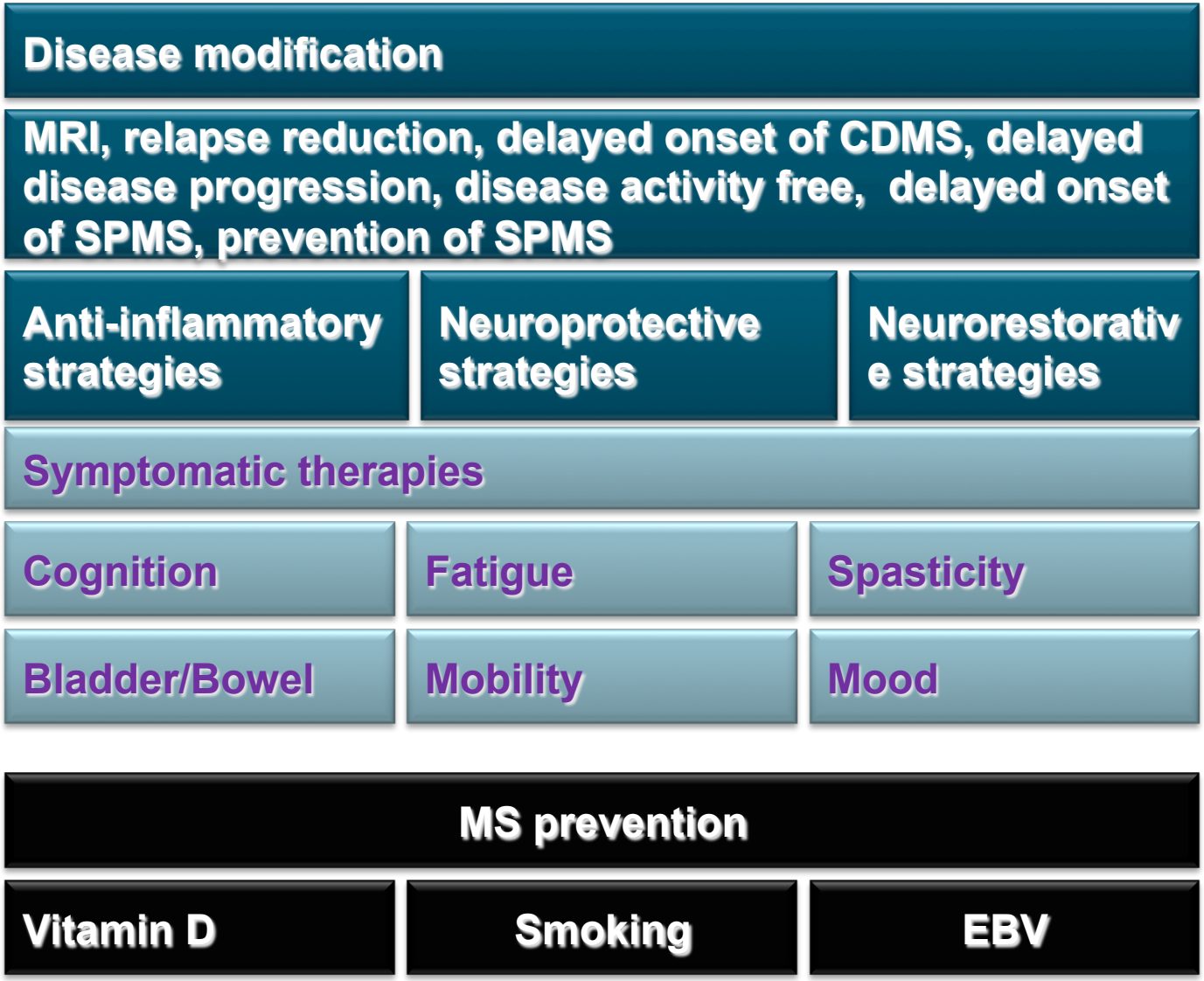
Chris H. Polman, MD, PhD,[1] Stephen C. Reingold, PhD,[2] Brenda Banwell, MD,[3] Michel Clanet, MD,[4] Jeffrey A. Cohen, MD,[5] Massimo Filippi, MD,[6] Kazuo Fujihara, MD,[7] Eva Havrdova, MD, PhD,[8] Michael Hutchinson, MD,[9] Ludwig Kappos, MD,[10] Fred D. Lublin, MD,[11] Xavier Montalban, MD,[12] Paul O'Connor, MD,[13] Magnhild Sandberg-Wollheim, MD, PhD,[14] Alan J. Thompson, MD,[15] Emmanuelle Waubant, MD, PhD,[16] Brian Weinshenker, MD,[17] and Jerry S. Wolinsky, MD[18]

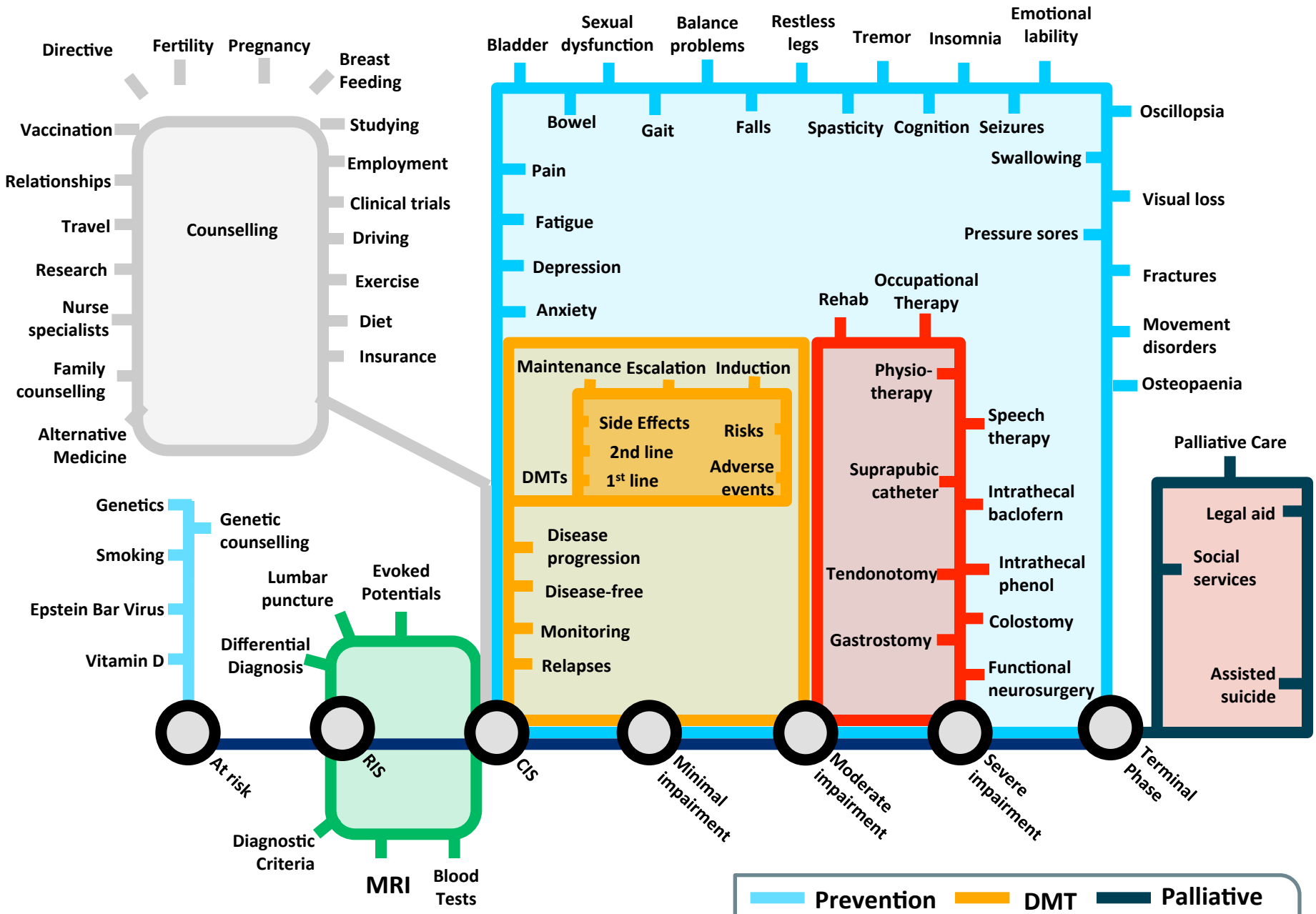
MS Survey of 1,500 people with MS in 2015

‘Survey reveals many people are misdiagnosed and live in uncertainty for years before MS diagnosis’

- **1 in 4 people with MS misdiagnosed with a trapped nerve**
- **1 in 10 people with MS told they’d had a stroke**
- **39% of people with MS waited over a year for diagnosis**
- **25% visit GP four or more times before referred**

The unmet need is massive





An holistic approach to MS

Guidelines in MS 2014 -15

- NICE guidelines
-
- NHS England

- Association of British Neurologists

The Practitioner September 2015 - 259 (1785):xx-xx

Early accurate diagnosis crucial in multiple sclerosis

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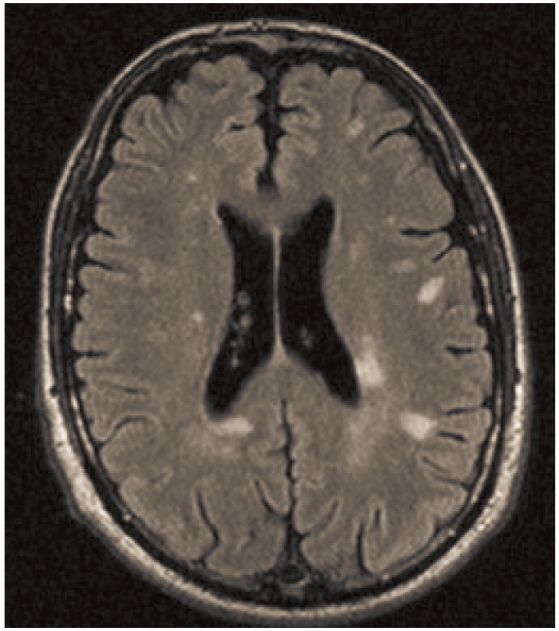


FIGURE 1
Axial FLAIR image that shows typical MS lesions: small and ovoid hyperintensities in T2-weighted sequences. Here they are located in the periventricular white matter and juxtacortical white matter

What are the different types of MS?

How should MS be diagnosed?

What are the management approaches?

MULTIPLE SCLEROSIS (MS) IS AN INFLAMMATORY-DEMYELINATING DISEASE OF THE CNS.

It is the most frequent disabling neurological disease among young adults, affecting around 2.3 million people worldwide.[1] Around 100,000 people[2] in the UK have MS, giving an average prevalence of 1.5/1,000 (varying from 1.2/1,000 in England and Wales to 1.9/1,000 in Scotland).[3]

In about 85% of cases, MS starts with an acute neurological episode, a clinically isolated syndrome (CIS), considered to be the first clinical episode of relapsing-remitting MS (RRMS). It is characterised by the presence of acute relapses, after which there is normally a good functional recovery.[4]

About 15-20 years after symptom onset, most patients develop secondary progressive MS (SPMS), characterised by a gradual and irreversible neurological decline.[5] Although relapses can still be present in SPMS, the accrual of disability is typically independent of any relapses. In about 15% of cases, MS starts with progressive neurological deterioration, i.e. primary progressive MS (PPMS).[6]

MS affects women more frequently than men, with a ratio of 2-3:1.[7,8] Age at disease onset varies depending on the type of MS. In RRMS the disease generally starts in the late 20s. Symptom onset in those with PPMS occurs around the age of 40.[5,8] Once progression starts, the overall rate of neurological decline is similar for both SPMS and PPMS. Yet this progression rate may vary greatly between individuals and predicting which patients will follow a more rapid accrual of disability is still a challenge.

Recently, the International Advisory Committee on Clinical Trials of MS has re-examined the MS disease phenotypes.[9] Although the main phenotype categories have not changed, these are now described in terms of the amount of disease activity observed, either inflammatory activity, i.e. presence of relapses and/or active lesions on MRI or neurodegenerative activity, i.e. disease progression. The goal of treatment in MS should be to prevent all disease activity.

The cause of MS is unknown. It is believed that a combination of risk factors can trigger an autoimmune response against the CNS leading to the development of MS. Risk factors can be either genetic or environmental and»

Management

Education

Treatment & monitoring

- Disease-modifying treatments (DMD)
  - Treatment of relapses
  - Symptomatic treatment

Multidisciplinary approach

Self-management

Management : Education

Education should **aim** at:

•Improving the understanding of the disease

•Increasing the knowledge about healthy lifestyles and their consequences

•Increasing awareness of noxious factors such as smoking

•Promoting patients' empowerment

Management: Multidisciplinary approach

- Comprehensive annual assessments

- Focused on:
  - Mobility, balance, and falls
  - Mobility aids including wheelchair assessments
  - Use of arms and hands
  - Muscle spams and stiffness

- Healthcare professionals involved
  - Consultant neurologists
  - MS nurses
  - Physiotherapists, occupational therapists, speech and language therapists, and continent nurses
  - Psychologists and social care specialists
  - Dieticians

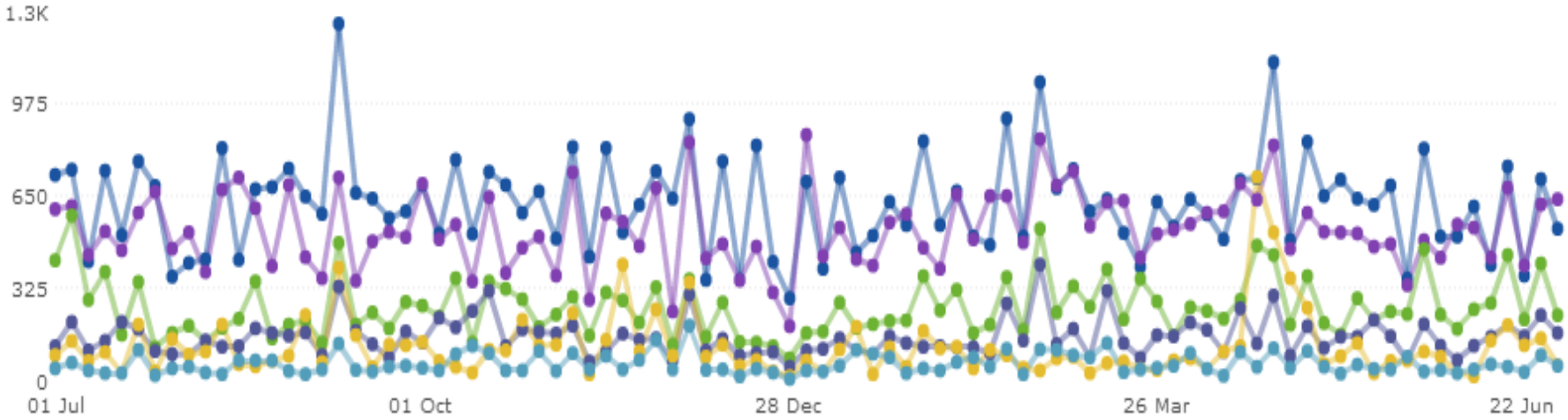
Management: Self-management

- Patients are aware of their condition and their symptoms
- Patients can adopt self-management strategies to solve day-to-day issues and gain independence
- Patients are at the centre of all decision-making processes
- Important decisions include
  - Healthy lifestyle
  - Start of treatment and compliance
  - Stop of treatment
  - Pregnancy and other family-related decisions

Dimensions of Wellness

The dimensions of wellness act and interact in ways that contribute to well-being.
They are influenced by health and other factors and involve lifestyle behaviors and activities

Top Traditional & Social Media Topics July 2014- June 2015



35.5% symptoms
230,511 mentions

30.4% wellness
197,051 mentions

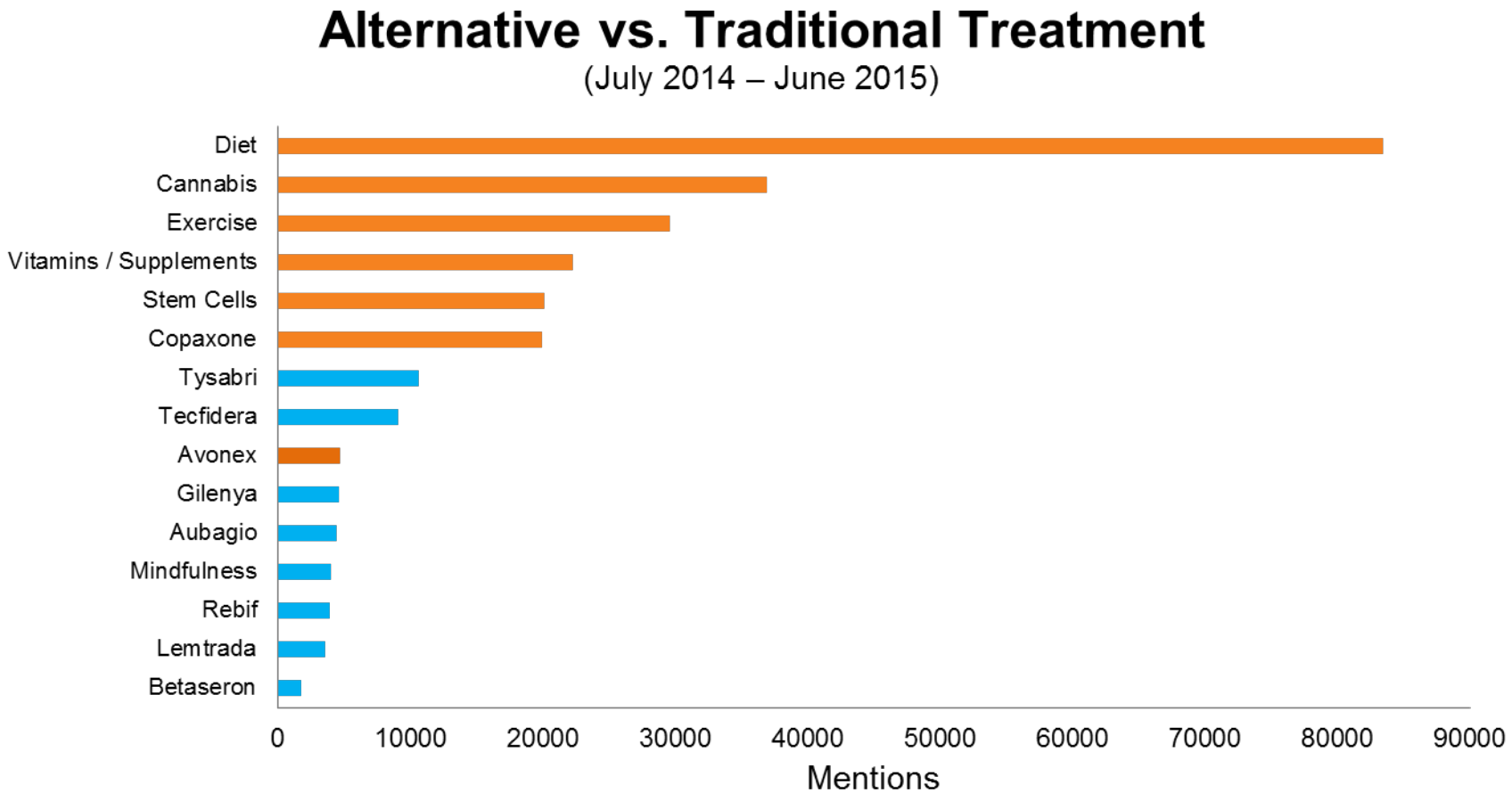
14.8% diagnosis
95,905 mentions

8.9% providers
57,680 mentions

6.9% medication
44,881 mentions

3.5% insurance
22,794 mentions

Social Media Wellness Themes



Current Wellness Evidence
Diet, Exercise and Mood Interventions

- Insufficient evidence to establish efficacy or effectiveness in MS
  - Specific diets
  - Dietary supplements
    - Vitamin D
    - PUFA's
  - Specific exercise program
  - Mindfulness or other practices to reduce stress or depressive symptoms.
- Poor identification of depressive symptoms and major depressive disorder

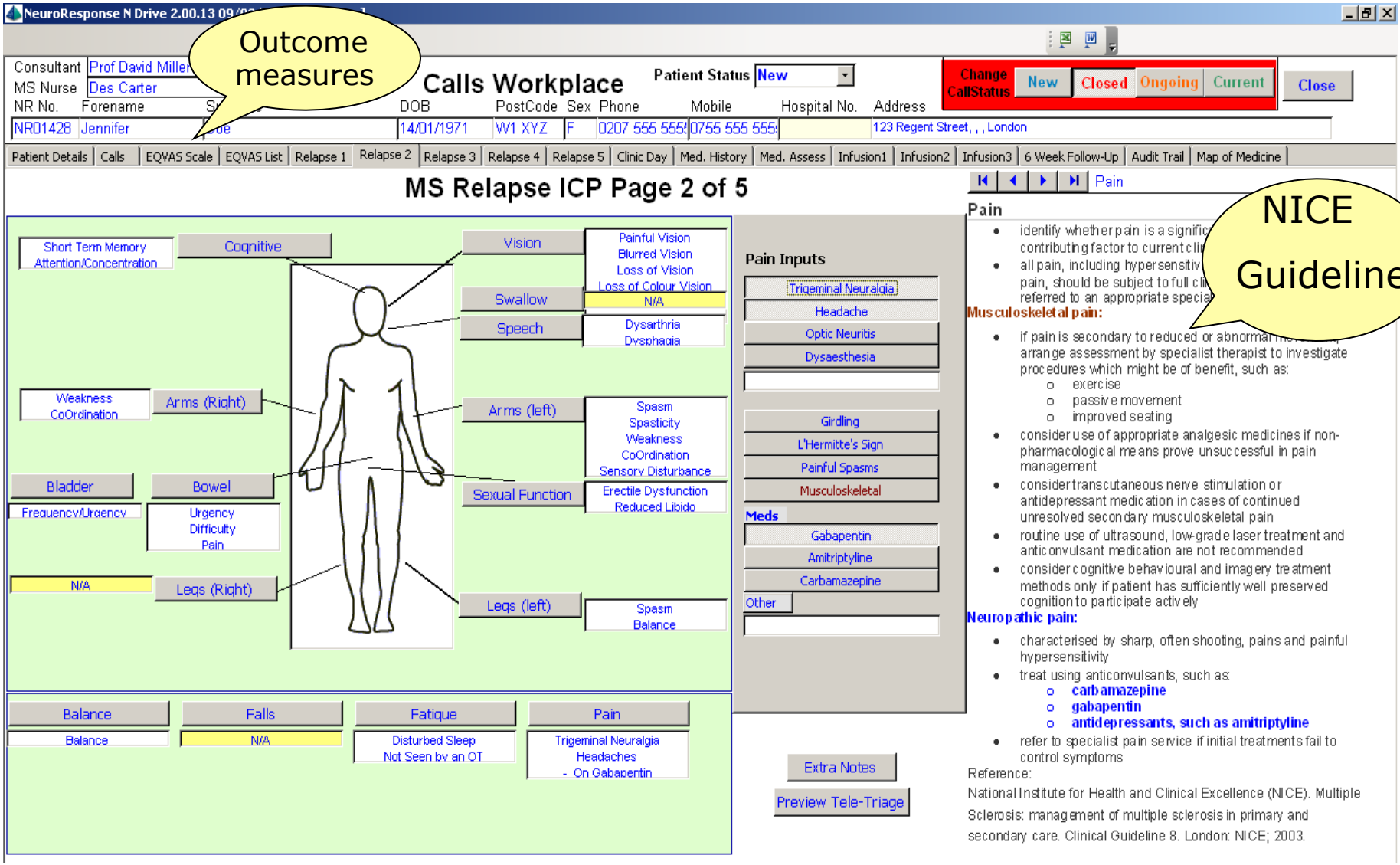
HEALTHCARE WITHOUT WALLS

NeuroDirect

NeuroView

NeuroMail

Integrated Care Pathway



Key Elements of Self Management

1. Electronic Health Records

2. Goal Orientated Care Plan

3. Motivational coaching

OptiMiSe Vision

- Own electronic records
- Goal orientated care plan
- Information & Evidence
- Ability to self-assess
- Ability to Benchmark to Peers
- Access to Motivational Coach

Therapeutic era of Multiple Sclerosis

- 1993 - First positive trial of therapeutic agent
- 1998 - Four agents available - reduce relapse rate
- 2004 - Second line agent licensed for more aggressive MS
- 2005 - Withdrawn because of serious side-effect
- 2006 - Reintroduced
- 2010 - First oral agent licensed
- 2015 – 12 treatments

Early treatment seems to be desirable

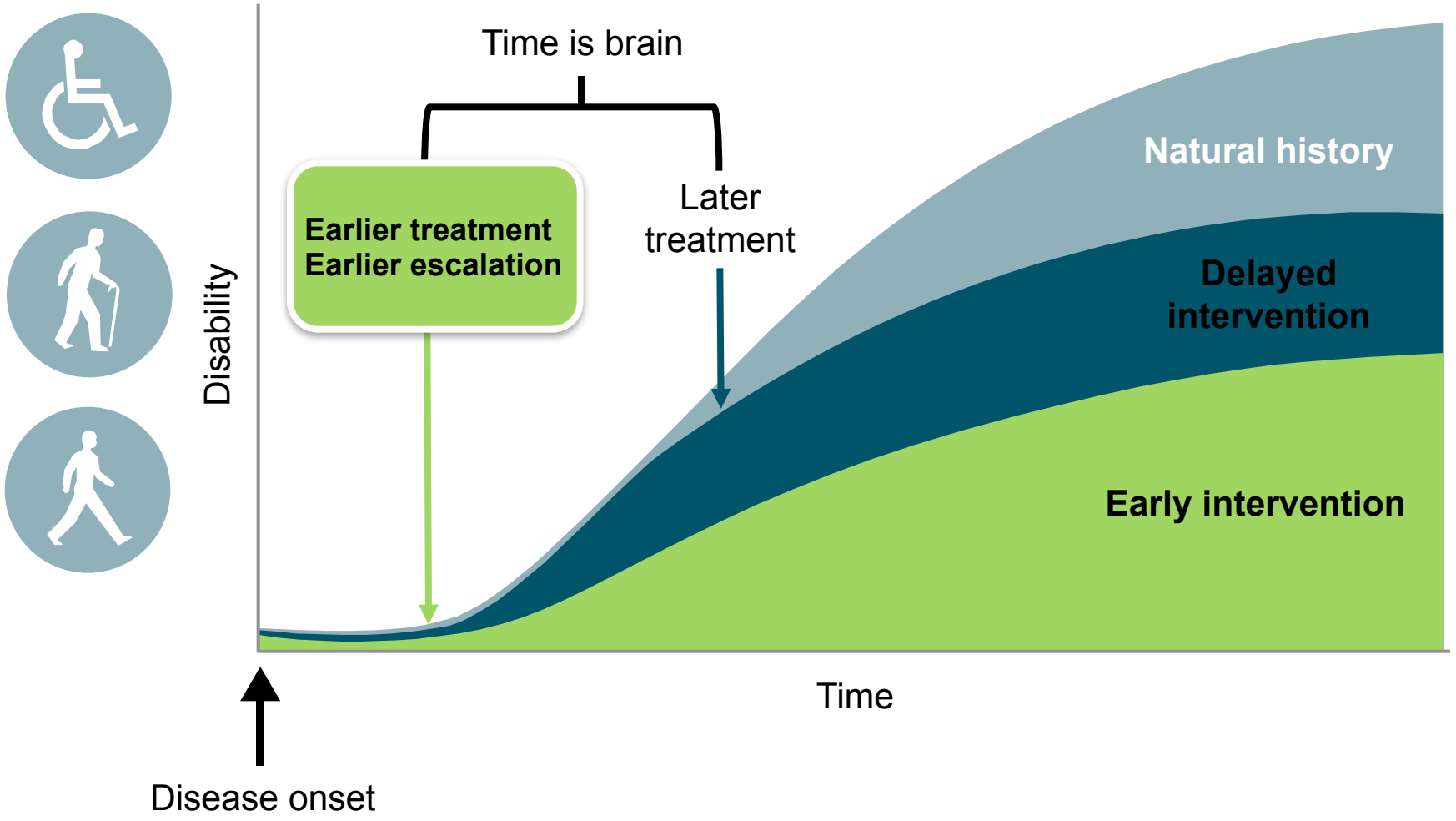


Figure: http://multiple-sclerosis-research.blogspot.co.uk/2012/06/research-dmt-slow-onset-of-progression.html Accessed 4 June 2013. Based on a review of Bergamaschi R *et al. Mult Scler* 2012

Brain health

Time matters in multiple sclerosis

Gavin Giovannoni
Helmut Butzkueven
Suhayl Dhib-Jalbut
Jeremy Hobart
Gisela Kobelt
George Pepper
Maria Pia Sormani
Christoph Thalheim
Anthony Traboulsee
Timothy Vollmer

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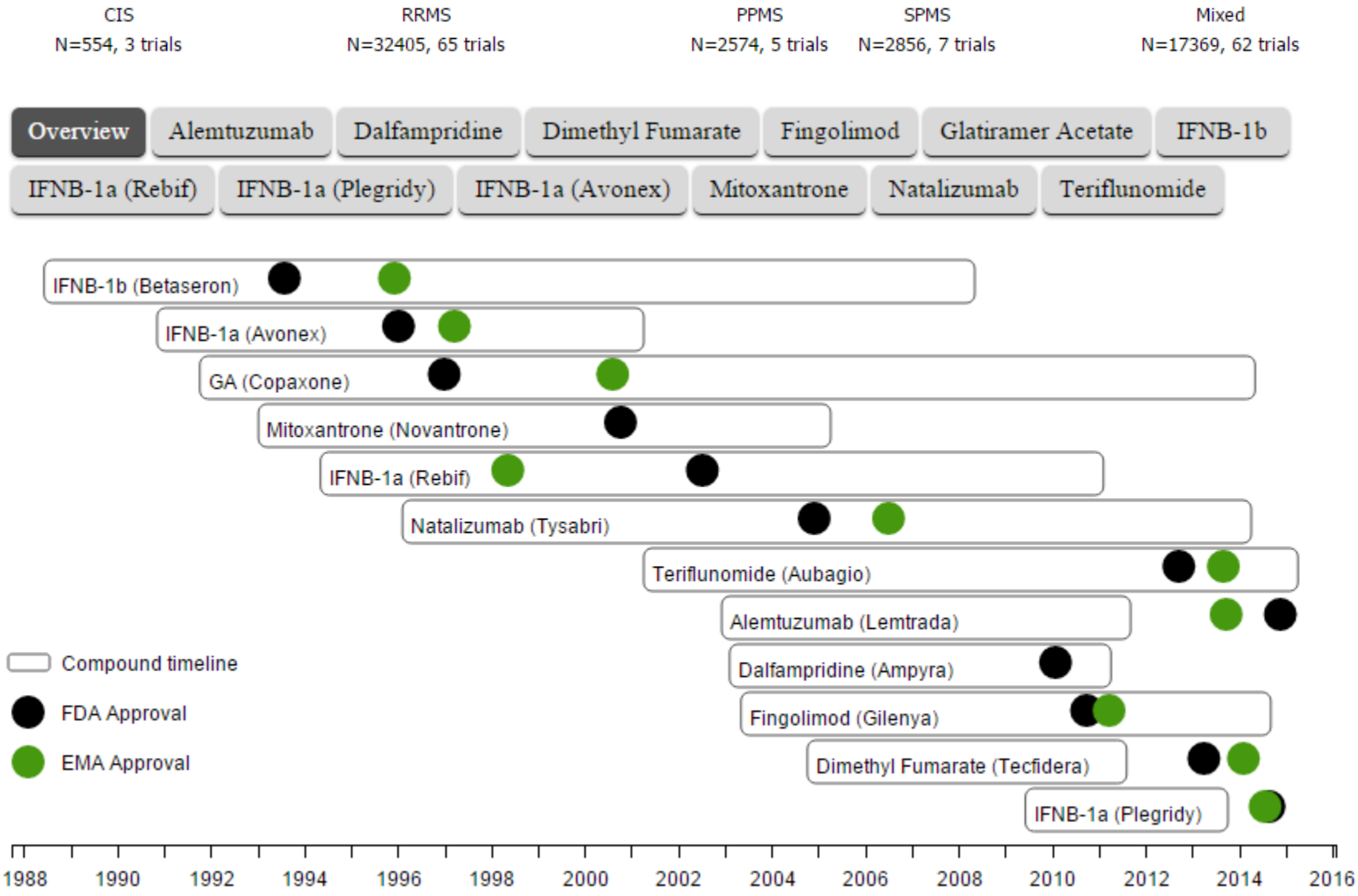
DRUGS LICENCED TO TREAT RELAPSING MS

ON THE WAY.....

- ✓ Interferon beta 1a s.c.
- ✓ Interferon beta 1 a pegylated
- ✓ Interferon beta 1b s.c.
- ✓ Interferon beta 1a i.m.
- ✓ Glatiramer acetate 40 tiw
- ✓ Mitoxantrone
- ✓ Natalizumab
- ✓ Fingolimod
- ✓ Teriflunomide
- ✓ DMF
- ✓ Alemtuzumab
- ✓ Daclizumab

Timeline of MS Treatment Approvals



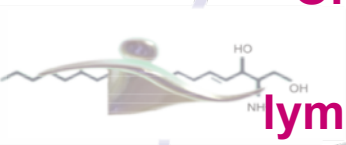
Treatment

Treatment & monitoring – DMD: First-line treatments

Drug, administration route	Reduction (%) in clinical activity (relapses) in clinical trials		Main side effects	Recommended safety monitoring
	Vs. placebo	Vs. first-line DMD		
Beta-interferon, SC or IM	30%	NA	-Flu-like symptoms -Mild-moderate lymphopenia -Elevated liver enzymes -Hypersensitivity	-Regular blood tests -Regular brain MRI scans
Glatiramer acetate, SC	30%	NA	-Immediate post-injection reaction -Local injection-site skin reaction -Hypersensitivity	-Regular brain MRI scans
Dimethyl fumarate, oral	45-50%	22%	-Flushing -Gastrointestinal events -Lymphopenia -Elevated liver enzymes	-Regular blood tests -Regular brain MRI scans
Teriflunomide, oral	40-50%	No proved superiority of teriflunomide vs. SC beta-interferon	-Hair loss -Elevated liver enzymes -Leukopenia -Peripheral neuropathy -Elevated blood pressure	-Regular blood tests -Regular brain MRI scans

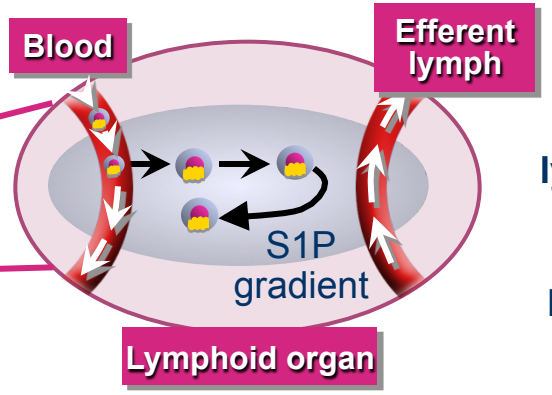
Oral fingolimod – mechanism of action

Neural cells express S1P receptors known to modulate neuropathological processes relevant to MS



Oral fingolimod modulates S1P receptors on lymphocytes and neural cells

It targets MS via actions in both the immune system and CNS



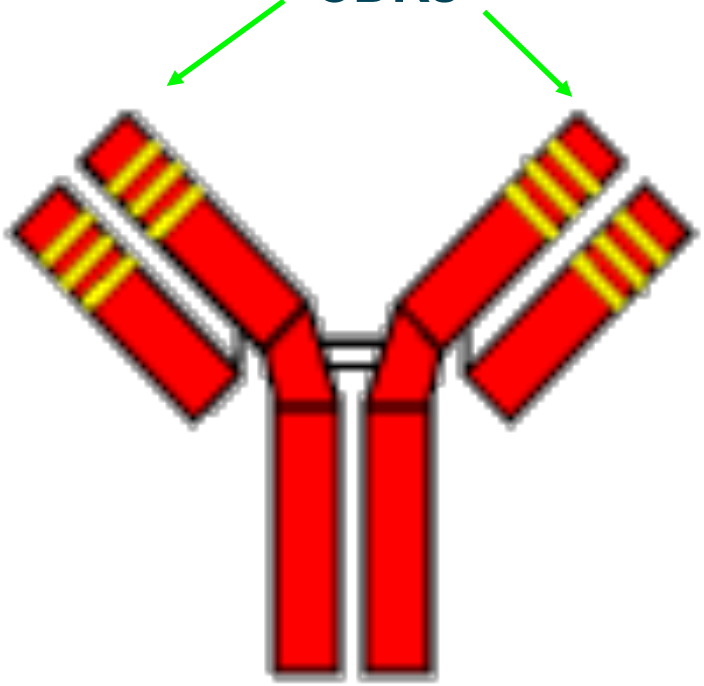
Autoaggressive lymphocytes remain in the lymph nodes, away from the CNS → reversible REDISTRIBUTION, not depletion

CNS, central nervous system; MS, multiple sclerosis; S1P, sphingosine 1-phosphate

Natalizumab: A Humanized, Monoclonal Antibody (mAb) Against α4 Integrins

Complementarity-Determining Regions

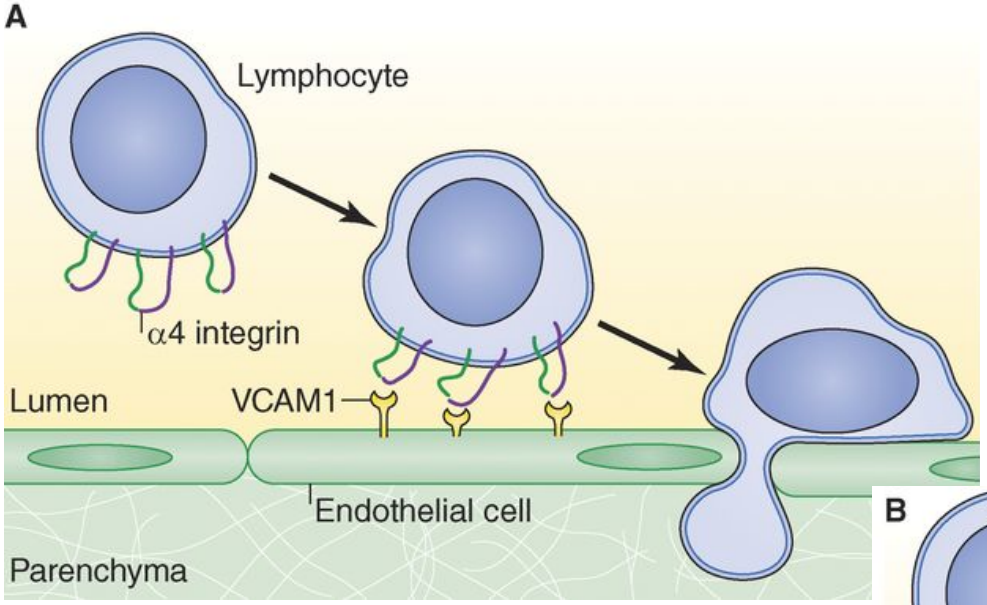
CDRs

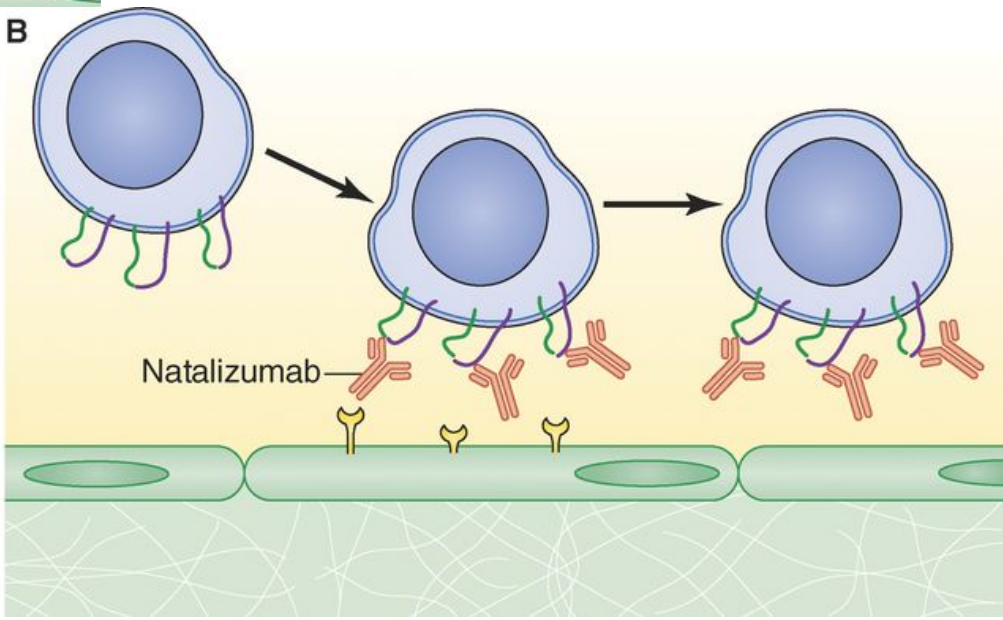


Framework

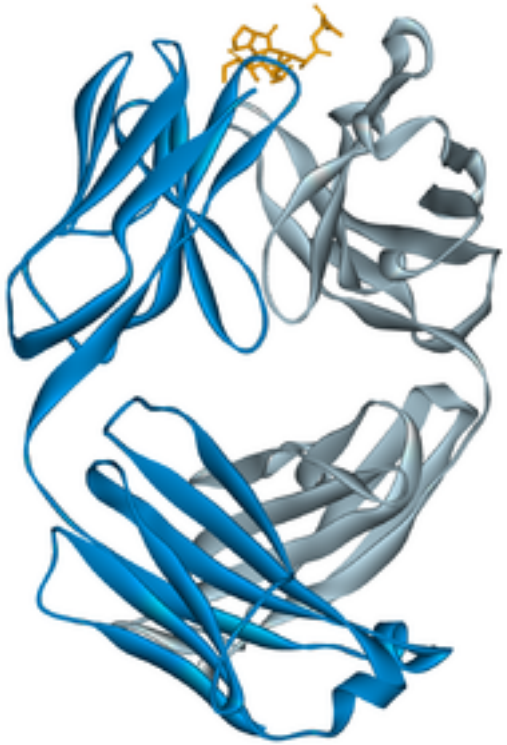
- **CDR grafted from murine Ab**
- **Human IgG4 framework**
- **Retains full potency**

NATALIZUMAB





Alemtuzumab



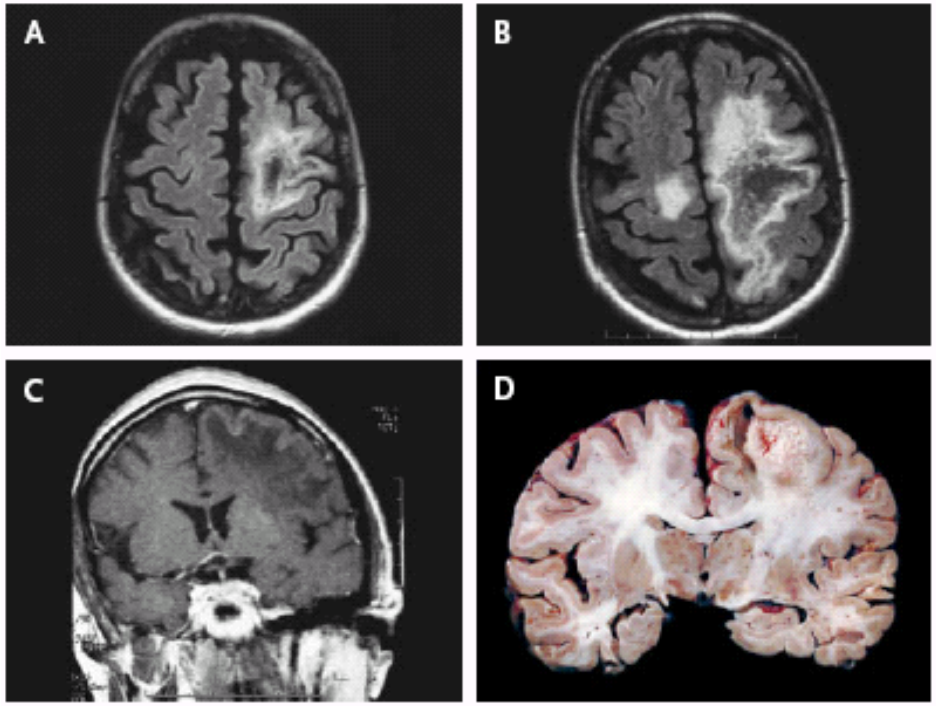
Treatment

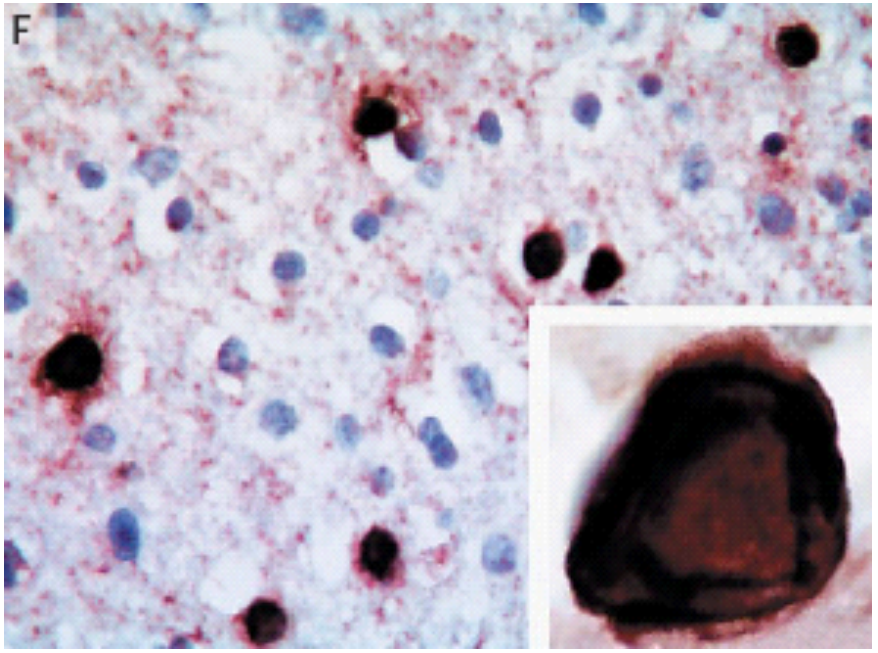
Treatment & monitoring – DMD: Second-line treatments

Drug, administration route	Reduction (%) in clinical activity (relapses) in clinical trials		Main side effects	Recommended safety monitoring
	Vs. placebo	Vs. first-line DMD		
Fingolimod, oral	55-60%	51-52%	-Bradycardia and other heart conduction abnormalities -Lymphopenia -Macular oedema -Elevated liver enzymes -Elevated blood pressure	-Regular blood tests -Regular brain MRI scans -Continuous ECG monitoring during first 6 hours after first dose -OCT exam -Vaccination against VVZ is recommended before starting fingolimod treatment
Natalizumab, IV	68%	NA	-Perfusion reaction (nausea, vomiting, generally mild) -Hypersensitivity -Immunogenicity (antibodies against natalizumab) -Infections, including PML -Elevated lymphocyte count in peripheral blood	-Regular blood tests -Regular brain MRI scans (i.e. every year or more frequently, every 6 or 3 months, if high risk of PML)
Alemtuzumab, IV	NA	55%	-Perfusion reaction (marked) -Marked lymphopenia -Infections -Secondary autoimmunity	-Regular blood tests -Regular urine tests -Regular brain MRI scans

PML in association with Natalizumab

Cells with inclusions have positive nuclear signal for JC virus



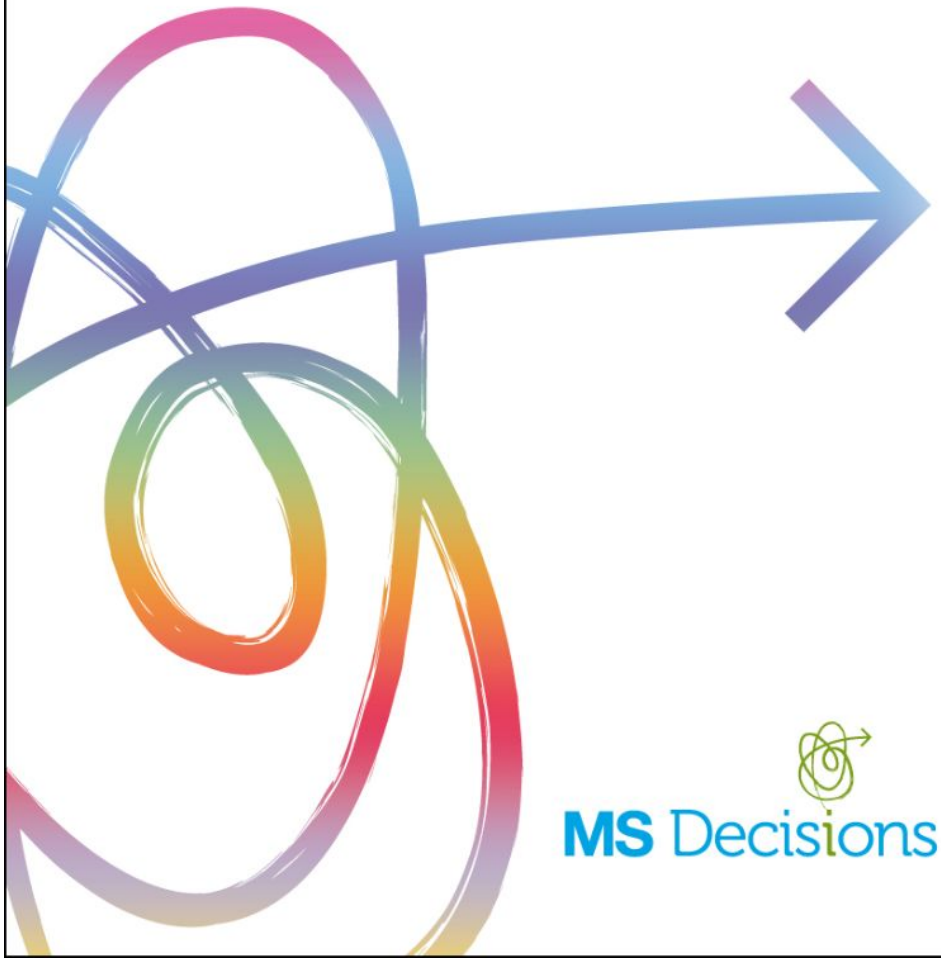


Disease modifying drugs

a guide to treatments for relapsing MS

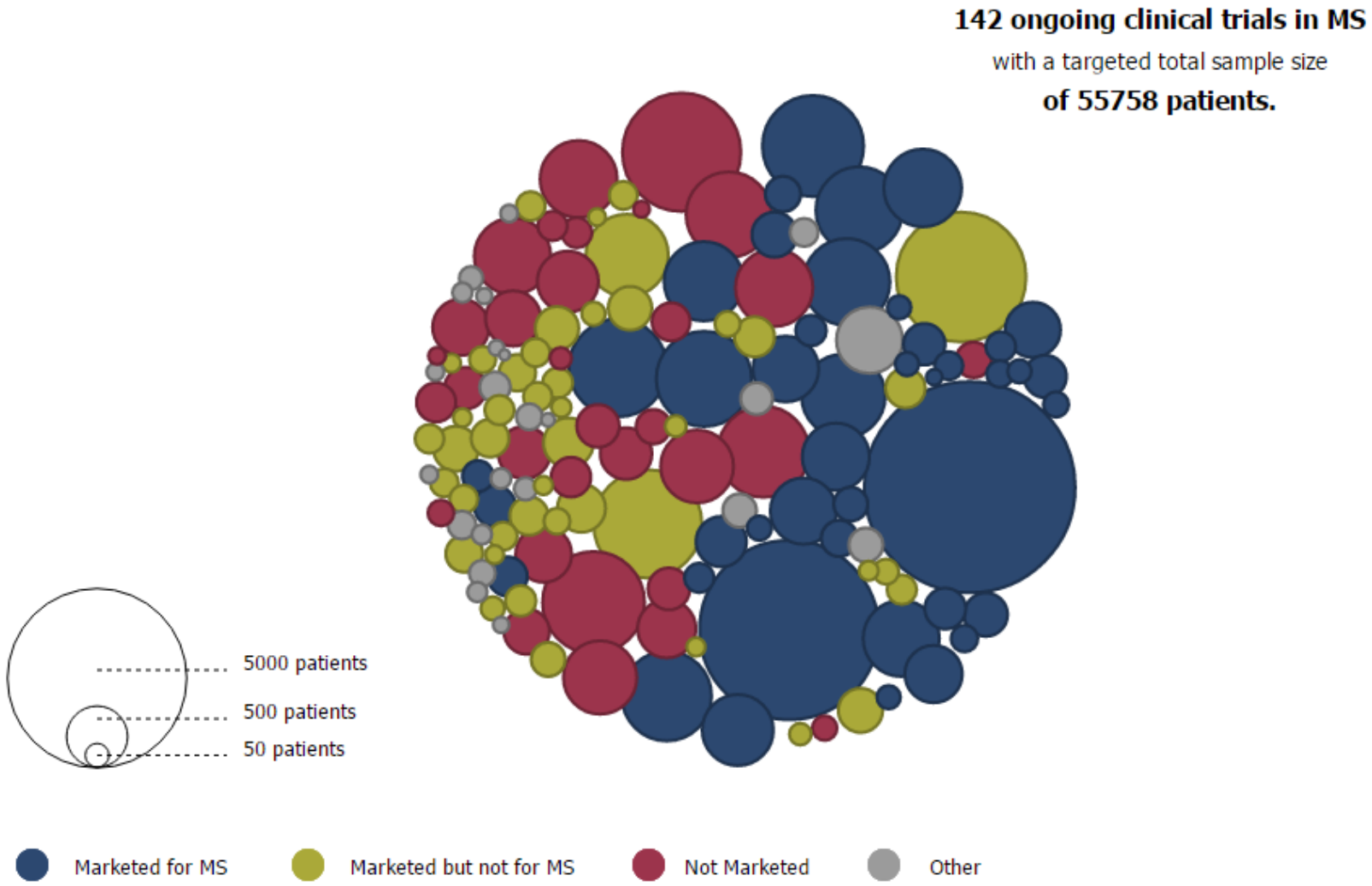
Multiple Sclerosis Trust

MS



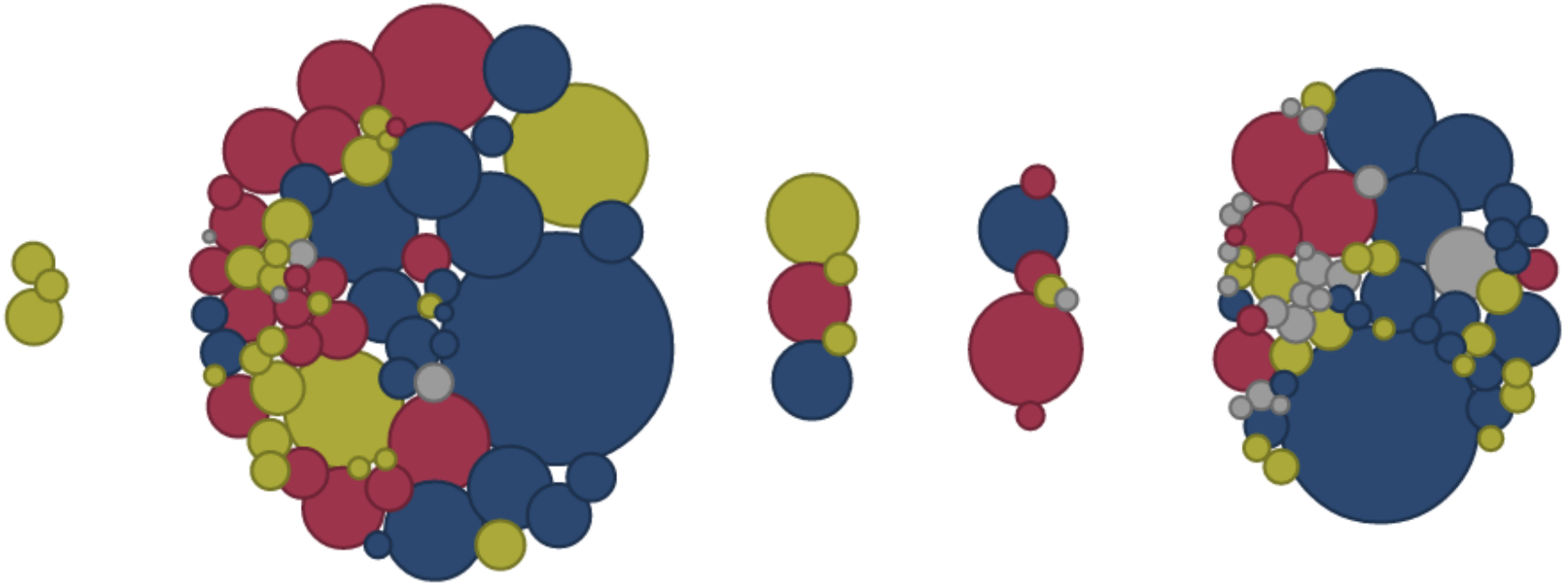
MS Decisions

Visual Map of MS Clinical Trials



MS Trials by Patient Population

CIS	RRMS	PPMS	SPMS	Mixed
N=554, 3 trials	N=32405, 65 trials	N=2574, 5 trials	N=2856, 7 trials	N=17369, 62 trials



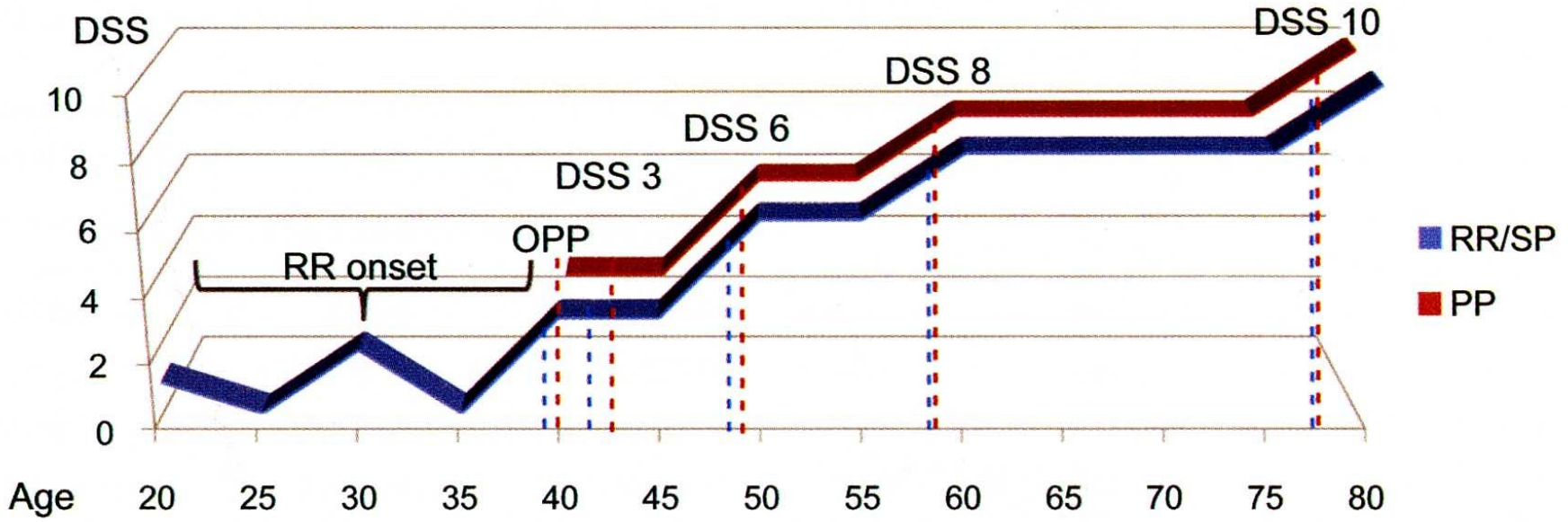
Despite the identified need for more clinical trials in PPMS and SPMS, RRMS remains the main focus for the Pharma industry.

Marketed for MS Marketed but not for MS Not Marketed Other

Urgent need to find solutions for people with Progressive MS

- Large worldwide impact: at least half of all (2.3million) MS patients
- Currently no effective treatment for progressive MS
- Onset of progression is the main determimant of disability
- Finding treatments for progressive MS is one of the top priorities for patients
- Every time another therapy is approved for RRMS, a large proportion of our constituents feel left out

Figure 2 Ages at attainment of disability endpoints according to type of disease course



Age at	OPP	*p*	DSS 3	*p*	DSS 6	*p*	DSS 8	*p*	DSS 10	*p*
RR/SP	40.2 (39)	0.09	41.6 (41)	0.82	49.7 (48)	0.05	59.2 (58)	0.44	76.1 (78)	0.63
PP	38.6 (40)		42.3 (43)		48.0 (49)		58.4 (58)		73.8 (78)	

Onset of progressive phase determines disability

Scalfari et al Neurology 2011

Challenges

- **Defining phenotype**
- Clarifying pathological mechanisms underpinning progression
- Identifying treatment targets
- Outcomes/Biomarkers
- Trial design

Defining the clinical course of multiple sclerosis

The 2013 revisions

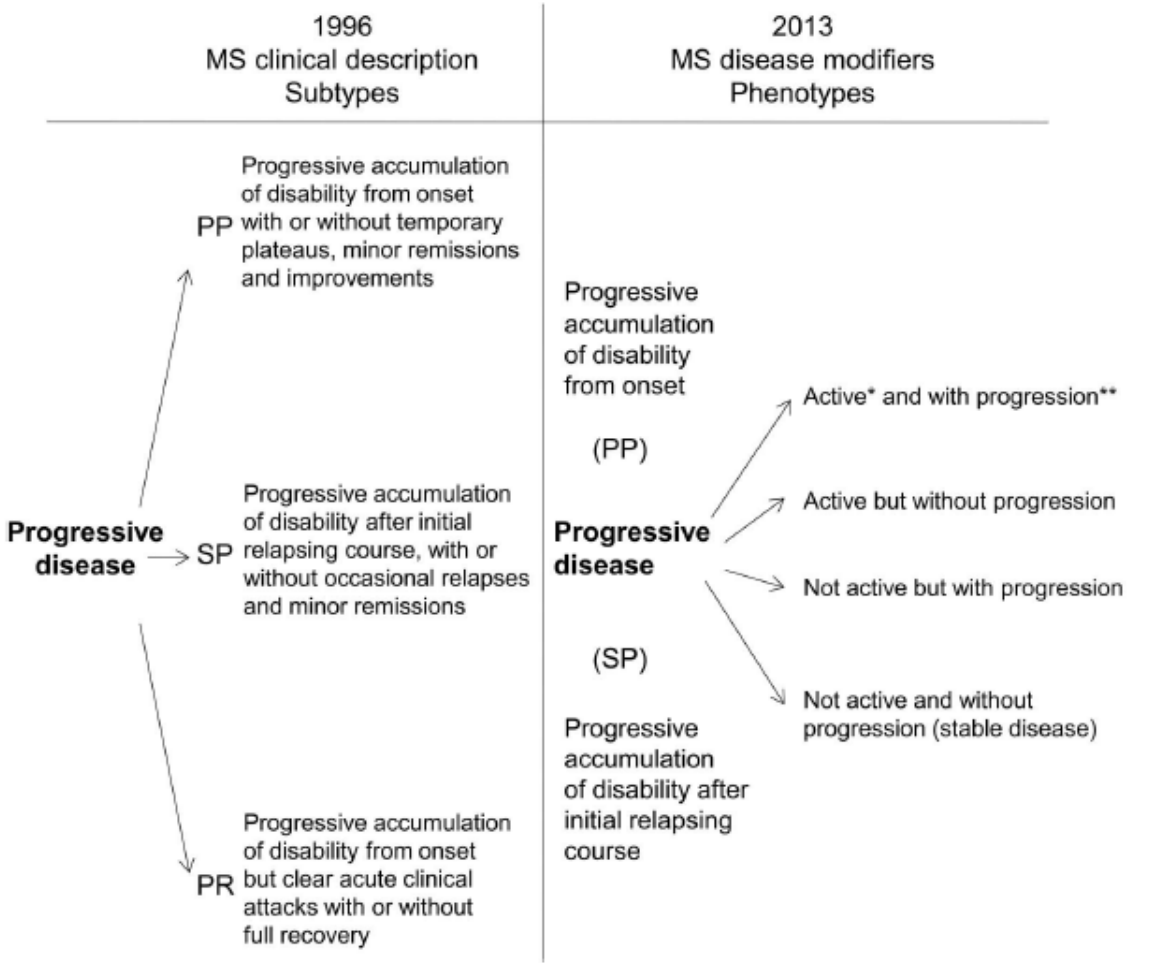
OPEN

Fred D. Lublin, MD
Stephen C. Reingold, PhD
Jeffrey A. Cohen, MD
Gary R. Cutter, PhD
Per Soelberg Sørensen, MD, DMSc
Alan J. Thompson, MD

Neurology® 2014;83:278-286

MS Clinical Forms: revised classification

Figure 2 The 1996 vs 2013 multiple sclerosis phenotype descriptions for progressive disease



*Activity determined by clinical relapses assessed at least annually and/or MRI activity (contrast-enhancing lesions; new and unequivocally enlarging T2 lesions). **Progression measured by clinical evaluation, assessed at least annually. If assessments are not available, activity and progression are "indeterminate." MS = multiple sclerosis; PP = primary progressive; PR = progressive relapsing; SP = secondary progressive.

Lublin FD et al. Neurology. 2014;83:1-9.

Trials in Progressive MS

Phase II
–MS STAT – high dose simvastatin
–PROXIMUS Trial - oxcarbazepine in SPMS
–MS Smart Trial – riluzole, amiloride, fluoxetine in SPMS
–SPRINT-MS – ibudilast in PPMS/SPMS
–Biotin in SP/PP MS

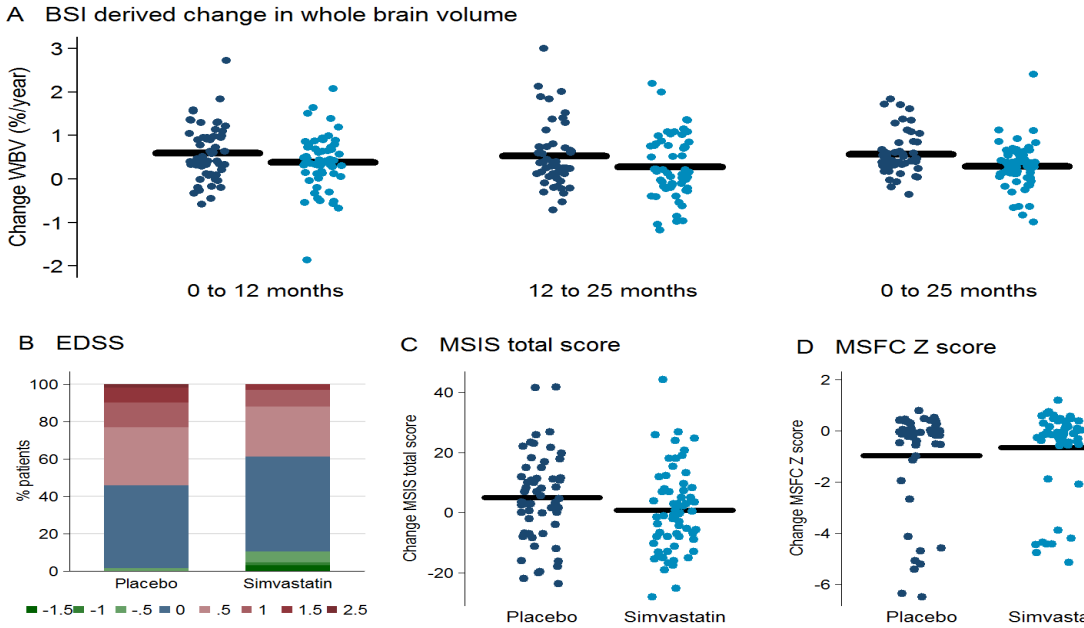
Phase III
–INFORMS – fingolimod in PPMS
–ASCEND – natalizumab in SPMS
–ORATORIO – ocrelizumab (related to rituximab) in PPMS
–EXPAND – siponimod (related to fingolmod) in SPMS
–ARPEGIO – laquinimod in PPMS

Others

Rituximab, mesenchymal stem cells, mastitinib, lipoic acid, erythropoietin, hydroxyurea, idebenone, minocycline, anti-nogo, anti-lingo

Simvastatin trial in secondary progressive MS

- Placebo-controlled, 2-year trial
- 70 patients/arm (simvastatin 80mg/day or placebo)
- 42% ↓rate of brain atrophy in simvastatin-treated patients (0.30% vs. 0.59% per year)
- No effect on relapses or new T2 lesions

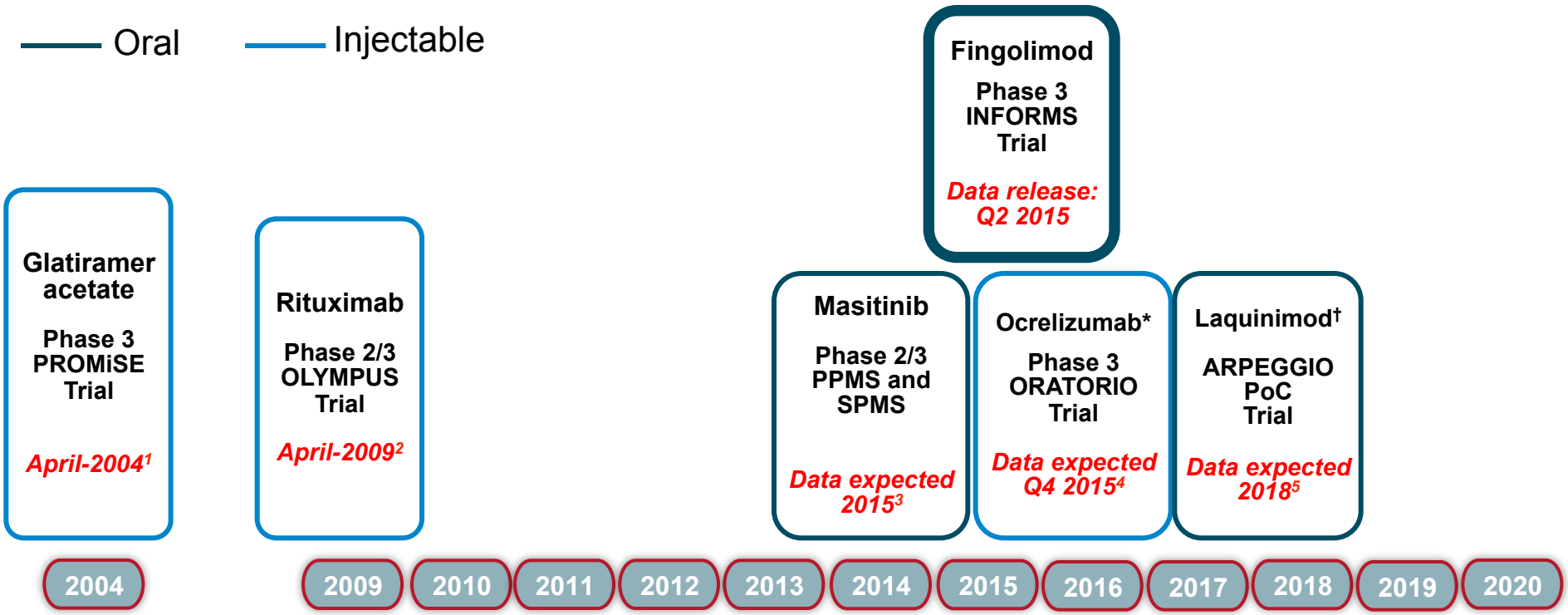


Mechanism of action?

Chataway et al, Lancet 2014; 383; 2113-21

Key PPMS clinical trials

Completed, ongoing and planned trials in primary progressive MS (PPMS)



- PROMiSE (N=943) and OLYMPUS (N=439) are the two largest randomized trials in PPMS patients completed to date

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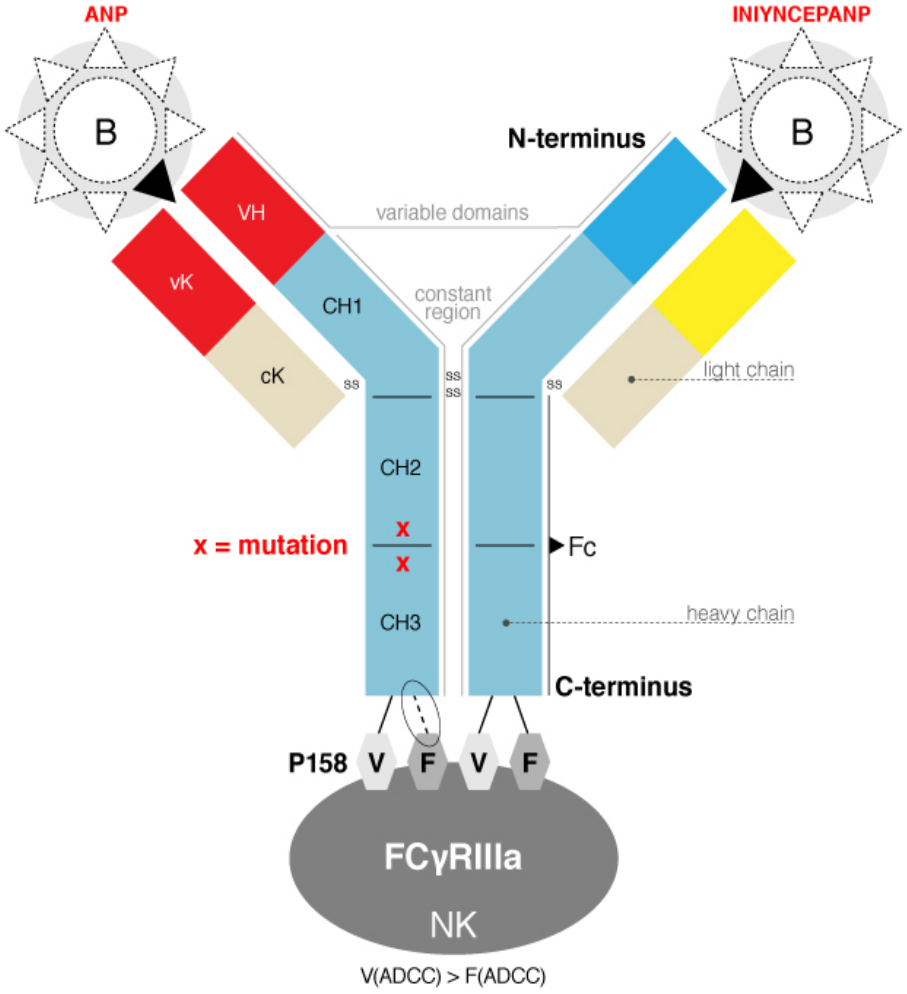
MEDIA RELEASE • COMMUNIQUE AUX MEDIAS • MEDIENMITTEILUNG

Novartis provides update on fingolimod Phase III trial in primary progressive MS (PPMS)

- *Phase III study in primary progressive multiple sclerosis (PPMS) did not meet the primary endpoint*

Ocrelizumab

- Fully humanised anti-CD20 monoclonal antibody
- Targets different epitopes to rituximab
- Stronger Ab-dependent cell-mediated cytotoxicity and less complement dependent cytotoxicity than rituximab



Genentech's Ocrelizumab First Investigational Medicine to Show Efficacy in People with Primary Progressive Multiple Sclerosis in Large Phase III Study

Genentech, a member of the Roche Group), today announced positive results from a pivotal Phase III study that evaluated the investigational medicine ocrelizumab in people with primary progressive multiple sclerosis (PPMS). The study (ORATORIO) **met its primary endpoint**, showing treatment with ocrelizumab significantly reduced the progression of clinical disability sustained for at least 12 weeks compared with placebo, as measured by the EDSS.

September 27, 2015

Neuroprotection

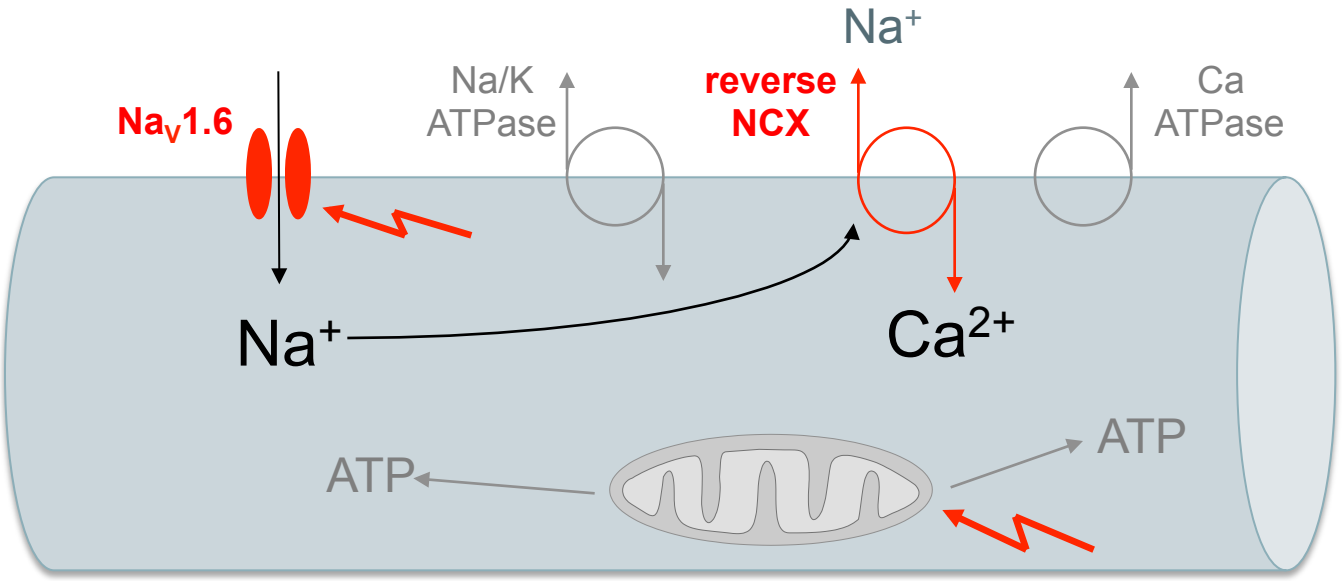
Repair/Remyelination

Lifestyle

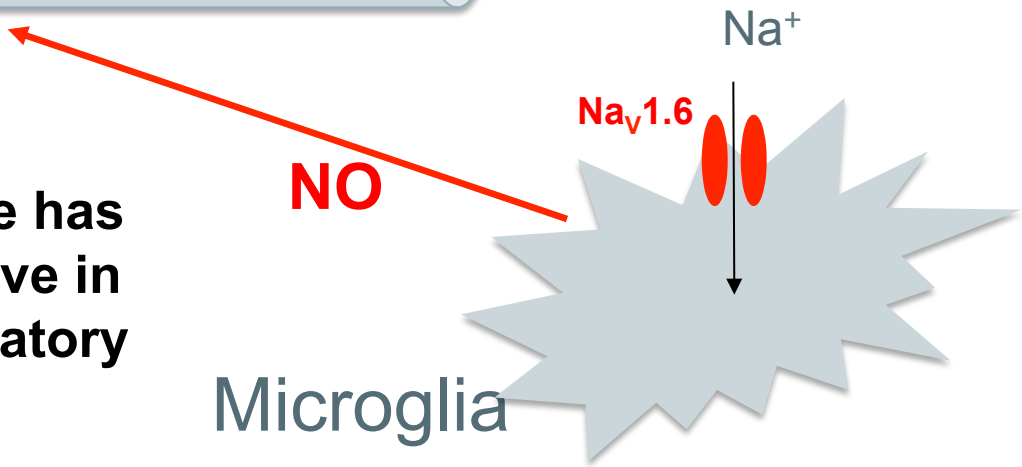
Rehabilitation

Enhancing plasticity

Treatment target
Neuroprotection: sodium channel blockers



Axons



Microglia

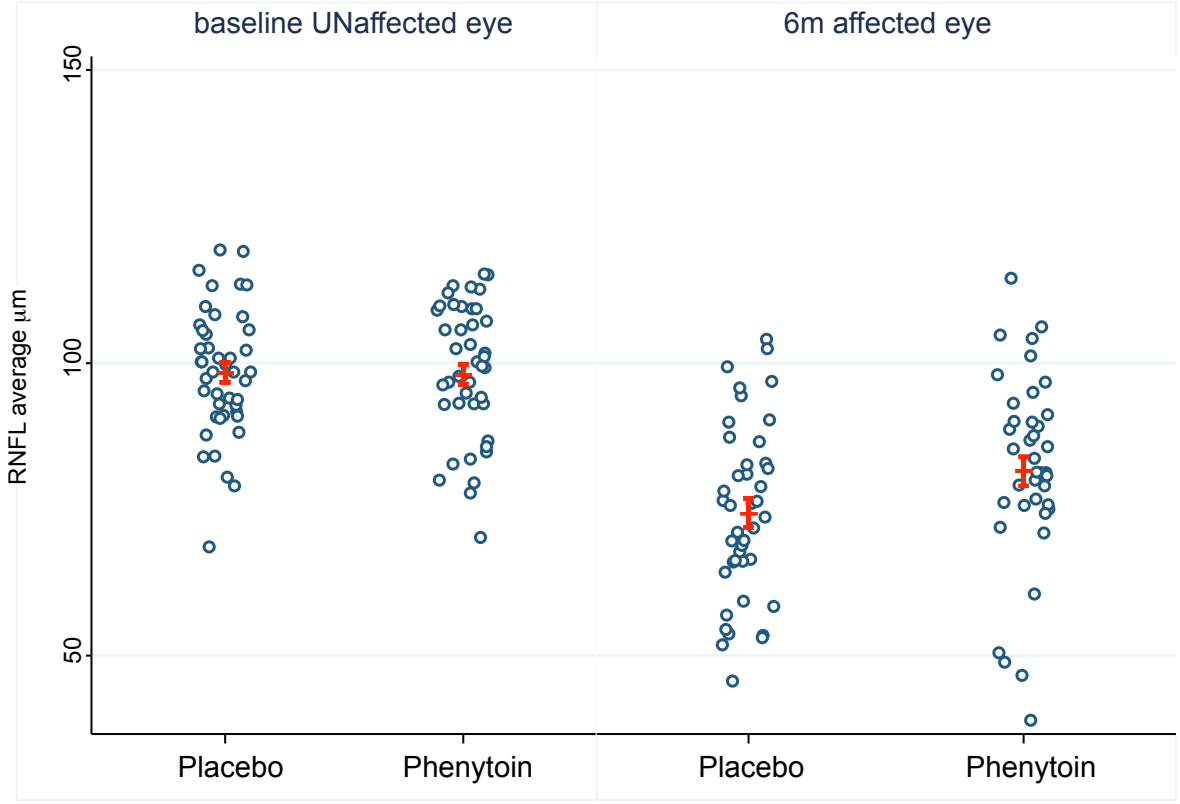
Partial sodium channel blockade has been shown to be neuroprotective in experimental models of inflammatory axonal injury

Phenytoin is neuroprotective in acute optic neuritis:
Results of a phase 2 randomized controlled trial

R Kapoor[1, 2], R Raftopoulos[1,2], S Hickman[4], A Toosy[1,2], B Sharrack[4], S Mallik[1,2], D Altmann[2], P Malladi[1], M Koltzenburg[1,2], C Wheeler-Kingshott[2], K Schmierer[3], G Giovannoni[3], and DH Miller[2]

National Hospital for Neurology and Neurosurgery[1], UCL Institute of Neurology[2], and Queen Mary University of London[3], London UK, and Royal Hallamshire Hospital, Sheffield UK[4]

Primary outcome: RNFL

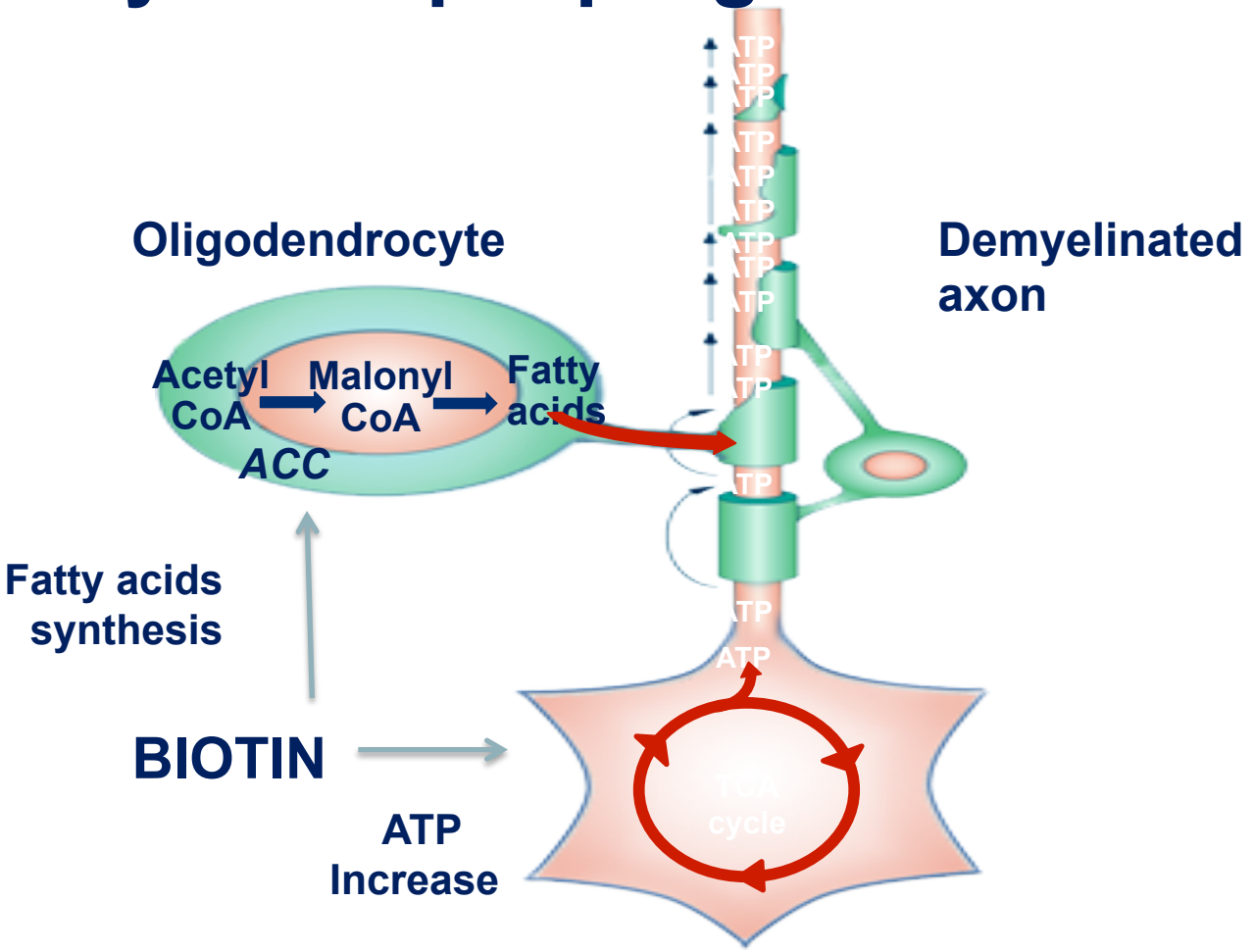


Bars are standard errors around the unadjusted group means

- Active-placebo adjusted difference 7.15 µm (95% CI 1.08, 13.22 p=0.02)
- 30% reduction of atrophy in active group

- PP comparison: Active-placebo adjusted difference 7.40 µm (95% CI 0.76, 14.04 p=0.03)

Biotin targets two mechanisms that may underpin progressive MS



ACC: acetyl CoA carboxylase

Primary Endpoint results

	MD1003 n(%)	Placebo n(%)	p-value [1]
ITT population	N=103	N=51	
	13 (12.62%)	0 (0.0%)	0.0051
Per protocol population	N=87	N=42	
	13 (14.9%)	0 (0.0%)	0.0093

(1) Fisher's Exact test

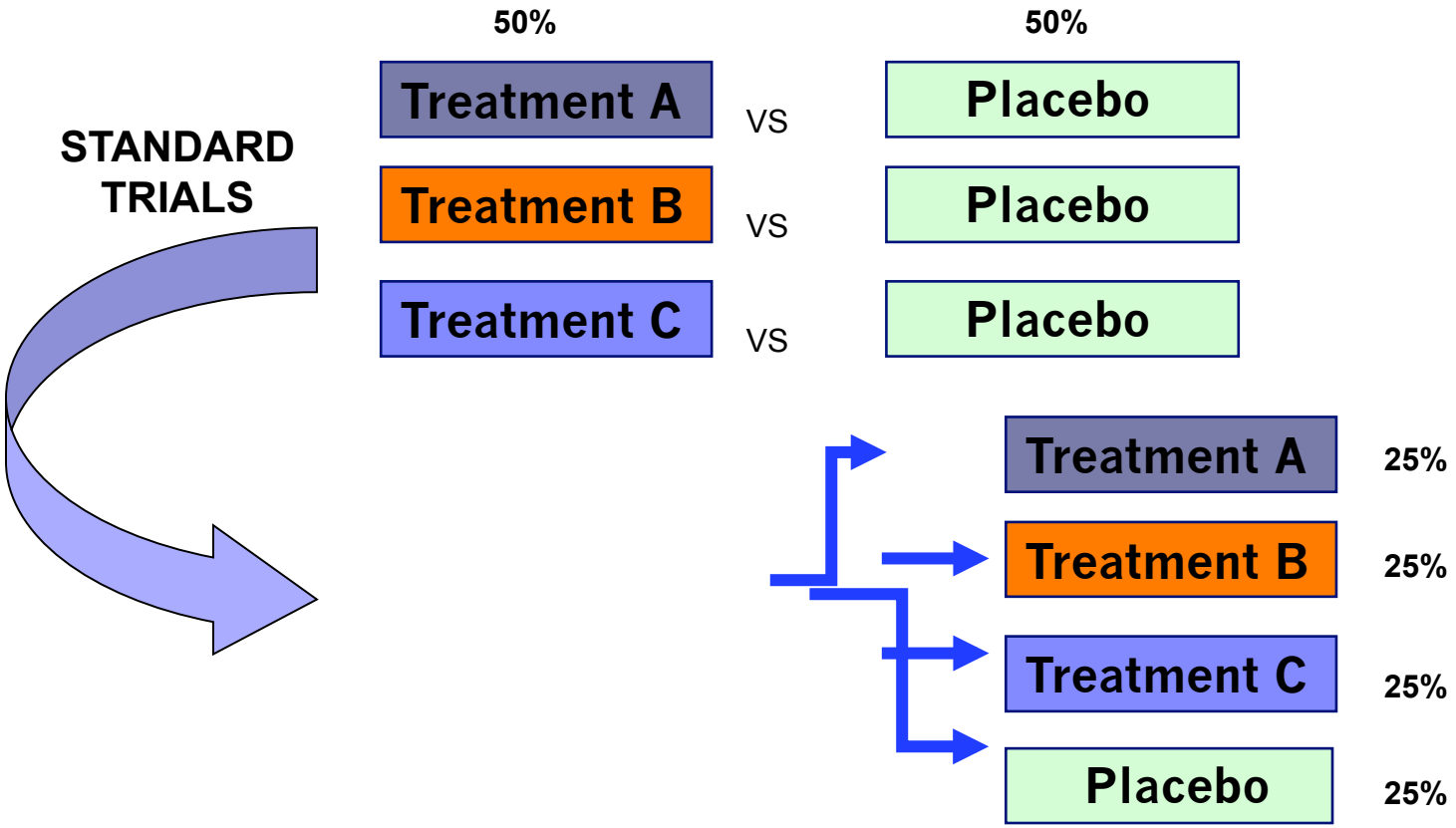
- Primary endpoint met with EDSS: 76.9%
- Primary endpoint met with TW25: 38.5%

Multiple Sclerosis-Secondary Progressive Multi-Arm Randomisation Trial

MS-SMART Trialists

Dr Jeremy Chataway

MULTI-ARM trials: an effective way of speeding up the therapy evaluation process!



Interventions

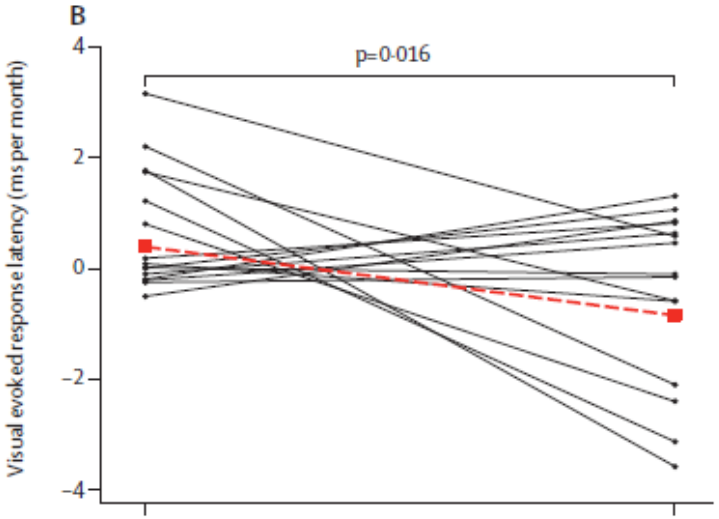
- Amiloride 5 mg bd
- Riluzole 50mg bd
- Fluoxetine 20mg bd

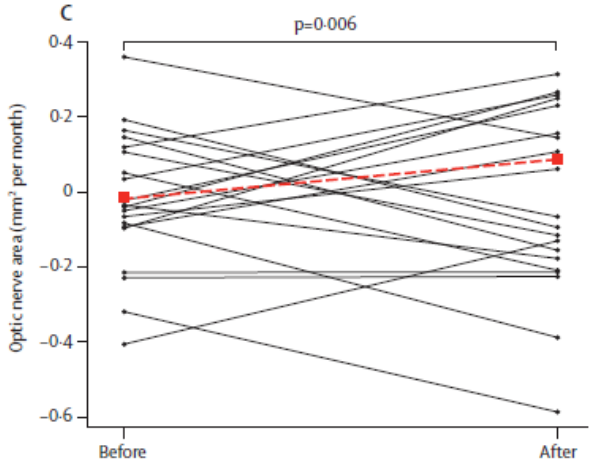
Autologous mesenchymal stem cells for the treatment of secondary progressive multiple sclerosis: an open-label phase 2a proof-of-concept study

Peter Connick,* Madhan Kolappan,* Charles Crawley, Daniel J Webber, Rickie Patani, Andrew W Michell, Ming-Qing Du, Shi-Lu Luan, Daniel R Altmann, Alan J Thompson, Alastair Compston, Michael A Scott, David H Miller, Siddharthan Chandran

Lancet Neurol 2012; 11: 150–56

Visual system of 10 patients with secondary progressive MS





↓VEP latency (p=0.016)

↑optic nerve area (p=0.006)

Progressive MS Alliance

Mission

To expedite the development of effective disease modifying and symptom management therapies for progressive forms of multiple sclerosis

ms international federation

MS National Multiple Sclerosis Society

SCLEROSI MULTIPLA fondazione italiana un mondo libero dalla SM

MS Multiple Sclerosis Society

MS AUSTRALIA

MS Multiple Sclerosis Society of Canada

Sclerose foreningen

New Perspectives

MULTIPLE SCLEROSIS JOURNAL | MSJ

Multiple Sclerosis Journal
0(0) 1–7

DOI: 10.1177/1352458512458169
msj.sagepub.com
SAGE

Setting a research agenda for progressive multiple sclerosis: The International Collaborative on Progressive MS

Robert J. Fox[1], Alan Thompson[2], David Baker[3], Peer Baneke[4], Doug Brown[5], Paul Browne[4], Dhia Chandraratna[4], Olga Ciccarelli[2], Timothy Coetzee[6], Giancarlo Comi[7], Anthony Feinstein[8], Raj Kapoor[9], Karen Lee[10], Marco Salvetti[11], Kersten Sharrock[12], Ahmed Toosy[2], Paola Zaratin[13] and Kim Zuidwijk[14]

Priority areas :

- Underlying Mechaniasm/Experimental Models
- Target pathways and drug repurposing
- Proof of concept trials (phase II)
- Phase III clinical trials & outcome measures
- Symptom management and rehabilitation

INTERNATIONAL

PROGRESSIVE MS ALLIANCE

CONNECT TO END PROGRESSIVE MS

Nationale Belgische Multiple Sclerose Liga vzw
Ligue Nationale Belge de la Sclérose en Plaques asbl

Lancet Neurol 2015; 14: 183–93

Series

Progressive multiple sclerosis 1

Pathological mechanisms in progressive multiple sclerosis

D

Series

Lancet Neurol 2015; 14: 194–207

Progressive multiple sclerosis 2

Treatment of progressive multiple sclerosis: what works, what does not, and what is needed

Anthony Feinstein, Jenny Freeman, Albert C Lo

Series

Lancet Neurol 2015; 14: 208–23

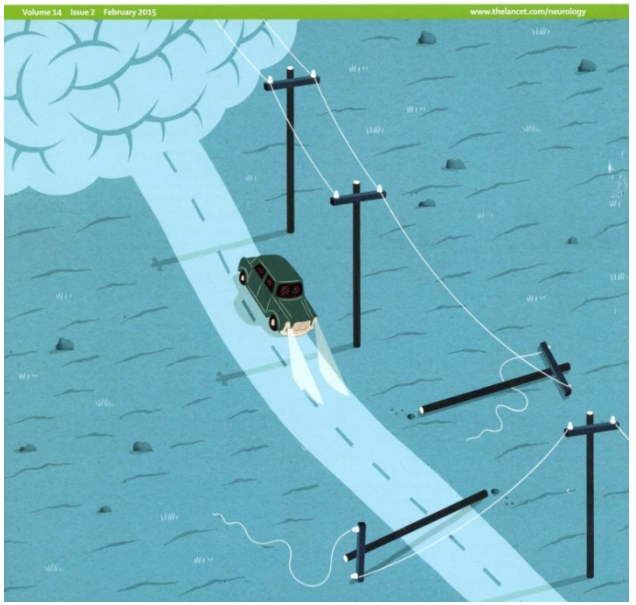
Progressive multiple sclerosis 3

Clinical trials in progressive multiple sclerosis: lessons learned and future perspectives

Daniel Ontaneda, Robert J Fox, Jeremy Chataway

THE LANCET Neurology

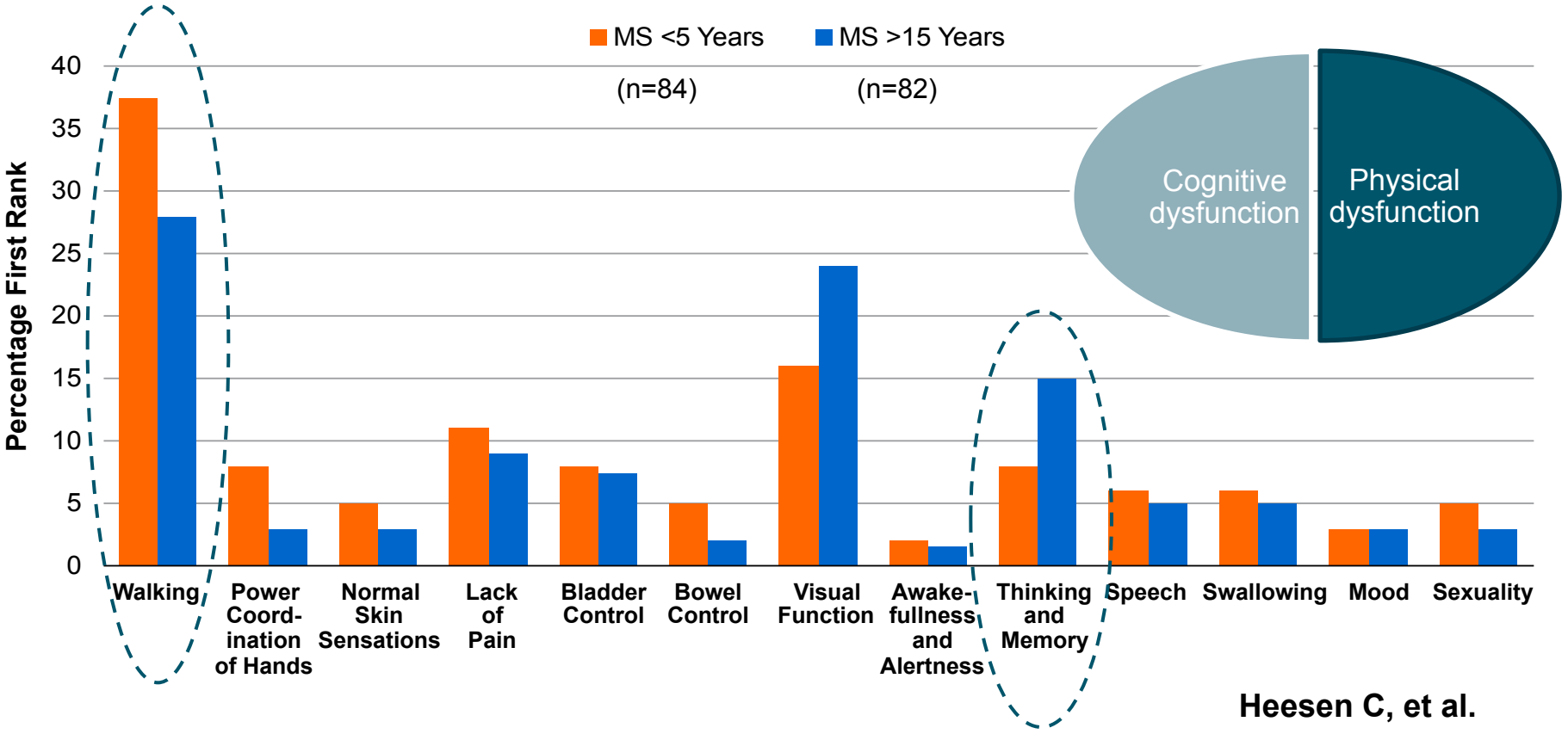
Volume 14 Issue 2 February 2015 www.thelancet.com/neurology




Rehab in MS
Working together for practical solutions to everyday problems

Patient Perspective on Valuable functions

- Gait function, visual function and thinking/memory perceived are the most valuable functions in pwMS with >15 yrs of MS



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