

The live webinar series

# MS Matters: The evolving patient profile in MS – approaches to management



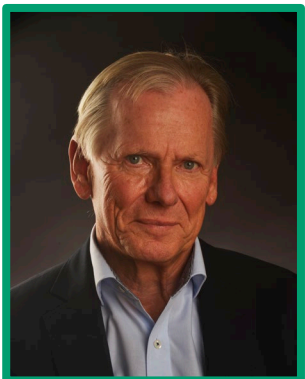
The live webinar series

# MS Matters: The evolving patient profile in MS – approaches to management

Welcome and introduction



# Your faculty today



## **Professor Per Soelberg Sørensen, moderator**

Professor of Neurology at the University of Copenhagen  
Senior Consultant at Rigshospitalet, Copenhagen



## **Dr Melinda Magyari, co-presenter**

Associate Professor at the University of Copenhagen  
Director of The Danish Multiple Sclerosis Registry and  
Consultant Neurologist at Rigshospitalet, Copenhagen

# Disclosures

## Professor Per Soelberg Sørensen

Personal compensation for serving on scientific advisory boards, steering committees, independent data monitoring committees or speaker honoraria from Biogen, Celgene, GlaxoSmithKline, Merck, Novartis and Teva.

## Dr Melinda Magyari

- Served on scientific advisory board for AbbVie, Biogen, Merck, Novartis, Roche, Sanofi.
- Received honoraria for lecturing from Biogen, Genzyme, Merck, Novartis, Sanofi.
- Received research support and support for congress participation from Biogen, Genzyme, Merck, Novartis, Roche.

# Agenda

Time	Session	Presenter
13:30–13:35	Welcome and introduction	Per Soelberg Sørensen
13:35–13:45	<b>The evolving patient profile in MS</b>	Per Soelberg Sørensen
13:45–13:50	Audience Q&A	
13:50–14:05	<b>Managing the modern patient with MS</b>	Melinda Magyari
14:05–14:10	Audience Q&A	
14:10–14:15	<b>Case study discussion: Adapting management approaches for a diverse patient cohort</b>	Per Soelberg Sørensen & Melinda Magyari
14:15–14:25	Audience Q&A	
14:25–14:30	Summary and close	Per Soelberg Sørensen

# Relatively recent changes in how we diagnose and treat MS

## Treatment availability



1990s

Disease-modifying therapy<sup>1</sup>

## Diagnostic criteria



2017

Revision to McDonald criteria<sup>2</sup>

## Treatment guidelines



2018

EAN/ECTRIMS guidelines<sup>3</sup>

1. Rolak LA. The history of MS – the basic facts. 2015. Available from: <https://www.nationalmssociety.org/NationalMSSociety/media/MSNationalFiles/Brochures/Brochure-History-of-Multiple-Sclerosis.pdf> (accessed 15 Jan 2020); 2. Thompson AJ, et al. *Lancet Neurol.* 2018;**17**:162–73; 3. Montalban X, et al. *Mult Scler.* 2018;**24**:6–120.

# How the profile of a patient with MS has changed...



More young patients and overall lower levels of disability<sup>1,2</sup>



More elderly patients with MS who may suffer from a range of age-related comorbidities<sup>3</sup>

**How does the MS care team need to adapt their management approach to the modern MS patient population?**

# The evolving patient profile in MS

**Professor Per Soelberg Sørensen**

University of Copenhagen and Rigshospitalet, Copenhagen, Denmark



# What are the reasons for the apparently milder course of MS?



Updates to the **McDonald diagnostic criteria**: 2001,<sup>1</sup> 2005,<sup>2</sup> 2010 and 2017<sup>3</sup>



Changes in **neuroepidemiology** in MS: sex ratio, environmental factors and improvement of the general health of the population<sup>4</sup>



**Treatment**: earlier treatment, evolved treatment strategies, i.e. 'treat-to-target', and more efficacious drugs to prevent relapses and disability progression and to treat progressive MS<sup>3,5</sup>



**New classification of disease course**: active disease, progressive disease and stable disease<sup>6</sup>

1. McDonald WI et al. *Ann Neurol*. 2001;**50**:121-71; 2. Polman CH et al. *Ann Neurol*. 2005;**58**:840-6; 3. Dobson R & Giovannoni G. *Eur J Neurol*. 2019;**26**:27-40;

4. Magyari M & Sorensen PS. *Curr Opin Neurol*. 2019;**32**:320-26; 5. Comi G, Radaelli M, Soelberg Sørensen P. *Lancet*. 2017;**389**:1347-56;

6. Lublin FD et al. *Neurology*. 2014 Jul 15;**83**(3):278-86



# How the updates to the McDonald criteria impact on whether a patient is diagnosed with CIS, RIS or MS

	2001 <sup>1</sup>	2005 <sup>2</sup>	2010 <sup>3</sup>	2017 <sup>4</sup>
<b>≥2 attacks; ≥2 clinical lesions</b>	MS	MS	MS	MS
<b>≥2 attacks; 1 clinical lesion (needs MRI DIS)</b>				
MRI DIS 2001	MS	MS	MS	MS
MRI: 2 T2 lesions + CSF-OB	MS	MS	CIS	CIS
MRI DIS 2005	MS	MS	MS	MS
MRI DIS 2010	CIS	CIS	CIS	MS
MRI DIS 2017	CIS	CIS	CIS	MS
<b>1 attack; 2 clinical lesions (needs MRI DIT)</b>				
MRI DIT 2010	CIS	CIS	MS	MS
MRI DIT 2017	CIS	CIS	CIS	MS
MRI DIS 2017 + CSF-OB	CIS	CIS	CIS	MS
<b>1 attack; 1 clinical lesion (needs MRI DIS and DIT)</b>				
MRI DIS 2010 + MRI DIT 2010	CIS	CIS	MS	MS
MRI DIS 2017 + MRI DIT 2017	CIS	CIS	CIS	MS
MRI DIS 2017 + CIS-OB	CIS	CIS	CIS	MS
<b>0 attacks; 0 clinical lesions; MRI suggested diagnostic criteria for RIS</b>	RIS	RIS	RIS	RIS

CIS, clinically isolated syndrome; CSF-OB, cerebrospinal fluid oligoclonal bands;

DIS, dissemination in space; DIT, dissemination in time;

MRI, magnetic resonance imaging; RIS, radiologically isolated syndrome

1. McDonald WI et al. *Ann Neurol.* 2001;**50**:121-71; 2. Polman CH et al. *Ann Neurol.* 2005;**58**:840-6;

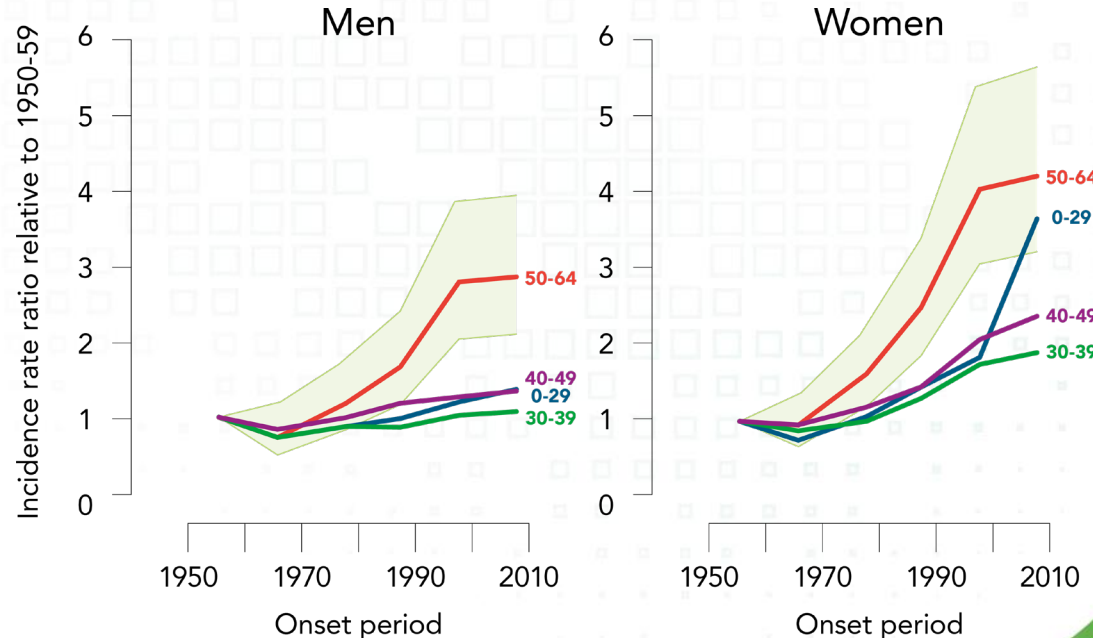
3. Polman CH et al. *Ann Neurol.* 2011;**69**:292-302; 4. Thompson AJ et al. *Lancet Neurol.* 2018;**17**:162-73



# Incidence of MS has increased over six decades in Denmark, particularly late-onset MS and MS in women

- The incidence did not change uniformly for all age groups
- The incidence rate ratio between the 2000–2009 and 1950–1959 periods was highest with age at onset of 50–64 years

Incidence rate ratio in onset decades relative to incidence in the 1950–1959 decade, in four age-at-onset groups

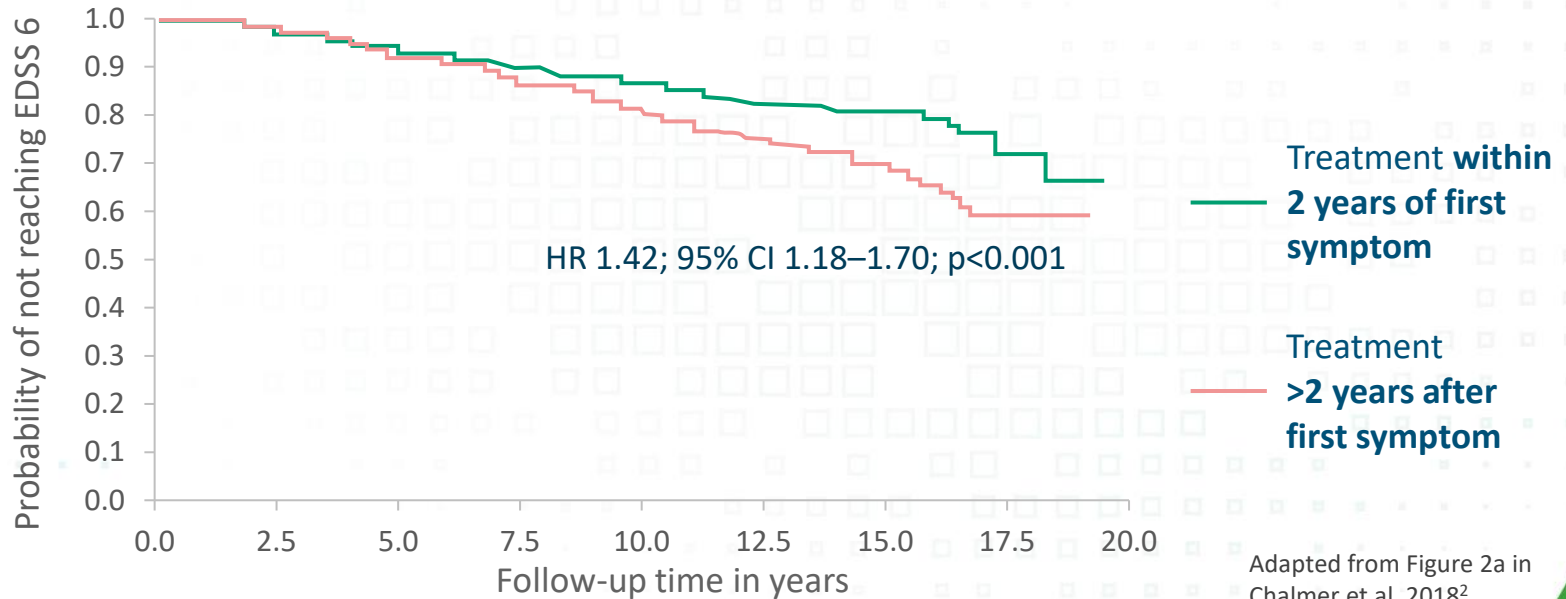


Shaded areas: 95% confidence interval for rate ratio for the 50–64 years group



# There is a shift towards early treatment approaches in MS,<sup>1</sup> with improvement in disease progression outcomes<sup>2</sup>

Adjusted Kaplan–Meier curve of time to a confirmed EDSS score of 6



Treatment >2 years after first symptom

1,480 1,322 1,056 621 339 172 83 21 0

Treatment within 2 years of first symptom

2,316 2,076 1,634 1,044 630 352 136 28 0

CI, confidence interval;

EDSS, Expanded Disability Status Scale; HR, hazard ratio





# Improved efficacy of DMTs is associated with a milder MS course

Since the first DMTs in MS, the following advances in efficacy have been made:

A. Reduction in **annualised relapse rate** vs placebo<sup>1</sup>

B. Reduction in **disability worsening (EDSS)** vs placebo<sup>1</sup>

C. An increased percentage of patients achieving **NEDA** vs comparator in Phase III trials<sup>2</sup>

1. Comi G, Radaelli M, Soelberg Sørensen P. *Lancet*. 2017;**389**:1347–56;

2. Dobson R & Giovannoni G. *Eur J Neurol*. 2019;**26**:27–40

DMT, disease-modifying therapy; EDSS, Expanded Disability Status Scale;

NEDA, no evidence of disease progression



# Changes in classification of the MS disease course from 1996 to 2013

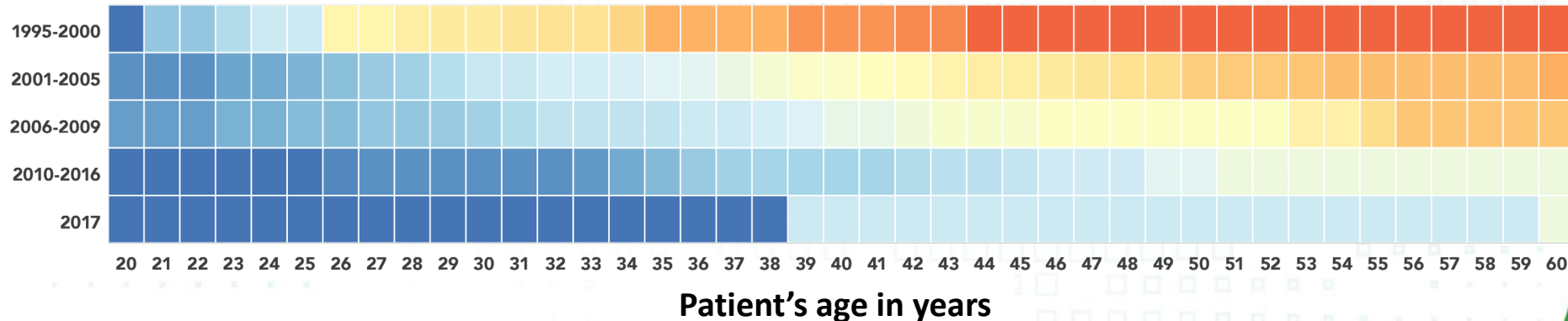
Classification	1996	2013
<b>Clinically isolated syndrome<sup>1</sup></b>	N/A (introduced to the official nomenclature in 2012)	The first episode of inflammatory demyelination in the central nervous system that could become MS if additional activity occurs <sup>†</sup>
<b>Relapsing–remitting MS<sup>1</sup></b>	Basic descriptor	Additional subsets: <b>active OR not active</b>
<b>Primary progressive MS<sup>1</sup></b>	Basic descriptor	Additional subsets: <b>active OR not active AND with progression OR without progression</b>
<b>Secondary progressive MS<sup>1</sup></b>	Basic descriptor	Additional subsets: <b>active OR not active AND with progression OR without progression</b>
<b>Progressive relapsing MS<sup>1</sup></b>	Basic descriptor	<b>No longer classified as a disease course</b>

<sup>†</sup>With the revisions of the McDonald criteria, an **increasing proportion of patients previously classified as CIS are being classified as relapsing-remitting MS** based on MRI findings and cerebrospinal fluid oligoclonal bands<sup>2</sup>

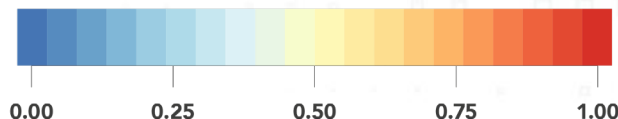
# An example of improving MS outcomes: At a certain age, the proportion of patients with confirmed EDSS 3 has been decreasing since 1995<sup>1</sup>

MS diagnosis era

Confirmed EDSS 3<sup>1</sup>



Proportion



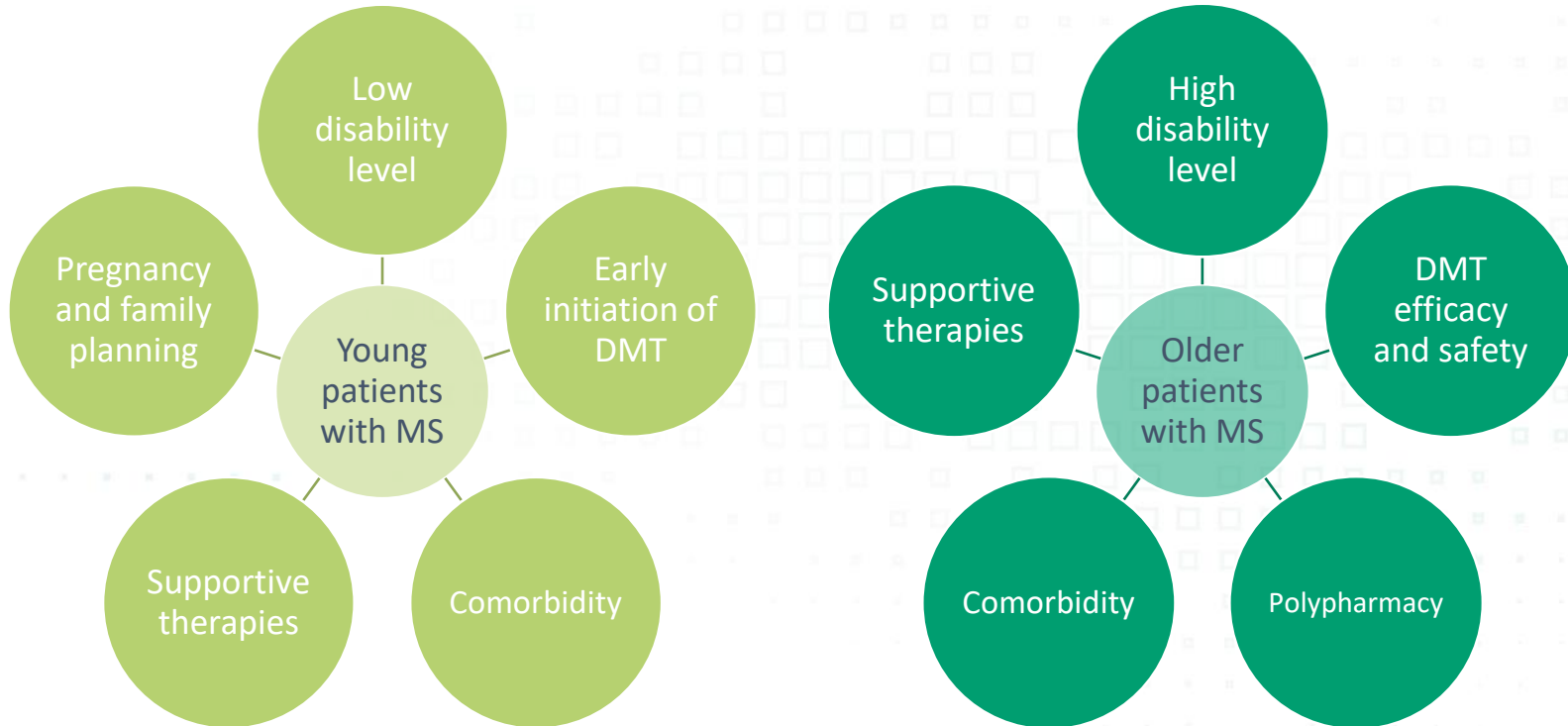
# Managing the modern patient with MS

**Dr Melinda Magyari**

University of Copenhagen and Rigshospitalet, Copenhagen, Denmark

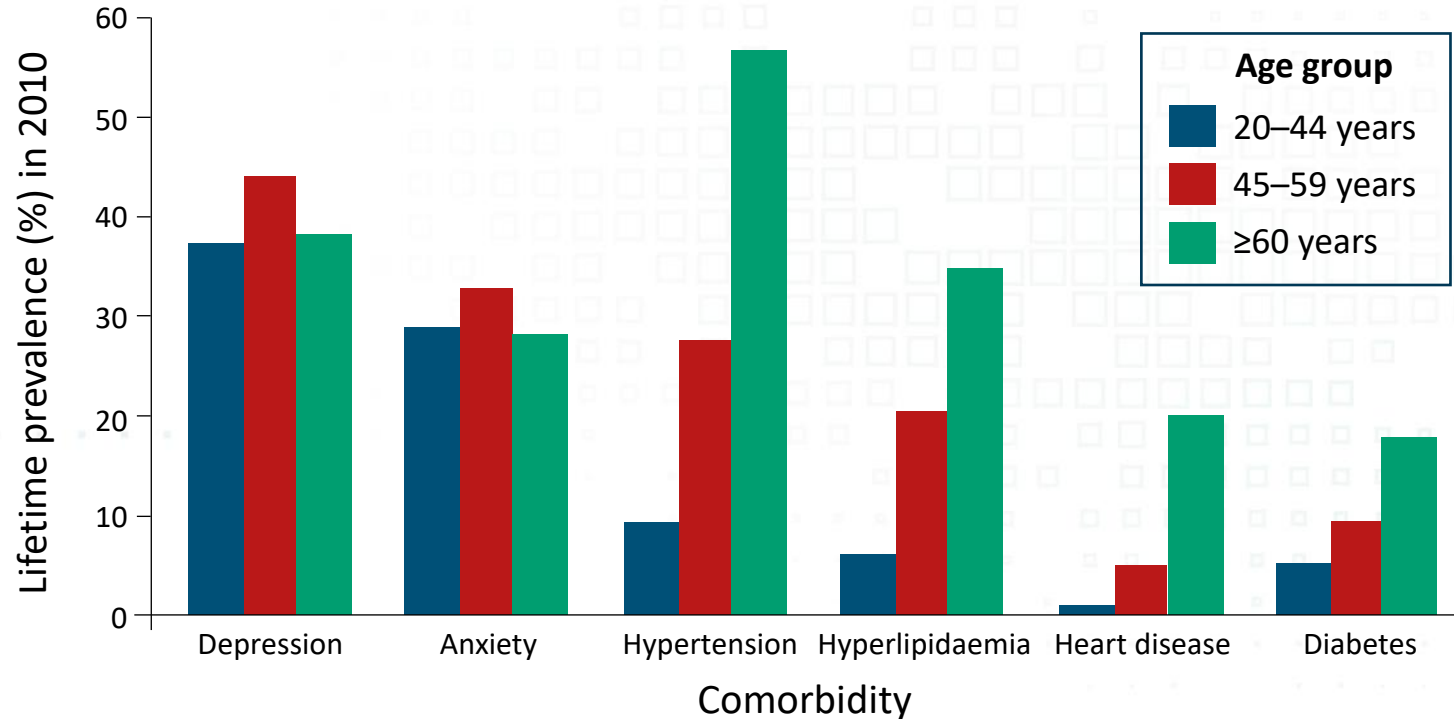


# What may need to be considered when managing the modern patient with MS?



# The prevalence of comorbidities differs by age group in patients with MS

Age-specific prevalence of common comorbidities in a prevalent MS cohort

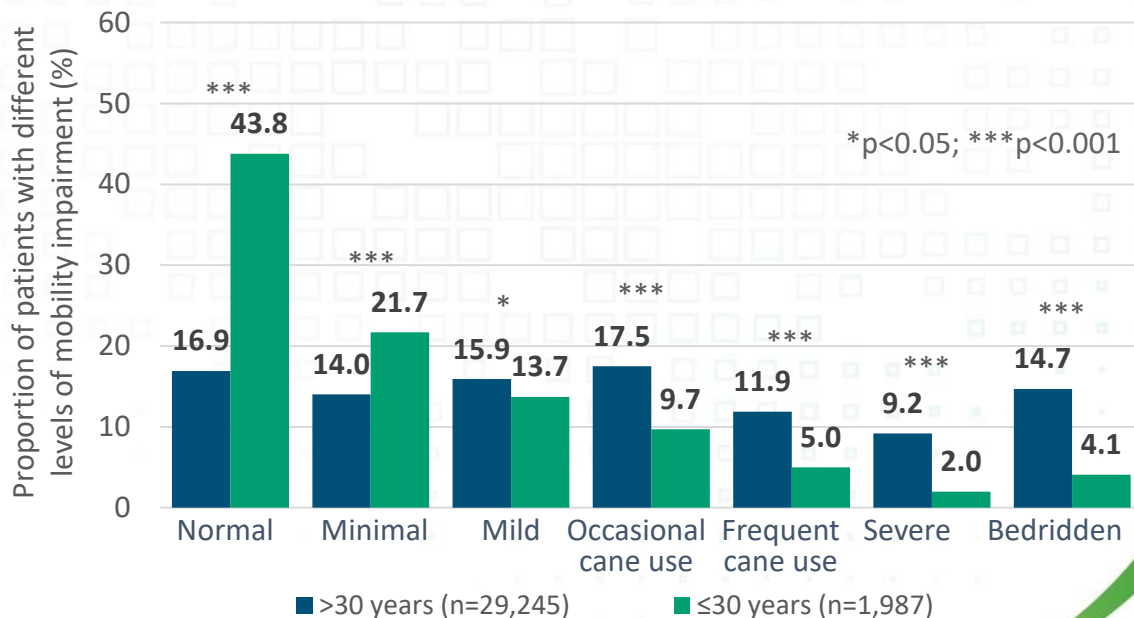


# Patients in different age groups show different levels of disability

In an analysis of NARCOMS registry data:

- **44%** of young patients ( $\leq 30$  years) reported normal mobility vs **17%** of older patients ( $>30$  years)
- Older patients were more likely to experience **fatigue, poor bowel/ bladder control, spasticity, pain and tremor**

Level of mobility impairment of patients in different age groups in a 2009 analysis of NARCOMS registry data



# Management of young patients with MS



# Early treatment with DMT in patients with MS may reduce future disability

Several studies have shown that early initiation of DMT is associated with slower disability progression compared with later initiation

- Each year of delay in treatment initiation was associated with a **7.4% increase in risk of EDSS  $\geq 4$**  in a single-centre, real-world study<sup>1</sup>
- Early therapy was associated with a **42% decreased risk of reaching EDSS  $\geq 6$**  in a cohort study by the Danish MS group<sup>2</sup>
- The risk of EDSS progression was lowest if treatment was initiated within 6 months of disease onset in an analysis of the MSBase registry<sup>3</sup>

DMT should be initiated as soon as possible in young or newly diagnosed patients with MS to reduce future disability<sup>4</sup>



# Management considerations for psychiatric comorbidities, which are prevalent in younger patients with MS<sup>1</sup>

## Why is it important to consider psychiatric comorbidities?

Independently associated with greater disability at diagnosis<sup>1</sup>

They may lead to negative changes in health behaviours, e.g. poor diet<sup>1</sup>

Associated with a higher mortality rate<sup>3</sup>

Depression increases risk of disability worsening<sup>4</sup>

- **Psychiatric specialists and clinical psychologists** have been proposed as core members of collaborative MS management teams<sup>1,2</sup>
- There is a need for **early recognition** and **appropriate treatment** of psychiatric comorbidities in patients with MS<sup>3,4</sup>

# Supportive therapies in young patients with MS

Intellectually enriching activities to enhance cognitive reserve<sup>1</sup>

**Strength training activity:**  
2 sets of 10–15 reps,  
heavy enough that you can  
barely finish the last set<sup>2</sup>



Occupational therapy?

**Treating and managing MS requires a comprehensive approach, which is started as early as possible<sup>1</sup>**

Exercise therapy:  
a disease-modifying effect?<sup>3</sup>

Support with limiting alcohol consumption and smoking cessation<sup>1</sup>

Counselling?

**Aerobic activity:** 2x per week,  
30 mins, moderate intensity<sup>2</sup>





# Family planning is a key consideration for young patients with MS

- MS is increasingly being diagnosed in young women<sup>1</sup>
- Guidelines recommend that:<sup>2,3</sup>
  - All women of childbearing age should receive pre-pregnancy counselling (repeated yearly)
  - Women considering pregnancy should be advised to discuss this with their MS care team
  - Discussions on the risks and benefits of DMTs should occur as early as possible and before any planned pregnancy

Am I able to have a child?

Will I and the baby be able to stay healthy?

What treatment decisions will I need to make?

Will I be able to breastfeed?



1. Coyle PK. *Mult Scler Relat Disord*. 2019;**32**:54–63; 2. Dobson R, et al. *Pract Neurol*. 2019;**19**:106–14; 3. Langer-Gould AM. *Continuum (Minneapolis)*. 2019;**25**:773–92.



# Management of older patients with MS



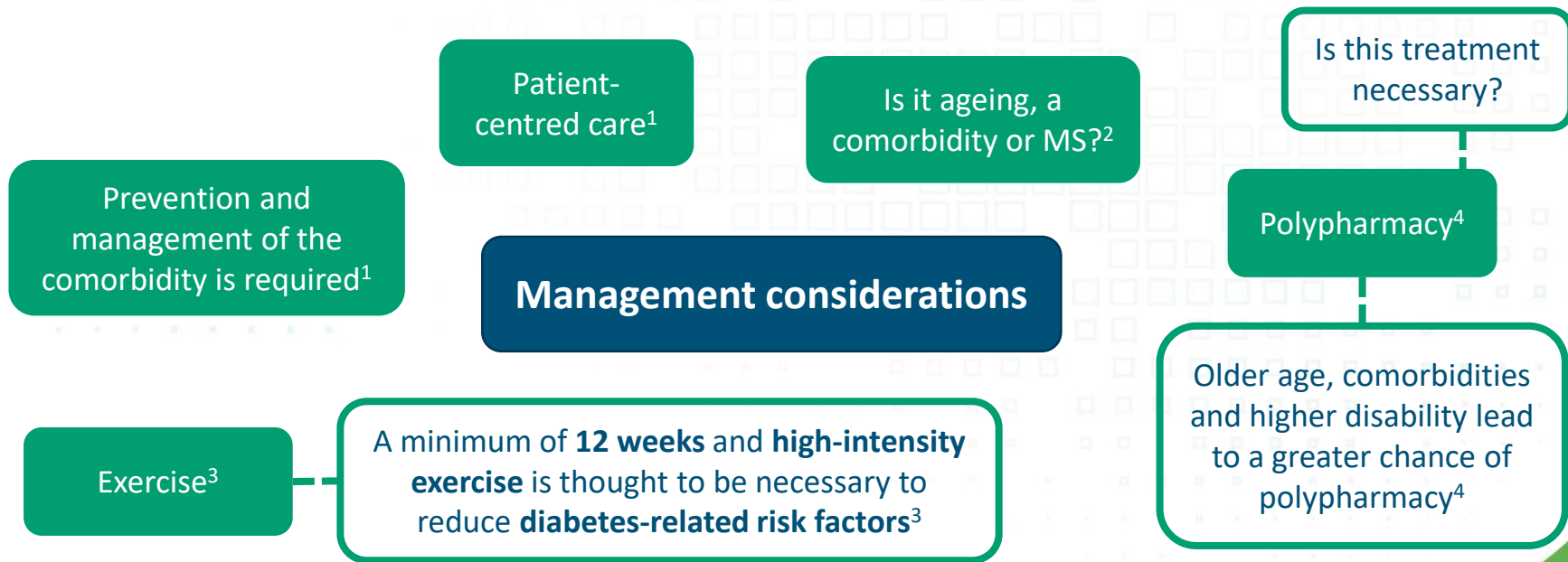
# What is the value of DMT in older patients with MS?

- Most patients aged >65 years have progressive forms of MS and fewer DMT options are available, compared with relapsing–remitting MS<sup>1</sup>
  - There is a transition from an inflammatory to a neurodegenerative phenotype<sup>1</sup>
- The safety and efficacy of many commonly used DMTs have often not been established in elderly patients<sup>1</sup>
- A meta-analysis of clinical trial data showed that the effect of DMTs on MS disability decreases with increasing age<sup>2</sup>
  - A regression model predicts that DMT efficacy may be zero for patients aged >53 years
  - High-efficacy drugs outperform low-efficacy drugs at inhibiting MS disability only for patients younger than 40.5 years

Immunosenescence, which occurs during ageing, complicates the management of MS in elderly patients<sup>1</sup>

# Managing comorbidities in elderly patients with MS

- Hypertension, hyperlipidaemia, heart disease and diabetes are more prevalent in elderly patients with MS than in younger patients with MS<sup>1,2</sup>



1. Marrie RA. *Nat Rev Neurol*. 2017;**13**:375–82; 2. Vaughn CB, et al. *Nat Rev Neurol*. 2019;**15**:329–42;  
3. Ewanchuk BW, et al. *Mult Scler Relat Disord*. 2018;**26**:19–32; 4. Frahm M, et al. *Biol Sex Differ*. 2019;**10**:27.

# Supportive therapies for older patients with MS

- Older patients (>30 years) with MS were more likely to use supportive therapies, such as acupuncture, physical therapy and occupational therapy, compared with younger patients ( $\leq 30$  years) in an analysis of the NARCOMS registry data<sup>1</sup>
- Multidisciplinary rehabilitation in the Danish MS hospitals is an example of how supportive therapies can be used to manage patients with MS<sup>2</sup>

**Cognitive behavioural therapy  
in patients with MS is helpful  
for managing**

**Fatigue<sup>3</sup>**

**Depression<sup>3</sup>**

1. Buchanan RJ, et al. *NeuroRehabilitation*. 2009;**25**:271–8;

2. Personal communication of the speaker;

3. Dennison L & Moss-Morris R. *Expert Rev Neurother*. 2010;**10**:1383–90.

# Summary

- DMT should be offered as soon as possible after diagnosis<sup>1,2</sup>
- When treating patients with MS, clinicians need to incorporate the prevention and management of comorbidities, which vary between different age groups<sup>3</sup>
  - It is also key to distinguish normal ageing phenomena from worsening MS and to identify other neurological disorders that are common in ageing, but may mimic some of the symptoms of MS<sup>4</sup>
- Including supportive therapies in MS management strategies can improve long-term health and well-being<sup>1,5,6</sup>
- Pregnancy counselling is important to successfully control disease activity in women with MS throughout pregnancy and the postpartum period while minimising harm to the infant<sup>7</sup>

# Case study discussion: Adapting management approaches for a diverse patient cohort

**Professor Per Soelberg Sørensen & Dr Melinda Magyari**

University of Copenhagen and Rigshospitalet, Copenhagen, Denmark

# Case study: Young female

What are the unique challenges in managing this type of patient?

<b>Age</b>	30 years
<b>Sex</b>	Female
<b>Occupation</b>	Primary school teacher
<b>Age at disease onset</b>	28
<b>Age at diagnosis</b>	30
<b>Current treatment</b>	<ul style="list-style-type: none"><li>• Newly diagnosed, so no treatment</li><li>• Once-weekly physical therapy</li></ul>
<b>EDSS score</b>	3
<b>Further considerations</b>	<ul style="list-style-type: none"><li>• Thyroid disorder, well managed</li></ul>

# Case study: Older male

What are the unique challenges in managing this type of patient?

<b>Age</b>	59 years
<b>Sex</b>	Male
<b>Occupation</b>	Early retired (disability pension)
<b>Age at disease onset</b>	41
<b>Age at diagnosis</b>	44
<b>Current treatment</b>	<ul style="list-style-type: none"><li>• Moderate-efficacy DMT with breakthrough disease</li><li>• Twice-weekly physiotherapy sessions</li></ul>
<b>EDSS score</b>	6 (no EDSS worsening in the past 3 years)
<b>Further considerations</b>	<ul style="list-style-type: none"><li>• Aged 55, he was diagnosed with hypertension and type 2 diabetes</li><li>• He is taking 3 medications for difficult-to-control high blood pressure</li><li>• Previous smoker and overweight</li><li>• Mild and slow worsening of gait, mobility and cognitive functions</li></ul>



# Summary and close

**Professor Per Soelberg Sørensen**

University of Copenhagen and Rigshospitalet, Copenhagen, Denmark

# Closing remarks

- Changes in diagnosis, neuroepidemiology, available treatments, treatment approaches and classification are reasons for the changing patient profile in MS
- Different management challenges exist depending on the age of patients with MS, in terms of:
  - Disability levels
  - Comorbidity profile
  - Changing benefits of DMTs
  - Polypharmacy
  - Pregnancy considerations

**Thank you for your time and participation!**

