

# Multiple Sclerosis: Understanding the Impact & Mitigation Strategies

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# Disclosures

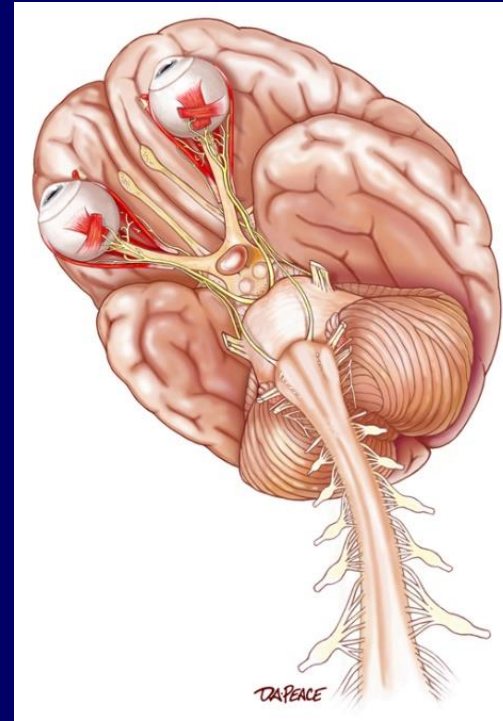
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- CIHR, MS Society of Canada, MS Scientific Research Foundation, NMSS, CMSC, Research Manitoba, US Department of Defense, Waugh Family Chair in Multiple Sclerosis, Brain Canada
- Co-investigator on studies funded by Roche, Biogen Idec (no funds to me or my institution)

# Objectives

- To recognize the impact of MS on health & productivity
- To recognize the potential effect of comorbidity including psychiatric disorders on outcomes
- To understand how we can mitigate the impact of MS
  - Disease-modifying therapy
  - Management of comorbidity

# Multiple Sclerosis: Definition

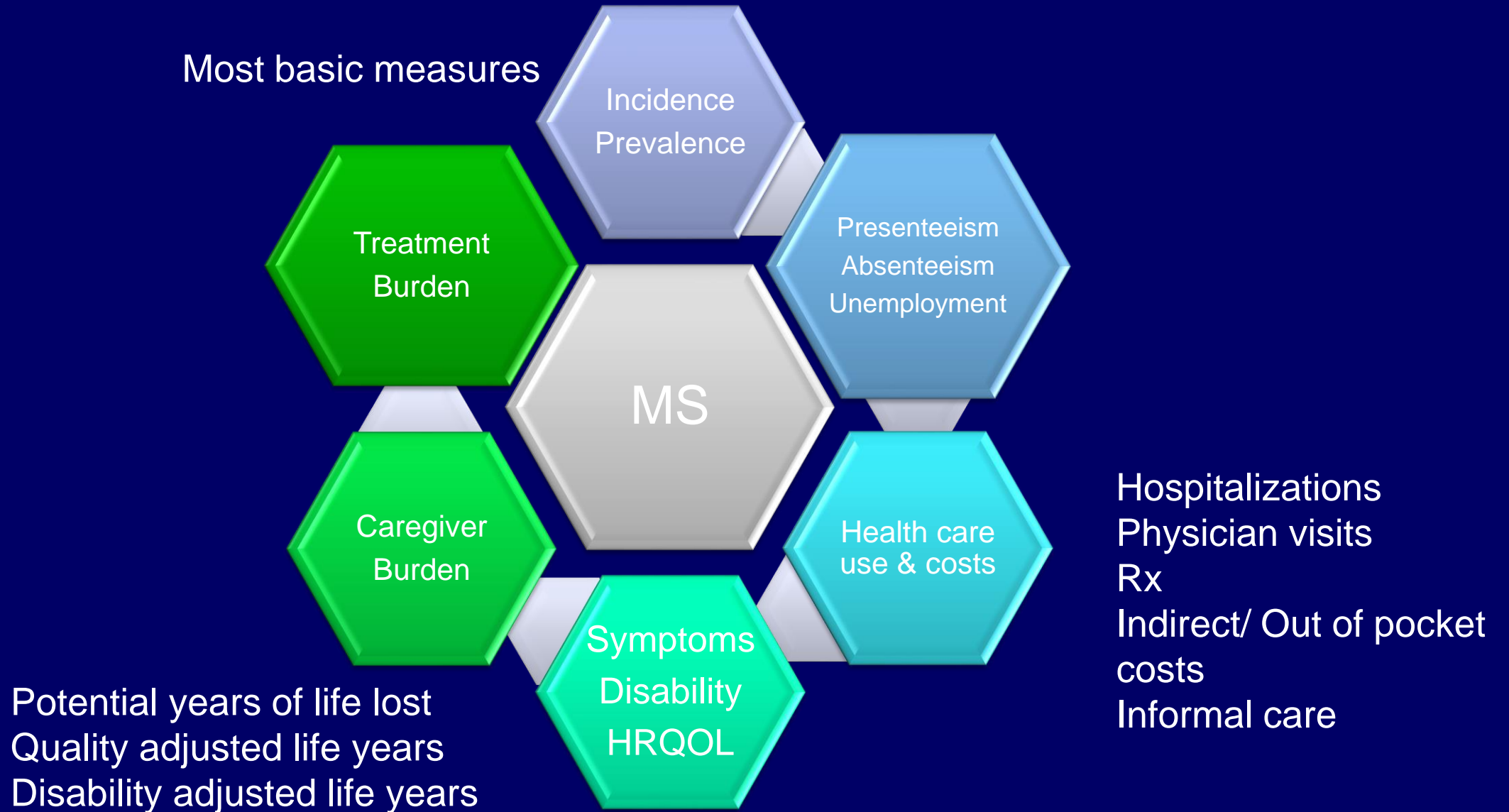
- An immune-mediated, demyelinating disease of the **central nervous system**



# Measuring the Impact of MS

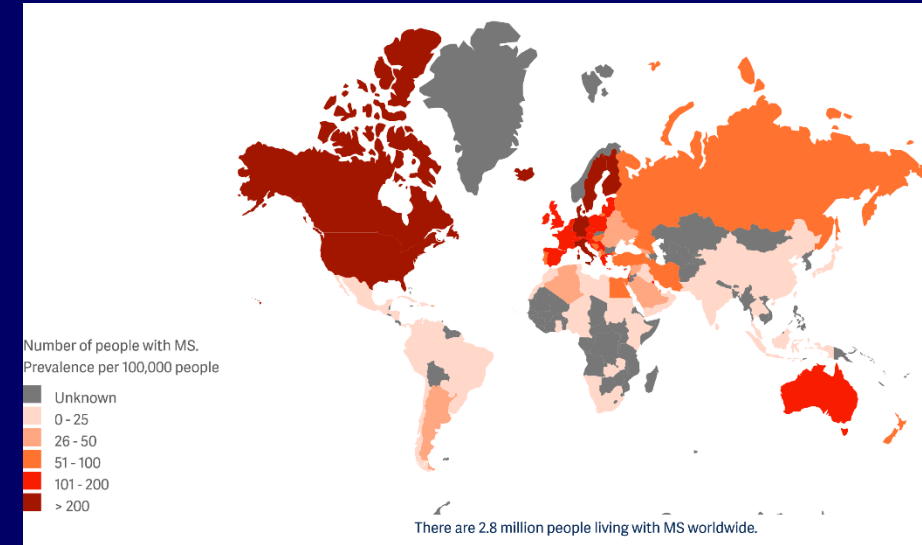
- WHO: “health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity”

# Measuring the Impact

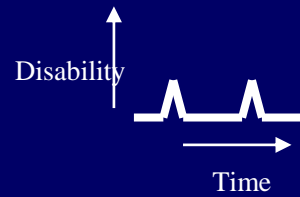


# Epidemiology of MS

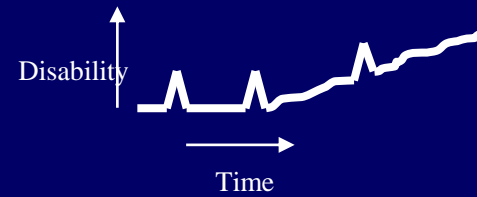
- Affects ~ 100,000 Canadians
- Female > Male: ratio incr. from 2:1 to 3:1
- Onset typically 20-50 years
  - may occur in childhood (5%) or after age 60 (0.5%)
- Most common, non-traumatic cause of disability in young adults
- Life expectancy: ↓ 6-7 years



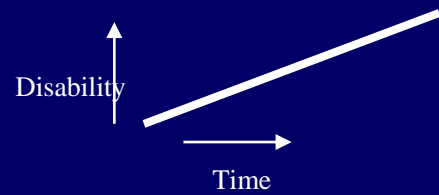
# Course of MS



Relapsing Remitting



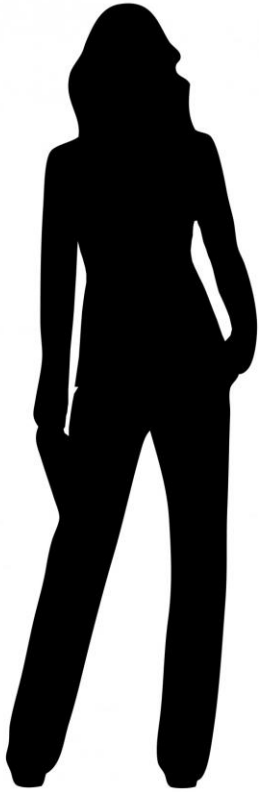
Secondary Progressive  
(following Relapsing Remitting)



Primary Progressive



# Symptoms



Cognitive impairment  
Involuntary crying/emotions

Impaired speech, swallowing, double vision, visual loss, vertigo

Spasticity, weakness, difficulty walking, poor balance,  
numbness, tremor, impaired coordination

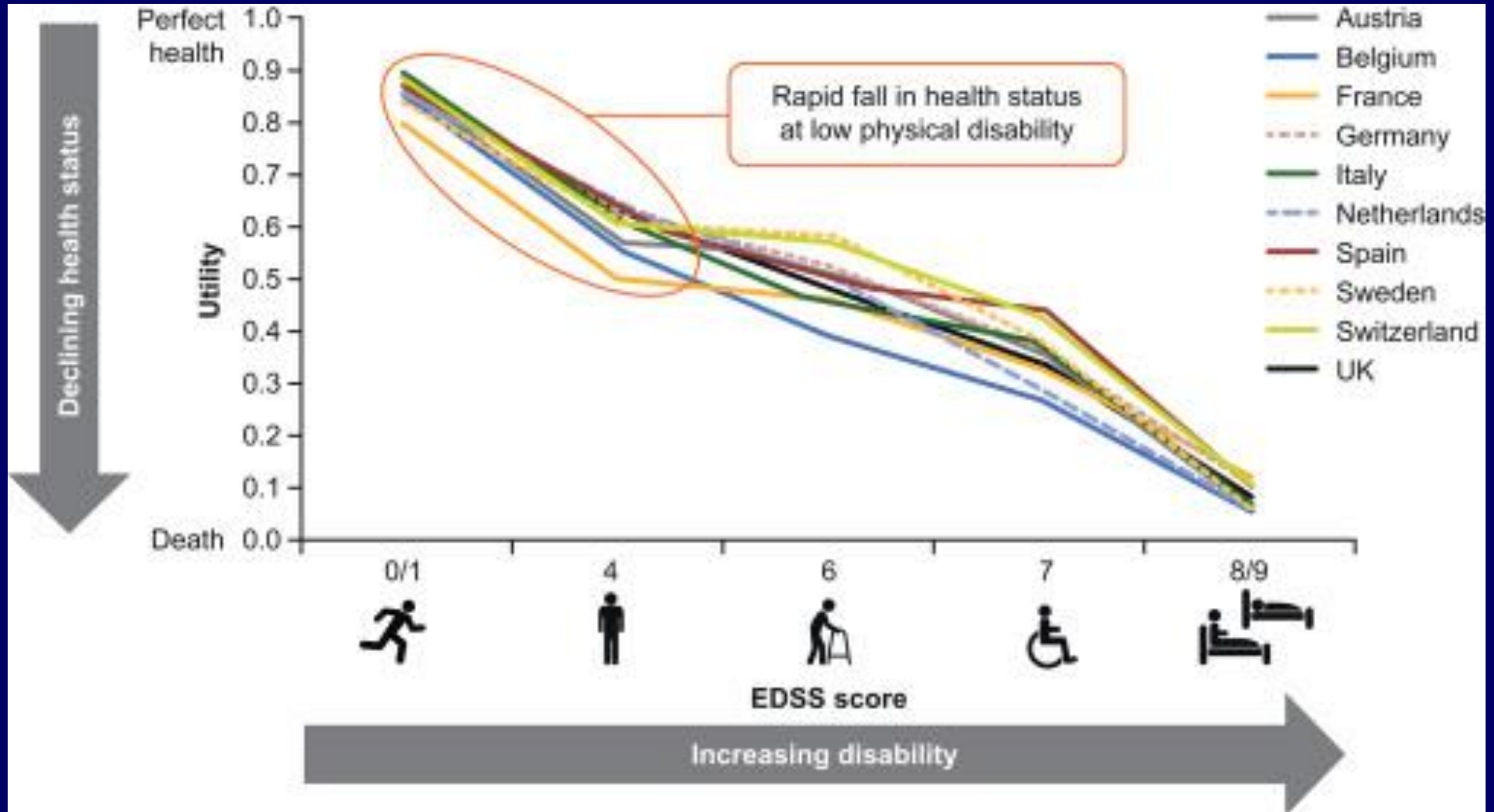
Pain, fatigue, heat intolerance

Bowel/bladder problems  
Sexual dysfunction

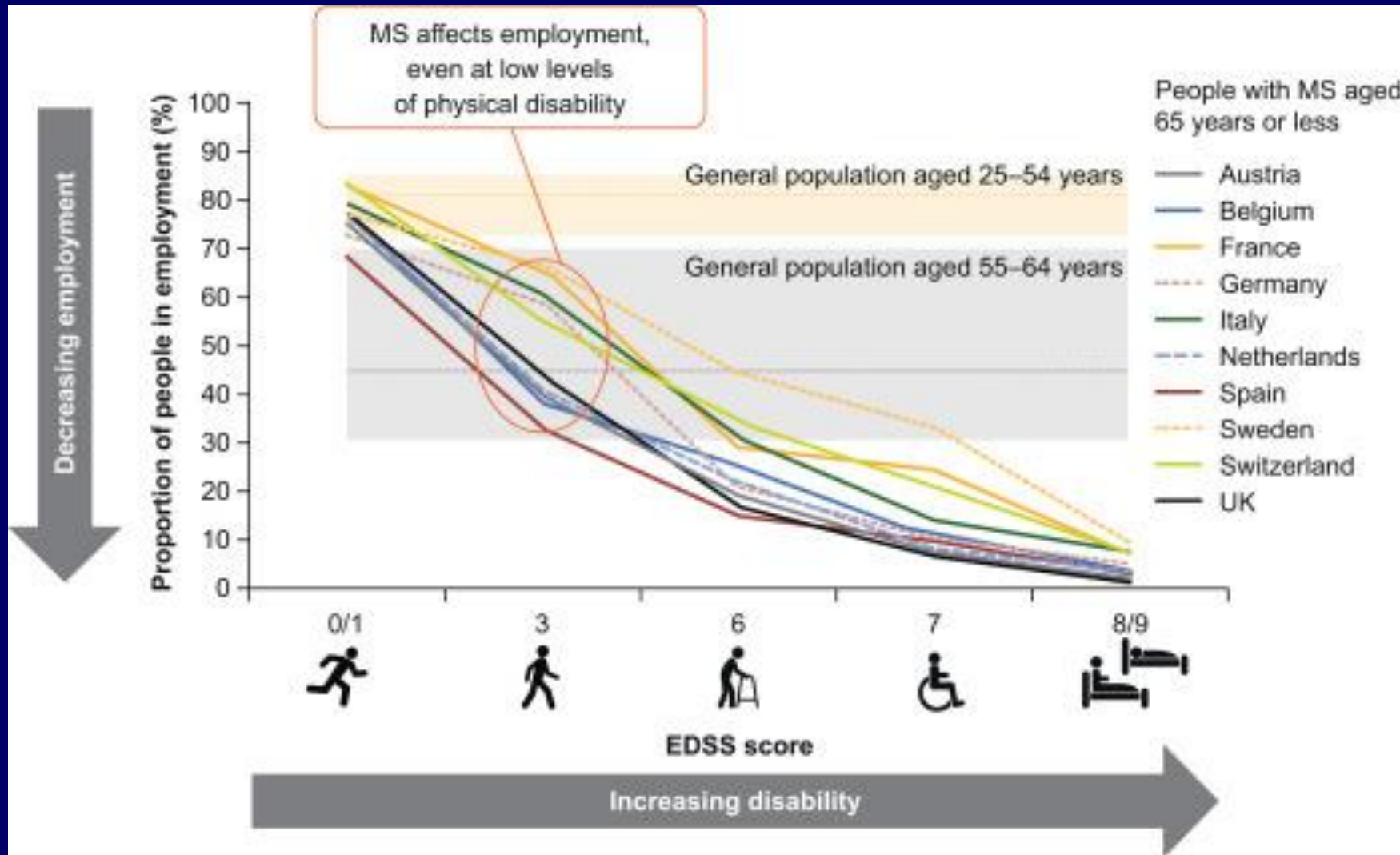
# Expanded Disability Status Scale (EDSS)



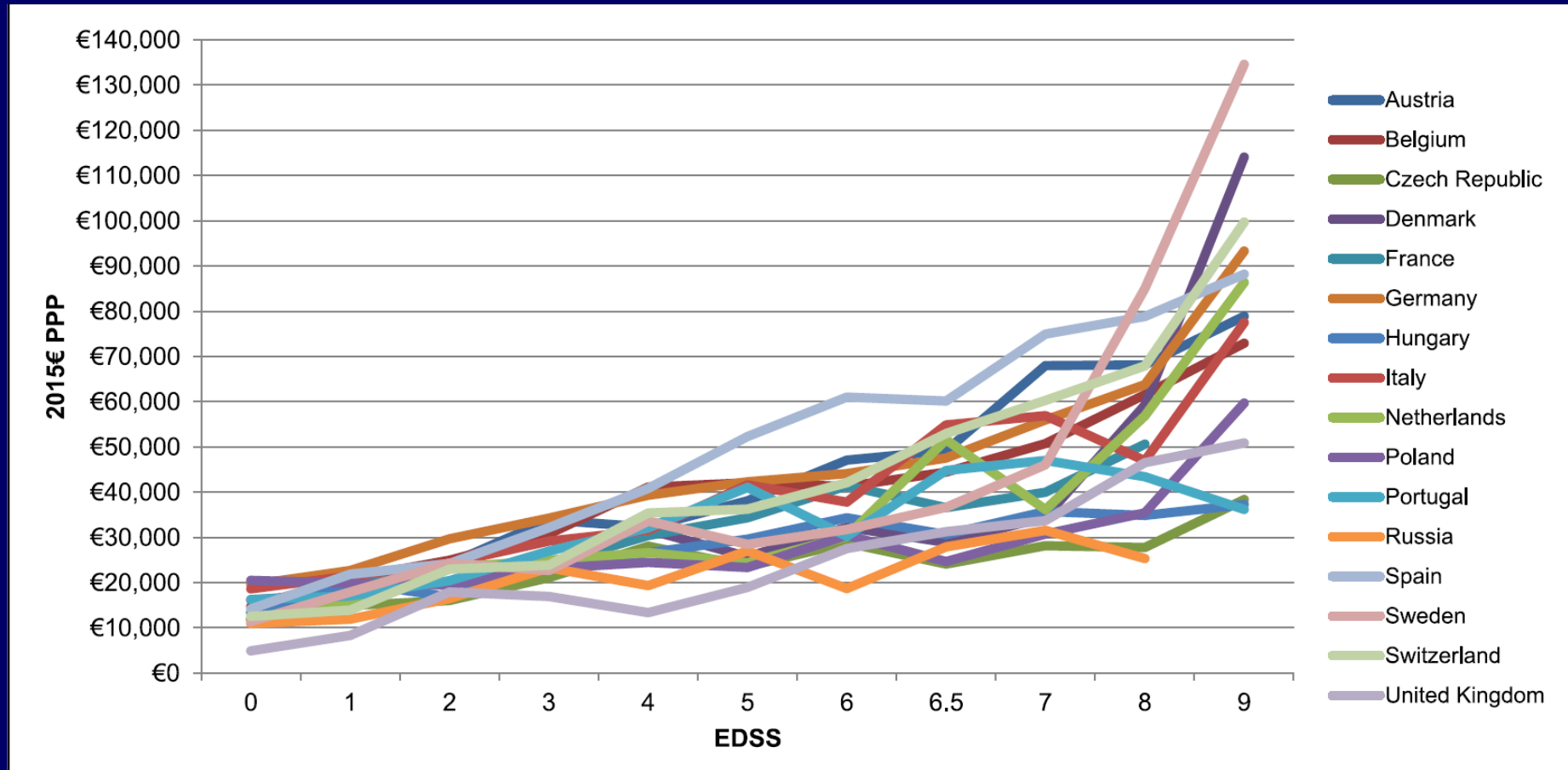
# HRQOL declines with rising EDSS



# Employment declines with rising EDSS

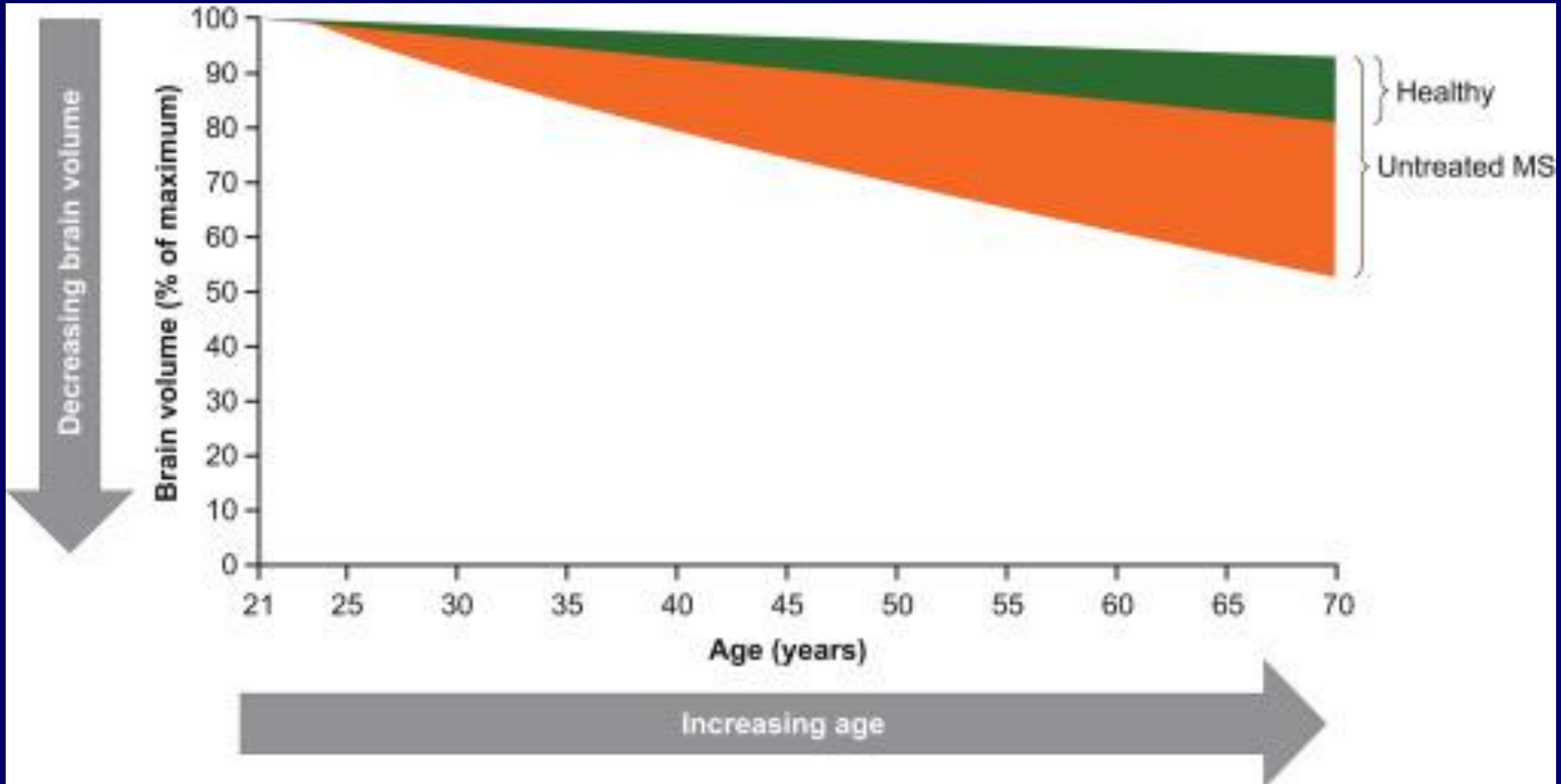


# Health care costs rise as disability rises



Canada's projected annual direct costs in 2031: \$2 Billion

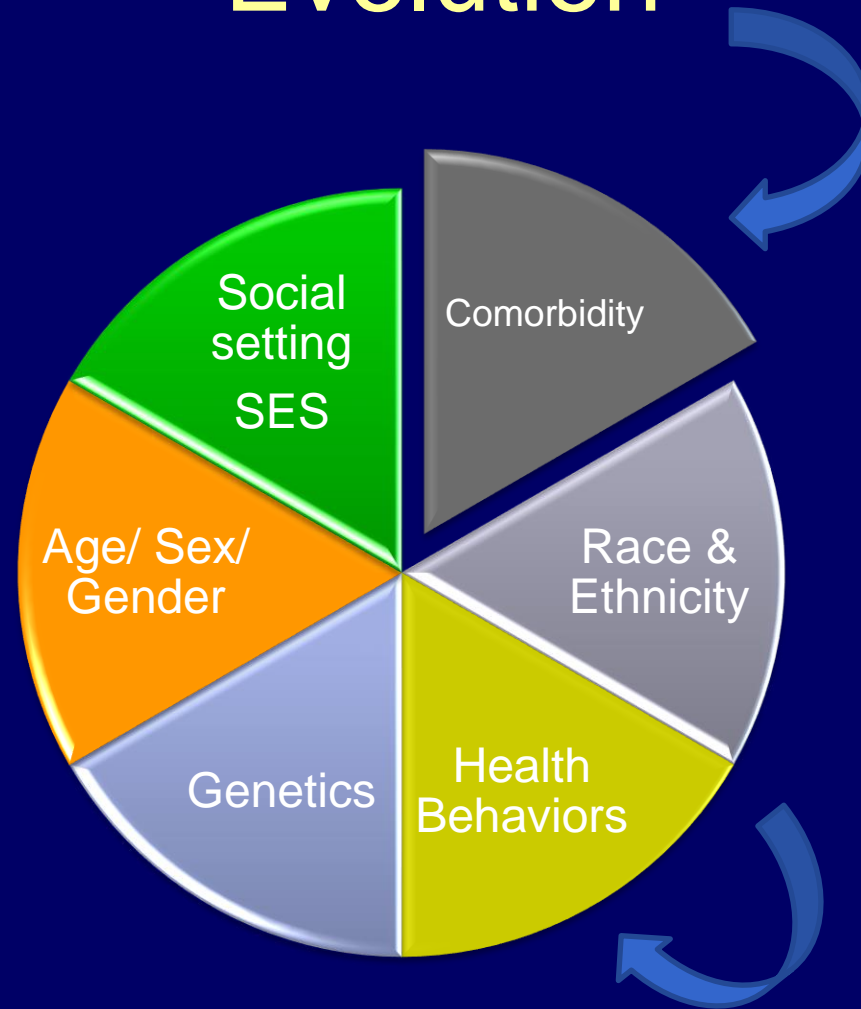
# Brain tissue loss



# Demographic, Clinical, Radiographic Factors at Diagnosis Associated with Worse Prognosis

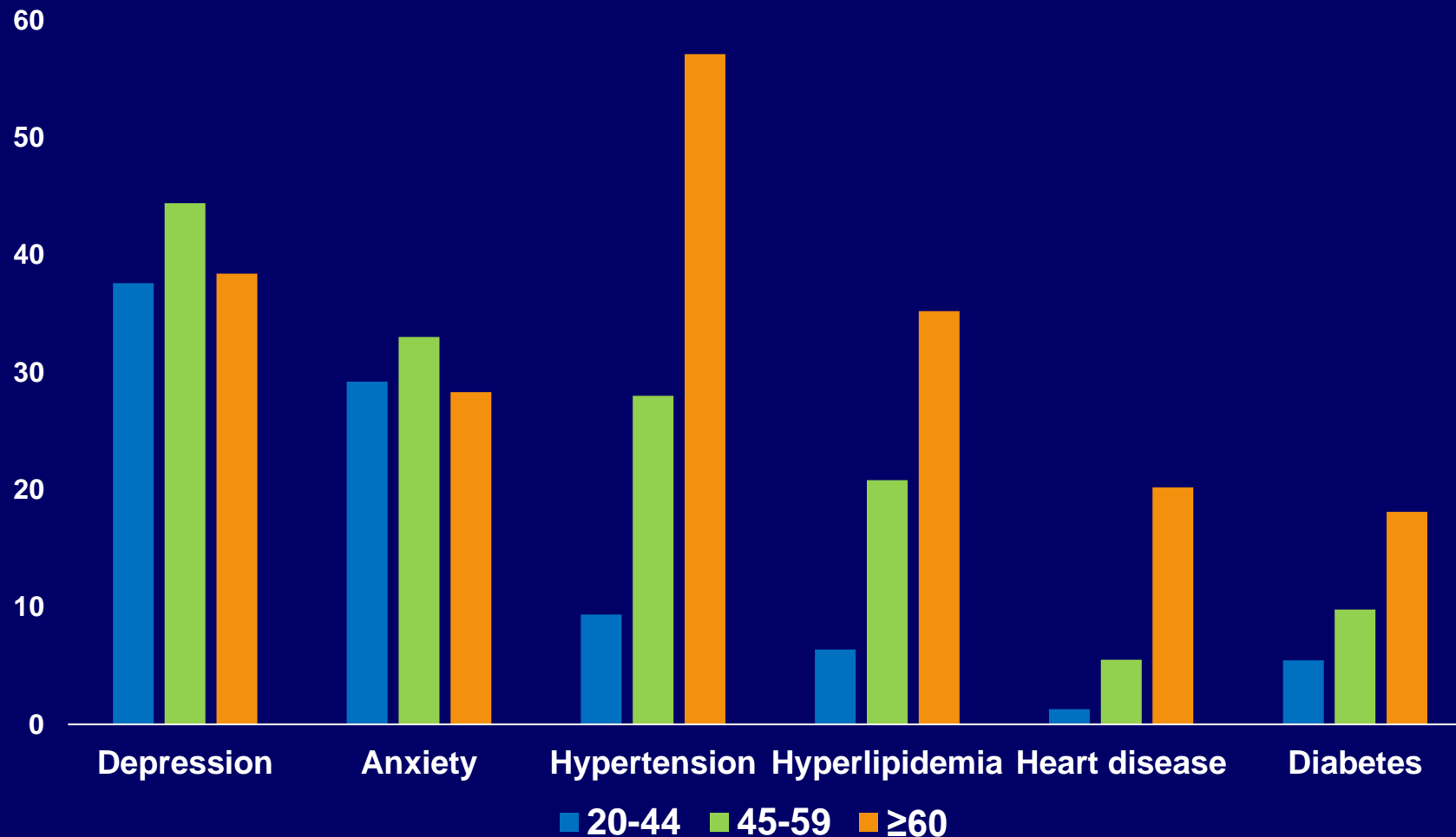
- Demographic & clinical
  - Age >40 years
  - Male sex
  - Non-White ethnicity
  - Comorbidity
- MRI
  - New Gd+/T1/T2 lesions
  - T2 lesion volume
  - Spinal cord lesion
  - Brain atrophy
- Relapse characteristics
  - frequency
    - >1 mod/ severe
  - severity
    - Steroids/hosp. required
    - Severe effect on ADL
    - >1 functional system affected
    - Severe motor/cerebellar/ brainstem
  - Recovery
    - Incomplete recovery

# Biology & Biography Influence Disease Evolution

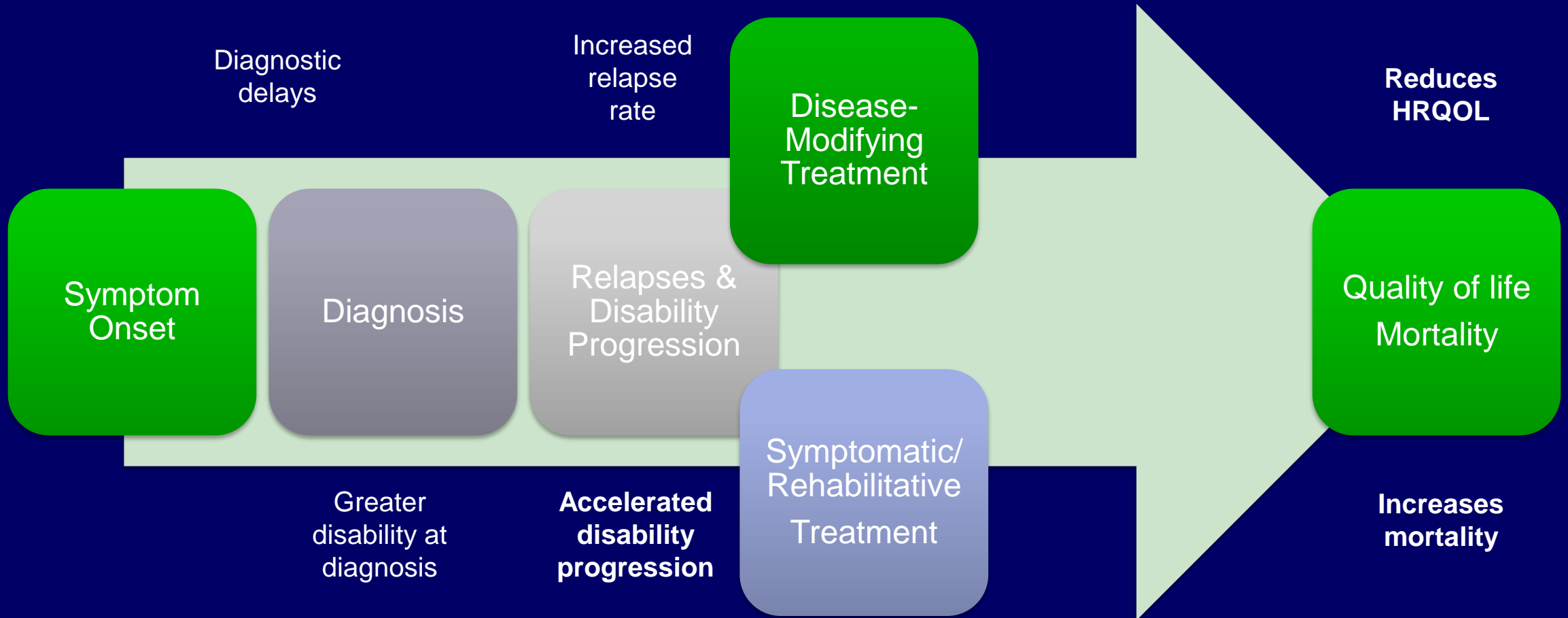




# Prevalence of Physical Comorbidity Increases with Age & Psychiatric Comorbidity Persists



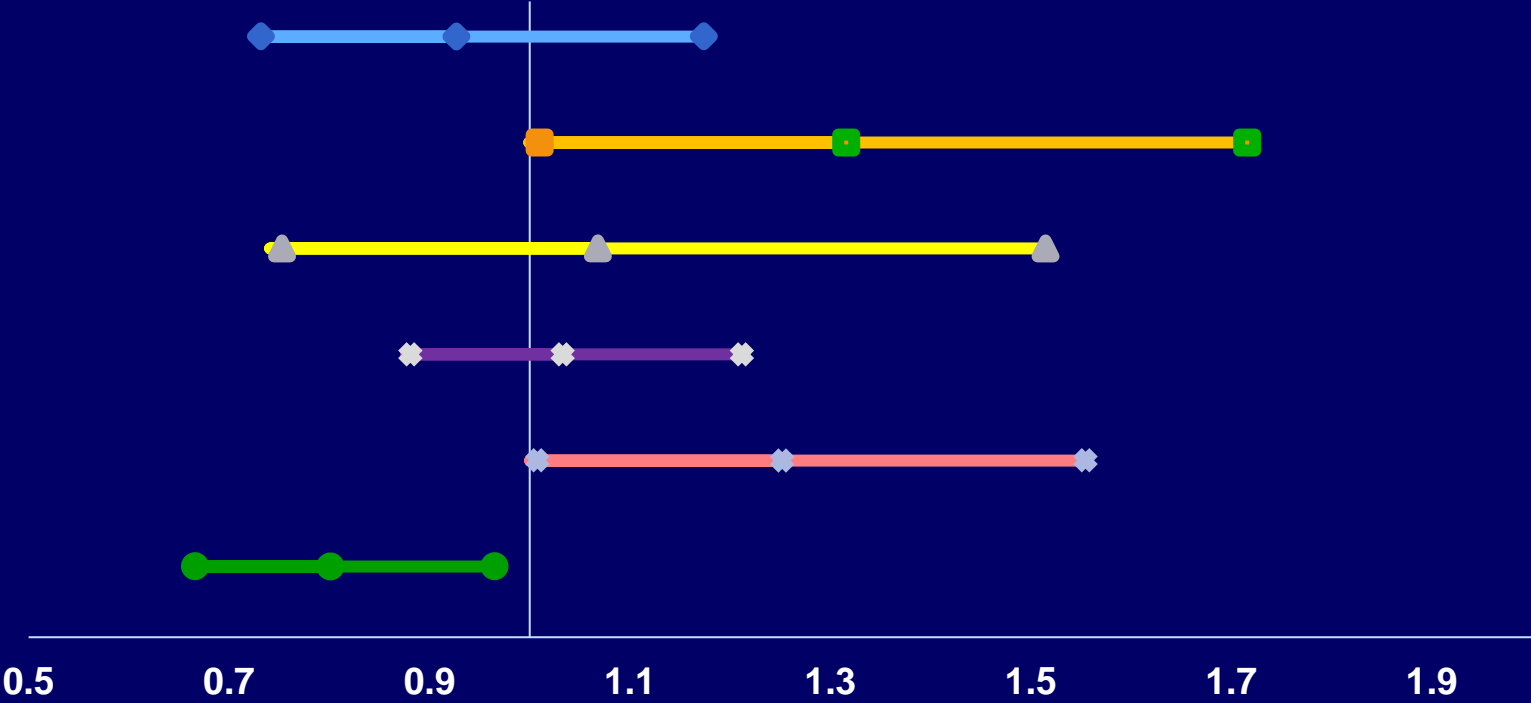
# Comorbidity Affects MS Throughout the Disease Course



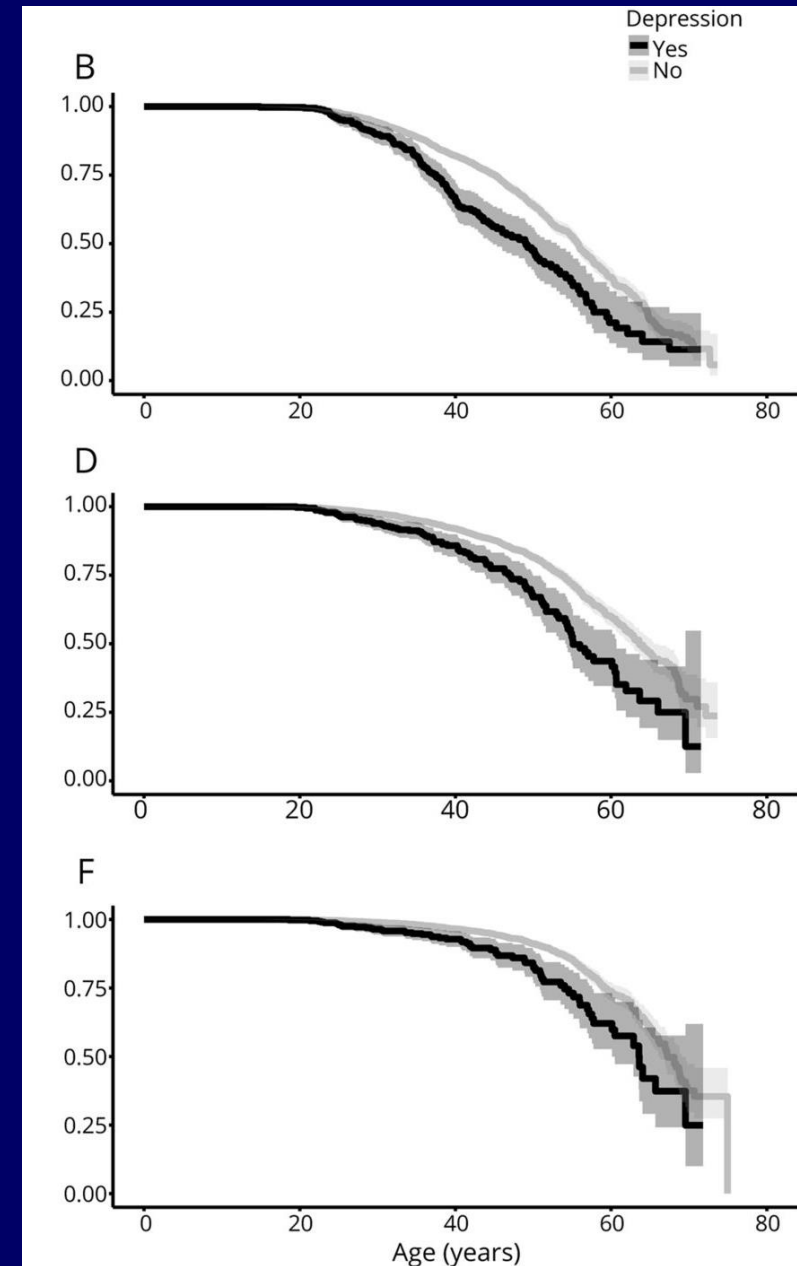
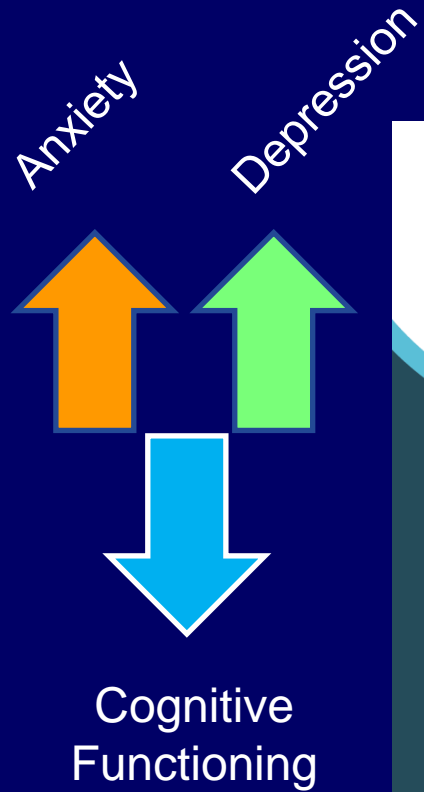
# Dyslipidemia Affects Relapse Activity

CombiRx Trial, n = 959

● Hypertension ● Dyslipidemia ▲ Diabetes ● Depression ● Anxiety ● Migraine



# Psychiatric disorders have broad impacts



# Employment Barriers

- Most common factors reported to affect employment
  - Mobility
  - Upper limb impairment (eg affects keyboarding, writing)
  - Cognitive impairment\*\*\* (eg affects learning, memory, ability to multi-task)
  - Fatigue
- Heat sensitivity, other symptoms in combination also contribute
- Inability to modify work environment or work hours also play a role

# Mitigation:

## Refer people with suspected MS to specialists



MS neurologists have access to specialist equipment and personnel

MS specialist nurses can implement programmes and support people with MS

Access to MS HCPs increases the likelihood of people with MS taking DMTs

MS neurologists have knowledge of rapidly evolving treatment options

A multidisciplinary team offers an integrated approach to care in which different aspects of the disease are managed by different specialists

Specialist clinics enable rapid diagnosis

# Mitigation: Use DMT Early

## Rationale For Early Treatment

- Most patients ultimately develop permanent disability
- Ability to prognosticate limited
- Clinical features correlate poorly with ongoing inflammation & irreversible tissue destruction
- DMT reduce disease activity & disability progression
- Available therapies are preventative not restorative
- Effectiveness is greater early and less later d/t accumulating irreversible pathology, ↓ inflammation, & evolution to a degenerative process

# Strategies: Escalation vs. Early Use of Higher Efficacy Therapy

- Escalation <<historical paradigm>>:
  - Begin with lower efficacy, generally safer therapy.
  - Escalate if treatment response is inadequate (do this early!)
  - Inadequate treatment response = worse long-term outcomes
- Early use higher efficacy therapy
  - Use more effective therapy first.
  - May incur higher risks, but may produce better outcomes
  - Important for those with higher risk for poor outcomes\*
- In Canada, only one higher efficacy therapy is available first-line (i.e. in the treatment-naïve) : ocrelizumab



# Observational comparison of medium vs. high efficacy Rx

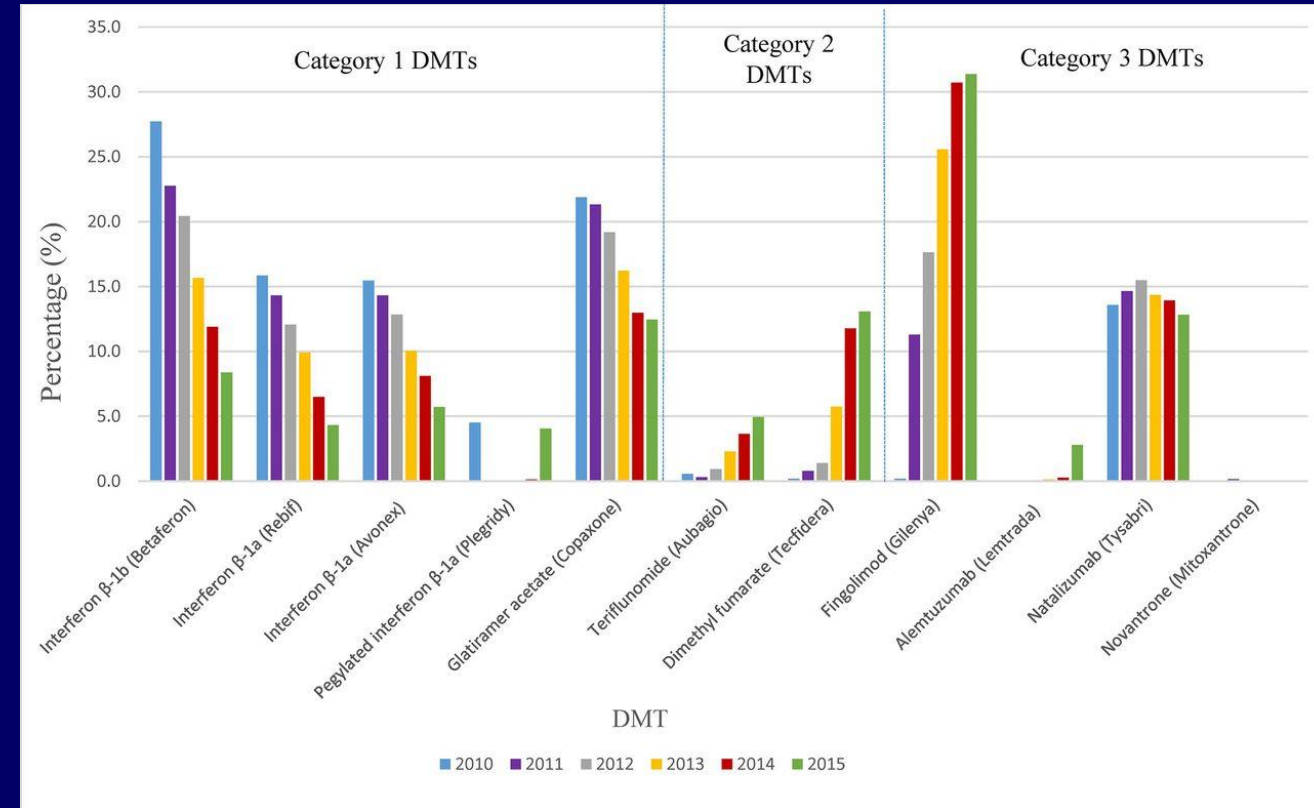
- N = 8953 treatment naïve pts with RRMS
- Propensity score matches
- heDMT = natalizumab, fingolimod, alemtuzumab, cladribine, daclizumab, ocrelizumab

Outcome	meDMT	heDMT
6-mo EDSS worsening		
At 2 years	18.3% (12.7-23.9%)	11.5% (6.7-16.3)
At 4 years	30.1% (23.1-37.1%)	16.7% (10.4-23.0)
First relapse		
At 2 years	51.8% (43.8-59.8%)	30.6% (23.5-37.7%)
At 4 years	66.9% (58.1-75.8%)	41.4% (32.7-50.0%)

Outcomes better with heDMT

# Effect of higher efficacy DMT on employment

- Employment rate in Australians with MS ↑ since 2010 (48.8%) as higher efficacy therapies used (57.8% in 2013)
- ↑ in amount of work vs. no change
  - Category 3 vs. 1:
    - RR 2.84 (1.90-4.25)
- ↑ in work attendance vs. no change
  - Category 3 vs. 1
    - RR 3.14 (1.98-5.00)



# Key Messages

- MS has a broad impact on affected individuals, society & health system
- **Early, effective intervention** is key to reducing disability progression and some of these adverse impacts
- Better identify & treat most prevalent comorbidities → depression & anxiety & vascular comorbidities
  - Need better supports/funding to achieve this goal:
    - smoking cessation
    - behavioral coaches,
    - exercise programs,
    - extended mental health support
- Improve work accommodations
  - Tailored to the individual: good communication, more freq. breaks, unlimited bathroom access, ability to limit sensory stimulation, modified work hours....

