Time matters in multiple sclerosis – international consensus recommendations on diagnosis, management and access to treatment

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Background

- Diagnostic criteria, treatment options, monitoring procedures and our understanding of multiple sclerosis (MS) are rapidly evolving.
- Relapsing MS is no longer considered to consist solely of episodic attacks on myelin in the central nervous system (CNS); diffuse damage to white and grey matter is ongoing throughout the disease course.[1]
- To compensate for damage, the brain appears to have a neurological reserve – a finite capacity to reroute signals or adapt undamaged areas to take on new functions.[2,3]

Objective

- To develop international consensus recommendations for improving diagnosis, management and access to treatment in MS based on advances in disease understanding.

Methods

- An international working group comprising clinicians, researchers, specialist nurses, health economists and representatives from patient groups conducted structured discussions during 2015 to examine:
  - the personal and economic impact of MS
  - current practice in diagnosis, treatment and management
  - definitions of disease activity
  - barriers to accessing disease-modifying therapies (DMTs).

Policy recommendations

- The resulting recommendations for policy change (**Figure 1**) have been widely endorsed by professional and patient organizations.

1. Speed up referral and diagnosis

- Significant delays often occur before a person with symptoms suggestive of MS sees a neurologist. Improved access to MS healthcare professionals and services is therefore required.
- Neurologists with interest and expertise in MS are the healthcare professionals best placed to provide routine diagnosis and to establish an integrated multidisciplinary approach to specialist care and management.
- Campaigns are needed to raise public and professional awareness of MS and the detrimental effect on brain health of delays in diagnosis and treatment.

2. Intervene early to maximize lifelong brain health

- Cognitive impairment in early MS reduces quality of life,[4] daily functioning and employability.[5]
- Preserving brain volume and cognitive reserve (the two components of neurological reserve) protects against disease-related cognitive decline[6] and disability progression[7,8] in MS.
- Adopt a clear treatment goal: maximize neurological reserve, cognitive function and physical function by reducing disease activity in order to preserve CNS tissue.
  - Using the term 'brain health' to describe neurological reserve can help people with MS to conceptualize their disease.
- Start treatment early, with DMT and lifestyle measures.

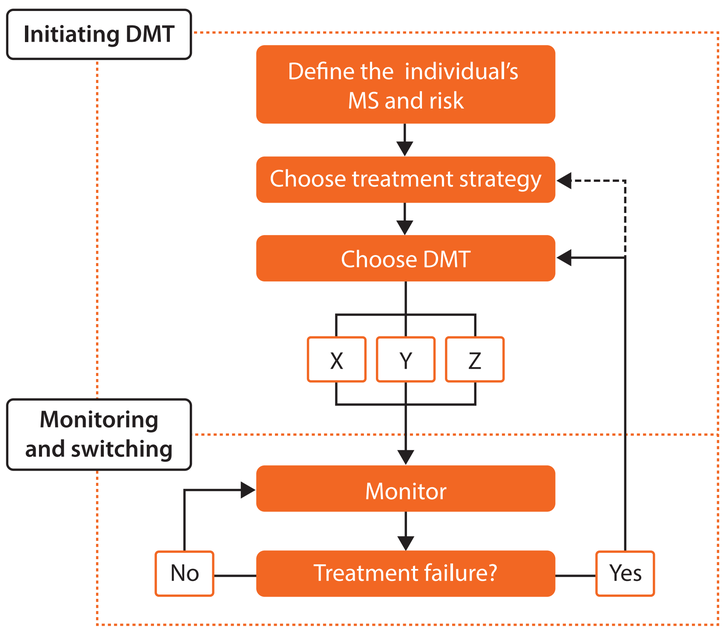

Figure 2. Monitoring is crucial to identifying treatment failure and enabling timely switching to a different DMT.

X, Y and Z represent DMT options.
DMT, disease-modifying therapy.
Adapted with permission from Gavin Giovannoni from Personalizing treatment choice. International MS Physician Summit, 22–23 March 2014, Prague, Czech Republic.[9] © Gavin Giovannoni 2014.

- Implement a shared decision-making process that:
  - embodies dialogue between people with MS and healthcare professionals
  - considers all appropriate DMTs when initiating or switching treatment.

3. Monitor disease activity and treat to a target

- Adopt clear management principles to identify treatment failure and enable timely switching (**Figure 2**):[9]
  - set an explicit treatment target
  - monitor disease activity proactively
  - collect and record data.
- Adopt a definition of disease activity that includes all parameters predicting future relapses and disability progression, and evolves as the evidence base grows.
- Perform MRI brain scans to monitor lesions and brain volume (if possible) at predefined intervals and when necessary.
- Record monitoring data formally in databases and registries to facilitate individual treatment decisions.

4. Act swiftly and generate evidence

- Act swiftly on suboptimal control of disease activity by considering switching to a DMT with a different mechanism of action.
- Generate real-world evidence from registries about the long-term effectiveness and safety of DMTs and therapeutic strategies for use by regulators, health technology assessors, payers and healthcare professionals.

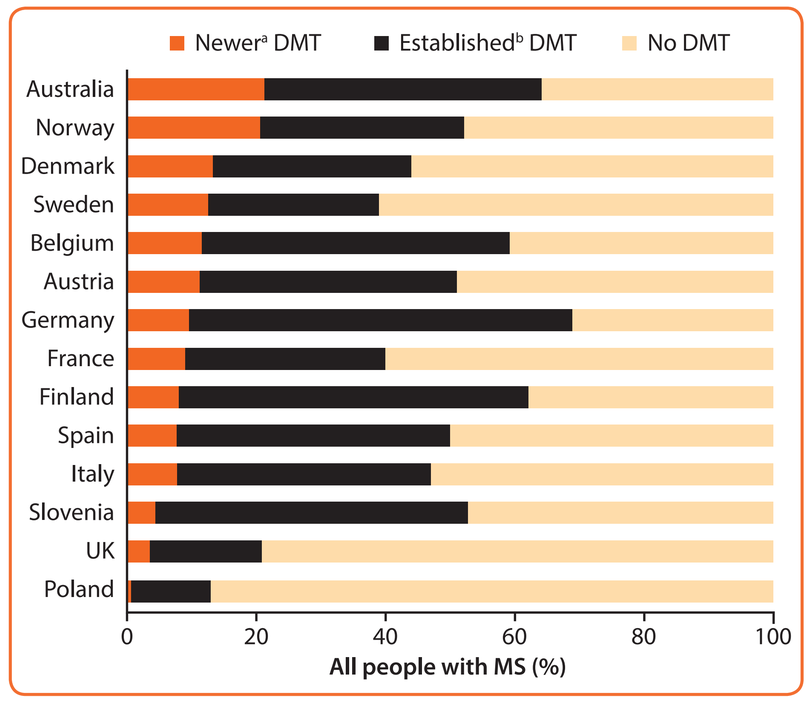

Figure 3. The proportion of people with all forms of MS receiving a newer DMT in 2013 varied considerably between countries.

Data were generated from DMT sales figures as described in the original sources,[11,12] and therefore potentially include people with all forms of MS (relapsing or progressive), and do not differentiate between treatment initiation and treatment switching. All DMTs for Australia: calculation based on sales figures,[12] population[13] and number of people with MS.[14]
[a]Newer DMT is defined as a DMT approved for relapsing forms of MS that has a different mechanism of action from established DMTs.
[b]Established DMT is defined as a DMT approved for relapsing forms of MS during the 1990s or a reformulation or generic version of one of these agents.
DMT, disease-modifying therapy.

5. Take a comprehensive economic approach to evaluating treatment cost-effectiveness

- Costs – especially indirect and informal care costs – increase significantly as disability progresses.[10]
- The recommended therapeutic strategy (**Figure 1**) has the potential to reduce disability progression and avoid some of these long-term costs.
- In many jurisdictions, however, access to DMTs is limited. In 14 upper-middle- and high-income countries, the proportion of people with MS receiving a DMT in 2013 was in the range of 13–69% (**Figure 3**).[11–14]
- To improve access to treatment, the relevant bodies should consider all costs to all parties when conducting economic evaluations, not just those borne by healthcare and social services.
- The continuing investigation, development and use of cost-effective therapeutic strategies and alternative financing models should be encouraged.

Conclusions

- Major policy changes are needed in order to translate advances in diagnostic criteria, treatment options, monitoring procedures and disease understanding into better outcomes.
- The overarching recommendations below aim to facilitate a therapeutic strategy involving proactive monitoring, shared decision-making, and improved treatment access.
  - Minimize delays in the diagnosis of MS and in the time to treatment initiation.
  - Set goals for treatment and ongoing management that will optimize outcomes for every person with MS.
  - Consult the most robust evidence base possible when making treatment and management decisions.
  - Formally record the results of monitoring to generate further real-world evidence.
- This more urgent approach will enable MS healthcare professionals and other stakeholders to strive towards the highest possible standards of care.

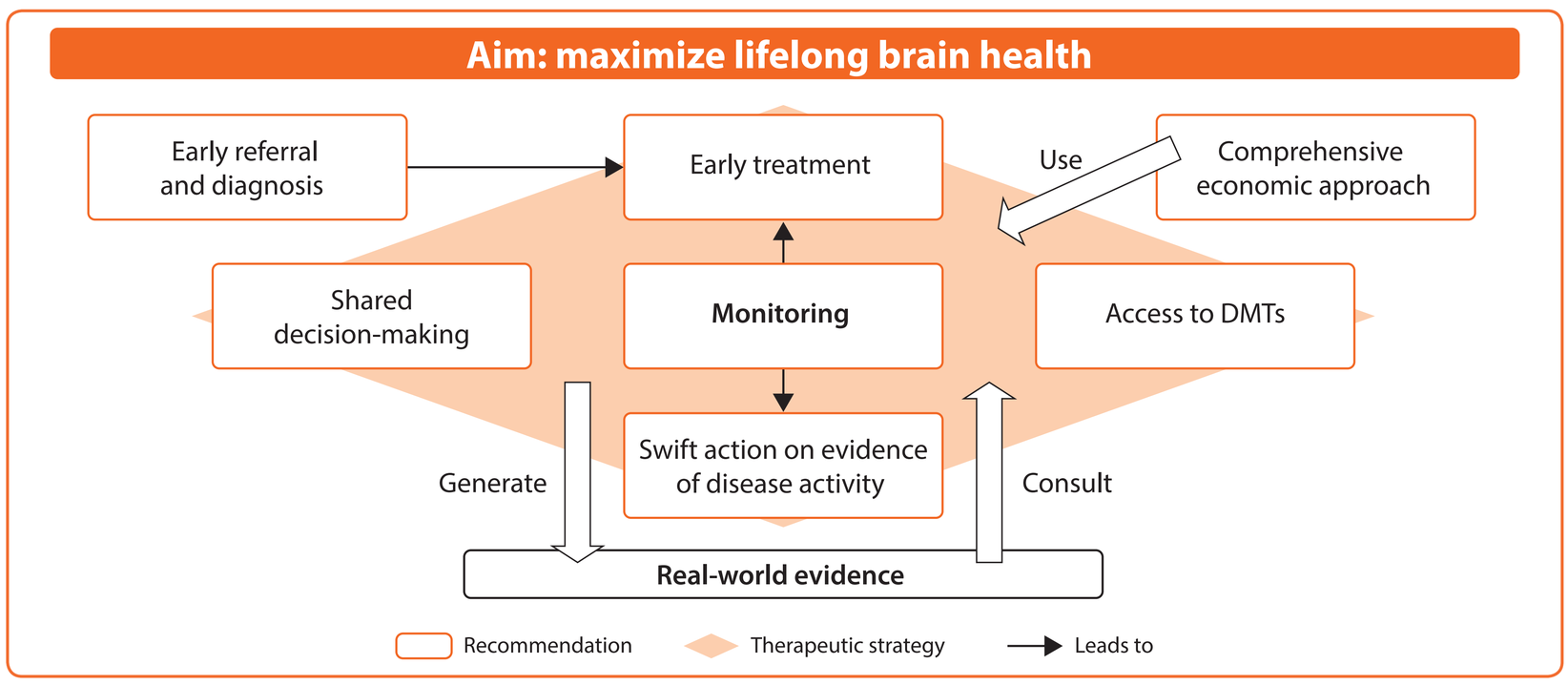

Figure 1. We recommend a therapeutic strategy based on regular monitoring that aims to maximize lifelong brain health while generating robust real-world evidence.

DMTs, disease-modifying therapies.

To read the full report and consensus recommendations, visit **www.msbrainhealth.org**

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Disclosures

G Giovannoni has received consultancy fees for advisory board meetings from Biogen Idec, Genzyme Sanofi, Merck Serono and Novartis, relating to a phase 3 trial programme in MS from GSK and relating to data safety monitoring board activities from Synthon BV; has served on steering committees for AbbVie, Biogen Idec, Novartis, Roche and Teva; and has received honoraria for speaking at medical education meetings from Genzyme Sanofi, and for speaking at a physicians' summit from Biogen Idec. H Butzkueven has received consultancy/adviser fees, honoraria and/or research support from Biogen, CSL Limited, Genzyme, Merck Serono, and Novartis. S Dhib-Jalbut has received consultancy fees from Bayer, Genentech, Genzyme, Serono and Teva; and grant support from Biogen and Teva Pharmaceuticals. J Hobart has received consultancy fees, honoraria, support to attend meetings or research support from Acorda, Asubio, Bayer Schering, Biogen Idec, Genzyme, Merck Serono, Novartis and Teva. G Kobelt has received consultancy fees for health economic topics related to multiple sclerosis from Biogen, Genzyme, Merck Serono, Novartis and Teva. G Pepper has nothing to declare; his organization, Shift.ms, has received support from Biogen, Genzyme, Merck Serono, Novartis, Roche and Teva. MP Sormani has received consultancy fees from Biogen, Teva, Genzyme, Merck Serono, Novartis, Roche and Synthon. C Thalheim has acted as a speaker and adviser on non-product specific subjects for Almirall, Bayer, Biogen, GSK, Novartis, Roche, Synthon and Teva. A Traboulsee has received grant funding from the MS Society of Canada, the Canadian Institute for Health Research, the Lotte and John Hecht Foundation, the Vancouver Hospital Foundation, Bayer, Roche and Biogen; honoraria or travel grants from Biogen, Teva Canada Innovation, Roche, Merck/EMD Serono and Chugai Pharmaceuticals; and has served on the data safety monitoring board for Merck Serono and a clinical trial steering committee for Roche. T Vollmer has received consultancy fees from Acorda, Biogen Idec, Consortium of MS Centers (CME presentation), DeltaQuest, Genentech, Medscape, Mylan, Novartis, Novartis Canada, Novartis Japan, Teva, Teva Canada and Xenoport; and research support from Accelerated Cure Project, Acorda, Avanir, Biogen Idec, EMD Serono, Genzyme, Jensen Research, MedImmune, the US National Institutes of Health, Novartis Pharmaceuticals, Ono Pharmaceuticals, Rocky Mountain MS Center, Roche, Teva Neuroscience and Vaccinex.

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