

NICE guideline practical summary

Management of multiple sclerosis in primary care

A summary of NICE guideline CG186 and the practical implications for GPs, covering diagnosis, information and support, relapse treatment and management of MS-related symptoms, but not including disease-modifying treatments.

Written by:

Dr Jeremy Chataway

Jeremy Chataway is a consultant neurologist at The National Hospital for Neurology and Neurosurgery, University College Foundation NHS Trust (UCLH) and Queen Square Multiple Sclerosis Centre, Department of Neuroinflammation, University College London (UCL), London, UK. He was also on the NICE Guideline Development Group for the management of multiple sclerosis guideline.

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Peer reviewed by:

Dr Paul Cooper

Paul Cooper is a consultant neurologist at Salford Royal Foundation Trust, Salford, UK. He was also on the NICE Guideline Development Group for the management of multiple sclerosis guideline.

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Multiple sclerosis (MS) is a disease of young people that affects 2.5 million worldwide and over 120,000 in the UK.[1] While the cause is unknown, the last 20 years has seen a fantastic increase in approved disease modifying treatments (DMTs) that can reduce the relapse (attack) rate by up to 80%.[2] This is the good news. The bad news is that progression, with onward accumulation of disability (eg, affecting walking, bladder function, and cognition) remains intractable and is where the global therapeutic effort is most needed and increasingly most concentrated. How do these recent NICE offerings (CG186 replacing CG8) help us in a primary care setting? The scope of this guideline is not about DMTs (where technology appraisals exist [3-8]), but rather about the diagnosis, symptom and relapse management, and support of adults with MS.

What shines through the guideline, is that the care and treatment of this complex and unpredictable condition, where the key players include GPs, MS nurses, neurologists, physiotherapists, occupational and speech therapists, psychologists, and, of course, the individual affected by MS, must take place in a joined up environment, to achieve an optimal outcome.

Key practice-changing points

1. Exclude alternative diagnoses before referring a person suspected of having MS to a neurologist

The formal diagnosis of MS by the neurologist is complex and involves stitching the history and examination together with investigations such as magnetic resonance imaging (MRI) and spinal fluid analysis. There are, however, some fairly straightforward principles that GPs can follow from the outset, that are important for avoiding under- and over-diagnosing MS.

- Apart from routine blood tests, the following should be included:
 - Vitamin B12 levels
 - HIV
 - An Inflammatory profile (eg erythrocyte sedimentation rate (ESR) and antinuclear antibody (ANA))
- Be aware of likely common symptoms:
 - Loss or reduced vision typically in *one* eye with pain or ache (optic neuritis)
 - An ascending sensory disturbance with or without weakness (eg from feet to abdomen)
 - Double vision
- Do not routinely suspect MS if the main symptoms are dizziness or fatigue
- MRI alone is not used to diagnose MS
- MS should only be diagnosed by a consultant neurologist using current criteria.

2. Ensure at each follow-up appointment that patients are given relevant ongoing information and support

It is vital that when a diagnosis of MS is made (and at subsequent follow up) it is carried out in a fully supportive environment where appropriate knowledge (oral and written) is available about the disease, its manifestations, and treatments. While this will take place in secondary care at the time of diagnosis, this should be reinforced subsequently. It is therefore important to ensure that:

- People with MS have been given information about charities (see Resources) and local social services
- People with MS have informed the DVLA of their condition and are also aware of their legal rights including employment and benefits advice
- There is appropriate on-going follow-up with the MS team with a clear point of contact
- Care sits within a coordinated multidisciplinary approach
- A yearly comprehensive review is mandated by healthcare professionals with expertise in MS and its complications.

3. Advise people with MS, including those with mobility problems and/or fatigue, to exercise and consider exercise referral schemes to encourage patients to continue exercising after treatment programmes have been completed

Exercise is beneficial both for the disease and for general health. It is worth specifically emphasising to patients that exercise will not have any harmful effects on their MS as well explaining the benefits. Recommendations about exercise in the guideline include:

- Consider a supervised exercise programme involving moderate progressive resistance training and aerobic exercise to treat people with MS who have mobility problems and/or fatigue
- Ensure those with mobility problems have access to a rehabilitation team/physiotherapist with expertise in MS
- Do not prescribe fampridine for lack of mobility in people with MS, as it is not a cost effective treatment.

4. Address the vaccination needs of people with MS to reduce the risk of relapse or progression of the disease

- Be aware that live vaccinations may be contraindicated for people with MS who are on DMTs
- When offering flu vaccination note that the benefits and risks should be individualised and discussed (considering the most recent advice from the Department of Health), it is not compulsory, and there is a possible risk of relapse post vaccination in people with relapsing MS.

5. Discuss issues surrounding pregnancy with women of childbearing age with MS

Pregnancy is not a contraindication in people with MS but it should be planned carefully, particularly with regard to stopping and re-starting DMTs, breast feeding, current disability, and on-going relapse rate. Note that:

- Relapse rates may reduce during pregnancy and relatively increase for three to six months post partum
- Pregnancy does not increase the risk of progression of MS.

6. Advise people with MS not to smoke and explain its effects on disease progression

Patients with MS should not smoke as this may negatively affect disability progression. There appears to be a clear association of deterioration in function and for the conversion of relapsing to progressive MS, even when corrected for other factors. For example, in one study of nearly 900 people, conversion occurred faster in current smokers than never-smokers, but was similar in never- or ex-smokers.[9]

7. Do not use dietary supplements to treat MS or its symptoms unless they are specifically indicated

A number of diets (with a variable evidence base) have been devised for people with MS, and in my experience patients can find these helpful). In terms of formal supplements:

- Do not use vitamin B12 injections to treat fatigue unless the patient has a deficiency
- Do not use omega-3 or omega-6 fatty acid compounds as there is no evidence that they affect relapse frequency or progression of MS
- Vitamin D should not be used solely to treat MS because there is no convincing evidence for its efficacy in managing the condition (though research is on-going). However, vitamin D may be given to at risk groups for other health benefits according to national guidelines.[10]

8. Offer treatment for factors that may aggravate spasticity in people with MS (eg constipation, urinary tract or other infections, inappropriately fitted mobility aids, pressure ulcers, posture, and pain)

Intense muscle stiffness, spasm, and muscle jerking are all manifestations of spasticity. There are a number of straightforward pharmacological approaches available to alleviate it. The best approach is to start at a low dose and gradually build up in divided doses to the maximum tolerated dose with the maximum effectiveness.

- Gabapentin and/or baclofen are first line options, depending on contraindications and the person's comorbidities and preferences. If one drug is not tolerated consider switching to the other
- Tizanidine or dantrolene are second line options
- Benzodiazepines (eg clonazepam) are used third line but can also be useful for nocturnal spasticity
- Cannabis extract (Sativex) is not a cost-effective option for treating spasticity in people with MS
- You should refer your patient to specialist spasticity services if these approaches are ineffective
- Non-pharmacological approaches (eg resistance and aerobic exercise) are complementary and advice should be taken from physiotherapists and occupational therapists.

9. In people with MS and fatigue, assess and treat anxiety, depression, insomnia, and relevant medical problems such as anaemia and thyroid disease

Fatigue is pervasive and hard to treat, and you should follow these principles:

- Explain that there will be natural fluctuation and temperature effects (eg a hot humid day may in some people worsen the neurological symptoms)
- Amantadine can sometimes be helpful (though note that at the time of publishing [DATE] the drug is not licensed for this indication)
- Consider fatigue management courses. NICE did not recommend specific courses, but many GPs find FACETS courses helpful. Consider mindfulness-based training for anxiety
- Consider exercise programmes incorporating aerobic and resistance activity, stretches, and yoga
- Vestibular rehabilitation can help fatigue in those with balance impairment.

Comorbidities are highly prevalent in people with MS and can have compound effects on disability. A comprehensive review of all aspects of the person's care should be carried out once a year and should include an assessment of anxiety and depression, in line with the relevant national guideline. [11, 12] Other issues to consider are insomnia, anaemia, thyroid disease, and skin integrity.

10. Assess and treat relapses urgently according to local pathways

Relapses — changes in the neurological status that come on generally over days or weeks, and can be differentiated from natural fluctuation — are, of course, part of the core of the condition and may occur even in the face of sustained progression, though less so. Examples might be visual blurring in one eye (optic neuritis), leg weakness (spinal cord relapse) or balance issues (cerebellum or brainstem). The guiding principles are to:

- Treat infection (often urinary) promptly
- Use high dose steroids for a significant relapse, typically methylprednisolone orally or intravenously, to hasten recovery, but
- Note that high dose steroids might temporarily worsen mental health and should be used with caution if there is significant depression. Blood sugar control may worsen in people with diabetes
- Ensure the MS team is informed about significant relapses because they may indicate that the prescribed DMTs need to be changed
- Consider the bone health status.

Pearls of wisdom

1. Don't rely on the MRI alone to make a correct diagnosis

MS is a feared diagnosis and, of course, a serious neurological condition of the brain and spinal cord. It typically affects young people of working age, perhaps with young families, and can have a devastating effect on their hopes, plans, and aspirations for their life. Saying that, the therapeutic scene has changed dramatically for the better over the last 20 years with up to a dozen DMTs available and symptomatic approaches that are more logical than previously and with greater reach. It is clearly vital that the correct diagnosis is made, that correct information is given about the biology of the disease at the outset, and that all disciplines are engaged. General practice is at the core of this.

From this NICE document I would highlight and reinforce the maxim that MRI alone does not at all make the diagnosis. The radiological statement 'high T2 lesions seen, consider MS', may ultimately be true, but such appearances can be seen with natural aging and other conditions (eg vascular, migraine). A health warning in this era of the explosive use of MRI should be applied.

2. All exercise is good exercise

Physical exercise suitable for patients with MS may take a wide variety of forms, from solo use of the gym, a personal trainer, out-patient physiotherapy, and formal neuro-rehabilitation assessment. All are highly valuable depending on the needs of the particular patient at the particular stage of their MS, and will change through the course of the disease.

I would personally say that:

- All exercise is good exercise
- Timely advice from an appropriately trained profession (eg a physiotherapist with neurological skills) should always be thought about
- Early engagement with rehabilitation services, particular if function is worsening, should take place
- A thorough occupational therapy review, including a home visit, is vital, particularly if the disease is progressive.

3. Tackling spasticity effectively

One of the miseries of MS is the pain of spasticity and its impact on daily life, even of the most basic of daily tasks: sitting in a chair or getting a good night's sleep. My approach to management is to start with a low dose of a first line drug (eg baclofen) and gradually titrate up over weeks (often in divided doses) until relief is achieved, side effects occur, or a maximum tolerated dose is reached. If the situation at this point is satisfactory then stay at this dose. If there is a partial improvement, then slowly and carefully add another drug (eg gabapentin). If there is no response to that, then I would try another agent (eg tizanidine or dantrolene). If there had been no response at all to the first drug, then I would switch completely to another of these agents and start again. It is not a race and with patience, relief should follow in most situations

Remember:

- Treating spasticity can be a fine equation to balance: if you use too much drug then (reversible) weakness can occur
- Underlying conditions can worsen the spasticity (eg infection or constipation) so make sure you treat these
- Expert patients can auto-titrate their own spasticity medication and should be encouraged to do so
- Gabapentin will also be effective for relieving neuropathic pain if present.

If these approaches are not successful you should refer your patient to a spasticity service, where advanced management can include botulinum toxin and intrathecal baclofen.

4. Don't forget to identify and address cognition problems

Cognition is increasingly reported as being affected in people with MS, with some relationship to disability.[13] Anxiety and depression should be treated as appropriate and may masquerade as cognitive issues, which will improve with treatment of the underlying anxiety/depression. A formal neuro-psychological assessment and intervention may be required. You should also consider and address the effect on work and family life.

Clinical tip: Urinary dysfunction

Urinary dysfunction is very common in patients with urgency and frequency dominating, and compounded by infection, but it is eminently treatable. The NICE guideline on MS does not cover urinary symptoms, but I would offer the following advice.

- A simple post-void bladder ultrasound will establish whether more than 100ml of urine is being accumulated
- If <100ml urine, work through agents such as oxybutynin (modified release), solifenacin, and tolterodine, titrating to the maximum dose and discarding if ineffective
- If >100ml urine then intermittent catheterisation is likely to work.

Tricky patient case studies

1. You are asked to see a 34 year woman who reports numbness in her toes that has come on over the last month. During this time she has been abroad where she had a brain MRI scan. She was told by a doctor there that she has MS. Is this likely to be correct?

While she may well have MS – she is at an appropriate age and has neurological symptoms – there are many stages to go through before a correct diagnosis can be made. In terms of the history, you need to ask is this her first neurological manifestation or has she had previous events? Is she systemically well or is there evidence of other systemic disease (eg rash, weight loss)? On examination is there objective evidence of altered sensation? Are there other signs (eg leg weakness or altered reflexes)? You should carry out routine blood tests along with vitamin B12 levels, HIV, and an inflammatory profile (ESR and ANA) as described earlier. If these are negative you should refer the patient to the neurology department for review of both patient and MRI scan — urgently if her symptoms are deteriorating.

2. You see a 25 year old man with known relapsing-remitting MS. He says that over the past eight weeks he has gradually become weaker in his legs and he now has difficulty getting to the corner shop. You confirm that he is significantly weak in his legs. What should you do next?

This certainly sounds like a relapse and an infection screen should take place, especially for a urinary tract infection, which should be promptly treated. In addition he should receive timely high dose corticosteroids according to local policy, with a neuro-physiotherapy review. You should inform his neurologist that he has had a significant relapse, to evaluate the need for a change or commencement of a DMT.

3. He is kept under regular review, but complains of on-going spasticity, which makes it difficult to sleep and to get in and out of his car. How should you proceed?

First, you should look for and treat any provoking factors, such as infection and constipation. Next, he should be prescribed an anti-spasticity agent, such as gabapentin, and the dose of this should be gradually increased until a positive effect occurs or side effects intervene. The maximum dose of gabapentin is 1200 mg tds and you should titrate up to this before discarding for lack of effect or side effect.

4. A 47 year old woman with established progressive MS comes to see you. She works as a company director in a medium sized firm, but feels that her decision making ability is 'not as sharp' as it should be, and that she has made some small mistakes recently. She wonders if it's the stress of the job and would like your advice.

Certainly stress, anxiety, and depression will impair cognitive performance and must be considered first and treated. Once these have been eliminated, it is possible that this patient might be experiencing some early cognitive change due to her MS. It would be useful at this point to arrange a dedicated neuro-psychological evaluation and to consider of what strategies would be useful to manage the issues. If available, vocational rehabilitation would also be valuable.

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Resources

The following UK charities offer useful resources for healthcare professionals and for people with MS.

- Multiple Sclerosis Society: <http://www.mssociety.org.uk/>
- Multiple Sclerosis Trust: <http://www.mssociety.org.uk/>

Shift MS (www.shift.ms/) is targeted at younger people with the condition.