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Association for Palliative Medicine of Great Britain	Guideline	010	013 - 020	We welcome the inclusion and guidance around supporting people with advanced Multiple Sclerosis, with signposting to palliative care services, guidance around recognising the end-of-life phase and links to information and support for advance care planning. The recommendation to explain to the person with Multiple Sclerosis about advance care planning 'when appropriate' needs greater clarification as health care professionals may not acknowledge this phase early enough and miss opportunities to do it. We would suggest the following recommendation: Think about discussing advance care planning with people at an earlier opportunity if you expect their communication ability, cognitive status or mental capacity will deteriorate. Be prepared to discuss end of life issues whenever people wish to do so; consider future care planning and decision making for people without mental capacity as per the Mental Capacity Act 2005 legislation.	Thank you for your comment. We have incorporated your suggestion into recommendation 1.2.18
Association of British Neurologists	Guideline	015	003	Section 1.5.12 – The evidence to support the use of Modafinil and SSRIs in the pharmacological management of fatigue in MS is extremely weak and there are also specific concerns in the case of Modafinil regarding its safety. We are concerned about the recommendation for the use of Modafinil except in the clear circumstance of	Thank you for your comment. The committee acknowledge that there is only limited evidence of benefit for amantadine, modafinil and SSRIs (see committee discussion of the evidence in evidence review D. However, in their clinical experience and opinion some people do respond to these treatments and given the

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				significant daytime sleepiness and the use of a SSRI unless it is felt that anxiety and depression were key drivers for the fatigue the person with MS was experiencing. We feel that only a trial of amantadine should be routinely recommended pharmacologically.	potential impact of fatigue on daily life they made a recommendation to consider these interventions. In recommendation 1.5.12 we now refer to considering safety of the drugs. In recommendation 1.5.15 we now refer to monitoring and reviewing response to treatment. The guidance in the summary of product characteristics has now also been highlighted in the rationale and impact. The 2020 MHRA safety advice on modafinil (Provigil) is now referred to in recommendation 1.5.14 and rationale. Recommendation 1.5.4 highlights the importance of recognising other causes of fatigue including anxiety and depression.
Association of British Neurologists	Guideline	018	003	Section 1.5.23 onwards – We agree with the naming of baclofen and gabapentin as initial spasticity therapies and also the recognition of the issues around gabapentin prescription. We feel there should also be mention and a view expressed on other oral therapies used in this area – particularly tizanidine, dantrolene and benzodiazepines. Although cannabinoids are mentioned and reference made to the 2019 NICE consultation we feel the Guideline should make more clear what role they feel this group of drugs has in spasticity treatment as there remains considerable access difficulties to this group of therapies. If the guideline does see the use of cannabinoids as favourable in certain circumstances then this would be extremely helpful in trying to solve current issues of	Thank you for your comment. The committee removed the recommendations on third- and fourth-line options due to the lack of clinical and health economic evidence. These treatments should only be considered by specialists (see recommendation 1.5.31). Cannabinoids were outside of the scope of this guideline and therefore we cross-referred to the existing NICE guidance but no evidence review was undertaken for this update.

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				availability which can be frustrating to some people with MS.	
Association of British Neurologists	Guideline	021	007	Section 1.5.38 – Additional guidance would be helpful as to when the guidelines feel a full neuropsychology referral would be helpful to assess cognition as access to such services are often dictated by local availability. Further clarity would be appreciated to help service development in this area.	Thank you for your comment. When a referral for a full neuropsychological assessment would be appropriate varies according to a number of factors and the committee considered that these cannot be captured in a recommendation.
Association of British Neurologists	Guideline	022	004	Section 1.6 - Given the widening availability of disease modifying therapies especially to progressive patients and blueteq requirements there is now we believe a strong case for all specialist comprehensive reviews to have as a minimum requirement a defined recorded EDSS value.	Thank you for your comment. As not all people conducting the comprehensive review will be able to assess the EDSS we have edited recommendation 1.6.3 to refer to the nature and extent of the disability.
Association of British Neurologists	Guideline	025	021	Section 1.7.8 – it is also common practice to recommend a PPI medication such as omeprazole to be co-prescribed with a high dose steroid course for MS relapses.	Thank you for your comment. These recommendations were not updated by this guideline update.
Association of British Neurologists	Guideline	028	002	Section 1.8.1 – although the evidence for routine prescribing of vitamin D to 'treat' MS does not exist there are consensus guidelines which do incorporate an evidence base for vitamin D supplementation for people with MS. We feel this should be acknowledged and although not favouring routine prescribing should recognise many people with MS are already taking high dose vitamin D supplementation.	Thank you for your comment. Vitamin D was not included in the scope of this guideline. The government guidance on vitamin D supplements can be found here https://www.gov.uk/government/publications/vitamin-d-supplements-how-to-take-them-safely?msclkid=e3328675b4bb11ec81f79f46befed6e3
Association of British Neurologists	Guideline	028	016	It would be helpful to know further how the choice of key research recommendations was arrived at.	Thank you for your comment. See the NICE methods manual

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					https://www.nice.org.uk/process/pmg20/chapter/writing-the-guideline#formulating-research-recommendations
Association of British Neurologists	Guideline	General	General	We feel that it would be helpful for the guidelines also to look at issues regarding employment in people with MS and strategies such as vocational support/rehabilitation.	Thank you for your comment. Employment was outside of the scope of this guideline. Recommendation 1.6.3 states that employment should be covered by the comprehensive review and the committee have added for example vocational support/rehabilitation.
Barts Health NHS trust	Guideline	007	008	It would be useful to signpost to approropriate online resources eg MS Trust, MS society, Shift MS and other charitable groups	Thank you for your comment. The MS Trust and MS Society are included in the section on information for the public on the NICE webpage for the MS guideline.
Barts Health NHS trust	Guideline	007	018	MS patient should be given details of who to contact before the next appointment (which maybe 6 weeks away)	Thank you for your comment. Recommendation 1.2.6 ensures that people with MS and their family members or carers have a point of contact if their symptoms change and recommendation 1.3.1 recommends a single point of contact to coordinate care or access services.
Barts Health NHS trust	Guideline	008	006	The management plan should be sent to the GP and clearly identified as a management plan (not just a routine letter with information within), with a national template	Thank you for your comment. This recommendation was not within the scope of this update but the committee would expect that the management plan would be sent to the GP.
Barts Health NHS trust	Guideline	010	004	Advanced MS patients should still see HCPs with expertise in MS (which may be neurorehabilitation)	Thank you for your comment. The committee agree with your comment and the recommendations in the sections on coordination of care and symptom management are applicable to all people with MS and refer to seeing people with expertise in MS where appropriate.
Barts Health NHS trust	Guideline	014	003	There is no current evidence on diet – it may come in the future	Thank you for your comment. This point is noted in the rationale and any new evidence will be identified through a surveillance review

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Barts Health NHS trust	Guideline	026	006	If had multiple relapses treated with high dose steroids – need to supply an emergency steroid card	Thank you for your comment. These recommendations were not updated by this guideline update.
Biogen Idec Limited	Appendix A	014 & 022	Table 2 - Table 8	Cost-utility analysis - It is not clear within the publications of the data source used for the base case utilities. The Economic Analysis Report states utilities used in the base case are described within Section 2.3.1, Table 2: *Overview of parameters and parameter distributions used in the model* and Section 2.3.5 Table 8: *Base-case utilities informing treatment effect (Base case: Pooled estimates using pooled BSC as baseline).* However, the data sources described appear to be different. In Table 2 is described as Pooled estimates from ENHANCE and MOBILE mean over 24 weeks), while section 2.3.5 describes the base case for the utilities, in which the pooled BSC baseline utility was used. Furthermore, in the economic model, the base case is described as "BASECASE POOLED (FE) (ENHANCE and MOBILE 3L) Using pooled ENHANCE and MOBILE placebo as baseline" (sheet D1 QoL row 50:54).	Thank you for your comment. The write-up had not been updated to match the final model at the end of development but has since been corrected to reflect the final model. The utilities in the model are based on the mean utility over 24 weeks. In the base case this was calculated by pooling the ENHANCE and MOBILE data. Mean utility for each comparator over 24 weeks was calculated by applying the pooled BSC change from baseline and pooled mean difference in change from baseline (for fampridine arms only) to the pooled baseline BSC utility. The model write up has been reworded to clarify this approach.
Biogen Idec Limited	Appendix A	032 - 033		Cost-utility analysis - The reported utility data in Table 14 are not accurately described. The values do not match the Acosta study, nor in the economic model (Sheet: D1 QoL cells G88:G89; Sheet: Settings&inputs cells C97:C99).	The write up had not been updated to match the final model at the end of model development but has since been corrected to reflect the final model. Tables 2, 8 and 14 have been updated to reflect the model.

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				e.g. SA8 Acosta et al. pooled utility for BSC in the report states a mean of 0.665, while in the Acosta publication and accompanying MS Guideline economic model provides adjusted EQ-5D values of 0.5906. Furthermore, in reporting the respective mean difference from baseline for responders, the value for mean difference provided is 0.020; whereas in Acosta et al., this value is 0.0292. e.g 2. SA7 ENHANCE utilities reported in Table 14 do not match the utilities reported in the economic model	
Biogen Idec Limited	Evidence review E	005	011	Biogen suggests adding the statement **'Fampridine is the only licenced treatment for MS-related walking impairment.'** This would make it clearer that the evidence review is concerned with fampridine only.	Thank you for your comment. We have added your suggestion to the introduction of the evidence review E.
Biogen Idec Limited	Evidence review E	043	Table 6	Table 6: Utilities - As described in item 4, data source in the report is not entirely clear and seems to be different to the data described in the economic model "BASECASE POOLED (FE) (ENHANCE and MOBILE 3L) Using pooled ENHANCE and MOBILE placebo as baseline" (sheet D1 QoL row 50:54)	Thank you for your comment. The write up had not been updated to match the final model at the end of model development but has since been corrected to reflect the final model.

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Biogen Idec Limited	Guideline	General	General	Biogen thank NICE for their diligence in their assessment of fampridine. Biogen welcome the clinical and economic analysis of fampridine. It should be noted that Biogen welcome the opportunity to continue a discussion on the commercial arrangements with relevant commissioners to ensure that NICE can consider a price of fampridine that would enable them to recommend it as a cost-effective use of NHS resources and enable suitable NHS patients in England & Northern Ireland to access fampridine as is already available to NHS patients in Scotland & Wales.	The independent guideline committee acknowledged that it is a clinically effective treatment for some people, however it is not cost effective at the current price the NHS is expected to pay. The availability of treatments in Scotland and Wales is a matter for the devolved administrations. In these countries it is made available under a confidential patient access scheme that provides the drug at a lower cost. Patient access schemes are negotiated by the relevant NHS commissioning body and the company (manufacturer). In England this process is led by NHS England
Birmingham Community Healthcare NHS Foundation Trust	General	049	General	Patient comments for information and their experiences with Functional Electrical Stimulation (FES) -NICE IPG278 The reference to NICE IPG278 Functional Electrical Stimulation (FES) has been removed from previous Guideline and we would like to have it referred to again in the draft guideline due to the difference it makes for please not just for walking but fatigue, spasticity, pain, safety of walking, mood and quality of life. Patient 1"Dear NICE, **MS NICE guidelines consultation** **Re: Functional Electrical Stimulation (FES) for mobility:**	Thank you for your comment. The non-pharmacological management of spasticity and mobility were not identified by the surveillance review as having new evidence and was not included in this update. We have added a cross-reference to the NICE IPG on functional electrical stimulation https://www.nice.org.uk/guidance/ipg278. Functional electrical stimulation is being considered in the new guideline on rehabilitation for chronic neurological conditions including acquired brain injury currently in development (https://www.nice.org.uk/guidance/indevelopment/gid-ng10181).

Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees

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				I am a dual stakeholder; a GP (GMC No 2581729) and a patient with Primary Progressive Multiple Sclerosis. I was referred for assessment and treatment to the FES Clinic (SellyOak, Birmingham) in 2010 by my physiotherapist and have used it daily since. It has been a massive help in terms of increasing walking speed, reducing effort of walking + accompanying fatigue and reducing risk of falls. It has been of more benefit to me than a trial of fampridine. I'm surprised at the omission of FES from the consultation document and will continue to personally and professionally support its use in appropriate MS patients. In terms of value for money and evidenced based clinical outcomes it is a really useful facilitator of mobility and independence. Please contact me if you have any queries. Patient 2) "I have had MS for 38 years and believe that using fes daily has helped hold back the increasing disability caused by this condition. The ability to walk a little and be upright also lightens my mood." Patient 3 " Although my MS continues to progress, and my walking becomes more difficult, my FES machine allows me to enjoy a quality of life I couldn't dream of without it. I can visit the gym for a workout, I can go out for dinner alone, without the risk of falling, I can shop, and carry out	

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				all sorts of domestic chores that I couldn't without the FES." Patient 4 "FES has been and is a key part of the management of my symptoms and greatly improves the quality of my life. " Patient 5 "My experience with using an FES. I have used an FES device for bilateral foot drop due to MS for over 10 years, and using during all my waking hours. If the FES stops working ex. I let it run out of power, I am virtually immobile The FES reduces the effort I need to use when walking, resulting in less fatigue and as a result being able to walk further. Before the FES I had used a drop foot orthosis. However the latter only 'carried' my foot, which still made practically no contribution to walking. Also, my leg muscles became visibly atrophied due to disuse. Since using the FES, my leg muscle atrophy has reversed and I have noticed improved circulation (my leg feels warmer). Tripping is now rare and I feel more confident walking. The overall result has given me the confidence to feel confident managing day to day activities independently and also stay in full time employment.	

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				I am also sure that other benefits follow-on the increased mobility in a similar way that walking/exercise benefit able bodied people. Patient 6: My association with FES devices dates back to 2002 when I attended an assessment clinic. I only found about the FES by serendipity when I, by chance encountered another patient attending the same physiotherapy session as me and I was curious about the device she was using. At the time, I was walking with the help of a stick for short distances of about 100 metres, after this my foot would drop and drag. I had tried the use of a manual foot orthotic (AFO) but this had proved unhelpful for me. I realised the benefit of the drop foot stimulator (FES) almost immediately and was able to walk further and with less fatigue. Initially I used the stimulator on one leg and then progressed to two as my condition deteriorated. I have no doubt that the stimulator helped me to keep working for longer and delayed my transition to the use of a wheelchair. Even when I started using a wheelchair the stimulator was invaluable for helping the movement of my feet for transfers such as using the toilet. In addition, I use the stimulator as an exerciser for my legs and arms. This is particularly beneficial for users like myself who cannot move themselves and would normally need a person assisting them to exercise. Also, as my hand function has recently deteriorated, the arm stimulator	

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				has helped me maintain the use of my computer, mobile phone and other electronic devices. As an FES user and living with MS for 38 years, I fully support the inclusion of the FES stimulator within the MS NICE guidelines. Patient 7: As I have had very limited help from other sources, other than our local rehab, FES (*Functional Electrical Stimulation)* has been greatly welcomed by myself " Whilst the guideline is limited for comments on mobility the above comments are an indication of the experiences people with MS have had from Specialist support for management of symptoms and medical devices such as Functional Electrical Stimulation (FES).	
Birmingham Community Healthcare NHS Foundation Trust	General	General	General	There is limited mention of Specialist rehabilitation services and Specialist HCP for assessment of, specialist wheelchairs, postural support, medical devices, communication aids, mobility aids, Functional Electrical Stimulation (FES) or orthtoics for the management of pain, fatigue and spasticity	Thank you for your comment. Recommendation 1.6.4 covers referral for identification of issues identified in the comprehensive review to MS multidisciplinary teams and other appropriate teams. The specific interventions you refer to were not covered by the evidence reviews (see Appendix A evidence reviews C and G). The committee prioritised interventions where there is variation in current practice or uncertainty regarding their clinical and cost effectiveness.

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Birmingham Community Healthcare NHS Foundation Trust	Guideline	013	016	Recommend a referral to an Occupational therapist for fatigue management	Thank you for your comment. The role of occupational therapists is acknowledged in the committee discussion of the evidence in evidence review C. The evidence of interventions used to support this recommendation was provided by a number of different health professionals and the committee were therefore unable to be specific in the recommendation.
Birmingham Community Healthcare NHS Foundation Trust	Guideline	013	023	Additional suggestion to provide advice on aids and adaptations to help with day to day activities	Thank you for your comment. This is covered by recommendation 1.6.3.
Birmingham Community Healthcare NHS Foundation Trust	Guideline	014	009	Recommend use of FES to reduce fatigue of walking by reducing effort (Refer to NICE IPG278 for Functional Electrical Stimulation (FES) additional evidence from DOI: 10.7224/1537-2073.2016-094 Five year follow-up of a Longitudinal Cohort study of the effectiveness of Functional Electrical Stimulation (FES) for people with MS. Patient comments "The *(FES)* Stimulators have been invaluable for me, they have considerably improved and sustained my ability to walk, reduced the physical effort involved and considerably reduced the risk of me tripping and falling further to my dropped foot". Another patient	Thank you for your comment. The non-pharmacological management of mobility was not identified by the surveillance review as having new evidence and was not within the scope of this update. We have added a cross-reference to the NICE IPG on functional electrical stimulation https://www.nice.org.uk/guidance/ipg278 . Functional electrical stimulation is being considered in the new guideline on rehabilitation for chronic neurological conditions including acquired brain injury (https://www.nice.org.uk/guidance/indevelopment/gid-ng10181).

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				”For many years my heart rate and walking speed were much better when wearing my FES with a reduction in fatigue”. Another patient “Dear NICE, **MS NICE guidelines consultation** **Re: Functional Electrical Stimulation (FES) for mobility:** I am a dual stakeholder; a GP (GMC No 2581729) and a patient with Primary Progressive Multiple Sclerosis. I was referred for assessment and treatment to the FES Clinic (SellyOak, Birmingham) in 2010 by my physiotherapist and have used it daily since. It has been a massive help in terms of increasing walking speed, reducing effort of walking + accompanying fatigue and reducing risk of falls. It has been of more benefit to me than a trial of fampridine. I'm surprised at the omission of FES from the consultation document and will continue to personally and professionally support its use in appropriate MS patients. In terms of value for money and evidenced based clinical outcomes it is a really useful facilitator of mobility and independence. Please contact me if you have any queries. Another patient: The FES reduces the effort I need to use when walking, resulting in less fatigue	

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Birmingham Community Healthcare NHS Foundation Trust	Guideline	017	008	Suggest change physiotherapist to – Neurophysiotherapist – as they have a greater understanding of the needs for people with MS	Thank you for your comment. The committee were unable to refer to neurophysiotherapists due to their limited availability and therefore the potential resource impact.
Birmingham Community Healthcare NHS Foundation Trust	Guideline	017	023	Suggest adding the use of Functional Electrical Stimulation (FES) to manage spasticity as increases the power of agonist when antagonist have received pharmacological spasticity management Patient comment "I have also used FES *(Functional Electrical Stimulation)* on both legs to keep the tone down during periods of illness which has helped in recovery."	Thank you for your comment. The non-pharmacological management of spasticity was not identified by the surveillance review as having new evidence and was not included in this update. We have added a cross-reference to the NICE IPG on functional electrical stimulation https://www.nice.org.uk/guidance/ipg278 . Functional electrical stimulation is being considered in the new guideline on rehabilitation for chronic neurological conditions including acquired brain injury (https://www.nice.org.uk/guidance/indevelopment/gid-ng10181).
Birmingham Community Healthcare NHS Foundation Trust	Guideline	017	026	Refer to NICE IPG278 for Functional Electrical Stimulation (FES) as helps to reduce pain of walking as described in DOI: 10.7224/1537-2073.2016-094 Five year follow-up of a Longitudinal Cohort study of the effectiveness of Functional Electrical Stimulation (FES) for people with MS.	Thank you for your comment. The non-pharmacological management of mobility was not identified by the surveillance review as having new evidence and was not within the scope of this update. We have added a cross-

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					reference to the NICE IPG on functional electrical stimulation https://www.nice.org.uk/guidance/ipg278 . Functional electrical stimulation is being considered in the new guideline on rehabilitation for chronic neurological conditions including acquired brain injury (https://www.nice.org.uk/guidance/indevelopment/gid-ng10181).
Birmingham Community Healthcare NHS Foundation Trust	Guideline	018	001	Suggest combine Functional Electrical Stimulation (FES) with spasticity management for assistance with walking	Thank you for your comment. The non-pharmacological management of spasticity and mobility were not identified by the surveillance review as having new evidence and were not included in this update. We have added a cross-reference to the NICE IPG on functional electrical stimulation https://www.nice.org.uk/guidance/ipg278 . Functional electrical stimulation is being considered in the new guideline on rehabilitation for chronic neurological conditions including acquired brain injury (https://www.nice.org.uk/guidance/indevelopment/gid-ng10181).
Birmingham Community Healthcare NHS	Guideline	019	015	Suggest adding refer to Functional Electrical Stimulation (FES) services - NICE IPG278 – for impairments in mobility caused by spasticity	Thank you for your comment. The non-pharmacological management of spasticity and mobility were not identified by the surveillance review as having new evidence and

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Foundation Trust					were not included in this update. We have added a cross-reference to the NICE IPG on functional electrical stimulation https://www.nice.org.uk/guidance/ipg278 . Functional electrical stimulation may is being considered in the new guideline on rehabilitation for chronic neurological conditions including acquired brain injury (https://www.nice.org.uk/guidance/indevelopment/gid-ng10181).
Birmingham Community Healthcare NHS Foundation Trust	Guideline	034	014	Advice from an Occupational Therapist for management of fatigue and impact of caring for a child might have on their symptons	Thank you for your comment. In the experience and opinion of the committee a number of different health professionals may provide this advice and they were therefore unable to recommend an occupational therapist.
Birmingham Community Healthcare NHS Foundation Trust	Guideline	036	029	Suggest adding aids and adaptation including electrical devices , such as Functional Electrical Stimulation (FES) - NICE IPG278 as management interventions for fatigue	Thank you for your comment. The non-pharmacological management of spasticity and mobility were not identified by the surveillance review as having new evidence and were not included in this update. We have added a cross-reference to the NICE IPG on functional electrical stimulation https://www.nice.org.uk/guidance/ipg278 . Functional electrical stimulation is being considered in the new guideline on rehabilitation for chronic neurological

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					conditions including acquired brain injury (https://www.nice.org.uk/guidance/indevelopment/gid-ng10181).
Birmingham Community Healthcare NHS Foundation Trust	Guideline	043	023	Suggest – to offer Neurophysiotherapist assessment for pain caused by musculoskeletal causes as they have a greater understanding of people with MS	Thank you for your comment. In the absence of evidence on who should provide physiotherapy assessments a specific profession was not recommended.
Brain and Spinal Injury Charity (BASIC)	Guideline	008	General	1.2.9 How can we ensure that up to date information is given to clients who attend charitable organisations for therapy	Thank you for your comment. We are unable to ensure that charities provide up to date information but this would be part of good practice on the part of the charitable organisations.
Brain and Spinal Injury Charity (BASIC)	Guideline	013	General	1.5.2 It is important that clients/ patients with MS are able to access the MS nurse/ consultant when fatigue is identified 1.5.5. Not always easy for people with MS to access psychology services for CBT due to limited resources within community settings	Thank you for your comment. The committee agree and have made recommendations for the treatment of fatigue including to discuss if medication might be appropriate 1.5.12. The non-pharmacological management of fatigue was not identified by the surveillance review as an area that needed updating at this time https://www.nice.org.uk/guidance/cg186/documents/surveillance-review-proposal.
Brain and Spinal Injury Charity (BASIC)	Guideline	014	General	1.5.6 please can chair based assisted exercises / virtual reality be included for exercise	Thank you for your comment. No evidence was found to support a recommendation on these interventions and the committee were therefore unable to include them in a recommendation. The committee has made a research recommendation see appendix J evidence review C.

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Brain and Spinal Injury Charity (BASIC)	Guideline	017	General	1.5.20. Even when spasticity has been identified can be a delay for the individual to be seen by the relevant clinician …	Thank you for your comment.
Brain and Spinal Injury Charity (BASIC)	Guideline	General	General	Rec 1.1.2– How are we going to ensure that all charity/ private health care are aware of these guidelines and how whom to refer to if patient/ client is not known to a specialist team …………..	Thank you for your response. We are unable to ensure that charities and private health care follow these guidelines but it would be considered good practice.
Coloplast Limited	Guideline	022	019	Coloplast Ltd would like to raise again renewed concern that lack of signposting health care professionals and patients to other NICE Clinical Guidelines (CG 148 & CG 49) means in practice that adults with multiple sclerosis (MS) who have bladder and bowel symptoms may not be given the appropriate opportunity or time to discuss these symptoms as part of the Comprehensive Review. Burkhard Domurath et al; Neurourological assessment in people with multiple sclerosis (MS): a new evaluated algorithm (Multiple Sclerosis and Related Disorders 44 (2020)) cites in conclusion that "*All patients with MS should be examined for NLUTD irrespective of their urological complaints. The proposed algorithm with four easy to collect parameters - PVR, micturition frequency, UTI-rate, incontinence, and additionally uroflowmetry can complete the neurological assessment standards to ameliorate diagnosis and management of NLUTD in patients with MS*." With reference to the NHS Long Term Plan (and in the spirit of Making Every Contact Count: MECC principles)	Thank you for your comment. The NICE guidelines CG148 urinary incontinence due to neurological disease and CG49 faecal incontinence in adults have been signposted to in recommendation 1.6.3.

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				under the heading of *"More NHS action on prevention and health inequalities"*, section 2.7 of the Long Term plans states *The role of the NHS includes secondary prevention, by detecting disease early, preventing deterioration of health and reducing symptoms to improve quality of life. Every 24 hours, the NHS comes into contact with over a million people at moments in their lives that bring home the personal impact of ill health. This Long Term Plan sets out practical action to do more to use these contacts as positive opportunities to help people improve their health. This will contribute to the government's ambition of five years of extra healthy life expectancy by 2035* Therefore, Coloplast Ltd would request the addition of these 4 "red flags" to be added to the comprehensive review before patients or health care professionals are signposted to other NICE Clinical Guidelines 148 and CG49. The 4 "red flags" would be: i) No of UTI's in the preceding 6 months; ii) Micturition frequency in past 24 hours; iii) incontinence (Yes/No) iv) Post Void Residual (10 ml scale) If any of these red flags are present, an adult with multiple sclerosis would then be offered Uroflowmetry and signposted to local continence specialist/services for appropriate management (utilising relevant NICE clinical Guidelines 148 and CG 49). The addition of this algorithm would ensure adults with multiple sclerosis were offered a	

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				structured standardised approach in the comprehensive review ensuring sufficient time to disclose and discuss their symptomology. Coloplast also believes this aligns with the *Patient Experience in Adult NHS Services Overview* (2021) from NICE under section 5; *"Tailoring health care services to each patient"* by adopting an individualised approach to healthcare services that is tailored to the patient's needs and circumstances, taking into account their ability to access services, personal preferences and coexisting conditions. Alongside giving the patient information about relevant treatment options and services that they are entitled to, even if these are not provided locally. It ensures discussions can be held in a way that encourages the patient to express their personal needs and preferences for care, treatment, management and self-management and allows for adequate time to discuss an aspect of their care that is often stigmatised and challenging for a patient to proactively raise themselves. This approach aligns with the principles in this overview.	
Coloplast Limited	Guideline	022	020	Coloplast Ltd would like to raise again renewed concern that the lack of signposting health care professionals and patients to other NICE Clinical Guidelines (CG 148 & CG 49) means in practice that adults with MS who have bladder and bowel symptoms may not be given the	Thank you for your comment. The NICE guidelines CG148 urinary incontinence due to neurological disease and CG49 faecal incontinence in adults have been signposted to in recommendation 1.6.3.

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				appropriate opportunity or time to discuss these symptoms as part of the Comprehensive Review. Burkhard Domurath et al; Neurourological assessment in people with multiple sclerosis (MS): a new evaluated algorithm (Multiple Sclerosis and Related Disorders 44 (2020)) cites in conclusion that "*All patients with MS should be examined for NLUTD irrespective of their urological complaints. The proposed algorithm with four easy to collect parameters - PVR, micturition frequency, UTI-rate, incontinence, and additionally uroflowmetry can complete the neurological assessment standards to ameliorate diagnosis and management of NLUTD in patients with MS*." With reference to the NHS Long Term Plan (and in the spirit of Making Every Contact Count: MECC principles) under the heading of *"More NHS action on prevention and health inequalities"*, section 2.7 of the Long Term plans states *The role of the NHS includes secondary prevention, by detecting disease early, preventing deterioration of health and reducing symptoms to improve quality of life. Every 24 hours, the NHS comes into contact with over a million people at moments in their lives that bring home the personal impact of ill health. This Long Term Plan sets out practical action to do more to use these contacts as positive opportunities to help people improve their health. This will contribute to the government's ambition of five years of extra healthy life expectancy by 2035*	

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				Therefore, Coloplast Ltd would request the addition of these 4 "red flags" to be added to the comprehensive review before patients or health care professionals are signposted to other NICE Clinical Guidelines 148 and CG49. The 4 "red flags" would be: v) No of UTI's in the preceding 6 months; vi) Micturition frequency in past 24 hours; vii) incontinence (Yes/No) viii) Post Void Residual (10 ml scale) If any of these red flags are present, an adult with multiple sclerosis would then be offered Uroflowmetry and signposted to local continence specialist/services for appropriate management (utilising relevant NICE clinical Guidelines 148 and CG 49). The addition of this algorithm would ensure adults with multiple sclerosis were offered a structured standardised approach in the comprehensive review ensuring sufficient time to disclose and discuss their symptomology. Coloplast also believes this aligns with the *Patient Experience in Adult NHS Services Overview* (2021) from NICE under section 5; *"Tailoring health care services to each patient"* by adopting an individualised approach to healthcare services that is tailored to the patient's needs and circumstances, taking into account their ability to access services, personal preferences and coexisting conditions. Alongside giving the patient information about	

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				relevant treatment options and services that they are entitled to, even if these are not provided locally. It ensures discussions can be held in a way that encourages the patient to express their personal needs and preferences for care, treatment, management and self-management and allows for adequate time to discuss an aspect of their care that is often stigmatised and challenging for a patient to proactively raise themselves. This approach aligns with the principles in this overview.	
Coloplast Limited	Guideline	022	021	Coloplast Ltd would like to raise again renewed concern that the lack of signposting health care professionals and patients to other NICE Clinical Guidelines (CG 148 & CG 49) means in practice that adults with MS who have bladder and bowel symptoms may not be given the appropriate opportunity or time to discuss these symptoms as part of the Comprehensive Review. Burkhard Domurath et al; Neurourological assessment in people with multiple sclerosis (MS): a new evaluated algorithm (Multiple Sclerosis and Related Disorders 44 (2020)) cites in conclusion that "*All patients with MS should be examined for NLUTD irrespective of their urological complaints. The proposed algorithm with four easy to collect parameters - PVR, micturition frequency, UTI-rate, incontinence, and additionally uroflowmetry can complete the neurological assessment standards to*	Thank you for your comment. The NICE guidelines CG148 urinary incontinence due to neurological disease and CG49 faecal incontinence in adults have been signposted to in recommendation 1.6.3.

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				ameliorate diagnosis and management of NLUTD in patients with MS." With reference to the NHS Long Term Plan (and in the spirit of Making Every Contact Count: MECC principles) under the heading of *"More NHS action on prevention and health inequalities"*, section 2.7 of the Long Term plans states *The role of the NHS includes secondary prevention, by detecting disease early, preventing deterioration of health and reducing symptoms to improve quality of life. Every 24 hours, the NHS comes into contact with over a million people at moments in their lives that bring home the personal impact of ill health. This Long Term Plan sets out practical action to do more to use these contacts as positive opportunities to help people improve their health. This will contribute to the government's ambition of five years of extra healthy life expectancy by 2035* Therefore, Coloplast Ltd would request the addition of these 4 "red flags" to be added to the comprehensive review before patients or health care professionals are signposted to other NICE Clinical Guidelines 148 and CG49. The 4 "red flags" would be: ix) No of UTI's in the preceding 6 months; x) Micturition frequency in past 24 hours; xi) incontinence (Yes/No) xii) Post Void Residual (10 ml scale) If any of these red flags are present, an adult with multiple sclerosis would then be offered Uroflowmetry and	

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				signposted to local continence specialist/services for appropriate management (utilising relevant NICE clinical Guidelines 148 and CG 49). The addition of this algorithm would ensure adults with multiple sclerosis were offered a structured standardised approach in the comprehensive review ensuring sufficient time to disclose and discuss their symptomology. Coloplast also believes this aligns with the *Patient Experience in Adult NHS Services Overview* (2021) from NICE under section 5; *"Tailoring health care services to each patient"* by adopting an individualised approach to healthcare services that is tailored to the patient's needs and circumstances, taking into account their ability to access services, personal preferences and coexisting conditions. Alongside giving the patient information about relevant treatment options and services that they are entitled to, even if these are not provided locally. It ensures discussions can be held in a way that encourages the patient to express their personal needs and preferences for care, treatment, management and self-management and allows for adequate time to discuss an aspect of their care that is often stigmatised and challenging for a patient to proactively raise themselves. This approach aligns with the principles in this overview.	

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Faculty of Pain Medicine of the Royal College of Anaesthetists	Guideline	020	026	There is not enough importance attached to MSK pain in general due to spasticity and there is evidence for the benefit of cannabis (albeit, evaluated as secondary outcomes in the main Sativex studies). One area of interest to the FPM is the issue that NICE guidelines may fall well-short of providing the necessary benefit for people with MS pain leaving people distressed. At a minimum, this could be acknowledged as an area for either research (eg consensus approaches or otherwise) or further consideration.	Thank you for your comment. The importance of assessing and investigating the cause of pain is covered in recommendation 1.5.23. Due to the lack of evidence no recommendations could be made for the non-pharmacological management of MSK pain but the committee has made a research recommendation (covering all types of pain). The NICE guidance on cannabis-based medicinal products is referred to in recommendation 1.5.32.
Faculty of Pain Medicine of the Royal College of Anaesthetists	Guideline	020 - 021	017	The draft guideline lists only limited information on the pharmacological management of pain in MS and simply references to other NICE guidelines for pharmacological management. In contrast, there is detailed evidence gathering for non-pharmacological management. There is an absence of a pathway or algorithm for pain specific to MS. The other NICE guidance on Neuropathic pain or Lower Back Pain does not address MS specifically. There is an absence of detailed discussion of pains that arise in MS and why. What seems to be lacking altogether - possibly for lack of publications on this subject- is the role of pain services in the delivery of intrathecal Baclofen. Several pain services	Thank you for your comment. The committee agreed that the pharmacological management of pain was covered by the NICE guideline on neuropathic pain and that the management of other causes of pain, for example muscular-skeletal pain was not different to other conditions. The causes of pain are referred to in the rationale for these recommendations. The role of pain services in the delivery of intrathecal baclofen is a service delivery issue and this is outside the scope of this guideline.

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				in institutions, without direct on-site neurosurgical services, provide care for patients with intrathecal Baclofen delivery devices.	
Faculty of Pain Medicine of the Royal College of Anaesthetists	Guideline	031	001	There is a research recommendation for non-pharmacological guidance and the same should be recommended for research into pharmacological agents for management of pain in MS.	Thank you for your comment. An evidence review for the pharmacological management of pain was not conducted and the committee are therefore unable to make a research recommendation.
GW Pharmaceuticals	Evidence Review F	005	019	We are concerned by the language used to describe cannabis-derived medications in the evidence review. It is inappropriate to refer to these medications as 'complex pharmacological management' as this indirectly implies that cannabis-derived medications (such as Sativex) are associated with more complexities than other treatments at the same line of therapy without explaining what these complexities may be and if/how they may impact the patient's care.	Thank you for your comment. We have removed the word 'complex'
GW Pharmaceuticals	Evidence Review F	005 & 037	019 & 012 – 016	As previously mentioned, it is a concern that a newly developed guideline on the management of MS would make such little mention of a licensed treatment for the symptom of spasticity, in particular when the evidence review itself acknowledged the existence of NICE guidance on this topic, published since the MS guideline was last revised.	Thank you for your comment. Cannabis-based products were outside of the scope of this guideline. Recommendation 1.5.30 refers to the NICE guideline on cannabis-based medicinal products.
GW Pharmaceuticals	Guideline	018	007 – 014	We are concerned that this recommendation does not clarify that in addition to off-label gabapentin, there are licensed second-line options (e.g. THC:CBD [Sativex]) available at this line of therapy	Thank you for your comment. Recommendation 1.5.32 refers to the NICE guideline on cannabis-based medicinal products.

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GW Pharmaceuticals	Guideline	018	007 – 014	Although we understand that the recommendation faithfully cites the title of an MHRA document, we are concerned that this also provides the brand names for two products, whereas the brand names for other products are not provided in the guideline draft.	Thank you for your comment. The brand names have been removed.
GW Pharmaceuticals	Guideline	019	001 – 013	We are concerned that this recommendation does not clarify that there are licensed options (e.g. THC:CBD spray [Sativex]) for combination therapy at this line of treatment, as alternatives to using off-label gabapentin.	Thank you for your comment. Recommendation 1.5.32 refers to the NICE guideline on cannabis-based medicinal products.
GW Pharmaceuticals	Guideline	019	001 – 013	As per the above, although we understand that the recommendation faithfully cites the title of an MHRA document, we are concerned that this also provides the brand names for two products, whereas the brand names for other products are not provided in the guideline draft.	Thank you for your comment. The brand names have been removed.
GW Pharmaceuticals	Guideline	019	018 – 019	This recommendation introduces THC:CBD spray (Sativex) for the first and only time in this document. The licensed indication for Sativex is "*indicated as treatment for symptom improvement in adult patients with moderate to severe spasticity due to multiple sclerosis (MS) who have not responded adequately to other anti-spasticity medication and who demonstrate clinically significant improvement in spasticity related symptoms during an initial trial of therapy*". Given this is a licensed treatment for this purpose, it is of concern that any new guideline on the management of MS would make such little reference to a licensed therapy whilst giving more focus on an off label treatment option (gabapentin). In the interest of balance, it	Thank you for your comment. Cannabis-based products were outside of the scope of this guideline and we therefore did not include these in the review protocol for this question (appendix A evidence review F). No evidence review was undertaken for this update. We cross-refer to the existing NICE guidance on cannabis-based medicinal products in recommendation 1.5.32.

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				is appropriate to state within this section of the guideline that other treatments are an option for this disabling symptom of MS.	
GW Pharmaceuticals	Guideline	019	018 – 019	Acknowledging that this was also the case in the prior revisions of the guidelines, the position of recommendation 1.5.28 at the bottom of this subsection, may indirectly imply that THC:CBD spray (Sativex) is a last-line option for this disabling symptom of MS. This is a concern as within its licensed indication, "*indicated as treatment for symptom improvement in adult patients with moderate to severe spasticity due to multiple sclerosis (MS) who have not responded adequately to other anti-spasticity medication and who demonstrate clinically significant improvement in spasticity related symptoms during an initial trial of therapy*", Sativex can be offered to manage spasticity earlier in the pathway than is implied by its current introduction within the draft guidelines.	Thank you for your comment. The ordering of the recommendations does not reflect the order in which interventions should be offered. However, we note the guidance in NG144 which we cross-refer to in recommendation 1.5.32.
GW Pharmaceuticals	Guideline	019	018 – 019	We note that through the wording of this recommendation in combination with NICE NG144 cited in 1.5.28 further contributes to Sativex being positioned as a later option in the treatment pathway compared with the Sativex indication.	Thank you for your comment. The ordering of the recommendations does not reflect the order in which interventions should be offered. However, we note the guidance in NG144 which we cross-refer to in recommendation 1.5.32.
International Functional Electrical Stimulation	Guideline	017	001	Section:- Non pharmacological management of mobility problems. The guidelines fail to mention Functional Electrical Stimulation as an intervention to aid mobility.	Thank you for your comment. The non-pharmacological management of mobility was not identified by the surveillance review as having new evidence and was not within the scope of this update. We have added a cross-

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Society (IFESS) UK chapter				Please note that similar clinical guidelines for cerebral palsy (NG119) and stroke (CG162) do include guidelines on FES and we strongly feel that the guidelines for MS should include similar recommendations. Below, I copy our previous submission made to NICE, which outlines our argument for including FES in the guidelines: **The case for updating the guidance on FES for correction of dropped foot in CG186 (2016)** Paul Taylor, International Functional Electrical Stimulation Society (IFESS) stake holder representative, Salisbury District Hospital. Dropped foot is the inability to clear the ground with the foot as it I brought forward in the swing phase of gait. It is a common problem for people with multiple sclerosis (pwMS) and is associated with weakness and spasticity of the muscles in the leg, hip and lumbar region. Dropped foot significantly increases the risk of falls and makes walking less efficient. It leads to reduced participation in daily life and reduced quality of life. Traditionally it is addressed with orthotics, although there are no major studies that demonstrate the effectiveness of orthotics for pwMS.	reference to the NICE IPG on functional electrical stimulation https://www.nice.org.uk/guidance/ipg278 . Functional electrical stimulation is being considered in the new guideline on rehabilitation for chronic neurological conditions including acquired brain injury (https://www.nice.org.uk/guidance/indevelopment/gid-ng10181).

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				Functional Electrical Stimulation (FES) is a means of producing movement in paralysed or weak muscles. By stimulating the common peroneal nerve it is possible to induce dorsiflexion and eversion and when timed to the walking using a footswitch in the shoe or inclinometer mounted on the leg, it can effectively correct the dropped foot. FES is provided using a small battery powered body warn device and is used as practical day to day orthosis, increasing the safety, efficiency and effectives of waling. FES has become a central part of the clinical interventions used to improve mobility following MS and is routinely used at major therapy centres such as; the National Hospital for Neurology and Neurosurgery, London; The West Midland Rehabilitation Centre, Birmingham; Salisbury District Hospital; The Northern General, Sheffield; Derby Royal Infirmary and Chapple Adlington Hospital, Leeds. Guidance on FES is given in IPG278 (2009). The current edition of the MS guidelines CG186 do not mention FES within the section on Non-pharmacological management of mobility (section 10.4). However IPG278, are listed in the list of related guidelines in section 2.3. This is often missed by readers of the guidelines because it is not within the section on recommended interventions.	

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				The original guidance on FES (IPG278) was published in 2009 and is largely based on published studies in stroke populations. One of the recommendations for future research questions in CG186 is "What is the optimal frequency, intensity and form of rehabilitation for mobility problems in people with MS?" Since 2016 a significant number of studies specific to the use of FES with pwMS have been published, including economic evaluations that demonstrate cost effectiveness of the technique. Further, the evidence base has grown significantly since the publication of IPG278. It is evident that there is now sufficient evidence to justify specific guidance on the technique within the main recommendations of the guidelines. Its absence from the guidelines gives the false impression that it is not an evidence bases intervention in routine clinical use. **FES-MS studies published since the current MS guidelines were published (2016 -2019)** 1. Angela Davies Smith, Terezie Prokopiusova, Rosemary Jones, Tania Burge, Kamila Rasova. Functional electrical stimulation for foot drop in people with multiple sclerosis: The relevance and importance of	

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				addressing quality of movement. Mult Scler. 2021 Apr;27(5):653-660. doi: 10.1177/1352458520923958 2. Miller Renfrew L, Lord AC, Warren J, Hunter R.Evaluating the Effect of Functional Electrical Stimulation Used for Foot Drop on Aspects of Health-Related Quality of Life in People with Multiple Sclerosis: A Systematic Review. Int J MS Care. 2019 Jul-Aug;21(4):173-182. doi: 10.7224/1537-2073.2018-015. 3. Juckes FM, Marceniuk G, Seary C, Stevenson VL A cohort study of functional electrical stimulation in people with multiple sclerosis demonstrating improvements in quality of life and cost-effectiveness. Clin Rehabil. 2019 Apr 10:269215519837326. doi: 10.1177/0269215519837326. [Epub ahead of print] 4. Renfrew LM, Paul L, McFadyen A, Rafferty D, Moseley O, Lord AC, Bowers R, Mattison P. The clinical- and cost-effectiveness of functional electrical stimulation and ankle-foot orthoses for foot drop in Multiple Sclerosis: a multicentre randomized trial. Clin Rehabil. 2019 Apr 11:269215519842254. doi: 10.1177/0269215519842254. [Epub ahead of print] PMID: 30974955 5. Renfrew ML, Flowers P, Lord AC, Rafferty D, McFadyen AK, Bowers R, Mattison P, Paul L. An	

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				exploration of the experiences and utility of functional electrical stimulation for foot drop in people with multiple sclerosis. Disabil Rehabil. 2018 Oct 9:1-9. doi: 10.1080/09638288.2018.1501100. [Epub ahead of print] 6. Miller Renfrew L, Lord AC, McFadyen AK, Rafferty D, Hunter R, Bowers , Mattison P, Moseley O, Paul L. A comparison of the initial orthotic effects of functional electrical stimulation and ankle-foot orthoses on the speed and oxygen cost of gait in multiple sclerosis. J Rehabil Assist Technol Eng. 2018 Feb 2;5:2055668318755071. doi: 10.1177/2055668318755071. eCollection 2018 Jan-Dec 7. Street T, Singleton C Five-Year Follow-up of a Longitudinal Cohort Study of the Effectiveness of Functional Electrical Stimulation for People with Multiple Sclerosis Int J MS Care. 2018 Sep-Oct;20(5):224-230. doi: 10.7224/1537-2073.2016-094. 8. Andreopoulou G, Mercer TH, van der Linden ML. Walking measures to evaluate assistive technology for foot drop in multiple sclerosis: A systematic review of psychometric properties. Gait Posture. 2018 Mar;61:55-66. doi: 10.1016/j.gaitpost.2017.12.021. Epub 2017 Dec 25	

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				9. Miller L, McFadyen A, Lord AC, Hunter R, Paul L, Rafferty D, Bowers R, Mattison P. Functional Electrical Stimulation for Foot Drop in Multiple Sclerosis: A Systematic Review and Meta-Analysis of the Effect on Gait Speed. Arch Phys Med Rehabil. 2017 Jul;98(7):1435-1452. doi: 10.1016/j.apmr.2016.12.007. Epub 2017 Jan 11. 10. Springer S, Khamis S Effects of functional electrical stimulation on gait in people with multiple sclerosis - A systematic review. Mult Scler Relat Disord. 2017 Apr;13:4-12. doi: 10.1016/j.msard.2017.01.010. Epub 2017 Jan 18 11. Khurana SR1, Beranger AG, Felix ER. Perceived Exertion Is Lower When Using a Functional Electrical Stimulation Neuroprosthesis Compared With an Ankle-Foot Orthosis in Persons With Multiple Sclerosis: A Preliminary Study. Am J Phys Med Rehabil. 2017 Mar;96(3):133-139. doi: 10.1097/PHM.0000000000000626 **FES-MS studies published since IPG278 FES guidelines were published (2009 – 2016)**	

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				12. L. Miller, D. Rafferty, L. Paul, and P. Mattison. The impact of walking speed on the effects of functional electrical stimulation for foot drop in people with multiple sclerosis. Disabil Rehabil Assist Technol. 2015 Mar 31:1-6. [Epub ahead of print] 13. Linda Miller, Danny Rafferty, Lorna Paul, and Paul Mattison A comparison of the orthotic effect of the Odstock Dropped Foot Stimulator and the Walkaide functional electrical stimulation systems on energy cost and speed of walking in Multiple Sclerosis. 2015 Disabil Rehabil Assist Technol, Early Online. ISSN 1748-3107 print/ISSN 1748-3115 online, DOI: 10.3109/17483107.2014.898340 14. Street TD, Taylor PN, Swain ID. The Effectiveness of Functional Electrical Stimulation on Walking Speed, Functional Walking Category and Clinically Meaningful Changes for People with Multiple Sclerosis. Archives of Physical Medicine. Volume 96, Issue 4, April 2015, Pages 667–672 15. Dapul GP, Bethoux F. Functional Electrical Stimulation for Foot Drop in Multiple Sclerosis. US Neurology, 2015;11(1):10–8 DOI: 10.17925/USN.2015.11.01.10	

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				16. Flisher L, Norman S, Wilkinson H, Seary C, Stevenson V. The sustained benefit of lower limb functional electrical stimulation in people with multiple sclerosis. Multiple Sclerosis Journal 2014;20:(7) 1004 17. van der Linden ML, Hooper JE, Cowan P, Weller BB, Mercer TH (2014) Habitual Functional Electrical Stimulation Therapy Improves Gait Kinematics and Walking Performance, but Not Patient-Reported Functional Outcomes, of People with Multiple Sclerosis who Present with Foot-Drop. PLoS ONE 9(8): e103368. doi:10.1371/journal.pone.0103368 18. van der Linden ML, Scott SM, Hooper JE, Cowan P, Mercer TH. Gait kinematics of people with Multiple Sclerosis and the acute application of Functional Electrical Stimulation. Gait Posture (2014), http://dx.doi.org/10.1016/j.gaitpost.2014.01.016 19. van der Linden M, Hooper J, Mercer T. Functional Electrical Stimulation to treat foot drop for people with MS; user perception of benefit, disadvantages and service provision in Edinburgh. Multiple Sclerosis Journal 2014;20:(7) 999	

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				20. Wening J, Ford J, Jouett D. Orthotic and FES for maintenance of walking in patients with MS. Disease-a-Month 59 (2013) 284-2894 21. S. Khurana, T. Ference, A. Beranger. Comparison of functional electric stimulation neuroprosthesis and ankle foot orthosis in persons with multiple sclerosis. 26th ECTRIMS congress &15th RIMS meeting 2013 22. Scott SM, van der Linden ML, Hooper JE, Cowan P, Mercer TH. Quantification of gait kinematics and walking ability of people with multiple sclerosis who are new users of functional electrical stimulation. J Rehabil Med. 2013 Apr;45(4):364-9. doi: 10.2340/16501977-1109 23. Taylor P., Barrett C., Mann G., Wareham W., Swain I. 2013. A Feasibility Study to Investigate the Effect of Functional Electrical Stimulation and Physiotherapy Exercise on the Quality of Gait of People With Multiple Sclerosis. Neuromodulation. 2014 Jan;17(1):75-84; discussion 84. doi: 10.1111/ner.12048. Epub 2013 Apr 19. 24. Taylor P, Humphreys L, and Swain I, The long-term cost-effectiveness of the use of functional Electrical stimulation for the correction of dropped foot Due to upper motor neuron lesion. J Rehabil Med 2013; 45: 154–160	

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				25. Courtney AM, Castro-Borrero W, Davis SL, Frohman TC and Frohman EM. Functional treatments in multiple sclerosis. Current Opinion in Neurology 2011, 24:250–254 26. Stevens P, Hunsaker RB. Recent Findings Regarding the Efficacy of functional electrical stimulation in patients with chronic hemiplegia and multiple sclerosis: a narrative literature review. J Prosthet Orthot. 2010;22:166-171 27. JE Esnouf, PN Taylor, GE Mann, CL Barrett. Impact on falls and activities of daily living of use of a Functional Electrical Stimulation (FES) device for correction dropped foot in people with multiple sclerosis. Mult Scler 2010;16 1141-1147 28. Barrett CL, Taylor PN. The effects of the Odstock Drop Foot Stimulator on Perceived Quality of Life for People with Stroke and Multiple Sclerosis. Neuromodulation 2010 13, 1, pp: 58-64 29. Stein RB, Everaert DG, Thompson AK, Chong SL, Whittaker M, Robertson J, Kuether G. Long-term therapeutic and orthotic effects of a foot drop stimulator on walking performance in progressive and nonprogressive	

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				neurological disorders. Neurorehabil Neural Repair. 2010 Feb;24(2):152-67. Epub 2009 Oct 21. 30. Sheffler LR, Bailey SN, Chae J. Spatiotemporal and kinematic effect of peroneal nerve stimulation versus an ankle-foot orthosis in patients with multiple sclerosis: a case series. PM R. 2009 Jul;1(7):604-11 31. Sheffler LR, Hennessey MT, Knutson JS, Chae J. Neuroprosthetic effect of peroneal nerve stimulation in multiple sclerosis: a preliminary study. Arch Phys Med Rehabil. 2009 Feb;90(2):362-5. 32. CL Barrett, GE Mann, PN Taylor and P Strike. A randomized trial to investigate the effects of functional electrical stimulation and therapeutic exercise on walking performance for people with multiple sclerosis. Mult Scler. 2009 Apr;15(4):493-504 Studies published before IPG278 FES guidelines were published (2008 – 1999) 33. Sheffler LR, Hennessey MT, Knutson JS, Naples GG, Chae J. Functional Effect of an Ankle Foot Orthosis on Gait in Multiple Sclerosis: A Pilot Study. 87(1):26-32, January 2008	

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				34. L Paul, D Rafferty, S Young, L Miller, P Mattison and A McFadyen. The effect of functional electrical stimulation on the physiological cost of gait in people with multiple sclerosis Mult Scler 2008; 14; 954 originally published online Jun 23, 2008; http://msj.sagepub.com/cgi/content/abstract/14/7/954 35. Burridge JH, Elessi K, Pickering RM, Taylor PN. Walking on an uneven surface: the effect of common peroneal nerve stimulation on gait parameters and relationship between perceived and measured benefits in a sample of participants with a drop foot. Neuromodulation, 10(1): 59-67, 2007 36. Swain ID, Taylor PN. The clinical use of functional electrical stimulation in neurological rehabilitation. In: Horizons in Medicine 16 – Updates on major clinical advances. Ed. Franklyn J. Pub. Royal College of Physicians, ISBN 1-86016-233-9, London, pp. 315-322, 2004. 37. Taylor PN. The use of electrical stimulation for correction of dropped foot in subjects with upper motor neuron lesions. Advances in Clinical Neuroscience and Rehabilitation, 2(1): 16-18, 2002.	

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				38. Taylor PN, Burridge JH, Wood DE, Norton J, Dunkerley A, Singleton C, Swain ID. Clinical use of the Odstock Drop Foot Stimulator its effect on the speed and effort of walking. Archives of Physical Medicine and Rehabilitation, 80: 1577-1583, 1999. 39. Taylor PN, Burridge JH, Wood DE, Norton J, Dunkerley A, Singleton, C, Swain ID. Patient perceptions of the Odstock Drop Foot Stimulator. Clinical Rehabilitation, 13: 333-340, 1999. 40. Taylor PN, Burridge JH, Wood DE, Norton J, Dunkerley A, Singleton, C, Swain ID. Clinical audit of five years provision of the Odstock Drop Foot Stimulator. Artificial Organs, 23(5): 440-442, 1999.	
Medtronic Ltd	Evidence Review	005	026	The PICO Table 1, line 26 lists "*Baclofen (intrathecal) – to be kept separate to oral"* however *a* section for Intrathecal Baclofen has not been included in the draft guideline. We ask that an overview of intrathecal baclofen is included in the spasticity symptom management section, to provide *guidance* on *general principles*, *testing* and *administration* using a similar framework to the guidance on intrathecal baclofen in *CG145: Spasticity in under 19s: management).*	Thank you for your comment. Creamer 2018 has been added to the evidence review after it was identified by stakeholders. The committee has now re-considered intrathecal baclofen in light of new clinical and cost effectiveness evidence (a threshold analysis was conducted using Creamer 2018 evidence as well as updated costing of intrathecal baclofen) and agreed that this does not warrant a change in the recommendations. Please see

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					evidence review F for the update clinical and health economic evidence review and committee discussion.
Medtronic Ltd	Evidence Review	037	007	Page 37, line7: *The <u>committee removed the recommendations on third- and fourth-line</u> <u>options due to the lack of clinical and health economic evidence</u>. These treatments should only be considered by specialists* **Clinical Evidence** There is a significant body of evidence to support the use of intrathecal baclofen in patients with multiple sclerosis. The comparator in the PICO table is described as "Interventions will be compared to each other (both within and between classes), to placebo/sham, or to usual care or no treatment". The evidence review for intrathecal baclofen seems to have focussed on the placebo comparator only, which may have missed other relative studies comparing to usual care. We would like to highlight the studies and real-world evidence below, including a 2018 RCT, which have not been considered in the evidence review and provide additional evidence on the effectiveness of intrathecal baclofen in patients with multiple sclerosis and in other conditions.	Thank you for your comment. The studies referenced in the comment, with the exception of Creamer 2018, are all non-randomised studies which do not fit our protocol and therefore could not be included in the evidence review. The two health economic references could not be included as one pre-dates our 2005 cut-off for health economic study inclusion (as stated in the health economic protocol) and other is not a health economic analysis. Thank you for highlighting the Creamer 2018 study which we had been missed. This has now been added to the evidence review. In addition, a threshold analysis based on this paper and a more detailed costing of intrathecal baclofen were undertaken. The intervention was not found to be cost effective based on the currently available data. The uncertainties of this analysis and costing are detailed in the evidence review. The committee re-considered intrathecal baclofen in light of this new clinical and cost effectiveness evidence and agreed that there was too much uncertainty to warrant a change in the recommendations. As the committee made no recommendations on intrathecal baclofen we have also not provided guidance on general principles, testing and administration.

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				Although some of the studies below relate to different patient populations, we note that the Guideline Development Group decided to include studies with mixed populations because "there were no good physiological reasons why the alternative neurological diagnoses should unduly influence the effects of the drug on spasticity". - *Creamer M, Cloud G, Kossmehl P, et al. Effect of intrathecal baclofen on pain and quality of life in poststroke spasticity: A Randomized Trial (SISTERS). Stroke. 2018;49(9):2129-2137. doi:10.1161/STROKEAHA.118.022255* - *Creamer M, Cloud G, Kossmehl P, et al. Intrathecal baclofen therapy versus conventional medical management for severe poststroke spasticity: Results from a multicentre, randomised, controlled, open-label trial (SISTERS). J Neurol Neurosurg Psychiatry. 2018;89(6):642-650. doi:10.1136/jnnp-2017-317021 - Significant treatment effects in favor of ITB vs. CMM in health-related quality of life.* - *Abbatemarco JR, Griffin A, Jones NG, et al. Long-term outcomes of intrathecal baclofen in ambulatory multiple sclerosis patients: A single-center experience. Mult Scler. July*	

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				2020:1352458520936912. doi:10.1177/1352458520936912 - *Reis PV, Vieira CR, Midoes AC, Rebelo V, Barbosa P, Gomes A. Intrathecal Baclofen Infusion Pumps in the Treatment of Spasticity: A Retrospective Cohort Study in a Portuguese Centre. Acta Med Port. 2019;32(12):754-759. doi:10.20344/amp.10482* - *Sammaraiee Y, Yardley M, Keenan L, Buchanan K, Stevenson V, Farrell R. Intrathecal baclofen for multiple sclerosis related spasticity: A twenty-year experience. Mult Scler Relat Disord. 2019;27:95-100. doi:10.1016/j.msard.2018.10.009* - *Sammaraiee Y, Stevenson VL, Keenan E, et al. Evaluation of the impact of intrathecal baclofen on the walking ability of people with Multiple Sclerosis related spasticity. Mult Scler Relat Disord. 2020;46:102503. doi:10.1016/j.msard.2020.102503* - *Ordia JI, Fischer, Edward, Adamski, Ellen, Chagnon, Kimberly G, Spatz, Edward L. Continuous intrathecal baclofen infusion by a programmable pump in 131 consecutive patients with severe spasticity of spinal origin. Neuromodulation. 2002;5(1):16-24* - *Yoon YK, Lee KC, Cho HE et al. Outcomes of intrathecal baclofen therapy in patients with*	

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				cerebral palsy and acquired brain injury. H. Medicine (Baltimore). 2017 Aug;96(34):e7472 - *Rawicki B. Continuous intrathecal baclofen delivered via an implantable pump: long-term follow-up review of 18 patients. J Neurosurg. 1999;91(5):733-736* - *Meythaler JM, McCary A, Hadley MN. Intrathecal infusion of baclofen for spasticity caused by acquired brain injury: a preliminary report. J Neurosurg. 1997;87(3):415-419.* - *Meythaler JM, Guin-Renfroe S, Grabb P, Hadley MN. long-term continuously infused intrathecal baclofen for spastic-dystonic hypertonia in traumatic brain injury: 1-year experience. Arch Phys Med Rehabil. 1999;80(1):13-19* - *Schiess MC, Oh IJ, Stimming EF et al. Prospective 12-month study of intrathecal baclofen therapy for poststroke spastic upper and lower extremity motor control and functional improvement. Neuromodulation. 2011;14(1):38-45* - *Ivanhoe CB, Francisco GE, McGuire JR et al. Intrathecal baclofen management of poststroke spastic hypertonia: implications for function and quality of life. Arch Phys Med Rehabil. 2006;87(11):1509-1515*	

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				- *Francisco GE, Boake C. Spastic hemiplegia after intrathecal baclofen therapy: a preliminary study. Arch Phys Med Rehabil. 2003;84(8):1194-1199.* - *Meythaler JM, Guin-Renfroe S, Brunner RC, Hadley MN. Intrathecal baclofen for spastic hypertonia from stroke. Stroke. 2001;32(9):2009-2109* - *Farrell R et al. Evaluation of the cognitive benefits of intrathecal baclofen pump implantation in people with intractable multiple sclerosis related spasticity. Multiple Sclerosis and Related Disorders. Volume 50 (2021) 102831* - *Feller CN et al. Low Rate of Intrathecal Baclofen Pump Catheter-Related Complications: Long-Term Study in Over 100 Adult Patients Associated With Reinforced Catheter. Neuromodulation 2021; 24: 1176–1180* - *Berntsson SG et al. Inherited Ataxia and Intrathecal Baclofen for the Treatment of Spasticity and Painful Spasms. Stereotact Funct Neurosurg 2019;97:18–23* - *Comi G et al. Italian consensus on treatment of spasticity in multiple sclerosis. European Academy of Neurology 2019* **Health Economic Evidence**	

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				Intrathecal baclofen has been shown to Need to answer this point please be cost effective from a UK NHS perspective[1] and is routinely commissioned by NHS England in line with the criteria set out in *NHSCB/D04/P/c Clinical Commissioning Policy: Intrathecal Baclofen (ITB)*[2] 1. *Sampson FC, Hayward A, Evans G, Morton R, Collett B. Functional benefits and cost/ benefit analysis of continuous intrathecal baclofen infusion for the management of severe spasticity. J Neurosurg. 2002;96(6):1052-1057.* 2. *NHSCB/D04/P/c Clinical Commissioning Policy: Intrathecal Baclofen (ITB). https://www.england.nhs.uk/wp-content/uploads/2013/04/d04-p-c.pdf* We ask that an overview of intrathecal baclofen is included in the spasticity symptom management section, to provide *guidance* on *general principles*, *testing* and *administration* using a similar framework to the guidance on intrathecal baclofen in *CG145: Spasticity in under 19s: management).*	
Medtronic Ltd	Evidence Review F	029	009	Table 12: Clinical evidence profile: The evidence review of intrathecal baclofen versus placebo. found no evidence relating to quality of life. We would like to highlight the 2018 SISTERS RCT[ref] which reported Significant	Thank you for your comment. Creamer 2018 has been added to the evidence review after it was identified by stakeholders. In addition, a threshold analysis based on this paper and a more detailed costing of intrathecal

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				treatment effects in favor of ITB vs. CMM in health-related quality of life. - *Creamer M, Cloud G, Kossmehl P, et al. Effect of intrathecal baclofen on pain and quality of life in poststroke spasticity: A Randomized Trial (SISTERS). Stroke. 2018;49(9):2129-2137. doi:10.1161/STROKEAHA.118.022255* - *Creamer M, Cloud G, Kossmehl P, et al. Intrathecal baclofen therapy versus conventional medical management for severe poststroke spasticity: Results from a multicentre, randomised, controlled, open-label trial (SISTERS). J Neurol Neurosurg Psychiatry. 2018;89(6):642-650. doi:10.1136/jnnp-2017-317021 - Significant treatment effects in favor of ITB vs. CMM in health-related quality of life.* Although the RCT above relates to post stroke spasticity, we note that the Guideline Development Group decided to include studies with mixed populations because "there were no good physiological reasons why the alternative neurological diagnoses should unduly influence the effects of the drug on spasticity".	baclofen were undertaken. The intervention was not found to be cost effective based on the currently available data. The uncertainties of this analysis and costing are detailed in the evidence review. The committee re-considered intrathecal baclofen in light of this new clinical and cost effectiveness evidence and agreed that there was too much uncertainty to warrant a change in the recommendations.

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Medtronic Ltd	Evidence Review F	029	009	Table 12: Clinical evidence profile: The evidence review of intrathecal baclofen versus placebo. found no evidence relating to functional / mobility issues. We would like to highlight several retrospective studies in people with multiple sclerosis patients which report on these outcomes: • *Sammaraiee Y, Yardley M, Keenan L, Buchanan K, Stevenson V, Farrell R. Intrathecal baclofen for multiple sclerosis related spasticity: A twenty-year experience. Mult Scler Relat Disord. 2019;27:95-100. doi:10.1016/j.msard.2018.10.009* • *Sammaraiee Y, Stevenson VL, Keenan E, et al. Evaluation of the impact of intrathecal baclofen on the walking ability of people with Multiple Sclerosis related spasticity. Mult Scler Relat Disord. 2020;46:102503. doi:10.1016/j.msard.2020.102503* • *Abbatemarco JR, Griffin A, Jones NG, et al. Long-term outcomes of intrathecal baclofen in ambulatory multiple sclerosis patients: A single-center experience. Mult Scler. July 2020:1352458520936912. doi:10.1177/1352458520936912* • *Reis PV, Vieira CR, Midoes AC, Rebelo V, Barbosa P, Gomes A. Intrathecal Baclofen Infusion Pumps in the Treatment of Spasticity: A*	Thank you for your comment and for providing the references. The protocol for the evidence review states that only RCTs and systematic reviews of RCTs would be included and therefore these retrospective studies could not be included.

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				Retrospective Cohort Study in a Portuguese Centre. Acta Med Port. 2019;32(12):754-759. doi:10.20344/amp.10482	
Medtronic Ltd	Evidence Review F	037	032	*Furthermore, it was highlighted to the committee that the actual cost of intrathecal baclofen includes the cost of administering the drug as well as the drug costs (which are between £3,650 and £18,250, depending on whether an ampoule can be used for multiple treatments). The administration costs although not presented to the committee are considered to be significant.* We ask that the cost assumptions are reassessed as the suggested drug costs, as highlighted to the Committee, seem excessively high. A 2000 study by Sampson et al reported that the cost of the pump and implantation procedure is estimated at around £11,800, with further annual costs of £500 to £900 for follow-up and refill. The pump is refilled with intrathecal baclofen every 2 - 3 months by inserting a needle through the skin into the pump. This may require a local anaesthetic. The pump	Thank you for your comment. The two health economic references could not be included as one pre-dates our 2005 cut-off for health economic study inclusion (as stated in the health economic protocol) and other is not a health economic analysis. Creamer 2018 has been added to the evidence review after it was identified by stakeholders. As a result, the unit cost of the intrathecal baclofen drug cost (and dose) has been reviewed and adjusted. Furthermore, a threshold analysis based on EQ5D data from Creamer 2018 was undertaken as well as a more detailed costing of intrathecal baclofen. The intervention was not found to be cost effective based on the currently available data. The uncertainties of this analysis and costing are detailed in the evidence review. The committee re-considered intrathecal baclofen in light of this new clinical and cost effectiveness evidence and agreed that there was too much uncertainty to warrant a change in the recommendations.

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				device requires replacement approximately every five to seven years. Intrathecal baclofen has been shown to be cost effective from a UK NHS perspective[1] and routinely commissioned by NHS England in line with the criteria set out in *NHSCB/D04/P/c Clinical Commissioning Policy: Intrathecal Baclofen (ITB)*[2] 3. *Sampson FC, Hayward A, Evans G, Morton R, Collett B. Functional benefits and cost/ benefit analysis of continuous intrathecal baclofen infusion for the management of severe spasticity. J Neurosurg. 2002;96(6):1052-1057.* 4. *NHSCB/D04/P/c Clinical Commissioning Policy: Intrathecal Baclofen (ITB). https://www.england.nhs.uk/wp-content/uploads/2013/04/d04-p-c.pdf*	
MS Society	General	General	General	For future updates of this guideline we would request a longer consultation period. 6 weeks, over the Christmas holidays, did not allow enough time for us to adequately consult the MS community and healthcare professionals on the updated draft. We would very much like to meet with the committee to discuss our response.	Thank you for your comment. We recognise the burden on stakeholders of our consultation process, and in this instance allowed more time than usual because of the timing of the consultation.

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				Given the length of the evidence reviews produced, NICE should consult for 12 weeks so that all stakeholders can fully engage in all the material.	
MS Society	Guideline	005	012	**Referral and diagnosis** The previous guideline explicitly stated only a consultant neurologist should make a diagnosis of MS. The update states to refer people suspected of having MS to a consultant neurologist for confirmation of the diagnosis. This strongly implies there is nothing wrong with another doctor diagnosing MS. This appears to contradict the conclusion from the supporting consultation document "Committee discussion for diagnostic criteria for multiple sclerosis; possible multiple sclerosis; neuromyelitis optica and clinically isolated syndrome". This states at 1.1.1.5 "the committee confirmed that due to the importance of obtaining an accurate diagnosis a referral to a consultant neurologist is essential". Furthermore, the optimal clinical pathway for MS (developed in 2020 by a working group of MS healthcare professionals as part of an NHS England neurology transformation programme, see: https://www.neural.org.uk/wp-content/uploads/2020/07/Optimum-pathway-for-patients-	Thank you for your comment. Recommendation 1.1.5 states that a person should be referred to a consultant neurologist or specialist under their supervision for diagnosis. The committee confirmed that in their clinical experience and opinion a neurologist does not necessarily have to be specialist in MS to make the diagnosis but the recommendation does not preclude their advice or a referral being made if appropriate. How a GP contacts a neurologist for specialist advice varies according to local protocols/pathways. The committee agree that a consultant advice line is a good example of how this may occur.

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				with-MS_updated.1.pdf) states: *'a person with suspected MS should be referred directly to an MS specialist neurologist. People with MS diagnosed by general neurologists (and other doctors), should be referred to an MS specialist neurologist for categorisation of the patients' disease and access to therapies.'* While acknowledging there is currently increasing demand on a limited number of neurology specialists, we recommend the guideline reflects the optimal clinical pathway and states all of the following: • 'MS should be diagnosed by a consultant neurologist, ideally an MS specialist neurologist'. • 'people with MS diagnosed by general neurologists (and other doctors) should ideally be referred to an MS specialist neurologist, for categorisation of their disease and access to therapies.' • 'refer people suspected of having MS to a consultant neurologist, ideally an MS specialist neurologist'. Appreciating the need to avoid inappropriate referrals, we suggest the committee considers evidence in favour of GP-consultant advice lines. This approach has been demonstrated to work very well in the Walton Centre in Liverpool and was included in NHS England's RightCare	

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				Toolkit for progressive neurological conditions (see: https://www.england.nhs.uk/rightcare/products/pathways/progressive-neurological-conditions-toolkit). An evaluation found that between April to December 2017, 43% (189) of total calls (443) to the Walton's Consultant Advice Line received advice and guidance only, thereby potentially avoiding an outpatient's or specialist's appointment. This equates to a saving of £37,303 across the 9 CCGs in the Walton Centre catchment. Where GPs asked for and subsequently received specialist advice and guidance, only 33% of patients went on to be referred to secondary care (see: https://www.edgehill.ac.uk/health/files/2018/11/WC-NEURO-network-evaluation-KAEHNE-09052018.pdf). A statement could be included in the guideline that where the referrer is not certain if a referral is appropriate they consider seeking advice from a consultant neurologist with expertise in MS, where possible. The Neurological Alliance made a similar suggestion in their submission to the consultation on the draft NG127, namely that GPs ought to be advised in certain circumstances to seek a second opinion from a neurologist and that 'a phone call to a neurologist is far more efficient than a wasted neurology outpatient appointment – and more likely to lead to the better pathway for the patient' (see comment 2:	

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				https://www.neural.org.uk/wp-content/uploads/2021/04/2017-09-nice-response-2017-1.pdf).	
MS Society	Guideline	005	021	**Clarifying what is meant by 'MS mimics'** The guideline states that diagnosis of MS should include 'excluding alternative diagnoses (targeted laboratory tests to exclude MS mimics may be indicated if the history, examination or MRI findings are atypical)'. It is not necessarily well understood by the public and patients what is meant by 'MS mimics', so it would be helpful to be explicit. On a related point, it would be helpful to include a definition of Clinically Isolated Syndrome within the guideline.	Thank you for your comment. We have removed the term 'mimics' from the recommendation. We have added a bullet point to recommendation 1.1.7 to see the McDonald criteria for a definition of clinically isolated syndrome.
MS Society	Guideline	006	001	**Annual review of people suspected of having MS** We welcome the fact the update suggests as an example that people with suspected MS be reviewed annually. Living with uncertainty about your health for long periods of time can be distressing.	Thank you for your comment
MS Society	Guideline	006	001	**Clarity regarding meeting McDonald criteria 'completely'** The updated guideline implies that all the McDonald criteria must be met to diagnose MS ('if MS is suspected but the McDonald criteria are not completely met…'). It would be helpful to define what is meant by 'completely'	Thank you for your comment. We have removed the word 'completely' from the recommendation.

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				and state which criteria are essential, so that patients know what they can expect from the diagnostic process both when they are first diagnosed, and possible subsequent diagnosis of secondary progressive MS.	
MS Society	Guideline	007	008	**Information and support at time of diagnosis** We welcome that online resources have been added to the information that should be provided at point of diagnosis, given this is how many people with MS prefer to access information.	Thank you for your comment
MS Society	Guideline	007	019	**Ongoing information and support** We welcome the addition of '*Explain to* people with MS that they should have a comprehensive review of their care at least once a year and what this should cover. Advise them to ask their healthcare professional for a review if it has not taken place.' It is really important patients know what care they should expect and are empowered to ask for that. We welcome the addition of 'Provide ongoing information and support tailored to the person's changing needs or circumstances, for example, for people planning to have children or for people as their MS becomes more advanced.' We welcome the addition of 'Explain to carers (including young carers) about their right to a carer's assessment	Thank you for your comment.

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				and tell them about other sources of information and support that may be available'.	
MS Society	Guideline	009	003	**Information and support for people planning to have children or who are pregnant** We welcome the addition of this section. It is a topic that matters hugely to people with MS. At 1.2.12 it would be helpful to add that *MS is not directly inherited from parent to child and* that pregnancy does not increase the risk of disease progression, rather than at section 1.2.14. This would be in order to increase the likelihood this information is proactively offered by professionals given it could be important to help inform prospective parents' decision-making. There is no mention that MS symptoms can be affected by pregnancy, which seems a significant omission. The guideline should mention breastfeeding and the fact that some DMTs should be avoided if you want to breastfeed and that this should be discussed with your neurologist. The guideline ought to advise proactively signposting to support groups and local services for parents during pregnancy and post-birth.	Thank you for your comment. We merged the two recommendations (recommendation 1.2.2). This recommendation covers that MS can be well managed in pregnancy and does not increase the rate of progression which are based on the clinical experience and opinion of the committee. We have added that breastfeeding is safe unless the person is taking certain disease-modifying therapies. We are unable to signpost to support groups and local services except for the section on the NICE webpage for this guideline.
MS Society	Guideline	009	016	**Information and support for people planning to have children or who are pregnant**	Thank you for your comment. With have incorporated your suggestion into recommendation 1.2.12.

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				The guideline states '**I**f a person with MS is thinking about or planning pregnancy, or is pregnant offer opportunity to discuss…changes to medicine use before and during pregnancy'. We very much welcome this, however the guideline should also advise and empower patients directly to initiate this conversation, not just healthcare professionals, given treatment may need to be changed urgently i.e. 'if you're trying to have a baby, or if you become pregnant, and you are on a DMT, let your neurologist know straight away'.	
MS Society	Guideline	011	004	**Coordination of care** We welcome that a single point of contact remains and there has been an additional note that that person should have knowledge of MS services. We welcome the additional MDT members that have been added, reflecting more of the professionals that are and should be involved in the treatment and care of people with MS.	Thank you for your comment.
MS Society	Guideline	014	017	**Pharmacological management of fatigue** We consulted our medical advisors, a number of whom expressed serious concern at the recommendations in this section, specifically the recommendations for modafinil and SSRIs. We would like to meet with experts and	Thank you for your comment. The committee acknowledge that there is only limited evidence of benefit for amantadine, modafinil and SSRIs (see committee discussion of the evidence in evidence review D. However, in their clinical experience and opinion some people do respond to these treatments and given the

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				committee members to discuss this further given the concerns. The 2014 guideline stated there was not enough evidence to recommend either modafinil or paroxetine as treatments for MS-related fatigue and it warned of the potential harms. We are not convinced that the evidence presented in this updated draft guideline supports changing the treatment pathway in this way. Clinicians felt that the only drug with reasonable evidence is amantadine. Clinical opinions expressed were that the evidence in favour of modafanil in MS is poor. Clinicians cited the risks associated with modafanil, that it is not often used outside of the sleep context and that there is restricted use of the drug even in relation to sleep now. As an unlicensed product, prescribers would have to take all the risk and responsibility of prescribing. It was felt there would be significant pushback to prescribing in primary care, placing more burden on specialists in secondary care. It was felt that a recommendation would be counterproductive in that it would raise expectations among patients that specialist clinicians do not have confidence in.	potential impact of fatigue on daily life they made a recommendation to consider these interventions. In recommendation 1.5.12 we now refer to considering the safety of the drugs. In recommendation 1.5.15 we now refer to monitoring and reviewing response to treatment. The guidance in the summary of product characteristics has now also been highlighted in the rationale and impact to raise awareness of potential harms. In the experience of the committee these drugs are prescribed in primary care and locally arrangements for prescribing occur only if a person responds to treatment. We have made a new recommendation on shared care (1.5.16) The 2020 MHRA safety advice on modafinil (Provigil) is now referred to in recommendation 1.5.14 and in the rationale. Recommendation 1.5.4 highlights the importance of recognising other causes of fatigue including anxiety and depression.

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				Clinical opinions expressed regarding SSRIs were similarly unsupportive. It was felt that SSRIs should only be contemplated if it is felt that fatigue was the result of concomitant anxiety and depression. Concern was expressed about increased burden being placed again on secondary care, because primary care will be reluctant to prescribe for an unlicensed indication. Specialists often refer patients to their GP to manage depression. Given the pressure on MS services, concern was expressed about ability to monitor and manage prescribing of SSRIs in secondary care. In the three studies the committee cites (Chataway, Ehde and Cambron), evidence is taken from secondary outcome measures. None of these studies were designed to measure the effect of the SSRIs on fatigue in MS.	
MS Society	Guideline	016 & 040	General	1.5.14 - We disagree with the decision not to offer fampridine to treat mobility problems in people with MS. MS has a substantial impact on people's lives in a variety of ways. One of most profound effects is felt in relation to mobility, with consequences on ability to work, to care for oneself and others, as well as to maintain a social life and other life activities.	Thank you for reaching out to the MS community and highlighting the importance of this issue. The independent guideline committee acknowledged that it is a clinically effective treatment for some people, however it is not cost effective at the current price the NHS is expected to pay. The availability of treatments in Scotland and Wales is a matter for the devolved administrations. In these countries it is made available under a confidential patient access scheme that provides the drug at a lower cost. Patient access schemes are negotiated by the relevant

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				Whilst we understand that fampridine is only an effective treatment for mobility problems in some people with MS, when it does work, the effects can be profound and wide ranging. We appreciate that NICE has conducted a very detailed cost analysis and review of available evidence to calculate the price at which fampridine may be deemed cost effective. We note that NICE's preferred quality of life measure, EQ-5D-3L, has just three options to describe level of mobility, and thus may not be sufficiently sensitive to capture the changes in mobility that may be conferred by use of fampridine, which can be modest but nevertheless life-changing as explained further below. We understand that other measures like the 12-item Multiple Sclerosis Walking Scale (MSWS-12), and the Timed 25-foot walk (T25FW) were also used in the analysis. However, we are unclear to what extent this was factored into the central cost effectiveness calculations and feel it may be extremely difficult capture the full effect of fampridine on overall quality of life for people with MS without a range of qualitative descriptions of experience. The MS Society issued a call-out to people with MS, asking what it would mean to them to have access to fampridine. We also asked respondents whether they had previously taken fampridine, and, if so, what their	NHS commissioning body and the company (manufacturer). In England this process is led by NHS England.

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				experience had been. The aim of this was to allow people with MS to have their say on this decision and to present the NICE committee with qualitative experiences of people with MS we hope will be of some help. 388 people responded to our call out, 56 of whom had current or previous experience of taking fampridine. We have anonymised responses for data protection purposes. A number of consistent themes emerged in our responses, which we have set out below. **The profound effects of restriction of mobility on daily living and overall physical health** Many people wrote to us about the profound effects that restricted mobility had on multiple aspects of daily living - on their ability to work and to support themselves, to carry out caring responsibilities, to socialise and to go outdoors. They also spoke about the impact on their fitness and overall physical health. One person told us *"I've had MS for 20 years now and my mobility is really poor. I use a powered wheelchair when outside of my home as my walking is so limited. To be able to walk even a little easier would mean the world to me. Each step I take needs so much effort and despite*	

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				using a rollator I regularly fall. To retain the independence that walking brings is beyond cost and will reduce care costs and the burden on the NHS." Another person with MS said simply *"It would help me walk, which means more than you will ever understand if you can walk".* Person E said "{if I could access fampridine} *my overall fitness would improve immensely as I walk at a snail's pace, so no cardio benefits for me."* Person I said- *"To retain the independence that walking brings is beyond cost and will reduce care costs and the burden on the NHS from dealing with the fallout of dealing with injuries associated with falls."* Many people expressed modest hopes for their lives which they felt might come with an improvement in walking ability or mobility. Person J - *"If the therapy successfully improved my mobility it could mean that I could walk to the top of my drive unaided and maybe take my dog for a walk. I could maybe get on the floor and play with my baby grandson and be able to get up again. Perhaps I could have a bath instead of a shower and not struggle to get out. In other*	

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				words possibly it would have the potential to restore a degree of normality to my day-to-day life." Person K - *"I would be able to get some fresh air instead of staying indoors all the time."* Person L told us the idea of being able to try fampridine would mean she could hope for *"The ability to walk for longer than 10 minutes, and the chance after that to consider having a small dog."* Responders talked of a restricted ability to care for children or grandchildren, and of their hope that the difference that an improvement in mobility could make to this. Person A told us *"I'm already dependant on crutches to walk and I've got children to raise, one of them disabled. I would like to have that option to improve my walking as it's very important for me as a single parent to be able to take care of my children like any other parent."* Person C said "*I can't walk very far and can't do all the things I would like to do with my toddler son. If this medicine was available to me, I could take him a walk, I could take him to the park or the beach."*	

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				The link between mobility and mental health and emotional wellbeing Multiple people wrote to us about the knock-on effect of reduced mobility on their mental health-and their hope that a treatment that increased mobility (even a small improvement) might help with this. Some people talked about a loss of confidence and increased fearfulness that had developed along with loss of mobility, as well as a sense of a loss of dignity and independence. Person G said *"This treatment could possibly help with my walking ability. If successful I would be able to take physical exercise, go for walks etc and not feel scared to go out on my own again. It would also lessen my anxiety issues around a fear of being on my own in case of trips. My walking has been severely impaired due to relapse, life changing in fact."* Person H said that if fampridine was able to help them *"I would feel more confident when out and about, feeling less of a target for being attacked or mugged."* **The profound improvements in quality of life and mental health seen when fampridine increases mobility**	

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				Of those who contacted us who were currently using or had previously used fampridine, many gave striking accounts of its effects on their mobility, and of the downstream effects of this on their fitness, mental health and quality of life. Person M told us –"*Fampridine significantly improves my MS. It reduces fatigue massively and makes all motor skill movements more controllable. This allows me to exercise and maintain my muscle condition."* Person N said "*I went on the trial about six years ago and have been on the drug fampridine for about 5 1/2 years. It was life changing for me. I can tell instantly if I forget to take it- I wonder why I can't get up the stairs anymore. It is literally the difference between a life and none. It massively improves my energy levels, both physically and mentally. Without it life wouldn't be worth living, it's as simple as that."* Person O said "*During the trial I participated in for fampridine, I was actually on the placebo. When I was given the actual drug it was like a miracle I could walk without a stick for the first time in years actually carry something without falling over. I've been on the drugs 5 1/2 years and it is life changing for me my MS has progressed very slowly so I am less able than when I*	

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				started taking the drug however without it I'm scuppered. I've been on the drugs 5 1/2 years and it is life changing for me my MS has progressed very slowly so I am less able than when I started taking the drug however without it I'm scuppered. I can tell instantly if I Forget to take it as suddenly I can't get up the stairs anymore. It improves my productivity both mentally and physically." Person P told us *"I have been on fampridine for two months now and I have noticed a substantial difference in leg movement. I can walk easier and a little quicker, move better in bed and lift my legs onto the bed, my fatigue is better and I feel remarkably better in myself. Getting upstairs is better and I am able to stand for a little longer than before."* Person Q *"I already have access to fampridine, after seeing my neurologist earlier this month. This last week I have found that I can now stand upright, WITHOUT using support or a stick. And that is after taking fampridine for less than a week! I was diagnosed with M.S. 28 years ago, and have been using a wheelchair for just over 8-9 months now…So now being able just to stand up is WONDERFUL, and I would hate it if I was not able do that."*	

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				Person R told us "*Earlier in the year there was a mix up with my prescription and I was without Famprya for 10 days. I could hardly walk and had to use a wheelchair around the home.*" Person S said "*Fampridine is what has kept me walking & out of a wheelchair, thus helping me to maintain my independence.*" Person T said "It *has made a huge difference to my walking ability! Given me back a bit of my lost confidence & made it possible to move a leg which has been a dead weight for so long!*" Person U said "*I had a trial of the drug fampridine, which was a huge success. Before I started it, I was house bound and struggled to move around my home. After taking the drug I was able to go out and even walked a full mile without my walking sticks or frame. The positive impact on my quality of life was phenomenal. Since the trial has ended, my health and mobility have seriously deteriorated. This has been exacerbated by the stress caused when I was denied access to this drug by my clinicians. I've since had a number of falls in the home owing to my condition, and have also been diagnosed with Type 2 Diabetes. These can be directly attributed to my lack of mobility due to my Multiple Sclerosis. The best way*	

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				to manage my diabetes is plenty of exercise, but unfortunately because of my MS, this isn't possible." Person V said "*Fampyra is one of the most important drugs to me. It helps with not only walking but {with} movement of all my limbs enabling me to pick things up and drink and it just generally makes me feel stronger with less spasticity which results in me feeling better physically and mentally. Because I pay for the drug myself, I have frequently tested how I feel when I stop the drug and when I restart it. The results are 100% in favour of the beneficial effects of Fampyra on my MS symptoms. I struggle to pay for the drug but the benefits to me are indisputable and I would struggle without it."* Person W said "I *am fortunate enough to be able to access fampridine. It has been a game changer in my quality of life. If it was available on the NHS it would mean that I and so many others would be able to benefit from the immense advantages it brings to those suffering from reduced mobility. It is not just about walking speed, it helps in so many other ways not recognised in this restricted measurement of success."* Person Y said "*I have PPMS and have taken fampridine for several years now and have found it very helpful for mobility issues. I still do exercise classes and my walking*	

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				is a lot stronger, so it would be great if this were available on the NHS." Person X said- *"Fampridine is the only drug that helps my husband to stand & walk on his frame. To stand long enough to pull up his trousers, long enough to get himself a mug - long enough to do the things we all take for granted every day. He can only walk a very short distance but Fampridine helps his balance so that he doesn't fall as often."* **Impact on the quality of life and wellbeing of unpaid carers** People responded to our call out about to tell us about the impact of MS on family life and family members' wellbeing. Person B told us *"My husband's walking had deteriorated significantly meaning he cannot partake in normal everyday activities as a dad. The children miss out on so much as he cannot walk very far or even stand for short periods. It is very upsetting and distressing for him."* Person D contacted us on behalf of her partner. She said "*My partner has RRMS and often cannot walk further than 250m. At only 38 that makes our life significantly poorer. If you can't walk, you can't exercise and that's not great for*	

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				other aspects of your physical health as well as causing terrible mental health consequences such as depression." Person F said *"I get quite depressed now I am not able to walk very far and it is not just me but it has an impact on my family too."* The progressive, fluctuating nature of MS presents particular challenges for those family members, friends and unpaid carers supporting them. It can make balancing work, education and taking care of one's own health and wellbeing very difficult. 6,842 people with MS in England took part in our 2019 'My MS, My Needs' survey (see: https://www.mssociety.org.uk/sites/default/files/2020-08/MMMN3-nations-data-tables.pdf), which found 4 in 10 respondents relied on unpaid care and support from family members and friends to some extent. Our 2019 survey of 549 friends, family members and unpaid carers of people with MS in the UK (see: https://www.mssociety.org.uk/sites/default/files/2020-08/MS-family-and-friends-2019-survey-findings.pdf) found 41% of respondents spent the equivalent of a full-time job or more each week supporting someone with MS. An overwhelming 90% of respondents reported negative impacts on their health and wellbeing, which is particularly concerning considering 41% said they were living with a	

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				long-term condition themselves. Half of respondents said they didn't have the practical, emotional or financial support they needed in their caring role, while one in three (34%) had given up work as a result of supporting the person with MS. Access to treatments that can improve people with MS's mobility and independence, in turn improves the wellbeing of unpaid carers, family members and friends, and their ability to be more independent - including to work, if they wish to do so. **The impact of paying to access fampridine on people with MS** Of those who contacted who were taking, or had previously taken fampridine, many specified they were paying for a private prescription, with an average stated monthly cost of around £191 per month. Many of those paying privately emphasised the difficulty they had in affording the monthly cost of fampridine. Person U, who had previously able to access fampridine through a trial but is now paying privately for his prescription, told us "*The impact of {being on the} the fampridine trial was huge. I was housebound beforehand, but by the end I could walk for a mile and a half. I was finally able to walk over to my mum's house with no walking aids.*	

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				Being less active had a terrible effect on me, I developed type 2 diabetes and muscle ache. I was battling for a year or so, and just couldn't cope – so I made the difficult decision to start paying for it privately, which costs £200 a month. I've had to make huge sacrifices and cut down on things like food and heating to be able to afford it. I know that there will come a point where I can't afford it anymore and I have to stop. Fampridine has made such a huge impact on me. It helps me to shower and go to the toilet more easily, get in and out of bed and get about more. It enables me to live a full, independent life without relying on others. Everyone who's eligible should be able to get it on the NHS." Person Y told us "*Fampridine got me off crutches. Having not worked for over 12 months {I worked at an airport, prior to the pandemic}, I am really struggling to pay for the fampridine…Please rethink this decision, it is very unfair."* Person Z said "*With an EDSS of 6.5 life is very tough. I've been on fampridine for about 4 months now and while it's not a miracle cure I can climb stairs, drive better and go out more}. Paying privately is a huge strain on my finances and I'm not sure I can continue paying, which would be a massive step backwards for me. Consider how making people more independent can have a wider benefit to the*	

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				economy and the calculations on value for money isn't perhaps quite so clear. It's certainly a huge increase in quality of life." Person AA said "*I have to budget very carefully to pay for fampridine as it is so expensive - not being licensed!"* Person AB said "*As a disabled pensioner this saving would make a massive difference to my finances. Please license it as it is in Wales and Scotland! Please."* Person AC said "I *have to pay £191.00 month for it- I have to have it as my life isn't as good without it. I still work two days a week and think without it I would have to give up working. I have to go without other things to afford to pay for it"* Person AD said "*I would save £185.64 every 4 weeks. It's a lot of money to pay out of my PIP. Earlier in the year there was a mix up with my prescription and I was without Famprya for 10days. I could hardly walk and had to use a wheelchair around the home".* Person AE said -*"My wife takes fampridine which we privately fund. Sometimes we have to stop dues to financial constraints. My wife suffers with MS and has*	

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				done for 20 years. She struggles to walk at all now. Without fampridine she can't at all" Person AF said -"*Having 1st trialled fampridine in 2012 on private prescription {from} Newcastle RVI, I continued using it until 2017, paying £200/month. It allowed me to keep on working and improved my ability to walk tremendously. I know longer can afford to pay for it now, have been made redundant and to get this on NHS England would improve my life so much. Since I have stopped using it I now use a wheelchair 24/7 to cope with daily tasks."* Person AG said to us -*"It's quite simple, I have tried fampridine before and it worked, it improved my walking and it reduced the time I took to walk the same distance twice by half, but unfortunately I could not stay on it as I could only get it privately and could not afford it. I cannot see how someone {NICE} who is able bodied can decide it's not cost effective when it enabled me at the time to carry on working within the building trade. Not at all fair."* Person AH said "*fampridine stops me tripping and falling over. Without fampridine I could fall and break bones costing the NHS more money than the prescription costs."*	

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				Person AI said *"I am appalled and bitterly disappointed by this decision. I have been paying privately for fampridine since 2013, and am absolutely convinced that it has kept me more mobile and given me more stamina than would have been the case otherwise. Before starting to take it walking and balance were gradually deteriorating, but since using it regularly my condition has stabilised. … why has NICE seen fit to ignore the evidence? It feels as if maintaining as much independence as possible is unimportant to NICE - and it also feels as though NJCE has no understanding of the mental and physical benefits for people with MS of maintaining as much mobility as possible. .. I have absolutely no doubt that without it I would by this time be using a wheelchair permanently and my quality of life would have deteriorated markedly. I would probably have had more falls and worse general health because of not being able to move around adequately - and would be costing the NHS more in other ways!"* Person AJ said *"I take fampridine daily on private prescription. Apart from the huge financial cost the difference that fampridine makes to me is literally the difference between being able to walk 5 feet or 100. Without it my quality of life is significantly reduced."*	

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				The potential financial benefits to society of providing fampridine on the NHS Some people stated they felt the decision not to fund fampridine on the NHS England was counterproductive, due to the perceived savings to society of providing the drug. Such as: enabling people to stay in employment, reducing the requirement for disability benefits, and the savings for the NHS due to improved mental and physical health if mobility improved, or the savings in the cost of the care and support required. Person AK said- "*fampridine made a massive impact on my mobility. I strongly believe that if I were able to get this medication it would greatly improve my quality of life and extend my working life. Keeping me working and off benefits, therefore financially be fitting the public purse in the long run."* Person AL said *"fampridine helps me to walk! Don't talk about speed of walking- it helps me to walk! {fampridine} is cost effective. How much would going into care cost the local authority for me, who hasn't got a house to sell? Thousands and thousands compared to £993.72p per year. "*	

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				Person AM said -"*My son is an MS sufferer. He is not yet fifty and had changed his way of life to enable him to continue working and supporting his wife and two children. I realise that fampridine is very expensive, but if it enables him to continue to support his family it saves the state the cost of supporting him and his family which would be the case if his health deteriorated further.* *It is essential that the NHS is able to supply drugs which enable people to maintain their self-sufficiency."* Person AN said *"Having been diagnosed over 16 years {ago}, my condition is beginning to decline, the availability of this drug gives hope and longer independence to people like me! Meds should be available to all in the UK, rather than on a regional/postcode basis. The government needs to make this right, as a taxpayer that hopes to stay in employment and remain independent this drug is vital for people like me."* Person AO said "*This is further indication that NHS funding for MS treatments is inadequate. I'm fortunate to have had a prescription for Functional Electrical Stimulation since 2016 which has kept me walking safely despite continued MS progression. Even though my muscles are very weak now, I have no problems with pressure sores, my right foot and leg muscles haven't atrophied entirely and I continue to mobilise as much as*	

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				possible despite reliance on an electric chair. Surely the continued good health achieved through supporting walking treatments costs less in the long run?" Person AP said "*Why are {NICE} saying {fampridine} is not cost effective for approval because of the cost?- how much cost would it be to the NHS to provide carers morning noon and night for each person, rehabilitation to help with the person to cope to help the person deal with everyday life?"* Person AQ said *"{I would} need less caring and intervention from other services and save the NHS money".* Person AR said "*I rely entirely on a powerchair but can manage a few steps with a frame. If I was able to walk just a little further it would mean the world. I would be able to keep those muscles and joints mobile for as long as possible, which would generally improve my health and wellbeing and help to prevent further deterioration and/or complications, saving the NHS money in the end* Person AS said "*I am sure that there are many fellow sufferers that would be able to continue in employment much longer if they had access to Fampridine, this would not only benefit the individual but also help the economy and reduce benefit costs."*	

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				Different decisions on approval of fampridine in different nations of the UK A third strong and consistent theme in our responses was the differing decisions on approval of fampridine between health services in Scotland, Wales, England and Northern Ireland. Whilst not all people with MS may be aware that the "NHS" in the UK represents four separate systems, with different bodies governing approval of medicines in these systems, there was clearly a very strong sentiment about differential access to fampridine around the UK. There was confusion as to why, if authorities in Scotland and Wales had decided that fampridine was cost effective, NICE had not reached the same conclusion. Person AT said *"I think that if it has been approved in Scotland and Wales it seems unreasonable that NICE will not approve a drug that has been shown to benefit MS sufferers walking difficulties which from my own experience is my main form of disability."* Person AU said *"Fampridine has given me my life back. I do more, get out more and have more energy. The benefits for me have gone far beyond increasing my walking speed. I can manage the few side effects I have occasionally experienced. Although the drug only treats*	

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				symptoms and is not a cure then so what. The longer I can keep fit and well, manage to live without care, keep doing things with my friends and keep off antidepressants the better for family and the NHS. I dread the day I may have to stop taking it. It's also unacceptable that it is available on the NHS in Scotland and Wales but not England." Person AV said *"This is not a case of what fampridine does for me this is downright discrimination …if fampridine is not economical for England it's not economic for Wales or Scotland."* **The lack of access to treatments for some people with MS** A fourth theme in our responses was a perception of a lack of access to other treatments for mobility, especially amongst those with progressive forms of MS. Whilst several DMTs have been approved by NICE for progressive forms of MS, only some patients with progressive disease are eligible for these treatments. Person AY told us "I *have PPMS and I am at the stage where I cannot walk unaided and will soon be confined to a wheelchair. When I heard about this drug, it gave me such hope that I could be mobile for a few extra years. To*	

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				have it so cruelly withdrawn, when there is little else to treat primary progressive MS, is a body blow especially when my near neighbours in Wales will have access to this treatment". Person AZ with progressive MS able to access fampridine through a trial, said *"Fampridine significantly improves my MS. It reduces fatigue massively and makes all motor skill movements more controllable. This allows me to exercise and maintain my muscle condition. Fampridine takes effect quickly, missing one pill is very noticeable. I am lucky that following stage three trials I was allowed to stay in the drug. It is the only drug I take for my PPMS."* Person BA said "*I was diagnosed with primary progressive MS in 1991….I have been on a trial of {fampridine} for 5 years and it has improved my walking considerably. I was about to get a stair lift but after taking fampridine I have managed to climb the stairs on my own."* Person BB said *"I have PPMS and have taken Fampridine for several years now and have found it very helpful for mobility issues. I still do exercise classes and my walking is a lot stronger, so it would be great if this were available on the NHS."*	

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				There is a perception amongst some of those with progressive forms of MS than the system has "abandoned" them. Our 2019 'My MS, My Needs' survey found that people with progressive forms of MS were less likely to be able to access MS specialists when they needed to, compared to people with relapsing forms of MS {40% need met vs 65%}. In addition, people with progressive forms of MS were also less to have received the emotional support they needed than people with relapsing forms of MS {58% with unmet need v 44%}. Our survey showed that overall access to symptom management treatments is poor, with just 13% of those with progressive MS able to access a symptom management treatment, compared to 7% with relapsing forms of MS. This included those who were paying to access such treatments privately.	
MS Society	Guideline	017 - 019	General	1.5.20-1.5.28 - **Treatment combination** The MS Society consulted with our medical advisors (all consultant MS neurologists, see: https://www.mssociety.org.uk/what-we-do/our-people/ms-society-medical-advisers) on NICE's updated guidance for the management of spasticity. They emphasised that many people with MS required a combination of treatment to manage their spasticity, and that it would be helpful if	Thank you for your comment. The protocol for this review did state that combinations of pharmacological treatments would be included (see appendix A evidence review F.) However, the search did not identify any studies on combinations of drugs that fulfilled our inclusion criteria.

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				the guideline were to make this explicit as a general point, beyond the specific recommendation that baclofen and gabapentin can be combined.	
MS Society	Guideline	017 - 019	General	1.5.20-1.5.28 - **Specialist and multidisciplinary team management of spasticity** The draft guideline states that if initial treatments for spasticity are unsuccessful, referral should be made to a multidisciplinary team experienced in the management of spasticity. The implication in the guideline, stated more explicitly in the evidence recommendation, is that if a patient's treatment goals for spasticity are not being met by baclofen and gabapentin, other treatment approaches - delivered by a service dedicated to the specialist management of spasticity- should be considered. However, there is no guidance as to the optimal escalation cascade for other treatments that may be given considered in a specialist clinic, including Botulinum toxin or intrathecal Baclofen, although these latter treatments were included in the evidence review. Some of our medical advisors questioned why these treatments were not referred to in the draft NICE guideline.	Thank you for your comment. The committee removed the recommendations on third- and fourth-line options due to the lack of clinical and health economic evidence. These treatments should only be considered by specialists and a recommendation is made to refer to a multidisciplinary team experienced in the management of spasticity (1.5.31). Due to the limited evidence the committee made a research recommendation for future studies to be conducted on all of the interventions stated in the review protocol (appendix A evidence review F).
MS Society	Guideline	018	003 - 030	1.5.23 -1.5.25 - **The recommendations for first and second line treatment of spasticity** We agree with the committee's recommendation to offer oral baclofen as a first line pharmacological treatment in the management of spasticity, and gabapentin second	Thank you for your comment.

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				line. We also agree with the recommendations on dose escalation, tolerance of these treatments.	
MS Society	Guideline	019	014 - 018	1.5.27-1.5.28 - **The use of nabiximols in the management of spasticity** The committee's recommendation on the treatment of spasticity in people with MS sets out that prescribers should consider oral baclofen as a first line treatment in those people with MS spasticity who have specific treatment goals such as improving mobility or easing pain, with gabapentin to be offered as a second line option. The guideline states that a combination of these two treatments can be offered if the individual medicines do not provide relief or are not tolerated at higher doses. It is implied that referral to a multidisciplinary team experienced in the management of spasticity should follow if these initial treatments are unsuccessful. Following this, reference is then made to NICE's guideline NG144 on cannabis-based medicinal products, for guidance on the use of THC:CBD spray for treating spasticity in people with MS. We strongly object to the lack of clarity about where nabiximols (as the sole licenced THC:CBD spray, brand name Sativex), should come in the treatment cascade for	Thank you for your comment. Cannabis-based products were outside of the scope of this guideline and we therefore did not include these in the review protocol for this question (appendix A evidence review F). We cross refer to the existing NICE guidance on cannabis-based medicines in recommendation 1.5.32.

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				spasticity, given its licenced indication as an "add-on" treatment for those with moderate to severe MS spasticity for whom other treatments have not been effective. Our 2021 Approved but Denied report (see: https://www.mssociety.org.uk/sites/default/files/2021-10/ApprovedButDenied_Dev17_0.pdf) on access to nabiximols for eligible people with MS found that fewer than half of CCGs in England had chosen to put nabiximols on their formulary, with just 13% of those NICE estimated as eligible for a trial of nabiximols able to access the treatment at the time of our report in August 2021. Some of this can be attributed to an acknowledged confusion about when licenced cannabis-based medicines should be prescribed. Our report also highlighted issues with stigma around the prescription of such medicines, even amongst specialists. In September 2021 NHS England's Chief Pharmaceutical Officer wrote to NHS England's CCGs and Trust to draw attention to NICE's prescribing recommendations for Sativex as set out in NG144. The NICE MS management guideline represents an opportunity to clarify to prescribers when nabiximols should be considered for people with MS with spasticity. In addition, our Approved but Denied report found that, of those NHS CCGs who had chosen to put nabiximols on	

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				formulary, just 37% had instigated a shared care agreement. NICE's cannabis-based medicines guideline indicated that prescriptions of cannabis based medical products may be issued by another prescriber as part of a shared care agreement under the direction of the initiating specialist prescriber. It would be helpful if the updated MS management guideline could indicate that shared care can be considered in the prescription of nabiximols.	
MS Society	Guideline	023	010 - 014	**Comprehensive review** Welcome that the review now includes assessing MS evidence of progression, evidence of active disease and eligibility for disease modifying treatment. However it would be helpful to include what constitutes evidence of progression, particularly the role and frequency of MRI scans.	Thank you for your comment. An evidence review was not conducted as part of this guideline and therefore only minor changes could be made https://www.nice.org.uk/process/pmg20/chapter/updating-guideline-recommendations#refreshing-the-guideline-recommendations. We are therefore unable to specify how disease progression should be assessed.
MS Society	Guideline	023	013	**DMTs** We welcome the inclusion of eligibility for disease modifying treatments being considered in the comprehensive review, as they are a key aspect of MS management.	Thank you for your comment.
MS Society	Guideline	027	020	**DMT algorithm** The guideline should cross-refer to NHS England's DMT algorithm (March 2019, see: https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2019/03/Treatment-Algorithm-for-Multiple-Sclerosis-Disease-Modifying-Therapies-08-03-	Thank you for your comment. As disease modifying therapies was outside of the scope of this guideline, we are unable to cross refer to this guidance.

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				2019-1.pdf) as the national commissioning policy for disease modifying treatments in England. It is a framework to aid decision-making for multiple sclerosis (MS) specialists and patients, to help reduce excessive variation in practice, and ensure safe and effective prescribing. The algorithm is due to be updated soon.	
MS Society	Guideline	049	General	**Table 1 Recommendations that have been deleted** We disagree with proposal to delete the following from the guideline: **'**Offer people suspected of having MS, information about support groups and national charities' on the basis that, quoting the committee, 'providing information and support on MS without a confirmed diagnosis increases anxiety. There are so many possible diagnosis due to the diversity of symptoms information and support should be provided once a diagnosis of MS in confirmed'. People with MS can often face delays and long waits before being seen by a consultant neurologist and diagnosed with MS. The Neurological Alliance Patient Experience Survey in 2019 (England) found 27% (n=259) of respondents with MS who saw a GP did so five or more times before being told they needed to see a neurologist, and a further 22% (n=210) saw their GP three to four times. The same survey found 23% (n=222) of	Thank you for your comment. We have added that information should be provided to recommendation 1.1.9

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				respondents who needed to see a neurologist waited more than 12 months. Meanwhile, patients may be dealing with painful and confusing symptoms, anxiety and most certainly questions. Support groups and national charities are well placed to provide information and support at this time. If health care professionals do not signpost to reliable sources, patients will seek information anyway and this could be from unreliable sources, leading to potentially dangerous misinformation and an increase in unwarranted anxiety. Many people contact the MS Society before they are diagnosed seeking information about the condition. Information related to this is among our most popular. In 2021 for example, 7154 people downloaded our pdf factsheet, Have I got MS and why…?, and there were 226,707 visits to our webpage on early signs of MS, making this our most visited information page. The proposed deletion of this line also contradict the recommendations to offer patients with suspected neurological conditions information and advice as set out in guideline 127 on recognition and referral of suspected neurological conditions (https://www.nice.org.uk/guidance/ng127/resources/suspected-neurological-conditions-recognition-and-referral-pdf-66141663923653).	

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				The committee acknowledges that 'a prompt and accurate diagnosis will ensure that people have timely access to interventions to manage their symptoms' and we couldn't agree more. However, the reality is that many people do not get a prompt diagnosis and while they are waiting it is important they are aware they can access information and support from patient charities etc.	
MS Society	Guideline	General	General	**Functional Electrical Stimulation** Functional Electrical Stimulation (FES) for foot drop should be recommended in the MS guideline. Evidence demonstrates FES can improve walking performance and quality of life, reduce trips and falls, and is cost-effective. Evidence outlined as follows. FES improves walking speed A systematic review and meta-analysis (included 19 studies involving 490 people with MS) was carried out in 2017 (Miller et al. 2017). The review found that the majority of studies reported a significant increase in walking speed following the initial use of FES for MS related foot drop. On average, FES increased walking speeds by 5% to 18% in those studies. A small number of studies reported mixed results or no immediate change in walking speed.	Thank you for your comment. The non-pharmacological management of mobility was not identified by the surveillance review as having new evidence and was not within the scope of this update. We have added a cross-reference to the NICE IPG on functional electrical stimulation https://www.nice.org.uk/guidance/ipg278 . Functional electrical stimulation is being considered in the new guideline on rehabilitation for chronic neurological conditions including acquired brain injury (https://www.nice.org.uk/guidance/indevelopment/gid-ng10181).

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				The meta-analysis combined the data of all these studies to find out the initial orthotic effect. It found a statistically significant initial orthotic effect with an average increase in walking speed of 0.05 meters per second (m/s), or 7.1% The majority of studies reported a statistically significant positive ongoing orthotic effect. The meta-analysis combined the results of all eligible studies that used short walking tests. It revealed a statistically significant long-term orthotic effect with an average increase in walking speed of 0.08 m/s (11.3%) (Miller et al. 2017). FES improves quality of life A systematic review of the effects of FES on health-related quality of life in people with MS which included quantitative studies with QoL measures, was published in 2019 (Miller Renfrew et al. 2019). It found that quality of life improvements were reported in all but one of the included studies. Results reported in the studies suggest that FES can improve quality of health and related measures, including physical (such as fatigue) and psychological (such as self-esteem) outcomes. In 2015 study (Bulley et al. 2015), participants reported that FES reduced fatigue, improved their walking ability,	

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				fitness and physical activity, reduced trips and falls, and increased confidence and participation in daily activities. In another study (Renfrew et al. 2020), participants reported an improvement in walking ability, including a reduction in trips and in the worry relating to trips and falls when walking. This is important, since previous research shows that fear of falling is a big issue for people with MS. In a study of 1064 people with MS over the age of 45, 63% reported a fear of falling. Of those, 83% of participants said that they reduced their activities as a result of this fear (Peterson et al. 2007). It also reported reduced dependency on walking aids. A reduction in the mental effort of walking (similar to findings by Bulley et al. 2015) can reduce fatigue and enable people with foot drop to take part in social and daily activities with greater ease and comfort (Renfrew et al. 2020). Participants reported increased engagement in social, leisure and vocational activities that would have been a struggle before – such as shopping, gardening, accessing public transport etc. They also reported increased confidence, self-esteem, restored sense of personal autonomy, feeling more in control than before. Cost-effectiveness	

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				Since the 2009 FES guidance, three further cost-effectiveness studies have been published (Taylor et al. 2013, Juckes et al. 2019, Renfrew et al. 2019). Although the methodologies differ between studies, all three find FES to be a cost effective treatment option for foot drop.	
MS Society	Recommendations for research	General	General	We would like to see an additional research recommendation relating to the effect of MS on people from different ethnic backgrounds. There is some evidence that your likelihood of getting different types of MS, your response to certain DMTs, and the rate at which MS may cause disability all can vary depending on your ethnic background. MS clinical trials have predominantly involved white people with MS and disproportionately excluded people from ethnic minority backgrounds. This means that some estimates of DMT efficacy cannot be robustly applied to everyone. Much more research is needed to fully understand these disparities and the drivers for them. We need research to better understand the demographics of people with MS and the representativeness of past and ongoing studies, as well as specific studies that investigate the impact of MS and current treatment regimes in minority ethnic groups. See here and here for useful and up-to-date summaries on these topics. The lack of research in this area could also usefully be noted in the equality impact assessment for the guideline.	Thank you for your comment. The committee agree that this is an important area of research but disease modifying therapies were outside of the scope of this guideline.

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				The MS Society's research priorities are outlined here: https://www.mssociety.org.uk/sites/default/files/2020-11/MS-Society-Research-Strategy-2018-2022_0.pdf The James Lind Alliance priorities for MS research are outlined here: https://www.jla.nihr.ac.uk/priority-setting-partnerships/multiple-sclerosis/top-10-priorities/ The EDI action plan for MS Society research can be found here: mssociety.org.uk/sites/default/files/2021-12/EDI%20action%20plan%20for%20MS%20Society%20research%20Dec%202021.pdf	
MS Society	Research recommendations	042	General	We agree with the research recommendation made on the identification of clinical and cost-effective pharmacological interventions for the management of spasticity in adults with MS, including people receiving palliative care	Thank you for your comment.
Multiple Sclerosis Trust	Guideline	005	012	This recommendation should be amended such that people suspected of having MS should be referred to a consultant neurologist **with expertise in MS**. We would also recommend that people diagnosed with MS by general neurologists should be referred to an MS	Thank you for your comment. Recommendation 1.1.5 states that a person should be referred to a consultant neurologist or specialist under their supervision for diagnosis. The committee confirmed that in their clinical experience and opinion a neurologist does not necessarily have to be specialist in MS to make the

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				specialist neurologist to clarify disease type and activity and for access to disease modifying treatments.	diagnosis but the recommendation does not preclude their advice or a referral being made if appropriate.
Multiple Sclerosis Trust	Guideline	006 049	007 001	The guideline should reinstate the recommendation that people with suspected, but unconfirmed, MS should be offered information about support groups and national charities. Table 1 - This recommendation was included in the 2014 guideline and should also be retained in the 2022 guideline. People with suspected MS describe being in a state of limbo, are often distressed by living with unexplained symptoms and generally do not have contact with an MS team. They often face long delays before being seen by a consultant neurologist. The Committee states that "Providing information and support on MS without a confirmed diagnosis increases anxiety." Our experience is exactly the opposite – a diagnosis of suspected MS **without** access to information and support leads to increased anxiety. We are frequently contacted by people who have been given a diagnosis of suspected MS or Clinically Isolated Syndrome who are worried about on-going symptoms and what they can do to minimise the risk of developing confirmed MS. Support groups and national charities are well-placed to provide information and support.	Thank you for your comment. We have added that information should be provided to recommendation 1.1.7. The purpose of this recommendation is ensuring that people know who to contact if their symptoms change and so we have not specified information on support groups.

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Multiple Sclerosis Trust	Guideline	011	005 - 010	We welcome the addition of a single point of contact **with knowledge of MS services**. We welcome the additional health professionals added to the multidisciplinary team, however, a growing number of teams have established the role of disease modifying treatment coordinator and this role should be included in the list.	Thank you for your comment. This list is not exhaustive and the committee have provided a few examples.
Multiple Sclerosis Trust	Guideline	012	001	**Modifiable risk factors** There is now considerable evidence that early and effective treatment with disease modifying treatments reduces the risk of progression. See comment number 12 below.	Thank you for your comment.
Multiple Sclerosis Trust	Guideline	013	General	**Assessment and non-pharmacological management of fatigue** **1.5.3 Do not assume that fatigue is caused by MS.** This statement is incorrect and may give the false impression that fatigue reported by someone with MS is not be genuine. In these examples, fatigue <u>**is**</u> caused by MS – it is a consequence of living with MS. It would be better to note that fatigue may be caused directly by MS-related nerve damage (primary fatigue) or could be a consequence of living with MS, such as sleep problems, symptoms of MS, side effects of medicines etc (secondary fatigue). Each of these potential causes of	Thank you for your comment. The committee have modified recommendation 1.5.4 to refer to the fact that a person's fatigue is not always caused by MS. They confirmed that it is important to identify and manage all sources of fatigue and that the wording of the recommendation does not imply that the fatigue is not genuine.

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				MS-related fatigue should be considered and addressed where appropriate and then monitored for improvements in fatigue. We would agree that other health issues could be responsible for fatigue and should be ruled out by initial investigations. This applies to all symptoms that might cause problems for someone with MS; all symptoms should be thoroughly investigated and not assumed to have been caused by MS to ensure that appropriate treatment is offered.	
Multiple Sclerosis Trust	Guideline Evidence Review D	015	006 - 008	**Pharmacological management of fatigue** We are very concerned by the recommendation to offer modafinil and SSRIs as treatments for fatigue. The 2014 guideline makes a very clear statement that there is insufficient evidence to recommend either modafinil or paroxetine as treatments for MS-related fatigue and warns of potential harms. The quality of the new evidence presented in the draft guideline and evidence review does not justify a change to this recommendation. **Modafinil** As noted in this NICE Evidence Summary published in April 2013, the European Medicines Agency concluded that modafinil should be prescribed for narcolepsy alone https://www.nice.org.uk/advice/esuom9/chapter/Key-	Thank you for your comment. The committee acknowledge that there is only limited evidence of benefit for amantadine, modafinil and SSRIs (see committee discussion of the evidence in evidence review D. However, in their clinical experience and opinion some people do respond to these treatments and given the potential impact of fatigue on daily life they made a recommendation. In recommendation 1.5.12 we now refer to considering safety of the drugs. In recommendation 1.5.15 we now refer to monitoring and reviewing response to treatment. The guidance in the summary of product characteristics has now also been highlighted in the rationale and impact. The 2020 MHRA safety advice on modafinil (Provigil) is now referred to in recommendation 1.5.14 and rationale. Recommendation

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				points-from-the-evidence. This change to the indication was reached after a careful risk/benefit analysis of modafinil. **SSRIs** We are very concerned by the weak evidence used to support the recommendation to consider SSRIs as treatments for MS fatigue. In the three studies (Ehde, Cambron and Chataway), evidence is taken from secondary outcome measures; none of these studies were powered to measure the effect of the SSRIs on MS fatigue. Having carefully reviewed these studies, we do not accept that the data reported in these studies show clinically relevant changes. In all three studies, fatigue levels fluctuated considerably over the time course of the study; neither paroxetine nor fluoxetine showed a consistent effect on fatigue levels over the duration of the studies. In the case of paroxetine, evidence is drawn from a single study (Ehde 2008) which assessed paroxetine for the treatment of major depressive disorder in people with MS (n=42, 22 participants took paroxetine, 5 of the 22 (23%) were lost to follow-up). Not only is this a very small number of participants, but also the population (major depressive disorder) is not representative of people with MS in general. We do not believe that study results can	1.5.4 highlights the importance of recognising other causes of fatigue including anxiety and depression.

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				be extrapolated to support the recommendation. Furthermore, the study failed to find a significant effect of paroxetine on the primary outcome measure, depression. A Cochrane review[1] of this study was critical of the high number of people who were lost to follow-up or for whom outcome measurements were missing; they considered the methodology used to impute missing data could have a big influence on results. In the case of fluoxetine, evidence for clinical effectiveness is drawn from two studies (Cambron 2019 and Chataway 2020). In both cases, fluoxetine was assessed as a treatment for progressive MS; as noted above fatigue was measured as a secondary outcome and the studies not powered to assess effect on fatigue. Cambron 2019 (FLUOX-PMS study): the authors report that they did not find any difference between the two treatment groups (fluoxetine and placebo) for cognitive, depression or fatigue tests and concluded that fluoxetine had no effect on fatigue. Chataway 2020 (MS-SMART study): the appendix to the published paper reveals that 10.8% of those taking	

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[1] Koch MW, Glazenborg A, Uyttenboogaart M, Mostert J, De Keyser J. Pharmacologic treatment of depression in multiple sclerosis. Cochrane Database of Systematic Reviews 2011, Issue 2. Art. No.: CD007295. DOI: 10.1002/14651858.CD007295.pub2. Accessed 26 January 2022

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				fluoxetine were also taking unspecified anti-fatigue medication compared to 2.7% of the placebo group. This makes it very difficult, if not impossible, to draw conclusions about improvement in fatigue due to fluoxetine. The authors conclude that secondary outcomes accord with insufficient evidence of therapeutic effect. Given all these points, we are very surprised the committee has updated the recommendation to consider modafinil and SSRIs in addition to amantadine. At the least, the recommendation should note that modafinil can be considered where there is excessive daytime sleepiness and SSRIs considered where there is evidence that severe depression is a major contributor to fatigue; this will avoid inappropriate prescription of these treatments.	
Multiple Sclerosis Trust	Guideline Cost-utility analysis: Fampridine for the treatment	016 044	010 04.1	**Pharmacological management of mobility problems** The MS Trust is disappointed that the Committee has not recommended fampridine to treat mobility problems. While the Committee acknowledges that fampridine is clinically effective, it is not considered cost effective at list price. A cost-utility analysis has determined that fampridine would be cost effective at a price of £202.	Thank you for your comment. Thank you for reaching out to the MS community and highlighting the importance of this issue. The independent guideline committee acknowledged that it is a clinically effective treatment for some people, however it is not cost effective at the current price the NHS is expected to pay. The availability of treatments in Scotland and Wales is a matter for the devolved administrations. In these countries it is made available under a confidential patient access scheme that

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	of MS mobility			It is a frustration for all stakeholders that the process for developing NICE Guidelines does not provide for discussions with the manufacturer on prices. NICE has previously turned down an application to review fampridine through the Technology Appraisal route, which would have included an opportunity to review pricing. We urge NICE, NHS England and the manufacturer to find a way to resolve this. The Guideline Development Process provides very limited opportunity to hear from the people most affected – in this case people with MS. A relatively small improvement in walking ability can have a much greater perceived benefit for the person with MS, which is not captured by clinical measures such as time taken to walk 25 feet or quality of life measures such as EQ-5D. To illustrate the more intangible benefits that an improvement in walking can achieve, we have gathered the views of people currently taking fampridine, some through private prescriptions. Walking around the house, the garden, to the shops and in the office should be automatic and effortless and is something that we all take for granted. The value we place on our mobility is reflected by the fact that walking problems and consequent loss of independence is one of the greatest fears of people diagnosed with MS.	provides the drug at a lower cost. Patient access schemes are negotiated by the relevant NHS commissioning body and the company (manufacturer). In England this process is led by NHS England.

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				Walking problems can have a major impact on all aspects of work, social and family life. They often compound other MS symptoms such as increased fatigue due to the effort of walking, bladder and bowel incontinence because it becomes difficult to reach the toilet in time, increased risk of falls leading to fractures and further complications, general weakness and social isolation through becoming housebound. Spending more time sitting down leads to deconditioning. Increasing mobility problems lead to greater dependence on informal carers, straining relationships and resulting in poorer quality of life and economic burden not only for the individual, but also for their family, friends, work colleagues and wider society. Someone with walking problems will need housing adaptations and equipment such as walking frames or wheelchairs. As well as the cost of providing these, they can also have a big impact on family life as they make the house feel less like a home, may be difficult to accommodate when floor space is limited and affect how other members of the household perceive the person with MS. We asked people with MS how the loss of mobility has affected their lives. These quotes demonstrate how devastating this can be:	

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				"As my mobility has reduced I have become a bit more depressed. I finally, but reluctantly, had to give up work as I could no longer function well enough to continue. This has upset me a great deal." "I know that if I didn't pay for regular physiotherapy my mobility would be a lot worse." "I miss the social activities walking with friends, gardening with my husband etc." "I used to like walking, swimming, shopping etc but all these have become very difficult." "I have had to give up activities like going to the gym where I used to meet people. Accessing restaurants, cinema, theatre etc are now more difficult because of mobility issues and there is a tendency to go less often to these venues and socialise. Consequently I don't see much of certain friends anymore." "Very limited mobility, no longer drive. Can't be a proper nanny and look after my grandson." "Wheelchair access is very poor when out anywhere. Can no longer be spontaneous, everything now is like a military operation - going out, going on holiday, going shopping, the hairdresser..... Every day is hard work." Fampridine is currently the only licensed medicine for mobility problems in people with MS. There are a number of causes for walking problems and not all will be resolved	

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				by fampridine. A two-to-four-week trial of fampridine can identify responders. Any improvement in mobility will bring many benefits to the individual as well as to their family and carers. Improvement in mobility helps people stay engaged in the activities which matter to them which will have a positive effect on the person and on their relationships with family and carers. Increased independence and the ability to remain in employment, both for the individual and informal carers, reduces the financial burden of MS and improves the psychological and emotional impact that MS can have on relationships. Improved mobility enhances participation in family commitments, day-to-day activities and social life. It allows people to be more physically active, keep exercising and spend less time sitting, resulting in maintained muscle tone and flexibility of joints. All of these benefits contribute to improved quality of life and mental well-being. In the words of people with MS who have taken fampridine:	

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				Independence "Not being able to cut my food is a horrible indication of what the future might hold. Thank goodness for fampridine." "I'm only just walking, but only just walking is better than sitting in a wheelchair. In a wheelchair I would be dependent on others. With fampridine I can get out and do stuff, I managed to go to hospital on my own, I can drive using hand controls." "I've had MS for 40 years, my brain is still very active, I work full-time. Without fampridine I couldn't walk out to car, wouldn't be able to drive, I would lose a lot of independence." "I live on my own and before I started taking fampridine I was very near the point of not being able to cope on my own anymore." "For me it has helped movement in all parts of my body not just my legs giving back my independence and confidence. My MS affects my left side more than my right. Everything and I mean everything was incredibly difficult and slow before taking fampridine. I was constantly having to call upon my neighbours to help me out as I was always getting into difficulties. The joy of once again being able to walk a few metres to the kitchen and do some washing up, some cooking or put things in the dishwasher."	

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				"Fampridine has given me independence, go to MS centre quite a lot, can do things on my own, can meet friend at café, can drive, walking to car, getting into car." **Improvement in mobility results in improvements in activities of daily living** "Before I started on Fampridine I used one stick as my balance was poor. Within two weeks of starting I was walking through the kitchen holding a cup of coffee in each hand." "Huge improvement in balance, stopped having to walk with stick." "If I forget to take my evening tablet I can't get out of bed in the morning, I can't walk without moving my legs with my hands, I can't stand in the shower, I don't have enough strength in my hands to cut my food." "I've had a special procedure so that I self-catheterise through my tummy button, with fampridine I can stand up to empty my bladder, it's very difficult to do it sitting down." "Fampridine hasn't been a miracle, I'm still using sticks but it's taken away some of the heaviness, so my feet aren't dragging." "Whole body feels better, more movement in arms helps enormously, feel able to move better, getting up from chair, do more around house." "It's all of those little bits like getting in out of bed, washing, in and out of bathroom, loo."	

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				"Fampridine has been a lifeline. I can do housework, it still takes some time but I can do it, I don't have to rely no others." "I feel safer coming up and down stairs, my balance is better and feel more confidence with movement." **Staying engaged in activities** "I've been on Fampyra for a year now. Fampyra is amazing. It helps me walk, swim, get up the stairs and much more." "I came off fampridine for two weeks in 2019. Going back onto it showed an astounding doubling of walking speed." "I couldn't have answered the door just now [doorbell rang during our conversation], I can go upstairs to get changed and take the dog out for a walk – it's just normal things, nothing special, but I can do them." "When I'm planning stuff, I don't have to wait and see how I will be tomorrow." "I was on fampridine for 6 years, it kept me in work. When I was made redundant, I couldn't afford it anymore, now I have to use a wheelchair, an Oswestry standing frame, I'm getting a electric wheelchair. Had I stayed on fampridine, I would still be walking with a struggle, but now I'm a burden on the NHS." "Fampridine means I can get into the passenger seat of the car. Without fampridine, it's very hard, if not impossible."	

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				"With fampridine I can get out to car, it's easier to get in and out of car, my legs wouldn't swing into car and I needed a lot of help, I still need a bit of help but it's much easier." **Improved symptoms** "Less fatigue – MS nurses were surprised when I told them of this benefit. Maybe it's because signals from my brain don't have to take such a long route to get to my muscles." "Fatigue is so much better." "Bladder control is better." "Improves strength in my hands so I can cut up food." "Pain doesn't feel so severe, feels like I can deal with it better." "Legs don't drag, so has lessened fatigue." "I had relapsing remitting MS which progressed to secondary quite rapidly, but since starting fampridine my EDSS has stayed at 6.5, something my neurologist believed wouldn't be possible." "My arms and hands have improved." "Fampridine is very good for my hands especially my right hand which is curling into a fist. It means I can stretch my hand out and move my finger quite well. If I forget to take fampridine I can't open my hand." "I have noticed other improvements generally ie arms, hands and brain improvement. I also had several people	

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				say I was far more alert that before as well as my walking improvement." "Before starting fampridine, I was stuck in a chair and developed a deep vein thrombosis in my upper thigh, had to stay in hospital. It's taken a while to get my strength back and for swelling in my legs to go down. Swansea team suggested fampridine, they said my walking speed needed to improve by 25% or I would not be prescribed it. I knew my walking was better after 5-6 days, but at the second walking test, my speed had improved by 50%, apparently I'm a super-responder." "I'm brighter, more alert, brain working better, generally feel healthier, other people have commented on improvement in cognition, family can see it as well." "It feels like fampridine has pushed my MS back by about 3 years." "It helps mentally – I feel more switched on, everything works better, I have gained several years on MS." **Physical activity** "Thanks to fampridine I can do press-ups every morning, this makes a big difference, helps my core muscles, my heart is fitter. Without fampridine I wouldn't be exercising." "I can stand, so I can do yoga. Fampridine has improved my all-round fitness."	

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				"Rain or shine, every day I drive to the local beach for a mile's walk with my rollator. It's great for my mental health." **Family relationships** "Fampridine allows me to allow my family to get on with life, so it doesn't just help me, it helps my family too." "With fampridine my wife can go out to work. Without fampridine, she would need to be at home and caring for me." "I can be a dad with kids. Taking fampridine has massively improved my relationship with my youngest daughter, I'm not shouting at her because I'm frustrated. If she's in the kitchen doing her homework and calls for help, I can walk into the kitchen and help her. If she's in the back garden I can join her and her mates, I'm just a dad, that's a huge thing for me. I can go and watch her play rugby on a Saturday. Her relationship was all Mum, now it's Dad as well. My middle daughter is getting married next weekend – I'll be able to walk her down the aisle, rather than use a buggy." "Having been on fampridine for 15 months, I am more physically capable, with my self-confidence increasing as a result. Overall, I am a more content and relaxed person and more than ever I enjoy visits from my friends and family as visitors, rather than as care helpers and worrying about over burdening them."	

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				"My wife has better quality of life, helps with her mental state." **Psychological benefits - self-esteem and motivation** "When I was diagnosed, I had been a paratrooper for 27 years old, getting MS was a shock. My walking deteriorated quickest, fampridine has been a game-changer, it's given me back my individuality, put me back in control. In my head I know I have a disability, but fampridine means I can do something about it, it's given me back my masculinity." "MS destroys your mind. Before it was 'why me?' Now I just get on with it." "I was presented with an award at Buckingham Palace, I managed to walk up to receive it. I really wanted to do this; it was my trigger for starting fampridine." "Fampridine has transformed my life by making everyday activities less stressful leading to improved mental health." "I'm more relaxed and content, when I feel better everyone else does, neighbours particularly see difference since starting." "Quality of life and mental health is better as well I feel mentally more with it." **Side effects** Few people reported side effects.	

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				"I have developed a rash, possibly caused by fampridine, waiting to hear from consultant. I stopped taking fampridine, my walking speed has dropped again." "It affects my sleep, I wake up early and can't get back to sleep, this has improved a bit, but is the only thing I've noticed since starting." Given the impact of walking problems on daily activities and the lack of alternative treatments, we would expect most people to view these side effects as an acceptable risk. However, there will always be individual preferences about benefit and risk balance and practicalities linked to daily routines. **Dosing schedule** Fampridine must be taken on an empty stomach one tablet twice a day and tablets must be taken 12 hours apart. People find the best times for their morning and evening doses which fit around their daily routines, often using mobile phones to remind them to take next dose. Most people noticed that their walking deteriorated rapidly if they forgot a dose or if they had to stop fampridine.	
Multiple Sclerosis Trust	Guideline	017	002	**Non-pharmacological management of mobility problems** Non-pharmacological management of mobility problems should be updated to include a link to	Thank you for your comment. The non-pharmacological management of mobility was not identified by the surveillance review as having new evidence and was not within the scope of this update. We have added a cross-

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				Functional electrical stimulation for foot drop of central neurological origin NICE Interventional procedure guidance 278 (2009) https://www.nice.org.uk/guidance/ipg278.	reference to the NICE IPG on functional electrical stimulation https://www.nice.org.uk/guidance/ipg278 . Functional electrical stimulation is being considered in the new guideline on rehabilitation for chronic neurological conditions including acquired brain injury (https://www.nice.org.uk/guidance/indevelopment/gid-ng10181).
Multiple Sclerosis Trust	Guideline	019	018	THC:CBD spray is unlikely to be recognised as Sativex by a significant proportion of users of the guideline, particularly people affected by MS. The reference to THC:CBD spray should be qualified with the inclusion of the marketed name ie Sativex, as it is in the NICE guideline on cannabis-based medicinal products. This recommendation should read: 1.5.28 For guidance on THC:CBD spray [Sativex] for treating spasticity see NICE's guideline on cannabis-based medicinal products. We would also welcome more detail in the guideline on Sativex's position in the spasticity treatment pathway.	Thank you for your comment. We have cross-referred to the name of the existing NICE guidance which does not include the trade name Sativex. The recommendations on spasticity in the guideline on cannabis-based medicinal products do not use the name Sativex. Cannabis-based products were outside of the scope of this guideline and we therefore did not include these in the review protocol for this question (appendix A evidence review F).
Multiple Sclerosis Trust	Guideline	022	001	**Ataxia and tremor** Non-pharmacological management	Thank you for your comment. The scope of this guideline included only the pharmacological management of ataxia and tremor. The committee are therefore unable to make recommendations on referral for non-pharmacological

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				We recognise that no specific therapy intervention could be recommended by the Committee for ataxia and tremor. However, this devalues the significant contribution made by physiotherapists and occupational therapists to management of these very disabling symptoms. Without therapist interventions and management, there will be a significant increase in the care and caregiver burden, particularly in relation to activities of daily living. We would like: • a general recommendation that people with MS experiencing ataxia are referred to physiotherapy services for assessment and treatment. Without this recommendation there is a risk that commissioners will not fund services for this small but very disabled patient group. • a general recommendation that people with MS who have tremor are referred to occupational therapy for assessment for treatment with orthoses; there may not be much evidence for these in any neurological condition, but they are a first line of treatment and without a recommendation it is likely that people with MS and tremor in primary care will not be supported to control their tremor • a signpost to the relevant NICE Guidance for deep brain stimulation for treatment of tremor.	management. We have added a cross-reference to the NICE guidance for deep brain stimulation as suggested.

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Multiple Sclerosis Trust	Guideline	027	017	**Other treatments** **Disease modifying treatments** We welcome the inclusion of links to technology appraisals for disease modifying treatments (DMTs) in the draft guideline. However, the committee has missed an opportunity to provide general guidance on treatment pathways for DMTs which is not provided in technology appraisals. At the MS Guideline workshop (12 December 2019) there was a strong view from all discussion groups that the guideline should include recommendations for a general pathway for DMT treatment, however, this feedback has been completely disregarded in drawing up the draft scope and subsequently the draft guideline. Technology appraisals cover each of the DMTs approved for relapsing remitting, primary progressive and secondary progressive MS. The treatments are listed in the NICE pathway for MS. However, none of these documents give any guidance on when or how services should initiate and manage treatment with DMTs. The 2014 guideline makes very limited reference to DMTs. This makes it of limited value to commissioners and	Thank you for your comment. The committee recognised the importance of disease modifying therapies but this is outside of the scope of this guideline because the NICE technology appraisals on DMTs which we cross refer to. We are also aware of the NHS England guidance on this referred to in your later comment.

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				providers of services as there is no recognition of this vital aspect of MS services. Furthermore, the public version of the current guideline makes no reference to DMTs at all. As a result, people affected by MS are given no indication of what they can expect from MS services, in terms of timescales for initial discussions about their treatment options and then for starting a DMT or a review of their current treatment. This contrasts with other NICE guidelines, such as those for rheumatoid arthritis and Parkinson's disease, which give significantly more detail of treatment options, recommend timescales for initial discussions and for treatment reviews. The value of NICE guidance has been documented recently in the NICE Impact report on arthritis, noting, for example, that between 2019 and 2020, the number of people starting a disease modifying antirheumatic drug withing 6 weeks of referral increased form 54% to 64% https://www.nice.org.uk/about/what-we-do/into-practice/measuring-the-use-of-nice-guidance/impact-of-our-guidance/nice-impact-arthritis. The introduction to the draft scope acknowledged the importance of initiating treatment early in the course of MS. Starting people on treatments and monitoring of DMTs represent a very significant proportion of MS teams'	

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				workload. A lack of guidance on the treatment pathway for DMTs is likely to have contributed to considerable variance in DMT prescribing in England and Wales. **We consider it vital that the guideline provides at least basic recommendations for the treatment pathway. There is considerable published evidence to inform these recommendations.**	
Multiple Sclerosis Trust	Guideline	General	General	We acknowledge the enormous amount of work that has gone into preparing the guideline both from the Committee and from NICE members of staff. We were pleased that the Committee drew on a wealth of experience, including people who have MS or have MS in the family, and full representation of the multidisciplinary team. Overall, we are pleased to see extra detail added to recommendations throughout the guideline. We welcome the additional sections on information and support for people planning to have children and for people with advanced MS. We also welcome more extensive links to related NICE guidelines and Technology Appraisals.	Thank you for your comment.

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NHS England and NHS Improvement	Guideline	004 - 006	General	Overall follows good practice for diagnosis and referral for possible MS and: • 1.1.3 Do not routinely suspect MS if a person's main symptoms are… or vague sensory phenomena, unless they have a history or evidence of focal neurological symptoms or signs. [2022]. This is well worded with the addition of "not routinely" as this group are sometimes referred and sometimes do have MS. The recommendation on performing blood tests to exclude alternative diagnosis and instead highlighted that these need to be tailored to the individual and their presenting symptoms, makes clinical sense and would be expected clinical practice. But having looked at the previous recommendations I do wonder if some that would be missed and have to be requested by the neurologist. They will have a blood test, is there any harm in advising ones the neurologist would expect? Avoids duplication, improves the patient journey. The diagnosis is outside primary care and by a consultant neurologist as expected. The above are generally accepted and in practice currently so there would be no additional service provision or resource implications.	Thank you for your comment. The committee confirmed that the blood tests need to be tailored to the individual.
NHS England and NHS Improvement	Guideline	006 - 009	General	The provision of support and information both written and oral at the time of diagnosis is as expected. I appreciate that the information list was not intended to be	Thank you for your comment. We have added the detail on sending a letter to the GP to the diagnostic criteria committee discussion. The timing of reviews should be

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				comprehensive but should a copy of the clinic letter detailing the discussion and diagnosis be an expectation for the patient? It would be helpful if the letter to the GP could be both sent quickly (as often the patient will contact the GP shortly after the diagnosis) and include the contact details and resources that the patient has been signposted to, including legal requirements and rights as mentioned. A review six weeks after diagnosis makes sense, but should there be another after six months before the annual reviews? "Advise them to ask their healthcare professional for a review if it has not taken place. [2022]", should this not be their single point of contact as mentioned below? (i.e not their GP if possible) "If a person with MS is thinking about or planning pregnancy, or is pregnant, offer the opportunity to talk with a healthcare professional with knowledge of MS to answer any questions they have." And it would be helpful to have that as a letter to the GP to enable appropriate prescribing of supplements and understanding of potential risks and understanding some misconceptions possibly held by the patient and GP.	tailored to the individual and recommendation 1.2.6 ensures that people know who to contact if their symptoms change. Who is appropriate to conduct the comprehensive review will vary from individual to individual and we have therefore not specified who should conduct it. In section 1.2 we signpost to the NICE guideline on patient experience which makes recommendations on health professionals communicating with each other.
NHS England and NHS Improvement	Guideline	011	General	"Offer the person with MS an appropriate single point of contact with knowledge of MS services to coordinate care and help them access services. [2022]"	Thank you for your comment. The committee expect a referral to be made to the healthcare professional most appropriate to meet the needs of the person with MS which may include those working in primary care.

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				Essential from a primary care perspective and usually fulfilled by a dedicated MS nurse who can advise on urgent treatment of acute exacerbations and sooner OPD appointments for problems less urgent but need an MDT review. Impact is huge when this works and equally detrimental when it doesn't so requires a robust service. It should not have a significant resource impact as most have a system in place but it needs to be resilient. Referrals from the MDT should be within the team and not passed to primary care to refer on as this sometimes means the appropriate service is not appropriate for the specific needs of the patient with MS and delays referral.	Recommendation 1.3.1 refers to a single point of contact with knowledge of MS to support this.
NHS England and NHS Improvement	Guideline	013	General	Assessment for fatigue could be highlighted for contacts in primary care and that they should be assessed, investigated, and treated as you would expect in a person without MS. If considered MS related then advice can be sought through their single point of contact If a person with MS wishes to try a medicine for fatigue then it would be helpful for the communication to the GP to be clear that the medication is off label and have clear instructions on dosing, side-effects and follow up (usual practice anyway from neurologists on the whole) as these are medications that they will be unfamiliar with. For the treatment of spasticity the recommendations could be co-ordinated though the MS team to the primary care team to manage with their advice? Most are comfortable	Thank you for your comment. Recommendation 1.6.3 on a comprehensive review which includes fatigue may be carried out by a GP. If a pharmacological intervention is prescribed by a specialist the committee would expect that clear instructions are provided to the GP on dosing, side effects and follow up. The committee agree primary care may offer the interventions in recommendation 1.5.25 and 1.5.26. This guideline also cross-refers to the NICE guideline on medicines optimisation which makes recommendation on medicines-related communication systems when patients move from one care setting to another.

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				with gabapentin prescribing even though it would be off-label	
NHS England and NHS Improvement	Guideline	022	General	Comprehensive review outputs would be useful to have in primary care to avoid duplication and help organise monitoring that can be done in primary care. From a practical perspective is it worth a look at whether all patients with MS have had an annual review? Suspect there may be some with a diagnosis pre-dating this who may not be benefiting from this care.	Thank you for your comment. The recommendations on comprehensive review assume that the results would be communicated to relevant health professionals. In section 1.2 we refer to the NICE guideline on patient experience in adult NHS services which includes recommendation on communicating information to other health professionals also the recommendation. We also cross-refer to the NICE guideline on medicine optimisation which makes recommendations on medicines-related communication systems when patients move from one care setting to another. Recommendation 1.2.4 advises people to ask their healthcare professional (including non-specialists) for a review if it has not taken place.
NHS England and NHS Improvement	Guideline	025	General	Ruling out infection needs to be co-ordinated through primary care and some may not be aware of this as a requirement before diagnosing a relapse. This can cause confusion as ruling out infection can mean different things to different people. If completely asymptomatic do they still need an examination and/or a urine dipstix or MSE? Should they have blood tests eg CRP? This may require a further assessment if the initial exacerbation is based on symptoms via a non-FTF consultation. Treating relapses and specifically whether to treat with steroids has usually been via the MS nurse for the patient.	Thank you for your comment. These recommendations were not updated by this guideline update.

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				They advise accordingly but accessibility can cause delays and this may lead to primary care treating a relapse without that advice. 14 days is too long, it should be within a week given the impact exacerbations can have on a persons life. There is a sense that the sooner you treat the better the outcome (which adds to the above pressure) but not sure that has been borne out in studies? (maybe a research topic?) Not giving a supply of steroids to the patient to self administer for future relapses is sensible but the above scenario isn't far off that type of management anyway.	
NHS England and NHS Improvement	Research recommendations	028	General	Research into co-ordination of care would be helpful to confirm their value. As you may have guessed my frontline experience is that they are invaluable when available.	Thank you for your comment. The committee has made a research recommendation on the clinical and cost effectiveness of coordination of care.
Novartis Pharmaceuticals UK Limited	Guideline	005	012 - 014	This is a positive addition to the guidelines encouraging referral to a Neurologist upon suspecting Multiple Sclerosis	Thank you for your comment
Novartis Pharmaceuticals UK Limited	Guideline	005	029	The guidelines have added new guidance on the diagnosis of primary progressive multiple sclerosis which is a welcome addition. However, guidance on diagnosing secondary multiple sclerosis is missing. The guidelines should set out to provide clear guidance on diagnosing secondary progressive multiple sclerosis, in addition to clarity on referral and management pathways for those with relapsing remitting multiple sclerosis who progress to a secondary progressive form of the disease	Thank you for your comment. The purpose of this review was to update the recommendations in accordance with the revised McDonald criteria (2017) which do not cover secondary progressive MS. Recommendations 1.2.7 and 1.6.3 cover progression of MS.

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Novartis Pharmaceuticals UK Limited	Guideline	006	001 - 005	This is positive addition to the guidelines ensuring a review is planned if Multiple Sclerosis is suspected.	Thank you for your comment
Novartis Pharmaceuticals UK Limited	Guideline	008	018	The guidelines point towards providing information if a person's Multiple Sclerosis becomes more advanced. Health care professionals are hesitant to provide a secondary multiple sclerosis diagnosis (Duddy et al, MSARD 55, 2021, 103174). The NICE guidelines should set out clear guidance on how early information on progression should be provided to the patients.	Thank you for your comment. How early information should be provided was not included in the evidence review (see appendix A evidence review A) and varies according to individual circumstances to be included in a recommendation. The committee have added a recommendation (1.2.7) to raise awareness of discussing advance care planning and power of attorney.
Novartis Pharmaceuticals UK Limited	Guideline	010	006	The guidelines should state that information on advanced Multiple Sclerosis should be given before a patient reaches this stage. The guidelines refer to advanced Multiple Sclerosis but should clearly refer to Secondary Progressive Multiple Sclerosis where appropriate to avoid confusion. Disease modifying therapies are reimbursed for relapsing remitting multiple sclerosis, secondary progressive multiple sclerosis, or primary progressive multiple sclerosis, and therefore the guidelines should refer to these terms	Thank you for your comment. Recommendation 1.2.9 refers to providing ongoing information and support tailored to the person's changing need for example if their MS is changing to a more progressive phase or as their MS becomes more advanced. The term advance MS is used to refer to any progression of MS and the recommendations where this is used are not specific to types of MS.
Novartis Pharmaceuticals UK Limited	Guideline	011	004 - 006	The guidelines should encourage care closer to the home for people with multiple sclerosis. This would reduce travel demands when they are already facing challenges with mobility and will free up resources in the specialist	Thank you for your comment. Where care is provided should be discussed with the person with MS, their families and carers and would vary depending on individual circumstances. Recommendation 1.3.2 states

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				centres. There should be fast and efficient access to a multi-disciplinary team to enable access to high efficacy treatments without delay due to restricted capacity of multidisciplinary teams.	that care for MS should be by a coordinated multidisciplinary approach.
Royal College of Nursing	Guideline	General	General	We do not have any comments to add on this consultation. Thank you for the opportunity to contribute.	Thank you for your comment
Royal College of Occupational Therapists	Guideline	010	011	Highlight to increase awareness, in relation to supporting employment, that Allied Health Professionals are able to complete an AHP Health and Work Report.	Thank you for your committee. This has been added to the committee discussion of the evidence in evidence review A
Royal College of Occupational Therapists	Guideline	013 & 036	003 & 023	Suggested rewording: 'Ask people with MS if they are experiencing fatigue, sudden tiredness or a change in their energy levels affecting their daily living.' A broader use of accessible language may assist people to identify a range of symptoms affecting participation in activities amenable to intervention.	Thank you for your comment. We have incorporated your suggestion in recommendation 1.5.3
Royal College of Occupational Therapists	Guideline	013	004	Consider changing: 'Do not assume that fatigue is caused by MS'. Due to the multifaceted nature of MS fatigue, difficult to determine if MS fatigue is/is not present, even if other causes of fatigue are clearly present. Suggested rewording: 'Assess for potential other causes or contributing factors of fatigue and manage these or refer the person for management, if indicated.'	Thank you for your comment. We now highlight that fatigue may not always be related to in recommendation 1.5.4.
Royal College of Occupational Therapists	Guideline	013	016 - 023	The recommendations for the content of a personalised discussion about fatigue are important considerations, however, the guideline needs to be explicit that a referral could (or should) be made to an occupational therapist.	Thank you for your comment. The role of occupational therapists is acknowledged in the committee discussion of the evidence in evidence review C. The interventions in the evidence used to support this recommendation

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				The points listed would be included in a holistic assessment by an occupational therapist and compliment the skills used regularly by the profession. Occupational therapists often have the most involvement in the assessment and intervention of fatigue including group management programmes when compared to the rest of the multidisciplinary team. Also, a specific health professional is named in the mobility and cognitive recommendations and this should also be considered for fatigue.	were provided by a number of different health professionals and the committee were therefore unable to be specific.
Royal College of Occupational Therapists	Guideline	013	017	Additional suggestions: • Advice on keeping a fatigue diary, to record activities and self-rated fatigue scores at regular intervals across the day. • Consider referring people with MS and persistent fatigue to an occupational therapist* and/or fatigue management programme according to the person's needs. • Signpost to employment rights and consider referring to vocational rehabilitation service should fatigue be interfering with the individual's employment (and as comment (1), highlight AHP Health and Work Report to support remaining in employment). *neurological occupational therapists can provide tailored fatigue management for individuals with MS (or run	Thank you for your comment. We have added using a fatigue management diary to the committee's discussion of the evidence in evidence review C. It has not been explicitly mentioned in the recommendations but may be used to inform the discussion referred to in 1.5.6. Recommendation 1.6.3 refer to employment and the committee have added for example vocational support/rehabilitation.

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				FACETS group fatigue management programmes, depending on service remit) *social services occupational therapist can undertake environmental assessment and suggest adaptations and/or equipment to improve energy efficiency	
Royal College of Occupational Therapists	Guideline	017	017	Add: 'a deterioration in hand function with typical activities'	Thank you for your comment. The committee has incorporated your suggestion into recommendation 1.5.24.
Royal College of Occupational Therapists	Guideline	017	024	Add somewhere to promote self-management: 'educate the person with MS (and carers where relevant) to prevent / manage these potentially contributing factors to spasticity'	Thank you for your comment. The committee has incorporated your suggestion into recommendation 1.5.23
Royal College of Occupational Therapists	Guideline	021	003	Highlight potential of cognitive impairment (executive functioning) on mental capacity to make decisions, which may not be initially evident without a thorough assessment.	Thank you for your comment. We now refer to the NICE guideline on decision-making and mental capacity in section 1.2.
Royal College of Occupational Therapists	Guideline	033 & 035	010 & 005	The guidelines can be useful to prompt the minimum standards of a comprehensive review, particularly for non-specialists. There must be careful consideration of what aspects to include and remove as cannot be assumed that the breadth and depth of expertise required is available across systems.	Thank you for your comment.
Royal College of Occupational Therapists	Guideline	035	001	Consider advocating development of services for people with MS (and carers where relevant) to be able to self-refer to services to address their needs	Thank you for your comment. The recommendation supported by this rationale does not preclude a person or carers self-referring.

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Salford Royal NHS Foundation Trust	Evidence review A	020	040 - 041	Feel that these statements need more context rather than blanket statements. Gives no indication as to what medication, so this needs quantifying. Was it high efficacy medication and was the advice given on what was known about the medication at the time and the risks of continuing a pregnancy outweighed the benefits based on the best knowledge available at the time? For the final document this needs to be clearer for none health care professionals working in MS.	Thank you for your comment. These statements summarise the themes identified in the studies. Unfortunately, the level of detail you request was not reported.
Salford Royal NHS Foundation Trust	Evidence review A	General	General	Agree with the overall statements however, could the structure of the groups of people with MS be more logical? Starting with people with CIS, then pregnancy then palliative then families & carers rather than starting with palliative? This reflects the usual disease trajectory but pleased that specific reference is made to people with MS who require palliative care.	Thank you for your suggestion. This has been changed accordingly.
Salford Royal NHS Foundation Trust	Evidence Review B	035 - 036	049 - 003	You have described the current situation of most MS nurses' day to day practice. Due to the lack of recognition of the value of MS nurse specialists in the previous guidance, the subsequent lack of job security and funding, has led to most having to become a "jack of all trades" and undertake a plethora of none specialist tasks for the best interests of the patient, to ensure they can navigate the care system. Utilising specialist personnel this way not	Thank you for your comment. A recommendation specifically mentioning MS nurses could not be made as no relevant health economic evaluation studies comparing interventions to improve coordination of care were included in the evidence review. Several studies were identified that reported on the value of the MS specialist nurse, however, none of these studies met the criteria for assessment of applicability or methodology as

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				only undermines their value but also does not allow for true evaluation of the role as you have highlighted.	they were not economic evaluations and/or did not include a comparator. The committee has made a research recommendation (see appendix K) so that evidence may be available if this guideline is considered for update. Recommendation 1.3.1 on coordination of care does not specify which health care professionals should do this and in the experience of the committee it could be a number of different people.
Salford Royal NHS Foundation Trust	Evidence Review B	General	General	Again, disappointing that the extensive work carried out by the MS Trust with MS specialist nurses and MS specialist allied health care professionals has not been felt good enough to be taken as evidence. It is noted that on other sections under review (E or example), the experiences of the panel have been considered and these experiences, and ultimately their impact, have shaped the recommendations for that section. Why couldn't the same principles be applied here? Plus in Evidence review E, a positive decision was made by the panel despite "low quality evidence", so the panel could have advocated for the specialist nurse given available evidence examined. You have consistently referenced patients experiences of point of contact with a MS nurse throughout the subthemes (mostly positive), however, by failing to endorse the importance of the role we are concerned that the implication of this will continue to see the eroding of the role and loss of specialist nurse input to more generic	Thank you for your comment. The experience and opinion of the guideline committee can be used to inform recommendations but if there is a substantial resource impact, as is the case with the 'interventions' covered by this review, then there needs to be evidence of cost effectiveness. Due to a lack of available evidence on the clinical and cost effectiveness of the MS nurse role which met the evidence review protocol criteria (see appendix A evidence review B) and from the call for evidence the committee were unable to recommend an MS nurse. No relevant health economic evaluation studies comparing interventions to improve coordination of care were included in the evidence review. Several studies were identified that reported on the value of the MS specialist nurse, however, none of these studies met the criteria for assessment of applicability or methodology as they were not economic evaluations and/or did not include a comparator. Due to lack of clinical data it was not possible to undertake any further health economic

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				and a continued lack of willingness of management to invest in specialist roles. This will impact on the consultant neurologist's role at a time when follow up of people with long term conditions is being encouraged to be undertaken by a healthcare professional with expert knowledge in a disease area.	analyses. The committee has made a research recommendation (see appendix K) so that evidence may be available if this guideline is considered for update.
Salford Royal NHS Foundation Trust	Evidence Review E	049	008 - 020	Whilst the "consider" recommendation for modafinil is welcome as another treatment option for fatigue, the issue of who would be prescribing this needs to be determined and recommendations made re the prescribing to reduce the impact that this will have on secondary care. Also, the responsibility re the vigilance of the drug once started as per SmPC, needs to eb stated.	Thank you for your comment. The committee highlighted that modafinil is typically prescribed in secondary care but in the absence of evidence specifics on who this should be could not be provided. We have added that monitoring and re-evaluation of long-term use should be carried out (recommendation 1.5.15) to the committee's discussion of the evidence in evidence review D.
Salford Royal NHS Foundation Trust	Evidence review H	232	010 - 011	Whilst this would have an impact on the current set up of most clinical practice/ settings, this is a fundamental requirement of a comprehensive review. The positive recommendation of this will allow for service to try to restructure to incorporate this, and determine the best person to do this within individual teams	Thank you for your comment
Sanofi	Guideline	006	007	Sanofi supports calls from MS Trust for clarity around how soon a newly diagnosed MS patient should meet with their specialist.	Thank you for your comment. Recommendation 1.2.3 specifies within 6 weeks
Sanofi	Guideline	023	009	We agree that there are additional important elements when assessing MS disease course. However, "evidence	Thank you for your comment. An evidence review was not conducted as part of this guideline and therefore only

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				of progression" and "evidence of active disease" should be elaborated on further to make it clear that relapse rates alone are not a sufficient means of assessing disease progression.	minor changes could be made https://www.nice.org.uk/process/pmg20/chapter/updating-guideline-recommendations#refreshing-the-guideline-recommendations . We are therefore unable to specify how disease progression should be assessed.
Sanofi	Guideline	028	022	As per the findings from evidence review B, the recommendation for further research into clinical and cost-effectiveness of care should extend to social care as well as healthcare professionals.	Thank you for your comment. The evidence review for this question (appendix A evidence review B) did not include social care and the committee are therefore unable to include in the research recommendation. Research recommendations can only include interventions that were part of the evidence review.
Sanofi	Guideline	General	General	Sanofi supports prioritisation of the patient voice in shaping these MS guidelines.	Thank you for your comment
UK Multiple Sclerosis Specialist Nurses Association (UKMSSNA)	Guideline	006	021	The UKMSSNA agree with point but would like to add that support around diagnosis in terms of verbal and written material should be given by not just the consultant Neurologist but MS nurses or MS practitioners who will be involved in the patients care.	Thank you for your comment. This recommendation is specific to when a diagnosis is made and it is therefore aimed at consultant neurologists. The recommendations in the section on ongoing information and support are aimed at all relevant health professionals
UK Multiple Sclerosis Specialist Nurses Association (UKMSSNA)	Guideline	007	020	1.2.4 and 1.2.9 and 1.2.10 - The UKMSSNA agrees with these statements but would like to add that the patient should be made aware of basic information around their care, in terms of who is involved in their care, when they can expect a review, who is their point of contact if they have a question or an issue with their MS and who to contact if they are not happy with their care.	Thank you for your comment. Recommendation 1.2.6 ensures that people with MS and their family members or carers has a point of contact if their symptoms change and 1.3.1 recommends a single point of contact to coordinate care or access services. Recommendation 1.2.4 advises people to ask their healthcare professional (which could be a GP) for a review if it has not taken

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				The UKMSSNA feels strongly that any health or social care professionals involved in a MS patient's care at any point of the patient's care pathway has a duty of care to sign post the patient to the correct service to manage patient's symptoms. This point is felt to be especially important for when a patient has been lost to follow up or has no MS team involved in their care.	place. The NICE guideline on patient experience of adult NHS services https://www.nice.org.uk/Guidance/CG138 also makes recommendations on continuity of care and relationships (section 1.4).
UK Multiple Sclerosis Specialist Nurses Association (UKMSSNA)	Guideline	009	005 - 016	The UKMSSNA agrees that MS care and care outcomes are improved by early discussions around family planning, fertility, and pregnancy. This allows for better planning and discussion of treatment options in terms of disease modifying therapies but also in terms of managing symptoms with pharmacological interventions. It allows the patient to voice their thoughts and concerns around family issues and allows them control to plan their future.	Thank you for your comment
UK Multiple Sclerosis Specialist Nurses Association (UKMSSNA)	Guideline	010	006 - 020	The UKMSSNA agrees with this section but feels that the transition for a patient to a more advanced stage of MS can be as life changing and devastating for the patient and their carer as when they received their original diagnosis. We recommend that the MS nurse/practitioner is equipped to deal with this and counsel them through this period of transition, to sign post the patient to services such as mental health services, palliative care, carer support and continuing health care. It is also important to recognise that cognitive impairment may impact on the persons	Thank you for your comment. The committee agree that it is very important to provide information and support when the MS is progressing to a more advanced stage. The committee support the needs for health professionals to be equipped to support people should this occur. In recommendation 1.2.18 we highlight the importance of discussing advance care planning if you expect the person's cognitive status will deteriorate.

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				ability to retain information and make decisions on their care and the MS professional should have the knowledge to recognise this and support the patient and their carers appropriately by sign posting to other services for support.	
UK Multiple Sclerosis Specialist Nurses Association (UKMSSNA)	Guideline	011	004	UKMSSNA agrees with this statement and the literature review (Evidence review B) which suggests care is enhanced with a single point of access and a MS nurse or MS practitioner may be best place to be this point of access. Although the UKMSSNA acknowledges that MS services throughout the country look different and work differently in terms of location (urban, rural, secondary primary care), a professional working autonomously or as part of a Multidisciplinary team, we agree that in most services the specialist MS nurse is best placed to be the main point of contact and to provide the following:- • Patient carer well being • Patient education • Family/ carer education • Symptom management and support • Counselling and coping skills in terms of diagnosis transition to progressive MS end of life care • Management/ monitoring of Disease Modifying Therapies • Coordination of care, • Sign posting to other services	Thank you for your comment. The experience and opinion of the guideline committee can be used to inform recommendations but if there is a substantial resource impact, as is the case with the 'interventions' covered by this review, then there needs to be evidence of cost effectiveness. Due to a lack of available evidence on the clinical and cost effectiveness of the MS nurse role which met the evidence review protocol criteria (see appendix A evidence review B) and from the call for evidence the committee were unable to recommend an MS nurse. No relevant health economic evaluation studies comparing interventions to improve coordination of care were included in the evidence review. Several studies were identified that reported on the value of the MS specialist nurse, however, none of these studies met the criteria for assessment of applicability or methodology as they were not economic evaluations and/or did not include a comparator. Due to lack of clinical data it was not possible to undertake any further health economic analyses. The committee has made a research

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				• Educating other clinicians • Safety and Safeguarding issues • Reduction in GP and Neurologist appointments • Prevention hospital admission This list is not inclusive of what the MS Nurse roles consist of but are the components that our members feel are paramount to their role The UKMSSNA accepts that it is difficult to quantify this in research due to variations in services study designs and the difficulties in finding comparisons to compare and evaluate what is central to or required to provide best practice MS service. However, our organisation feels that the research the MS trust and MS society has done over the years including GEMSS the advanced MS nurse champions program is reflective of and shows how paramount an MS nurse role is to the running of MS services, patients' satisfaction, and cost of an MS service. Although the NICE committee were unable to quantify this in the systematic review due to the studies design and lack of comparators. In real-world data these studies have been responsible for creating MS nurse posts funded by the NHS due to the differences that MS nurse posts have made to the MS service.	recommendation (see appendix K) so that evidence may be available if this guideline is considered for update.
UK Multiple Sclerosis Specialist	Guideline	021	004 - 017	The UKMSSNA agree with the points but would like to point out that the cognition problems also impact on family and carers and the organisation feels that it is important to	Thank you for your comment. Recommendation 1.2.10 and 1.6.9 discussed the needs of carers including their right to a carer's assessment.

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Nurses Association (UKMSSNA)				be aware of their needs and support them when assessing cognition problems through a referral to appropriate services or and a carers assessment.	
UK Multiple Sclerosis Specialist Nurses Association (UKMSSNA)	Guideline	027	013	Along with consideration for disease modifying treatments the UKMSSNA would add if the patient is on a disease modifying treatment (DMT) and relapses occur then MS team should consider neurological review of patient, imaging and disease modifying therapy review to look at whether escalation of treatment is needed.	Thank you for your comment. These recommendations were not updated by this guideline update. Recommendation 1.6.3 recommends that evidence of progression or active disease should be assessed as part of the comprehensive review.
University College London NHS Foundation Trust	Guideline	004	007	Patients with primary progressive multiple sclerosis typically present with progressive walking/gait problems. This is not included among the typical presentations of MS listed.	Thank you for your comment. We have edited recommendation 1.1.1 in accordance with your suggestion.
University College London NHS Foundation Trust	Guideline	005	010	1.1.4 - We are concerned that the guideline recommends patient assessment but not physical examination which is important before referral to secondary care to identify more common conditions, and is relevant to changing care models in primary care	Thank you for your comment. We have edited recommendation 1.1.4 to now refer to physical examination
University College London NHS Foundation Trust	Guideline	013	016	The FACETS intervention, which is supported by class I evidence from a randomized control trial is not included in the non-pharmacological management of fatigue.	Thank you for your comment. The FACETS trial has been included in evidence review C. The intervention was not found to be cost effective compared to current local practice and therefore was not specifically recommended.
University College London	Guideline	015	003	We are concerned about the recommendation to offer pharmacological treatments to manage MS-related fatigue. Evidence in this area is generally low-quality, and	Thank you for your comment. The committee acknowledge that there is only limited evidence of benefit for amantadine, modafinil and SSRIs (see committee

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NHS Foundation Trust				a very recent randomized trial (Nourbakhsh et al Lancet Neurology 2021) showed no benefit of amantadine or modafinil over placebo in term of fatigue, and a number needed to harm to cause side effects from these medicines between 2-3. We are particularly concerned about the recommendation to use Modafanil, given the EMA recommendation to not use it in anything other than narcolepsy due to risk of serious side effects. What is NICE's opinion on the medico-legal position of following the NICE guidance and prescribing an off-label drug which the EMA has specifically recommended not to use if the person then has a serious side effect e.g. suicide. The evidence to support the use of SSRI's for MS-related fatigue is very limited and in our practice we would only recommend use of SSRI's in the setting of fatigue with depression or anxiety.	discussion of the evidence in evidence review D. However, in their clinical experience and opinion some people do respond to these treatments and given the potential impact of fatigue on daily life they made a recommendation to consider these interventions. In recommendation 1.5.12 we now refer to considering safety of the drugs. In recommendation 1.5.15 we now refer to monitoring and reviewing response to treatment. The guidance in the summary of product characteristics has now also been highlighted in the rationale and impact The 2020 MHRA safety advice on modafinil (Provigil) is now referred to in recommendation 1.5.14 and rationale. Recommendation 1.5.4 highlights the importance of recognising other causes of fatigue including anxiety and depression.
University College London NHS Foundation Trust	Guideline	016	005	In managing mobility problems in people with MS requires MDT management with specialist neurophysiotherapy review, access to spasticity management, orthotics and electrical stimulation and a combination of interventions should be considered and effect of intervention monitored.	Thank you for your comment. This review focuses on the pharmacological management of spasticity as this is the area where the surveillance report suggested there may be sufficient new evidence since the last guideline (2014) to warrant updating the evidence review https://www.nice.org.uk/guidance/cg186/documents/surveillance-review-proposal.

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University College London NHS Foundation Trust	Guideline	016	008	1.5.13 - There is no mention of appropriate management of foot drop, a very common feature of MS-related walking impairment. Consideration of referral to Orthotics or for Functional Electrical Stimulation should be mentioned here. Functional Electrical Stimulation is a NICE approved treatment for people with foot drop to improve their mobility and reduce falls, there is a large body of evidence proving efficacy in people with MS. The published NICE guidance [IPG278] should be cross referenced: Functional electrical stimulation for drop foot of central neurological origin. Interventional procedures guidance [IPG278] Street T, Taylor P and Swain I. Effectiveness of functional electrical stimulation on walking speed, functional walking category, and clinically meaningful changes for people with multiple sclerosis. *Arch Phys Med Rehabil* 2015; 96(4): 667–672. Street T and Singleton C. Five-year follow-up of a longitudinal cohort study of the effectiveness of Functional Electrical Stimulation for people with multiple sclerosis. *International Journal of MS Care* 2018 20: 224-230. Juckes F, Marceniuk G, Seary C, Stevenson VL. A cohort study of functional electrical stimulation in people with multiple sclerosis demonstrating improvements in quality of life and cost effectiveness. Clin Rehabil. 2019; 2019;33(7):1163-1170.	Thank you for your comment. The non-pharmacological management of mobility was not identified by the surveillance review as having new evidence and was not within the scope of this update. We have added a cross-reference to the NICE IPG on functional electrical stimulation https://www.nice.org.uk/guidance/ipg278 . Functional electrical stimulation is being considered in the new guideline on rehabilitation for chronic neurological conditions including acquired brain injury (https://www.nice.org.uk/guidance/indevelopment/gid-ng10181).

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University College London NHS Foundation Trust	Guideline	016	010	The guideline states"Do not offer prolonged release fampridine to treat mobility problems in people with MS. Fampridine- PR is a clinically effective treatment for some people, but it is **not cost effective at the current list price."** In view of this statement it is imperative the NICE engage with the company to ensure that a discounted price is obtained in line with NHS Wales and the Scottish Medicines Consortium which has enabled access to this treatment in Wales and Scotland. The treatment is highly effective for some people and can lead to increased independence, ability to work and reduced falls. If this is achieved the provision of Fampridine-PR should be as an adjunct to managing mobility with specialist assessment of gait and use of other aids, devices if more appropriate than medication. There is a large placebo effect in trials and as such response to treatment with Fampridine – PR needs to have defined outcome measures before and after treatment and objective measures such as a timed 25 foot walk and patient reported measure such as MSWS-12 are advised. Goal setting and goal attainment are also recommended	Thank you for your comment. The independent guideline committee acknowledged that it is a clinically effective treatment for some people, however it is not cost effective at the current price the NHS is expected to pay. The availability of treatments in Scotland and Wales is a matter for the devolved administrations. In these countries it is made available under a confidential patient access scheme that provides the drug at a lower cost. Patient access schemes are negotiated by the relevant NHS commissioning body and the company (manufacturer). In England this process is led by NHS England.
University College London	Guideline	018	003	The initial choice of drug to treat MS-related spasticity should take into account other symptoms, comorbidities, and preferences. For example, gabapentin may be more	Thank you for your comment. These factors are covered by recommendation 1.5.25. Caution when using baclofen is provided in the rationale

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NHS Foundation Trust				appropriate than baclofen in patients with spasticity plus neuropathic pain. A comment/caution about the use of baclofen is missing from the guideline about the need for slow titration, and the risks of sudden withdrawal.	
University College London NHS Foundation Trust	Guideline	022	004	This section recommends covering employment in the MS annual review, however, no recommendation is made in this section about sign-posting people with work difficulties to sources of vocational support or referred for vocational rehabilitation.	Thank you for your comment. The committee have added for example vocational support/rehabilitation.
University Hospitals of North Midlands NHS Trust	Guideline	013	016	1.5.5 - Management of fatigue- draft version of the guidelines have covered width and depth around management of fatigue. I would perhaps like to make a comment on the semantics. The use of terminology "Self-management" gives an explicit message about the concept and empowers our patients. I would like to recommend committee to incorporate this in the management plan of fatigue and other relevant symptoms' management in MS.	Thank you for your comment. We have incorporated your suggestion into 1.5.6.