National Institute for Health and Clinical Excellence

Multiple Sclerosis
Scope Consultation Table
8 May 2012 – 7 June 2012

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
SH	Addenbrookes Hospital Foundation Trust dept of Neurology	1	general	We welcome the extensive scope of the new NICR MS Guideline	Thank you for your comment.
SH	Addenbrookes Hospital Foundation Trust dept of Neurology	2	4.3.1	We are keen to see a detailed evaluation of sativex, as this has not been subject t a NICE TA. There is wide variation across commissioners in provision of Sativex across the Country, and thewrfore something of a postcode lottery. It has a role for MS related pain, spasticity and bladder symptoms, and we would be pleased to see detailed clinical and cost effectiveness guidelines toi allow its use and funding in an appropriate seeting	Thank you for your comment. The appropriate treatment of bladder related problems is included in the NICE guideline on Incontinence in Neurological disease which is due for publication October 2012. The NICE guideline on Neuropathic pain is being updated and Sativex is included in that draft scope. We will liaise with the team developing the neuropathic pain guideline during development of this guideline.
SH	Addenbrookes Hospital Foundation Trust dept of Neurology	3	4.3.1	We would also welcome a detailed review on the clinical benefits and cost effectiveness of Dalfampradine. Again, most commissioners are not funding it as it has not had a NICE TA, missing an opportunity for its use. By improving mobility and walking speed, it should provide an economic benefit that would offset its cost, but the data needs both acquiring and reviewing. We would ask the scope of the guidance to include detailed observationos on this	Thank you for your comment. The use of fampridine for mobility is included in the scope.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
SH	ASSOCIATION OF BRITISH NEUROLOGISTS	1	4.1.2	Whilst recognising that NICE protocols normally separate adult from children's care, we firmly believe that this rule is not appropriate in the current instance, and that this proposed Guideline document should include childhood onset multiple sclerosis.	Thank you for your comment. We recognise the problems that children may have in terms of diagnosis and management and have carefully considered the guideline population. Following consideration of stakeholder comments we have altered the guideline population to people of 18 years and over only. We considered we could not adequately address the needs of younger people with MS within this guideline. As your comment indicates making recommendations for people under 18 years requires a different approach and include different GDG constitution, reviews of different evidence and consideration of licensing issues in under 18s.
SH	Association of physiotherapists interested in neurology	1	3	should there be a sub-heading that addresses the incidence of MS within ethnicity (e.g. low or high incidence within certain ethnic groups?	Thank you for your comment. We have considered this but are not aware of any issues related to ethnicity and MS in the UK.
SH	Association of physiotherapists interested in neurology	2	3.2	There is considerable literature and research since the original guideline about the benefits of exercise for people with MS also the type and intensity of exercise. Also the use of CBT for fatigue management and Adjustment to diagnosis	Thank you for your comment. The areas included in section 3.2(d) are examples of developments and are not meant to be exhaustive.
SH	Association of	3	4.1	Should the guidance be divided into age 16 and up, then age	Thank you for your comment. We

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
	physiotherapists interested in neurology			65 and up. This will then incorporate the individual needs of the older MS population, (that isn't so great and a recognised diagnosis?), this could also highlight that there is a small population of much older patients with MS.	specify subgroups or populations in the scope if it is considered that they have specific needs that need to be addressed. We have considered whether we should include people over 65 years as a specific subgroup and decided not to do this. The needs of people with MS are likely to be specific to that individual and their disease, and less to do with their age. The individual needs of people with MS will be assessed in our section on structured review.
SH	Association of physiotherapists interested in neurology	3	4.2	Guideline needs to ensure that NHS services include community. I'm not sure if there is much evidence of early supported discharge for MS (longer term conditions), but this could be mentioned? even to say that there isn't much evidence?	Thank you for your comment. The guideline is relevant in all areas where NHS services are delivered and this includes community. The guideline plans to specifically look at setting of rehabilitation for people with MS which will inform treatment at home.
SH	Association of physiotherapists interested in neurology	4	4.3.1	Sexual health (this was addressed extensively in 2003). Seating and positioning. Access to wheelchairs and equipment? Palliative care, end of life care. Long-term neurological conditions: management at the interface between neurology,	Thank you for your comment and the references you have provided. We acknowledge the importance of the issues you raise to people with MS. We have had to prioritise what we cover in the guideline and have prioritised those areas where an

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				rehabilitation and palliative care NATIONAL GUIDELINES March 2008 Occupational rehabilitation / return to employment. Vocational rehab for people with long term neurological conditions. Recommendations for Best Practice BSRM 2010 Ready to Work? Meeting the Employment and Career Aspirations of People with Multiple Sclerosis. Work Foundation report 2011 Dignity and privacy? Should every neurological service within hospital aim to have an MS champion? Pilates, yoga. Prescription of exercise / exercise groups Expert patient groups'.include a reference/section on `self-management' (National policy initiative: NHS Improvement plan 2004, Dr Fiona Jones research). There isn't an inclusion of telemedicine. This is a really expanding area of management of longer term conditions. Management in rural areas? Potentially socio-economic disadvantages, re: access to services and travelling to services/hospital?	assessment of the clinical and cost effectiveness evidence will inform care. People's individual needs in regard to sexual health, vocational rehabilitation etc will be included in the structured review as in 4.3.1 (b) but we do not consider that there is any MS specific treatment to review. The GDG will consider whether to make recommendations about facilitating onward referral. We have added to 'end of life care' to 4.3.1. (c). Non-pharmacological management programmes, including self care are already in the scope. We have not pre-defined the exercise component in these which may include the types of exercise you mention. We understand the issues faced by people who need access to equipment and services. NICE clinical guidelines provide recommendations based on clinical and cost effectiveness and do not have a role in ensuring appropriate availability locally. NICE has an implementation team who support the dissemination of the guideline and MS

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				New Ataxia guidelines 2009 Ataxia UK National clinical guideline for diagnosis and management in primary and secondary care RCP and CSP 2004. Medical rehabilitation in 2011 and beyond RCP 2010. Home Care reablement study 2010 Investigating the longer-term impacts (prospective longitudinal study) Evidence-Based Management Strategies for Spasticity Treatment in Multiple Sclerosis Clinical Practice Guidelines 2005 intra-thecal baclofen? Pressure sore Prevention Oct 2003 Management of neuropathic pain NICE guidance 2010	is on the list of Quality Standards referred to NICE. We do not consider telemedicine and needs of people in rural areas as issues specific to MS. We will however include consideration of equality of access when making recommendations.
SH	Association of physiotherapists interested in neurology	4	4.3.1	• There is mention of the specialist nurse but where is the specialist physiotherapist and OT needed within a MDT and as a single service • acupuncture was strongly evidence-based for pain relief and was recommended in the NICE guideline CG88 for Low Back Pain. The analgesic effect is mediated by afferent stimulation causing release of endogenous opiates and a segmental inhibitory effect. • acupuncture is widely used in clinical practice for pain relief in MS (and this was supported by colleagues in the group whose patients had been treated with acupuncture). • other symptoms of MS such as fatigue, anxiety,	Thank you for your comment. The guideline will examine physiotherapy and occupational therapy interventions and make recommendations about these where appropriate as part of non-pharmacological interventions. Specialist nurses are specifically mentioned in the scope to examine the clinical and cost effectiveness of their role. Acupuncture is included in the scope as

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				depression, sensory and motor disorders, autonomic dysfunction and secondary effects such as insomnia, oedema and sleep disturbance responded well to acupuncture and were found to improve quality of life, engagement with therapy, positive attitude, coping strategies and so reduced the burden on carers. 'Quality of Life' outcome measures, as mentioned, would be appropriate to measure these effects. • more research is needed to validate these outcomes. • acupuncture is extremely cost-effective and safe	an option for treatment.
SH	Association of physiotherapists interested in neurology	5	4.4	• MS Walking scale • Leeds MS quality of life scale • MSIS (MS impact scale)	Thank you for your comment. We have added these to the list of outcomes
SH	Bayer plc (Bayer HealthCare)	1	4.1.1	**Groups that will be covered** Although multiple sclerosis (MS) in children is rare. It has been suggested that around five to ten per cent of people with MS experience its onset before the age of 16.[1] The age range of this guideline should therefore be extended to provide guidance regarding the management of MS in those younger than 16 years of age. 1. Multiple Sclerosis Society. MS in Children. Multiple Sclerosis Society Web Site. [cited 30/05/2012]; Available from: URL:http://www.mssociety.org.uk/what-is-ms/types-of-ms/ms-in-children	Thank you for your comment. We recognise the problems that children may have in terms of diagnosis and management and have carefully considered the guideline population. Following consideration of stakeholder comments we have altered the guideline population to people of 18 years and over only. We considered we could not adequately address the needs of younger people with MS within this guideline. Making recommendations for people under 18

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
					years requires a different approach and includes having a different GDG constitution, reviews of different evidence and consideration of licensing issues in under 18s.
SH	Bayer plc (Bayer HealthCare)	2	4.3.1	**a)** We support the inclusion of the appropriate investigation for people with clinically isolated syndrome (CIS) as a key clinical issue, however, we are concerned that the subsequent management of people with CIS with disease modifying treatments will not be covered, as this is not an area encompassed by previous NICE appraisals nor by the Risk Sharing Scheme for MS. This may lead to uncertainty as to the appropriate management of this group. We propose that the management of people with CIS who are at high risk of developing MS should be included in the scope.	Thank you for your comment. Clinically isolated syndrome will be included in the review for update of NICE technology appraisal TA32 on Beta interferon and glatiramer acetate for the treatment of multiple sclerosis.
SH	Bayer plc (Bayer HealthCare)	3	general	The national audit of services for people with multiple sclerosis (2011)[2] highlighted that none of the six key recommendations made by NICE in 2003 have been implemented widely or fully. As such we recommend that key recommendations from the guideline are carried through to relevant quality standards and consequently included in the Commissioning Outcomes Framework (COF) and appropriate provider payment mechanisms to encourage implementation. 2. The Royal College of Physicians and the Multiple Sclerosis Trust. The national audit of services for people with multiple sclerosis. 2011. Royal College of Physcians	Thank you for your comment and suggestion for informing the Quality Standard development.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				Website. [cited 23/05/2012]; Available from: URL:http://www.rcplondon.ac.uk/sites/default/files/ms_audit_national_report_2011_0.pdf	
SH	Bayer plc (Bayer HealthCare)	4	4.3.1	**g)** We support the inclusion of Sativex for the pharmacological management of spasticity in this guideline. Randomised placebo-controlled trials have demonstrated that Sativex is well tolerated and improves symptoms in patients with moderate to severe spasticity due to MS who had insufficient benefit from their existing oral anti-spasticity medication, and who have shown capacity to respond to treatment. Early phase III trials in a broad population resulted in outcomes of questionable treatment effect or clinical relevance,[3-5] however, it was postulated that a clinically useful treatment effect in some patients might be partly masked by data from non-responders. In analyses comparing NRS scores with patient global impression of change (PGI), a 19% NRS response was estimated to represent a clinically relevant improvement on the PGI and a response of 28% "much improved" on the PGI. In post hoc exploratory combined analyses of the early studies, a 4-week trial period using a 20% NRS response threshold was predictive of eventual response defined as a 30% reduction.[6] Consequently a phase 3 trial was designed which aimed to assess the benefit of continued treatment for patients who achieve an initial response to treatment.[7] The trial incorporated a formalised 4-week therapeutic trial period prior	Thank you for your comment and this information.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				to randomisation to allow responders to be identified. 572 patients with MS and refractory spasticity all received single blind Sativex for four weeks. After four weeks on active treatment 272 met the entry criterion of a reduction of at least 20% on the spasticity symptom NRS. 241 of these patients were then randomised to either continue to receive active or switch to placebo for the 12 week double-blind phase, for a total of 16 weeks treatment overall. The mean change in spasticity 0-10 NRS at the end of the single-blind treatment with Sativex was a decrease (improvement) of 3.01 points. During the double-blind phase the mean NRS scores for patients receiving Sativex further improved by 0.04 units (baseline 3.87), whereas an increase of 0.81 units (baseline 3.92) was seen in the placebo group. At the end of the 12 weeks, the estimated treatment difference between the 2 groups in the mean spasticity NRS was 0.84 points (95% CI -1.29, -0.40) p=0.0002. During the double-blind phase the overall adverse event rate was similar between Sativex and placebo. The most common adverse events in the Sativex group were vertigo, fatigue, muscle spasms and urinary tract infection. This trial design reflects the proposed clinical practice, and in principal the difference between active and placebo should be a fair reflection of efficacy in the population treated with Sativex in clinical practice. The benefit of continued treatment in the long-term was studied in a placebo controlled, parallel group, randomised withdrawal trial in subjects taking long-term Sativex (at least 12 weeks).[8] Thirty six patients with a mean duration of	

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				Sativex use prior to the trial of 3.6 years were randomised to either continue with Sativex treatment or switch to placebo for 28 days. The primary endpoint was time to treatment failure, defined as the time from the first day of randomised treatment to a 20% increase in NRS or premature withdrawal from randomised treatment. Those randomised to placebo reached treatment failure significantly faster than those on Sativex (p=0.013) Treatment failure was experienced by 94% of placebo patients and 44% of Sativex patients, hazard ratio 0.335 (95% CI 0.16, 0.69). Despite the small numbers of subjects in the study, this trial suggests that the effect of Sativex is maintained with long-term use, and it also suggests that there is no evidence of a withdrawal syndrome in those subjects who stopped Sativex, despite a prolonged period of time on treatment. In a study designed to identify its abuse potential, Sativex at a dose of 4 sprays taken at one time did not differ significantly from placebo. Higher doses of Sativex of 8 to 16 sprays taken at one time did show abuse potential comparable to equivalent doses of dronabinol, a synthetic cannabinoid.[9] 3. Wade DT, Collin C, Stott C, Duncombe P. Meta-analysis of the efficacy and safety of Sativex (nabiximols), on spasticity in people with multiple sclerosis. *Mult Scler* 2010; 16(6):707-714. 4. Collin C, Davies P, Mutiboko IK, Ratcliffe S. Randomized controlled trial of cannabis-based medicine in spasticity caused by multiple sclerosis. *Eur J Neurol* 2007; 14(3):290-296.	

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				5. Collin C, Ehler E, Waberzinek G, Alsindi Z, Davies P, Powell K et al. A double-blind, randomized, placebo-controlled, parallel-group study of Sativex, in subjects with symptoms of spasticity due to multiple sclerosis. *Neurol Res* 2010; 32(5):451-459. 6. GW Pharma Ltd c/o Bayer plc. Sativex Oromucosal Spray Summary of Product Characteristics. 28-7-2011. 7. Novotna A, Mares J, Ratcliffe S, Novakova I, Vachova M, Zapletalova O et al. A randomized, double-blind, placebo-controlled, parallel-group, enriched-design study of nabiximols* (Sativex®), as add-on therapy, in subjects with refractory spasticity caused by multiple sclerosis. *Eur J Neurol* 2011; 18(9):1122-1131. 8. Notcutt W, Langford R, Davies P, Ratcliffe S, Potts R. A placebo-controlled, parallel-group, randomized withdrawal study of subjects with symptoms of spasticity due to multiple sclerosis who are receiving long-term Sativex(R) (nabiximols). *Mult Scler* 2012; 18(2):219-228. 9. Schoedel KA, Chen N, Hilliard A, White L, Stott C, Russo E et al. A randomized, double-blind, placebo-controlled, crossover study to evaluate the subjective abuse potential and cognitive effects of nabiximols oromucosal spray in subjects with a history of recreational cannabis use. *Hum Psychopharmacol* 2011; 26(3):224-236.	
SH	Bayer plc (Bayer HealthCare)	5	4.3.1	**g)** Gabapentin is not licensed for the management of spasticity.[10] Recommendations regarding off-label or unlicensed medicines should only be made where an	Thank you for your comment and references. We include careful consideration of medicine licensing when making recommendations.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				appropriate licensed alternative would not meet the patient's needs to avoid conflict with the professional codes and ethics of healthcare professional statutory bodies.[11,12] 10. BMJ Group and the Royal Pharmaceutical Society of Great Britain. British National Formulary 63. March 2012. 11. General Medical Council (GMC). Good practice in prescribing medicines - guidance for doctors. September 2008. http://www.gmc-uk.org/static/documents/content/Good_Practice_in_Prescribing_Medicines_0911.pdf 12. Nursing & Midwifery Council. Standards of proficiency for nurse and midwife prescribers. June 2006. Available at: http://www.nmc-uk.org/Documents/Standards/nmcStandardsofProficiencyForNurseAndMidwifePrescribers.pdf	
SH	Bayer plc (Bayer HealthCare)	6	4.3	In light of the findings of the national audit of services for people with multiple sclerosis (2011)[2] highlighted on page 3 of the scope, it is particularly important that access to specialist neurological and neurological rehabilitation services is covered by this guideline. 2. The Royal College of Physicians and the Multiple Sclerosis Trust. The national audit of services for people with multiple sclerosis. 2011. Royal College of Physcians Website. [cited 23/05/2012]; Available from: URL:http://www.rcplondon.ac.uk/sites/default/files/ms_audit_national_report_2011_0.pdf	Thank you for your comment. Clinical guidelines make recommendations for clinical and cost effective treatment. NICE clinical guidelines do not have a role in ensuring appropriate availability of services locally. . NICE has an implementation team who support the dissemination of the guideline and MS is on the list of Quality Standards referred to NICE.
SH	Bayer plc (Bayer HealthCare)	7	4.3.3 c	The Risk Sharing Scheme for Disease Modifying Therapies in	Thank you for your comment. We are unable to signpost to non-NICE

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				MS should also be included under this section as it is this that enables the supply of these treatments on the NHS.[13] Ministers have issued a statutory direction in respect of the scheme which places NHS bodies under a funding obligation equivalent to that for positive NICE guidance.[13] 13. Department of Health. Health Service Circular HSC 2002/004: Cost Effective Provision of Disease Modifying Therapies for People with Multiple Sclerosis. February 2002. Department of Health Website. [cited 23/05/2012]; Available from: URL:http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@en/documents/digitalasset/dh_4012214.pdf	guidance but we are aware of the Risk Sharing Scheme. The Guideline Development Group will be kept up to date on the progress of the Risk Sharing Scheme.
SH	Bayer plc (Bayer HealthCare)	8	4.3.3 c	We note that pharmacological management of MS with disease modifying treatments is not covered by the scope with the rationale that "they are covered by other technology appraisals or other NICE guidance to which the new guideline will cross refer." However these other references do not discuss the important issue of early treatment in patients with CIS. This is an important gap as early treatment with interferon beta-1b in patients CIS has been shown to delay conversion to clinically definite multiple sclerosis (CDMS). In the placebo controlled BENEFIT study, interferon beta-1b reduced the probability of the development of CDMS over 2 years from 45% in the placebo group to 28%.[14] Following on from this trial, early versus delayed initiation of treatment also showed significant benefits in the development of CDMS at 3,[15] 5[16]	Thank you for your comment. Clinically isolated syndrome will be included in the review for update of NICE technology appraisal TA32 on Beta interferon and glatiramer acetate for the treatment of multiple sclerosis subject to a review proposal consultation.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				and 8 years,[17] Overall, early treatment with IFNB-1b reduced the risk of CDMS by 32.2% over the 8-year observation period compared with delayed treatment (hazard ratio=0.678, 95% CI 0.525-0.875; *p*=0.0029). Time to CDMS in the early-treatment group was delayed by 3.7 years at the 50th percentile.[16] The risk for confirmed disability progression was at significantly lower at 3 years,[15] but not at 5[16] or 8 years.[17] Whilst it can be argued that not all patients with CIS go on to develop MS,[18] MRI evidence can predict the likelihood of development; in the placebo arm of the BENEFIT trial, including patients with at least two clinically silent brain MRI lesions, 85% converted to McDonald's MS after a period of 2 years.[15] It has been recommended that patients with CIS who have been shown to be at high risk could be considered for initiation of treatment with disease modifying therapies: The Association of British Neurologists Revised (2009) guidelines for Prescribing in Multiple Sclerosis state that neurologists may consider advising treatment for patients within 12 months of a clinically significant clinically isolated syndrome when MRI evidence predicts a high likelihood of recurrent episodes (i.e. development of multiple sclerosis)."[19] Similarly, the American National MS Society Disease Management Consensus Statement also states that "Initiation of treatment with an interferon beta medication or glatiramer acetate may be considered for selected patients with a first attack who are at high risk of MS."[20] This is also of relevance because the scope covers the investigation for people with clinically isolated syndrome	

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				under 4.3.1 a), but does not propose to discuss their subsequent treatment which will lead to uncertainty as to the appropriate management of this group. We propose that the management of people with CIS who are at high risk of developing MS should be included in the scope. 14. Kappos L, Polman CH, Freedman MS, Edan G, Hartung HP, Miller DH et al. Treatment with interferon beta-1b delays conversion to clinically definite and McDonald MS in patients with clinically isolated syndromes. *Neurology* 2006; 67(7):1242-1249. 15. Kappos L, Freedman MS, Polman CH, Edan G, Hartung HP, Miller DH et al. Effect of early versus delayed interferon beta-1b treatment on disability after a first clinical event suggestive of multiple sclerosis: a 3-year follow-up analysis of the BENEFIT study. *Lancet* 2007; 370(9585):389-397. 16. Kappos L, Freedman MS, Polman CH, Edan G, Hartung HP, Miller DH et al. Long-term effect of early treatment with interferon beta-1b after a first clinical event suggestive of multiple sclerosis: 5-year active treatment extension of the phase 3 BENEFIT trial. *Lancet Neurol* 2009; 8(11):987-997. 17. Edan G, Kappos L, Montalbán X, Polman C, Freedman M, Hartung HP et al. Long-Term Effect of Early Treatment With Interferon Beta-1b After a First Clinical Event Suggestive of Multiple Sclerosis: 8-year Observational Extension of the Phase 3 BENEFIT Trial. Presented at the	

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				5th Joint Triennial Congress of the European and Americas Committees for Treatment and Research in Multiple Sclerosis, Amsterdam, The Netherlands, 19-22 October 2011 . 2011. 18. Miller D, Barkhof F, Montalban X, Thompson A, Filippi M. Clinically isolated syndromes suggestive of multiple sclerosis, part I: natural history, pathogenesis, diagnosis, and prognosis. *Lancet Neurol* 2005; 4(5):281-288. 19. Association of British Neurologists. Revised (2009) Guidelines for Prescribing in Multiple Sclerosis. Association of British Neurologists Website. [cited 29/05.2012]; Available from: URL:http://www.abn.org.uk/abn/userfiles/file/ABN_MS_Guidelines_2009_Final%281%29.pdf 20. National Multiple Sclerosis Society. Treatment Recommendations for Physicians - Disease Management Consensus Statement. 2008. National Multiple Sclerosis Society Website. [cited 29/05/2012]; Available from: URL:http://www.nationalmssociety.org/for-professionals/healthcare-professionals/publications/expert-opinion-papers/index.aspx	
SH	Bayer plc (Bayer HealthCare)	9	4.4	**d)** Consideration should be given to the fact that symptomatic treatments may be better measured by patient reported outcomes as opposed to clinician- related measurements which may not give an accurate representation of the patient experience of spasticity or be sensitive to changes that are	Thank you for your comment. We have added patient reported outcomes to the list

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				meaningful to the patient.[21] A Cochrane review of anti-spasticity agents for multiple sclerosis suggests "under implications for research" that assessment tools developed for spasticity and other components of the upper motor neurone syndrome should correspond to the daily patient experience of spasticity.[22] 21. Farrar JT, Troxel AB, Stott C, Duncombe P, Jensen MP. Validity, reliability, and clinical importance of change in a 0-10 numeric rating scale measure of spasticity: a post hoc analysis of a randomized, double-blind, placebo-controlled trial. *Clin Ther* 2008; 30(5):974-985. 22. Shakespeare DT, Boggild M, Young C. Anti-spasticity agents for multiple sclerosis. *Cochrane Database Syst Rev* 2003;(4):CD001332.	
SH	British Association of Urological Surgeons Ltd	1	3.2 c	Our Comments are as follows. I would include a paragraph stating 'bladder management may include pharmacological treatment or catheter techniques to improve symptoms and to reduce complications and prevent long term renal damage.'	Thank you for your comment. Section 3.2 (c) lists some of the symptoms that require management and is not intended to be a complete list. Bladder management is covered by the Management of Incontinence in Neurological Disease guideline which is due for publication in August 2012 and to which this guideline will refer.
SH	British Association of Urological Surgeons Ltd	2	4.3.1 e	Our comments are as follows… Include a sentence stating' use of intermittent catheterisation techniques for bladder emptying'.	Thank you for your comment. We do not intend to cover bladder emptying as bladder management has been covered in Management of Incontinence in Neurological Disease guideline which

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
					will be published in October 2012 and to which this guideline will refer.
SH	British Association of Urological Surgeons Ltd	3	4.3.1	Our comments are as follows…. I would before g or h have another section stating 'the pharmacological management of bladder dysfunction including Antimuscranics and/ or Intra-vesical Botulinum toxin injections'.	Thank you for your comment. The management of bladder dysfunction is covered by the Management of Incontinence in Neurological Disease guideline which is due for publication in October 2012 and to which this guideline will refer.
SH	British Association of Urological Surgeons Ltd	4	General	The guideline should include advice on the management of sexual dysfunction and pregnancy. It is unfortunate that there is so much overlap with other guidance so that there is a danger that the final guideline will be reliant on signposting to other guidance (such as the Neurogenic Incontinence one) which will make it appear a bit disjointed and fragmented.	Thank you for your comment. We have considered the specific inclusion of sexual dysfunction and pregnancy and did not consider that either have MS specific treatment to review. NICE will produce a NICE pathway where easy reference to all guidance relevant to people with MS will be found.
SH	British Dietetic Association	1	4.3.1	Re. 'vitamin D for the management of MS'. Ideally should give an indication of optimal vitamin D dosage recommended, route(s) of administration and should consider safety aspects of megadoses of vitamin D. Should explicitly relate to sub-types of MS i.e. relapsing-remitting vs. progressive forms in terms of proposed efficacy.	Thank you for your comment and suggestions regarding this question. We will consider these issues when planning the review of evidence.
SH	British Dietetic Association	2	4.3.1	Re. 'use of complementary and alternative therapies such as linoleic acid….' Should consider polyunsaturated fatty acids (PUFA) in the broader sense, not just linoleic acid (as there are published journal articles relating to other PUFA and MS, e.g. omega-3 fatty acids).	Thank you for your comment. We have changed this to include omega 3 and omega 6 fatty acids.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
SH	British Dietetic Association	3	4.3.3	Re. 'swallowing difficulties'. Consider re-phrasing as 'swallowing difficulties and nutritional support'. The NICE guideline cited ('Nutrition Support in Adults, 2006) is not specific to swallowing difficulties per se but to nutritional support in a wider context, including artificial nutritional support (e.g. gastrostomy feeding). It is very relevant to cross-reference this NICE guideline.	Thank you for your comment. The scope now cross refers to the nutrition support in adults NICE guideline.
SH	British Paediatric Neurology Association	1	3.1	Children under age 16 years with MS will need to be considered too. Recent studies report an annual incidence figure for the first inflammatory demyelination event (i.e. Clinically Isolated Syndrome) in children to be around 10 per million in the UK. Around 5% of people diagnosed with MS in their adulthood actually experienced their first MS symptom in childhood.	Thank you for your comment. We recognise the problems that children may have in terms of diagnosis and management and have carefully considered the guideline population. Following consideration of stakeholder comments we have altered the guideline population to people of 18 years and over only. We considered we could not adequately address the needs of younger people with MS within this guideline. Making recommendations for people under 18 years requires a different GDG constitution, reviews of different evidence and consideration of licensing issues in under 18s.
SH	British Paediatric Neurology Association	2	3.2 a	The diagnosis of MS in children should be addressed, as it is often delayed. Paediatricians often do not consider MS as a possible diagnosis in children, leading to delay. This is likely to reflect their lack of familiarity with this relatively uncommon	Thank you for your comment. We recognise the problems that children may have in terms of diagnosis and management and have carefully

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				group of disorder. Conditions which share some symptoms with MS occur more frequently in children than in adults and there is a wider differential diagnosis. Treatments of other recurrent non MS demyelination provide further challenges.	considered the guideline population. Following consideration of stakeholder comments we have altered the guideline population to people of 18 years and over only. We considered we could not adequately address the needs of younger people with MS within this guideline. As your comment indicates making recommendations for people under 18 years requires a different approach and include different GDG constitution, reviews of different evidence and consideration of licensing issues in under 18s.
SH	British Paediatric Neurology Association	3	3.2 c	There is wide variation in paediatric prescribing practice. Many paediatric neurologists are unfamiliar with disease modifying drugs and may therefore are reluctant to prescribe them. Optimal and timely treatment as recommended by the International (Chitnis et al 2012 *Mult Scler.* 18(1):116-27) and European MS group (Ghezzi et al 2010 *Mult Scler.*16 (10):1258-67) are often initiated only in a small number of patients eg. disease modifying treatments in children with MS. These drugs are prescribed off label and are unlicensed for children (under 18 years), requiring time consuming 'named patient' basis local commissioning approval for funding and resulting delays in treatment. Indeed some children may not be offered treatment, whilst others may have been started on treatment which are no longer used as first-line treatment in adults e.g. azathioprine, because of easier	Thank you for your comment. We recognise the problems that children may have in terms of diagnosis and management and have carefully considered the guideline population. Following consideration of stakeholder comments we have altered the guideline population to people of 18 years and over only. We considered we could not adequately address the needs of younger people with MS within this guideline. As your comment indicates making recommendations for

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				availability	people under 18 years requires a different approach and include different GDG constitution, reviews of different evidence and consideration of licensing issues in under 18s.
SH	British Paediatric Neurology Association	4	4.1.2	The NICE guideline should include children. All those affected by the condition should have access to the same support regardless of age. Delay in diagnosis in children with MS and access to specific therapies are issues identified in the UK (National MS Society Meeting, London 2007).	Thank you for your comment. We agree that all those affected by a condition should have access to appropriate supports and treatment. We have considered inclusion of children but decided that we cannot to justice to the requirement of this group. The diagnostic process is different with a different differential diagnosis and making recommendations for people under 18 years requires a different approach and include different GDG constitution, reviews of different evidence and consideration of licensing issues in under 18s.
SH	British Paediatric Neurology Association	5	4.3.1 a	The diagnosis of paediatric MS should be addressed, as it is often delayed. Paediatricians rarely consider MS as a possible diagnosis, which leads delays in diagnosis, assessment, information and treatment. Also there is a wider differential diagnosis of inflammatory demyelination in children than in adults.	Thank you for your comment. We have carefully considered the inclusion of children and adolescents in the guideline. Following consideration of stakeholder comments we have altered the guideline population to people of 18 years and over only. We considered we could not adequately address the

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
					needs of younger people with MS within this guideline. Making recommendations for people under 18 years requires a different approach which would include a different GDG constitution, reviews of different evidence and consideration of licensing issues in under 18s.
SH	British Paediatric Neurology Association	6	4.3.1 b	For childhood sufferers of MS, continuing education is a major issue. Childhood MS can lead to significant morbidity - motor, speech, bladder and bowel, fatigue, emotional and cognitive difficulties. Children with MS often struggle at school and need educational psychology/neuropsychometric assessments to assess and remedy underlying cognitive difficulties.	Thank you for your comment. We have carefully considered the inclusion of children and adolescents in the guideline. Following consideration of stakeholder comments we have altered the guideline population to people of 18 years and over only. We considered we could not adequately address the needs of younger people with MS within this guideline. Making recommendations for people under 18 years requires a different approach which would include a different GDG constitution, reviews of different evidence and consideration of licensing issues in under 18s.
SH	College of Occupational Therapists	1	General	The College would like to take this opportunity to confirm its endorsement of the response submitted by the MS Society in relation to this draft scope consultation. We fully support all the comments made in the MS Society response and the view that the remit should be extended to	Thank you for your comment. The remit from the Department of Health is for a clinical guideline for the management of MS in primary and secondary care and does not include social care or public health. We

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				produce an integrated guideline to cover both health and social care.	acknowledge the importance of social care for people with MS and anticipate that some of the interventions we recommend may be delivered by social care depending on local arrangements. As NICE will have a remit for social care from April 2013NICE is considering how best to address the issues of integration of health and social care.
SH	College of Occupational Therapists	2	General	The College of Occupational Therapists is pleased to offer further comments on the draft scope of the guideline on the management of multiple sclerosis in primary and secondary care. We hope that the guideline development group will give careful consideration to the points listed below.	Thank you
SH	College of Occupational Therapists	3	General	In its current state the scope appears to be biased towards a medical model of management of people with MS. People with MS often require support from a range of health and social care professionals and organisations, and we would recommend that this is reflected in the new guideline. Retention of the existing guideline on teamwork (section 1.2) would help to resolve this.	Thank you for your comment. The remit is for a clinical guideline but we recognise that people with MS may require support from a wide range of people and services. We will refer to the NICE Patient Experience guidance which makes recommendations about communication and co-ordination of services.
SH	College of Occupational Therapists	4	General	Long-term access to specialist multidisciplinary services to review and manage symptoms is not mentioned and we suggest this is included (Khan et al 2007, Craig et al 2003).	Thank you for your comment and these references. Appropriate structured review is included in the scope.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				References: Khan F, Turner-Stokes L, Ng L, Kilpatrick T, Amathya B (2007) *Multidisciplinary rehabilitation for adults with multiple sclerosis*. Cochrane Database of Systematic Reviews 2007, Issue 2. Art. No.: CD006036. DOI: 10.1002/14651858.CD006036.pub2 Craig J, Young CA, Ennis M, Baker G, Boggild M (2003) A randomised controlled trial comparing rehabilitation against standard therapy in multiple sclerosis patients receiving intravenous steroid treatment. *Journal of Neurology, Neurosurgery and Psychiatry, 74:* 1225-1230.	
SH	College of Occupational Therapists	5	General	The scope does not appear to include treatment of sexual dysfunction for people with MS. We would suggest retaining section 1.7.18 in the existing guideline on Sexual Dysfunction.	We have had to prioritise what we cover in the guideline and have prioritised those areas where an assessment of the clinical and cost effectiveness evidence will inform care. People's individual needs in regard to sexual health, will be included in the structured review as in 4.3.1 (b) but we do not consider that there is any MS specific treatment to review. The GDG will consider whether to make recommendations about facilitating onward referral.
SH	College of Occupational Therapists	6	General	Inclusion of innovative practice such as the use of assistive technology to support self-management would be useful.	Thank you for your comment.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
SH	College of Occupational Therapists	7	General	Although the scope mentions anxiety and depression, psychological adjustment and access to psychological therapies are not included.	Thank you for your comment. We will refer to the Patient Experience guideline
SH	College of Occupational Therapists	8	4.1.1	The guideline needs to be relevant for any person with a diagnosis of MS or possible MS, regardless of their age.	Thank you for your comment. When developing NICE guidelines we always specify the population that the guideline is relevant to. MS in childhood is uncommon and children and young people require different considerations when making recommendations. The guideline that is being replaced (CG8) included adults only.
SH	College of Occupational Therapists	9	4.3.1	Access to services to maintain health could be included here e.g. social and leisure opportunities. This could be achieved by retaining section 1.6.3 in the existing guideline on Leisure and Social Interaction.	Thank you for your comment. We have had to prioritise what we cover in the guideline and have prioritised those areas where an assessment of the clinical and cost effectiveness evidence will inform care. People's individual needs in regard to social and leisure opportunities will be included in the structured review as in 4.3.1 (b) but we do not consider that there is any MS specific intervention to review. The GDG will consider whether to make recommendations about facilitating onward referral.
SH	College of Occupational	10	4.3.1 b	While vocational activities are mentioned as part of diagnosis, assessment and information, vocational rehabilitation is not	Thank you for this reference. Thank you for your comment.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
	Therapists			mentioned as an actual intervention. We would recommend that referral to vocational rehabilitation and occupational therapy services are considered in the guideline to address vocational activities for people with MS (Sweetland et al 2007). Reference: Sweetland J, Riazi A, Cano SJ, Playford ED (2007) Vocational rehabilitation services for people with multiple sclerosis: what patients want from clinicians and employers. *Multiple Sclerosis 13(9)*, 1183-1189. This could be achieved by retaining section 1.6.2 in the existing guideline on Vocational Activities – employment and education.	We have had to prioritise what we cover in the guideline and have prioritised those areas where an assessment of the clinical and cost effectiveness evidence will inform care. People's individual needs in regard to areas such as vocational rehabilitation will be included in the structured review as in 4.3.1 (b) but we do not consider that there is any MS specific treatment to review. The GDG will consider whether to make recommendations about facilitating onward referral.
SH	College of Occupational Therapists	11	4.3.1 b	Although assessment of functional problems such as activities of daily living is included in this section, the scope does not provide guidance on what the intervention should include. There is an important role for goal setting, rehabilitation and access to equipment and adaptations which needs to be included within this section. Section 1.6. of the previous guideline does include recommendations, and reference should be made to these.	Thank you for your comment. We have had to prioritise what we cover in the guideline and have prioritised those areas where an assessment of the clinical and cost effectiveness evidence will inform care. People's individual needs in regard to areas such as functional problems will be included in the structured review as in 4.3.1 (b) but we do not consider that there is any MS specific intervention to review. The precise intervention will need to be tailored to individual patient.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
					The GDG will consider whether to make recommendations about facilitating onward referral
SH	College of Occupational Therapists	12	4.3.1 b	It is important that this includes the involvement of social services for full integration of care for people with MS. This should include both social workers for assistance with care package assessment and for Social Services based occupational therapists for home equipment and adaptations (Hill 2006). There is no mention of this in the current NICE guideline. Reference: Hill S (2006) Independent living: equipment and cost savings. Chelmsford: Essex Learning and Social Care. [Unpublished].	Thank you for your comment. The remit from the Department of Health is for a clinical guideline for the management of MS in primary and secondary care and does not include social care or public health. We acknowledge the importance of social care for people with MS and anticipate that some of the interventions we recommend may be delivered by social care depending on local arrangements. As NICE will have a remit for social care from April 2013 NICE is considering how best to address the issues of integration of heath and social care.
SH	College of Occupational Therapists	13	4.3.1 e	Fatigue management programmes to include CBT and occupational therapy-led fatigue management programmes should be included as this not just about self-management (Mathiowetz et al 2005; 2007). References Mathiowetz VG, Finlayson ML, Matuska KM, Chen HY, Luo P (2005) Randomized controlled trial of an energy conservation course for persons with multiple sclerosis. *Multiple Sclerosis, 1(5),* 592–601. Mathiowetz VG, Matuska KM, Finlayson ML, Luo P, Chen HY	Thank you for your comment. We will be including therapist led courses when considering management programmes.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				(2007) One-year follow-up to a randomized controlled trial of an energy conservation course for persons with multiple sclerosis. *International Journal of Rehabilitation Research, 30(4),* 305–313.	
SH	College of Occupational Therapists	14	4.3.1 e	Access to specialist equipment and technology should be included in the non-pharmacological management of spasticity, mobility and pain, for example, specialist seating.	Thank you for your comment. We understand the issues faced by people who need access to equipment and services. NICE clinical guidelines provide recommendations based on clinical and cost effectiveness and do not have a role in ensuring appropriate availability locally.
SH	College of Occupational Therapists	15	4.3.1 m	Whilst the role of the MS Nurse Specialist is very important, people with MS also need support from a multidisciplinary team, including specialist occupational therapists.	Thank you for your comment. The role of MS nurse is specifically mentioned as this was considered an issue where specific guidance is required. The role of interventions provided by other specialists such as occupational therapists are included in the sections on specific interventions. The scope has been amended to include consideration of coordination of care and support including the role of the MS nurse.
SH	College of Occupational Therapists	16	4.3.2 b	It is important that management of contractures is addressed, including their prevention wherever possible. A 24-hour approach to postural management should be included here.	Thank you for your comment. The prevention of contractures will be included in 4.3.1 (e) and 4.3.1 (g)
SH	College of	17	4.4 b	It is welcome that the impact on carers is being used as an	Thank you for your comment. The list of

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
	Occupational Therapists			outcome, but further detail is needed on how this will be achieved. It is recommended that care is coordinated between health and social care, with advice being given by all relevant professionals. For example, occupational therapists can advise on maintaining independence, use of assistive technology and environmental modifications.	outcomes here is the outcomes that will be prioritised when reviewing the evidence.
SH	College of Occupational Therapists	18	General	It would be useful to see a review of research on the full range of interventions that are recommended for people with MS, including, for example, interventions made by the multidisciplinary team.	Thank you for your comment. We have to prioritise the areas included in a guideline and not able to include the full range of interventions for people with MS.
SH	Department of Health	1	general	The Department of Health has no substantive comments to make, regarding this consultation	Thank you for your comment.
SH	Ferring Pharmaceuticals	1	4.3.3 e	Ferring would like to highlight that our DDAVP Melt 60, 120 and 240 micrograms oral lyophilisate may be of use in patients who have difficulty swallowing and/or who would prefer an alternative to a nasal formulation. It has comparable efficacy to the tablet recommended in the previous 2003 guidelines (section 1.7.2.4), as shown in the Lottman et al 2007 study in children (enclosed). DDAVP Melt (like the Desmopressin tablets) is not licenced in Multiple Sclerosis.	Thank you for this information.
SH	Ferring Pharmaceuticals	2	4.4.4 d	Ferring would like to highlight that our DDAVP Melt 60, 120 and 240 micrograms oral lyophilisate may be of use in patients who have difficulty swallowing and/or who would prefer an alternative to a nasal formulation. It has comparable efficacy to the tablet recommended in the previous 2003 guidelines (section 1.7.2.4), as shown in the Lottman et al 2007 study in children (enclosed). DDAVP Melt (like the Desmopressin tablets) is not licenced in Multiple	Thank you for this information.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				 Lottmann H et al 2007.pdf Sclerosis.	
SH	G W PHARMACEUTICALS PLC	1	general	The national audit of services for people with multiple sclerosis (2011)[1] highlighted that none of the six key recommendations made by NICE in 2003 have been implemented widely or fully. As such we recommend that key recommendations from the guideline are carried through to relevant quality standards and consequently included in the Commissioning Outcomes Framework (COF) and appropriate provider payment mechanisms to encourage implementation. 23. The Royal College of Physicians and the Multiple Sclerosis Trust. The national audit of services for people with multiple sclerosis. 2011. Royal College of Physcians Website. [cited 23/05/2012]; Available from: URL:http://www.rcplondon.ac.uk/sites/default/files/ms_audit_national_report_2011_0.pdf	Thank you for your comment. MS is on the list of Quality Standards that have been referred to NICE and we will work with the guideline implementation team and QS teams to encourage implementation.
SH	G W PHARMACEUTICALS PLC	2	4.3.1	**g)** We support the inclusion of Sativex for the pharmacological management of spasticity in this guideline. Randomised placebo-controlled trials have demonstrated that Sativex is well tolerated and improves symptoms in patients with moderate to severe spasticity due to MS who had insufficient benefit from their existing oral anti-spasticity medication, and who have shown capacity to respond to treatment[1].	Thank you for your comment and this information. The NICE guideline on Neuropathic pain is being updated and sativex is included in the draft scope. The management of bladder function for people with MS as included in the NICE guideline for Incontinence in

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				Early phase III trials in a broad population resulted in statistically significant outcomes in favour of Sativex, but of uncertain clinical relevance.[2-4] It was postulated that a clinically useful treatment effect in some patients might be partly masked by data from non-responders. In analyses comparing NRS scores with patient global impression of change (PGI), a 19% NRS response was estimated to represent a clinically relevant improvement on the PGI and a response of 28% "much improved" on the PGI. In post hoc exploratory combined analyses of the early studies, a 4-week trial period using a 20% NRS response threshold was predictive of eventual response defined as a 30% reduction.[5] Consequently a phase 3 trial was designed, in formal consultation with the MHRA, which aimed to assess the benefit of continued treatment for patients who achieved success in a therapeutic trial.[6] The trial therefore incorporated a formalised 4-week therapeutic trial period prior to randomisation to allow patients with the capacity to respond to treatment to be identified. 572 patients with MS and refractory spasticity all received single blind Sativex for four weeks. After four weeks on active treatment 272 met the entry criterion of a reduction of at least 20% on the spasticity symptom NRS. 241 of these patients were then randomised to either continue to receive active or switch to placebo for the 12 week double-blind phase, for a total of 16 weeks treatment overall. The mean change in spasticity 0-10 NRS at the end of the single-blind treatment with Sativex was a decrease (improvement) of 3.01 points. During the double-blind phase	Neurological Disease which is due for publication in October 2012.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				the mean NRS scores for patients receiving Sativex further improved whereas a deterioration of 0.81 units (from a baseline of 3.92) was seen in the placebo group. At the end of the 12 weeks, the estimated treatment difference between the 2 groups in the mean spasticity NRS was 0.84 points (95% CI -1.29, -0.40) p=0.0002. During the double-blind phase the overall adverse event rate was similar between Sativex and placebo. The most common adverse events in the Sativex group were vertigo, fatigue, muscle spasms and urinary tract infection. This trial design reflects the proposed clinical practice, and in principal the results should be a fair reflection of effectiveness in the population treated with Sativex in clinical practice. Overall, 74% of patients with a successful trial of therapy went on to be responders (equivalent to feeling "much improved") on Sativex (compared with 51% on placebo). In the clinical setting, where these patients had exhausted conservative treatment options, this response rate indicates that Sativex can be a useful addition to the therapeutic armamentarium. Various secondary endpoints, notably sleep quality, were also improved on Sativex. Of particular interest in this study was the observation that the Barthel Activities of Daily Living Index was significantly improved on Sativex compared with placebo, indicating functional improvement. The benefit of continued treatment in the long-term was studied in a placebo controlled, parallel group, randomised withdrawal trial in subjects taking long-term Sativex (at least 12 weeks).[7] Thirty six patients with a mean duration of Sativex use prior to the trial of 3.6 years were randomised to	

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				either continue with Sativex treatment or switch to placebo for 28 days. The primary endpoint was time to treatment failure, defined as the time from the first day of randomised treatment to a 20% increase in NRS or premature withdrawal from randomised treatment. Those randomised to placebo reached treatment failure significantly faster than those on Sativex (p=0.013) Treatment failure was experienced by 94% of placebo patients and 44% of Sativex patients, hazard ratio 0.335 (95% CI 0.16, 0.69). This trial shows that the effect of Sativex on spasticity is maintained with long-term use, and it also shows that there is no evidence of a withdrawal syndrome in those subjects who stopped Sativex, despite a prolonged period of time on treatment. The results are consistent with previously published open-label long-term studies showing maintenance of clinical effectiveness[8]. In commenting on the results of this study, the MHRA Clinical assessor commented "*Robust evidence of long-term efficacy of Sativex in the relief of spasticity in MS patients , (which was lacking in the previous application), is provided by the new placebo controlled, parallel group, randomised withdrawal study GWSP0702"* A questionnaire survey, designed in consultation with the MS Trust, was sent to patients with MS who had been receiving Sativex for a median of 27 months. Results showed that patients report a reduction in the number of visits to the doctor, a reduction in the number of physiotherapy visits, a reduction in the use of concomitant medication, and an overall improvement across 15 activities of daily living[9].	

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				Furthermore, the number of falls requiring medical attention was low (at 4%) compared with recently published UK reference groups. These results suggest that health service utilisation is reduced in people with advanced MS treated with Sativex for their spasticity. The survey also showed that Caregivers experienced an improvement in their sleep quality. **Other Symptoms of MS.** **There are 2 notable absences from this section of the guideline, with regard to their pharmacological management. Both chronic neuropathic pain and bladder dysfunction are causes of substantial disability, and both are conventionally treated with medicines, as well as with other non-pharmacological interventions. Sativex has been reported to be of value in both these areas.** 24. **Central neuropathic pain.** Data from randomised controlled clinical studies, published in peer-reviewed medical journals, indicates that Sativex provides significant relief of central neuropathic pain in people with MS. The extent of available data is substantially greater than that available to support the use of gabapentin in the treatment of spasticity for example. Rog et al[10] studied compared Sativex with placebo as	

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				add-on therapy in 66 patients with central neuropathic pain due to MS. In all patients, other analgesic medications, (including strong opioids) had not provided adequate relief from pain. Results showed that treatment with Sativex reduced mean baseline pain severity by 2.4 units from a baseline of 6.5, a mean improvement of 37%. This was significantly superior to placebo (p=0.003). The authors concluded "Cannabis-based medicine (Sativex) is effective in reducing pain and sleep disturbance in patients with MS-related central neuropathic pain, and is generally well-tolerated." The same authors continued to follow the patients and were able to document maintenance of pain relief and sleep improvement over a 2 year period of continuing treatment[11]. 25. **Overactive Bladder**. Bladder instability is a common problem in people with MS. A small pilot study conducted at The Institute of Neurology showed Sativex to have potential to improve bladder symptoms[12]. Subsequently Kavia et al reported the results of a randomised controlled study in 135 patients with advanced MS and bladder problems[13]. They showed significant improvements (compared with placebo) in urinary frequency, nocturia, bladder symptom severity and patient global impression of change.	

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				1. GW Pharma Ltd. Sativex Summary of Product Characteristics. 2011 2. Wade DT, Collin C, Stott C, Duncombe P. Meta-analysis of the efficacy and safety of Sativex (nabiximols), on spasticity in people with multiple sclerosis. *Mult Scler* 2010; 16(6):707-714. 3. Collin C, Davies P, Mutiboko IK, Ratcliffe S. Randomized controlled trial of cannabis-based medicine in spasticity caused by multiple sclerosis. *Eur J Neurol* 2007; 14(3):290-296. 4. Collin C, Ehler E, Waberzinek G, Alsindi Z, Davies P, Powell K et al. A double-blind, randomized, placebo-controlled, parallel-group study of Sativex, in subjects with symptoms of spasticity due to multiple sclerosis. *Neurol Res* 2010; 32(5):451-459. 5. Farrar JT, Troxel AB, Stott CG, Duncombe P, Jensen MP. Vailidity, Reliability and Clinical Importance of Change in a 0-10 Numeric Rating Scale measure of spasticity: a post-hoc analysis of a randomised, double-blind, placebo-controlled trial. Clin Ther. 2008; 30: 974-985. 6. Novotna A, Mares J, Ratcliffe S, Novakova I, Vachova M, Zapletalova O et al. A randomized, double-blind, placebo-controlled, parallel-group, enriched-design study of nabiximols* (Sativex®), as add-on therapy, in subjects with refractory spasticity caused by multiple sclerosis. *Eur J Neurol* 2011; 18(9):1122-1131.	

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				7. Notcutt W, Langford R, Davies P, Ratcliffe S, Potts R. A placebo-controlled, parallel-group, randomized withdrawal study of subjects with symptoms of spasticity due to multiple sclerosis who are receiving long-term Sativex(R) (nabiximols). *Mult Scler* 2012; 18(2):219-228. 8. Notcutt W. A questionnaire survey of patients and Carers of Patients Prescribed Sativex as an unlicensed Medicine. Prim HealthCare Res Dev Journal. 2012 (in press). 9. Wade DT, Makela PM, House H, Bateman C, Robson P. Long-term use of a cannabis-based medicine in the treatment of spasticity and other symptoms in multiple sclerosis. Mult Scler. 2006 Oct;12(5):639-45. 10. Rog DJ, Nurmikko TJ, Friede T, Young CA. Randomised controlled trial of cannabis-based medicine in central pain in multiple sclerosis. Neurology. 2005; 65: 812-819. 11. Rog DJ, Nurmikko TJ, Young CA. Oromucosal THC/CBD for neuropathic pain associated with multiple sclerosis:an uncontrolled, open-label, 2 year extension trial. Clin Ther. 2007; 29: 2068-2078. 12. Brady CM, DasGupta R, Dalton C, Wiseman OJ, Berkley KJ, Fowler CJ. An open-label pilot study of cannabis based extracts for bladder dysfunction in advanced multiple sclerosis. Mult Scler. 2004; 10: 425-437. 13. Kavia RBC, De Ridder D, Constantinescu CS, Stott CG, Fowler CJ. Randomised ciontrolled trial of Sativex	

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				to treat detrusor overactivity in multiple sclerosis. Mult Scler. 2010; 16: 1349-1359.	
SH	G W PHARMACEUTICALS PLC	3	4.3.1	**g)** Gabapentin is not licensed for the management of spasticity.[14] Recommendations regarding off-label or unlicensed medicines should only be made where an appropriate licensed alternative would not meet the patient's needs to avoid conflict with the professional codes and ethics of healthcare professional statutory bodies.[15,16] 14. BMJ Group and the Royal Pharmaceutical Society of Great Britain. British National Formulary 63. March 2012. 15. General Medical Council (GMC). Good practice in prescribing medicines - guidance for doctors. September 2008. http://www.gmc-uk.org/static/documents/content/Good_Practice_in_Prescribing_Medicines_0911.pdf 16. Nursing & Midwifery Council. Standards of proficiency for nurse and midwife prescribers. June 2006. Available at: http://www.nmc-uk.org/Documents/Standards/nmcStandardsofProficiencyForNurseAndMidwifePrescribers.pdf	Thank you for your comment and references. We include careful consideration of medicine licensing when making recommendations.
SH	G W PHARMACEUTICALS PLC	4	4.3	In light of the findings of the national audit of services for people with multiple sclerosis (2011)[1] highlighted on page 3 of the scope, it is particularly important that access to specialist	Thank you for your comment. Clinical guidelines make recommendations for clinical and cost effective treatment.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				neurological and neurological rehabilitation services is covered by this guideline. 1. The Royal College of Physicians and the Multiple Sclerosis Trust. The national audit of services for people with multiple sclerosis. 2011. Royal College of Physcians Website. [cited 23/05/2012]; Available from: URL:http://www.rcplondon.ac.uk/sites/default/files/ms_audit_national_report_2011_0.pdf	NICE clinical guidelines do not have a role in ensuring appropriate availability of services locally. NICE has an implementation team who support the dissemination of the guideline and MS is on the list of Quality Standards referred to NICE.
SH	G W PHARMACEUTICALS PLC	5	4.4	**d)** Consideration should be given to the fact that symptomatic treatments may be better measured by patient reported outcomes as opposed to clinician- related measurements which may not give an accurate representation of the patient experience of spasticity or be sensitive to changes that are meaningful to the patient.[17] A Cochrane review of anti-spasticity agents for multiple sclerosis suggests "under implications for research" that assessment tools developed for spasticity and other components of the upper motor neurone syndrome should correspond to the daily patient experience of spasticity.[18] 17. Farrar JT, Troxel AB, Stott C, Duncombe P, Jensen MP. Validity, reliability, and clinical importance of change in a 0-10 numeric rating scale measure of spasticity: a post hoc analysis of a randomized, double-blind, placebo-controlled trial. *Clin Ther* 2008; 30(5):974-985. 18. Shakespeare DT, Boggild M, Young C. Anti-spasticity agents for multiple sclerosis. *Cochrane Database Syst*	Thank you for your comment. We have added patient reported outcomes to the list

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				Rev 2003;(4):CD001332.	
SH	Humber NHS Foundation Trust	1	4.1.2	I am commenting on this area as in my sub group at the scoping exercise we had a consultant who specialised in MS in paediatrics. This was not an area that I was previously aware of, however I feel it is worthy of consideration in the guidelines as this population will move into adult services and if their needs are dealt with appropriately when they are children there is likely to be less secondary complications when moving to adult services. It will also allow for consistency of services between adult and paediatric services.	Thank you for your comment. We recognise the problems that children may have in terms of diagnosis and management and have carefully considered the guideline population. Following consideration of stakeholder comments we have altered the guideline population to people of 18 years and over only. We considered we could not adequately address the needs of younger people with MS within this guideline. As your comment indicates making recommendations for people under 18 years requires a different approach and include different GDG constitution, reviews of different evidence and consideration of licensing issues in under 18s.
SH	Humber NHS Foundation Trust	2	4.3.1 e	I am keen to see a greater acknowledgement of the role that specialist seating and postural management can play in the management of MS. Correct seating can have a positive effect on pain, tremor, fatigue, pressure care and spasticity.	Thank you for your comment**.** We will examine the effectiveness of programmes of care for these problems. We do not intend to specify the individual components as consider these will need to be individualised to each patient by their therapist.
SH	Humber NHS Foundation Trust	3	4.3.2 b	I would query as to the non inclusion of contractures as this can cause a great deal of pain, distress and ultimately	Thank you for your comment. The prevention of contractures will be

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				difficulty in completing basic activities of daily living such as dressing and feeding if not well managed. It can also cause pressure damage depending on the area of the contracture, so I feel it is worthy of inclusion due to the wider implications.	included in 4.3.1 (e) and 4.3.1 (g)
SH	Humber NHS Foundation Trust	4	4.3.3 d	As stated above in regard to seating, this can play a critical role in the management of pressure care and there needs to be a greater emphasis on good seating and positioning early on in the disease process so intervention can be proactive rather than reactive.	Thank you for your comment. This guideline is currently being updated.
SH	Medtronic Ltd	1	4.3.1 g	• Medtronic thanks NICE for the opportunity to comment on the scope and we are in agreement with the inclusion of baclofen in the pharmacological management of spasticity. • Although not specifically mentioned within the scope can NICE confirm that the mode of baclofen delivery will include continuous intrathecal infusion which is currently used in the management of the MS patient.	Thank you for this information. Baclofen is included in the scope and we will agree with the GDG which method of delivery of baclofen to include.
SH	Multiple Sclerosis Society	1	General	This is an MS Society submission endorsed by the following Royal Colleges and Professional Bodies: • **College of Occupational Therapists** • **Chartered Society of Physiotherapy** • **Royal College of Nurses** • **Sue Ryder Care** • **UK MS Specialists Nurses Association**	Thank you for your comments and information.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
SH	Multiple Sclerosis Society	2	General	**Introduction** The MS Society welcomes the opportunity to offer our comments on the draft consultation scope for 'Multiple Sclerosis: the management of multiple sclerosis in primary and secondary care'. We hope that our comments will be helpful. This consultation response builds on several major pieces of work; the MS Society's light touch review submitted to NICE in December 2010 (MS Society Review of MS Clinical Guideline, submitted Dec 2010), the MS Society's response to the NICE consultation on "Review of Clinical Guideline (CG8) – Multiple Sclerosis" submitted in May 2011, and a one day workshop with over 30 health and social care professionals, including people affected by MS. Consensus was sought on all areas for inclusion in the scope; from initial diagnosis and access to disease modifying treatments to diagnosis and management of symptoms, rehabilitation, access to specialists to integration between health and social care. The MS Society has also sought the views of our team of medical advisors who have extensive expertise, experience and knowledge of MS. This submission is endorsed by the following Royal Colleges and Professional Bodies: • **College of Occupational Therapists** • **Chartered Society of Physiotherapy** • **Royal College of Nurses**	Thank you for your comment.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				• **Sue Ryder Care** • **UK MS Specialists Nurses Association** The review and update of the MS clinical guideline is an opportunity for NICE to produce an integrated guideline covering both health and social care; a guideline that is forward looking and able to support best practice in the coming years and not simply a reflection of the status quo. The MS Society has written to NICE regarding the opportunity to produce an integrated health and social care guideline (Appendix A). This proposal of an integrated guideline is supported by the UKMSSNA, Royal College of Nurses, the Royal College of Psychiatrists, Sue Ryder Care, Carers UK and the Carers Trust.	
SH	Multiple Sclerosis Society	3	general	**Executive Summary** Whilst we are encouraged to see some of our comments shared at the scoping workshop taken on board, we are concerned that there are still some outstanding issues to be addressed. These issues are summarised below. • **Integration.** Due to the complex needs of people with MS we strongly advocate the need for an integrated guideline. A guideline which sets out best practice for joint-working between health and social care would help ensure the coordination of services and seamless care. The integrated guideline for Dementia (CG42, 2011) has set a precedent. NICE will formally take on the remit of developing guidance in social care in 2013; given the remit of NICE will be extended to social care we believe the MS guideline should reflect this.	Thank you for this summary of your comments. We have responded to each comment individually where they are outlined in more detail. Please see the responses made in each section to the more detailed comments made by the MS society.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				• **Treatment.** The guideline needs to address the large variation in prescribing practice that exists across the country with the inclusion of a full list of current first and second line treatments. Furthermore, we recommend that NICE should work with the MS Society, the Association of British Neurologists (ABN) and the UK MS Specialists Nurses Association to develop a treatment pathway to reflect the real options that clinicians have when prescribing. • **Population.** The MS Society disagrees that the guideline should only be for those aged 16 and above. We believe all those affected by the condition should have access to the same support regardless of age. A decision against this would be regarded as discriminatory. • **Diagnosis.** The diagnosis criteria should be updated to reflect the revised McDonald criteria and to include information on how a diagnosis should be given and by whom. • **Maintaining independence.** The provision of appropriate equipment and the opportunity to engage in leisure, vocational and social activities is vital if people are to retain maximum independence and the impact on carers to be minimised. Currently the draft scope makes no reference to equipment, adaptations and personal support.	

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				• **Rehabilitation.** Timely rehabilitation is essential for disability management and the maintenance of independence. It should be an ongoing service that is provided to those who need it, tailored to individual personal goals, and at timely points in the life course of the condition e.g. following relapses or after progression of the condition in secondary progressive multiple sclerosis (SPMS) or primary progressive multiple sclerosis (PPMS) which might require additional rehab. Continued…..	
SH	Multiple Sclerosis Society	3	general	Continued… • **MS Specialists.** People with MS should be able to access a comprehensive multi-disciplinary team which includes a range of MS specialist services. The new guideline should make greater reference to MS specialists; providing a definition of who they are, the role they fulfil and the expected standard. Within the specialist team there should be a lead coordinator who would act as a single point of contact. This would ensure joint-working and lead to a seamless experience of care. • **Management of symptoms.** People with MS experience a range of symptoms throughout the life course of the condition. Many of these, in particular fatigue and spasticity, are treated with pharmacological management but can also be treated with non-pharmacological management programmes such as CBT for fatigue and or depression and physiotherapy for spasticity. The scope of	We have responded to each comment individually where they are outlined in more detail. Please see the responses made in each section to the more detailed comments made by the MS society

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				the guideline should fully consider both non-pharmacological and pharmacological management of the condition. Whilst the draft scope does cover the wide range of symptoms that can be experienced by people with MS, pain, swallowing issues and sexual dysfunction are currently not included and we would expect them to be reviewed. In order to self manage effectively people affected by MS need appropriate information, tools, the opportunity to learn about self-management, support and a named point of contact. • **Families and Carers**. Currently there is a lack of information guidance on how to support the specific needs of the family of people with MS and their carers. Access to support and information needs to be readily available. • **Main outcomes.** We agree with the main outcomes listed in the draft scope but would advocate the inclusion of a range of additional outcomes. This includes: o A record of the case load of the MDT o The percentage of people with a definitive diagnosis of MS within 12 weeks of a GP referral o The percentage of people with MS with an	

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				agreed care plan ○ The percentage of people with a named point of contact ○ The percentage of people with MS experiencing a significant and disabling relapse referred to an MS specialist services within 48 hours ○ We would also want to see the impact on carers included as a main outcome ○ Maintenance or improvement in quality of life of people with MS and their carers	
SH	Multiple Sclerosis Society	4	General	**1) Integration** As the remit of NICE extends to include social care, this presents an opportunity to include social care within the update of the Guideline. The Clinical Guideline on Dementia (CG42, 2011) is a best practice example in that it was the first to cover health and social care; indeed, NICE are now committed to developing a Quality Standard for dementia focussing on social care. A precedent has been set and we believe that due to the complex care needs of people with MS; the need for integrated, timely and responsive care; and prevention of unnecessary hospital admission during a crisis, the same logic should apply to MS. **Rationale:** For people affected by MS integration between health and social care is essential. The government is encouraging integration between health and social care to result in better outcomes for individuals. In order for integration to become a	We have responded to each comment individually where they are outlined in more detail. Please see the responses made in each section to the more detailed comments made by the MS society.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				reality, there needs to be joint commissioning and integrated guidelines. There are trigger points when this is particularly important including: • Discharge from hospital • Preventing avoidable harm, particularly during a relapse; in more advanced stages of secondary progressive MS; and for those with primary progressive MS • Providing emotional, health and wellbeing support to carers and extended family, as well as the individual There are already existing indications within the guideline to social care, this presents a base on which to build and improve coordination across health and social care organisations: "All parts of the healthcare system, social services and other statutory services should have agreed protocols that specify: • how responsibility for people with MS is shared with other groups or organisations to prevent duplication • what agreed descriptive information (that is, a common dataset) about the person with MS should always be shared • the point of contact within any service or organisation, and how contact should be made." (p. 11, CG08, 2003) In addition, social workers are currently included as part of the multidisciplinary team that all people with MS should be	

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				able to access. To ensure effective integration this guideline must be extended to include recommendations on social care. Continued…	
SH	Multiple Sclerosis Society	4	General	Building on the precedent set by the Dementia guideline, we have considered the principal areas in the dementia guideline that we believe would map onto the care of multiple sclerosis and suggest the following: • The rights of carers to access psychological therapy and assessment of their psychological and emotional needs • Integrated working across all agencies involved in the treatment of people with MS including jointly agreed policies, procedures and goals. Improved cross organisational communication and teamwork across health, social care, benefits and employment, mental and physical health, community and acute settings can help maintain and optimise the quality of life of people with and affected by MS. • The inclusion of local service users and carers in joint planning • Care plans to coordinate all aspects of health and social care needs agreed by health and social services. Care plans should consider the changing needs of the person with MS and his or her carer's needs. This would include environmental	We have responded to each comment individually where they are outlined in more detail. Please see the responses made in each section to the more detailed comments made by the MS society

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				modifications to aid independent functioning, assistive technology, and advice from an occupational therapist, clinical psychologist and physiotherapists. A care plan should include support for people to participate in activities they enjoy • Care plans should have a named health and/or social care staff to coordinate the care plan; ownership of the care plan should be held by the individual or their carer(s); establish formal reviews of the care plan, at an agreed frequency between professionals involved and the person with MS and/or carers and recorded in the notes • Appropriate training in MS for all professionals in health and social care in regular contact with people with MS • Comprehensive range of respite/short-break services to meet the needs of the person with MS and their family and/or carer. • Information about direct payments and individual budgets • Information about the statutory difference between NHS care and care provided by local authority social services (adult services) so that they can make informed decisions about their eligibility for NHS Continuing Care Employment needs to be included as an overarching consideration with vocational rehabilitation as part of the MDT. Consideration needs to be given to refer to a trained Disability Employment Advisor, benefits reviews and referral	

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				back to health and social care support.	
SH	Multiple Sclerosis Society	5	General	For children with MS, education needs to be considered. Children should have access to educational psychology assessments and support, so that they can reach their full potential, and later a suitable vocation.	We have responded to each comment individually where they are outlined in more detail. Please see the responses made in each section to the more detailed comments made by the MS society
SH	Multiple Sclerosis Society	6	General	The move from child to adult services is currently disjointed. Specific guidance is required to improve the transition from childhood to adulthood, as well as to end of life care; also life changes such as pregnancy, marriage, jobs and homes. Joint working and communication to ensure continuity of care when someone moves to a new area is particularly important.	We have responded to each comment individually where they are outlined in more detail. Please see the responses made in each section to the more detailed comments made by the MS society
SH	Multiple Sclerosis Society	7	General	The sections on communication and the specific needs of people affected by MS need to be more prominent. We agree that the guideline on patient experience should be referred to but we strongly recommend that the specific requirements of people with MS are referred to within the MS guideline. This is particularly important when considering both visible and invisible symptoms that health care professionals should be aware of when communicating with people affected by MS.	We have responded to each comment individually where they are outlined in more detail. Please see the responses made in each section to the more detailed comments made by the MS society
SH	Multiple Sclerosis Society	8	General	There is a lack of information and guidance on how to support the family and carers, including young carers. Whilst the guideline aims to improve outcomes for carers and families it is difficult to see how this will be achieved unless there is	Thank you for your comment. The impact of carers has been added to the structured reviewed in 4.3.1 (b), Section 4.3.1 (c) includes information

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				guidance. Health and social care professionals need to be accessible to and supportive of carers' and family needs at every point of contact. Access to support and information needs to be readily available. Carers need to be viewed as expert care partners and included. For example: "Family members (including any schoolchildren) living in the same house as the person with MS, and any family members delivering substantial support even if living elsewhere, should be supported by: • asking about their physical and emotional health and well-being, especially in the case of children aged 16 years or less, and offering advice and referring on for additional support if necessary • providing them with general factual information about MS; this should only be extended to include more specific information related to the person with MS with the permission of that person • ensuring that they are willing to undertake support of personal activities of daily living (such as dressing and toileting), are safe and competent at such tasks, and that the person with MS is happy for them to provide such assistance • informing them about social services carer assessment and support procedures. (CG08, p.7, 2003)	and support for patients and carers. We will refer to the Carers (equal opportunities) act 2004. Thank you for this information.
SH	Multiple Sclerosis	9	3.2 c	**Current practice**	Thank you for your comment. The

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
	Society			As outlined in the scope in section 3.2.c) "The coordination of the assessment and treatment of often complex needs and symptoms is pivotal for high quality care". We agree with this statement and as such it is important that the guideline includes a list of current first and second line treatments. The guideline should also include best practice on discussing the risks and benefits of treatments with the individual, their family and potentially their carer. There is variation in prescribing practice between MS specialist centres across the UK (MS 2015 Vision Report, 2011) with some centres regularly prescribing more aggressive treatments, and others prescribing first line treatments. The update of the guideline presents an opportunity to provide clarity regarding what to prescribe, when to prescribe and when it is appropriate to stop prescribing. We would strongly encourage NICE to defer to the prescribing guideline of the Association of British Neurologists, and to work with the MS Society, the ABN and the UKMSSNA to develop a treatment pathway for MS. There is even greater variation in prescribing practice in children. Many paediatric neurologists are not familiar with these drugs and therefore, many are reluctant to prescribe them. Optimal and timely treatment as recommended by the International (Chitnis et al, 2012 *Mult Scler.* 18(1):116-27)	guideline will refer to related Technology Appraisals when available. In the areas included in the scope we will endeavour to provide clear guidance on first and second line treatments. We will refer to both NICE Patient Experience guidance and NICE Medicines Adherence guideline, both of which provide more comprehensive recommendations on communication about medicines and risk than could be covered in this guideline. Information and support for patients and carers is included in this guideline and we will include any additional MS specific area the GDG consider important. NICE develops recommendations using clinical and cost effectiveness reviews of evidence and would not usually defer to guidelines of other organisations. We recognise the problems that children may have in terms of diagnosis and management and have carefully considered the guideline population.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				and European MS group (Ghezzi et al, 2010 *Mult Scler.*16 (10):1258-67) are often initiated only in a small number of patients e.g. disease modifying treatment (various interferons and glatiramer acetate) in children with multiple sclerosis. These drugs are prescribed off label as they are unlicensed for children (usually under 18), thus requiring a time consuming process of securing local commissioning approval for funding. Treatment is inevitably delayed. Indeed some children may not be offered treatment, whilst others may have been started o a treatment which is no longer used as first line treatments for adults e.g. azathioprine, because of easier availability. There is a clear need for an MS treatment pathway that seeks to incorporate: • those treatments approved by NICE • those treatments that are licensed for MS but have not been through a NICE appraisal such as botulinum toxin, fampridine and sativex • those medicines covered by the MS Risk Sharing Scheme • those treatments that are not licensed for MS but used in clinical practice such as alemtuzumab and mitoxantrone.	Following consideration of stakeholder comments we have altered the guideline population to people of 18 years and over only. We considered we could not adequately address the needs of younger people with MS within this guideline. Making recommendations for people under 18 years requires a different approach and include different GDG constitution, reviews of different evidence and consideration of licensing issues in under 18s. NICE will develop a NICE pathway which links recommendations from this guideline, other related NICE guidelines and TAs.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				• the treatment pathway should include off licence DMT treatments for under 16s.	
SH	Multiple Sclerosis Society	9	3.2 c	A treatment pathway needs to reflect the real options that clinicians have when prescribing. Incorporating all relevant guidance into one place would be advantageous and help to improve implementation of the recommendations. We would not expect or wish for an update of technology appraisals but we would expect to see them all referenced within the guideline and included in the pathway to provide clinicians with a recommended approach. Given that we are expecting treatments to increase in the coming years it will be important that the recommendations are kept up to date with newly licensed treatments and not just those appraised by NICE. As outlined above, one approach would be for NICE to defer to the ABN prescribing guideline. We also strongly recommend that NICE work with the MS Society and other professional bodies to develop an accredited treatment pathway. **Updated ABN guidance:** The most recent Association of British Neurologists prescribing guidance should be included and reflected in all guidance and publication. The Risk Sharing Scheme currently uses 2001 ABN guidance. **New Evidence:** There is new evidence on the effect of early versus delayed treatment in addition to further publications on the Risk Sharing Scheme.	Thank you for your comment and information about updated ABN guidance. NICE will produce a NICE pathway which will include all related NICE guidelines, and all relevant technology appraisals in one place. We acknowledge the importance of keeping recommendations up to date and that new options for treatment are likely to become available in the coming years. NICE would not usually defer to guidelines from another organisation and develops recommendations using reviews of evidence. We are unable to include drugs in the guideline when those drugs are not licensed, or not in common use or where there is not evidence of their effectiveness. As such we cannot include very new drugs. We are not planning to review any disease modifying treatments but are including drugs not licensed for MS in

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				New Treatments: There are a number of new treatments that have been developed and approved since the original guideline; Gilenya, Extavia and Tysabri are the most notable. The guidance on these treatments should be cross referenced in the updated guideline. There are also other drugs in the pipeline such as Alemtuzumab, laquinimod, BG-12 and Teriflunomide which do not yet have a licence but are expected to apply. These drugs should be considered for inclusion in the guideline and or referencing. In addition, there are drugs which do not have a licence for MS but are used in the treatment and care of someone with MS. This should be acknowledged in the update of the guideline and include reference to treatments such as mitoxantrone, azathioprine and IVIg. In order to provide comprehensive information and to reduce variation in prescribing practice, all this information needs to be included or referenced.	scope where appropriate.
SH	Multiple Sclerosis Society	10	3.2 d	New evidence is also available regarding physiotherapy: *Management of the Ataxias: Guideline towards Best Clinical Practice, 2009, Ataxia UK; Treatment of Ataxia in MS, 2009, Mills et al.* and regarding rehabilitation: *Medical rehabilitation in 2011 and beyond Report of a joint working party of the Royal College of Physicians and the British Society of Rehabilitation Medicine, November 2010; Winchcombe M.,*	Thank you for your comment and this information.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				(2012) A life more ordinary: Findings from the Long-Term Conditions Research Initiative. An independent Overview Report for the Department of Health: Research Initiative for Long Term Neurological Conditions.	
SH	Multiple Sclerosis Society	11	3.2 e	The recent National Audit Office (NAO) report highlights the lack of integration, generally, not just within health. For this reason we believe that social care should be included within the scope of the guideline. The need for improved integration extends beyond health and it will not happen unless there is guidance to drive improvement in practice. The Public Accounts Committee has asked the NAO to return to the topic before the end of parliament so that the PAC can review the impact of the lessons learned. NICE has a key role in bringing about improvement in integration and service provision. Unless social care is included within the scope of the guideline it is difficult to foresee how this improvement will be realised.	Thank you for your comment. The remit from the Department of Health is for a clinical guideline for the management of MS in primary and secondary care and does not include social care or public health. We acknowledge the importance of social care for people with MS and anticipate that some of the interventions we recommend may be delivered by social care depending on local arrangements. As NICE will have a remit for social care from April 2013, NICE is considering how best to address the issues of integration of heath and social care.
SH	Multiple Sclerosis Society	12	4	**The guideline** We would strongly encourage NICE to engage in further discussions with the Department of Health regarding the remit of the MS clinical guideline. We strongly advocate for the inclusion of social care within the scope to enable the government to turn its rhetoric of integration into action.	Thank you for your comment. We acknowledge the importance of social care for people with MS and anticipate that some of the interventions we recommend may be delivered by social care depending on local arrangements. As NICE will have a remit for social care from April 2013, NICE is considering how best to address the issues of integration of heath and social

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
					care.
SH	Multiple Sclerosis Society	13	4.1	**Population** The MS Society disagrees that the guideline should only be for those aged 16 and above. Recent studies report an annual incidence figure for the first demyelinating event (i.e. clinically isolated syndrome) is 9.83 children per million in the UK (Absoud et al., *Multiple Scelrosis Journal* , April 2012). Studies have also shown that around 5% of people diagnosed with MS in their adulthood actually experienced their first MS symptom in childhood. We believe that all those affected by the condition should have access to the same support regardless of age. Any decision against this would give us cause for concern regarding discrimination. **Specific issues to be addressed in children with MS.** Delay in diagnosis in children with acquired demyelinating disorders, in particular Multiple Sclerosis, and access to specific therapies are issues identified (in the UK National MS Society Meeting, London 2007). To address these significant shortfalls, the guideline needs to be a resource for : 1. Early and rapid diagnosis 2. Optimal Management enabling treatment when appropriate 3. Provide a resource to support professionals	Thank you for your comment. We recognise the problems that children may have in terms of diagnosis and management and have carefully considered the guideline population. Following consideration of stakeholder comments we have altered the guideline population to people of 18 years and over only. We considered we could not adequately address the needs of younger people with MS within this guideline. As your comment indicates making recommendations for people under 18 years requires a different approach and include different GDG constitution, reviews of different evidence and consideration of licensing issues in under 18s.
SH	Multiple Sclerosis Society	14	4.2	**Healthcare setting** We believe that this should extend to settings where there is a provision of social care as well, in line with an extended remit to include social care.	Thank you for your comment. The remit from the Department of Health is for a clinical guideline for the management of MS in primary and secondary care and

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
					does not include social care or public health. We acknowledge the importance of social care for people with MS and anticipate that some of the interventions we recommend may be delivered by social care depending on local arrangements. As NICE will have a remit for social care from April 2013, NICE is considering how best to address the issues of integration of heath and social care.
SH	Multiple Sclerosis Society	15	4.3.1 a	**Key clinical issues that will be covered** **Diagnosis, assessment and information** We agree with the decision to review the diagnostic criteria, including neuromyelitis optica and appropriate investigation for people with clinically isolated syndrome (CIS). The updated guideline should incorporate treatment options for those with CIS including immediate referral to an MS nurse for those at high risk of developing MS. Diagnosis criteria should reflect the revised McDonald criteria. Given the importance of MRI for application of these criteria, the updated guideline should also include guidance on scanning protocols for MS. The diagnosis of children with MS should be addressed, as the diagnosis is often delayed. Doctors looking after children do not necessarily consider MS as a possible diagnosis, leading to delayed diagnosis. This is likely to reflect lack of familiarity in this relatively uncommon group. In children,	Thank you for your comment. Clinically isolated syndrome will be included in the review for update of NICE technology appraisal TA32 on Beta interferon and glatiramer acetate for the treatment of multiple sclerosis. The guideline will review of the role of the MS nurse

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				conditions which share some symptoms with MS occur more frequently than in adults. Therefore, when deciding whether a child has MS or another condition ("the differential diagnosis") it is more complex than in adults. Treatments of other recurrent non MS demyelination provide further challenges. The guidance should outline primary and secondary treatment options in line with ABN recommendations. There should also be a recommendation on how diagnosis should be given and by whom, i.e. a consultant neurologist with a special interest in MS and recommendation to refer to an MS nurse for a follow up appointment.	We have carefully considered the inclusion of children and adolescents in the guideline. Following consideration of stakeholder comments we have altered the guideline population to people of 18 years and over only. We considered we could not adequately address the needs of younger people with MS within this guideline. Making recommendations for people under 18 years requires a different approach which would include a different GDG constitution, reviews of different evidence and consideration of licensing issues in under 18s. Thank you for your suggestion about outlining treatment options. NICE makes recommendations on the basis of clinical and cost effectiveness reviews carried out for the guideline.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
					Diagnosis is included in the scope as is information and support for patients and carers. We will discuss with the GDG whether they wish to make a recommendation about who gives a diagnosis. The role of the MS nurse is also included in the scope.
SH	Multiple Sclerosis Society	16	4.3.1 b	We agree with the recommendation, however, in addition to the examples given we would expect to see: a specific review of mobility and the following activities: **Vocational activities:** The current guideline provides guidance on vocational activities, including employment, education and voluntary work. The new guideline needs to outline the support and assessments by the appropriate specialists that people should expect in education and voluntary work as well as paid employment. Advice on strategies, equipment and services linked to vocational activities should be given, including information for employers and information on disability employment advisors when applicable. Services should also include vocational rehabilitation services and occupational therapists (Sweetland, J. et al (2007) "Vocational rehabilitation services for people with multiple sclerosis: what patients want from clinicians and employers", *Multiple Sclerosis* 13(9), 1183-1189.	Thank you for your comment and suggestions about appropriate review of people with MS. We have to prioritise what we cover in the guideline and have prioritised those areas where an assessment of the clinical and cost effectiveness evidence will inform care. People's individual needs in regard to areas such as vocational rehabilitation, leisure and social activities will be included in the structured review as in 4.3.1 (b) but we do not consider that there is any MS specific treatment to review. As NICE will have a remit for social care from April 2013, NICE is considering how best to address the

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				Leisure and social interaction: The new guideline should cover both vocational and leisure activities. It is important that people affected by MS, both individuals and their carers, are supported to continue leisure activities that they enjoy. The guideline should outline the support services that people should be able to access. Services should include occupational therapy and rehabilitation services to enable people to continue their leisure and social activities. **Activities of daily living**: The new guideline should outline comprehensive support and services that people should be able to access in order to maintain their independence and carry out daily living activities. This should include personal, domestic and community activities and a multidisciplinary assessment. There should be a person centred approach whereby the individual identifies the goals that they want to achieve and what is most important to them in a variety of settings. **Educational activities in children:** MS can lead to a range of symptoms but, in particular, it is fatigue, emotional and cognitive difficulties which are the symptoms which trouble children. Children with MS can struggle in education, and may need educational psychology or more extensive neuropsychometric assessment to support and develop coping strategies, so that they can reach their potential. As such there remains a need that even specialised tertiary paediatric neurology centres struggle to meet. Assessments for all people with MS should consider the	issues of integration of heath and social care. We have carefully considered whether children should be included in the guideline and have decided not to include people under 18 years as we feel we cannot do justice to their needs in this guideline. We have added the impact on carers to the structured review.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				support provided by family and carers, the limitation of this support and the wellbeing of those providing it.	
SH	Multiple Sclerosis Society	16	4.3.1 b	The assessment should result in an agreed care plan outlining the interventions, support and services that the individual and their carer needs. It is important that this includes the involvement of social services, for both social workers for assistance with care package assessment and for Social Services based occupational therapists for home equipment and adaptations. This should be reviewed at least annually but also if an individual experiences a relapse so that their changed needs can be picked up on and relevant treatment and support can be provided. **Equipment, adaptation and personal support:** The current scope makes no mention of equipment, adaptations and personal support. The provision of appropriate equipment is vital if people with MS are to retain their independence and minimise dependency on carers. The new guideline will need to consider equipment and the assessments of individuals' surroundings. Individuals should be supported to retain maximum independence and carers should be supported with training and information to allow them to care for the person with MS whilst not negatively impacting on their own health and wellbeing.	Thank you for your comment and for providing an outline of what an assessment should provide. We understand the issues faced by people who need access to equipment and services. NICE clinical guidelines provide recommendations based on clinical and cost effectiveness and do not have a role in ensuring appropriate availability locally.
SH	Multiple Sclerosis Society	17	4.3.1 c	We agree that the guideline should include information and support for patients and carers but we believe support for families should also be included as outlined in our general	Thank you for your comment. We will use the evidence review on information and support (section 4.3.1 (c)) and the

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				comments. Information given to people with MS should be given both orally and followed up in writing. Whilst we support the reference to CG138 we believe that it would be helpful to have an appendix, as in the current guideline, outlining key considerations when communicating. This section will also need to consider the appropriate timing of information given and how people can seek support when required. A key contact would be an effective way to support the needs of people over time. The amount and type of information given should be tailored to the person's need at the time to avoid overwhelming the individual during a time of great stress. There needs to be guidance on what information people with MS and their family and carers should be given and when this information should be provided e.g. at point of diagnosis. This should include information relating to self management, access to courses following diagnosis and guidance on changes in health which would warrant self referral and who to contact in those situations. Sources of further information such as contact details for relevant third sector and voluntary sector organisations should also be given to enable ongoing support. Information should also include additional support, employment and benefits information and respite care. The guideline should also encourage people to provide information on the MS register. The MS register[1] is an online	expertise of the GDG to consider the specific needs of people with MS and their carers in relation to information and support. Thank you for information about the MS register.

[1] The MS Register: www.ukmsregister.org

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				survey and a first of its kind. It seeks to combine information collated from people with MS, neurologists and data collected by the NHS to build a national picture of how MS affects each individual and what impact it has on lives. In doing so the MS register has the potential to transform the development and delivery of care and services for people with MS. The MS register will therefore be of significant use for commissioners when re-designing services and will also have an important role to play in the future implementation of the guideline.	NICE guidelines to not make reference within the recommendations to specific non NHS resources.
SH	Multiple Sclerosis Society	18	4.3.1 d	As well as immunisations and pregnancy, modifiable risk factors should also include information relating to stress, infections and surgery.	Thank you for your comment. Immunisation and pregnancy are included here as examples. The GDG will make the final decision as to which modifiable risk factors to include. We will include your suggestions in the discussion with them. The emphasis is intended to be on modifiable risk factors.
SH	Multiple Sclerosis Society	19	4.3.1	**Disability management and rehabilitation** **General:** Rehabilitation needs to focus on prevention, maintenance and optimal functionality for people with MS. Regular assessment by an MDT will encourage appropriate rehabilitation, maintenance and reablement with goal setting which is person centred and includes family and carers. Reassessment should also follow relapses and people should be able to self refer at a point of need. However, rehabilitation should not be restricted to when a person has a relapse but	Thank you for your comment. The appropriate setting for rehabilitation is included in the scope and the important outcomes will be agreed by the GDG. We will use your suggestions to inform the discussion. The performance of a structured review is included in the scope and will outline appropriate assessment. We will not

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				should be an ongoing service provided to those who need it. The rehabilitation team needs to be consistent with the MDT and take a holistic approach including an occupational therapist, physiotherapist, a continence nurse, neuropsychologist, speech and language therapist, dietician, rehabilitation nurses, psychologist, social worker, neurologist, GP, MS nurse and potentially third sector representatives. **General:** There is no mention of rehabilitation following acute episodes. We believe that, whilst it is important to outline the management of symptoms, it is important to ensure that there is guidance on the management and rehabilitation following relapses or change in capability. The guideline should outline the standard of care and support required by individuals including practical care, equipment and personal care. There should also be specific guidance on relapse referrals to specialist services to support rehabilitation (Craig, J, Young, C.A. Ennis, M., Baker, G. & Boggild, M (2003) "A randomised controlled trial comparing rehabilitation against standard therapy in multiple sclerosis patients receiving intravenous steroid treatmen", *Journal of Neurology, Neurosurgery & Psychiatry*, *74:1225-1230.* We would stress that this section needs to include relevant equipment, adaptations and personal support including both physical and occupational therapy. Examples of equipment that should be included within the guideline are functional electrical stimulation (FES) and other orthotic equipment, programmable baclofen pumps, home adaptations such as hoists supported by social services OTs, infra-red technology,	make specific recommendations about the structure of MDTs but will make recommendations about who should be providing interventions if the evidence review enables this. We are not making a distinction between acute rehabilitation and other rehabilitation. We have included a number of specific areas to evaluate that cover the management of particular symptoms in people with MS. We are including both disability management and rehabilitation. Clinical guidelines make recommendations on appropriate interventions based on clinical and cost

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				computerised technology, speech assisted technology, telecare, mobility aids, wheelchairs.	effectiveness reviews. Clinical guidelines do not have a role in ensuring appropriate availability in services locally.
SH	Multiple Sclerosis Society	20	4.3.1 e	Relating to the specific points as per section 4.3.1.e of the scoping document: **Fatigue:** The scope should include energy effectiveness, cognitive behavioural therapy based approaches, and exercise or physiotherapy and occupational therapy based energy conservation programmes options to manage fatigue (Mathiowetz VG, Finlayson ML, Matuska KM, Chen HY, Luo P (2005) "Randomized controlled trial of an energy conservation course for persons with multiple sclerosis", *Multiple Sclerosis*, 1(5): 592–601; Mathiowetz VG, Matuska KM, Finlayson ML, Luo P, Chen HY (2007) "One-year follow-up to a randomized controlled trial of an energy conservation course for persons with multiple sclerosis", *International Journal of Rehabilitation Research*, 30(4):305–313.).. **Spasticity:** We would want to see non-pharmacological management programmes to include rehabilitation and physiotherapy. We also note that the current guideline omits spasms and we would expect this to be rectified so that the section is entitled "Spasticity and spasms". Emphasis should be placed on a collaborative approach to treatment: pharmalogical and MDT options **Mobility:** exercise interventions, physical devices (e.g. FES,	Thank you for your comment and your suggestions for the guideline. We are not pre-specifying the components to include in the programmes on fatigue, mobility and spasticity and will be guided by the GDG and the evidence available. We consider that the treatment of spasticity to include treatment of spasms. We do not intend to look at specific interventions provided by therapists such as devices and orthoses. This degree of detail is beyond the scope of a guideline on MS and is likely to be

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				orthoses) and neuro-physiotherapy interventions will all have a role (e.g. stretching) and we would want these to be included in the guideline. **Pain:** the MS clinical guideline needs to address musculoskeletal pain incorporating all approaches – psychological, ultrasound, exercise, physiotherapy, devices, pharmacological approaches and complementary therapy including mindfulness to present a comprehensive and up to date guideline. **Self management:** • The guideline needs to improve the prevention, diagnosis, early intervention and management of symptoms. Appropriate treatment should be outlined through regular reviews by an MDT to re-assess an individual's symptoms and changes. This will reduce impact on the individual; improve chances of staying in employment; maintain or improve quality of life and reduce long term costs. Reviews need to take a holistic, lifestyle approach involving appropriate members of the MDT. In between reviews, access needs to be available through self-referral. • Guidance on adjustment after diagnosis, support and therapies on adjustment to change in MS. • MS and behaviour change approaches should be included within the guideline. • People with MS need an integrated care plan, across both health and social care. It should be held by the individual with MS to provide advance and	individual to each patient and best assessed by appropriate therapist using their professional knowledge. We recognise the importance of the areas you outline under self management for people with MS. We are unable however to include recommendations on all aspects of treatment for people with MS. We have had to prioritise what we cover in the guideline and have prioritised those areas where an assessment of the clinical and cost effectiveness evidence will inform care.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				preventative care planning and enable self management. This should be shared with whomever the person with MS would like to inform.	
SH	Multiple Sclerosis Society	20	4.3.1 e	• In order to self manage effectively individuals need to have a lead contact to provide answers to questions or concerns. Information needs to be given at appropriate points without overwhelming individuals at vulnerable times e.g. point of diagnosis. This might be given as a 'welcome pack' following admission. • Appropriate information, tools, and the opportunity to learn about techniques to effectively self manage and be an 'expert patient' addressing confidence and skills development to communicate, self manage and understand symptoms; support to apply the learning should be offered. MS and behaviour change approaches should be embedded within the guideline. • The role of the third sector, technology and peer to peer support should be considered within these recommendations. • Following the diagnosis of a symptom, a referral to the appropriate specialist should be made to confirm the diagnosis. • The guideline should look at the support that is needed for those in later stages of MS. The change in roles that people experience, both the person with MS and those of the family and carers need to be	Thank you for your comment and your suggestions for the guideline. We recognise the importance of the areas you outline for people with MS. We are unable however to include recommendations on all aspects of treatment for people with MS. We have had to prioritise what we cover in the guideline and have prioritised those areas where an assessment of the clinical and cost effectiveness evidence will inform care.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				identified to allow for coping strategies and support to be given to help people adjust to change. • Information on relapses, symptoms and rehabilitation should be recommended within the guideline so individuals know when to self refer and GPs know when to refer to MS specialists and share information. Following a relapse, people should be referred to a relapse clinic within one week of a relapse being diagnosed.	
SH	Multiple Sclerosis Society	21	4.3.1 f	We agree that the pharmacological management of fatigue should be included covering amantadine, and selective serotonin reuptake inhibitors (SSRIs) but also modafinil. Clarification should be made that B12 injections are for the treatment of pernicious anaemia and only may help with MS fatigue.	Thank you for your comment. Modafanil has not been included because of the European wide restriction limiting its used to narcolepsy. Thank you for your information on B12 injections.
SH	Multiple Sclerosis Society	22	4.3.1 g	We agree that the pharmacological management of spasticity should be addressed in the guideline including all treatments listed and Pregabalin	Thank you for your comment. We have added Pregabalin to this section
SH	Multiple Sclerosis Society	23	4.3.1 h	We agree that the pharmacological management of mobility with fampridine should be included.	Thank you for your comment.
SH	Multiple Sclerosis Society	24	4.3.1 i	We agree that the management of visual problems should be included within the scope, this should include diplopia, optic neuritis.	Thank you for your comment. We will agree with the GDG which visual problems to include
SH	Multiple Sclerosis Society	25	4.3.1 j	We agree that the management of ataxia and tremor should be covered in the guideline. We would expect to see the inclusion of physiotherapy within this section and to reflect evidence including *Management of the Ataxias: Guideline*	Thank you for your comment and information. We will agree with the GDG what to include in this section.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				towards Best Clinical Practice, 2009, Ataxia UK; Treatment of Ataxia in MS, 2009, Mills et al.	
SH	Multiple Sclerosis Society	26	4.3.1 k	We agree with the inclusion in the scope of the management of emotionalism, memory and cognitive impairments including anti-depressants and neuropsychological rehabilitation. It is important to stress that the guideline should reflect that cognitive symptoms should be referred to the appropriate professional; depression and anxiety should be assessed aside from MS and not assumed that it relates to MS.	Thank you for your comment. Recommendations on appropriate care of people with cognitive impairments will be informed by the evidence review. NICE has already produced guidance on Depression with a chronic physical problem (CG91) which addresses diagnosis in people with physical illness and is included as related guidance.
SH	Multiple Sclerosis Society	27	4.3.1 l	The MS Society would like to stress that there needs to be a patient centred and integrated approach to rehabilitation in the home and hospital. Acute and community teams should be coordinating with social services to ensure that rehabilitation and support is provided in the most appropriate setting. Therefore, this should include the wider community setting. We recommend that a three pronged approach of home versus community versus hospital rehabilitation is carried out. Any change in setting should be seamless with good communication between teams and involvement of the individual in all decisions. Regardless of settings, rehabilitation goals need to be tailored and personalised to the goals of the individual and be pertinent to their needs, e.g. getting back to work; taking care of their children; doing their weekly shopping; doing voluntary work. A 'goals and choices plan' could be a potential way to communicate these goals and desired outcomes to all those	We have amended section 4.3.1 (i) to 'setting of rehabilitation' to enable the GDG to consider all setting including the community The structured review 4.3.2 (b) will identify functional problems including activities of daily living.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				involved in the rehabilitation. **General points relating to disability management and rehabilitation:** Within the clinical issues to be covered there should also be sections on: **Weakness and cardio-respiratory fitness:** The scope does not currently include guidance on weakness and cardio-respiratory fitness. The guideline should reflect the importance of addressing weakness and cardio-respiratory fitness in order to improve people's clinical state and to improve their ability to carry out activities. Guidance on exercise and techniques to improve strength should be included within the guideline. **Exercise:** The current guideline, as referenced in section 3.2, includes guidance on exercise however the proposed scope does not appear to include exercise within its remit. With an increased evidence base to support this intervention we would hope to see it included within the new guideline. **Contractures at joints:** the current guideline issues guidance on contractures at joints and it is important that this is included in the new guideline. It is important to identify the preventative measures that will need to be taken by the individual and/or their carer and suitable courses of action where contractures at joints exist. **Sensory losses:** the current scope does not include sensory	We have had to prioritise what we cover in the guideline and have prioritised those areas where an assessment of the clinical and cost effectiveness evidence will inform care. People's individual needs in regard to disability and functional problems caused by weakness will be included in the structured review as in 4.3.1 (b). The GDG will consider whether to make recommendations about facilitating onward referral. Exercise will be included in 4.3.1 (e) within non pharmacological management programmes. We have amended section 4.3.2 (a) to clarify that we will not be covering the treatment of contractures. The prevention of contractures is included in section 4.3.1.(e) non-pharmacological management programmes and 4.3.1 (g) the pharmacological management of

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				losses. We would expect the new guideline to follow previous guidance regarding referrals to a specialist rehabilitation team if an individual is experiencing sensory losses.	spasticity Sensory losses will be included in the structured review in 4.3.1 (b) but we do not consider that there is any MS specific treatment to review. The GDG will consider whether to make recommendations about facilitating onward referral.
SH	Multiple Sclerosis Society	27	4.3.1 l	**Speech difficulties:** the current scope makes no mention of guidance on speech difficulties. The new guideline should include guidance on access to specialist speech and language therapists for people who have dysarthia and whose communication is therefore being affected. All people with MS should be able to access sufficient support through both therapy, technology and communication devices to allow them to communicate both in person and over the phone. **Sexual dysfunction:** The current guideline provides guidance on support for both male and female dysfunction. It is important that the new guideline includes guidance on sexual dysfunction to support clinicians to address the invisible as well as the visible symptoms of MS. Without guidance in this area there is a risk that this might be overlooked and result in an unnecessary impact. Access to specialists, information on counselling and support, as well as	People's speech difficulties and sexual dysfunction will be included in the structured review as in 4.3.1 (b) but we do not consider that there is any MS specific treatment to review. The GDG will consider whether to make recommendations about facilitating onward referral. The NICE guideline on Neuropathic Pain is being updated and a review of sativex for pain is included in the draft scope.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				treatments should be included within the guideline. **Sativex:** The guideline should also include the use of Sativex beyond spasticity including neuropathic pain and bladder dysfunction. **Urthoff's Syndrome:** The guideline should include guidance on Urthoff's Syndrome.	We have considered the inclusion of Urthoffs syndrome but do not consider it a priority. We do not aim to include all aspects of a condition when developing a NICE guideline. We have to prioritise what we cover and have prioritised those areas where an assessment of the clinical and cost effectiveness evidence will inform care.
SH	Multiple Sclerosis Society	28	4.3.1 m	**Specialist Nurse** We disagree with the wording of this section and would urge it to be entitled "MS Specialists". We believe that the role of the MS specialist nurse is integral to the care and support of people affected by MS and that people with MS, their family and carers should have the support of an MS nurse locally to their home. Currently children with MS do not have access to MS specialist nurses. The effects on school/academic functioning, family interactions, and the specific issues of adolescence are poorly appreciated. There is currently	Thank you for your comment. The role of MS nurse is specifically mentioned as this was considered an issue where specific guidance is required. The role of interventions provided by other specialists such as occupational therapists are included in the sections on specific interventions. **The scope has been amended to include consideration of coordination of care and support including the role of the MS nurse.**

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				inadequate support and at times inappropriate service provision. We believe that the pivotal role of the MS nurse should be addressed in the guideline including support and education over time in both community and acute settings and the coordination of care. However, this should extend beyond the MS specialist nurse to include other MS specialists. The new guideline should make greater reference to MS Specialists providing a definition of who they are, what they do, the expectation of their role and the expected standard. People with MS should be able to access a comprehensive multi-disciplinary team many of whom should be in a range of settings, not solely acute settings. The following MS specialist services should be provided: • consultant neurologist with a special interest in MS • MS specialist nurse • clinical psychologist • MS specialist physiotherapist • MS specialist occupational therapist • continence specialist	The scope has been revised and now includes adults 18 yrs or over This guideline will make recommendations on which interventions are clinically and cost effective. We agree that the care of people with MS requires input from a wide range of specialists in both acute and non-acute settings.
SH	Multiple Sclerosis Society	28	4.3.1 m	Additional non-MS specialist services should also be available to people with MS including: • vocational rehabilitation • neuro-physiotherapist	Thank you for this comprehensive list of services that may be required by people with MS. This guideline will focus on the

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				• neuropsychologist • a social worker • counselling support • mental health support • orthotist • dietician • podiatrist • dentist • employment advisors • speech and language therapist and liaison role There should be a lead care coordinator, an MS nurse or anyone in the MDT with a special interest in MS. The care coordinator must have links to all involved and help improve the channels of communication between all parties. There needs to be an expectation of their geographical coverage and reach so that the commissioning of each specialist is sufficient in order to provide accessible, timely and appropriate service and care for both rural and urban settings. Consideration needs to be given to caseloads and the number of cases and their status (i.e. stable/aggressive, DMTs, SPMS, PPMS) that each MS specialist nurse is covering. There is an understanding that not every local area will be able to provide all aspects of specialist support. However, there needs to be access to and integration between specialist centres. The guideline has the potential to describe a hub and spoke model with specialist centres providing a specialist education role.	management of symptoms specific to MS. The scope has been amended to include consideration of coordination of care and support including the role of the MS nurse. NICE guidelines do not generally specify who should provide a service or how that service should be organised unless there is clear evidence about models of service provision. We agree however that involvement of appropriate expertise and integration of services is beneficial for patients. Competencies to fulfil a particular role is the remit of professional organisations and employing authorities.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				The model of service and care needs to be defined in order to remove barriers, improve referral management and enhance the known network of care and standards across both primary and secondary care. This needs to include the social model and a care pathway to allow people to understand who is involved in the MS care pathway, how to access services and what they do. To be regarded as an MS specialist professionals need to have a skills specification with specific training to give them the 'MS specialist' status. This could be part of their CPD and should require updating. This could potentially be given by the third sector or in partnership. The coordination of the network of care should be led by a named lead MS specialist such as an MS specialist nurse or other MS specialist professional. This will help improve the diagnosis of MS and particular symptoms improving the access to treatments and interventions. There is also the potential to improve people's understanding of MS, local knowledge, teamwork and cooperation.	
SH	Multiple Sclerosis Society	29	4.3.1 n	**Other treatments** We agree with the recommendation to review the administration of steroids (intravenous versus oral) for acute relapse.	Thank you for your comment.
SH	Multiple Sclerosis	30	4.3.1 o	We agree with the recommendation to review Vitamin D for	Thank you for your comment.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
	Society			the management of MS.	
SH	Multiple Sclerosis Society	31	4.3.1 p	We agree with the recommendation to review the use of complementary therapies.	Thank you for your comment.
SH	Multiple Sclerosis Society	32	4.3.2 b	Contractures at joints. We disagree with the decision to omit this from the scope and expect this to be included. It is important to identify the preventative measures that will need to be taken by the individual and/or their carer and suitable courses of action where contractures at joints exist.	Thank you for your comment. The prevention of contractures will be included in 4.3.1 (e) and 4.3.1 (g)
SH	Multiple Sclerosis Society	33	4.3.3 a	**NICE guidance to which the new guideline will cross-refer** **Communication** We agree with the decision to cross refer to the Patient Experience in adult NHS services (CG138) however, as explained, there needs to be greater emphasis in the guideline for MS on family and carers.	Thank you for your comment. Section 4.3.1 (b) structured review has been amended to included the impact on carers. The impact on carers is included as an outcome 4.4 (c)
SH	Multiple Sclerosis Society	34	4.3.3 b	We agree that the section on emotional support should refer to CG138 on Patient Experience however, the patient experience guideline only states that: "There should be recognition of the potential need for psychological and emotional support" (CG138, p.8) and this does not adequately reflect the need to offer a full assessment of their emotional status by a suitable specialist if an individual is experiencing extreme emotions with little provocation. Neither is there mention of potential treatments.	Thank you for your comment. We are distinguishing the provision of emotional support which is included in the Patient Experience guideline and the management of 'emotionalism' which is included in the scope.
SH	Multiple Sclerosis Society	35	4.3.3 c	We agree with the cross referencing of TA32 and TA127 however there should also be cross-referencing to Health Circular 2002/004. http://bit.ly/K8G5X7 This section has also omitted to cross reference TA254 on Fingolimod, we would expect this to be cross referenced within the guideline.	Thank you for your comment. This section is for NICE guidance only. We have amended the scope to include TA254 4.3.3 (c)

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
SH	Multiple Sclerosis Society	36	4.3.3 d	We agree that the cross referencing of CG29 should be in the guideline	Thank you for your comment.
SH	Multiple Sclerosis Society	37	4.3.3 e	We agree with the cross reference of the Guideline on Management of Incontinence in neurological disease but we would also advocate reference to the UK consensus on the use of botulinum toxin in clinical care (2009).	Thank you for your comment. The Management of Incontinence in Neurological Disease guideline provides guidance on the use of botulinum toxin for bladder management.
SH	Multiple Sclerosis Society	38	4.3.3 f	We support the cross reference of the updated guideline on Infection Control.	Thank you for your comment.
SH	Multiple Sclerosis Society	39	4.3.3 g	We agree with the cross referencing of CG49: Faecal incontinence: The management of faecal incontinence in adults, 2007	Thank you for your comment.
SH	Multiple Sclerosis Society	40	4.3.3 h	We agree with the cross referencing of CG96: Neuropathic pain: the pharmacological management of neuropathic pain in adults in non-specialist settings, 2010 .	Thank you for your comment.
SH	Multiple Sclerosis Society	41	4.3.3 i	We agree with the cross referencing of Depression: the treatment and management of depression in adults (update), 2009. NICE clinical guideline CG90.	Thank you for your comment.
SH	Multiple Sclerosis Society	42	4.3.3 j	We agree with the cross referencing of CG113: Generalised anxiety disorder and panic disorder (with or without agoraphobia) in adults, 2011.	Thank you for your comment.
SH	Multiple Sclerosis Society	43	4.3.3 k	We agree with the recommendation to cross reference *Nutrition support in adults,* (CG32, 2006) however, there are additional points in the current guideline that are not raised within CG32. These include specific references to bulbar dysfunction and assessments by appropriate professionals as well as further tests by a specialist speech and language	Thank you for your comment. We will discuss CG32 with the GDG and agree whether there are areas important in the care of people with MS that we need to include in structured assessment and where appropriate

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				therapists. The current guideline recommends advice on swallowing technique, on adapting food consistencies and dietary intake. There are also recommendations to refer to specialist neurological rehabilitation teams to assess for adjustments to seating, chest physiotherapy and short term nasogastric tube. The current guideline also makes recommendations to have advanced conversations regarding feeding and to discuss and record the individual's wishes. In addition guidance on alternative feeding will need to be included in the advanced directives section. The guideline will need to address nutrition and guidance on appropriate nutritional screening in both acute and community settings to identify those malnourished and at risk of malnutrition.	referral is facilitated.
SH	Multiple Sclerosis Society	44	4.3.3	In many of the guidelines to be cross referenced the applicable population is 18 and over. The current scope recommends that the population should be 16 and over, we would want to see clarification that all guidelines cross referenced are applicable to the entire population of the MS clinical guideline.	Thank you for your comment. Following consideration of stakeholder comments we have altered the guideline population to people of 18 years and over only. We considered we could not adequately address the needs of younger people with MS within this guideline.
SH	Multiple Sclerosis Society	45	4.4 a	**Main outcomes** We agree that one of the main outcomes should be linked to Health related Quality of Life and happiness and should be for both individuals with MS and their carers.	Thank you for your comment
SH	Multiple Sclerosis Society	46	4.4 b	The impact on carers should also be included as a main outcome. We would advocate that carers are offered a range of support such as:	Thank you for your comment. The impact on carers is included as an outcome.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				• Access to a comprehensive carer's assessment including psychological therapy and assessment • Integrated working across all agencies involved in the treatment of people with MS including jointly agreed policies and procedures • The inclusion of local service users and carers in joint planning • Care plans to coordinate all aspects of health and social care needs agreed by health and social services. Care plans should consider the changing needs of the person with MS and his or her carers including environmental modifications to aid independent functioning, including assistive technology, with advice from an occupational therapist, clinical psychologist and physiotherapists. A care plan should include support for people to participate in activities they enjoy. • Care plans should have a named health and/or social care staff to coordinate the care plan; ownership of the care plan should be held by the individual or their carer(s); formal reviews of the care plan should be planned at an agreed frequency between professionals involved and the person with MS and/or carers and recorded in the notes. • Support offered to people with MS and their family/carers to help to communicate, discuss issues and manage change. • Appropriate training in MS for all professionals in health and social care in regular contact with people with MS	

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				• Comprehensive range of respite/short-break services to meet the needs of the person with MS and the carer • Information about direct payments and individual budgets • Information about the statutory difference between NHS care and care provided by local authority social services (adult services) so that they can make informed decisions about their eligibility for NHS Continuing Care	
SH	Multiple Sclerosis Society	47	4.4 c	We agree with recommended outcomes on functional scales and would expect disability measures to be checked through an annual review.	Thank you for your comment
SH	Multiple Sclerosis Society	48	4.4 d	We agree with the list of outcomes but would also add pain, swallowing issues, and sexual dysfunction. Again, we would expect these functions and symptoms to be assessed by a regular health check and would also expect an outcome to be improved access to symptomatic treatments and therapies.	Thank you for your comment. The list of outcomes in this section are those to be included in the evidence review.
SH	Multiple Sclerosis Society	49	4.4 e	We agree with the recommended outcome of psychological symptoms but would also expect the outcome to include improved provision of psychological support.	Thank you for your comment. The outcomes listed in section 4.4 are those to be used when reviewing the evidence for clinical and cost effectiveness. The outcomes suggested are primarily outcomes for assessment of services and not usually relevant when assessing clinical and cost effectiveness.
SH	Multiple Sclerosis Society	50	4.4 f	We believe that the outcome should include an increased number of people on disease modifying treatments and symptomatic treatments with regular appointments to monitor	Thank you for your comment. The outcomes listed in section 4.4 are those to be used when reviewing the

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				and record adverse effects from all treatments.	evidence for clinical and cost effectiveness. The outcomes suggested are primarily outcomes for assessment of services and not usually relevant when assessing clinical and cost effectiveness.
SH	Multiple Sclerosis Society	51	4.4	We recommend NICE considers the following outcome measures for incorporation in the revised guideline: • The percentage of people contacted or seen by an MS Nurse within two weeks of diagnosis • The percentage of people affected by MS who upon diagnosis, are notified and receive information that an MS specialist nurse is available in their area • A record of the case load of the MDT including MS Nurses and Neuro-Physiotherapists and Neuro Occupational Therapists • The percentage of people with a definitive diagnosis of multiple sclerosis in less than 12 weeks of a GP referral • The number of people with Primary Progressive MS accessing physiotherapy • Maintenance or improvement in quality of life of people with MS and their Carers • The number of emergency admissions of people with MS • Percentage of people who are referred for DMT who are assessed within 6 weeks • Waiting time for referral to a first appointment with a specialist (psychologist, OT etc.) • The percentage of people with MS with an agreed care plan	Thank you for your comment. The outcomes listed in section 4.4 are those to be used when reviewing the evidence for clinical and cost effectiveness. The outcomes suggested here are primarily outcomes for assessment of services and not usually relevant when assessing clinical and cost effectiveness.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				• The percentage of people who have a single, named point of contact • The percentage of people who know how to self refer to specialist services following a relapse • The percentage of people with MS experiencing a significant and disabling relapse referred an MS specialist services within 48 hours • Percentage of staff who have participated and passed an e-learning module on MS as part of their Continuing Professional Development. • Percentage of people with MS in employment (including voluntary and parenting) • Percentage of people offered a course for newly diagnosed people with MS within a month of diagnosis	
SH	Multiple Sclerosis Society	52	General	**A Review of research recommendations** should be included as research has now accumulated in the areas of research recommended in the original review. We would hope to see recommendations for research to develop DMTs for progressive MS through both the commercial development of novel therapies and repurposing of treatments from other conditions and/or 'off patent' drugs. The focus should be on development of neuro-protective and myelin repair treatments; a head to head multi-therapy trial of the various licensed products; outcome measures, including patient reported outcome measures. Other research should include research into unproven therapies such as CCSVI (as per NICE recommendation "NICE interventional procedure guidance 420"), LDN and stem cells.	Thank you for your comment. As this guideline is replacing the previous guideline a new set of research recommendations will be developed.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				It would also be useful to see a review of research on the full range of interventions that are recommended for people with MS, including, for example, interventions made by the multi-disciplinary teams.	
SH	Multiple Sclerosis Society	53	5.1.3	We strongly recommend NICE cross reference CSGSP: Supportive and Palliative Care (2004) and the recently published End of Life Quality Standard and highlight the need for professionals to engage in conversations about end of life planning at an appropriate time. It is important to highlight the need for early recognition and identification of those who are in the last months/year of life, and to use of prognostic indicators to help identify such patients to promote access to good end of life care. Palliative and end of life care must be included the final guideline, as people with MS unfortunately still lack access to this kind of support and services.	Thank you for your comment. We have added the NICE Quality Standard on end of life care for adults to section 5.1.3. End of life care has been added to 4.3.1 (b)
SH	Multiple Sclerosis Society	54	general	We hope NICE will consider our comments carefully and thoroughly, and acknowledge that our submission has been informed through extensive consultation with people affected by MS, their carers, and professionals working in the field of MS. We believe that our suggestions will help to ensure that the new guideline is comprehensive and robust and will support	Thank you for your comments.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				professionals to provide a high standard of care for people affected by MS in order to improve both health outcomes and quality of life.	
SH	Multiple Sclerosis Society	55	General		
SH	Multiple Sclerosis Trust	1	General	The MS Trust welcomes the revision of the guideline. People with MS live a long time with an incurable disease that affects every aspect of their life. They deserve better services and the guideline is key to setting standards of service that can really make a difference for them. However in order to truly improve care for people with MS the guideline must come with the necessary levers to ensure full implementation. This will require leadership, collaboration and involvement from people who live with MS, their wider circle, and health professionals.	Thank you for your comments. The guideline will be supported by the NICE implementation team who will work with stakeholders to disseminate the guideline. A Quality Standard for MS is also included in library of quality standards referred to NICE. These will set out markers of high quality care and should be one of the levers to improve care.
SH	Multiple Sclerosis Trust	2	3.1 d	This section currently understates the impact of the disease on the lives of people with MS and their families. In particular • The relatively young age at which people are diagnosed (usually in their 20's and 30's), therefore they live with it for a long time. • The effect on the ability to work – a 2011 report by The Work Foundation suggested that on average people with MS miss out on 18 years of their working life.	Thank you for your comment. This section is not intended to be comprehensive. We have added specific comments about work and MS to this section.
SH	Multiple Sclerosis Trust	3	3.2 b	MS is a complex and unpredictable condition that varies from person to person and does not follow a set pattern. It is important to note that it is not always possible to say at diagnosis what type of MS a person has, this may only become apparent over time. Secondary progressive MS is not defined - *people who start off with relapsing remitting MS may go on to develop a*	Thank you for your comment. We have added further information about secondary progressive MS to this section.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				progressive form of the condition. The transition usually occurs somewhere between five to 20 years after diagnosis, but the change from relapsing remitting MS to secondary progressive MS can happen at any time. The severity and frequency of the relapses decrease, but disability slowly increases.	
SH	Multiple Sclerosis Trust	4	3.2 c	Symptoms should include bowel as well as bladder.	Thank you for your comment. The list is not meant to be exhaustive and we have highlighted those symptoms that the guideline with focus on.
SH	Multiple Sclerosis Trust	5	3.2 e	We assume the National Audit referred to is the one carried out in 2011 by the MS Trust in partnership with the Royal College of Physicians, which was also referenced in the National Audit Office Report on Services for People with Neurological Conditions. In particular the audit highlighted • that there is huge variation in the quality and quantity of care provided for people with MS • none of the 6 recommendations in CG8 have been implemented widely or fully and the relevant quality requirements of the NSF for people with long-term conditions show an unacceptably low level of attainment In responding to the audit people with MS emphasised:- • problems in getting help quickly, as there is often no single point of contact • basic symptoms such as pain, fatigue and cognition are not well managed • the lack of access to treatments and therapies that can aid mobility, as well as physical aids and equipment • the lack of co-operation between health and social care	Thank you for your comment. We recognise the importance of the issues raised by the audit and the difficulties experienced by people with MS. The guideline will be supported by the NICE implementation team. A quality standard for multiple sclerosis has also been referred to NICE by the Department of Health.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				• little evidence of involving them in decision making or service commissioning • poor access to rehabilitation generally and virtually no access to vocational rehabilitation • little support for their families or carers It was disappointing to report that little has changed in the 3 audits we have undertaken since 2006. This guideline must seek to address these issues and ensure the necessary levers are put in place to ensure full implementation.	
SH	Multiple Sclerosis Trust	6	4.1.1	The guideline should cover anyone affected by MS regardless of age. It is not clear whether people between 16 and 18 are treated in adult services. The guideline may need to consider service arrangements for transition between paediatric and adult services.	Thank you for your comment. When developing NICE guidelines we commonly specify the population that the guideline is relevant to. The guideline that is being replaced (CG8) included adults only. Following consideration of stakeholder comments we have altered the guideline population to people of 18 years and over only. We considered we could not adequately address the needs of younger people with MS within this guideline. Making recommendations for people under 18 years requires a different approach which would include a different GDG constitution, reviews of different evidence and consideration of licensing

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
					issues in under 18s.
SH	Multiple Sclerosis Trust	7	4.2	The MS Trust believes that it is vital to include social care as the interface between health and social care services is a key issue for people with MS.	Thank you for your comment. The remit from the Department of Health is for a clinical guideline for the management of MS in primary and secondary care and does not include social care or public health. We acknowledge the importance of social care for people with MS and anticipate that some of the interventions we recommend may be delivered by social care depending on local arrangements. As NICE will have a remit for social care from April 2013NICE is considering how best to address the issues of integration of heath and social care.
SH	Multiple Sclerosis Trust	8	4.3.1 a	The inclusion of CIS and NMO is welcome. The guideline should also include a recommendation on how a diagnosis is given and the support to be offered at the time including referral to an MS specialist nurse.	Thank you for your comment. We will refer to NICE Patient Experience guidance and make specific recommendations for people with MS if the GDG consider this is required. Information and support for patients and carers is included as 4.3.1 (c)
SH	Multiple Sclerosis Trust	9	4.3.1 b	Structured holistic review is essential and this should be done regularly not just at diagnosis. Assessment should also cover key relationships and carers including their own wellbeing.	Thank you for your comment and suggestions. We will discuss these with the Guideline development group.
SH	Multiple Sclerosis Trust	10	4.3.1 c	High quality, accessible information must be available for people with MS, their families, friends, employers and the health professionals who work with them. This is essential for shared decision making at all stages of the disease course.	Thank you for your comment. We will review the evidence on information needs for people with MS and their carers and consider what specific

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				However it may be useful to emphasise the key points when access to good information is vital for example at diagnosis, when considering disease modifying drugs, at transition between types of MS, and advanced decision making	recommendations are required for people with MS. We will also refer to the Patient Experience and Medicines Adherence guidelines.
SH	Multiple Sclerosis Trust	11	4.3.1 d	Should be expanded to include other lifestyle factors e.g. stress	Thank you for your comment. Immunisation and pregnancy are included here as examples. The GDG will make the final decision as to which modifiable risk factors to include. We will include your suggestions in the discussion with them. The emphasis is intended to be on modifiable risk factors.
SH	Multiple Sclerosis Trust	12	4.3.1 e	This section covers many of the issues people with MS highlighted in the audit. Access to all forms of rehabilitation is very important, as is the availability of mobility aids including FES, wheelchairs and all other equipment to aid daily living. This should cover therapies and equipment provided by both health and social services. Relapse management and rehabilitation should be included. Vocational rehabilitation is also important.	Thank you for your comment. We understand the issues faced by people who need access to equipment and services. NICE clinical guidelines provide recommendations based on clinical and cost effectiveness and do not have a role in ensuring appropriate availability locally. NICE has an implementation team who support the dissemination of the guideline and MS is on the list of Quality Standards referred to NICE. Relapse management and rehabilitation are included with respect to what intervention should be used to manage specific symptoms. The setting of rehabilitation (4.3.1 (e)) includes

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
					rehabilitation following a relapse. Vocational issues will be included in the structured review (4.3.1 (b))
SH	Multiple Sclerosis Trust	13	4.3.1 f k	Agreed. In addition sections should be included for the management of: • speech problems • swallowing problems • sexual dysfunction • bladder and bowel problems	Thank you for your comment. People's individual needs in regard to sexual health, vocational rehabilitation etc will be included in the structured review as in 4.3.1 (b) but we do not consider that there is any MS specific treatment to review. The GDG will consider whether to make recommendations about facilitating onward referral. Bladder problems are covered by the NICE guideline on the 'management of incontinence in neurological disease'. Bowel problems are covered by the NICE guideline on 'faecal incontinence'
SH	Multiple Sclerosis Trust	14	4.3.1 l	The availability of rehabilitation in all settings is key. In the audit less than 20% of people with MS could access rehabilitation at home.	Thank you for your comment. We understand the difficulties patients experience when accessing rehabilitation as home. NICE clinical guidelines provide recommendations based on clinical and cost effectiveness and do not have a role in ensuring appropriate availability locally.
SH	Multiple Sclerosis Trust	15	4.3.1 m	People with MS tell us how highly they value their MS specialist nurse, however there are still too few of them and	Thank you for your comment. The review will examine the role and effectiveness of MS nurses and if

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				not everyone with MS currently has access to this vital service. Understanding and articulating the content of their role over the disease course and the ensuing benefits for people with MS in this guideline will be welcome, and can inform the design, configuration and commissioning of services. The interface between specialist and generalist care should also be explored. We would request that the guideline should also add a section for MS specialist therapists as a multidisciplinary team approach is essential for people with MS. We provide professional development opportunities and resources for both nurses and therapists and continue to fund research to demonstrate the value of their services.	possible make recommendations about MS nurses for people with MS. The scope has been amended to include consideration of coordination of care and support including the role of the MS nurse. We have had to prioritise what is included in the guideline and MS nurses are specifically mentioned in the scope to allow consideration of their role. This is not intended as a comment on the importance of other professionals who contribute to the care of people with MS.
SH	Multiple Sclerosis Trust	16	4.3.3	Whilst it is practical to reference other NICE guidelines, their use should not be an excuse to devolve accountability for care of a person with MS to other clinical areas. Poor management of key symptoms e.g. continence can have a huge impact on their life with MS and ultimately the MS specialist team should retain responsibility for their overall care.	Thank you for your comment. NICE pathways will provide an overview of all guidelines relevant to people with MS.
SH	Multiple Sclerosis Trust	17	4.3.3 c	Also needs to include reference to Health Service Circular 2002/004	Thank you for your comment. This section is for NICE guidance only.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				and TA254 Fingolimod.	Thank you for your comment. The Guideline Development Group will be kept up to date on the progress of the Risk Sharing Scheme. We have amended the scope to include TA254 4.3.3 (c)
SH	Multiple Sclerosis Trust	18	4.4	There are outcome measures for shared decision making and patient activation measures for self management which may be appropriate. It would be useful for the development group to co-opt someone with the necessary expertise to review all these measures to ensure they are comprehensive and genuinely measurable.	Thank you for your comment. The GDG will specify which outcomes we should report for each evidence review. We can co-opt an expert is the GDG or technical team do not have appropriate expertise.
SH	National Council for Palliative Care (NCPC)	1	General	NCPC welcomes the opportunity to comment on the draft scope for the Multiple Sclerosis (MS) guideline. We are the umbrella charity for palliative, end of life and hospice care in England, Wales and Northern Ireland. We hope you find our comments useful. **We strongly recommend** that palliative and end of life care be included the scope and guideline. Palliative care, combined with rehabilitation, can significantly benefit people with MS and their carers from the point of diagnosis through to the end of life. It can help the person manage their condition and symptoms and maintain the best possible quality of life. Crucially, it can help people with MS think about, discuss and plan for the future and make decisions in advance in anticipation of times where they may	Thank you for your comment and information 4.3.1 (c) has been amended to include end of life care.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				lack the capacity or ability to communicate their wishes. As well as bringing peace of mind, planning ahead helps avoid costly hospital admissions which frequently occur in the last year of life. Referral to palliative care should be encouraged from an early stage, rather than being seen simply as an 'add on' at the end of life.[2] The draft scope talks about the importance of quality of life but does not mention palliative or end of life care. This is within a context of few people with MS receiving the palliative care they need.[3] We therefore **strongly recommend** that the guideline explicitly addresses palliative and end of life care. A number of specific suggestions for how you can amend the scope to remedy this omission are included below. This recommendation has been echoed by the MS Society in their response to the draft scope. **More information** We have been working for a number of years with our dedicated Neurological Conditions Group to improve and extend the provision of palliative care services for people with neurological conditions from diagnosis through to the end of	

[2] *Evaluation of a new model of short-term palliative care for people severely affected with multiple sclerosis: a randomised fast-track trial to test timing of referral and how long the effect is maintained* Higginson IJ, Costantini M, Silber E, Burman R, Edmonds P. Postgrad Med J. 2011 Nov;87(1033):769-75. www.ncbi.nlm.nih.gov/pubmed/21978993

[3] *Halfway through - are we half way there? A mid-term review of the NSF* (2011, Neurological Commissioning Support) found that none of the sites it reviewed fully met the palliative care Quality Requirement, and only 18% of services achieved 'part met' status. http://ltc-community.org.uk/articles.asp?id=6093 The National Audit Office chose not to include the palliative care requirement in its recent review of the NSF *Services for people with neurological conditions* (NAO, 2011) www.nao.org.uk/publications/1012/neurological_conditions.aspx

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				life. More information about this work can be found at www.ncpc.org.uk/neurological-conditions. We have intentionally kept our response here brief, but would be pleased to provide further assistance to the reference group in development of the guideline as needed.	
SH	National Council for Palliative Care (NCPC)	2	4.3.3	**We strongly recommend** that the new guideline cross-references: • End of life care Quality Standard (NICE, 2011) – 16 statements outlining what good looks like, all of which are applicable for people with MS. www.nice.org.uk/guidance/qualitystandards/endoflifecare/home.jsp • End of life care in long-term neurological conditions: a framework for implementation (National End of Life Care Programme, NCPC & Neurological Alliance 2010). www.endoflifecareforadults.nhs.uk/publications/end-of-life-care-in-long-term-neurological-conditions-a-framework • National end of life care strategy (Department of Health, 2008) – the government's commitment to ensuring that all people have the access to palliative and end of life care services they need, regardless of condition or setting. www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_086277 • The National Service Framework for Long-Term	Thank you for your comment and references. The NICE Quality Standard of end of life care for adults has been added to section 5.1.3. We can only reference to other NICE guidance in the scope.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				Conditions (DH, 2005) - Quality requirement 9 concerns palliative care (see footnote 2). www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_4105361 • *Improving Supportive and Palliative Care for Adults with Cancer* (NICE, 2004) – originally for cancer the principles have been applied to a range of life-limiting conditions including MS. www.nice.org.uk/csgsp	
SH	National Council for Palliative Care (NCPC)	3	4.3.1	Palliative care teams, through the provision of training, advice and services, can help control symptoms, improve quality of life and facilitate advance care planning, and as such have key role in helping to address many of the clinical issues included in this section. Specifically: • 4.3.1 c) 'Information and support for patients and carers including advanced decision making' will need to include the impact of advance care planning on improved quality of life and reduction in the number of unnecessary hospital admissions. The guideline should include a clear message that professionals work together to provide the person with MS opportunities to discuss and plan for the future. • 4.3.1 e)-l) The guideline must reference the role of palliative care services in disability management. Specialist palliative care has a distinctive role to play in helping to manage specific symptoms experienced towards the end of life including spasms, depression,	Thank you for comment. We have added 'end of life' care to 4.3.1 to make explicit our intention to comment on this. NICE guidelines do not generally specify who should provide a service or how that service should be organised unless there is clear evidence about models of service provision. We agree however that involvement of appropriate expertise and integration of services is beneficial for patients.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				cognitive change, difficulty swallowing with reduced nutrition and hydration, skin fragility and mobility problems (NEOLCP 2010). • 4.3.1 m) The role of other professionals working alongside the specialist nurse, including rehab and palliative care professionals, must be included. Partnership working, communication and integration is absolutely key.	
SH	National Council for Palliative Care (NCPC)	4	4.4	**We recommend** that outcomes from the NICE End of life care Quality Standard are adopted: • *The care that people approaching the end of life receive is aligned to their needs and preferences.* • *Increased length of time spent in preferred place of care during the last year of life.* • *Reduction in unscheduled care hospital admissions leading to death in hospital (where death in hospital is against their stated preference).* • *Reduction in deaths in inappropriate places such as on a trolley in hospital or in transit in an ambulance.* See also the Palliative care Outcome Scale - Symptoms (POS-S) developed for people with advanced multiple sclerosis - www.csi.kcl.ac.uk/pos-s.html	Thank you for your comment. The outcomes in Quality Standard are primarily outcomes for assessment of services and not usually relevant when assessing clinical and cost effectiveness.
SH	National Council for Palliative Care	5	5.1.3	See (NCPC) point 3	

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
	(NCPC)				
SH	National Council for Palliative Care (NCPC)	6	4.1.1	Note that the MS guideline as it stand will cover people aged 16 and over, but other NICE guidance covers only those aged over 18 (e.g. the End of life care Quality Standard). We would support the MS Society's call for specific guidance from NICE to improve the transition from childhood to adulthood.	Thank you for your comment. Following consideration of stakeholder comments we have altered the guideline population to people of 18 years and over only. We considered we could not adequately address the needs of younger people with MS within this guideline. Making recommendations for people under 18 years requires a different approach which would include a different GDG constitution, reviews of different evidence and consideration of licensing issues in under 18s.
SH	NHS Salford (Salford Primary Care Trust)	1	4.3.3 c	Our comments are as follows: • The consultation should include the recent guidance on fingolimod • The consultation should include a caveat regarding the use of "off-label" drugs such as mitoxantrone, azathioprine and alemtuzumab to ensure that commissioners understand the possible need to use such drugs in exceptional circumstances. • The consultation should clarify the use of low dose naltrexone.	Thank you for your comment. This section is for NICE guidance only. We have amended the scope to include TA254 4.3.3 (c) Thank you for your comment. We include drugs that are licensed, are in common usage and if there is evidence for their use which is not the case for new treatments and therefore these are not included. The use of steroid sparing medicines is related to chronic use of steroids and to recommendations affecting disease

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
					progression which we are not including.
SH	NHS South of England	1	4.3.3	You need to refer to the importance of good end of life care and that this is not covered as its covered in the NICE EoLC Standard	Thank you for your comment. 4.3.1 (c) has been amended and now includes end of life care
SH	Novartis	1	4.2.2	We suggest this also needs to include Personal Social Services (PSS) so that it matches the new NHS structure.	The remit from the Department of Health is for a clinical guideline for the management of MS in primary and secondary care and does not include social care or public health. We acknowledge the importance of social care for people with MS and anticipate that some of the interventions we recommend may be delivered by social care depending on local arrangements. As NICE will have a remit for social care from April 2013NICE is considering how best to address the issues of integration of heath and social care.
SH	Novartis	2	4.3.1 m	This section references MS specialist nurses. We suggest the review should also examine access to MS nurses because we believe access across the UK is patchy – good in many places but some areas have no service at all or have only partial services. We believe that NICE guidance on this would be impactful.	Thank you for your comment. The review will examine the role and effectiveness of MS nurses and if possible make recommendations about MS nurses for people with MS.
SH	Novartis	3	4.3.3	We agree with NICE that the update of the MS clinical guideline should refer to the existing NICE Health Technology Appraisals. In addition, guidance on fingolimod for the treatment of highly	Thank you for your comment. We have amended section 4.3.3 (c) to refer to fingolimod

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				active relapsing-remitting multiple sclerosis is now published (TA 254) and the guideline needs to cross-refer to this.	
SH	Novartis	4	4.5	We note that the scope states that NICE economic evidence reviews usually only consider an NHS and PSS perspective. However, this perspective is not universally accepted in the UK or outside the UK. There is a wealth of evidence demonstrating the high impact of MS on patient's and carer's out-of pocket expenditure (e.g. loss of income and cost of informal care). We suggest that this evidence is discussed in the guideline.	Thank you for your comment. We recognize the impact of MS on patient's and carer's expenditure however when reviewing the economic evidence, the NICE guidelines manual has to be followed to ensure comparability across all guidelines. This currently states that "productivity costs and costs borne by patients and carers that are not reimbursed by the NHS or PSS are not included either in the reference-case or non-reference case". The manual is currently under consultation and there are proposals to include costs borne by carers. If this change goes ahead, these costs will be considered during the development of this guideline.
SH	RCGP	1	General	Brief seems appropriate provided the cross referenced guidelines are up to date.	Thank you for your comment.
SH	Roche Products Ltd	1	4.3.1 b	As part of the structured review of people with MS, some acknowledgement of the frequency of assessments should be specified to address any issues with treatment compliance and/or treatment side effects.	Thank you for your comment. We will refer to the Medicines Adherence guideline which makes recommendations for regular review to cover the areas you suggest.
SH	Roche Products Ltd	2	4.3.2	We understand that disease modifying treatments will be 'cross referred' to other technology appraisal guidance. As such, should disease modifying treatments be listed under	Thank you for your comment. Disease modifying treatments has now been added under the clinical areas not

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				this section (Clinical areas not covered)?	covered section of the scope.
SH	Roche Products Ltd	3	4.3.3 c	'Fingolimod for the treatment of highly active relapsing-remitting multiple sclerosis, 2012. NICE Technology Appraisal TA254' should also be listed under this section (for technology appraisals that will be cross referred). Fingolimod is currently only listed under section 5.1.3: 'other related NICE guidance'.	Thank you for your comment. This section is for NICE guidance only. We have amended the scope to include TA254 4.3.3 (c)
SH	Roche Products Ltd	4	4.3.3 c	The technology appraisal TA32 'Guidance on beta interferon and glatiramer acetate for the treatment of multiple sclerosis' has not been updated since 2002. As disease modifying treatments are not being reviewed as part of this clinical guideline, is there consideration for reviewing this technology appraisal?	Thank you for your comment. Please refer to the NICE website for information about the review plans for TAs.
SH	Roche Products Ltd	4	4.4 a	In addition to the generic QOL scales listed (EQ-5D, SF-36), we would recommend the consideration of MS specific scales such as Multiple Sclerosis Impact Scale (MSIS-29).	Thank you for your comment. We have added this to the list outcomes. The list of outcomes will be specified by the GDG and will vary for each evidence review.
SH	Roche Products Ltd	5	4.4 b	We would recommend that in addition to 'Impact on carers' being included as a main outcome, social impact should also be included.	Thank you for your comment. Impact on carers is specified in the list of outcomes
SH	Roche Products Ltd	6	4.4 c	We would recommend that in addition to the functional scales listed, some assessment of mobility should also be included.	Thank you for your comment. We have added this to the list outcomes. The list of outcomes will be specified by the GDG and will vary for each evidence review.
SH	Royal College of Nursing	1	2	The Royal College of Nursing welcomes the revision of the guideline as the management of MS has developed considerably in the last decade.	Thank you for your comment. The remit from the Department of Health is for a clinical guideline for the management of MS in primary and secondary care and

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				This remit would benefit from representation from social services and public health on the CCG and in anticipation of the shared outcomes of public health and social care. People with MS (PwMS) span across all services over their lifetime and can anticipate fifty years of potential debilitating or disabling symptoms that will benefit from early intervention from all services.	does not include social care or public health. We acknowledge the importance of social care for people with MS and anticipate that some of the interventions we recommend may be delivered by social care depending on local arrangements. As NICE will have a remit for social care from April 2013, NICE is considering how best to address the issues of integration of health and social care.
SH	Royal College of Nursing	2	3.1	It is only presumed that MS is an acquired chronic auto-immune mediated condition; we have no irrefutable evidence as yet. MS is increasing in women (cause unknown) in the RRMS group but remains relatively stable in men; this could have implications for work patterns, social care and health services, including maternity services, in the next decade. The migratory pattern of MS and its' implications for BME groups should be considered.	Thank you for your comment. We have amended this information in the scope. Thank you for the information. We have not identified any data that indicates there is a difference in the incidence of MS in different BME groups in the UK.
SH	Royal College of Nursing	3	3.2	ABN Guidelines on prescribing treatments were updated in 2009. The Recommendations on Rehabilitation services for PwMS in Europe have just been published (EMSP 2012)	Thank you for this information.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
SH	Royal College of Nursing	4	3.2	We would welcome guidance in early prescribing and examination of evidence on early and limited prescribing of DMDs.	Thank you for your comment. We will refer to NICE technology appraisals which are relevant to MS but will not review this evidence.
SH	Royal College of Nursing	5	3.2	We would welcome GP prescribing of exercise programmes similar to those offered to other LTCs.	Thank you for your comment. The guideline will make recommendations following a review of the evidence.
SH	Royal College of Nursing	6	4.1.2	Inclusion of adolescents and children with MS should be considered as their numbers are likely to increase and evidence accruing on early, effective intervention.	Thank you for your comment. We have carefully considered the inclusion of children and adolescents in the guideline. Following consideration of stakeholder comments we have altered the guideline population to people of 18 years and over only. We considered we could not adequately address the needs of younger people with MS within this guideline. Making recommendations for people under 18 years requires a different approach which would include a different GDG constitution, reviews of different evidence and consideration of licensing issues in under 18s.
SH	Royal College of Nursing	7	4.2	Inclusion of social care environments is relevant to PwMS	Thank you for your comment. We acknowledge the importance of social care environment for people with MS. The remit from the Department of Health is for a clinical guideline for the management of MS in primary and

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
					secondary care and does not include social care or public health. We acknowledge the importance of social care for people with MS and anticipate that some of the interventions we recommend may be delivered by social care depending on local arrangements. As NICE will have a remit for social care from April 2013NICE is considering how best to address the issues of integration of heath and social care.
SH	Royal College of Nursing	8	4.3.1 a	The inclusion of clinically isolated syndrome and NMO is welcomed and guidance on minimum (cost effective) investigation required would be helpful as would guidance on who can undertake what investigation and where.	Thank you for your comment.
SH	Royal College of Nursing	9	4.3.1 a	We welcome proposals to use the new McDonald criteria in the diagnosis of MS.	Thank you for your comment.
SH	Royal College of Nursing	10	4.3.1 b	Holistic assessment and regular review is welcomed as is focus on vocational rehabilitation. Lifestyle coaching and a focus on living well with MS will enable self managing with MS.	Thank you for your comment.
SH	Royal College of Nursing	11	4.3.1 b	Assessment should include family members; MS is a family affair	Thank you for your comment. We have added 'impact on carers' to this section.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
SH	Royal College of Nursing	12	4.3.1 b	Assessment should also include competency of carers	Thank you for your comment. We have added 'impact on carers' to this section and will consider carer competency in relation to interventions and setting of rehabilitation.
SH	Royal College of Nursing	13	4.3.1 b	Annual Review and self referral would be good practice	Thank you for your suggestion.
SH	Royal College of Nursing	14	4.3.1 c	Shared decision making using evidenced based information, including advanced decisions for end of life is welcomed.	Thank you for your comment.
SH	Royal College of Nursing	15	4.3.1 c	All guidance should be mindful of the subtle, complex nature of cognitive deficits in MS that occur early in the course of the disease.	Thank you for your comment.
SH	Royal College of Nursing	16	4.3.1 c	Evidenced decision aid tools that are evidenced and proven would be welcomed Guidance for employers on how to set out the workplace for PwMS would be invaluable.	Thank you for your comment. The NICE guidance on Patient Experience, to which we will refer, already recommends the use of decision aids if these are high quality and available. We would expect that guidance for employers will need to be specific to the type of employment and to the particular disabilities the employee has and as such outside of advice a general guideline can provide.
SH	Royal College of Nursing	17	4.3.1 d	Should include other lifestyle factors; smoking (and HLADRB1) risk, stress, atypical infection etc	Thank you for your comment. Immunisation and pregnancy are included here as examples. The GDG will make the final decision as to which

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
					modifiable risk factors to include. We will include your suggestions in the discussion with them. The emphasis is intended to be on modifiable risk factors.
SH	Royal College of Nursing	18	4.3.1 e	This is really important and should play a major role in the guideline. We would welcome inclusion on managing relapse: a) with steroids b) without steroids (see 4.3.1 n) Self determination and self managing is a key theme. Strategies for family/meaningful others is also key	Thank you for your comment. The management of acute relapse with steroids is included in section 4.3.1 (n) administration of steroids. The management of rehabilitation following a relapse will be included in 4.3.1 (i) setting of rehabilitation. Self management programmes are included in 4.3.1 (e) The structured reviews 4.3.1 (b) included impact on carers.
SH	Royal College of Nursing	19	4.3.1 f k	Pharmacological management should include new and future available treatments including: ▪ Peristeen anal irrigation ▪ Use of Cognitive behavioural therapy for anxiety and depression	Thank you for your comment. The guideline will refer to the NICE Faecal Incontinence guideline which recommends referral to specialist service for people who require rectal irrigation. This guideline will cross refer to the NICE guideline on 'the treatment and management of depression in adults with chronic physical health problems; and on 'generalised anxiety disorder and panic disorder (with or without

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
					agrophobia'.
SH	Royal College of Nursing	20	4.3.1 f k	We welcome inclusion of these symptoms and would add Seasonal Affective Disorder as a differential diagnosis Sexual dysfunction would be a welcome addition to managing symptoms	Thank you for this information People's individual needs in regard to sexual health will be included in the structured review as in 4.3.1 (b) but we do not consider that there is any MS specific treatment to review. The GDG will consider whether to make recommendations about facilitating onward referral.
SH	Royal College of Nursing	21	4.3.1 l	Inclusion of rehabilitation using local community resources and remote and IT/Computerised/Robotic guided rehabilitation would be relevant here	Thank you for your comment and suggestions which we will consider with the GDG.
SH	Royal College of Nursing	22	4.3.1 m	We very much welcome the inclusion of the role of the MS Specialist nurse. The UK leads the way in MS nursing and is seen as the gold standard in Europe (MS NEED 2012) Setting out the key elements of role of MS Specialist nursing would be welcomed in this guideline and would inform commissioning/configuration/tariffs of services for MS Specialist nursing. This could include the referral pathway to a MS Specialist nurse and the role of the generalist in MS care. There is a competency framework for MS Specialist services (MS Trust - RCN 2011) Currently there is a paucity of evidence and guidance on type and cost of MS nurse activity although work is in progress (Generating Evidence in Multiple Sclerosis Services	Thank you for your comment. . The recommendations will be informed by the evidence review and GDG.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				(GEMSS) MS Trust 2012)	
SH	Royal College of Nursing	23	4.3.1 m	Clarification on the breadth of the role, case management of whole episodes of care, extended practice and independent non medical prescribing for the MS Specialist nurse may be relevant.	Thank you for your comment. . The recommendations will be informed by the evidence review and GDG.
SH	Royal College of Nursing	24	4.3.1 m	The MS Specialist nurse should be set out in this guidance as managing responsive, pro-active care beyond diagnosis and across the MS trajectory, that is key to effective self managing and best use of resources	Thank you for your comment. The recommendations will be informed by the evidence review and GDG.
SH	Royal College of Nursing	25	4.3.1 m	Exploring the MS Specialist nurse's role telephone triage skills, remote/online working and life coaching would be welcome in this guidance	Thank you for your comment. The recommendations will be informed by the evidence review and GDG.
SH	Royal College of Nursing	26	4.3.1 n p	We would recommend inclusion of when NOT to use steroids for relapse Vitamin D would require consideration in light of the general population We would recommend the removal of specifics such as linoleic acid but include such things as mindfulness as there is some evidence of effectiveness in MS.	Thank you for your comment. The GDG will decide what areas should be covered with respect to the administration of steroids. Vitamin D for the management of MS is included in 4.3.1 (O). We have not pre-specified the components of programmes and will discuss the explicit inclusion of mindfulness based therapies with the

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
					GDG.
SH	Royal College of Nursing	27	4.3.3	We welcome proposals to cross reference to other relevant NICE guidelines e.g. Pain, epilepsy.	Thank you for your comment.
SH	Royal College of Nursing	28	4.4	Remaining in work/study is a key outcome for a young adult group and almost 50% are prematurely retired (Ready to Work: Meeting the employment and career aspirations of people with multiple sclerosis Work Foundation 2011). Remaining in a stable relationship is a key outcome; PwMS have 75% annualised divorce rate Episodes of clinical depression is a key marker as PwMS have a 50% incidence of at least one episode of clinical depression and a high suicide rate. It is currently managed at a sub optimum level.	Thank you for your comment. We have added this to the list of outcomes. The list of outcomes will be specified by the GDG and will vary for each evidence review.
SH	Royal College of Nursing	29	General	The guideline should include reference to the following: • Mental health assessment, mental health capacity, Independent Mental Capacity Advocate (IMCA)	Thank you for your comment. NICE include standard wording in all guidelines about mental capacity and this will be included in this guideline. Cognitive impairment is also included in the guideline scope.
SH	Royal College of Nursing	30	General	This guideline is welcomed and long awaited. The complexity of MS is increasingly understood and acknowledged and new markers of successful treatment outcomes being identified. Self managing and early intervention are recognized hallmarks of MS care and clear guidance on how best to implement these principles are awaited. Health care	Thank you for your comment.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				professionals outside this specialist field will benefit from updated guidance. The guidance should be mindful of the rapid pace of development in managing MS.	
SH	Royal College of Nursing	31	General	We reiterate the importance of integrated working across health acute and community, social and voluntary sectors and suggest that the guideline should make this explicit.	Thank you for your comment. The remit is for a clinical guideline
SH	Royal College of Paediatrics and Child Health	1	general	Thank you for inviting the Royal College of Paediatrics and Child Health to comment on the draft scope, *multiple sclerosis.* We have not received any responses to this guideline.	Thank you for your comment.
SH	Sheffield Teaching Hospitals NHS Foundation trust	1	4.3.1 f	I think the second or third line use of modafanil for severe fatigue should be considered	Thank you for your comment. Modafanil has not been included because of the European wide restriction limiting it's use to narcolepsy.
SH	Sheffield Teaching Hospitals NHS Foundation trust	2	4.3.3 c	The use of conventional disease modifying therapy with interferon and glatiramer acetate use was governed by the health service circilar 2002/4 and 2003 guidelines and not the technology appaisal use of newer drugs such as natalizumab and fingolimod uses that information for their baseline. There are also several drugs where phase III trials have shown positive benefits and there needs to be scope to include Teriflunomide, fumarate and laquinimod soon to treat MS. Better guiance on the treatment of secondary progressive MS needed too.	Thank you for your comment. We are aware of the Risk Sharing Scheme and we will keep up to date with its progress.
SH	Sheffield Teaching Hospitals NHS Foundation trust	3	4.3.3 h	The NICE guidelines mentioned is for non specialist use and neurologist are specialist. Different drugs work better for different types of nerve pain and we use a much boarder	Thank you your comment. The NICE guideline on neuropathic pain is currently being updated. The scope

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				range. Some pains such as trigeminal neuralgia respond more often to drugs like carbamazepine than amitryptiline. Also attention to non neuropathic pain needs to be mentioned.	outlines the broad range of drugs that will be covered. Symptoms such as non neuropathic pain will be covered in the structured review in 4.3.1 (b) and the GDG will consider whether to make recommendations about facilitating onward referral.
SH	Sheffield Teaching Hospitals NHS Foundation trust	4	4.4 d	Cognitive screens with MMSE, Addenbrooks and MOCHA are in common use too	Thank you for your comment
SH	Teva UK	1	4.3.3 c	Refer to HS-2002/004 which followed TA32 and is still in force, and also RSS letter (Gateway reference 16971, dated 1 December 2011)	Thank for this information. This section is for related NICE guidance.
SH	Teva UK	2	3.1 a	The definition of MS focuses on the inflammatory effects of the disease but overlooks the diffuse pathology in regard to such as brain atrophy / T1 / T2 lesions	Thank you for your comment. Section 3.1 provides general background information and we are unable to include all of the issues.
SH	Teva UK	3	4.1.1	Add Clinically Isolated Syndrome term into the guidelines as per the ABN guidelines	Thank you for your comment. This is included in 4.3.1 (a).
SH	Teva UK	4	4.3.3 c	Should products that are anticipated to be launched during the review phase, such as BG-12, laquinimod and teriflunomide, be included in the scope?	Thank you for your comment. We include drugs that are licensed, are in common usage and if there is evidence for their use which is not the case for new treatments and therefore these are not included.
SH	Teva UK	5	5.1.3	**Regarding the use of Gilenya following glatiramer acetate** TA254 - Fingolimod has been given a restricted recommendation as a second line therapy i.e. as an option for the treatment only of patients with high disease activity	Thank you for these comments on the use of disease modifying treatments. We are not making recommendations for disease modifying treatments in this

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				'failing' on treatment with INFβ for relapsing-remitting multiple sclerosis The second-line funding recommendation for Gilenya is a small proportion of the total MS population NICE indicated that they cannot provide funding guidance on the use of Gilenya following on from glatiramer acetate or other therapies There is neither a positive *nor* a negative recommendation to fund Gilenya following on from glatiramer acetate and, therefore, in the absence of guidance the decision is a clinical one. Interferons **and** glatiramer acetate are the established first-line best supportive care in the UK. Glatiramer acetate is recognised as an element of best supportive care and this should be clarified. Clinicians should have freedom to prescribe Gilenya following glatiramer acetate as it is a cost neutral option vs Interferon-beta The majority of the UK population have mild to moderate RRMS, a group for which glatiramer acetate is licenced and has long-term evidence to demonstrate its favourable benefit-risk profile.	guideline.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
SH	The Society and College of Radiographers	1	general	There are a range of implications for imaging services here, not just the CNS but also arising from complications such as UTI and possibly dysphagia. As usual, a plea for appropriate imaging resources, support and collaboration around protocols and development opportunities for specialist radiographer roles.	Thank you for your comment. NICE clinical guidelines make recommendations about appropriate interventions following a review of evidence. Resources, protocols and collaboration are not within our remit.
SH	The Society and College of Radiographers	2	general	Overall a much more holistic approach it seems from the document.	Thank you for your comment.
SH	Therapists in Multiple Sclerosis (TiMS)	1	3.1	Of significance is the fact that diagnosis frequently occurs between the ages 20-40	Thank you for this information.
SH	Therapists in Multiple Sclerosis (TiMS)	2	4.2	Integration with social care is fundamental to the care pathway for people with MS. Voluntary services also have a part to play	Thank you for your comment. The remit from the Department of Health is for a clinical guideline for the management of MS in primary and secondary care and does not include social care or public health. We acknowledge the importance of social care for people with MS and anticipate that some of the interventions we recommend may be delivered by social care depending on local arrangements. As NICE will have a remit for social care from April 2013NICE is considering how best to address the issues of integration of heath and social care.
SH	Therapists in Multiple Sclerosis (TiMS)	3	4.3.1	The disability management and rehabilitation section should include vocational rehabilitation, management of swallow and	Thank you for your comment. We have had to prioritise what we cover in the

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				communication difficulties, end of life care and modification of the person with MS' environment. Self management should also be emphasised	guideline and have prioritised those areas where an assessment of the clinical and cost effectiveness evidence will inform care. People's individual needs in regard to areas such as vocational rehabilitation will be included in the structured review as in 4.3.1 (b) but we do not consider that there is any MS specific treatment to review for these aspects of care. The GDG will consider whether to make recommendations about facilitating onward referral. Self management programmes are already included in the scope.
SH	Therapists in Multiple Sclerosis (TiMS)	4	4.3.1 b	the WHO classification of impairment, activity and participation should be used Communication and swallow issues should be included in structured review	Thank you for your suggestion which we will discuss with the GDG.
SH	Therapists in Multiple Sclerosis (TiMS)	5	4.3.1 e	If 4.3.1 j does not specifically cover non – pharmacological management of ataxia and tremor, it should be included in e	Thank you for your comment. We intend to include pharmacological and non-pharmacological treatment of ataxia and tremor.
SH	Therapists in Multiple Sclerosis (TiMS)	6	4.3.1 l	This is broader than just home versus hospital and should be expanded to look at the range of places rehabilitation takes place including community settings (not necessarily a person's home) specialist rehab units either as inpatient or	Thank you for your comment. We have altered this heading to 'Setting of rehabilitation' to cover the issues you raise.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				outpatient and generalist neuro rehab units	
SH	Therapists in Multiple Sclerosis (TiMS)	7	4.3.1 m	There are also specialist therapists working with people with MS and have a significant impact on the care of people with MS. They play a role in rehabilitation, reablement and prevention, often working at the boundaries of services to link and co-ordinate them. Therefore the scope should be expanded to cover all specialist healthcare professionals working with people with MS	Thank you for your comment. We recognise that many different healthcare professionals work with people with MS. The guideline does not aim to cover all aspects of care that a person with MS will require. The scope describes those areas where specific review of evidence is considered to be useful for the NHS.
SH	Therapists in Multiple Sclerosis (TiMS)	8	4.3.2 b	Why are contractures and other secondary problems not included. These can lead to major functional difficulties and pain for people with MS	Thank you for your comment. The prevention of contractures will be included in 4.3.1 (e) and 4.3.1 (g)
SH	Therapists in Multiple Sclerosis (TiMS)	9	4.3.3 a	This is really communication *with service users* rather than communication difficulties that an individual may have per se	Thank you for your comment. In addition, people's individual needs in regard to communication difficulties will be included in the structured review as in 4.3.1 (b).
SH	Therapists in Multiple Sclerosis (TiMS)	10	4.3.3 k	Specific management (rehab) of physical swallow problems (dysphagia) are not covered in CG32 and therefore should be in scope	Thank you for your comment. We have prioritised management of symptoms which are MS-specific. The structured review 4.3.1. (b) will include swallowing problems.
SH	Therapists in Multiple Sclerosis (TiMS)	11	4.5	The impact on work and economic productivity is significant in this patient group particularly given the young age profile	Thank you for your comment.
SH	Therapists in Multiple Sclerosis (TiMS)	12	general	The terminology should be consistent throughout particularly People with MS rather than patient in some places	Thank you for your comment. This scope has been amended to people

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
					with MS
SH	UK Multiple Sclerosis Specialist Nurse Association (UKMSSNA)	1	General	The UKMSSNA supports and endorses the submission made by the MS Society. The UKMSSNA agrees with the MS Society that NICE should take the opportunity to produce an integrated guidelines covering both health and social care and has written a joint letter with the MS Society to NICE regarding this.	Thank you for your comment. The remit from the Department of Health is for a clinical guideline for the management of MS in primary and secondary care and does not include social care or public health. We acknowledge the importance of social care for people with MS and anticipate that some of the interventions we recommend may be delivered by social care depending on local arrangements. As NICE will have a remit for social care from April 2013NICE is considering how best to address the issues of integration of health and social care.
SH	UK Paediatric Demyelinating and Multiple Sclerosis Working Group	1	3.1	Children with MS need to be considered. Studies consistently show that around 5% of people diagnosed with MS inadulthood actually experienced their first MS symptom in childhood. A recent national paediatric surveillance study into childhood demyelination reported that 80 children per year present with a clinically isolated syndrome in the UK (Absoud et al 2012 Mult Scler. Apr 19 Epub)	Thank you for your comment. We recognise the problems that children may have in terms of diagnosis and management and have carefully considered the guideline population. Following consideration of stakeholder comments we have altered the guideline population to people of 18 years and over only. We considered we could not adequately address the needs of younger people with MS within this guideline. Making

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
					recommendations for people under 18 years requires a different GDG constitution, reviews of different evidence and consideration of licensing issues in under 18s.
SH	UK Paediatric Demyelinating and Multiple Sclerosis Working Group	2	3.2 a	The diagnosis of children with MS should be addressed, as the diagnosis is often delayed. Doctors looking after children often do not consider MS as a possible diagnosis, This is likely to reflect lack of familiarity in this relatively uncommon group of disorder. In children, conditions which share some symptoms with MS occur more frequently than in adults. Hence deciding whether a child has MS or another condition ("the differential diagnosis") is more complex than in adults. Treatments of other recurrent non-MS demyelination provide further challenges in childhood.	Thank you for your comment. We recognise the problems that children may have in terms of diagnosis and management and have carefully considered the guideline population. Following consideration of stakeholder comments we have altered the guideline population to people of 18 years and over only. We considered we could not adequately address the needs of younger people with MS within this guideline. As your comment indicates making recommendations for people under 18 years requires a different approach and include different GDG constitution, reviews of different evidence and consideration of licensing issues in under 18s.
SH	UK Paediatric Demyelinating and Multiple Sclerosis Working Group	3	3.2 c	There is a great variation in prescribing practise in children. Many paediatric neurologists are not familiar with these drugs and may therefore are reluctant to prescribe them. Optimal and timely treatment as recommended by the International (Chitnis et al 2012 *Mult Scler.* 18(1):116-27) and European	Thank you for your comment. We recognise the problems that children may have in terms of diagnosis and management and have carefully considered the guideline population.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				MS group (Ghezzi et al 2010 *Mult Scler.*16 (10):1258-67) are often initiated only in a small number of patients eg. disease modifying treatment (interferons and glatiramer acetate) in children with multiple sclerosis. These drugs are prescribed off label as they are unlicensed for children (usually under 18), thus requiring a time-consuming process of securing local commissioning approval for funding. Treatment is inevitably delayed. Indeed some children may not be offered treatment, whilst others may have been started on treatments, which are no longer used as first line treatment adults e.g. azathioprine, because of easier availability. Children should be seen and treated by a paediatric Neurologist with an interest in demyelinating disorders.	Following consideration of stakeholder comments we have altered the guideline population to people of 18 years and over only. We considered we could not adequately address the needs of younger people with MS within this guideline. As your comment indicates making recommendations for people under 18 years requires a different approach and include different GDG constitution, reviews of different evidence and consideration of licensing issues in under 18s.
SH	UK Paediatric Demyelinating and Multiple Sclerosis Working Group	4	4.1.2	The guideline should include children. All those affected by the condition should have access to the same support regardless of age. Delay in diagnosis in children with Multiple Sclerosis, and access to specific therapies are issues (amongst a host of others) identified in the UK (National MS Society Meeting, London 2007), one that can best be addressed by this guideline.	Thank you for your comment. We agree that all people affected by a condition should have access to the same support regardless of age. We have carefully considered the inclusion of children and adolescents in the guideline. Following consideration of stakeholder comments we have altered the guideline population to people of 18 years and over only. We considered we could not adequately address the needs of younger people with MS within this guideline. Making recommendations for people under 18 years requires a different approach which would include a different GDG

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
					constitution, reviews of different evidence and consideration of licensing issues in under 18s.
SH	UK Paediatric Demyelinating and Multiple Sclerosis Working Group	5	4.3.1 a	The diagnosis of children with MS should be addressed, as the diagnosis is often delayed as described in section 3.2.a. Ideally children should be seen by a paediatric Neurologist with an interest in demyelinating disorders.	Thank you for your comment. We have carefully considered the inclusion of children and adolescents in the guideline. Following consideration of stakeholder comments we have altered the guideline population to people of 18 years and over only. We considered we could not adequately address the needs of younger people with MS within this guideline. Making recommendations for people under 18 years requires a different approach which would include a different GDG constitution, reviews of different evidence and consideration of licensing issues in under 18s.
SH	UK Paediatric Demyelinating and Multiple Sclerosis Working Group	6	4.3.1 b	Despite having better a better motor disability score, children share many common morbidity with adult sufferers. Problems such as emotional and cognitive deficits are frequently encountered but often overlooked. Compounded by other morbidities like fatigue, these contribute to the major challenges encountered the child's educational setting. It is envisaged that this guideline would facilitate the recognition of this but also map out a pathway for which this could be addressed. For children with MS, education needs to be considered.	Thank you for your comment. Following consideration of stakeholder comments we have altered the guideline population to people of 18 years and over only. We considered we could not adequately address the needs of younger people with MS within this guideline. Making recommendations for people under 18 years requires a different GDG constitution, reviews of

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				Children struggle in education, and may need access to educational psychology for a more extensive neuropsychometric assessment to support and develop coping strategies.	different evidence and consideration of licensing issues in under 18s.
SH	UK Paediatric Demyelinating and Multiple Sclerosis Working Group	7	General	As the guideline is to include children, the authorship must include a Paediatric Neurologist.	Thank you for your comment. Following consideration of stakeholder comments we have altered the guideline population to people of 18 years and over only. We considered we could not adequately address the needs of younger people with MS within this guideline. As your comment indicates making recommendations for people under 18 years requires a different approach and include different GDG constitution, reviews of different evidence and consideration of licensing issues in under 18s.
SH	UKCPA Neurosciences Group	1	General	The UKCPA Neurosciences group welcomes the initiative to update the existing MS guidelines.	Thank you for your comment.
SH	UKCPA Neurosciences Group	2	general	The purpose of the new clinical guidelines is about lifestyle measures, rehabilitation support and symptomatic management. It would be helpful if it was clear in the title of the document that disease-modifying therapies were not part of the scope.	Thank you for your comment. Disease modifying treatments has now been added under the clinical areas not covered section of the scope.
SH	UKCPA Neurosciences Group	3	General	The group is concerned about cross-referencing the GL to existing TAs in the context of emerging evidence. → Clinically isolated syndrome and the role of interferon are not featured in TA 32 but there is emerging evidence for the treatment.	Thank you for your comment. Clinically isolated syndrome will be included in the review for update of NICE technology appraisal TA32 on Beta interferon and glatiramer acetate for the

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
					treatment of multiple sclerosis.
SH	UKCPA Neurosciences Group	4	1.3.2.3	The UKCPA group feel that the diagnosis of MS should be specifically linked to the latest McDonald diagnostic criteria, as this is the consensus opinion of the International Panel on the Diagnosis of Multiple Sclerosis. The 2010 criteria increase specificity and/or sensitivity and may facilitate an earlier diagnosis of MS.	Thank you for your comment. The section number you refer to is from the CG8 guideline which this new guideline will replace. The diagnostic criteria for MS, including the revised McDonald criteria are included in the scope.
SH	UKCPA Neurosciences Group	5	1.4.3.3	Although from the scoping meeting in London it appears that the recommendations for interventions affecting disease progression may be removed from the updated guidance, the UKCPA feels that describing steroid-sparing oral immunomodulatory medicines such as azathioprine would continue to be useful.	Thank you for your comment. We have considered your suggestion about the inclusion of steroid sparing medicines and do not think it is appropriate to include these. The use of steroid sparing medicines is related to chronic use of steroids and to recommendations affecting disease progression which we are not including.
SH	UKCPA Neurosciences Group	6	1.4.3.3	Intravenous immunoglobulin (IVIg) is NOT recommended for the treatment of MS and is a black indication as per the Department of Health guidelines. Its use is not recommended or funded. References to IVIg should be removed.	Thank you for your comment. The section number you refer to is from the CG8 guideline which this new guideline will replace. Intravenous immunoglobulin is not included in the scope for the new guideline.
SH	UKCPA Neurosciences Group	7	1.4.3.3	If mitoxantrone is not to be subject to a TA, then reference to the place of mitoxantrone therapy for MS within the updated CG would be beneficial.	Thank you for your comment. We recognise the importance of disease modifying drugs for people with MS but consider appropriate use of mitoxantrone is outside scope of this guideline as we are including management of MS in primary and secondary care only. NICE guidance

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
					on these will be displayed together with the guideline recommendations in the NICE pathway.
SH	UKCPA Neurosciences Group	8	1.4.3.4	If this paragraph is to remain, then the wording around cladribine should be modified to differentiate between oral and intravenous cladribine. Oral cladribine DOES significantly reduce relapse rates versus placebo, however its toxicity limits its place in practice.	Thank you for your comment. The section number you refer to is from the CG8 guideline which this new guideline will replace. The paragraph you refer to will not remain.
SH	UKCPA Neurosciences Group	9	1.7.1.6	Medicines for the treatment of fatigue in practice extend beyond amantadine. The MS Trust recommended treatment with modafinil and this should be evaluated. Evidence is compelling e.g. Rammohan et al, *J Neurol Neurosurg Psychiatry* 2002; 72: 179-83 – using 200mg daily. The magnitude of benefit using the same scales for efficacy has been demonstrated to be greater than for amantadine, which is included in the current CG.	Thank your for your comment. The European Medicines Agency has recommended that the use of modafinil should be restricted to treat only sleepiness associated with narcolepsy following a safety review and we would not be able to recommend its use in primary or secondary care under these circumstances.
SH	UKCPA Neurosciences Group	10	1.7.6.5	Treatment of spasticity is only to extend beyond baclofen or gabapentin if side effects are troublesome (where the therapy should be stopped) or if treatment is unsuccessful. There are no recommendations to withdraw medicines not shown to be of benefit in the current guidelines. Can you please consider if it is appropriate to include such advice?	Thank you for your comment and for raising this important point. We agree that medicines that are not of benefit should be withdrawn but do not consider that this is a MS specific issues. The guideline will refer to the NICE Medicines Adherence guideline which includes regular review of repeat medicines.
SH	UKCPA Neurosciences Group	11	1.7.6.6	Intrathecal baclofen is sometimes combined with intrathecal morphine in an implanted infusion device for painful MS spasticity in specialist centres. This is not described in the current CG.	Thank you for this information. Baclofen is included in the scope and we will agree with the GDG which method of delivery of baclofen to include.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
SH	UKCPA Neurosciences Group	12	1.7.6.6	"Phenol injections to motor points or intrathecally". Differentiation between liquefied phenol and oily phenol must be made for safety reasons. High strength & liquefied phenol if injected cause tissue necrosis, which could be life threatening if inadvertently given intrathecally. See NPSA signal 1162D; Feb 2010. Only low strength oily phenol injections should be used for pain and spasticity indications.	Thank you for your comment. The section you refer to is from the previous guideline which this guideline will replace.
SH	UKCPA Neurosciences Group	13	1.7.11	The group is concerned about a simple cross-reference regarding the treatment of MS-related pain in the GL to existing TAs and CG96 (currently under review for accuracy) in the context of emerging evidence and condition specific requirements. Furthermore, it could be argued that MS patients experience more treatment resistant pain which is not covered in CG 96. MS patients occasionally require treatment with off-license medicines for neuropathic pain not covered in CG96 such as mexitiline.	Thank you for your comment. We recognise that patients may be resistant to standard treatments and that off licence use may be required in individual cases. We do evaluate off license treatments if there is significant evidence for their use and they are commonly used. Mexetiline is off license for treatment of pain and only available in the UK by special order. We would not be able to recommend a treatment which is not marketed in the UK and so cannot include mexelitine.
SH	UKCPA Neurosciences Group	14	1.7.13	The treatment of emotionalism is stated as "usually [with] a tricyclic antidepressant". Conventionally where a co-indication of neuropathic pain and emotionalism/depression is present, a larger dose of e.g. amitripytline is beneficial. The use of a TCA and an SSRI is not recommended owing to the risks of serotonin syndrome and hyperserotonin symptoms (such as nausea). However, an SSRI is usually the first choice of treatment for emotionalism / depression where there are no pain issues or where gabapentin is being used. This should be reflected in the updated CG.	Thank you for your comment. The section number you refer to is from the CG8 guideline which this new guideline will replace. The management of emotionalism is included in the scope for this guideline.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
SH	UKCPA Neurosciences Group	15	1.7.16	We would recommend that a patient with swallowing difficulties that affected the patient's ability to take his/her prescribed medicines should be referred to a hospital pharmacist for a medicines review where alternative formulations, routes of administration or alternative agents could be recommended. This is, of course, dependent on the local resources available.	Thank you for your comment. The section number you refer to is from the CG8 guideline which this new guideline will replace. The ability of a patient to take his/her medicine should be part of regular medication review and the need for regular medicines review is included in the Medicine Adherence guideline which is included in the related guideline section.
SH	UKCPA Neurosciences Group	16	General	Sporadic shortage of oral methylprednisolone tablets is leading to a variety of regimens being used across the different hospital centres. Recommendations as to what can be done if first-line treatment with methylprednisolone becomes unavailable can be included.	Thank you for your comment. We will bring this issue to the attention of the GDG.
SH	UKCPA Neurosciences Group	17	General	The group has been asked to comment on the decision to exclude acetylcholinesterase inhibitors from the scope. The group would welcome inclusion of treatment options for dementia related to MS if this will not be part of the dementia guidelines.	Thank you for your comment. Acetylcholinesterase inhibitors have been excluded from the scope as they are not licensed; we are not aware they are commonly used or are of any significant benefit.
SH	United Kingdom Clinical Pharmacy Association (UKCPA)	1	general	We have no comments to make at this time	Thank you for your comment.