

# APPENDICES

# Appendix A: Expanded model of illness (WHO ICF plus)<sup>467,468</sup>

## A way of describing someone's situation

People with long-term conditions such as MS may face a large range of changes in, or effects on, their life. When considering their situation and how it might be analysed and improved, it is helpful to have a consistent framework or way of categorising the important factors that need consideration. The World Health Organisation developed their International Classification of Impairments, Disabilities and Handicaps (ICIDH) in 1980 as a way of classifying the consequences of disease. This was revised and expanded into the International Classification of Functioning (ICF) in 2001.<sup>8</sup>

**Table A1 Expanded model of illness (WHO ICF plus)**

'Location' of description	Subjective/internal (experience, attributions and beliefs of the patient)	Objective/external (observations made by, and implications drawn by, others)
<b>Level of description (term used)</b>		
<b>Organ within person (pathology)</b>	<i>Disease:</i> Label attached by person, usually on basis of belief and experience.	<i>Diagnosis:</i> Label attached by others, usually on basis of investigation.
<b>Person (impairment)</b>	<i>Symptoms:</i> Somatic sensation, experienced moods, thoughts etc.	<i>Signs:</i> Observable abnormalities (absence or change), often elicited explicitly; <i>and</i> deficits assumed from observations.
<b>Person in environment (behaviour/'activities')</b>	<i>Perceived ability:</i> What person feels they can do and cannot do, and opinion on quality of performance.	<i>Disability/activities:</i> What others note person does do, quantification of that performance (not what others think should do).
<b>Person in society (roles/'participation')</b>	<i>Life satisfaction:</i> Person's judgement or valuation of their own role performance (what and how well).	<i>Handicap/participation:</i> Judgement or valuation of important others (local culture) on role performance (what and how well).
<b>Context of illness</b>		
<b>Personal</b>	<i>'Personality':</i> Person's attitudes, expectations, beliefs, goals, outlook, reasoning style, etc.	<i>'Past history':</i> Observed/recorded behaviour prior to and early on in this illness.
<b>Physical</b>	<i>Personal importance:</i> Person's attitude towards specific people, locations.	<i>Resources:</i> Description of physical (buildings, equipment etc) and personal (carers etc), resources available.
<b>Social</b>	<i>Local culture:</i> The people and organisations important to person, and their culture; especially family and people in same accommodation.	<i>Society:</i> The society lived in and the laws, duties and responsibilities expected from and the rights of members of that society.
<b>Totality of illness</b>		
<b>Quality of life –summation of effects</b>	<i>Contentment:</i> Person's assessment of and reaction to achievement or failure of important goals; <i>or</i> sense of being a worthwhile person.	<i>Social involvement:</i> Extent of positive interaction with society, contributing to social networks.

## Appendix B: Issues for people with MS and their carers<sup>14</sup>

**Table B1 Issues raised through focus groups and interviews**

Issue	Links to recommendations
<b>Diagnosis</b>	
The time diagnosis takes – variation in services, from speedy to experiences of long delays.	Section 3.3.1 recommends the provision of ready access to a specialist neurological service for diagnosis. A local implementation point recommends that guidelines are set for how timescales for the confirmation of a diagnosis will be met locally. Diagnosis is primarily based on clinical history and examination – further tests to be carried out only if diagnosis in doubt (Section 4.1).
Misdiagnosis and the impact of this on peoples' lives.	Referral system recommended such that the diagnosis is made by a doctor with specialist neurological experience (Section 4.1).
Poor communication with or by medical staff at a devastating moment in your life.	General recommendations on communication are made in Table 2 (Section 3). Specific recommendations on communicating the diagnosis can be found in Section 4.2.
<b>Support and information needs</b>	
Access to support – the need for immediate access to someone knowledgeable to talk to at the time of diagnosis.	Recommendation in Section 3.1.2 to consider the provision of emotional support to the person with MS from the time of diagnosis onwards. Section 4.2 also deals with immediate needs for support and information – ‘the person with MS should be put in touch with or introduced to a skilled nurse or other support worker, ideally with specialist knowledge of MS ... and counselling experience’.
Importance of a single contact point for people with MS, to provide ongoing information and support; provision of advice and sign-posting to other advice and support services. Could be an MS nurse, a GP, generic supporter or key worker knowledgeable about MS. Able to provide immediate advice and treatment in times of crisis.	Recommendation in Section 3.3.2 states that there should be someone within the MS-related services that ensures services are coordinated and collaborative. For the person with MS, they should have access to a person to assist in identifying and communicating local information sources and to facilitate access to resources and services needed.
Carers identified the need for someone to take responsibility for coordinating all aspects of care, eg organising annual review of drugs.	Recommendation to provide an annual review of support needs for people with MS who are ‘severely impaired and markedly dependent’, in Section 3.5.
To be in contact with people who look at physical disability in the context of the whole person, not as problems in isolation.	There are acknowledgements of the need to consider all aspects of a person with MS’s situation in the introductions to sections 3, 5 and 6. It is a theme that the guideline developers have been committed to, and which runs through the whole document.
Importance of access to advice on how to stay in work, including the adaptation of the physical environment.	Recommendations in Section 5.3 includes this. Reference is made to accessing specialist advisers and services where necessary in order to stay at work.

*continued*

Table B1 Issues raised through focus groups and interviews – *continued*

Issue	Links to recommendations
<b>Support and information needs – <i>continued</i></b>	
Important role of voluntary sector recognised, providing access to information.	Table 2 (Section 3) refers to the provision of information, including national sources, as does Section 4.2 – in particular recommendation R38.
<b>GP role</b>	
People with MS are positive about the general care provided by GPs, but acknowledge a GP isn't an expert in MS (and they need support and information themselves) – would like to see a person in each practice trained in the needs of people with MS.	This is covered by the two recommendations in Section 3.3.2.
<b>Hospital services</b>	
Patchy provision of neurologists – people with MS often fall through the net. Not enough emphasis on the social or practical side of having MS.	Section 3.3.1 recommends that every health commissioning authority should ensure its population has ready access to specialist neurological services for the initial diagnosis of MS and subsequent symptoms. Reference to the importance of considering leisure and social interaction is made in Section 5.4.
Problems with lack of access to case notes and full information at the time of a relapse – like starting again each time.	Importance of information sharing at the interfaces described in Section 3.3.2.
<b>Physical problems mentioned specifically by people with MS</b>	
There was very little discussion about specific physical problems associated with having MS. Participants recognised there is no 'cure' and were more interested in being able to get on with their lives. The following were mentioned, but not discussed: <ul style="list-style-type: none"> <li>• bladder problems</li> <li>• mobility and balance</li> <li>• gait</li> <li>• speech</li> <li>• vision</li> <li>• hearing.</li> </ul>	Sections 5 and 6 deal with these areas. Recommendations about bladder problems can be found in Section 6.2. Issues around mobility, balance and gait are dealt with in Sections 5.5 and 6.4. Section 6.15 makes recommendations about dealing with speech problems. Section 6.8 deals with the assessment, provision of equipment and referral to specialist ophthalmology clinic where necessary, for problems of vision.
<i>continued</i>	

Table B1 Issues raised through focus groups and interviews – *continued*

Issue	Links to recommendations
<b>Psychological problems mentioned specifically by people with MS</b>	
Cognitive problems.	Section 6.10 includes offering a cognitive assessment and specialist advice when appropriate.
Frustration/lack of confidence.	
<b>Psychological problems mentioned specifically by people with MS – <i>continued</i></b>	
Mood swings.	Section 6.11 deals with emotionalism and Section 6.12 depression, each of which could be factors associated with mood swings.
Depression.	This is discussed in Section 6.12.
Isolation. For people with mild-moderate MS this was about having someone to talk to, with counselling skills. For people with more severe MS it was isolation in the home and lack of mental stimulation.	The need for access to support and counselling is referred to in Section 4.2. Section 5.4 emphasises the need for people with MS to be supported in maintaining their chosen leisure and social activities.
<b>Relationships</b>	
Problems with relationships with partner – including breakdown or new relationships. Family carer feels they become a nurse, rather than a partner.	Sections 3, 5.7 and 6.16 all deal with different aspects of this. Support for carers is a recurring theme.
Impact on family life, children – young carers carrying out inappropriate tasks, including missing school to provide care.	A recommendation to consider the emotional and physical health of any children in the household of a person with MS is included in Section 3.1.4.
Recognition needed of the immensely difficult task of caring, both physically and emotionally.	Recommendation in Section 3.1.4 (also Section 5).
Anxiety within the family and the person with MS about possible hereditary influences.	This should be dealt with in the information given to people with MS about the disease (Section 4.2).
Support needs of partners and families must be recognised – should include advice and information, counselling and access to respite care.	Recommendations about the provision of support to family and informal carers are given in Section 3.1.4.
<i>continued</i>	

Table B1 Issues raised through focus groups and interviews – *continued*

Issue	Links to recommendations
<b>Respite care</b>	
Better information needed on access to and availability of respite care – for person with MS and carer.	Reference to the provision of respite support can be found in Section 3.5 with a specific recommendation.
Variability in costs and quality of respite care highlighted – participants felt there was a need for a national benchmark.	
Need for a choice in styles and facilities of respite care, tailoring to the needs of an individual.	
Important factors for people with MS in respite care – care staff with time to talk to residents, treating the person with MS as a person.	
<b>Treatment</b>	
Physiotherapy – highly regarded, but strong feeling that continuous provision is needed rather than one-off sessions. Limited NHS provision criticised. Most provision currently in hospital settings – very little in the community – often stops once at home.	Section 5 (on rehabilitation) and Sections 6.4 and 6.6 (weakness and ataxia) relate to physiotherapy interventions.
Occupational therapy – long waits for assessment and provision of equipment criticised. Assessment usually only as a result of a hospital admission.	Section 5.7 deals specifically with the provision of equipment adaptations.
Speech and language therapy – regular treatment not available.	Recommendations about dealing with speech and swallowing difficulties can be found in sections 6.14 and 6.15.
Importance of adapting support and provision to individuals' needs stressed throughout.	Throughout the document/recommendations.
Need for more MS specialists (all professions) in hospital and the community – real anxiety about quality of care, particularly from carers.	Reference to the need for specific specialist members of a rehabilitation team in Section 3.3.1.

Source: Focus groups and interviews held with people with MS and their carers in July – September 2001

## Appendix C: Literature searches

**Table C1 Databases searched**

Database	Date range searched
Cochrane Library	Pre Sept 2002
DARE	Pre Sept 2002
DARE (admin database)	Pre Sept 2002
Current Controlled Trials	Pre Sept 2002
National Research Register	Pre Sept 2002
Clinical Trials	Pre Sept 2002
Inside Conferences	1993 to September 2002
SIGLE	1976 to September 2002
Medline	1966 to September 2002
Embase	1980 to September 2002
Cinahl	1982 to September 2002
PsycINFO	1887 to September 2002
AMED	1985 to September 2002

### Inclusion criteria

Studies identified by the searches were screened for relevance. Papers considered to be potentially relevant were ordered and screened for inclusion. Due to time constraints studies were assessed for relevance and inclusion by one reviewer only. Where any difficulties were encountered these were resolved by discussion between the two reviewers working on the project. All papers were assessed for inclusion using the same form and the reviewer made the decision on whether to include the study based on the criteria listed below.

**Table C2 Inclusion criteria for 3.1.2 and 3.1.4**

<b>Study design</b>	SRs and primary studies of any design
<b>Intervention</b>	Any intervention aimed at supporting people with MS, family members or other socially important people
<b>Condition</b>	People with MS, stroke, TBI or spinal cord injuries
<b>Outcomes</b>	Any outcomes reported

Sections 3.1.1, 3.1.3, 3.2, 3.3, 3.4 and 3.5 were not included in the review process

Table C3 Inclusion criteria for 4.1 and 4.3

<b>Study design</b>	SRs or diagnostic accuracy studies
<b>Index test</b>	Any test used for the initial diagnosis or diagnosis of a subsequent relapse, to monitor disease progression, or to determine the sub-type of MS
<b>Reference standard</b>	Any reported reference standard was considered acceptable (including patient follow-up)
<b>Outcome</b>	Studies must report at least sensitivity and specificity, the DOR or a ROC analysis
<b>Population</b>	Studies should aim to diagnose patients with MS

Table C4 Inclusion criteria for 4.2

<b>Study design</b>	SRs or primary studies of any design
<b>Intervention</b>	Any intervention related to the provision of information regarding the condition or on how patients should be informed of their diagnosis
<b>Condition</b>	Only primary studies conducted with people with MS. SRs for any condition
<b>Outcomes</b>	Any outcomes reported

Table C5 Inclusion criteria for 4.4 and 4.6

<b>Study design</b>	SRs, RCTs and CCTs
<b>Intervention</b>	Any intervention aimed at treating acute worsening, optic neuritis, transverse myelitis or reducing disease progression
<b>Condition</b>	People with MS
<b>Outcomes</b>	Studies must report at least one clinical outcome

Table C6 Inclusion criteria for 4.7.1, 4.7.2, 4.7.3, 5.2, 5.3, 5.4, 5.5, 5.6 and 5.7

<b>Study design</b>	SRs and primary studies of any design
<b>Intervention</b>	Any intervention related to the assessment of rehabilitation or disability or which aim to alter the environment to maximise independence and safety
<b>Condition</b>	People with MS
<b>Outcomes</b>	Any outcomes reported by the studies will be considered

Table C7 Inclusion criteria for Section 6	
<b>Study design</b>	<i>Assessment:</i> SRs and diagnostic accuracy studies <i>Intervention:</i> SRs, RCTs and CCTs
<b>Intervention</b>	Any intervention aimed at treating specific symptoms associated with MS
<b>Condition</b>	Only primary studies conducted with people with MS. SRs in relevant conditions for symptoms on which there is insufficient MS specific evidence available*
<b>Outcomes</b>	<i>Assessment:</i> studies must report at least a diagnostic outcome measure <i>Intervention:</i> studies must report at least one clinical outcome
*Insufficient MS evidence was available for the 6.2, 6.3, 6.5.2, 6.6, 6.9, 6.11, 6.13, 6.14, 6.15, 6.16, 6.17. Therefore SRs were included for the relevant conditions	

# Appendix D: Searching for health economics evidence

## Searches and data sources

No study design criteria were imposed *a priori* as it was already known that little economic evidence was available, and it was thought best not to restrict the searches at this stage. The search strategies were designed and implemented by Catherine Beverley, Systematic Reviews Information Officer in the School for Health and Related Research at the University of Sheffield. All reviewing was carried out by the health economist. The following databases were searched: Medline, Embase, the Centre for Reviews and Dissemination (CRD) (including the Database of Abstracts of Review of Effectiveness (DARE), the NHS Economic Evaluation Database (NHS EED) and the Health Technology Assessment Database (HTA)), the Office of Health Economics Health Economic Evaluations Database (OHE HEED) and Econlit.

### ▷ Inclusion assessment

The titles, and where available the abstracts, were screened to assess whether the study met the following inclusion criteria.

*Patients* – At least some of the patients had MS. After the initial searches, supplementary searches in relation to specific questions were carried out, without the requirement that some patients had MS.

*Economic evidence* – The study was an economic evaluation or included information on resources, costs or specific quality of life measures. Selected quality of life measures were SF-36, EQ-5D or HUI (in conjunction with EDSS). These measures are the most useful for economic analysis of outcomes since they can be used to generate utility values in a modelling framework, and since they are generic measures they are useful for comparative purposes.

*Study design* – No criteria for study design were imposed.

## Summary results

The searches found 464 unique papers. The titles, abstracts and CRD/OHE HEED commentaries (where available) were reviewed, and 139 potentially useful papers were identified. The vast majority of these studies included only people with MS, but a small number make comparisons with other diseases. It was found that:

- 32 studies were solely concerned with quality of life (QoL) and contained no cost or resource information
- 38 studies were general resource use/cost studies, which consider the cost of MS to society and/or the individual with MS
- five studies were ‘needs assessments’.

▷ Summary by type

Six systematic reviews (of which four were HTA reports) covered:

- one on treatments for pain and spasticity (HTA)
- one on treatments for fatigue (HTA)
- one on immunomodulatory drugs (HTA)
- one on role of specialist nurses (HTA)
- one on corticosteroids for acute exacerbations
- one on overview of azathioprine treatment.

Nine economic analyses based on RCTs included:

- three on intrathecal baclofen therapy for spasticity
- three on oral *vs* intravenous corticosteroids in acute relapses
- one on immunoglobulin in secondary progressive MS
- one on the effect of rehabilitation on disability
- one on reducing the period of immobilization following pressure sore surgery
- one on the effects of physiotherapy on mobility.

Thirty-eight studies considering the general costs and/or resource use of MS, all based in Europe, the US or Canada, included:

- 12 on cost of illness (COI) studies (eight using a bottom-up costing method)
- two reviews of COI studies
- a further three studies use bottom-up costing but do not consider a full COI
- 13 cost studies considering indirect costs, as well as direct costs\*
- eight studies considering resource use but not including any cost information (of which five are patient surveys).

Five studies considered needs, specifically unmet needs, and included:

- three patient/carer surveys (from Europe, the UK and the US)
- one review
- one local study in Oxfordshire, which used a variety of data sources including observational data, audit and interviews.

Thirty-nine studies considered QoL as measured by the generic instruments outlined above, and included:

- 32 QoL studies containing no cost or resource data
- one study (a survey in Canada) considering QoL for carers of people with MS
- four studies making comparisons with QoL in other chronic conditions.

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\* 'Direct costs' are defined as all the goods, services and other resources that are consumed in the provision of an intervention, or dealing with side effects linked to the intervention. These costs can be medical and non-medical and can be incurred by the NHS, by patients and/or their carers and by wider society (eg social services). 'Indirect costs' are the lost productivity suffered by the economy as a result of an individual absence from work through illness, decreased efficiency or premature death.

# Appendix E: Health economics of comparing different methods of administration of methylprednisolone in the treatment of acute relapses in multiple sclerosis

## Introduction

The group were interested in finding out more about the potential costs and benefits of different methods of administering high-dose corticosteroids for the treatment of acute relapse. It is important to note that clinical practice varies widely and this document is based on 'usual' treatment, to the extent that it is possible to state what this is.

There is little clinical evidence available in this area. The evidence review (see Section 4.4) identified four trials comparing methylprednisolone with placebo and two trials comparing oral with intravenous methylprednisolone. The latter two trials are relevant to the current question and they were both carried out in the UK; unfortunately they are small and also difficult to compare given the different regimens used. Neither included any collection or analysis of resource use data. A further search for economic evidence in this area, which imposed no quality criteria on studies, found only one relevant paper. This is a survey of 212 consultant neurologists carried out in March 1997, which questioned them on their use of corticosteroids in the treatment of MS.

Formal economic modelling which attempts to systematically evaluate costs and benefits is not possible without relevant clinical data. Instead the costs and benefits of these three methods of administration were itemised in a way that facilitates comparisons.

While there are a number of choices of drugs and methods of administration, the focus here was on the use of methylprednisolone administered in three ways:

- hospital intravenous (inpatient or day case)
- home intravenous
- oral.

## Background

Hospital administration of intravenous methylprednisolone is the most common treatment for relapse. In many cases the person with MS will need to be admitted to hospital as a result of the disability caused by the relapse and in these cases they will usually receive intravenous methylprednisolone during their hospital stay. Where admission for disability is not necessary, many people will still be admitted in order to administer intravenous corticosteroids.

The hospital intravenous category considered here largely refers to inpatient stays, as day case administration is rare. A recent survey suggested that only 7% of neurologists could offer administration as day case.<sup>462</sup> Admission to hospital is probably more common in those areas

where specialist neurology units are not available, as there are few alternatives for administering high dose corticosteroids in these cases. Day case administration (and home intravenous) will be more common in areas with specialist units.

It is important to note that the only efficacy information considered here comparing oral and intravenous methylprednisolone comes from trials where intravenous administration was offered as a day case by the pharmacy at hospitals with specialist centres. This may not be representative of the usual method of administration of intravenous methylprednisolone across England and Wales.

Home intravenous administration is included here as it was of interest to the group. However, it is not readily available in most parts of the country. The same survey suggested that only 5% of neurologists had the facilities to offer home intravenous treatment with methylprednisolone.<sup>462</sup> There is no information on the number of GPs who may be able to offer this service.

The survey of neurologists may be misleading as in many parts of the country people experiencing a relapse will be managed by their GP (who would usually take advice from a neurologist). Once GP contact is established the care pathway will depend on the GP's and patient's experience of MS and relapse, the GP's relationship with the patient and local access to neurology services.

Oral corticosteroids are used by some GPs and some neurologists to treat relapse.

The Tremlett survey found that 74% of neurologists would recommend oral administration instead of intravenous methylprednisolone at sometime, although the most popular response (48%) was for 'occasional use' (<25% of cases).<sup>462</sup> Oral prednisolone was the most common treatment, with only 23% recommending oral methylprednisolone. There is no evidence on the comparative efficacy of prednisolone against methylprednisolone.

## Making comparisons

In the absence of appropriate clinical or economic evidence Table E1 is 'think piece' in an effort to encourage full consideration of potential costs and benefits when different methods of administration are being compared.

The potential costs and benefits have been classified under six headings.

### ▷ Effectiveness

The methods are compared in relation to their effect on relapse. The only formal comparative clinical evidence comes from two RCTs comparing oral methylprednisolone with intravenous administration as a hospital day case;<sup>124,125,134</sup> these show equal efficacy. There is no formal clinical evidence comparing home intravenous administration with either hospital intravenous or oral administration. Assuming comparable regimens there is probably no reason to expect a difference in efficacy between home and hospital intravenous administration. However, this does not take into account potential problems or side effects of treatments.

▷ NHS resources

There is no formal evidence on the NHS resource use involved in any of the methods of administration. In terms of the pure drug cost, an intravenous course of methylprednisolone costs just over twice as much as an oral course.<sup>6</sup> The costs of intravenous administration are much higher, especially if they involve an inpatient stay (although the stay may not always be solely for drug administration). Day case administration is likely to be cheaper than an inpatient stay, but this facility is probably only available at larger hospitals with specialist services.

Home intravenous administration requires equipment provision and involves staffing costs for home visits.

A study in a Toronto teaching hospital which followed 92 patients for 12 months showed that inpatient administration of methylprednisolone was more expensive than outpatient or home administration.<sup>463</sup> This finding was robust to all sensitivity analysis. However there was no clear finding on the comparative costs of home against outpatient treatment, and this depended on assumptions made about the relevant overheads and staff costs.

▷ Quality of life

There is no formal evidence on the effect of alternative methods of methylprednisolone delivery on quality of life. Positive effects on quality of life would be expected to result from alleviation of the symptoms associated with relapse. It is also probably reasonable to assume that intravenous procedures would have a greater adverse affect on QoL than oral administration. It is usually assumed that QoL is adversely affected by hospital admission, but it is also important to consider the substantial burden imposed by daily hospital visits.

Home treatment is likely to be preferred in terms of QoL. An Italian study by Pozzilli *et al* comparing a home-based management program with hospital care for MS found a significant benefit in favour of home-based care for four of the eight dimensions of the SF-36:\* general health, bodily pain, emotional role and social functioning.<sup>464</sup>

▷ Patient and carer costs

There is no formal evidence on the patient burden associated with alternative methods of methylprednisolone delivery. The main costs will arise from absence from work which are due to the relapse itself and also from any costs of drugs or equipment borne by the patient. In addition day case administration will require travel to hospital which involves time and possibly direct financial burden.

▷ Side effects, tolerability etc

The trials of oral *vs* intravenous administration reported similar (minor) side effects in both arms. The risk of infection is greater from intravenous treatment, but it is not clear whether there may be a greater risk at home or in hospital.

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\* The SF-36 is a generic health-related quality of life instrument that has been used in many studies of multiple sclerosis treatments and has been shown to be a valid and sensitive measure of QoL in the population of people with MS. The SF-36 contains 36 items covering eight dimensions of health: general health, bodily pain, physical functioning, emotional role, physical role, mental health, social functioning and vitality.

It has been argued that oral therapy, being easier than intravenous, might be used more frequently or courses extended when clinical response is lacking. This increased 'routine' use would increase the chances of corticosteroid-induced side effects. It may also increase the chances of the therapy being used inappropriately.

▷ NHS delivery issues

There is geographical variation in the availability of home-based intravenous treatment and day case treatment at hospital. Home treatment requires equipment and the availability of appropriate staff, while day case treatment requires facilities that are unlikely to be available at DGHs.

## Summary

Many factors should be considered when comparing alternative methods of methyl-prednisolone delivery and there is little formal evidence on any of these. There is no clearly dominant treatment in terms of clinical effectiveness or resource use.

Table E1 Comparing methods of administering methylprednisolone (compare row with column)

	Oral	Hospital IV	Home IV
Oral		<p><b>Effectiveness: equal (2 RCTs)</b></p> <p><b>NHS resources (no evidence)</b></p> <ul style="list-style-type: none"> <li>• lower drug &amp; admin costs*</li> <li>• no hospitalisation</li> <li>• Quality of Life (no evidence)</li> <li>• = relief of symptoms?</li> <li>• non-invasive vs invasive</li> <li>• higher than if in hospital?</li> </ul> <p><b>Patient/carer costs (no evidence)</b></p> <ul style="list-style-type: none"> <li>• absence from work</li> <li>• prescription charges?</li> </ul> <p><b>Side effects etc (little evidence)</b></p> <ul style="list-style-type: none"> <li>• equal ('minor')</li> <li>• increased routine use?</li> </ul> <p><b>NHS delivery issues (no evidence)</b></p> <ul style="list-style-type: none"> <li>• no major issues?</li> </ul>	<p><b>Effectiveness: no evidence</b></p> <p><b>NHS resources (no evidence)</b></p> <ul style="list-style-type: none"> <li>• lower drug &amp; admin costs*</li> <li>• Quality of Life (no evidence)</li> <li>• = relief of symptoms?</li> <li>• non-invasive vs invasive.</li> </ul> <p><b>Patient/carer costs (no evidence)</b></p> <ul style="list-style-type: none"> <li>• absence from work?</li> <li>• prescription charges ?</li> </ul> <p><b>Side effects etc (little evidence)</b></p> <ul style="list-style-type: none"> <li>• increased routine use?</li> </ul> <p><b>NHS delivery issues (no evidence)</b></p> <ul style="list-style-type: none"> <li>• no major issues?</li> </ul>
Hospital IV	<p><b>Effectiveness: equal (2 RCTs)</b></p> <p><b>NHS resources (no evidence)</b></p> <ul style="list-style-type: none"> <li>• higher drug &amp; admin costs*</li> <li>• hospitalisation (or day case)</li> </ul> <p><b>Quality of life (no evidence)</b></p> <ul style="list-style-type: none"> <li>• = relief of symptoms?</li> <li>• invasive vs non-invasive</li> <li>• hosp. (or daily visits)</li> </ul> <p><b>Patient/carer costs (no evidence)</b></p> <ul style="list-style-type: none"> <li>• absence from work</li> <li>• travel for day case</li> </ul> <p><b>Side effects/tolerability</b></p> <ul style="list-style-type: none"> <li>• equal ('minor')</li> <li>• risk of infection</li> </ul> <p><b>NHS delivery issues (no evidence)</b></p> <ul style="list-style-type: none"> <li>• Avail. of day case service</li> <li>• appropriateness of bed use</li> </ul>		<p><b>Effectiveness: no evidence</b></p> <p><b>NHS resources (no evidence)</b></p> <ul style="list-style-type: none"> <li>• = drug costs?</li> <li>• hospitalisation (unless day case)</li> </ul> <p><b>Quality of life (no evidence)</b></p> <ul style="list-style-type: none"> <li>• relief of symptoms</li> <li>• hospitalisation (or daily visits)</li> </ul> <p><b>Patient/carer costs (no evidence)</b></p> <ul style="list-style-type: none"> <li>• absence from work</li> <li>• travel for day case</li> </ul> <p><b>Side effects/tolerability</b></p> <ul style="list-style-type: none"> <li>• no evidence</li> <li>• risk of infection</li> </ul> <p><b>NHS delivery issues (no evidence)</b></p> <ul style="list-style-type: none"> <li>• availability of day case service</li> <li>• appropriateness of bed use</li> </ul>
Home IV	<p><b>Effectiveness: no evidence</b></p> <p><b>NHS resources (no evidence)</b></p> <ul style="list-style-type: none"> <li>• higher drug &amp; admin costs*</li> <li>• costs of monitoring</li> <li>• home equipment costs</li> </ul> <p><b>Quality of life (no evidence)</b></p> <ul style="list-style-type: none"> <li>• = relief of symptoms?</li> <li>• invasive vs non-invasive</li> </ul> <p><b>Patient/carer costs (no evidence)</b></p> <ul style="list-style-type: none"> <li>• absence from work</li> </ul> <p><b>Side effects/tolerability</b></p> <ul style="list-style-type: none"> <li>• risk of infection</li> <li>• less tendency for routine use?</li> </ul> <p><b>NHS delivery issues (no evidence)</b></p> <ul style="list-style-type: none"> <li>• availability of equipment</li> <li>• staff for home visits</li> </ul>	<p><b>Effectiveness: no evidence</b></p> <p><b>NHS resources (no evidence)</b></p> <ul style="list-style-type: none"> <li>• = drug costs?</li> <li>• costs of monitoring</li> <li>• home equipment costs</li> </ul> <p><b>Quality of life (no evidence)</b></p> <ul style="list-style-type: none"> <li>• relief of symptoms</li> <li>• home vs hospital</li> </ul> <p><b>Patient/carer costs (no evidence)</b></p> <ul style="list-style-type: none"> <li>• absence from work</li> </ul> <p><b>Side effects/tolerability</b></p> <ul style="list-style-type: none"> <li>• risk of infection</li> </ul> <p><b>NHS delivery issues (no evidence)</b></p> <ul style="list-style-type: none"> <li>• availability of equipment</li> <li>• staff for home visits</li> </ul>	

\* Drug costs have been estimated using regimens from Barnes *et al*<sup>134</sup> and drug costs from BNF43 (September 2002). Intravenous methylprednisolone 1000mg daily for 3 days = £41.31. Oral methylprednisolone 48mg day for 7 days, 24mg day for 7 days, 12mg day for 7 days = £18.48.

## Appendix F: Economic evidence for nuclear magnetic resonance imaging scans in the diagnosis of MS

Magnetic resonance imaging (MRI) is a relatively expensive diagnostic technology (costing approximately £200 per scan\*), and a relevant question is whether the benefits of MRI are worth the additional cost. While safety evaluations indicate that non-contrast MRI is safe for most people including pregnant women,<sup>465</sup> and the procedure is not painful or invasive, many people find it uncomfortable. Benefits from MRI in diagnosis of MS may arise from the medical information it provides (which in turn informs disease management) and also from the potential psychological value of the information to the patient. In addition MRI may reduce the need for other tests, and in particular the need for EPs, CSF examination and lumbar puncture has diminished in recent years.<sup>466</sup>

### How might MRI affect care?

In MS the majority of interventions are targeted at symptoms rather than the disease itself, and the extent to which symptom management is influenced by diagnosis is unclear. A review of evidence suggested that MRI has had little direct impact on therapeutics or patient outcomes.<sup>465</sup> However, it seems sensible to suggest that errors of diagnosis, delay in diagnosis and invasive tests will all occur more often if MRI is not carried out (expert opinion).

The availability of the disease-modifying therapies (DMTs) interferon beta and glatiramer acetate under the risk-sharing scheme may have implications for the use of MRI in diagnosing MS. DMTs are available to people with a diagnosis of relapsing-remitting MS (RRMS) or secondary progressive MS (SPMS) in which relapses are the dominant feature, and who meet the Association of British Neurologists' criteria for treatment. It is estimated that between 7,500–9,000 people in England and Wales may be eligible for treatment (approximately 12.5% to 15% of the estimated total number of people with MS). The ABN criteria are not dependent on diagnosis via MRI and it is unclear how many of the eligible population would require an MRI scan to confirm diagnosis before access to treatment (the majority of people will already have had an MRI scan before this point).

Nevertheless, in countries where DMTs have been more commonly used than the UK, MRI is often used to aid the decision on whether to start, stop or modify therapy. This may mean that the risk-sharing scheme does increase the requests for MRIs.<sup>466</sup> The new international panel criteria which recommends MRI for diagnosis on people with clinically isolated symptoms is also likely to increase demand for MRI scans.<sup>55</sup>

### Existing cost-effectiveness studies

Only two studies were identified;<sup>93,94</sup> these looked at the targeting and cost-effectiveness of MRI for people with equivocal neurological symptoms who may have MS. Both studies employ

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\* Cost estimates vary between £155 and £286 for an MRI within the NHS.

decision analytic models, which are particularly valuable in evaluating diagnostic technologies since they enable modelling of alternative scenarios with their associated costs and benefits given available information, and they also allow identification of key areas of uncertainty around clinical utility and cost-effectiveness which can guide future research. Both studies are by the same authors and represent developments of the same piece of work; only the latest study is included in the evidence tables.<sup>93</sup>

This study made good use of information available at the time (early 1990s) and also employed comprehensive sensitivity analysis to deal with the large amount of uncertainty surrounding the key model parameters. The study concluded that MRI was not cost-effective in people with low prior probability of MS (unless the diagnostic information has a very high psychological value to patients). As the probability of disease increases, further MRI use becomes cost-effective. Given the fact that this study is relatively old (in an area where the technology is developing) and that it is based in the US, there is little value in citing specific cost-effectiveness ratios. Nevertheless, the results do question the usefulness of routine use of MRI in people where the probability of MS being present is low unless there is a reasonable probability of an alternative diagnosis that can also be diagnosed using MRI being present.

The results from both studies revealed that the key areas of uncertainty were the diagnostic accuracy of MRI and the value of the diagnostic information to patients (over and above the affect of the test result on disease management); both of these factors will have an important influence on the cost-effectiveness of the technology. In addition, these studies were carried out before the availability of the DMTs interferon beta and glatiramer acetate, so they do not take account of any additional benefit arising from speeding up access to these therapies.

### Increasing the relevance of this information

In an effort to update these cost-effectiveness studies and improve their relevance to our recommendations, a further comprehensive search was carried out to find economic information on the use of MRI as a diagnostic technology in MS and other neurological diseases, ie to identify the potential costs and benefits of MRI. As well as updating the original search of standard bibliographic databases (and broadening this outside of MS) the new search also focused on a number of key websites and databases. In addition information was sought from a number of relevant professional and academic organisations.

This search (and the review of the clinical evidence) revealed that evidence on the diagnostic accuracy of MRI had improved very little since the US cost-effectiveness studies of the early 1990s. As a result it was not possible to construct a cost-effectiveness model within the required time. Furthermore, this model would probably be of little value since it would be characterised by the same key uncertainties as the earlier work.

As an alternative to cost-effectiveness modelling (and after taking further advice from some members of the GDG) the focus was on providing answers to some questions, which may help to inform our recommendations.

### What proportion of people with (suspected) MS receive an MRI scan at present?

There is no formal data source containing this information. Expert opinion suggests that almost all people with MS will have had an MRI scan at some point, but it is not clear how many people

with suspected MS (ie some evidence from clinical tests) will get a scan, or how long they would have to wait (see below).

The number of MRI scans carried out for the purpose of diagnosing MS can only be estimated from incidence figures. There is uncertainty in estimating the current incidence and prevalence of MS. The HTA systematic review on the natural history and epidemiology of MS, produced to inform these guidelines,<sup>4</sup> cites prevalence of 100–109 per 100,000 and incidence of 3.5 to 3.8 per 100,000. Expert opinion from Alistair Compston and David Miller suggests an incidence of 7 per 100,000. This amounts to around 2,100 to 4,200 first diagnostic scans per year, depending on which incidence figure you take and assuming that all new cases receive an MRI scan. David Miller has suggested that as many again are probably done to exclude a diagnosis of MS.

Despite much concern over extremes in geographical variation there is little formal data on this. In relation to access to a neurologist, an ABN survey in 1999 and 2001 ([www.theabn.org/ukneuro/acuteneurology.html](http://www.theabn.org/ukneuro/acuteneurology.html)) asked consultant neurologists how long was the wait until their next appointment for a routine referral from a general practitioner for any purpose. The results show waits varying from 13 weeks in North West Thames to 51 weeks in Wales. Some areas show improvement since 1999, but in others the situation has worsened.

MRI scanning facilities in the UK are heavily used and if scanners are not used for the purposes of diagnosing MS, the machinery and staff would almost certainly be involved in scans for other purposes, so any cost savings from fewer MS scans are unlikely to be realised. However, there is a true opportunity cost from using a scanner to aid in the diagnosis of MS.

### What is the value of MRI in the diagnosis of relapse?

From the research point of view there appears to be much interest in MRI results as a potentially more objective outcome measure than EDSS in measuring disease progression. However, it is not clear how MRI results can be translated into patient-based outcomes (like quality of life) and evidence on the relationship between MRI and clinical progression is not conclusive. Any recommendations on the role of MRI in the continued management of MS (ie after diagnosis) must consider the effect on waiting times for initial diagnostic scans.

### Other important questions for which it was not possible to find information

- Do patients have lower/higher subsequent treatment costs if they have had more MRIs?
- Do patients have different rates of disability/relapse/death if they have had more MRIs?
- Can the cost of an MRI be equated with any clinical gain?

## Appendix G: The McDonald Criteria<sup>55</sup>

**Table G1 Making the diagnosis**

Clinical presentation	Additional data needed to make diagnosis	Comment
Two or more attacks; objective clinical evidence of two or more lesions.	None.	If tests (MRI scans or CSF analysis) are undertaken and are negative extreme caution must be taken before making a diagnosis of MS. Alternative diagnoses must be considered. There must be no better explanation for the clinical picture.
Two or more attacks; objective clinical evidence of one lesion.	Dissemination in space demonstrated by MRI.	MRI scan must fulfil criteria for brain abnormality (overleaf).
	Two or more MRI-detected lesions consistent with MS plus positive CSF.	Positive CSF: oligoclonal bands detected by established methods, preferably isoelectric focusing, different from any such bands in serum; or by a raised IgG index.
	Await further clinical attack implicating a different site.	
One attack; objective clinical evidence of two or more lesions.	Dissemination in time demonstrated by MRI.	MRI scan must fulfil criteria for dissemination of lesions in time (overleaf).
	Second clinical attack.	
One attack; objective clinical evidence of one lesion (mono-symptomatic presentation; clinically isolated syndrome).	Dissemination in space, demonstrated by MRI scan.	MRI scan must fulfil criteria for brain abnormality (overleaf).
	Two or more MRI-detected lesions consistent with MS plus positive CSF <i>and</i> dissemination in space, demonstrated by MRI scan <i>or</i> second clinical attack.	Positive CSF: oligoclonal bands detected by established methods, preferably isoelectric focusing, different from any such bands in serum; or by a raised IgG index.
		MRI scan must fulfil criteria in the second paragraph of the criteria for dissemination of lesions in time (overleaf).
Insidious neurological progression suggestive of MS.	Positive CSF <i>and</i> dissemination in space, demonstrated by nine or more T2 lesions in brain <i>or</i> two or more lesions in spinal cord, <i>or</i> four to eight brain plus one spinal cord lesion.	Positive CSF: oligoclonal bands detected by established methods, preferably isoelectric focusing, different from any such bands in serum; or by a raised IgG index.
	Abnormal VEP associated with four to eight brain lesions, <i>or</i> with fewer than four brain lesions plus one spinal cord lesion demonstrated by MRI <i>and</i> dissemination in time, demonstrated by MRI.	Abnormal visual evoked potential of the type seen in MS (delay with well preserved wave form).
	Continued progression for one year.	MRI scan must fulfil criteria shown in criteria for brain abnormality (overleaf).

## Magnetic resonance imaging criteria

### ▷ Magnetic resonance imaging criteria for brain abnormality

Magnetic resonance imaging criteria for brain abnormality are based on **three of four** of the following:

- one gadolinium-enhancing lesion or nine T2-hyperintense lesions if there is no gadolinium enhancing lesion
- at least one infratentorial lesion
- at least one juxtacortical lesion
- at least three periventricular lesions.

Note that one spinal cord lesion can be substituted for one brain lesion. Data from Barkhof *et al* 1999 and Tintore *et al* 2000.

### ▷ Magnetic resonance imaging criteria for dissemination of lesions in time

If a first scan occurs three months or more after the onset of the clinical event, the presence of a gadolinium-enhancing lesion is sufficient to demonstrate dissemination in time, provided that it is not at the site implicated in the original clinical event. If there is no enhancing lesion at this time, a follow-up scan is required. The timing of this follow-up scan is not crucial, but three months is recommended. A new T2- or gadolinium-enhancing lesion at this time then fulfils the criterion for dissemination in time.

If the first scan is performed less than three months after the onset of the clinical event, a second scan done three months or more after the clinical event showing a new gadolinium-enhancing lesion provides sufficient evidence for dissemination in time. However, if no enhancing lesion is seen at this second scan, a further scan not less than three months after the first scan that shows a new T2 lesion or an enhancing lesion will suffice.

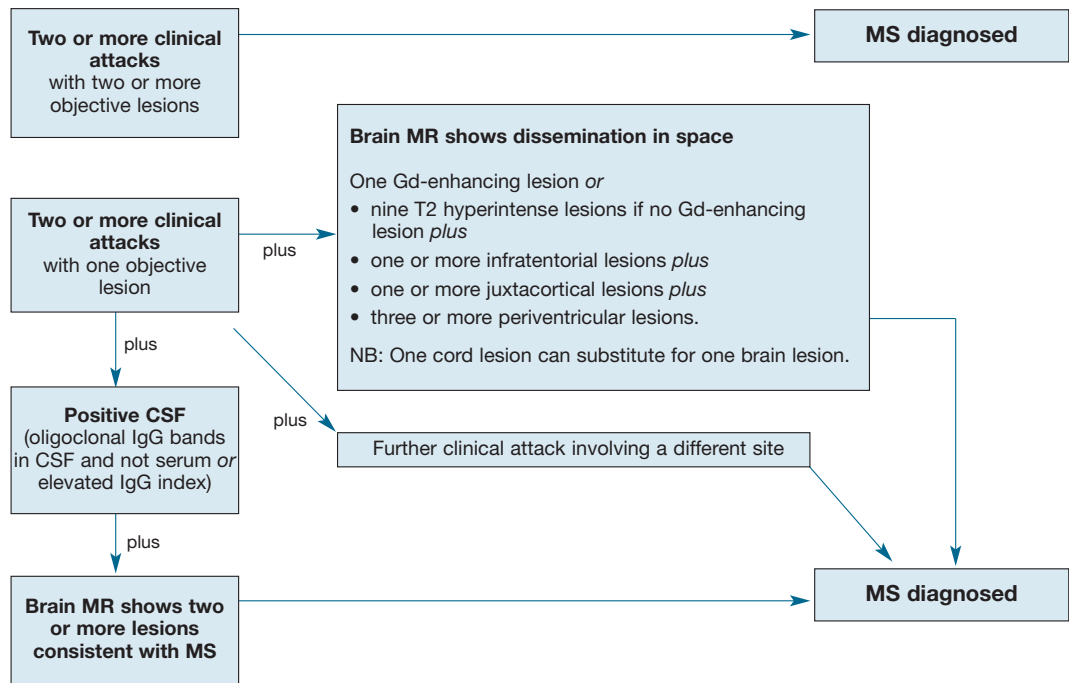
## Guidelines for the accurate diagnosis of MS according to the McDonald criterias

- 1) The diagnosis should be made by an experienced clinician with expert knowledge of MS and similar neurological conditions.
- 2) The prior probability that the individual has MS depends on factors such as age, ethnicity and geographical location.
- 3) Objective evidence of dissemination in time and space of lesions typical of MS is mandatory, as is the exclusion of other, better explanations for the clinical features.
- 4) Historical reports of symptoms may suggest previous episodes of demyelination, but cannot be used without objective evidence to satisfy the requirement of lesions disseminated in time and space.
- 5) MS can be diagnosed on purely clinical evidence of lesions separated in time and space.
- 6) Radiological (MRI) and laboratory evidence is desirable and may be essential where clinical evidence is insufficient for a secure diagnosis.
- 7) The choice of investigation will be determined by the clinical situation; for example, a delayed visual evoked potential is of value in a person with a spinal cord lesion but is of little value in a person with optic neuritis.

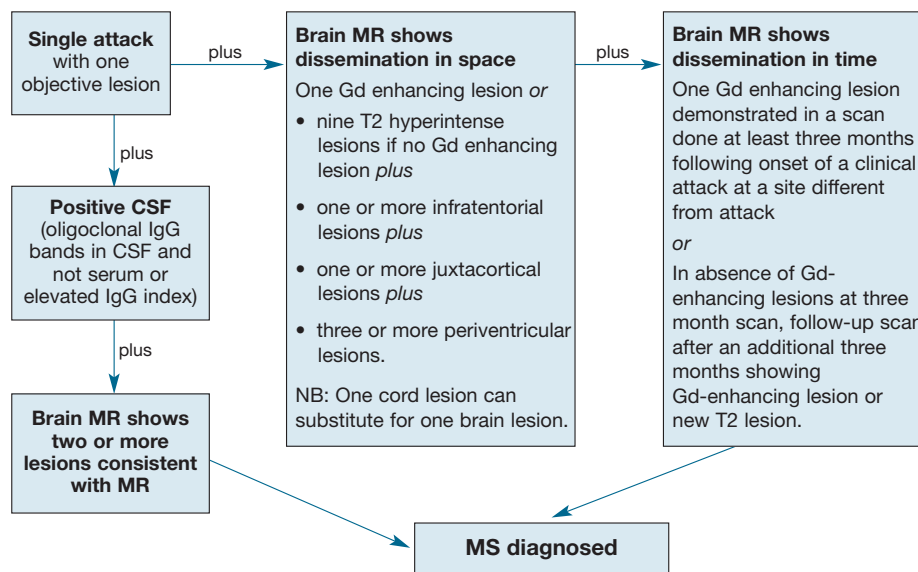
- 8) MRI is less useful in older people and in other inflammatory conditions such as acute encephalomyelitis where its specificity is lower. MRI is not applicable in people with metallic foreign bodies, pacemakers, etc or in those who cannot tolerate the procedure.

**Flow charts for diagnosis of MS using McDonald criteria**

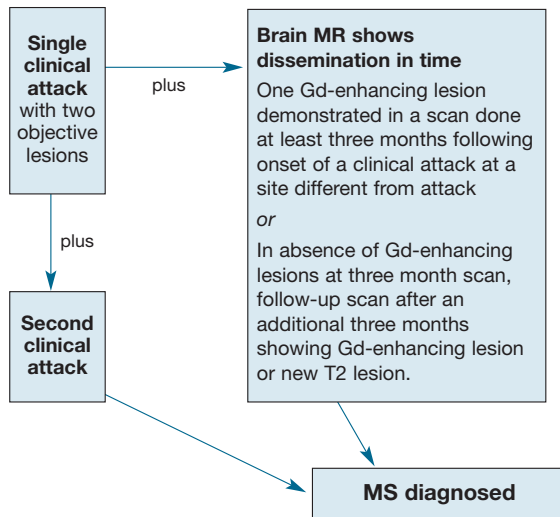
- ▷ Diagnostic criteria for suspected MS (two or more attacks)



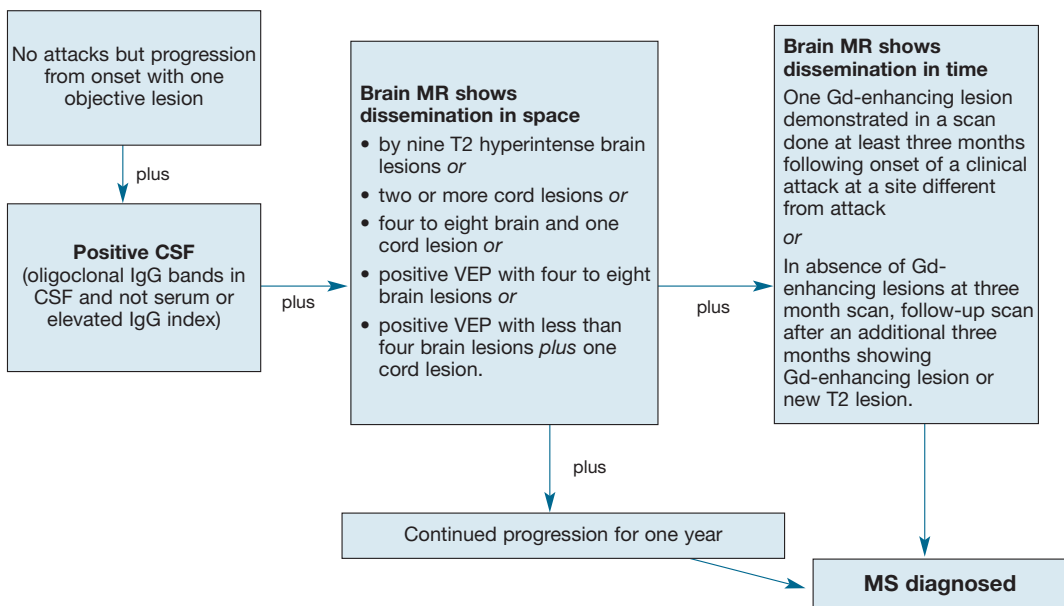
- ▷ Diagnostic criteria for suspected MS (monosymptomatic)



▷ Diagnostic criteria for suspected MS (single attack)



▷ Diagnostic criteria for suspected MS (progressive from onset)



## Appendix H: Assessments and measures

These guidelines do not recommend or even mention specific measures or assessments. A brief explanation is given in the introduction. This appendix gives a little more information. However, it must be emphasised that the measures mentioned here are not being recommended in any way.

First, the reader is reminded of the second paragraph in section 3.2.1:

The process of assessment refers both to the collection and to the interpretation of data needed to identify problems (screening) and to inform the solutions. The process of assessment may or may not include measurement, which is the quantification of data against some metric. In other words, an assessment procedure may be considered to have two purposes which may be distinct or combined:

- the **detection** of a phenomenon (ie diagnosis); and,
- the **measurement** of a phenomenon.

The questions faced are whether we are able to give recommendations that cover:

- how specific impairments or activity limitations should be detected
- how the severity of any impairment or activity limitation should be quantified, for example when measuring the outcome of an intervention
- what protocols should be used when first seeing a person with MS in order to detect most common or important difficulties.

In all three cases the first step is to collect data from or about the person with MS, and so the discussion is primarily concerned with whether or not the guidelines should mention or recommend specific data collection tools. These are referred to as ‘measures’ or ‘assessments’ interchangeably and loosely. A measure is a way of quantifying something; an assessment is a process of making a rehabilitation diagnosis through identifying and sometimes quantifying the presence of various abnormalities. The recommendations have emphasised the need for the process of assessment, and implied that measurement should be considered. The question is whether specific tools should be recommended.

### The problems

There are several problems, especially in the context of a document that is emphasising the need to base recommendations on evidence.

The evidence searches undertaken have not been appropriate for making decisions on which data collection tools to recommend. To give reasonable evidence we would need to search for evidence on what purposes each tool might be suitable for, how reliable it is, how sensitive to change if used for that purpose, its diagnostic sensitivity and specificity if used for that purpose, its feasibility, and its comparative utility with other tools.

For almost all tools only minimal published data are available. Specifically there are very little comparative data to guide any choice between tools that collect data on the same problem.

However, the number of tools used in research is vast. This appendix includes a list of measures mentioned in the studies tabulated in the evidence tables. This list is only a small proportion of the measures used in the totality of MS research. Moreover, in clinical practice a different set of measures is used (in as far as measures are used at all). The utility, validity etc of most of these measures is unknown.

It also needs to be recognised that many people hold strong views on what to use and will anyway disagree with and probably ignore any recommendations. The comments by stakeholders illustrated the wide variety of opinions on appropriate measures vividly – there was no agreement by stakeholders on any single measure.

At the same time those without strong views might not use any tools, whatever is recommended.

### **In favour of making recommendations**

In the guidelines we have suggested repeatedly that specific problems (such as swallowing difficulties) are identified, but not how. This omission lessens the likelihood of the recommendations being followed. Many stakeholders suggested that we should include recommendations, but usually recommended ones that others did not.

### **Against making recommendations**

Although we have not searched systematically for evidence on measures, there is in fact little useful evidence available and we have not searched for or found the relatively limited available evidence. Consequently any recommendations made will be arbitrary and will not be agreed. Therefore it is unlikely that any specific recommendations will be followed, making it unwise to make them.

We do not have the time or resources to undertake a proper systematic search for evidence even in one domain, let alone for the whole of neurological rehabilitation. It is wiser to make no recommendations than to make recommendations that are personal preferences, rather than based on firm evidence, and likely to be disputed by more people than agree on them.

### **What is available?**

In the process of formulating these guidelines and collating the evidence we have, however, produced some information.

First, there is a simple list of all the measures used in the research studies referred to in this document. Many of these measures are untested and few will be useful.

### **List of measures**

The tabulated list of measures is simply set out in order of frequency, with a brief note on some measures where known. The names given are those abstracted from the original papers, and some of the measures may have no further data available. To find further details the reader should identify the study that used the test and read the original paper.

## Conclusions

Several conclusions can be drawn from this appendix.

Firstly, future search strategies should focus on investigating:

- **validity:** what purposes the measure can fulfil (or what measures can fulfil a specific purpose)
- **reliability:** how consistent the tool is when used in different circumstances by different people or in different ways
- **sensitivity:** what change or difference can it detect
- **utility:** this is a review of such factors as the time and effort needed to use the measure, the amount of equipment needed, the training needed by the assessor, and how much the information gained alters clinical decisions.

Second, a large number of measures have been used, but many only once.

A research programme should be set up to investigate simple measures for routine use, preferably not limited to MS but covering all neurological conditions.

Table H1 Assessment tools used as outcome measures in multiple sclerosis RCTs and CCTs in evidence tables

Number of studies	Assessment tool	Number of studies	Assessment tool
84	EDSS	1	Fog scale
13	ADL otherwise unspecified	1	Global gait score
13	AI (Ambulation Index – Hauser)	1	Gottschalk and Gleser Scale
13	Ashworth scale	1	Gulick MS Specific Symptom Scale Score
12	SF-36	1	Health Attribution Test
11	FSS (Fatigue Severity Scale)	1	Hopkins Verbal Learning Test (HVLT)
10	BDI (Beck Depression Inventory)	1	HRSD
8	Alexander score	1	Imagery Assessment Tool
7	Nottingham health profile	1	Independence of activities of daily living (IADL)
6	9-HPT (Nine Hole Peg Test (manual dexterity))	1	Jebsen Test of Hand Function (JTHF)
6	Barthel Index ADL	1	Marital adjustment (Marital Adjustment Test – MAT)
6	Frenchay activities index – extended ADL		
6	Kurtske FSS (EDSS)	1	Memory concentration test
5	Rivermead mobility index	1	MFIS score
5	State Trait Anxiety Inventory (STAI)	1	MMPI D-30 scale
4	DSS (Disability Status Scale; precursor to EDSS)	1	MMSE (Mini-Mental State Examination)
4	General Health Questionnaire	1	MS self-efficacy function and control sub-scales
4	Incapacity Status Scale	1	MSIS
4	POMS (Profile of Mood States)	1	MSPSS (total social support)
4	RFSS	1	MSQOL-54
4	Scripps NRS (Neurological Rating Scale (impairments))	1	MSSE
4	FIM (Functional Independence Measure)	1	Nottingham Extended ADL index
4	HADS (Hospital Anxiety and Depression scale)	1	Oxford Handicap Scale Scores
3	GNDS (Guy's Neurological Disability Scale)	1	PASAT
3	NRS (Neurological Rating Scale Scripps)	1	Personality change (NEO-PI, Hogan Empathy Scale)
2	Berg Balance Test	1	Philadelphia Geriatric Center Morale Scale
2	ERP (Evoked Response Potential (EEG))	1	Prose Memory (MAS)
2	Hamilton Rating Scale	1	Rankin Scale
2	London handicap scale	1	Rehabilitation Institute of Chicago Functional Assessment Scale
2	MS Symptom Checklist		
2	Snellen test	1	RIC-FAS
1	Accommodation self-efficacy measure	1	Rivermead Behavioral Memory Test
1	Affect Balance Scale	1	Rivermead Motor Assessment (gross function, leg function, functional assessment)
1	AMB		
1	Anxiety Scale Score (ASQ)	1	Rosenberg Self-Esteem Scale
1	Arthritis impact measurement scale	1	SDDRE (how essential help with ADL is)
1	ASSS	1	SDDRO (help required in the last 24 hours with personal care, mobility, household tasks, leisure and employment)
1	Aulhorn Flicker Test		
1	Borg's post reading (perceived rate of exertion)	1	SDMT written (one of the attention/visuomotor search scales)
1	Boyarsky Scale		
1	Brief Assessment of Social Engagement and Life Satisfaction Index scores	1	SF-36
1	Bronx scale	1	SF-54
1	CDQ	1	Shiply Institute of Living Scales
1	Cerebellar Functional System Score		
1	Chalder Fatigue Scale Score	1	SOMC (Short Orientation Memory Concentration Test)
1	Community Integration Score	1	Spiral copying
1	COP Sway Centre of Pressure	1	SSEP (Somato-sensory evoked potential (EEG))
1	Cybox flexion score (quadriceps spasticity)	1	Standardised neurological status
1	Dartmouth Co-Op Chart	1	Symbol Digit Modalities Test (oral version)
1	DRS Disability Rating Scale	1	Symptom rating questionnaire (patient assessment)
1	Environmental status score	1	Symptom Trait Scale (physical symptoms)
1	EQUISCALE	1	Tempelaar Social Experience Checklist (SET)
1	Esteem (SES)	1	Visual Faces Scale Rating (patient rating of pain and spasticity)
1	Everyday memory problems (EMQ)		
1	FAMS symptoms (Functional Assessment in MS)	1	WAIS similarities and WAIS picture arranging
1	Fatigue Impact Scale (FIS)		
1	FDS (pyramidal functions and bladder and bowel functions)		

## Appendix I: Evidence tables

These are available at [www.rcplondon.ac.uk/pubs/books/ms/](http://www.rcplondon.ac.uk/pubs/books/ms/)

The evidence tables provide full details of the studies identified and critically appraised as part of the formal systematic review. They are organised according to guideline section, clinical question and study design.

# Appendix J: The scope of the clinical guideline

## Preamble

The National Institute for Clinical Excellence is responsible for developing, disseminating and giving advice on the implementation of clinical guidelines to provide advice on best practice for patients and health professionals in the NHS in England and Wales.

## Title

*Multiple sclerosis: national clinical guidelines for diagnosis and management in primary and secondary care.*

## Summary

The guideline will be relevant to adults of all ages with MS and will cover the full range of care that should be routinely made available from the NHS, including appropriate use of mainstream pharmacological, physical therapy, rehabilitative and psychosocial treatments.

## Status

This scoping statement has been subject to a period of consultation and discussed with stakeholders. It has been approved by the Guidelines Advisory Committee and the Institute's Guidance Executive and will be posted on the Institute's website along with details of the commission and the developers of the guidelines.

## Issues and objectives

- Multiple sclerosis is a progressive neurological condition. It has a variable clinical course and patients present with a variety of problems. They can present with a relapsing-remitting disorder that, after a variable time course, may evolve to a secondary progressive disorder. They may also present with a primary progressive disorder particularly in older patients.
- The guideline will cover a very broad range of care services, and the developers will need to assess how best to approach this.
- This is an NHS guideline. Although it will comment on the interface with other services, such as those provided by social services and the voluntary sector, it will not include services exclusive to these sectors.
- The guideline will incorporate the Institute's guidance on the use of interferon beta and glatiramer acetate.

## Inclusions and exclusions

### ▷ Disease or condition

The guideline will be relevant to adults of all ages with MS. The guideline should offer best practice advice on the diagnosis of MS and on the NHS care of patients diagnosed with various forms of MS. Diagnosis, early management, relapsing-remitting and progressive stages of the disease should be considered. Severe and advanced stages of the condition, and the management of rarer symptoms and treatment side effects will also be covered. Supportive and palliative care will be covered only to the extent that they relate specifically to MS.

### ▷ Health care setting and professions

The guideline will cover the care provided by clinicians who have direct contact with and make decisions concerning the care of patients with MS. It will address the needs of patients and carers in whatever setting NHS care is provided.

The guideline will need to comment on the way health care services need to interact with services provided by Social Services and the voluntary sector, but will not seek to guide the practice of social care or services provided by the voluntary sector.

### ▷ Interventions and treatment modalities

The guidelines will cover the full range of care that should be routinely made available from the NHS, including appropriate use of mainstream pharmacological, physical therapy, rehabilitative and psychosocial treatments.

These will include:

- **the diagnosis of the disease**
- **pharmacological treatments:** the guideline will consider the long established and widely used drugs such as steroids (various forms) and azathioprine but the brief specifically excludes evaluation of the interferon betas and glatiramer acetate which are being appraised by the Institute.
- **consideration of alternative treatments that might modify disease progress:** although the evidence base is much weaker for these therapies, many patients use them. By considering them, the developers will, amongst other observations, be able to point out where more data may be needed to enable a thorough appraisal of their value.
- **prevention of secondary disease processes:** including the prevention of pressure sores, contractures, and of incidental diseases that threaten life (eg 'flu vaccination) as these pertain to MS. The guideline will take account of the guideline on pressure ulcers.
- **management of impairments and disabilities:** the following will be considered as they apply to people with MS:
  - anti-spastic treatments
  - urinary and bowel problems
  - fatigue management
  - ataxia and other movement disorders
  - visual problems

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- mood/emotions
- swallowing/feeding/diet
- pain/sensory disturbance
- mobility and function posture
- **models of care:** the guideline will consider evidence on the effectiveness of models of care required to deliver the recommendations in this guideline.

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