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*The National Collaborating Centre  
for Chronic Conditions*

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*Funded to produce guidelines for the NHS by NICE*

# MULTIPLE SCLEROSIS

National clinical guideline for diagnosis  
and management in primary and secondary care

*With joint leadership from*

The Royal College  
of Physicians



The Chartered Society  
of Physiotherapy



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# Preface

It is a pleasure to welcome you to this guideline on the management of multiple sclerosis (MS). It describes best practice for the health care management of a complex disorder that affects individuals and their carers in many and varied ways. This variability has made it hard to plan a cohesive or effective NHS service, and the challenge now is for all those involved in health care (those that commission care, those that deliver care, and the patient and carer groups) to ensure that these guidelines are used.

We would particularly direct readers to the six key messages set out in the Executive Summary at the front of the document and to the audit/implementation criteria (Section 7) for measuring the implementation process. If these are acted upon, then service provision will be improved and those with MS will enjoy a better quality of life and less disability in the future.

The guideline has been developed by National Collaborating Centre for Chronic Conditions (NCC-CC) with a commission from the National Institute for Clinical Excellence (NICE). The commission stipulated that the guideline should concentrate on the health (ie NHS) aspects of multiple sclerosis, and that while it would include the interface with other agencies including social services, it would not discuss their detailed provision. An additional stipulation was that topics already covered by an existing NICE appraisal report would be incorporated without further assessment.

For many areas of MS there is little evidence upon which to base recommendations, and the gaps between the evidence have been filled with recommendations, based on a formal consensus of the experts on our guideline groups. In each section of the document the level of supporting evidence is made clear on the understanding that the stronger the evidence the greater likelihood that the recommendations based on it are sound. However the reader should not equate level of evidence with strength of recommendation – some of the most important recommendations, with the greatest consequences for the health service or for people with MS, have been made by group consensus because there was inadequate evidence. This is what the experts believe to be best practice – what they would recommend for their patients or relatives.

While the detail of local implementation of this guideline may vary (according to local facilities and geography), the main aims ought to be common across England and Wales, and if adopted should lead to better standards of care and thus better outcomes from this often distressing condition. There may be some readers who will find particular recommendations, especially those reached by consensus, hard to accept, and to them the challenge is to go out and produce and publish evidence to either confirm or refute what this guideline sets out. This additional research and thought applied to multiple sclerosis could make future versions of this guideline even stronger.

**Mike Pearson FRCP**  
Director, National Collaborating Centre for Chronic Conditions



## Executive summary

Multiple sclerosis (MS) is diagnosed in 3.5 to 6.6 people per 100,000 of the population each year, equivalent to about 1,800 to 3,400 people each year in England and Wales. Prevalence is between 100 to 120 per 100,000 of the population, equivalent to about 52,000 to 62,000 people with MS in total in England and Wales.

Some people with MS develop few symptoms, but for others the disease and society's interactions with them lead to problems affecting all aspects of their lives. The disease often has an impact upon the family.

Many people with MS need to make extensive use of primary and secondary health care, and social services. This guideline suggests how clinical services for people with MS can be improved both in terms of delivery and in terms of specific interventions. The needs of people with MS are similar to those of many other patients with long-term conditions, and this guideline will have general lessons which can be applied more widely than just MS.

The following recommendations have been identified as priorities for implementation.

### ▷ Specialised services

MS is a relatively rare condition often leading to complex problems that require expert services. We recommend that *specialist neurological and neurological rehabilitation services should be available to every person with MS when they need them, usually when they develop any new symptom, sign, limitation on activities or other problem, or when their circumstances change*. We have made suggestions about what this might mean for commissioners in the audit criteria section of the guideline (Section 7).

### ▷ Rapid diagnosis

Once a patient has experienced symptoms suggestive of MS, a rapid diagnosis is needed. This ensures that any required treatments are started, and reduces anxiety and uncertainty. We recommend that *an individual who is suspected of having MS should be referred to a specialist neurology service and seen rapidly within an audited time. The individual should be seen again after all investigations necessary to confirm or refute the diagnosis have been completed (also rapidly within an audited time)*.\*

### ▷ Seamless services

People with MS often have complex problems requiring input from many different groups both within and outside the NHS. Many find that bureaucracy and border disputes lead to stress and

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\* The Guideline Development Group debated the meaning of the word 'rapidly'. In this context, it is taken to mean that the exact time will vary according to clinical need but should, in the opinion of the development group, be no longer than six weeks from referral to being seen by a neurologist, and a further six weeks until any necessary investigations are completed.

delays in even the simplest of actions. Current policies should lessen this, but still we recommend that *every health commissioning organisation should ensure that all organisations in a local health area agree and publish protocols for sharing and transferring responsibility for and information about people with MS, so as to make the service seamless from the individual's perspective.* We recommend that these protocols are publicly available and that the timescales involved are audited to ensure that unnecessary delays do not occur.

▷ A responsive service

People with MS can experience one or more of a wide variety of symptoms and difficulties. Each person's needs are unique, and a flexible response is required from the NHS. We recommend that *all services and service personnel within the health care sector should recognise and respond to the varying and unique needs and expectations of each person with MS. The person with MS should be involved actively in all decisions and actions.* In other words, services should be patient centred. A patient-led system of audit can help address some of the difficulties in monitoring this.

▷ Sensitive but thorough problem assessment

The great variety of possible problems that people with MS may have can make it difficult for health care professionals to detect all relevant changes. We have recommended that *health service professionals in regular contact with people with MS, should consider in a systematic way whether the person with MS has a 'hidden' problem contributing to their clinical situation, such as fatigue, depression, cognitive impairment, impaired sexual function or reduced bladder control.* The main text of the guideline details the various problems that a person with MS may have and appropriate ways of treating these problems.

▷ Self-referral after discharge

There is no predictable pattern or progress of the condition in any individual with MS, but problems may arise quickly at any time. Some people therefore have routine appointments 'to keep in touch', which is wasteful and perpetuates a dependent approach, while many others 'fall out' of the system until a crisis occurs. We have strongly recommended that *every person with MS who has been seen by a specialist neurological or neurological rehabilitation service should be informed about how to make contact with the service when he or she is no longer under regular treatment or review. The individual should be given guidance on when such contact is appropriate.* This recommendation should mean that each specialist service (neurology, and neurological rehabilitation) has in place a mechanism for accepting and responding to direct contact by someone with MS, even when they are no longer under regular treatment or review by that service.

## Conclusion

The full document gives specific advice to clinical staff on a huge range of issues such as the management of bladder problems, the treatment of spasticity, therapy for reduced walking ability and the identification and management of difficulties in swallowing. One strong message

is that clinical staff need to be systematic in their approach to each person with MS so that all remediable problems are identified and managed effectively. This depends upon a well-trained body of staff working in a team with appropriate support from information systems.

Finally, the document emphasises the importance of prevention of ill health, which is a vital function of the NHS. Prevention is especially important in people with long-term conditions because they are often at risk of many specific secondary conditions. For example people with MS may experience infections, contractures, and falls. However, the occurrence of a pressure ulcer is perhaps the most serious and the best marker of service quality. We have suggested that the occurrence of a pressure ulcer in someone with MS should be considered an adverse event worthy of formal investigation.

If the NHS can deliver a good service to people with MS then it will also be delivering a good service not simply to other people with neurological disability but to all people with long-term conditions. This guideline should help set the NHS on course for this.



# Glossary

## Activities of daily living (ADL)

This phrase refers to activities or tasks undertaken as part of day-to-day life such as getting dressed, cooking or shopping. They can be subdivided into personal ADL, domestic (household) ADL, and community ADL.

## Adverse events

Sometimes known as side effects. Adverse events are any event that is not to the benefit of the person. Some are predictable, and some are only rare and unexpected. Adverse events from drugs might include, for example, rashes, feeling fatigued and being depressed. Adverse events can also follow rehabilitation treatments and might include falling while learning to walk and pain from stretching a joint.

## Allied health professionals

Health care professionals, other than doctors and nurses, directly involved in the provision of health care. Includes several groups such as physiotherapists, occupational therapists, dieticians, etc. (Also known as professions allied to medicine or PAMs.)

## Alternative therapies

A term that is difficult to define because the classification of therapies is not fixed. This usually refers to treatments of any type which are not prescribed or recommended by doctors, or are not given by health care professionals practicing within the NHS.

## Applicability

The extent to which the results of a study or review can be applied to the target population for a clinical guideline.

## Appraisal of evidence

Formal assessment of the quality of research evidence and its relevance to the clinical question or guideline under consideration, according to predetermined criteria.

## Area under curve (AUC)

See *receiver operating curve (ROC)*.

## Association of British Neurologists (ABN)

The professional body to which all neurological specialist physicians belong.

## ATG

Anti-thymus globulin.

## Bias

Systematic errors in the design and execution of a study which may lead to an over- or underestimation of the 'true' effect of a treatment or intervention.

## Blinding

The practice of keeping the investigators or subjects of a study ignorant of the group to which a subject has been assigned or of the population from which the subject has come. For example, a clinical trial in which the participating patients or their doctors are unaware of whether they are taking the experimental drug or a placebo (dummy treatment). The purpose of 'blinding' is to protect against bias.

## British National Formulary (BNF)

The BNF is the recognised authoritative source of up-to-date information on drugs and pharmaceutical products for health care professionals. The emphasis is on those that are prescribed in the UK, rather than over-the-counter medicines. It is a joint publication of the British Medical Association (BMA) and the Royal Pharmaceutical Society of Great Britain (RPSGB).

## CAM

Complementary and alternative medicine, eg acupuncture, homeopathy.

## Cardiorespiratory fitness

The extent to which the heart and lungs are able to respond to demand. Fitness depends upon a) muscles, primarily in the legs and b) the heart and lungs.

## Case-control study

A study that starts with the identification of a group of individuals sharing the same characteristics (eg people with a particular disease) and a suitable comparison (control) group (eg people without the disease). All subjects are then assessed with respect to other factors, such as things that happened to them in the past, eg things that might be related to getting the disease under investigation.

## Ceiling effects

See *floor and ceiling effects*.

## Cerebro-spinal fluid (CSF)

Fluid produced in hollow structures within the brain that circulates around the outside of the brain and also down the spinal canal. CSF is removed when a lumbar puncture is undertaken.

## Clinical audit

A systematic process for setting and monitoring standards of clinical care. Patients' notes and other clinical records are examined as part of the

audit process. Clinical audit should cover the practice of all relevant health care professional groups, as opposed to medical audit which only looks at the doctor's role in patient care.

Whereas 'research' defines what the best clinical practice should be, 'audit' investigates whether best practice is being carried out.

**Clinical effectiveness**

How well a drug, treatment or package of care works to produce good outcomes for patients.

**Clinical importance**

The importance of a particular guideline recommendation compared with other aspects of clinical management that may be under consideration.

**Clinical trial**

Research study conducted with patients, usually to evaluate a new treatment or drug. Each trial is designed to answer scientific questions and to find better ways to treat individuals with a specific disease. See also *randomised controlled trial*.

**Clinician**

A health care professional providing patient care, eg a doctor, nurse or physiotherapist.

**Cochrane Library**

The Cochrane Library consists of a regularly updated collection of evidence-based medicine databases including the Cochrane Database of Systematic Reviews (reviews of randomised controlled trials prepared by the Cochrane Collaboration). The Cochrane Library is available on CD-ROM and on the Internet.

**Cognitive status**

Cognition refers to the processes involved in thinking, concentrating, planning, solving problems, learning, analysing sensations and remembering. A person's cognitive status is the extent to which they can use their brain to undertake these processes.

**Cohort study**

A cohort study takes a group of patients and follows them forward in time and measures their outcome (eg disease or mortality rates). Patient subgroups are then identified from information collected about patients and these groups are compared with respect to outcome, eg comparing mortality between one group that received a specific treatment and one group which did not (or between two groups that received different levels of treatment). Cohorts can be assembled in the present and followed into the future (a 'concurrent cohort study') or identified from past records and followed forward from that time up to the present (a 'historical cohort study'). Because patients are

not randomly allocated to the two groups, the groups may be quite different in their characteristics and some adjustment must be made when analysing the results to ensure that the comparison between groups is as fair as possible.

**Competence**

In legal terms, this refers to the ability of someone to make an informed judgement and it depends upon being able to understand written or spoken material sufficiently, hold the information in the memory and use the material to make a considered judgement.

**Complementary therapies**

See *alternative therapies*.

**Computerised tomography (CT)**

A technique whereby X-rays are used to map the inside of the body, especially the brain.

**Confidence interval**

This helps us assess the likely effect of a clinical intervention by describing a range of possible effects that are consistent with the results of a study (or of a combination of studies). A wide confidence interval indicates a lack of certainty or precision about the true size of the clinical effect and is seen in studies with too few patients. Where confidence intervals are narrow they indicate more precise estimates of effects and a larger sample of patients studied. We usually interpret a 95% confidence interval as the range of effects within which we are 95% confident that the true effect lies.

**Confounding factor**

Something that introduces uncertainty and bias into an observed outcome, complicating interpretation.

**Consensus methods**

A variety of techniques that aim to reach an agreement on a particular issue. Formal consensus methods include Delphi and nominal group techniques, and consensus development conferences. In the development of clinical guidelines, consensus methods may be used where there is a lack of strong research evidence on a particular topic.

**Consistency**

The extent to which the conclusions of a collection of studies used to support a guideline recommendation are in agreement with each other. See also *homogeneity*.

**Control group**

A group of patients recruited into a study that receives no treatment, a treatment of known effect, or a placebo (dummy treatment) – in order to provide a comparison for a group

receiving an experimental treatment, such as a new drug.

**Controlled clinical trial (CCT)**

A study that includes some form of control that is not randomised.

**Correlation**

A measure of the strength of association between two or more variables. For example in children height, weight and age are all correlated because older children tend to be taller and heavier. A positive correlation indicates that one variable has been observed to increase as the other increases, a negative correlation indicates that one decreases as the other increases.

**Cost-benefit analysis**

A type of economic evaluation where both costs and benefits of health care treatment are measured in the same monetary units. If benefits exceed costs, the evaluation would recommend providing the treatment.

**Cost-effectiveness**

How expensive treatment and care are compared to how much benefit they offer to patients. In cost-effectiveness analysis, the outcomes of different interventions are converted into health gains for which a cost can be associated, for example, cost per additional heart attack prevented.

**Crossover study design**

The administration of two or more experimental treatments one after the other in a specified or random order to the same group of patients.

**Decision analytic model**

A method, in health economics, of establishing the best course of action when evidence, both clinical and cost, is uncertain.

**Department of Health**

A generic term for four UK government departments responsible for the health and well-being of people in England, Wales, Scotland and Northern Ireland, and having specific responsibility for the National Health Service (NHS) and Social Services Inspectorate (SSI).

**DGH**

District general hospital (non-teaching hospital).

**Diagnostic odds ratio (DOR)**

DOR is used as a summary measure of the accuracy of a diagnostic test. It is calculated as the odds of a correct positive result, divided by the odds of a false positive result. When a test provides no diagnostic evidence then the DOR is 1.0, but a valuable diagnostic test will tend to have a high DOR.

**Diagnostic study**

Any research study aimed at evaluating the utility of a diagnostic procedure. The methods employed are generally different to those in a *clinical trial* aimed at evaluating an *intervention*.

**Diagnostic work-up**

The process of making a diagnosis through tests, clinical history and clinical judgement.

**Disease modifying therapies (DMTs)**

Any treatment that slows down, stops or reverses the processes that damage the nervous system in MS.

**Disease progression**

This specifically refers to increasing damage to the nervous system. There is only a weak relationship between damage to the nervous system and increasing symptoms or signs. And some episodes of worsening are simply due to another illness (eg bladder infection) and not progression of the damage to the nervous system.

**Dominant**

An economic term for an intervention which is cheaper and clinically more effective than the alternative(s).

**Dysarthria**

Difficulty of articulating words caused by disease of the central nervous system, typically characterised by slurred speech, imprecise articulation and disorders of intonation.

**Economic evaluation**

Comparative analysis of alternative courses of action in terms of both their costs and consequences.

**Effectiveness**

The extent to which a specific treatment or intervention, when used under usual or everyday conditions, does what it is intended to do, eg control or cure an illness. (Clinical trials that assess effectiveness are sometimes called 'management trials'.)

**Efficacy**

The ability of a drug or other treatment to control or cure an illness. In research terms, 'efficacy' refers to the extent to which a specific intervention produces the intended (beneficial) result under ideally controlled conditions, eg in a laboratory.

**Episode of care**

A technical, Department of Health term that refers to the whole of a treatment episode from hospital admission to discharge or from starting to stopping a course of treatment.

**Evidence-based**

The process of systematically finding, appraising, and using research findings as the basis for clinical decisions.

**Evidence table**

A table summarising the results of a collection of studies which, taken together, represent the evidence supporting a particular recommendation or series of recommendations in a guideline.

**Evoked potentials**

Electrical changes in the brain that follow stimulation of the nervous system. The commonest example is to flash lights in the eyes, when an electrical change will occur over the occiput (back of the head) about 1/10th of a second later. They can only be detected using computers and many repeated stimulations because the potentials are so small.

**Experimental study**

A research study designed to test if a treatment or intervention has an effect on the course or outcome of a condition or disease.

**Extrapolation**

The application of research evidence based on studies of a specific population to another population with similar characteristics.

**Floor and ceiling effects**

Problems encountered in some *outcome* measures where there are limits to how low or high a numerical value they can assume, eg it is impossible to measure more than 100%. These can make it difficult to assess the true effect of an *intervention*.

**Focus groups**

Method of group interview or discussion of between 6 and 12 people focused around a particular issue or topic. The method explicitly includes and uses the group interaction to generate data.

**Functional status**

An individual's ability to continue normal social and physical activities.

**Grade of recommendation**

A code (eg A, B, C) linked to a guideline recommendation, indicating the strength of the evidence supporting that recommendation.

**Guideline**

A systematically developed tool which describes aspects of a patient's condition and the care to be given. A good guideline makes recommendations about treatment and care, based on the best research available, rather than opinion. It is used to assist clinician and patient decision making about appropriate health care for specific clinical conditions.

**Guideline recommendation**

Course of action advised by the guideline development group on the basis of their assessment of the supporting evidence.

**Health technology**

Health technologies include medicines, medical devices such as artificial hip joints, diagnostic techniques, surgical procedures, health promotion (eg the role of diet *vs* medicines in disease management) and other therapeutic interventions.

**Health technology appraisal (HTA)**

A health technology appraisal, as undertaken by NICE, is the process of determining the clinical and cost-effectiveness of a *health technology*. NICE health technology appraisals are designed to provide patients, health professionals and managers with an authoritative source of advice on new and existing health technologies.

**Heterogeneity**

Or lack of *homogeneity*. The term is used in *meta-analyses* and *systematic reviews* when the results or estimates of effects from separate studies seem to have different magnitude or even different sign or direction. Differences in the patient populations, outcome measures, definition of variables and duration of follow-up of the studies included in the analysis create problems of non-compatibility. See also *homogeneity*.

**Hierarchy of evidence**

An established hierarchy of study types, based on the degree of certainty that can be attributed to the conclusions of a well-conducted study. Well-conducted randomised controlled trials (RCTs) are at the top of this hierarchy. (Several large statistically significant RCTs which are in agreement represent stronger evidence than, say, one small RCT.) Well-conducted studies of patients' views and experiences would appear at a lower level in the hierarchy of evidence. See also *randomised controlled trial*.

**History, clinical**

The information collected and considered by a health care professional regarding an individual's previous health-related experiences.

**Homogeneity**

This means that the results of studies included in a systematic review are similar and there is no evidence of *heterogeneity*. Results are usually regarded as homogeneous when differences between studies could reasonably be expected to occur by chance. See also *consistency*, *heterogeneity* and *systematic review*.

**HTA**

See *health technology appraisal*.

**Iatrogenic**

Caused by a health care treatment.

**Incidence**

The rate of new occurrences of a condition or disease, often given as people per year or episodes per year.

**Inclusion criteria**

See *selection criteria*.

**Intention to treat analysis**

An analysis of a clinical trial where patients are analysed according to the group to which they were initially randomly allocated, regardless of whether or not they had dropped out, fully complied with the treatment, or crossed over and received the alternative treatment.

**Intervention**

Health care action intended to benefit the patient, eg prescribing drugs, surgical procedures, psychological therapy, etc.

**Intervention groups**

In a *clinical trial*, groups to which participants are allocated. Typically, these groups will receive different *interventions* or a *placebo*.

**Level of evidence**

A code (eg 1a, 1b) linked to an individual study, indicating where it fits into the hierarchy of evidence and how well it has adhered to recognised research principles. See also *hierarchy of evidence*.

**Literature review**

A process of collecting, reading and assessing the quality of published (and unpublished) articles on a given topic.

**Local protocols**

See *protocol*.

**Low vision service**

Any local health service provided to cater for people experiencing visual problems.

**Magnetic resonance imaging (MRI)**

An imaging technique which uses powerful magnetic fields rather than radiation to obtain accurate images of soft tissue inside the body. Some people cannot safely be scanned with MRI, for example those with pacemakers.

**Meta-analysis**

Results from a collection of independent studies are pooled, using statistical techniques to synthesise their findings into a single estimate of a treatment effect. A systematic review may or may not include a *meta-analysis*. It is always appropriate and desirable to systematically review a series of results but it may sometimes be inappropriate, or even misleading, to

statistically pool results from separate studies. See also *systematic review* and *heterogeneity*.

**Methodological quality**

The extent to which a study has conformed to recognised good practice in the design and execution of its research methods.

**Methodological weakness**

Any problem in the way in which a study has been conducted, which throws doubt on the conclusions. See *methodological quality*.

**Methodology**

The overall approach of a research project, eg the study will be a randomised controlled trial, of 200 people, over one year. See also *randomised controlled trial*.

**Multimodal intervention**

An *intervention* comprised of more than one aspect which can affect outcomes for the patient.

**Musculo-skeletal pain**

Pain arising from the muscular and skeletal systems, as distinct from neurogenic pain.

**National Institute for Clinical Excellence (NICE)**

NICE is a special health authority responsible for providing patients, health professionals and the public with authoritative, robust and reliable guidance on current 'best practice'. NICE commissioned and funded the development of this guideline.

**Neurogenic**

Arising from the nervous system.

**Neuropathic**

Pertaining to disorders of the nervous system.

**Non-experimental study**

A study based on subjects selected on the basis of their availability, with no attempt having been made to avoid problems of bias.

**Objective measure**

A measurement that follows a standardised procedure which is less open to subjective interpretation by potentially biased observers and study participants.

**Odds ratio**

Odds are a way of representing probability, especially familiar for betting. In recent years odds ratios have become widely used in medical reports. They provide an estimate (usually with confidence interval) for the effect of an intervention. Odds are used to convey the idea of 'risk' and an odds ratio of 1 between two treatment groups would imply that the risks of an adverse outcome were the same in each group. For rare events the odds ratio and the relative risk (which uses actual risks

and not odds) will be very similar. See also *control group, relative risk*.

**Oligoclonal banding**

A phenomenon which can be detected by testing *cerebro-spinal fluid*. It can help to diagnose MS.

**Optic neuritis**

Inflammation of the optic nerve, which carries visual information from the eye to the brain.

**Orthodox therapies**

See also *alternative therapies*. Any medical or physical therapy which is usually used or recommended by health care professionals working within the NHS

**Outcome**

The end result of care and treatment and/or rehabilitation. In other words, the change in health, functional ability, symptoms or situation of a person, which can be used to measure the effectiveness of care/treatment/rehabilitation. Researchers decide what outcomes to measure before a study begins. Outcomes are then assessed at the end of the study.

**Palliative care**

Care aimed at alleviating symptoms, pain and distress, and hence improving quality of life, rather than at curing or slowing progression of a disease or condition. It is often associated with, but is actually not limited to, the end of life.

**PCT**

See *primary care trust*.

**Pilot study**

A small scale 'test' of the research instrument. For example, testing (piloting) a new questionnaire with people who are similar to the population of the study, in order to highlight any problems or areas of concern, which can then be addressed before the full-scale study begins.

**Placebo**

A pill, medicine, or other treatment that has no physiological effect and is used as a dummy treatment. A placebo may be used as a comparison (control) in tests on new drugs etc.

**Placebo effect**

A beneficial (or adverse) effect produced by a placebo and not due to any property of the placebo itself. See *placebo*.

**Pooled estimate**

An estimate of the effect of a treatment, arrived at through a *meta-analysis*.

**Postpartum**

After childbirth.

**Pre-post study**

A study design which measures outcomes in one group of people, first before, and then after, an intervention is given or initiated.

**Prevalence**

The proportion of a population of people who are experiencing a condition or disease at a given time.

**Primary care**

Health care delivered to patients outside hospitals. Primary care covers a range of services provided by GPs, nurses and other health care professionals, dentists, pharmacists and opticians.

**Primary care trust**

A primary care trust is an NHS organisation responsible for improving the health of local people, developing services provided by local GPs and their teams (called primary care) and making sure that other appropriate health services are in place to meet local people's needs.

**Prior probability**

In a *diagnostic study*, the proportion of the population which has the condition in question, regardless of what the test result subsequently is.

**Probability**

How likely an event is to occur, eg how likely a treatment or intervention will alleviate a symptom.

**Prognostic factor**

Patient or disease characteristics which influence the course of a particular condition. In a randomised trial to compare two treatments, chance imbalances in variables (prognostic factors) that influence patient outcome are possible, especially if the size of the study is fairly small. In terms of analysis these prognostic factors become confounding factors. See *confounding factor*.

**Prospective study**

A study in which people are entered into the research and then followed up over a period of time with future events recorded as they happen. Prospective studies may be of several types, including cohort or randomised controlled trials. See *cohort study* and *randomised controlled trial*.

**Protocol**

A policy or strategy which defines appropriate action. A research protocol sets out, in advance of carrying out the study, what question is to be answered and how information will be collected and analysed. Guideline implementation protocols set out how guideline recommendations will be used in practice by the NHS, at both national and local levels.

**P-value**

If a study is done to compare two treatments then the P-value is the probability of obtaining the results, or something more extreme, if there really was no difference between treatments. Suppose  $P = 0.03$ . What this means is that if there really was no difference between treatments then there would only be a 3% chance of getting the kind of results obtained. Since this chance seems quite low we should question the validity of the assumption that there really is no difference between treatments. We would conclude that there probably is a difference between treatments. By convention, where the value of P is below 0.05 (ie less than 5% ) the result is seen as *statistically significant*. Where the value of P is 0.001 or less, the result is seen as highly significant. P values just tell us whether an effect can be regarded as statistically significant or not. In no way do they relate to how big the effect might be, for which we need the *confidence interval*.

**Qualitative methods**

Research techniques used to describe life's experiences and give them meaning, using a systematic, subjective approach. This type of research is conducted in order to describe and promote understanding of people's experiences, feelings, motivations and behaviour. Examples of qualitative methods include focus groups, in-depth interviews and participant observation. These techniques generate non-numerical data, eg a patient's description of their pain rather than a measure of pain.

**Quality-adjusted life years (QALYs)**

A measure of health outcome. QALYs are calculated by estimating the total life-years gained from a treatment and weighting each year with a quality of life score.

**Quantitative methods**

Research techniques that generate numerical data or data that can be converted into numbers. For example, census questions such as the number of people living in a household.

**Quasi-experimental study**

This is a study in which the treatment comparison groups are not assigned by randomisation.

**Randomised controlled trial**

A trial in which people are randomly assigned to two (or more) groups: one (the experimental group) receiving the treatment that is being tested, and the other (the comparison or control group) receiving an alternative treatment, a placebo (dummy treatment) or no treatment.

The two groups are followed up to compare differences in outcomes to see how effective the experimental treatment was.

**Receiver operating curve (ROC)**

A mathematical method of comparing diagnostic procedures involving their *specificity* and *sensitivity*. The closer the area under the curve (AUC) is to 1, the better the test.

**Reference standard**

In *diagnostic studies*, the test being evaluated is often compared to the best known diagnostic procedure, which is known as the reference standard or gold standard.

**Rehabilitation**

Rehabilitation is a process that focuses on ability and aims to optimise social participation and to minimise distress and stress for both the person with MS and any carers involved, mainly through a problem-solving approach that will involve multi-focal interventions from a specialist team over time.

**Relative risk**

A summary measure which represents the ratio of the risk of a given event in group of subjects compared to another group. When the 'risk' of the event of interest is the same in the two groups the relative risk is 1. Relative risk is sometimes used as a synonym for *risk ratio*. In a treatment comparison study a relative risk of 2 would indicate that patients receiving one of the treatments had twice the risk of an undesirable outcome than those receiving the other treatment.

**Relative risk-benefit ratio**

A method of comparing two interventions, balancing the risk and benefit of each to a defined population.

**Reliability**

Reliability refers to a method of measurement that consistently gives the same results. For example, someone who has a high score on one occasion tends to have a high score if measured on another occasion very soon afterwards. With physical assessments it is possible for different clinicians to make independent assessments in quick succession – and if their assessments tend to agree then the method of assessment is said to be reliable.

**Review**

Summary of the main points and trends in the research literature on a specified topic. A review is considered non-systematic unless an extensive literature search has been carried out to ensure that all aspects of the topic are covered and an objective appraisal made of the quality of the studies.

**Sample**

A part of the study's target population from which the subjects of the study will be recruited. If subjects are drawn in an unbiased way from a particular population, the results can be generalised from the sample to the population as a whole.

**Sampling**

Refers to the way participants are selected for inclusion in a study.

**Secondary**

Conditions and symptoms which are brought about by an existing disease or condition are described as secondary. For example, secondary pain can result from restrictions in mobility because of MS. The pain in this case is secondary to the MS.

**Secondary care**

Care provided in hospitals.

**Selection criteria**

Explicit criteria used by guideline development groups to decide which studies should be included and excluded from consideration as potential sources of evidence.

**Self-report measure**

An outcome measure which uses the views and experience of the person with MS rather than clinical measurements.

**Sensitivity**

The sensitivity of a diagnostic test is the proportion of people with MS who, when tested, have a true positive result.

**Sensitivity analysis**

A mathematical process, often employed in good quality health economics studies, which assesses the sensitivity of the conclusions to inaccuracy in the estimates regarding cost, clinical effectiveness of the treatments, and the structure of the health service.

**Sequelae**

A condition occurring as a consequence of a disease.

**Significance, statistical**

Also 'significant difference' or 'significant effect'.

**Specialist**

Health care professional with relevant qualifications, necessary knowledge and skills.

**Specificity**

The specificity of a diagnostic test is the proportion of people without MS who, when tested, have a true negative result.

**Stakeholder**

Any national organisation, including patient and

carers' groups, health care professionals and commercial companies with an interest in the guideline under development.

**Standard deviation**

A measure of the spread, scatter or variability of a set of measurements. Usually used with the mean to describe numerical data.

**Survey**

A study in which information is systematically collected from people (usually from a random sample within a defined population).

**Systematic**

Methodical, according to plan; not random.

**Systematic review**

A review in which evidence from scientific studies has been identified, appraised, and synthesised in a methodical way according to predetermined criteria. May or may not include a *meta-analysis*.

**Systemic**

Involving the whole body.

**Tertiary centre**

A major medical centre providing complex treatments, which receives referrals from both primary and secondary care. Sometimes called a tertiary referral centre. See also *primary care* and *secondary care*.

**Transverse myelitis**

Inflammation with neurological symptoms, caused by lesions on the spinal cord.

**Trial of treatment**

A planned period during which a person with MS receives a treatment to find out if it will be of benefit to them as individuals.

**Trust**

A trust is an NHS organisation responsible for providing a group of health care services. An acute trust provides hospital services. A mental health trust provides most mental health services. A primary care trust buys hospital care on behalf of the local population, as well as being responsible for the provision of community health services.

**Validity**

Assessment of how well a tool or instrument measures what it is intended to measure. See also *external validity*, *internal validity*.

**Well-being**

A concept combining an individual's health, their quality of life, and their satisfaction. There is no universally agreed definition that is useful in the context of health care.