

6 Diagnosis and treatment of specific impairments

Lesions within the CNS in MS may or may not cause the nervous system to function abnormally. There is evidence that most episodes of demyelination do not cause any specific symptoms or signs at the time.¹¹⁰ Moreover, factors other than episodes of demyelination may cause change in or occurrence of symptoms and signs. Nonetheless most people with MS will experience some specific impairments from time to time, if not constantly.

This section covers the assessment and management of many of the specific impairments that people with MS may experience. It considers each impairment individually, although in reality they will rarely occur in isolation. It does not cover the more general aspects of management nor does it cover the disabilities or other consequences of impairment. The primary outcome in the studies that support this section will generally be a change in the level of the impairment rather than the level of activities.

Effective management of any impairment depends upon its initial identification and so the first recommendation in most sections covers the detection of the impairment. While it is not necessary to ask every person with MS about every possible impairment, it is important to remember that any person with MS might have any of these impairments. Therefore the professional person in contact with the person with MS will need at least a mental checklist similar to that set out in Table 3. They should always ask specific questions in an appropriate and sensitive manner.

When considering how to act in any particular situation it is vital to take into account not only the recommendation(s) appropriate to the specific impairment but also all other aspects of the person's situation such as other impairments that they may have. **Thus for each impairment there is an unwritten first recommendation – do not start or modify treatment until all aspects of the person's clinical situation have been established and understood, and the wishes and expectations of the person with MS have been established.**

6.1 Fatigue

Fatigue is probably one of the commonest, most disabling and frustrating symptoms experienced by people with MS, although they may not explicitly complain about it. It varies widely both between people with MS and within a person from time to time. In a tertiary centre in the USA, fatigue limited activity in 78% of 224 people with MS, compared with 17% of 93 controls²⁶⁹ and in an epidemiologically sound sample of 124 people with MS in Norway, 39% reported frequent problems with fatigue limiting activity.²⁷⁰ A study in South Wales found that 48% of people with MS had fatigue at any one time.²⁷¹ In the audit of Oxfordshire people with MS, nearly half had fatigue on entry although only 3% (7/226) complained of new fatigue over a ten month period.⁶

Fatigue is associated with both disability and depression, and management of fatigue should consider all aspects of a patient's situation, not simply the fatigue. Furthermore, it is in practice often difficult to distinguish complaints of fatigue from complaints about weakness, both in research studies and in clinical practice.

Clinically, recommendations are needed to ensure that fatigue:

- is recognised as being present
- is analysed to determine whether it is primary or symptomatic
- is managed as far as possible, to try and ameliorate its effects.

▷ Evidence statements

Interventions for fatigue were investigated in one systematic review (Ia), one RCT, two randomised crossover trials (Ib) and one CCT (IIa).

Amantadine – The review included four RCTs which compared the effects of amantadine to placebo, and in addition one randomised crossover trial and one CCT also met the inclusion criteria. The review reported that all four RCTs showed a pattern in favour of amantadine but as the effect size was small there is considerable uncertainty about the validity and clinical significance of the findings.²⁷² The CCT also reported positive findings on the two outcomes assessed, namely overall improvement and patient's selection of drug for continuing therapy. The incidence and type of side effects reported were similar between the intervention and the control group.²⁷³ The randomised crossover trial²⁷⁴ examined the effects of amantadine on cognitive functioning in patients with fatigue. There were no differences reported on two of the three outcome measures assessed, with the only positive measure being attained on a test of stimulus selection with event-related potentials (ERP) as the outcome measure.

Pemoline – Pemoline was investigated in two RCTs included in the review and also one RCT and one randomised crossover trial not included in the review. The review showed that there was no beneficial effect of pemoline over placebo and an excess number of reports of adverse effects were recorded in the intervention groups.²⁷² The RCT not included in the review supports these findings, with no difference between the groups being evident on four of the five outcomes measures assessed.²⁷⁵ The final randomised crossover trial²⁷⁶ reported beneficial effects on the two patient report outcomes assessed. Drop outs were similar between the two intervention periods.*

▷ Economic evidence

The HTA systematic review found no formal economic evaluations of amantadine or pemoline. The review then attempted to identify indirect data on potential costs and benefits 'that might allow tentative modelling of cost-effectiveness'. Unfortunately, no information about the reduction in quality of life in MS due to fatigue, or the costs of managing fatigue, was identified. The HTA report concludes that:

if the interventions were of similar cost to amantadine [Amantadine costs £15.35 for 56 × 100mg tablets (BNF, 43) – therefore, a dose of 100mg twice a day costs approximately £200 per year] ... and costs of administration were minimal, it seems likely that such interventions would be cost-neutral. Although the NHS bears only a small proportion of the total burden of cost for MS, such is the size of this burden, that any savings in hospital and other treatment services may well outweigh the extra drug costs. Undoubtedly however, the bulk of the benefit arising from an effective treatment for

* NB Pemoline is no longer available in the UK

fatigue in MS would be to the individual themselves, who might be able to remain in full-time paid employment for longer.²⁷²

▷ From evidence to recommendations

The clinical significance of the benefits shown in the studies reviewed was judged to be too low to allow any firm recommendations in favour of amantadine. The GDG was also aware that modafinil is being used on the basis of one published study,²⁷⁷ but felt that until RCT evidence was available no recommendation should be made for this. The GDG therefore has recommended a simple approach, including traditionally used, though not researched approaches; this was agreed by consensus.

RECOMMENDATIONS

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| R85 | Each professional in contact with a person with MS should consider whether fatigue is a significant problem or a contributing factor to their current clinical state. | D |
| | <i>If fatigue is disrupting the individual's life, then the following recommendations apply.</i> | |
| R86 | The presence of significant depression should be considered; if significant depression is present, it should be treated. | D |
| R87 | Other factors causing fatigue, such as disturbed sleep, chronic pain and poor nutrition, should be identified and treated if possible. | D |
| R88 | Some medicines may exaggerate fatigue, thus any medication being taken should be reviewed. | D |
| R89 | General advice and training on how to manage fatigue should be given, including encouragement to undertake aerobic exercise and to use energy conservation techniques. | D |
| R90 | At present, no medicines targeted at fatigue should be used routinely, although people with fatigue should be informed that a small clinical benefit might be gained from taking amantadine 200mg daily. | D
A |

LOCAL IMPLEMENTATION POINTS

The local services should:

- identify which health workers have expertise in fatigue management for people with MS and how they are accessed
- decide whether a specific measurement tool is to be used, and if so which one.

6.2 Bladder problems

Urinary tract symptoms are common in people with MS. In a population-based sample in the USA, 25% of people with MS had intermittent or constant catheterisation for bladder dysfunction²⁶² and in a second American survey 59% had some bladder disturbance.²⁷⁸ A study in South Wales suggested that 14% of all people with MS had an indwelling urethral catheter and 44% of the remainder had bladder dysfunction.²⁷⁹ In the Southampton survey of

people with MS, 33% suffered urinary incontinence.²⁸⁰ In the Oxfordshire audit⁶ bladder problems were the most common presenting problem affecting 39/226 patients on 78 occasions over ten months, and they were the fifth most common problem in terms of prevalence.

Bladder dysfunction can be very disabling and may have many adverse consequences, including great emotional distress, curtailed social activities, and disturbed sleep. Incontinence also increases the risk of pressure ulcers. Its effects may be compounded by reduced mobility. Unfortunately matters are worsened by the reluctance of people with MS, their families and professional staff to discuss the problems.

While it is likely that disturbed bladder control is the commonest general cause of bladder symptoms, some bladder symptoms may be indicative of infection, and infection not only causes pyrexia (high temperature) and malaise but can also cause general exacerbation of all impairments, especially spasticity. Urinary tract infection (UTI) may also, rarely, cause pyelonephritis and septicaemia. The frequency of actual UTI is unknown and so, although the potential importance of urinary tract infection is great, its actual medical importance is unknown.

This section will first cover the assessment and management of disturbed bladder control leading to urinary frequency, nocturia, urgency of micturition, and incontinence. Then the specific issues of UTI will be covered. Many of the issues are not specific to people with MS, being similar to those faced by other people with neurogenic bladder disturbance and so some recommendations are based on generic evidence. The main issues to be covered are:

- detection and diagnosis of disturbed bladder physiology
- management of disruptive bladder function
- diagnosis and treatment of UTIs
- management of intractable incontinence.

6.2.1 *Bladder dysfunction*

This part considers disturbances in the control of bladder emptying. The use of catheters is mentioned, but 6.2 should also be consulted for further recommendations concerning the use and management of long-term catheters.

▷ Evidence statements

Ten systematic reviews were identified that assessed the efficacy of a number of different interventions for urinary incontinence, though some of these contained data from the same trials (IIa). Four reviews examined the effectiveness of different behavioural bladder training programmes for urge, mixed and stress incontinence. The first review compared bladder training to no intervention, drug therapy (oxybutynin and flavoxate hydrochloride plus imipramine), pelvic floor muscle training and electrical stimulation. The results showed that there was weak evidence to suggest that bladder training is more effective than no treatment, and that bladder training is better than drug therapy. There was insufficient evidence that electrical stimulation is more effective than sham electrical stimulation.²⁸¹ The second review assessed the efficacy of prompted voiding either alone or in combination with oxybutynin. The results indicated that prompted voiding was beneficial compared to no intervention, and that prompted voiding combined with oxybutynin was superior to prompted voiding alone.²⁸² The

third review compared the effectiveness of pelvic floor muscle training against placebo, electrical stimulation, vaginal cones and bladder training either alone or in combination. The results indicated that pelvic floor muscle training was superior to either no treatment or placebo, and that 'intensive' appeared to be better than 'standard' training. The effect of adding adjunctive treatments to pelvic floor training was unclear due to the limited amount of evidence.²⁸³ The last review compared bladder training to flavoxate hydrochloride and imipramine, electric prompting devices and combinations of training plus terodoline or oxybutynin. The results from the review tended to favour bladder training but data was only available for a limited number of prespecified outcomes.²⁸⁴

Four reviews were included that examined the use of different devices or surgical interventions as management options for incontinence. The first review compared suburethral slings to abdominal retropubic suspension and needle suspension. The results showed no differences between suburethral slings and abdominal retropubic suspension or needle suspension. However sling operations had a significantly higher complication rate.²⁸⁵ The second review compared the effect of weighted vaginal cones to control, electro stimulation, pelvic floor muscle training and these interventions in combination. The results showed that cones were better than no active treatment, but that there were no differences between cones and pelvic floor muscle training or electrostimulation. There was not enough evidence to show that cones plus pelvic floor muscle training was different to either cones alone or pelvic floor muscle training alone.²⁸⁶ The third review compared anterior vaginal repair to pelvic floor muscle training, open abdominal retropubic suspension and bladder neck needle suspension. The results indicated that anterior vaginal repair was less effective than open abdominal retropubic suspension both in the short and long term. There were no differences between anterior vaginal repair and bladder neck needle suspension.²⁸⁷ The last review assessed the efficacy of a number of different surgical procedures for stress incontinence. Overall, the results indicated that colposuspension may be more effective and the effect more long-lasting than that for anterior colporrhaphy and needle suspension. It was also found that second and subsequent operations to correct stress incontinence are less successful than first procedures.²⁸⁸

One small review compared the effectiveness of tolterodine to oxybutynin. The results showed that both drugs had similar effects on the number of micturitions in a 24-hour period, but that oxybutynin was marginally superior in decreasing incontinence and increasing the mean voided volume per micturation.²⁸⁹

The last review assessed the effects of different types of absorbent product for the containment of urinary and/or faecal incontinence. The results indicated favourable outcomes in terms of skin problems, the number of changes, ease of disposal and cost for disposable *vs* non-disposable body worn.²⁹⁰

Five RCTs and nine randomised crossover trials examined different interventions for bladder impairment (**Ib**).

Six placebo-controlled randomised crossover trials assessed the effect of desmopressin on voiding frequency and incontinence. Three of the trials specifically examined nocturia, whilst the other three assessed daytime voiding frequency. The three trials that reviewed nocturia all reported beneficial effects on the frequency of voiding, night-time urine volumes and sleep duration.^{291–293} No significant differences were reported in the number of episodes of incontinence. All three trials report a number of side effects of a minor nature. The trials that

examined daytime voiding frequency reported significant effects upon both frequency and volume up to six hours after drug intake.^{294–296} However, no benefit was observed on the frequency of night-time voiding; the 24-hour urine volume was unaffected. None of the trials reported side effects of a significant nature.

Four placebo-controlled trials assessed the efficacy of different drug interventions. One RCT examined the effect of synthetic capsaicin solution in patients with hyperreflexic bladder.²⁹⁷ The results showed an overall significant benefit in terms of voiding patterns, leakage, bladder pressure and the need to use pads. There were no differences in the incidence of side effects between the groups. The second RCT reviewed the use of indoramin in male patients with symptoms of urinary tract dysfunction.²⁹⁸ The study reported significant effects upon two of the five outcome measures assessed (flow rates) but not upon the overall symptoms score. Two randomised crossover trials assessed the efficacy of different drugs in patients with detrusor hyperreflexia. The first trial examining the use of atropine reported significant differences in bladder capacity.²⁹⁹ The second trial assessed the intervention of flurbiprofen.³⁰⁰ The study reported beneficial effects on five of the seven outcomes assessed. However, side effects were more common during the intervention phases although all of these were minor.

Two further placebo-controlled RCTs addressed the effectiveness of biofeedback and electrical stimulation of the pelvic floor muscles. The first RCT addressed biofeedback in combination with behaviour modification, pharmacological adjustment and pelvic floor training.³⁰¹ The results showed no significant differences between the groups on any of the outcome measures assessed. The other RCT examined the use of electrical stimulation of the pelvic floor muscles followed by pelvic floor exercises.³⁰² Significant beneficial effects were observed on all but one of the outcomes measures assessed.

Two studies, one RCT and one randomised crossover trial, compared different interventions against active comparators. One RCT compared oxybutynin to propantheline and reported no significant differences between the groups either in terms of benefits or the side effects observed.³⁰³ The randomised crossover trial examined the three interventions; methantheline bromide, meladrazine tartrate and flavoxate chloride in patients with detrusor hyperreflexia.³⁰⁴ The results showed that methantheline bromide was superior to the other two interventions on the outcomes measures of patient preference, entire cystometric pattern and micturition reduction. No significant differences were observed on measures of incontinence or residual urine volumes between the interventions. Meladrazine tartrate caused side effects so severe that the drug was discontinued. No serious adverse events were reported for the other two interventions.

At the time of writing there is insufficient evidence to comment on the use of cannabinoids in MS. However, we are aware that further evidence is likely to be published and that NICE intend to conduct a technology appraisal on cannabinoids in MS with a projected publication date of April 2004.

▷ Economic evidence

There are no formal economic evaluations of interventions for bladder impairment in MS. A study of the use of sacral rhizotomies and electrical bladder stimulation in people with spinal cord injury, showed this to be a cost-effective strategy in comparison to standard care, with

considerable savings on health care costs possible in the long run.³⁰⁵ This group of patients may be similar to the population of people with MS. However, this is a before-and-after study with a relatively small sample ($n = 52$), so the results should be treated with caution. A study of all people with MS in Hordaland County, Norway, between 1976 and 1986 ($n = 194$), showed that bladder impairment was a significant cause of reduced quality of life (as measured by the generic SF-36), underlying the need for identifying and treating this problem.³⁰⁶

▷ From evidence to recommendations

When considering the available evidence, the guideline developers recognised that the evidence was often primarily related to other causes of bladder disturbance, and lacking for many widely practiced procedures. They also recognised the need to suggest simple and safe interventions before more complex, more expensive or more risky interventions. However good consensus was achieved on the recommendations made.

RECOMMENDATIONS

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| R91 | Each professional in contact with a person with MS should consider whether the person has any problems controlling bladder function. Problems may include frequency or urgency of micturition, sleep disturbance from nocturia (awaking with need to empty bladder), difficulty in passing urine or incontinence of urine. | D |
| R92 | Any person with MS who has bladder symptoms should: <ul style="list-style-type: none"> ● have their post-micturition residual bladder volume measured using a simple measure such as ultra-sonography of the bladder ● be assessed for the presence of a urinary tract infection clinically and, if necessary, using an appropriate dipstick for nitrites and leucocyte esterase. Treatment should be provided, if necessary. <p>Urgency or urge incontinence sufficient to be bothersome or cause incontinence should be treated in the first instance using:</p> <ul style="list-style-type: none"> ● advice on changes to clothing and/or toilet arrangements (for example, provision of a commode downstairs) ● intermittent self-catheterisation if there is a high residual volume, and the person is able and willing ● anticholinergic medicines such as: <ul style="list-style-type: none"> – oxybutynin, or – tolterodine ● checking for an increased post-voiding residual volume if symptoms recur. | D
D
A
D
D |
| R93 | Any person who has nocturia should be offered desmopressin (100–400µg orally or 10–40µg intranasally) at night, to control the symptom. | A |
| R94 | Any person who wishes to control urinary frequency during the day (for example, when travelling), and who has failed with other measures, should be offered desmopressin (100–400µg orally or 10–40µg intranasally) but desmopressin should never be used more than once in 24 hours. | A |

- R95 Any person with MS who, despite treatment, has incontinence more than once a week should:
- be referred to a specialist continence service for further assessment and advice D
 - be considered for a course of pelvic floor exercises, A
 - preceded by a course of electrical stimulation of the pelvic floor muscles (if such a course is available). B
- R96 Any person with MS who experiences persistent incontinence should be offered a convene drain (for men) or pads (for women). D
- R97 Any person who has continued bladder symptoms despite pharmacological and other treatments should be considered: D
- for intermittent self-catheterisation taught by a suitably trained specialist, or
 - for longer-term urethral catheterisation as a means of control, with suprapubic catheterisation being considered especially when active sexual function is still wanted. See R99 to R102.
- R98 Intravesical botulinum toxin should only be used by suitably trained doctors in the context of clinical research. D

LOCAL IMPLEMENTATION POINTS

The local health system should identify:

- which community health workers have a particular expertise in managing incontinence and how they are accessed
- who can measure post-micturition bladder volume locally and how they are contacted
- the local urology service responsible for all managing aspects of neurologically-based bladder problems and incontinence and how it is contacted.

6.2.2 Urinary tract infections

This part discusses the prevention, identification and management of urinary tract infections (UTIs). It also specifically covers all aspects of long-term catheter use and management, drawing upon guidelines for preventing health care associated infections during long-term urinary catheterisation in primary and community care.³⁰⁷

▷ Evidence statements

All evidence statements for UTIs are level Ia.

Prevention of UTI – Five SRs were identified which assessed interventions for the prevention of UTI.^{308–311} A review of five studies looking at the effects of cranberry extract in elderly patients, patients needing intermittent catheterisation, and women with recurrent UTI, found no reliable evidence of the effectiveness of cranberry juice and other cranberry products.³⁰⁹ A review of eight RCTs comparing the effectiveness of indwelling silver coated urinary catheters and uncoated indwelling urinary catheters found that silver alloy catheters were significantly more effective in preventing UTIs as measured by the presence of bacteriuria than uncoated catheters but these studies were confined to relatively short-term use of catheters (2–10 days).³¹¹ The results from three of the eight trials indicated that women benefited from the silver-coated

urinary catheters more than men. The third review looked at risk factors for UTI and the effects of antibiotic prophylaxis in patients with neurogenic bladder due to spinal cord dysfunction.³¹⁰ This review found that indwelling catheterisation was associated with more frequent infections than intermittent catheterisation, which in turn is associated with more frequent infection than methods not involving a catheter. The literature did not support firm conclusions regarding most other risk factors. It also reported that antibiotic prophylaxis significantly reduces bacteriuria among acute spinal cord injury patients. However, antibiotic prophylaxis was not associated with a reduced number of symptomatic infections in the populations studied. Antibiotic prophylaxis resulted in a twofold increase in the occurrence of antibiotic-resistant bacteria. A second review assessing the effectiveness of antibiotic prophylaxis reported similar findings. However, this review only found reduced bacteriuria among patients with acute spinal cord injury, not in those with non-acute spinal cord injury.³⁰⁸ A final review of 11 studies assessed the efficacy of methenamine hippurate in patients at risk of developing a UTI. Four of the trials studied symptomatic bacteriuria and six studied bacteriuria as an outcome measure. The direction of six of the seven pooled trials was towards a favourable treatment effect for methenamine hippurate. However, due to heterogeneity interpretation of the pooled estimates could not be undertaken.³¹²

Health economic analysis of interventions to reduce the risk of UTIs – Only one economic study was identified with any relevance to the population of people with MS.³¹³ This was a decision analytic model to compare the cost-effectiveness of silver alloy-coated urinary catheters with standard (uncoated) catheters. Coated catheters are more expensive (per unit) than uncoated catheters but are more effective; hence the relevant decision is whether the improved efficacy is worth the additional per unit cost?

The base case simulation showed silver-coated catheters to be a *dominant strategy*, ie more effective and less costly, due to savings in costs of treating symptomatic UTIs and bacteraemia. One-way sensitivity analysis revealed that the strategy remained dominant throughout the ranges evaluated. In the multivariate sensitivity analysis the strategy provided clinical benefits over standard catheters in all cases and cost savings in 84% of cases.

Interventions to treat UTI – Two reviews which assessed the effectiveness of interventions for the treatment of UTI met inclusion criteria. The first review assessed the effectiveness of cranberry juice or cranberry products for the treatment of UTI, but did not find any RCTs which met inclusion criteria and so was unable to draw any conclusions.³¹⁴ The second review compared the effectiveness of single dose and multi-dose antibiotic treatment in female adult patients with UTI.³¹⁵ This review found no significant differences between women treated with single dose and multi-dose antibiotic therapy (1a). One further RCT comparing cranberry concentrate supplements to placebo found no significant difference between the groups in terms of the number of patients developing a UTI³¹⁶ (1b).

Areas where evidence was not found – No evidence was found to allow recommendations on several important clinical issues including altering fluid intake, the frequency of changing long-term catheters, the use of bladder wash-outs, the appropriate use of suprapubic catheters, and the best policy concerning routine monitoring of renal tract structure and function.

▷ From evidence to recommendations

The recommendations made draw largely on the published NICE document,³⁰⁷ which itself is largely based on consensus. However, where adequate evidence exists, grade A recommendations have been made

RECOMMENDATIONS

- R99 Any person with MS at risk of urinary tract infections should not be recommended prophylactic use of antibiotics or cranberry juice. A
- R100 If a person with MS experiences new urinary tract symptoms, or develops general malaise and/or worsening of existing symptoms with a raised temperature, they should:
- be given a urine dipstick test for infection, and culture, if necessary D
 - be offered treatment with an appropriate antibiotic. A
- R101 Any person with MS with more than three confirmed episodes of urinary tract infection in a period of one year should be assessed by a continence specialist for residual urine and other evidence of risk factors, and offered appropriate treatment and guidance. D
- R102 The general principles of care for people with long-term urinary catheters, as described in the NICE guideline on prevention of health care associated infection in primary and community care (see Table 6) should be followed. Of particular note in treating a person with MS are that long-term indwelling catheters should:
- be used only after all reasonable non-invasive methods have been tried
 - be reviewed regularly, to check whether less invasive methods can be used
- and that drainage systems from the catheter should:
- be emptied regularly, before the bag is overfull D
 - bladder installations and wash outs should not be routinely used. A

LOCAL IMPLEMENTATION POINTS

The local health system should identify:

- specific guidance on choice of antibiotics for suspected or confirmed urinary tract infection
- the local urology service responsible for all aspects of managing neurologically-based bladder problems and incontinence.

Table 6 The general principles of bladder management

Long-term indwelling bladder catheters should:

- only be used after all reasonable non-invasive methods have been tried **(D)**
- be inserted by fully trained and competent personnel using aseptic procedures with cleaning of the meatus and the use of an appropriate lubricant **(D)**
- be reviewed regularly, to check whether alternative less invasive methods can be used **(D)**
- be clearly documented, including insertion, changes and routine care **(D)**
- only be changed when clinically necessary or according to the manufacturer's recommendations **(D)**.

Drainage systems from the catheter should:

- be attached to a catheter valve outlet when the patient wishes and the system can be used **(D)**
- be kept sterile and continuously closed through ensuring clean handling whenever changes are required **(D)**
- be kept below the bladder but off the floor at all times to prevent stagnation or reflux of urine **(D)**
- emptied regularly, before the bag is over-full **(D)**
- have any samples taken using an aseptic technique through a sampling port **(D)**.

Bladder instillations and wash-outs should not routinely be used **(A)**.

From NICE's *Infection control: prevention of health care associated infection in primary and secondary care*.³⁰⁷

6.3 Bowel problems

People with MS may suffer bowel problems in two ways: reduced gut mobility may follow from immobility and the drugs used to treat various impairments; and neurological control of defecation may be directly impaired. One survey of 280 people found 43% to be suffering constipation.³¹⁷ More importantly the same survey found that 25% had been incontinent of faeces once a week or more frequently and 51% had been incontinent in a three month period. The total prevalence of bowel problems was 68%. In the South Wales survey, 29% of those with MS suffered faecal incontinence, and 54% suffered constipation.²⁷⁹ In another American study 39% had bowel problems.²⁷⁸ In the Oxfordshire audit, 19% of patients were experiencing problems with their bowels at any one time, and 26/226 presented with gastrointestinal problems over a ten month period, with 16 of these being specific problems with bowel control.⁶

Although constipation is probably clinically recognised in most instances, it is likely that health care professional staff are woefully unaware of how much faecal incontinence affects their patients with MS. The consequences of faecal incontinence are great: social embarrassment, risk of pressure ulcer, curtailing of activities etc.

Recommendations are needed to ensure that disturbed bowel control, both constipation and incontinence, is detected early, is evaluated to determine its aetiology, and is managed actively.

▷ Evidence statements

One systematic review of seven RCTs that assessed the effects of different management strategies for faecal incontinence and constipation in people with neurological diseases was identified. The results showed that psyllium was superior to placebo in terms of bowel movements and stool weight. A comparison of different suppositories indicated that

polyethylene glycol-based bisacodyl suppositories initiated defecation faster than hydrogenated vegetable oil-based bisacodyl suppositories. A comparison of bowel programmes indicated participants assigned to morning schedules were more likely to established successful bowel regimes than those assigned to evening schedules. No differences between the use of mandatory or optional suppositories was noted³¹⁸ (Ia).

▷ Economic evidence

No relevant economic evidence relating to bowel impairment was identified.

▷ From evidence to recommendations

The guideline developers noted the general lack of evidence concerning this important question and although a systematic review was found, the studies were small and of low quality and it was difficult to draw any firm conclusions. The recommendations made are largely on the basis of consensus, considering the experience of geriatric services that are faced with similar problems.

RECOMMENDATIONS

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| R103 | Each professional in contact with a person with MS should consider whether the person has any problems controlling bowel function. Potential problems include urgency, difficulty, pain, constipation or incontinence. | D |
| R104 | Any person with MS who has apparent constipation (pain on or difficulty with defecation, bowels open less than twice a week) should be offered advice on fluid intake and dietary changes that might help, and then be considered for oral laxatives. | D |
| R105 | Any person with faecal incontinence should be assessed for constipation with overflow, possibly exacerbated by laxative use. | D |
| R106 | If a person with MS has apparent constipation (pain on or difficulty with defecation, bowels open less than twice a week) despite treatment with oral laxatives he or she should be considered for the routine use of suppositories or enemas. | D |

LOCAL IMPLEMENTATION POINT

Local guidelines need to consider which local specialist (medical or surgical) services should be approached for advice in cases of difficulty.

6.4 Weakness and cardiorespiratory fitness

Many people with MS will experience 'weakness'. In a survey of 656 people with MS in the USA, 63% had 'weakness or paralysis' which affected 45% of those with limitations on personal ADL.²⁷⁸ In the same survey, 77% had fatigue and 74% had 'balance problems'. In South Wales weakness was the commonest single symptom experienced (89% at any time, 80% at any one time).²⁷¹ However, the term weakness may include many different phenomena and have many different contributing factors. This part specifically considers both actual or perceived weakness of voluntary muscle contraction and also more general lack of cardiorespiratory fitness.

Reduced strength of voluntary muscle contraction (weakness) is a common consequence of damage to ‘upper motor neurone’ tracts within the CNS, but it may be associated with several other impairments of motor function including clumsiness, spasms and spasticity. In people with MS muscle weakness may occasionally be a side effect of medication such as steroids or anti-spastic agents. Complaints of weakness may also be referring to or caused by: fatigue, the development of weakness only after some muscular exercise, reduced cardiorespiratory endurance, and depression. Consequently it is vital to establish exactly what the person with MS means when complaining of weakness.

In this guideline weakness and alterations in tone are considered separately as they may occur separately. Balance problems are not considered separately because they are also difficult to define, and will usually be associated with, if not caused, by weakness, spasticity, sensory loss or ataxia and all these are discussed. This section of the guideline needs to cover:

- detection and diagnosis of weakness and its associated phenomena
- management of and advice about weakness, especially relating to exercise
- management of secondary consequences.

▷ Evidence statements

No RCTs or CCTs in patients with MS were identified which assessed interventions to treat weakness. Four RCTs assessed interventions for cardiovascular dysfunction. Two trials examined the efficacy of expiratory muscle training *vs* sham training in patients who were bedridden or wheelchair bound (EDSS score 6.5–9.5). The first trial reported no overall significant improvement in the intervention group, whilst the second trial showed mixed results. Significant beneficial effects were reported for expiratory muscle strength, but not for inspiratory strength.^{319,320} The third study examined the effectiveness of an aerobic exercise training program. The results indicated positive effects on four out of eleven of the outcome measures assessed, namely aerobic capacity, physical work capacity, isometric strength and skinfold thickness. No effect however was seen on any of the general health indices measured.³²¹ The last trial assessed the use of music therapy with relaxation and diaphragmatic breathing in patients who were wheelchair bound. The results showed no significant effect³²² (Ib).

▷ Economic evidence

No relevant economic evidence relating to weakness in MS was identified.

▷ From evidence to recommendations

In the absence of any specific MS-related evidence the guideline developers drew on general principles often derived from research in patients with other neurological conditions such as stroke.

RECOMMENDATIONS

- R107** Each professional in contact with a person with MS should consider whether muscular weakness is a significant problem, or contributing factor, to the person’s current clinical state. If so, the person should be assessed to determine the nature and cause of the weakness. **D**

- R108 People with a limitation of their activities should be assessed for weakness of voluntary motor control using a valid technique. D
- R109 People with motor weakness should be shown and advised to undertake exercises and techniques to maximise strength and endurance appropriate to their circumstances (D), including aerobic training (B). Usually, specific exercises should be selected and explained by a neuro-physiotherapist, or other members of the neurological rehabilitation team (D).
- R110 People with motor weakness should be taught techniques and given equipment, such as orthoses, needed to optimise performance of activities appropriate to their circumstances. D
- R111 People with weakness sufficient to cause postural abnormalities should be assessed for specialist supportive equipment, including but not limited to seating. D

LOCAL IMPLEMENTATION POINTS

These should include:

- advice on measures and assessment techniques to be used locally
- list of gyms, health centres and other places where people with health conditions and/or disability can take exercise, with systems for collaboration and discussion between the NHS (likely to be physiotherapists) and gym instructors being developed. The Department of Health exercise referral national quality assessment framework provides more detail (www.doh.gov.uk/exercisereferrals/).

6.5 Spasticity, spasms and contractures at joints

6.5.1 Spasticity and spasms

Many patients with upper motor neurone weakness from any cause have altered tone in their limbs, and when increased this may be referred to as hypertonia or, most commonly, spasticity. There are continuing debates as to the meaning of the terms. However in practice it is characterised by increased stiffness and slowness in limb movement, the development of certain postures, an association with weakness of voluntary muscle power, and with involuntary and sometimes painful spasms of limbs. Spasticity and spasms are common in people with MS, and may be the dominant disabling impairment in some people. Spasms were present in 21% of the people surveyed in Oxfordshire, and new problems with spasms were the commonest single specific complaint relating to reduced mobility.⁶ Painful leg spasms were reported in 21% of 159 community patients with MS in Ontario, Canada³²³ and spasticity was reported in 49% of 656 people surveyed in the USA.²⁷⁸ The underlying neurophysiology in MS is likely to be similar to that seen in most other diseases associated with spasms and spasticity such as stroke, head injury and spinal cord injury. Consequently evidence from and recommendations for spasms and spasticity in these conditions will be applicable to people with MS.

It must be emphasised that treatment for spasticity and spasms may be necessary or justified simply to reduce the spasticity and/or spasms without expecting any other functional benefit for the patient. These impairments can cause pain and distress by their very presence. Furthermore it must be emphasised that amelioration of spasticity and spasms may be an integral part of a wider plan of management, for example through reducing the burden of care,

through enabling appropriate seating to be provided and used, or through reducing the risk of pressure ulcer. Lastly and of great importance, control of spasticity is vital in the prevention and management of joint contractures (fixed limitations on the range of movement available at a joint). Given the close connection between spasticity and contractures, contractures are also covered in this section (6.5.2).

The guideline recommendations need to ensure:

- identification of spasticity and spasms
- diagnosis and management of any treatable causes
- a stepped approach to management, tailoring interventions to each person's needs and wishes
- a cautious but appropriate use of more risky or expensive interventions
- prevention of complications of spasticity.

▷ Evidence statements

Two systematic reviews that examined interventions for spasticity were identified. In addition 46 studies that looked at a number of different interventions for spasticity and spasms in patients with MS met the inclusion criteria. These consisted of 16 RCTs, 27 randomised crossover trials, (Ib) two CCTs and three non randomised crossover trials (IIa).

Baclofen – One RCT and six randomised crossover trials compared baclofen to placebo (Ib). Overall three of the trials^{324–326} showed significant beneficial effects on the outcome measures assessed. All these measures were directly related to the number and intensity of spasms. Two further randomised crossover trials reported mixed results with significant differences being reported on direct measures of spasticity, but no benefit being evident on outcomes measures of ambulation or transfer activity.^{327,328} The last two small crossover trials reported no overall significant differences between the intervention groups.^{329,330} Six out of the seven trials that reported adverse events, stated that minor side effects were more common in the intervention phase than in the placebo phase. None of the trials reported serious adverse events.

Four RCTs, two randomised crossover trials and one CCT also examined the effect of baclofen against an active comparator. Three RCTs and one randomised crossover trial compared the efficacy of baclofen to tizanidine^{331–334} (Ib). All four of these trials reported no significant differences between the groups on any of the outcomes measured or in terms of side effects reported. A further RCT that compared baclofen to tetrazepam and tizanidine also reported no significant differences between any of the group.³³⁵ One randomised crossover trial examined the effects of baclofen alone against baclofen combined with stretching exercises, stretching exercises alone and placebo alone.³³⁶ The results showed significant differences upon a measure of spasticity for baclofen alone and baclofen combined with stretching exercises, but no differences were observed between the groups on the Ashworth scale score or a measure of functional abilities. A last CCT assessed baclofen against clonazepam and placebo³³⁷ (Ia). No differences were reported between the groups upon either the measure of spasticity or the number of side effects reported.

Baclofen pump – One systematic review of 27 studies conducted in patients with MS and other neurological conditions and one randomised crossover trial reviewed the efficacy of intrathecal baclofen via pump delivery. The review reported a beneficial effect with both the Ashworth scale score and Penn spasm score significantly reduced³³⁸ (Ia). The results of the crossover trial also indicated significant beneficial effects on all the outcome measures assessed.³³⁹

Tizanidine – Three RCTs and two randomised crossover trials compared the effect of tizanidine to placebo. One of the RCTs reported beneficial effects on four of eight of the outcomes measures assessed, including a reduction in muscle-tone score.³⁴⁰ One of the randomised crossover trials also reported beneficial effects on the number of patients in whom spasticity improved.³³⁴

However, none of the other three trials reported any overall effect on any of the outcome measures assessed.^{341–343} One further RCT compared tizanidine to the active comparator diazepam. The results indicated no difference in the clinical symptoms between the groups, and that diazepam was better tolerated.³³⁴

Dantrolene sodium – One non-randomised and two randomised crossover trials compared dantrolene sodium against placebo^{344–346} (Ib). Two of the trials reported no differences between the groups, whilst data from the third trial was not reported adequately. No serious adverse events were reported in any of the trials. One further randomised crossover trial compared dantrolene sodium to diazepam and placebo.³⁴⁷ The results showed that both dantrolene sodium and diazepam were superior to placebo on measures on spasticity, reflexes and clonus. However, dantrolene sodium was reported to have a negative effect relative to diazepam and placebo on both hip flexor strength and deltoid strength.

Gabapentin – Two placebo-controlled randomised crossover trials investigated the efficacy of gabapentin. The first trial reported significant differences between the groups on all of the eight outcomes measures assessed, with no minor or severe adverse effects being reported from the trial.³⁴⁸ The second trial reported significant effects on three of the seven outcomes measures, including the Ashworth scale score and the EDSS. Again no major side effects were reported in the trial.³⁴⁹

Progabide – One randomised and one non-randomised crossover trial compared progabide to placebo.^{350,351} Both of the trials reported no overall significant effects on either measures of spasticity or functional tests. The non-randomised trial reported eight cases of serious adverse events (IIa).

Progabide is not available in the UK.

Diazepam – Two randomised crossover trials compared diazepam to different active comparators. The first compared diazepam to ketazolam and placebo, with no significant differences between the groups being reported.³⁵² The second trial compared diazepam to dimethothiazine. However, the significances of the results for the trial was not reported³⁵³ (IIb).

Other pharmacological interventions – One systematic review and a further nine studies examined the efficacy of a variety of pharmacological interventions for spasticity. The systematic review of three RCTs, and one additional RCT assessed the efficacy of botulinum toxin. The review compared botulinum toxin to placebo and plaster casts for the treatment of lower limb spasticity in children with cerebral palsy. The results reported no significant differences between those treated with botulinum toxin and those treated with either placebo or plaster casts³⁵⁴ (Ia). The RCT compared three different doses of botulinum toxin to placebo.³⁵⁵ No overall significant differences were reported between the groups with a number of side effects reported for all three of the intervention groups, with these being proportional to the intervention dosage.

Two randomised crossover trials that assessed L-threonine and threonine respectively compared to placebo both reported no significant effects.^{356,357} Neither of the trials reported any major adverse events (Ib). Likewise a further non-randomised crossover trial examining brolitene and placebo reported no effect³⁵⁸ (IIa). One placebo-controlled randomised crossover trial that assessed 3,4 diaminopyridine reported significant differences on five of the six outcomes measures examined, including the ambulation index (AI). However side effects were reported by a high proportion of patients in the intervention group.³⁵⁹

Four placebo-controlled crossover trials examined the efficacy of different cannabis derivatives for spasticity. The first randomised crossover trial compared Delta-9-tetrahydrocannabinol (THC), cannabidiol (CBD), and a combination of THC and CBD to placebo. The results indicated that THC and the combination of THC and CBD showed beneficial effects on four of the seven outcome measures assessed, whilst CBD alone showed positive effects on three when compared to placebo.³⁶⁰ The second trial assessing Delta-9-THC reported no overall significant effects at lower doses, with a significant reduction in symptoms being noted only at high doses of the drug which was intolerable due to the number of side effects reported.³⁶¹ The third trial assessed the effect of active smoked marijuana on postural stability and reported negative effects on both outcome measures recorded.³⁶² The last randomised crossover trial compared THC and cannabis sativa plant extract to placebo. The results showed no overall beneficial effects for either of the interventions compared to placebo.³⁶³

Although four studies on the use of cannabinoids are reviewed, the totality of evidence is small with few patients included, so it was felt inappropriate to make any recommendations.

However, we are aware that further evidence is likely to be published and that NICE intend to conduct a technology appraisal on cannabinoids in MS with a projected publication date of April 2004.

Other non-pharmacological interventions – Seven RCTs investigated the efficacy of a number of different non-pharmacological interventions for spasticity (Ib). The first RCT assessed the utility of the interadductor *vs* the traditional approach to obturator nerve blockade for bilateral adductor muscle spasms. The results reported positive effects on four of the six outcomes examined, including discomfort, spasms and hygiene scores. No complications were reported with either approach.³⁶⁴ Two RCTs assessed different physiotherapy approaches. The first examined whether an inpatient physiotherapy rehabilitation program would lead to functional gains in mobility in the home.³⁶⁵ The trial reported no overall significant differences between the intervention group and the waiting list control group. The second RCT examined the utility of impairment-based physiotherapy approaches compared to disability-orientated approaches.³⁶⁶ Again no significant effects were observed on any outcome measures between the groups. Four further RCTs examined different interventions. The first assessed the use of muscle passive shortening with traction stress for patients with hip abductor hyposthenia.³⁶⁷ The results showed a positive benefit on the range of motion against gravity for the intervention, but other outcome measures assessed were not interpretable. The second RCT examined electrical neuromuscular stimulation (ENS) against sham stimulation.³⁶⁸ No significant benefits were seen for the intervention. The third examined the effects of magnetic stimulation. This RCT reported beneficial short-term effects on the stretch reflex but these did not persist at longer term follow-up, it also found no significant effect on ADL.³⁶⁹ The last RCT assessed the use of weighted leg extension exercises for strengthening the quadriceps against a standard prescribed exercise program.³⁷⁰ Again, no significant benefits were observed for the intervention.

▷ Economic evidence

The forthcoming HTA review of treatment for pain and spasticity in MS could identify no formal review of current clinical practice regarding the treatment of spasticity. Anecdotal evidence suggests that it may be variable, with an MS society survey reporting that 32% of people did not see a hospital specialist for treatment.³⁷¹ In the systematic review of economic evidence the forthcoming HTA report identified no formal economic evaluations. The only existing economic analysis considers the effect of continuous intrathecal baclofen infusion (CIBI) on hospitalisation rates. At present CIBI is not commonly used in Britain; in 1998 only around 200 people were implanted with a pump for intrathecal baclofen of which only around 60 had MS.^{371a}

None of the identified studies are based in the UK, they only include small numbers of patients, and they include people with spinal cord injury as well as MS. The studies all show significant savings in terms of hospitalisation, implying significant potential cost offsets and patient benefits.

A working group on acute purchasing report in 2000 attempted to model the costs and benefits of intrathecal baclofen in the management of people with severe spasticity (not only from MS).³⁷² The estimated cost per quality-adjusted life year (QALY) was around £20,000, which is relatively high but is within the acceptable range identified in historical NICE appraisal decisions. However, the report commented on the poor clinical evidence for CIBI, hence there is a large amount of uncertainty surrounding the cost per QALY estimate.

In general, though, the initial high cost of CIBI implantation could be offset by reductions in pressure ulcer and other admissions related to spasticity, orthopaedic procedures and reductions in requirements for aids. On the basis of the advice provided in this report, the Trent Development and Evaluation Committee recommended that CIBI be made available to those patient groups for which there is evidence of greatest benefit; that is 'patients who are bedbound due to severe spasticity, patients who cannot be seated in a wheelchair due to severe extensor spasms, and other wheelchair-bound patients in whom spasm-related pain or skin breakdown is a severe problem'.

▷ From evidence to recommendations

In formulating its recommendations, the guideline developers noted the relatively low level of evidence available for most of the commonly used drugs, that comparative studies were very rare, the absence of evidence for most of the commonly used physical therapies, and the difficulty in defining and measuring the benefits of treating spasticity in formal trials. Further, we recognise that cannabis derivative and extracts are currently being researched with several large studies to be published and that NICE is undertaking a review of cannabis drugs. It also recognized that the management of spasticity was an important topic, and hence derived a series of recommendations that drew on clinical consensus as well as the limited evidence.

RECOMMENDATIONS

- R112** Each professional in contact with a person with MS who has any muscle weakness should consider whether spasticity or spasms are a significant problem, or a contributing factor, to the person's current clinical state. **D**

R113	If spasticity or spasms are present, then simple causative or aggravating factors such as pain and infection should be sought and treated.	D
R114	Every person with MS who has persistent spasticity and/or spasms should be seen by a neurophysiotherapist to assess and advise on physical techniques, such as passive stretching and other physical techniques, to reduce spasticity and especially to avoid the development of contractures. Families and carers should be taught how to prevent problems worsening, and a monitoring system should be put in place.	D
R115	More active specific measures should be considered only if the spasms or spasticity are causing pain or distress, or are limiting (further) the individual's dependence and activities. In this case, both benefits and risks should be considered carefully. A specific goal (or goals) should be set, but will rarely include improved performance in activities.	D
R116	Initial specific pharmacological treatment for bothersome regional or global spasticity or spasms should be with: baclofen or gabapentin. The following should be given only if treatment with baclofen or gabapentin is unsuccessful or side effects are intolerable:	A
	<ul style="list-style-type: none"> ● tizanidine ● diazepam ● clonazepam or ● dantrolene. 	<p>A</p> <p>D</p> <p>D</p> <p>D</p>
	Combinations of medicines, and other medicines such as anticonvulsants, should only be used after seeking further specialist advice.	D
R117	People with MS who have troublesome spasticity and spasms unresponsive to simpler treatments should be seen by a team specialising in the assessment and management of spasticity. The team should consider using one or more of the following:	D
	<ul style="list-style-type: none"> ● standing and weight-bearing through legs ● splints ● serial casting ● special or customised seating, such as tilt-in-space chairs ● intrathecal baclofen ● phenol injections to motor points or intrathecally. 	<p>D</p> <p>D</p> <p>C</p> <p>D</p> <p>A</p> <p>D</p>
R118	Intramuscular botulinum toxin should not be used routinely, but can be considered for relatively localised hypertonia or spasticity that is not responding to other treatments. It should be used when specific goals can be identified, and:	B
	<ul style="list-style-type: none"> ● in the context of a specialist service that can consider all aspects of rehabilitation (for example, seating) ● by someone with appropriate experience and expertise ● followed by active input from a neurophysiotherapist. 	

LOCAL IMPLEMENTATION POINTS

These will need to:

- identify who within local neurological rehabilitations services will deal with difficult problems of spasticity and how they are accessed
- identify who may assess and give botulinum toxin injections and how they are accessed
- identify how preventative stretching and handling are delivered to people with MS in the community
- identify what assessment protocols and measures for spasticity should be used locally
- ensure collaborative working with those providing services such as specialized seating to give a comprehensive service to people with MS affected by spasticity
- agree funding arrangements (and prioritising mechanisms if any) for botulinum toxin, baclofen pumps and other specific treatments.

6.5.2 *Contractures at joints*

A contracture is a shortening in the soft tissues (ie tendons, muscles or ligaments) around a joint that limits the passive (and active) range of movement at that joint. Contractures generally arise when a joint is not moved through a full range of movement on a regular basis, for whatever reason. In people with MS the common reasons are spasticity and weakness. The prevalence of contractures in people with MS is not known, nor is it known how frequently they start to develop, but they are seen commonly in daily clinical practice, and much effort is devoted to their prevention and treatment. Contractures may cause pain, and may sometimes be the primary impairment limiting activities such as walking, feeding or dressing. Contractures frequently make caring for, and positioning, seating, walking, dressing and feeding people with MS extremely difficult, requiring expensive care packages to be set up and specialist seats to be made. Prevention and treatment of contractures always involves attempts to ameliorate underlying impairments or other causes.

The main aim of management is to prevent contractures, but some are inevitable and then specific treatments may be needed.

▷ Evidence statements

All evidence statements for contractures at joints are level **Ib**.

No SRs or primary studies in patients with MS were identified which assessed interventions to prevent contractures at joints. An ongoing study was identified on the national research register, which aims to investigate whether a daily muscle stretch regime prevents the development of contractures and muscle stiffness in stroke patients. However, this study is not due to be completed until December 2003.³⁷³

Five RCTs were identified which looked at interventions for the treatment of contractures (**Ib**). Three RCTs looked at various stretching programmes,^{374–376} one looked at a topical cream³⁷⁷ and the last looked at a bed positioning programme.³⁷⁶ Two of the studies, which assessed the effectiveness of a stretching programme, found a beneficial effect of treatment compared to the control group. The first of these studies evaluated the effectiveness of a low-load prolonged stretch in geriatric patients with bilateral knee flexion contractures and found a significant improvement in the passive range of motion in legs treated with the low-load prolonged stretch compared to those receiving a traditional high-load brief stretching programme. The other, a

crossover RCT, evaluated a below-the-knee cast and stretch in patients with traumatic head injury who had ankle contractures. This study reported a significant improvement in passive ankle dorsiflexion motion during the intervention period compared to the control period.³⁷⁶ The third study evaluated the ‘Dynasplint’, which applies a prolonged stretch unilaterally, in geriatric patients, and found no beneficial effect of treatment.³⁷⁴ An RCT, in people with joint disease, of a cream containing chlorprothazine, a muscle relaxant (not available in the UK), found significant improvements in a range of outcomes including pain intensity, tender point palpitation, patients evaluation of treatment, and contracture severity in patients receiving the active cream compared to those receiving a placebo cream. No effects were found for one of the outcomes investigated (limitation of movement).³⁷⁷ No beneficial effect was found for a bed-positioning treatment programme in older patients.³⁷⁸

▷ Health economics

No relevant economic evidence relating to contractures was identified.

▷ From evidence to recommendations

In the absence of much specific evidence the guideline developers drew upon consensus when developing recommendations in this area.

RECOMMENDATIONS

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|------|---|----------------------|
| R119 | Any person with MS who has weakness and/or spasticity sufficient to limit the regular daily range of movement around a joint should be considered at risk of developing a contracture at that joint, and should be considered for preventative measures. | D |
| R120 | Any person with MS at risk of developing contractures should have the underlying impairments assessed and ameliorated if possible (see sections on weakness (6.4) and spasticity (6.5)). | D |
| R121 | Any person with MS at risk of developing contractures should be informed; the individual, and/or carer(s) should be taught how to undertake preventative measures, such as regular passive stretching of the joint(s) at risk and appropriate positioning of limbs at rest. In more severe instances, specialist advice should be obtained on seating and positioning, including positioning in bed. | D |
| R122 | Any person with MS who develops a contracture should be assessed by a suitable specialist for specific treatment; the assessment should take into account the problems caused by the contracture, the discomfort and risk of any treatment and the wishes of the person. At the same time, renewed efforts should be made to reduce the underlying causes and to prevent further contracture. | D |
| R123 | Specific treatment modalities to be considered should include prolonged stretching using: <ul style="list-style-type: none"> ● serial plaster casts ● other similar methods, such as standing in a standing frame and removable splints. These are usually combined with: <ul style="list-style-type: none"> ● local botulinum toxin injection, and ● surgery when necessary. | A
D

D
D |

6.6 Ataxia and tremor

Ataxia refers to uncoordinated voluntary movement usually attributed to disturbed function of the cerebellum or associated pathways and not attributable to direct motor weakness or sensory loss. When present it may be extremely disabling. Ataxia may also arise from loss of adequate sensory feedback. Tremor is a broader term referring to any regular or rhythmic alternating movement affecting a joint or group of joints, and in practice it is difficult to distinguish the precise nature or cause of uncoordinated tremulous movements. The presence of ataxia often indicates lesions in areas that also control bulbar functions (articulation and swallowing) and eye movement control.

Although some people feel that ataxia and tremor are quite distinct,³⁷⁹ in practice there are great difficulties in describing and classifying tremor and ataxia in people with MS.³⁸⁰ Both will be considered at once because it is unlikely that most studies have made unequivocal distinctions. Generally the word 'tremor' will be used to include ataxia, but ataxia will be used primarily to refer to uncoordinated intentional movement thought to arise from cerebellar disturbance.

Tremor of some sort was a newly presenting symptom in 6 of 226 patients followed up over nine months in Oxfordshire.⁶ In a randomly selected group of 100 people with MS in London, tremor was reported by 37 but detected in 58: 15 had 'severe tremor' and 27 had disability attributable to the tremor.³⁸⁰ In another sample, 27% had shaking (tremor).²⁷⁸ In a South Wales survey, ataxia was experienced by 82% of people with MS, and had a point prevalence of 82%.²⁷¹

Although there are no proven treatments, the clinician will need guidance that describes possible managements, and also that alert them to possible complications that arise in people with tremor.

▷ Evidence statements

One RCT compared the use of Johnstone pressure splints as an addition to standard PNF physiotherapy approaches for ataxia. The results showed that the use of Johnstone pressure splints plus exercise using the proprioceptive neuromuscular facilitation technique was only beneficial on two of the eight outcome measures assessed, single limb stance time (right and left), compared to exercise alone³⁸¹ (Ib).

One RCT, two randomised crossover trials and one CCT assessed different interventions for tremor. The RCT examining thalamotomy compared to thalamic stimulation (implanting of electrodes) reported that thalamic stimulations was more beneficial. A large number of relatively serious adverse events were also reported in both groups in the six month period post surgery.³⁸² The first randomised crossover trial compared a single intravenous infusion of ondansetron to placebo, with positive results being reported on all three outcome measures at 60 minutes follow-up. The incidence of side effects was low and these were of a minor nature.³⁸³ The second crossover trial examined the efficacy of isoniazid with no effect being reported on either of the two outcome measures³⁸⁴ (Ib). The CCT which assessed the utility of unilateral stereotactic surgery also reported no overall effect, although beneficial results were reported for two out of the five outcomes examined.³⁸⁵ The trial also reported a number of adverse events both at the time of surgery and post-operatively (IIa).

▷ Economic evidence

No relevant economic evidence relating to ataxia or tremor was identified.

▷ From evidence to recommendations

The guideline development group recognises that many drugs are tried for this distressing and disabling impairment, although there is no evidence. It also noted that the only ‘positive’ drug trial was insufficient to make any recommendation, and that the evidence supporting neurosurgery was limited for such a risky and expensive procedure. The recommendations made reflect the lack of strong evidence or even consensus on specific interventions.

RECOMMENDATION

R124 Any person with MS who experiences a limitation of activities due to tremor should be assessed: D

- by a specialist rehabilitation team for medicines, treatment techniques and equipment (using the general principles of goal setting and evaluation recommended)

and, if problems remain severe and intractable, the person should be assessed:

- by a neurosurgical team from a specialist centre, for suitability for an operation to reduce ataxia (after being given a full explanation of its major risks and possible benefits).

LOCAL IMPLEMENTATION POINTS

These should identify:

- the local specialist rehabilitation service able to assess and advise on treatment and compensatory techniques and equipment
- the neurosurgical centre able to assess for and undertake neurosurgical interventions
- the preferred local measures and assessment techniques, if any.

6.7 Sensory losses

Altered sensation in the form of tingling, numbness, ‘odd’ feelings etc are common in people with MS. In one sample of 656 people, 63% with MS had ‘numbness, tingling or other sensory disturbance’.²⁷⁸ In one survey²⁷¹ sensory disturbance was the commonest first symptom (34%) and was the second most common symptom experienced (87%) and still existing at prevalence point (73%). Sensory losses may be associated with painful hypersensitivity and spontaneous neuralgic pain. The treatment of neurogenic pain is covered separately. Sensory disturbance can directly limit activities; for example numbness in a hand can make fine dextrous activities impossible and people may drop items or injure themselves. Abnormal sensation was present in 49/150 people surveyed at one point, and was a new problem in 6/226 people followed up over nine months in Oxfordshire.⁶

Although there are no proven treatments, the clinician will need guidance about possible managements, and also to alert them to possible complications that arise in people with sensory loss.

▷ Evidence statements

No RCTs or CCTs in patients with MS were identified which assessed interventions for the treatment of sensory losses.

▷ Economic evidence

No relevant economic evidence relating to sensory losses was identified.

▷ From evidence to recommendations

In the absence of any evidence even from other conditions or situations, the GDG has limited itself to simple advice, emphasising the risk that may follow on from loss of sensation.

RECOMMENDATIONS

R125 Any person with MS who experiences a limitation of activities not otherwise explained should be assessed for sensory losses. **D**

R126 Any person with sensory disturbance sufficient to limit activities should be seen and assessed by a specialist rehabilitation team; the individual should be given advice on techniques and equipment to ameliorate their limitations, and advice on personal safety. **D**

6.8 Visual problems

Demyelination within the optic nerve is a common if not universal occurrence in MS. Surprisingly, most people with MS do not have significant symptoms from this demyelination, though on formal testing visual acuity and colour vision are often impaired. Some people do suffer direct visual loss from optic nerve damage but more people suffer significant, sometimes severe visual problems from disturbed oculo-motor control (ie abnormalities in the control of eye movements) that may lead to double vision and movement of images. Reading is difficult for many people with MS. There are few studies on the frequency of significant limitations of visual function in people with MS but one survey did note that 30% had significant disturbance of visual function.²⁷⁸ In Southampton 10% had seriously impaired vision,²⁸⁰ and in South Wales 51% had experienced double vision and the prevalence of visual disturbance was 33%.²⁷¹ In Oxfordshire, 18 of 150 people mentioned problems with their eyes and eyesight at one point, and 3 of 266 developed new problems with their eyes and/or eyesight over nine months, with one having an episode of optic neuritis.⁶

This part aims to ensure that difficulties in this under-recognised area are identified and diagnosed accurately, and that people reach the services most equipped to help, and that the few specific treatments available are tried.

▷ Evidence statements

No RCTs or CCTs in patients with MS were identified which assessed interventions for the treatment of visual problems.

▷ Economic evidence

No relevant economic evidence relating to visual problems in MS was identified.

▷ From evidence to recommendations

Although there was no MS-specific evidence, the GDG has made several recommendations for two reasons. First, there was a strong view that visual impairments are often overlooked and that people with MS and visual impairment did not benefit from any specialist advice, which often may improve their abilities. Second, there is reasonable (RCT) evidence supporting the use of gabapentin for nystagmus, and it is widely used.^{386,387}

RECOMMENDATIONS

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|------|--|---|
| R127 | Each professional in contact with a person with MS should consider whether the individual's vision is disturbed, by considering, for example, the individual's ability to read the text of a newspaper, book or other written material and to see the television. | D |
| R128 | Any person with MS who is unable to read normal print or to see the television should be assessed for glasses by an optometrist. | D |
| R129 | Any individual who experiences reduced visual acuity, despite using suitable glasses, should be assessed in a specialist ophthalmology clinic. | D |
| R130 | Any person with MS who has nystagmus that causes reduced visual acuity or other visual symptoms, should be offered a time-limited trial of treatment with oral gabapentin. This should be initiated and monitored by a suitable specialist. | D |
| R131 | Any person with MS who is unable to read (due to low visual acuity) or to see television, despite all available treatment, should be: <ul style="list-style-type: none"> ● assessed for low-vision equipment and adaptive technology ● referred to the appropriate specialist social services team ● registered as partially sighted. | D |

LOCAL IMPLEMENTATION POINTS

These should identify:

- which local ophthalmologist has an interest in neuro-ophthalmology
- the nearest specialist low-vision service
- the social service team responsible for people with visual impairment.

6.9 Pain

People with MS may suffer pain in at least three ways: specific 'neuropathic' pain arising from areas of demyelination (trigeminal neuralgia is the most well known but not the most common); musculoskeletal pain secondary to postural and other consequences of the disease; and pain from an incidental medical problem unrelated to their MS. Unfortunately, anecdotal experience suggests that much pain is incorrectly diagnosed and poorly managed. A survey of 159 people with MS in Ontario found that 88 had had either an acute or chronic pain syndrome, and that

78 were experiencing chronic pain of one or more types: 46 had neuropathic pain, 22 had back pain, 21 had painful leg spasms.³²³ Pain was present in 42 of 150 people with MS surveyed in Oxfordshire, and 24 of 226 people with MS followed up for nine months developed new pain requiring diagnosis and management.⁶ Fifteen had neurogenic and eight had musculoskeletal pain (six more presented specifically with secondary musculoskeletal pain) and one had headaches (no specific cause). In another survey, pain was the second most frequent 'worst symptom' at 12% (fatigue achieved 17%).²⁶⁹ In a third survey, 36% of 656 people with MS had pain.²⁷⁸ One may conclude that pain is common, and anecdotal experience suggests that pain is often misdiagnosed and mistreated such that patients may suffer unnecessarily.

This section covers all aspects of pain management in people with MS. However the evidence relating to the management of non-neuropathic pain has not been reviewed, and only the evidence that concerns pain that is specific to neurological disease is included. The recommendations are intended to ensure that pain is adequately detected and correctly diagnosed so that the most specific and appropriate treatments available are used.

▷ Evidence statements*

A relatively large number of reviews were identified which assessed the effectiveness of a wide variety of interventions for the treatment of secondary pain. In total, 17 reviews met inclusion criteria. These can be grouped into three main categories: behavioural interventions ($n = 4$ SRs), pharmacological interventions ($n = 7$ SRs) and other therapies ($n = 6$ SRs).

Behavioural interventions showed mixed results in terms of effectiveness. A fairly poor review of cognitive coping strategies found that cognitive strategies were generally effective in enhancing pain tolerance, and that imagery methods were the most effective.³⁸⁸ A review of cognitive behavioural therapy also reported a beneficial effect of treatment on chronic pain.³⁸⁹ A review of multidisciplinary rehabilitation in patients with musculoskeletal pain reported no overall beneficial effects of treatment,³⁹⁰ and a review of non-pharmacological intervention for the treatment of chronic pain reported that studies were too heterogeneous to detect an effect of treatment.³⁹¹

The reviews of pharmacological interventions also reported mixed effects of the interventions evaluated. Two reviews assessed the effectiveness of antidepressants for the treatment of neuropathic pain,^{392,393} one of these also included patients with chronic pain.³⁹³ Both reviews found that antidepressants were more effective than placebo in the treatment of neuropathic pain.^{392,393} One of the reviews reported no difference between the different tricyclic antidepressants in terms of efficacy but that these were more effective than the benzodiazepines.³⁹² Three reviews looked at the effectiveness of anticonvulsant drugs in the treatment of chronic pain. Two looked at these drugs in general^{394,395} and one only looked at gabapentin.³⁹⁶ These reviews reported conflicting results. The first found that generally anticonvulsants were effective for trigeminal neuralgia, diabetic neuropathy, and migraine prophylaxis, but that minor adverse events occurred as often as benefit.³⁹⁵ The second reported that few trials

* Beard S, Hunn A, Wight J. Treatment for spasticity and pain in multiple sclerosis: a systematic review. *Health Technology Assessment* 2003;7:40, was published in December 2003, after the cut-off date for evidence in this guideline. It can be obtained at www.nchta.org/fullmono/mon740.pdf

showed analgesic effectiveness and concluded that these drugs should be withheld until other interventions have been tried for patients with chronic pain, with the exception of trigeminal neuralgia.³⁹⁴ The review which only considered gabapentin reported positive effects in diabetic neuropathy and post herpetic neuralgia compared to placebo, and found it similar in effectiveness to amitriptyline. However, intolerable side effects occurred in up to 10% of recipients.³⁹⁶ A poor quality systematic review found that chemical sympathectomy was effective in relieving pain in around half those receiving treatment.³⁹⁷ However, these results came mainly from uncontrolled studies, and the results of controlled studies were not reported separately. It is therefore difficult to draw conclusions from these results.

The remaining reviews looked at transcutaneous electrical nerve stimulation (TENS), phytodolor (a herbal preparation), acupuncture, ultrasound and low-level laser therapy (LLLT). TENS was reported to be better than inactive control but high frequency TENS (HFTENS) and low frequency TENS (LFTENS) were found to be similar.³⁹⁸ The effectiveness of phytodolor in treating osteoarthritis, chronic epicondylitis and rheumatic diseases was found to be superior to placebo and similar to synthetic drugs.³⁹⁹ There was limited evidence that acupuncture was more effective than no treatment in treating chronic pain, but the evidence was inconclusive as to whether it was more effective than placebo, sham acupuncture or standard care.⁴⁰⁰ Two reviews of ultrasound therapy and a review of LLLT for musculoskeletal pain reported no beneficial effects of treatment.^{401–403}

A review of cannabinoids for the treatment of cancer pain, post-operative pain and non-malignant pain found that cannabinoids were more effective than placebo in relieving pain but similar to codeine.⁴⁰⁴

At the time of writing there is insufficient evidence to comment on the use of cannabinoids in MS. Further evidence on the use of cannabinoids in MS is likely to be published and NICE intend to conduct a technology appraisal on cannabinoids in MS with a projected publication date of April 2004.

▷ Health economics

The forthcoming HTA review of treatment for pain and spasticity in MS found no studies that looked explicitly at the impact of pain on the quality of life of people with MS and no studies that considered the health economics of treatment for pain in MS. In addition, no formal review of current clinical practice was identified. However, there is some evidence that despite the high prevalence of pain as a symptom in MS, few patients are referred to pain specialists – fewer than 2% in an MS Society survey.³⁷¹

▷ From evidence to recommendations

When drawing up recommendations, the guideline developers was aware that although there were few MS-specific studies on pain and its treatment, much of the more generic evidence should be applicable. Consensus was achieved easily on the recommendations made.

RECOMMENDATIONS

- R132 Each professional in contact with a person with MS should ask whether pain is a significant problem for the person, or a contributing factor to their current clinical state. D
- R133 All pain, including hypersensitivity and spontaneous sharp pain, suffered by a person with MS should be subject to full clinical diagnosis, including a referral to an appropriate specialist service if needed. D
- Musculoskeletal pain*
- R134 Every person with MS who has musculoskeletal pain secondary to reduced or abnormal movement should be assessed by specialist therapists to see whether exercise, passive movement, better seating or other procedures might be of benefit. D
- R135 If non-pharmacological means are proving unsuccessful in managing the musculoskeletal pain (arising from reduced movement and/or abnormal posture), the individual should be offered appropriate analgesic medicines. D
- R136 Any person with MS who has continuing unresolved secondary musculoskeletal pain, should be considered for transcutaneous nerve stimulation or antidepressant medication. A
- R137 Treatments that should not be used routinely for musculoskeletal pain include ultrasound, low-grade laser treatment, and anticonvulsant medicines. A
- R138 Cognitive behavioural and imagery treatment methods should be considered in a person with MS who has musculoskeletal pain only if the person has sufficiently well-preserved cognition to participate actively. A
- Neuropathic pain*
- R139 Neuropathic pain, characterised by its sharp and often shooting nature, and any painful hypersensitivity, should be treated using anticonvulsants such as carbamazepine or gabapentin, or using antidepressants such as amitriptyline. A
- R140 If the neuropathic pain remains uncontrolled after initial treatments have been tried, the individual should be referred to a specialist pain service. D

LOCAL IMPLEMENTATION POINTS

These need to specify which specialist services can assess and advise on pain associated with MS, especially:

- musculoskeletal pain and the use of equipment and exercises
- neuropathic pain (neurology, neurorehabilitation or pain service).

6.10 Cognitive losses

About half of all people with MS experience cognitive losses. Indeed, MS is probably the commonest single cause of acquired severe cognitive loss in adults aged under 65 years. For example in the Oxfordshire audit, 12 of 150 individuals felt they had problems with concentration and 10 of 150 with thinking, and only 2 of 226 people present new cognitive problems over a nine month period of follow-up.⁶ In another community-based survey, 43 of

100 individuals had measurable cognitive losses⁴⁰⁵ and in a third community study of 200 people, 46% had measurable cognitive deficits with 34% having impaired memory and 33% impaired planning and other 'frontal lobe functions'.⁴⁰⁶ Other studies have shown similar findings.²⁷⁸

The main implication is that all people, professional and otherwise, who interact with the person with MS should be aware at all times that cognitive loss may be present. It is also important for the person with MS to be aware and to know how to minimise any problems. In practical terms cognitive losses will influence almost all aspects of life, but may be most important in their effects on more complex activities such as community and domestic ADL, making judgements and taking part in legally important decisions, work, and in communication. Other impairments such as disinhibition may also affect control of behaviour and social interaction.

Cognitive impairments in people with MS may have several causes and associated factors. They may be exacerbated by or associated with depression, drugs taken for other impairments, and fatigue. Relapses may cause cognitive impairment, in which case it may well improve. Cognitive loss may occasionally be the presenting or main feature of the disease. Its presence should always be considered but never assumed; formal assessment is usually necessary to clarify the situation. Although the severity of cognitive losses is generally associated with the severity of dependence, this is often not the case and the possible presence of cognitive impairment should always be considered.

The recommendations below should ensure that:

- cognitive impairments are always considered
- any factors that worsen cognitive impairment are identified and treated
- the effects of cognitive impairment are minimised
- any risks associated with cognitive impairment are identified and prevented if possible.

▷ Evidence statements

Four RCTs examined the efficacy of cognitive remediation programs for cognitive dysfunction. The first trial assessed the effectiveness of cognitive training and neuropsychotherapy in comparison to non-specific mental stimulation. The results showed no overall beneficial effect for the intervention at six month follow-up.⁴⁰⁷ The second trial examined the use of cognitive assessment plus remediation, compared to assessment alone, or no treatment. The results indicated no significant differences between the groups on any of the outcomes measures.⁴⁰⁸ The third study assessed the use of cognitive remediation strategies in patients who were resident in long-term nursing facilities. The results showed no beneficial effect for the intervention as compared to the no treatment control group.⁴⁰⁹ The last study compared the use of the story memory technique to no intervention. The results showed positive effects on three out of five of the outcomes assessed, including patients self report of memory functioning⁴¹⁰ (Ib).

▷ Economic evidence

No relevant economic evidence on treatment for cognitive losses was identified.

▷ From evidence to recommendations

The GDG noted that cognitive impairments affected at least half of all people with MS, and that cognitive impairments were often not recognised even though they have pervasive effects. The evidence does not currently support any specific intervention, but nonetheless it was felt important to ensure that cognitive impairments were identified, and that simple advice and actions were undertaken. The recommendations made were agreed by consensus.

RECOMMENDATIONS

- R141 Health care staff should always consider whether the person with MS has any impairment of attention, memory and executive functions sufficient to be a problem, or to be a contributing factor to their current clinical status. D
- R142 When a person with MS is being involved in making a complex medical decision, or is starting a course of complex treatment that requires their active participation, they should have their cognition sensitively assessed to ascertain their ability to understand and participate adequately, and to determine what support they may need. D
- R143 Any person with MS experiencing problems due to cognitive impairment should:
- have their medication reviewed, to minimise iatrogenic cognitive losses D
 - be assessed for depression, and treated if appropriate. D
- R144 Any person with MS complaining of cognitive problems, and any person where this is suspected clinically, should be:
- offered a formal cognitive assessment, coupled with specialist advice on the implications of the results
 - advised, if necessary, about any vulnerability to financial or other abuse that may arise, and how to reduce the risk
 - asked whether the results can be communicated to other people. D
- R145 Any person with MS whose level of dependence or whose social behaviour cannot be easily understood in terms of other known impairments or factors should be offered a formal neuropsychological assessment by a specialist clinical psychologist (and speech and language therapist if appropriate); it should be investigated whether cognitive or communicative losses are a contributing factor and, if so, appropriate management should be recommended. D

LOCAL IMPLEMENTATION POINTS

These need to:

- agree simple assessments of cognition for use by staff interacting with people with MS
- identify which specialist psychology service (usually that within the neurological rehabilitation service) should be approached for assessment and treatment, and how they are accessed.

6.11 Emotionalism

People with MS can suffer several disturbances in their emotions and emotional control. Emotionalism refers to a tendency to cry, or more rarely laugh, when this is not the felt emotion and often without any ability to control the behaviour. It is associated with depression, in stroke patients. It has also been referred to as pathological crying and laughing, pathological emotionalism, and one aspect of pseudobulbar palsy. There are no clear-cut, agreed definitions. It can be extremely distressing to the person with MS but fortunately rarely causes severe or prolonged problems.

The frequency of emotionalism is not known. One study suggests that 10% of people with MS experience 'pathological laughing and crying',⁴¹¹ and another that 32% found that they laughed or cried easily.²⁷⁸

▷ Evidence statements

One randomised crossover trial compared the effect of amitriptyline to placebo. The results showed a beneficial effect on both clinical improvement and the number of episodes of lability. No adverse events were reported⁴¹² (Ib).

▷ Economic evidence

No relevant economic evidence on treatment for emotionalism was identified.

▷ From evidence to recommendations

Although there is little MS-specific evidence; there is some evidence from other neurological conditions. Because emotionalism can be so distressing, the GDG drew on all this evidence to reach the consensus recommendations made.

RECOMMENDATIONS

- R146** A person with MS may comment (or it may be noticed) that they may cry or laugh with minimal provocation and with little control; the individual should be offered a full assessment of their emotional state by someone with suitable expertise. **D**
- R147** If the emotionalism is sufficient to cause concern or distress to the person with MS, or their family, then treatment with an antidepressant should be offered:
- usually a tricyclic antidepressant, or **B**
 - a selective serotonin re-uptake inhibitor. **D**
- R148** If the person with MS still has uncontrolled emotionalism, is unwilling or unable to take antidepressants, or is not responsive to antidepressants, then advice on behavioural management strategies should be offered by a suitable expert. **D**

LOCAL IMPLEMENTATION POINTS

These need to specify:

- which local specialist(s) (neurorehabilitationist, psychiatrist or clinical psychologist) has/have appropriate expertise to assess and manage emotional impairments
- whether one particular antidepressant is preferred.

6.12 Depression

Depression is a common emotional consequence in MS. For example, it was found in 36% of one sample.²⁷⁸ Depression may arise as a specific impairment secondary to neurological lesions and it may be secondary to disability, altered life circumstances, pain, or loss of employment.⁴¹³ It is also likely that depression in turn may cause or worsen some impairments and disabilities. There is some evidence that people with MS have a higher rate of suicide than people with most other chronic disabling conditions, and this risk may be highest within the first five years of diagnosis. In the Oxfordshire audit, 13 of 150 individuals complained of disturbed emotions or emotional control at one time, and 11 of 226 presented with depression or low mood over a nine month period.⁶ In the Southampton survey every person with MS was assessed formally using the Hospital Anxiety and Depression (HAD) scale and 7% were rated depressed and 9% borderline depressed.²⁸⁰

Consequently guidance needs to ensure that all professionals involved are aware of depression, and that it is identified and treated appropriately, not only by drugs but also through ameliorating some of the other causative factors. However it is also important that the important associations between depression, fatigue, social circumstances and other factors are always considered.

In the absence of strong evidence that depression in MS is different from depression in other people, the forthcoming NICE guideline on depression should be used once available.

▷ Evidence statements

Three RCTs examined the effect of cognitive behavioural therapy (CBT) compared to placebo or other active treatments. The first study compared weekly CBT, supportive expressive group (SEG) therapy and sertraline. The results showed that on all three of the outcome measures CBT was significantly superior to SEG; and that there were no differences in the results between CBT and sertraline. No adverse events were reported in the trial.⁴¹⁴ The other two trials both compared CBT to a waiting list control. The first trial reported positive effects on four of six outcome measures assessed, whilst the second that examined the use of individual telephone therapy also reported significant beneficial effects. Neither of the trials reported any adverse effects^{415,416} (**Ib**).

▷ Economic evidence

No relevant economic evidence on treatment for depression in MS was identified.

▷ From evidence to recommendations

The GDG felt that this was an important topic and in the absence of much evidence used consensus to develop the recommendations made.

RECOMMENDATIONS

R149	If depression is suspected, the person with MS should be assessed:	
	<ul style="list-style-type: none"> ● by asking ‘Do you feel depressed?’, or using a similar screening method ● clinically if necessary ● by a liaison psychiatrist if severe depression is present. 	DS D D
R150	In any person with MS who is depressed, a list of possible contributing factors (such as chronic pain and social isolation) should be drawn up.	D
R151	Assessment and interventions should be undertaken to ameliorate those contributing factors, where possible.	D
R152	Specific antidepressant medication, or psychological treatments such as cognitive behavioural therapy should be considered but only as part of an overall programme of depression management.	D A D
R153	Other concurrent psychological diagnoses, especially anxiety, should be considered.	D

LOCAL IMPLEMENTATION POINTS

These should consider:

- which screening question or questionnaire is recommended locally
- which formal depression questionnaire is recommended locally
- which psychiatrist and/or clinical psychologist should be approached when more specialist advice or treatment is required
- what antidepressants are preferred locally.

6.13 Anxiety

Although poorly studied, this is probably the commonest emotional impairment associated with MS. In one study the rate of anxiety at 25% (of 252 consecutive patients with MS) was three times the rate for depression in the same group.⁴¹⁷ In the Southampton survey using the HAD scale, 16% were anxious and 20% borderline anxious, over twice the rate of depression.²⁸⁰ The precise aetiology is not known, although it is probably not due to any specific lesions.⁴¹³ Nevertheless it can significantly increase dependence and distress. In the Oxfordshire audit only one patient (from 226) presented with anxiety over nine months.⁶

▷ Evidence statement

No RCTs or CCTs in patients with MS which assessed intervention for the treatment of anxiety were identified.

Three systematic reviews assessed different interventions for anxiety in patient populations other than MS (Ia). The first review examined the utility of self-help treatments for patients with anxiety presenting in primary care settings. The results showed advantages associated with self-help on at least one measure, although most studies reported multiple comparisons. There were no data available concerning the long term clinical benefits.⁴¹⁸ The second review of seven

trials compared the efficacy of kava extract (a herbal treatment) to placebo. All the trials showed superiority of kava extract, with any adverse effects being mild and transient.⁴¹⁹ However, it should be noted that kava extract has been voluntarily withdrawn from the market because of fears of liver toxicity. A more permanent ban of kava extract is currently being considered by the MCA. The last review compared the effectiveness of group therapy, individual therapy, couple therapy and relaxation therapy in patients with a diagnosis of cancer who were at risk of developing anxiety. The results indicated that all the four treatments were superior to placebo, with psycho-education and group therapy being the most effective.*⁴²⁰

Readers should note that there is a NICE guideline on anxiety in development.

▷ Economic evidence

No relevant economic evidence on treatment for anxiety in MS was identified.

▷ From evidence to recommendations

The recommendations made by the guideline developers depend largely on consensus because the limited evidence available was difficult to translate into useful guidance.

RECOMMENDATIONS

- | | | |
|------|---|---|
| R154 | Any person with MS whose function or happiness is being adversely affected by anxiety should be offered specialist assessment and management. | D |
| R155 | In people with MS with marked anxiety, psychologically-based treatment should be offered. | A |
| R156 | Pharmacological treatment of anxiety should be through using antidepressants or benzodiazepines. The Committee on Safety of Medicines (CSM) guidelines on the use of benzodiazepines (reproduced in the British National Formulary) should be used. | D |

LOCAL IMPLEMENTATION POINTS

These need to specify:

- how to access specialist psychological advice
- how to access specialist psychiatric advice.

6.14 Swallowing difficulties

Dysphagia is a difficulty with swallowing which may cause choking and aspiration of food or liquid into the lungs. There have been few studies on its actual prevalence, let alone its importance and treatment. One study found 49 of 143 consecutively identified people to have dysphagia, and that it was more common in more dependent people and in those with evidence of brainstem dysfunction such as dysarthria – compensatory treatment strategies were successful in 46.⁴²¹ In a second study, 43% of 79 people with MS had dysphagia and about half of these did

* Kapezinski F, Lima MS, Souza JS, Schmitt R. Antidepressants for generalized anxiety disorder. *Cochrane Database Syst Rev* 2003;(2):CD003592, has been withdrawn for updating and was therefore unavailable for inclusion.

not complain of swallowing difficulties.⁴²² Similar associations were found, and any complaint of difficulty swallowing, or coughing on swallowing, was a specific but insensitive marker. In the Oxfordshire audit 18 of 150 people had swallowing difficulties at one point in time, 5 of 226 people developed problems with swallowing over nine months.⁶

Dysphagia (choking, difficulty in swallowing, aspiration of food or fluid into the lungs) is not only distressing but it also may cause chest infections and death. Furthermore, inappropriate management may lead to malnutrition if the person fails to take an adequate diet. It is an important area of concern and the problem is quite common and probably underdiagnosed.

Fortunately, many patients will only have short-term difficulties with swallowing, usually associated with an acute relapse or an infection. Early detection is particularly important in these circumstances, but management is often only needed for a few days or weeks.

Guidance needs to consider various issues:

- early detection, before complications arise
- management that is appropriate to the nature and severity of the problem
- pro-active management to reduce complications
- clinical consideration of the ethical and resource implications of percutaneous endoscopic gastrostomy (PEG) feeding.

▷ Evidence statement

No RCTs or CCTs in patients with MS were identified which assessed interventions for the treatment of swallowing difficulties.

Two systematic reviews, both of good quality, investigated interventions for the treatment of dysphagia in patients with acute stroke or neurological disease^{423,424} (Ia). Both reviews compared PEG to nasogastric (NGT) feeding; there was some overlap in the studies included in these reviews. Both reported that PEG was superior to NGT for the various outcomes assessed, including a reduction in mortality.^{423,424} One of these reviews also investigated a variety of other interventions for the treatment of dysphagia. This review found that swallowing therapy, treatment with nifedipine, nutritional supplementation and fluid supplementation were not more effective than control in the treatment of dysphagia.⁴²⁴

▷ Economic evidence

No relevant economic evidence on treatment for swallowing difficulties was identified.

▷ From evidence to recommendations

The guideline developers recognized that the published evidence only covered a few of the important issues concerned with feeding, swallowing and nutrition and so used consensus to guide most of the recommendations in this important area.

RECOMMENDATIONS

- R157 Any person with MS who is unable to transfer from bed to chair independently, or who has any symptoms or signs of bulbar dysfunction such as any abnormality of eye movements, slurring of speech or ataxia, should be asked whether they have difficulties with chewing, or swallowing food or fluids (for example, coughing), and also whether they have altered their diet because of previous problems. D
- R158 Any person with MS with any bulbar symptoms or signs, and any person with MS who has a chest infection, should have their swallowing assessed by a competent person (using a standardised swallowing test). DS
- R159 People with MS who, on formal assessment, have an abnormality of swallowing should be further assessed by a specialist speech and language therapist. Advice should be given on specific swallowing techniques, and on adapting food consistencies and dietary intake. Further diagnostic assessment (for example, by videofluoroscopy) should be undertaken if:
- first-line therapy and advice are ineffective
 - a specific objective of the investigation can be identified.
- R160 Any person with MS who has difficulty swallowing for more than a few days should be assessed by a neurological rehabilitation team, to review the need for:
- adjustments to or provision of seating that will increase ease and safety of swallowing and feeding
 - chest physiotherapy
 - short-term use of nasogastric tube, especially if recovery is anticipated.
- R161 Any person with MS who has swallowing difficulties for more than one month should have his or her weight or nutritional status checked on a monthly basis (using a validated nutritional measure if needed). Dietary intake should be reviewed if there is continuing weight loss or evidence of malnutrition. D
- R162 If PEG feeding is anticipated as being a likely future option, discussions with the person with MS should be commenced at an early stage and their wishes documented. D
- R163 If swallowing difficulties persist, a PEG tube should be considered if any of the following occur:
- recurrent chest infections
 - inadequate food and/or fluid intake
 - prolonged or distressing feeding
 - nasogastric tube *in situ* for over one month. D
- R164 If PEG placement is indicated and agreed, the PEG tube should be inserted by a suitable specialist. Before the person with MS is discharged from hospital, full training should be given to any family members and carers who are going to be involved in feeding. A

LOCAL IMPLEMENTATION POINTS

These need to:

- produce brief guidance for health workers in contact with people with MS on warning signs of bulbar dysfunction and screening questions for swallowing problems
- agree which formal swallowing test should be used locally

- specify who may request and undertake additional investigative assessments
- specify how PEG tubes are requested, serviced and replaced
- agree who may train carers about PEG feeding
- specify funding arrangements for all equipment and feeds associated with PEG feeding.

6.15 Speech difficulties

Slurred speech (dysarthria) is another problem in people with MS where the prevalence and importance is little researched. In Oxfordshire the prevalence of speech difficulties was 11 of 150, but only one person of 226 developed a new speech difficulty over nine months.⁶ A survey in Sweden found that 44% of people with MS experienced speech or voice difficulties,⁴²⁵ and another study in Sweden found a prevalence of dysarthria of 51% in 77 people, and that a clinical dysarthria test was sensitive.⁴²⁶ The survey in the USA found that 23% had speech or communication difficulties.²⁷⁸ Undoubtedly a significant number of people have mild problems, and some people have problems so severe that communication is limited or prevented. This will usually be in people with severe disability, but sometimes it will be specifically associated with cerebellar disturbance and ataxia.

Other impairments may affect communication. Language disturbance (aphasia) is rare, although it can occur with a relapse leaving mild long-term word-finding difficulties. Cognitive losses can markedly affect communication. The voice can also be affected, causing changes in volume or pitch. Sometimes several impairments will combine to affect communication.

Guidance is needed to encourage recognition of the difficulty and its implications with appropriate management being followed.

▷ Evidence statements

No RCTs or CCTs in patients with MS were identified which assessed interventions for the treatment of speech difficulties.

Four systematic reviews assessed the effectiveness of various interventions for speech difficulties in patients with Parkinson's disease and/or stroke^{427–430} (Ia). Three reviews investigated the effects of different forms of speech and language therapy. The first concluded that it was impossible for the review to determine whether formal speech and language therapy is more effective than informal support.⁴²⁷ The second, which included only patients with Parkinson's disease, found that all trials reported a significant positive effect of speech and language therapy on dysarthria on a variety of outcome measures. However, this review concluded that it is unsafe to draw firm conclusions regarding the efficacy of speech and language therapy considering the small number of patients examined and the methodological flaws in the included studies.⁴²⁹ The third review also found that the limitations of the studies in terms of methodological inadequacies and small numbers of participants meant that it was not possible to draw conclusions regarding the efficacy of one form of speech and language therapy over another.⁴³⁰ The fourth review investigated the effectiveness of various forms of pharmacological therapy in the treatment of patients with aphasia due to stroke.⁴²⁸ This review found that there was some evidence that piracetam was more effective than placebo in the treatment of aphasia. For other interventions investigated (bifemelar, pirbedil, bromocriptine and idenone) the data was not in an appropriate format for analysis. No significant beneficial effects of treatment with dextran 40 were found.

▷ Economic evidence

No relevant economic evidence on treatment for speech difficulties was identified.

▷ From evidence to recommendations

Although four systematic reviews met inclusion criteria these did not provide conclusive evidence on any of the interventions investigated; consensus was therefore used to agree the recommendations.

RECOMMENDATIONS

- R165** Any person with MS who has dysarthria sufficient to affect communication with people outside the home or over the phone, and any person who is concerned about their speech sound or clarity, should be assessed and given advice by a specialist speech and language therapist. **B**
- R166** Any person with MS whose ability to communicate is affected significantly by dysarthria should be taught techniques to improve and maintain speech production and clarity; tuition should be provided by a specialist speech and language therapist, working with any other members of the neurological rehabilitation service who are involved. **D**
- R167** Any person who continues to have difficulties in communication should be considered for, and if appropriate taught the use of, alternative non-verbal means of assisting with or replacing speech. **D**
- R168** Any person with MS who cannot communicate effectively should be assessed by a specialist speech and language therapist for an augmentative aid to communication, which should then be provided as soon as possible. The family members, carers and other frequent communicators with any person with MS who has significant communication difficulties should have discussions with the speech and language therapist on how best to help the person communicate. **D**

LOCAL IMPLEMENTATION POINTS

These need to specify:

- which speech and language therapist should see people with dysarthria
- who may assess for and recommend augmentative equipment and adaptive technology to communication
- funding arrangements for augmentative aids to communication (AACs).

6.16 Sexual dysfunction

MS almost always affects the spinal cord, and disturbance of sexual functions is a common concomitant of any spinal cord damage. The precise frequency of direct sexual dysfunction is unknown. In the Southampton study, 55% of people with MS reported a change for the worse in their sexual relationships, although only 77 (44%) reported a change in their emotional relationship with a partner and 19 of these changes were reported as improvements.³²³ Another

study suggested that about 70% of people with MS had sexual dysfunction compared with 40% in non-neurological disabling conditions and 12% in the general population.⁴³¹ This study suggested that neurological damage was the single most common primary cause of sexual dysfunction. Nonetheless it must also be recognised that sexual behaviour will also be affected by many other impairments such as pain, sensory dysfunction, motor impairments, bladder dysfunction, bowel dysfunction, mood disturbance etc. Furthermore, physiological sexual dysfunction must always be considered in the much wider context of sexual behaviour and relationships. This section not only covers erectile dysfunction and disorders of sexual arousal mechanisms, but also covers wider aspects of sexual behaviour and social relationships that are probably of much greater importance.

Guidance needs to reflect the complexity of the problem, ensuring that problems are detected and then analysed fully so that targeted effective intervention is given where appropriate, while also ensuring that specific treatments are not given inappropriately.

▷ Evidence statements

No RCTs or CCTs in patients with MS were identified which assessed interventions for the treatment of sexual dysfunction.

Four systematic reviews which included men with erectile dysfunction were identified.^{432–435} All were of good quality (Ia). Two reviews examined the effects of sildenafil (Viagra), one looked at yohimbine (a herbal preparation) and the fourth looked at a variety of interventions including both yohimbine and sildenafil. There was overlap in the trials included in these reviews. All three reviews which looked at the effectiveness of sildenafil reported that it was significantly better than placebo in the treatment of sexual dysfunction in men.^{432,433,435} One review also reported that sildenafil was effective in all subgroups investigated.⁴³³ Both the review which looked exclusively at yohimbine⁴³⁴ and the review which also looked at a variety of other treatments⁴³² found that yohimbine was significantly better than placebo in the treatment of erectile dysfunction. The side effect profile of both drugs was reported to be good. The review which looked at a large variety of interventions for the treatment of erectile dysfunction found that inconsistent or lack of clinically relevant reported outcomes together with a lack of long-term follow-up or comparisons with active treatments and selection bias of enrolled patients limited study results.⁴³²

▷ Economic evidence

No relevant economic evidence on treatment for sexual dysfunction was identified.

▷ From evidence to recommendations

The only evidence available related to pharmacological treatments, but the GDG recognised that sexual activity and function depended upon far more than the neurophysiology of sexual structures.

The recommendations, agreed by consensus, therefore cover a much wider range of important issues.

RECOMMENDATIONS

- R169 Men with MS:
- should be asked whether they experience erectile dysfunction (relative or absolute) and, if so, whether it is of concern **D**
 - who have persisting erectile dysfunction and who do not have contraindications should be offered sildenafil 25–100mg **A**
 - who do not respond to sildenafil should be assessed for the general and specific factors that might cause or worsen erectile dysfunction and that are amenable to treatment (such as depression, anxiety, vascular disease, diabetes and taking medicines that may cause erectile dysfunction). Other specific treatments such as alprostadil or intracavernosal papaverine should then be considered. **D**
- R170 Women with MS should be asked whether they experience sexual dysfunction (such as failure of arousal or lubrication or anorgasmia) and, if so, whether it is of concern. **D**
- R171 Women with sexual dysfunction should be assessed for the general and specific factors that might cause or worsen sexual dysfunction and that are amenable to treatment (such as depression, anxiety, vascular disease, diabetes and taking medicines that may cause sexual dysfunction). **D**
- R172 Every person (or couple) with MS should be asked sensitively about, or given the opportunity to remark upon, any difficulties they may be having in establishing and/or maintaining wanted sexual and personal relationships; they should be offered information about locally available counselling and supportive services. **D**
- R173 Every person (or couple) with persisting sexual dysfunction should be offered the opportunity to see a specialist (with particular expertise in sexual problems associated with neurological disease) and offered, as appropriate, advice on lubricants and the use of sexual aids, and other advice to ameliorate their sexual dysfunction. **D**

LOCAL IMPLEMENTATION POINTS

These need to specify:

- urologist or other doctor with expertise in male sexual dysfunction
- gynaecologist or other doctor with expertise in female sexual dysfunction
- all local services available to individuals and couples with difficulties in establishing and maintaining personal and sexual relationships for whatever reason, and especially any that have experience of neurological diseases.

6.17 Pressure ulcers

A pressure ulcer (pressure sore or decubitus ulcer) is an area of broken skin that is secondary to unrelieved pressure on the skin, often exacerbated by slight trauma, for example when being moved. A pressure ulcer may range from a minor break to very large deep areas of dead tissue extending over many square centimetres and down to bone. Once present they can be difficult to heal, and can cause general malaise and worsening of most impairments, and they carry a risk of generalised or localised infections. Many people with MS are at high risk of developing a pressure ulcer because they may have, for example, limited mobility, impairment of sensory

functioning, and reduced cognitive function or undernutrition. In an audit of 226 people followed over 10 months, 10 people experienced 14 pressure ulcers, three acquiring them during hospital admission.⁶ Surveys and formal reports have repeatedly emphasised the costs of pressure ulcers both to the health service and to the patient with the ulcer.⁴³⁶ Prevention must be a high priority yet they continue to occur with monotonous regularity. This section covers both prevention and treatment.

Readers should be aware that a NICE guideline on pressure ulcer management is currently in development.

▷ Evidence statement

All evidence statements for pressure ulcers are level Ia.

Monitoring for the development of pressure ulcers – Two reviews were identified which looked at the assessment of pressure ulcers.^{437,438} The first review found great variation in the estimates of predictive validity both across scales and between assessment of the same scale, and that ultimately none of the scales appears to be unambiguously superior.⁴³⁷ The second reported similar findings, concluding that no scale appears to be more accurate in identifying those patients at most risk from developing pressure sores although the Braden scale has been the most extensively tested.⁴³⁸ This review also reported that there was no evidence that risk assessment scales are effective in reducing the incidence of pressure sores or that they improve preventive care.

Intervention to reduce the risk of pressure ulcers – Two reviews assessed the effectiveness of interventions to reduce the risk of pressure ulcers. Both reviews assessed the effectiveness of pressure-relieving interventions. Both reviews found that higher specification foam mattresses were more effective than ordinary foam mattresses in reducing pressure ulcer incidence in patients at risk of pressure ulcer.^{437,439} The first review reported that the relative merits of higher-tech constant pressure and alternating pressure beds and mattresses were unclear.⁴³⁹ However, the second found that these were more effective than standard hospital mattresses in preventing pressure ulcer. This review also reported that some types of large-cell alternating pressure devices (cell diameter 10cm or greater) may be more effective than simple, low-pressure mattresses, that low-air-loss beds are effective in preventing and treating pressure ulcer compared with foam mattresses and that there was no evidence to indicate the degree to which manual repositioning is effective, or what the optimum turning regime would be.⁴³⁷

Intervention for the treatment of pressure ulcers – Five reviews assessing the effectiveness of treatments for pressure ulcer met inclusion criteria.^{437,439–442} Two reviews, both of which also looked at the prevention of pressure ulcers, looked at the effectiveness of pressure supports. The first review found that standard hospital mattresses are outperformed by a range of foam-based, low-pressure mattresses and overlays, and also by ‘higher-tech’ pressure-relieving beds and mattresses, in the treatment of pressure ulcer. It also found that some types of large-cell alternating pressure devices may be more effective than simple, low-pressure mattresses, that low-air-loss beds are more effective in treating pressure ulcer than foam mattresses, and that there is no evidence to indicate the degree to which manual repositioning is effective, or what the optimum turning regime would be.⁴³⁷ The second review reported that air-fluidised supports and low-air-loss beds may improve pressure sore healing rates and that seat cushions have not been adequately evaluated.⁴³⁹

Two reviews looked at the effectiveness of topical agents for the treatment of pressure ulcers, one of these also looked at the effectiveness of various different dressings and compared dressings to topical agents. The first review found that there was not sufficient evidence to draw conclusions regarding the effectiveness of any topical agent. The second review reported that there was no significant difference in healing rates between topical agents and placebo. However, it found that topical hydrogel promoted healing more than hydrocolloid dressing, and that topical polysaccharide beads were less effective than calcium alginate dressings. It found good evidence (five RCTs) to suggest that hydrocolloid dressings were preferential to traditional therapies (saline gauze and antiseptics) for the treatment of pressure ulcer. Comparisons between dressings were unable to show any statistically significant difference in healing rates.

The fifth review looked at the effectiveness of therapeutic ultrasound, electrotherapy and electromagnetic therapy for the treatment of pressure ulcer.⁴⁴¹ This review found no evidence to support the use of ultrasound or electromagnetic therapy. It reported some evidence in favour of electrotherapy in the treatment of pressure ulcer, but highlighted that this evidence came from three small studies and so should be interpreted with caution.

One RCT assessed the effectiveness of providing personalized information and advice to patients with the aim of reducing the incidence of pressure ulcer and falls. This study found a negative effect of the intervention with an increase in the reports of pressure ulcer and falls in the group receiving information.⁴⁴³

- ▷ Health economic evidence on interventions to treat skins breaks and pressure ulcers

No formal economic evaluations of any interventions involving people with MS were identified. A systematic review in 1995 concluded that there was little evidence on the cost-effectiveness of methods of prevention or treatment (not MS specific).⁴³⁷ The pre-NICE guideline on the risk assessment and prevention of pressure ulcers does not consider the cost-effectiveness of interventions.⁴⁴⁴ A report by Touche Ross in 1993 estimated the costs of preventing and treating pressure ulcers in a 600-bed general hospital at between £600,000 and £3 million per year.⁴³⁶ A recent pilot study has attempted to estimate the cost-effectiveness of a potential prevention programme *vs* standard care of geriatric inpatients with pressure ulcers. This study concluded that the prevention programme was the dominant strategy reducing both the incidence of pressure ulcers and the costs of care. This study was of poor quality and is of limited relevance to the population of people with MS so it is *not* included in the evidence tables.⁴³⁶

RECOMMENDATIONS

- R174 Every person with MS who uses a wheelchair should be assessed for their risk of developing a pressure ulcer. The individual should be informed of the risk, and offered appropriate advice. **D**
- R175 Every person with MS who uses a wheelchair daily should be assessed by a suitably trained person, whenever they are admitted to hospital (for whatever reason), for their need for pressure-relieving devices and procedures. The assessment should be clinical,

specifically taking into account the risk features associated with MS, and not simply the recording of a pressure ulcer risk score; it should lead to the development and documentation of an action plan to minimise risk, including:

- optimisation of nutritional status D
 - provision of suitable equipment B
 - documentation of agreed manual handling techniques. D
- R176 Every person with MS who is provided with a wheelchair by a statutory organisation (NHS or social services), or whose wheelchair seating is being reassessed, should specifically be considered for pressure-relieving procedures and devices – not only in the wheelchair, but in all other activities, especially transfers and sleeping. D
- R177 For every person with MS considered to be at risk on their bed (in hospital or in the community):
- an appropriate specialist mattress should be provided wherever they are lying down A
 - regular turning should not be depended upon as a policy for preventing pressure ulcers A
 - the skin areas at risk should be inspected to ensure adequate protection is being provided. D
- R178 If a pressure ulcer occurs, it should be considered an adverse event worthy of investigation, and advice should be sought from a specialist service. D
- R179 Any person with MS who develops a pressure ulcer should be nursed on a low-loss mattress (while in bed). A
The ulcer should be dressed according to appropriate local guidelines. D
(See also the NICE Clinical Guideline on prevention of pressure ulcers.^{444,445})

LOCAL IMPLEMENTATION POINTS

The local services will need to consider:

- procedures and funding mechanisms to ensure that specialist pressure-relieving devices are made available promptly to people needing them wherever they are
- who has appropriate training to assess for risk of pressure ulcer
- which dressings are to be used locally
- which team specialises in prevention and management of pressure ulcer
- mechanisms for reporting the development of pressure sores and investigating why they occurred.

6.18 Other treatments including complementary therapies

Most people with MS take an active interest in managing their illness. This includes the use of unlicensed interventions that are not generally recognised by health professionals as influencing the disease process or ameliorating specific symptoms. A survey of 117 people in Cardiff showed that people with MS are high users of non-prescription medicines, and that these were usually purchased from sources where no health professional was available to give advice.⁴⁴⁶ These interventions are often referred to as alternative or complementary therapies. The stated

or expected effect of these treatments may not be clear. Where a rationale does exist it should be recognised that there may be an overlap between alternative therapies taken in the belief that they affect the disease process, and those taken in the belief that they ameliorate the effects of the disease in some way. Some benefit may arise through placebo mechanisms but for the individual this may be an important effect.

Some of these treatments may cost the person with MS substantial sums of money, or expose them to risk. Further information on complementary and alternative medicines and other lifestyle recommendations are available from various MS support organisations. It should also be recognised that the boundaries between complementary/alternative and orthodox treatments varies between countries, cultures, over time and even between members of the health care professions. This section covers a variety of interventions that are used in non-specific ways, usually to ameliorate several symptoms. It includes both standard interventions and those that may be considered alternative.

The aims of the recommendations are similar to those concerning all treatments, namely to ensure that people with MS:

- are facilitated in pursuing any treatments that they wish to
- are given or directed to any information that may be available concerning any proposed treatment
- are specifically recommended to consider risks, cost and benefits for any treatment
- keep the health care professionals aware of all treatments being pursued.

▷ Evidence statement

One systematic review of 12 RCTs assessed the efficacy of a variety of complementary and alternative therapies used by people with MS⁴⁴⁷ (Ib). The specific therapies addressed in the review were nutritional therapy ($n = 4$), Feldenkrais bodywork ($n = 1$), reflexology ($n = 1$), magnetic field therapy ($n = 2$), neural therapy ($n = 1$) and psychological counselling ($n = 2$). It reported some evidence to suggest some benefit of nutrition therapy, linoleic acid ($n = 3$) and fish oils ($n = 1$) for the physical symptoms of MS. Likewise, magnetic field therapy and neural therapy also appeared to have a short-term beneficial effect on physical symptoms. The results also showed that massage/bodywork and psychological counselling appear to improve depression, anxiety and self-esteem. However, the strength of evidence for any of the therapies was limited as many of the trials suffered from significant methodological flaws. One further CCT that also examined reflexology reported no effect on a range of symptoms, and although symptoms scores improved slightly during treatment this was not maintained at follow-up⁴⁴⁸ (IIa).

Two small randomised crossover trials examined the effectiveness of body cooling for heat sensitive patients^{449,450} (Ib). The first placebo-controlled trial reported beneficial effects on three out of four of the indices tested, namely visual acuity, timed walk test and muscle strength, but no effect on coordination.⁴⁵⁰ However, the length of follow-up was not reported and so it is impossible to determine whether these effects were transitory. The second trial reported no significant effects on either tympanic temperature decreases or on any of twelve performance tests.⁴⁴⁹

Three RCTs assessed the effectiveness of different exercise programmes for increasing the fitness and well-being of individuals with MS^{451,452,453} (Ib). The first that examined the effectiveness of a water exercise training program found positive effects upon pain, energy, social and sexual

function as assessed by the MSQOL-54, and tension, fatigue and vigour, assessed by the POMS-SF.⁴⁵² However, the second RCT that examined an exercise programme using a leg cycle ergometer found no improvement in either the physical fitness indices assessed or grades of fatigue, as assessed by the Fatigue Severity Scale.⁴⁵³ The last RCT examined the utility of lectures on exercise philosophy combined with nutrition, stress management and an individualised exercise programmes.⁴⁵¹ The results showed no effect on either graded exercise time or on EDSS scores.

Two RCTs (Ib) and one CCT (IIa) investigated the effects of antidepressants.^{454,456} The antidepressants assessed included imipramine, lofepramine combined with phenylalanine, and tranylcypromine. None of these trials reported an overall beneficial effect of the intervention, although one of the RCTs reported some beneficial effect. This good quality RCT found a greater improvement on the Chalder fatigue scale score in those receiving lofepramine combined with phenylalanine compared to those receiving placebo, however, it found no effect of treatment for any of the other five outcomes investigated.⁴⁵⁴ Side effects were relatively minor but occurred more frequently in the intervention group.

Two further RCTs (Ib) and two CCTs (IIa) examined the interventions of t'ai chi, Chinese medicine, relaxation training and a multimodal intervention program. The results of the CCT assessing t'ai chi reported significant changes in patients' assessment of their symptoms at three month follow-up.⁴⁵⁷ One CCT of a multimodal intervention program reported significant effects on five of the eight areas assessed. These included two measures of list learning and memory, improved BDI scores, one measure of grip strength and one of tactile sensitivity⁴⁵⁸ (IIb). One of the RCTs looked at relaxation training and biologically orientated imagery treatment.⁴⁵⁹ The results showed a significant improvement on state anxiety, but not on trait anxiety or the other three tests examining mood or health states. The last RCT compared the efficacy of traditional Chinese medicine combined with Western medicine to treatment with Western medicine alone. The results indicated beneficial effects upon remittance of symptoms.⁴⁶⁰

▷ Economic evidence

There are no economic studies of complimentary therapies in MS.

▷ From evidence to recommendations

This section, and the evidence in it, covers a wide range of potential treatments that are considered or used by a large number of people. The evidence does not support any particular treatment, though conversely it does not show that any are specifically harmful. The GDG felt it was important to steer readers towards any available information, while also making it clear that it was insufficient to recommend use or non-use. The GDG was also especially concerned that people with MS were encouraged to inform professionals about any treatments being used so that potentially harmful interactions or effects could be avoided.

RECOMMENDATIONS

- | | | |
|------|--|-------------------------------------|
| R180 | People with MS should be informed that there is some evidence to suggest that the following items might be of benefit, although there is insufficient evidence to give more firm recommendations: | A |
| | <ul style="list-style-type: none">● reflexology and massage● fish oils● magnetic field therapy● neural therapy● massage plus body work● t'ai chi● multi-modal therapy. |
A
A
A
A
A
A
A |
| R181 | A person with MS who wishes to consider or try an alternative therapy should be recommended to evaluate any alternative therapy themselves, including the risks and the costs (financial and inconvenience). | D |
| R182 | A person with MS should be encouraged to discuss any alternative treatments they are considering, and to inform their doctors and other professionals if they decide to use any. | D |

LOCAL IMPLEMENTATION POINTS

These should cover:

- how and where people may find more information about, and access/purchase, most common alternative therapies
- which alternative therapies are going to be supported by health funds, if any.