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[Intervention Review]

Information provision for people with multiple sclerosis

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ABSTRACT

Background

People with multiple sclerosis (MS) are confronted with a number of important uncertainties concerning many aspects of the disease. These include diagnosis, prognosis, disease course, disease-modifying therapies, symptomatic therapies, and non-pharmacological interventions, among others. While people with MS demand adequate information to be able to actively participate in medical decision making and to self manage their disease, it has been shown that patients' disease-related knowledge is poor, therefore guidelines recommend clear and concise high-quality information at all stages of the disease. Several studies have outlined communication and information deficits in the care of people with MS. However, only a few information and decision support programmes have been published.

Objectives

The primary objectives of this updated review was to evaluate the effectiveness of information provision interventions for people with MS that aim to promote informed choice and improve patient-relevant outcomes. Further objectives were to evaluate the components and the developmental processes of the complex interventions used, to highlight the quantity and the certainty of the research evidence available, and to set an agenda for future research.

Search methods

For this update, we searched the Cochrane Multiple Sclerosis and Rare Diseases of the Central Nervous System Group Specialised Register, which contains trials from CENTRAL (the Cochrane Library 2017, Issue 11), MEDLINE, Embase, CINAHL, LILACS, PEDro, and clinical trials registries (29 November 2017) as well as other sources. We also searched reference lists of identified articles and contacted trialists.

Selection criteria

Randomised controlled trials (RCTs), cluster-randomised controlled trials, and quasi-randomised trials comparing information provision for people with MS or suspected MS (intervention groups) with usual care or other types of information provision (control groups) were eligible.

Data collection and analysis

Two review authors independently assessed the retrieved articles for relevance and methodological quality and extracted data. Critical appraisal of studies addressed the risk of selection bias, performance bias, attrition bias, and detection bias. We contacted authors of relevant studies for additional information.

Main results

We identified one new RCT (73 participants), which when added to the 10 previously included RCTs resulted in a total of 11 RCTs that met the inclusion criteria and were analysed (1387 participants overall; mean age, range: 31 to 51; percentage women, range: 63% to 100%; percentage relapsing-remitting MS course, range: 45% to 100%). The interventions addressed a variety of topics using different approaches for information provision in different settings. Topics included disease-modifying therapy, relapse management, self care strategies, fatigue management, family planning, and general health promotion. The active intervention components included decision aids, decision coaching, educational programmes, self care programmes, and personal interviews with physicians. All studies used one or more components, but the number and extent differed markedly between studies. The studies had a variable risk of bias. We did not perform meta-analyses due to marked clinical heterogeneity. All five studies assessing MS-related knowledge (505 participants; moderate-certainty evidence) detected significant differences between groups as a result of the interventions, indicating that information provision may successfully increase participants' knowledge. There were mixed results on decision making (five studies, 793 participants; low-certainty evidence) and quality of life (six studies, 671 participants; low-certainty evidence). No adverse events were detected in the seven studies reporting this outcome.

Authors' conclusions

Information provision for people with MS seems to increase disease-related knowledge, with less clear results on decision making and quality of life. The included studies in this review reported no negative side effects of providing disease-related information to people with MS. Interpretation of study results remains challenging due to the marked heterogeneity of interventions and outcome measures.

PLAIN LANGUAGE SUMMARY

Information provision to help people with multiple sclerosis make informed decisions

Background

People with multiple sclerosis (MS) are confronted with many uncertainties in all phases of the disease. For example, the significance of a diagnosis for the future disease course remains unclear, as up to one-third of people will experience a benign disease course with little or even no disability progression. Uncertainty is also present for the effects and adverse effects of drug and non-drug therapies.

People with MS have the right and wish to receive accurate, recent, and relevant information in order to make informed choices on all relevant disease-related decisions and also on personal life-planning decisions. For this to occur, balanced information is a prerequisite. It has been shown that disease knowledge is poor in people with MS, therefore people with MS should receive interventions that provide information on all aspects relevant for them.

Results

We searched for relevant studies in the medical literature in November 2017 and identified 11 studies involving a total of 1387 participants. The studies evaluated a variety of approaches including the provision of written information or decision aids, coaching, educational programmes, and personal information. The quality of the study methods varied. Topics included disease-modifying therapy, relapse management, self care strategies, fatigue management, family planning, and general health promotion. Five studies assessing level of knowledge showed that information may successfully increase patients' knowledge (moderate-certainty evidence). Five studies reporting on the effects on decision making (low-certainty evidence) and six studies assessing quality of life (low-certainty evidence) showed mixed results. As the studies and the interventions used differed markedly, and the certainty of the evidence for our outcomes was not high, our results prevented a clear conclusion about the effectiveness of information provision interventions for people with MS.

SUMMARY OF FINDINGS

Summary of findings for the main comparison. Information provision compared to (optimised) standard care for people with multiple sclerosis

Information provision compared to (optimised) standard care for people with multiple sclerosis

Patient or population: people with multiple sclerosis
Setting: primary and secondary care
Intervention: information provision
Comparison: (optimised) standard care

Outcomes (see also Table 3)	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	Nº of participants (studies)	Certainty of the evidence (GRADE)
	Risk with (optimised) standard care	Risk with information provision			
Knowledge assessed with: RIKNO or MSKQ or self developed questionnaires (follow-up from directly after the intervention up to 6 months)	4 studies reported differences between groups in favour of the intervention groups. In 1 study (Rahn 2018), both intervention and control groups showed improved knowledge 3 and 6 months after the intervention.			505 (5 RCTs)	⊕⊕⊕⊖ MODERATE ¹
Decision making assessed with: different questionnaires (CPS, DCS, DSES, MMIC, PBMS, MAPPIN'SDM, or self developed) or analysis of videotaped coaching sessions (follow-up from 2 weeks up to 2 years after the intervention)	Only 1 study reported more active roles in decision making in the intervention group (Köpke 2009), while the other 4 studies showed no clear differences concerning decision making.			793 (5 RCTs)	⊕⊕⊖⊖ LOW ^{2 4}
Quality of life assessed with: SF-36 or HAQUAMS (follow-up from 6 weeks up to 2 years after the intervention)	2 studies found improvements in quality of life in favour of the intervention group (Ennis 2006, O'Hara 2002), while the other 3 studies found no differences between groups.			671 (6 RCTs)	⊕⊕⊖⊖ LOW ^{3 5}
Adverse events assessed with: HAQUAMS (quality of life), UNDS (disability status) or list of serious events or not specified	All 7 studies reporting this outcome found no adverse events.			751 (7 RCTs)	⊕⊕⊕⊖ MODERATE ⁶

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **CPS:** Control Preference Scale; **DCS:** Decisional Conflict Scale; **DSES:** Decision Self-Efficacy Scale; **MMIC:** Multidimensional Measure of Informed Choice; **HAQUAMS:** Hamburg Quality of Life Questionnaire in Multiple Sclerosis; **MAPPIN'SDM:** Multifocal Approach to Sharing in Shared Decision Making; **MSKQ:** Multiple Sclerosis Knowledge Questionnaire; **PBMS:** Planned Behaviour in MS questionnaire; **RCT:** randomised controlled trial; **RIKNO:** Risk Knowledge in Relapsing Multiple Sclerosis questionnaire; **SF-36:** 36-item Short Form Health Survey; **UNDS:** United Kingdom Neurological Disability Scale

GRADE Working Group grades of evidence

High certainty: We are very confident that the true effect lies close to that of the estimate of the effect.

Moderate certainty: We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low certainty: Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.

Very low certainty: We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

¹Of five studies, only [Köpke 2014](#) blinded participants and was rated as at low risk of bias.

²Of five studies, only [Kasper 2008](#) and [Köpke 2014](#) blinded participants and were rated as at low risk of bias.

³Of six studies, only [Köpke 2014](#) blinded participants and was rated as at low risk of bias.

⁴Different concepts were used to assess decision making, with only [Köpke 2009](#) showing a clearly positive effect on decision making.

⁵Two different instruments were used to assess quality of life, with only [Köpke 2014](#) and [O'Hara 2002](#) showing differences in favour of intervention groups for subscales of the SF-36.

⁶Of seven studies, only [Köpke 2014](#) blinded participants and was rated as at low risk of bias.

BACKGROUND

Description of the condition

Multiple sclerosis (MS) is an inflammatory and degenerative disorder of the central nervous system leading to damage of myelin and axons. It usually starts in early adult life, typically in the third decade (Reich 2018). Prevalence rates vary between geographical areas with the highest rates of 120 to 180 per 100,000 people reported for Northern Europe, North America, and Australia (Multiple Sclerosis International Federation 2010). In most people, the early disease course is characterised by inflammation causing relapses, that is episodes of neurological dysfunction that usually recover partially or in total. Relapses can lead to a number of clinical presentations ranging from mild sensory dysfunctions to severe symptoms (e.g. loss of vision or paraplegia). Over time, however, neurodegeneration seems to be more important than inflammation in leading to progression of disability. About 10% to 15% of people with MS have a primary progressive form. As the cause and mechanisms of the disease are mostly unexplained (Compston 2008), uncertainty remains a constant feature of the disease (Heesen 2011; NCC-CC 2004). Individual disease courses and prognoses are variable and hard to predict, with about one-third of people remaining relatively unaffected by the disease, experiencing a 'benign' course (Degenhardt 2009; Ramsaransing 2006). Prognostic information is a complex topic, and the information needs of people with MS with regard to this are rarely met (Dennison 2016; Dennison 2018). An increasing number of so-called disease-modifying drugs (DMDs) have been licenced for clinically isolated syndrome, relapsing, secondary progressive, and recently also for primary progressive MS aiming to reduce relapses rates and slow disease progression (Montalban 2018; Tramacere 2015). So far, however, interventions are only partially effective, and long-term effects remain unclear (Ebers 2010; Freedman 2008; Shirani 2012). Furthermore, DMDs are expensive and have adverse effects resulting in low treatment adherence (Bruce 2010; Tramacere 2015). The effectiveness of DMDs in progressive disease courses remains mostly unknown.

Taking into account recently licenced and further upcoming DMDs, and therefore the rapidly increasing complexity of treatment options, the availability of well-developed, unbiased, up-to-date information is increasingly necessary to enable informed treatment choices (Heesen 2011).

Apart from DMD choices, people with relapsing MS must make decisions on relapse therapies, where options range from high-dose intravenous or oral steroids to watchful waiting (Burton 2012; Galea 2015; Köpke 2004).

Despite the limited specificity of diagnostic tests in MS (Schäffler 2011), a 'hit hard and early' treatment approach is increasingly promoted by experts and pharmaceutical stakeholders (Freedman 2009; Montalban 2018). This is likely to result in overdiagnosis and overtreatment (Schäffler 2011; Whiting 2006).

These multiple uncertainties pose a challenge for the medical decision-making process between people with MS and their healthcare providers (Heesen 2011). Fifteen years ago it was shown in Europe that most people with MS claim autonomous roles in decision making (Heesen 2004), and this was recently confirmed in the USA by Cofield 2017. Notably, although cultural differences have been found on role preferences (Giordano 2008), the need to

be informed also applies to people with MS preferring a passive decision-making role. This contrasts with the poor disease-related knowledge among people with MS (Giordano 2010; Heesen 2004). Several studies have outlined communication and information deficits in the care of people with MS (Del Piccolo 2015; Heesen 2003; Solari 2007; Vickrey 2000; Wollin 2000), as well as differences between patients and physicians concerning perception of disease severity (Rothwell 1997), risk (Heesen 2010), and involvement in the decision process (Kasper 2011; Pietrolongo 2013). Multiple sclerosis management guidelines have therefore acknowledged the need for balanced information and patient participation in MS decision making (Montalban 2018; NCC-CC 2004). In 2007, the European Union published a 'Code of Good Practice' on the rights of people with MS (EMSP 2007), demanding the provision of clear and concise high-quality information, from diagnosis onwards, to empower people with MS to self manage their disease to the greatest degree possible.

A number of studies have addressed the decision-making competences of people with MS, some of them questioning such competences due to impaired mental capacities (Farez 2014; Neuhaus 2018). A recent systematic review on risk understanding of people with MS indicated underestimation of risks and overestimation of treatment effects together with seemingly insufficient methods to provide information on DMD risks and benefits (Reen 2017a). However, recent randomised controlled trials (RCTs) on communication of risk information are encouraging (Kasper 2017; Rahn 2016). Furthermore, numeracy competences of people with MS have recently been shown to be similar to a healthy population (and overall low) (Gaissmaier 2018). Finally, no data are available on the information needs of proxy decision makers of people with MS having severe cognitive compromise or dementia.

Description of the intervention

Various information tools have been developed for people with MS. Despite a large amount of available information, such as on the Internet, comprehensibility, up-to-dateness, relevance, accuracy, validity, and the efficacy of this information have rarely been studied (Heesen 2011). Available education and information materials include patient information handouts and booklets provided by pharmaceutical companies, charities, and self help groups. Other sources of information, such as on CD, DVD, or websites, are becoming increasingly important. Furthermore, information technologies commonly referred to as Web 2.0 systems (podcasts, blogs, and social networks), smartphones, and pocket PC technologies might be used to provide MS patient information. For this review update, we aimed to include studies assessing the effects of interventions providing information about MS to people with MS. The information may be provided in different formats such as printed materials, educational programmes, lectures, audiovisual aids, computer programmes or websites, decision support tools and personal information, or any combination of these.

How the intervention might work

Accurate and unbiased information may help to prevent unrealistic expectations, for example concerning disease courses and effects of therapies. In order to express preferences and to be involved in decision making, people with MS need sufficient and appropriate information that allows them to make informed decisions together with their physicians (Coulter 1999; Heesen 2011). Information

provision may therefore not only directly influence patients' knowledge, but also positively affect, for example, psychological outcomes, quality of life, sense of control, and health services utilisation (Heesen 2012). It is expected that informed treatment choices improve treatment adherence/persistence and reduce resource waste. Moreover, positive effects on the disease course could be expected as information provision can lead to more effective disease management strategies and healthier lifestyles (Heesen 2007a).

Why it is important to do this review

A few years ago Mulley and colleagues called for higher sensitivity towards patients' preferences in medicine, claiming that not taking into account patients' preferences and not addressing these preferences via adequate information and counselling is an important shortcoming of modern medicine comparable to medical misdiagnoses (Mulley 2012). This has been increasingly acknowledged by other authors. For example, in the UK, a national strategy on informed shared decision making has been proposed to achieve patient-centred care (Leng 2017). Recently Saini and colleagues identified factors associated with "knowledge, bias, and uncertainty" as one of three key drivers of poor medical care (Saini 2017). With the growing availability of various treatment options for MS, it seems increasingly important for patients to have access to adequate information in order to make informed choices. In this context, it is imperative to evaluate the effectiveness of different information strategies. A recently published systematic review on interventions to support the understanding of the risks and benefits of DMDs in MS patients that included any study design found some increase in risks understanding, but no effect in benefits understanding, and an unclear impact on decision making (Reen 2017b). The best evidence for the efficacy of interventions that aim to provide patients with information should come from large, well-conducted RCTs or from meta-analyses of these. Given the time since the original review, we considered an update to be appropriate to determine whether the evidence is any clearer regarding the effectiveness of information provision in this population. An updated systematic review was therefore required to identify all trials in this area and to summarise the existing evidence. A number of systematic reviews have addressed the different forms of information provision for patients, health professionals, and caregivers in other conditions. For example, a Cochrane Review that included 21 trials indicates that information provision to people following stroke may have positive effects on knowledge, patient satisfaction, and depression (Forster 2012). The results of this review showed a greater benefit with active information provision than with passive information provision for at least some outcome measures. The recently updated Cochrane Review on the effectiveness of decision aids, which included 105 trials, showed that decision aids are effective in increasing knowledge and may also positively influence decision making (Stacey 2017). However, this review included only one study addressing people with MS (Kasper 2008).

OBJECTIVES

The primary objectives of this updated review was to evaluate the effectiveness of information provision interventions for people with MS that aim to promote informed choice and improve patient-relevant outcomes.

Also we aimed to evaluate the components and the developmental processes of the complex interventions used, to highlight the quality and quantity of research evidence available, and to set an agenda for future research.

METHODS

Criteria for considering studies for this review

Types of studies

We included randomised, cluster-randomised, or quasi-randomised trials of information provision interventions provided with the intention of improving the outcome of patients compared to (optimised) standard care. We also included trials comparing two different strategies of information provision.

Types of participants

We considered patients of all ages with a diagnosis of any course of MS or in the diagnostic process (i.e. with suspected MS or clinically isolated syndrome) for inclusion. The criteria of diagnosis were any established diagnostic criteria (e.g. Schumacher (Schumacher 1965), Poser (Poser 1983), McDonald (Polman 2005), or McDonald 2010-revised (Polman 2011)) as used in the original studies.

Types of interventions

We considered any intervention or group of interventions providing disease-specific information given with the intention of improving the outcome of patients for inclusion. In the case of multifaceted interventions, information provision had to be the main or one of the main components of the intervention. Interventions that covered information on general disease issues, drug therapies, other (non-drug) therapies, or combinations of these, were eligible for inclusion. Information was expected to be provided by:

1. information leaflets, booklets, manuals, or pamphlets;
2. educational programmes or lectures;
3. audiovisual aids like videos, tape recordings, computer programmes, or websites;
4. Web 2.0 systems including podcasts, social networks or other information technologies such as smartphones;
5. decision support tools; and
6. personal information (e.g. house visits or telephone calls).

We expected some interventions (e.g. educational programmes) to be designed as complex interventions, that is comprising more than one of the components outlined above. Following the 'framework for design and evaluation of complex interventions' (Campbell 2000; Campbell 2007; Craig 2008), it may not be possible to extract the effective components of the interventions. Control interventions could be either standard care or optimised standard care, for example providing standard information in a structured way.

Types of outcome measures

Primary outcomes

As primary outcomes we considered:

1. disease-related ('risk') knowledge measured by any type of instrument used in the included studies (e.g. questionnaire or interview);

- measures of (shared) decision making, e.g. the OPTION scale (Elwyn 2005), the Shared Decision Making Questionnaire (SDM-Q) (Simon 2006), or the Decisional Conflict Scale (O'Connor 1995a).

Secondary outcomes

Further outcomes were:

- quality of life, e.g. Multiple Sclerosis Quality of Life-54 (MSQOL-54), Vickrey 1997, or Hamburg Quality of Life Questionnaire in Multiple Sclerosis (HAQUAMS) (Gold 2001);
- measures of informed choice, e.g. the Multidimensional Measure of Informed Choice (MMIC) (Marteau 2001);
- psychological status measures, e.g. Hospital Anxiety and Depression Scale (HADS) (Airlie 2001);
- treatment choices (e.g. invasive, less invasive, no treatment); and
- treatment adherence.

We also considered:

- satisfaction with the information received and with the decisional process;
- hospital admissions and use of health services;
- measures of activities of daily living (ADLs);
- coping, e.g. Coping Orientation to the Problems Experienced inventory (Goretti 2009);
- disability, e.g. Expanded Disability Status Scale (EDSS) (Kurtzke 1983);
- role preferences, e.g. Control Preference Scale (CPS) (Degner 1997); and
- adverse events, as suggested by the Cochrane Consumers and Communication Review Group (CCCG 2012).

Furthermore, reporting of process-related outcomes (e.g. qualitative data) was assessed using the Criteria for Reporting the Development and Evaluation of Complex Interventions in healthcare: revised guideline (CRDeCI 2) to allow for analysis and deeper understanding of the complex interventions used (Möhler 2015). Data on patient or consumer involvement and their perception of the intervention were extracted.

Search methods for identification of studies

We applied no language restrictions to the search.

Electronic searches

The Information Specialist searched the Cochrane Multiple Sclerosis and Rare Diseases of the Central Nervous System Group Trials Register which, among other sources, contains trials from the following sources.

- The Cochrane Central Register of Controlled Trials (CENTRAL) (the Cochrane Library 2017, Issue 11).
- MEDLINE (PubMed) (1966 to 29 November 2017);
- Embase (1974 to 29 November 2017);
- CINAHL (EBSCO host) (Cumulative Index to Nursing and Allied Health Literature; 1981 to 29 November 2017);
- LILACS (BIREME) (Latin American and Caribbean Health Science Information database; 1982 to 29 November 2017);

- PEDro (Physiotherapy Evidence Database; 1990 to 29 November 2017).
- US National Institutes of Health Ongoing Trials Register ClinicalTrials.gov (www.clinicaltrials.gov) and World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) (apps.who.int/trialsearch/) searched on 29 November 2017.

Updated search strategies are listed in [Appendix 1](#).

Information on the Group's Trials Register and details of the search strategies used to identify trials can be found in the 'Specialised Register' section within the Cochrane Multiple Sclerosis and Rare Diseases of the Central Nervous System Group [module](#).

Additionally, the review authors searched PsycINFO (OvidSP) (1967 to 29 November 2017) ([Appendix 2](#)).

Searching other resources

- We checked trial and dissertation registers ([Appendix 3](#)), as well as reference lists of published reviews, and retrieved articles for unpublished or ongoing trials.
- We also contacted experts in the field to identify unpublished or ongoing studies.

Data collection and analysis

Selection of studies

Two review authors (SK, AG) independently examined the titles and abstracts of citations obtained from the search and assessed articles for inclusion according to the above criteria. Disagreements were resolved by discussion. For primary studies in which review authors were involved, one review author (AS or FK) who was not involved in the primary study assessed the study for inclusion.

Data extraction and management

We used a data extraction form based on the Cochrane Consumers and Communication Group's data extraction template and entered data into Review Manager 5 ([Review Manager 2017](#)). Two review authors (SK, AG) independently extracted the data from the included studies using the standardised form and checked the data for accuracy. For primary studies in which review authors were involved, one review author (AS) not involved in the primary study checked data extraction. We extracted data for characteristics of participants, baseline data, interventions, duration of intervention, length of follow-up, outcome measures, and adverse events. For dichotomous data, we extracted the number in each treatment group and the numbers experiencing the outcome of interest. For each outcome measure, we extracted data for every participant assessed. To allow for an intention-to-treat (ITT) analysis, we extracted the data irrespective of treatment adherence and whether or not the participant was subsequently deemed ineligible or otherwise excluded from treatment or follow-up. If ITT data were not available in the publications, we retrieved 'on-treatment' data or the data of those who completed the trial. We did not mask study names. In case of disagreement, a third review author (CH) was involved to reach consensus. We aimed to collect any supplementary (e.g. qualitative) data produced as process evaluations to allow for deeper understanding of the complex interventions in the included studies and their components using the CRDeCI 2 criteria as a framework (Craig 2008; Möhler 2015).

One review author (AR) transferred the original CRDeCI ratings to the updated CRDeCI 2 criteria, which the two original raters (AG, SK) checked. We contacted study authors for additional information and data where necessary.

Assessment of risk of bias in included studies

Assessment of risk of bias followed the guidance in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). Two review authors (SK, AG) independently assessed and scored the risk of bias of studies to identify any potential sources of systematic bias through selection bias, performance bias, attrition bias, and detection bias. For primary studies in which review authors were involved, one review author not involved in the primary study assessed the risk of bias. As recommended in the *Cochrane Handbook for Systematic Reviews of Interventions*, we used a two-part tool, addressing six domains (sequence generation, allocation concealment, blinding, incomplete outcome data, selective outcome reporting, and other issues). The first part described what had been reported in the study. In the second part, we assigned a judgement concerning the related risk of bias for each entry based on the adequacy of the study in relation to the entry. The domains of sequence generation, allocation concealment (avoidance of selection bias), and selective outcome reporting (avoidance of reporting bias) were addressed in the tool by a single entry for each study. Blinding of participants, staff, and outcome assessors (avoidance of performance bias and detection bias) was considered separately for objective outcomes and subjective outcomes. Although initially planned, we did not consider incomplete outcome data (avoidance of attrition bias) separately for different lengths of follow-up (shorter and longer follow-up), as this was present in only one trial (Prunty 2008a). We assessed the certainty of the evidence for the four main outcomes (knowledge, decision making, quality of life, and adverse events) using the GRADE system (Schünemann 2013), employing GRADEpro GDT software (GRADEpro 2015), which we have presented in [Summary of findings for the main comparison](#).

Measures of treatment effect

As we detected clinical heterogeneity (see below), we have presented the study results in a narrative form. We extracted the data as reported in the [Characteristics of included studies](#) table. If meta-analyses become feasible in future updates, we will analyse treatment effects.

Unit of analysis issues

For each study we assessed whether individuals or groups of individuals were randomised together (in clusters) to the same intervention, whether individuals underwent more than one intervention, or whether there were multiple observations for the same outcome.

Dealing with missing data

Numbers and types of missing data related to participant dropout are described in the [Characteristics of included studies](#) table. As we did not perform meta-analysis and had no indication of data not

missing at random, we did not perform imputation of missing data or sensitivity analyses.

Assessment of heterogeneity

We analysed and presented the studies separately. To consider clinical heterogeneity, we analysed all studies in terms of participants, interventions, and outcomes. Due to apparent clinical heterogeneity, we did not perform meta-analyses and did not assess statistical heterogeneity. If data become available in future updates, we will consider both clinical heterogeneity and statistical heterogeneity.

Assessment of reporting biases

In order to minimise the risk of publication bias, we performed comprehensive searches in multiple databases, including searching for unpublished studies. Due to the small number of included trials for each endpoint, we did not analyse trial data using a funnel plot to investigate the likelihood of overt publication bias.

Data synthesis

Due to clinical heterogeneity we did not perform meta-analyses, and have presented the results narratively as we were unable to identify a feasible way to synthesise the included studies. Results are listed according to the study endpoints.

Subgroup analysis and investigation of heterogeneity

Due to insufficient data from the small number of included studies, we were unable to perform subgroup analyses as originally planned.

Sensitivity analysis

Because we presented results narratively, we did not perform sensitivity analyses. If meta-analyses become feasible in future updates, we will categorise and analyse interventions separately.

RESULTS

Description of studies

See [Characteristics of included studies](#), [Characteristics of excluded studies](#), and [Characteristics of studies awaiting classification](#).

Results of the search

The full details of the search results are presented in [Figure 1](#). We included 10 studies in the previous version of the review. The search strategy for this update yielded 657 records ([Table 1](#)), of which 647 were assessed as ineligible after title and abstract screening. We excluded nine further studies after full-text screening (see [Characteristics of excluded studies](#)). One record describing one new study was eligible for inclusion (Rahn 2018). We included a total of 11 studies in this update, described in [Characteristics of included studies](#) (Ennis 2006; Kasper 2008; Köpke 2009; Köpke 2014; Kos 2007; O'Hara 2002; Prunty 2008a; Rahn 2018; Shinto 2008; Solari 2010a; Young 1986). Additional information about all 11 studies was obtained from correspondence with the trialists and incorporated in [Characteristics of included studies](#).

Figure 1. Study flow diagram.

We did not identify any ongoing or unpublished studies.

Included studies

We included 11 randomised controlled trials (RCTs) with a total of 1387 participants in this updated review (Ennis 2006; Kasper 2008; Köpke 2009; Köpke 2014; Kos 2007; O'Hara 2002; Prunty 2008a; Rahn 2018; Shinto 2008; Solari 2010a; Young 1986). We found pronounced clinical heterogeneity with regard to the definitions of interventions and outcomes assessed, therefore we did not evaluate statistical heterogeneity and did not perform meta-analyses. We have thus presented the study results in a narrative format.

Settings and participants

All but three studies, Kasper 2008; Kos 2007; Prunty 2008a, were hospital-based (mostly outpatients). In Prunty 2008a, participants were recruited from members of regional MS societies, in Kos 2007 either through the national MS Society or by treating neurologists, whereas in Kasper 2008 participants were recruited from different locations including primary and hospital care. Four studies were carried out in Germany by the same research group (Kasper 2008; Köpke 2009; Köpke 2014; Rahn 2018), two in the UK (Ennis 2006; O'Hara 2002), two in the USA (Shinto 2008; Young 1986), one

in Australia (Prunty 2008a), one in Belgium (Kos 2007), and one in Italy (Solari 2010a) (see [Characteristics of included studies](#)). Participants' mean age ranged from 31 to 51 years across studies (mean of means 40.0 years (standard deviation (SD) 5.5)). The percentage of women ranged from 63% to 100% (mean of means 74.9% (SD 10.7)), and relapsing-remitting disease courses were most frequent, ranging from 45% to 100% (mean of means 72.2% (SD 21.5)). All but three studies mentioned levels of disability (O'Hara 2002; Prunty 2008a; Young 1986), and were moderate overall. More than 50% of participants had 12 or more years of education; level of education was not reported in two studies (Ennis 2006; Prunty 2008a). All participants had a confirmed MS diagnosis, Ennis 2006; Kasper 2008; Köpke 2009; Köpke 2014; Kos 2007; O'Hara 2002; Prunty 2008a; Rahn 2018; Shinto 2008; Solari 2010a; Young 1986, or a clinically isolated syndrome (Kasper 2008; Köpke 2014; Rahn 2018). Two studies included only people with relapsing-remitting MS (Köpke 2014; Shinto 2008). Most studies excluded patients with severe cognitive impairment. One study did not report any exclusion criteria (Young 1986).

Duration of follow-up

Study follow-up ranged from one month, Prunty 2008a; Young 1986, to two years (Köpke 2009) (see [Figure 2](#)).

Figure 2. Overview of the intervention components.

Figure 2. (Continued)

Description of interventions

All of the included studies provided the information using one or more components (see Figure 2). In four studies, participants took part in an educational programme: in Ennis 2006, the Optimisation of Prognosis and Treatment in Multiple Sclerosis Portal (OPTIMISE) programme aimed to provide knowledge, skills, and confidence to undertake health-promoting activities; in Köpke 2009 and Köpke 2014, participants received a four-hour educational programme and a preparatory booklet on the topics of the intervention: relapse management, Köpke 2009, or diagnosis, prognosis, and early MS therapy (Köpke 2014). In Köpke 2009, participants were also offered a prescription of oral corticosteroids. In Kos 2007, participants took part in four two-hour education sessions during four weeks, each consisting of information provision followed by an interactive component.

In Kasper 2008 and Prunty 2008a, participants received a decision aid. In Kasper 2008, this comprised a "comprehensive evidence-based MS patient information booklet about immunotherapy options and an interactive worksheet"; in Prunty 2008a, the decision aid consisted of an information booklet containing an exercise sheet that aimed to "help women consider their personal values and those of their partners" on family planning ("motherhood choice").

In three studies (O'Hara 2002; Shinto 2008; Young 1986), participants received personal information and a booklet on self care strategies (O'Hara 2002), information on specific aspects related to MS (Shinto 2008), or steroid medication (Young 1986). In Solari 2010a, participants received information specific for the newly diagnosed during a personal interview with a physician using a navigable CD, as well as a take-home booklet.

In one study (Rahn 2018), participants received nurse-based decision coaching and had access to a wiki-based information platform.

Development

Three interventions were based on psychological theories (Ennis 2006; Köpke 2009; Rahn 2018). Ennis 2006 stated that "the group setting provides opportunity for development of self-efficacy, Bandura 1977, through vicarious experiences and verbal persuasion from other people with MS". In Köpke 2009, the programme was based on the protection motivation model, Boer 1996; Rogers 1975, "applied to decisional autonomy" with the curriculum derived from the "practical oriented approach" (Meyer 1983). Rahn 2018 used the theory of planned behaviour, Airlie 2001; Kasper 2012a, as "underlying framework" (Rahn 2015). Four studies, Kasper 2008; Köpke 2014; Prunty 2008a; Solari 2010a, used as their theoretical background international standards (Campbell 2000; Coulter 1999; Elwyn 2006). Three studies were performed prior to trials to assess patients' needs and study feasibility (Heesen

2004; Kasper 2006; Solari 2007). Two studies, Kos 2007; O'Hara 2002, did not mention underlying theories but performed pre-trial studies. O'Hara 2002 reported a "pragmatic approach"; O'Hara 2000, based on previous publications of patients' needs, Robinson 1996, and pre-trial studies, O'Hara 2000. In two studies (Shinto 2008; Young 1986), the intervention was based on clinical practice with no theoretical basis mentioned.

Content and delivery

Content

Different information topics were addressed as part of the interventions (see Table 2), with seven studies including information on MS in general (Kasper 2008; Köpke 2009; Köpke 2014; O'Hara 2002; Prunty 2008a; Rahn 2018; Solari 2010a), nine studies information on drug therapies (Kasper 2008; Köpke 2009; Köpke 2014; Kos 2007; O'Hara 2002; Prunty 2008a; Rahn 2018; Solari 2010a; Young 1986), seven on non-drug therapies (Kasper 2008; Köpke 2009; Köpke 2014; Kos 2007; O'Hara 2002; Shinto 2008; Solari 2010a), and four including information of general interest for people with MS (Ennis 2006; Kos 2007; O'Hara 2002; Shinto 2008).

Delivery

In two studies (Kasper 2008; Prunty 2008a), participants received decision aids by mail. In O'Hara 2002, participants were assigned by a health professional to either group or individual sessions. Sessions were conducted either at participants' homes or in local therapy centres on two occasions during one month, and each session lasted between one and two hours. In Solari 2010a, the interviewing physician was a neurologist or trainee neurologist experienced in MS. Five physicians (one at each centre) were trained during one day in the personal interview and CD navigation. The physician and patient went through the topics of the CD guided by patient preferences. A take-home booklet matching CD contents was given to each participant at the end of the interview. In Young 1986, a physician and nurse gave an oral presentation (no information was available on presentation contents or on providers' training). In Köpke 2009, the participant received a 40-page preparatory information brochure two weeks before the programme, which was a structured four-hour education programme with 10 participants each (plus their partners or close relatives who were also invited). Mostly, two providers held the programme: a nurse and a specially trained patient with MS. In Köpke 2014, 10 participants with their partners or close relatives were invited per session. The programme was led by one "non-medical" person from the study centre and was based on structured presentation materials and moderation cards. Training of the provider was not reported. In Ennis 2006, eight weekly three-hour education sessions in small groups of approximately eight participants per group were held within a hospital. Sessions were delivered by healthcare professionals, as appropriate (occupational therapist, physiotherapist, dietician,

and MS nurse). The number and training of providers was not reported. In [Kos 2007](#), four weekly two-hour education sessions were held by "four different therapists", with no further information provided. In [Shinto 2008](#), besides usual care, participants received eight visits from an MS nurse over a period of six months. None of the studies provided information using Web 2.0 systems (podcasts, social networks, or smartphones). In [Rahn 2018](#), the intervention consisted of up to three coaching sessions and access to an online information platform.

Control groups

Three studies included control interventions that were similar in size to the active intervention ([Kasper 2008](#); [Köpke 2014](#); [Kos 2007](#)), and five provided some information ([Köpke 2009](#); [O'Hara 2002](#); [Prunty 2008a](#); [Rahn 2018](#); [Young 1986](#)). In the remaining studies ([Ennis 2006](#); [Shinto 2008](#); [Solari 2010a](#)), no intervention was offered to the control group (usual care). Characteristics of usual care were not reported in any of these studies.

Methods of data collection

In all of the included studies most primary and secondary outcomes were assessed using self reported measures (questionnaires or

scales), some of which had been validated in the target language and population.

Excluded studies

We excluded 29 studies as they did not meet the inclusion criteria relating to main outcomes, participants, or the type of intervention (see [Characteristics of excluded studies](#)), of which nine were added with this update.

Risk of bias in included studies

We contacted the first or senior authors of all but one study, [Kos 2007](#), asking them to provide further information on methodological details not reported in the publications. All authors responded to our requests, and all but one author was able to provide further information. Overall, two studies were of high methodological certainty ([Kasper 2008](#); [Köpke 2014](#)). The remaining studies all had at least some risk of bias ([Characteristics of included studies](#); [Figure 3](#); [Figure 4](#)).

Figure 3. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

Figure 4. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Ennis 2006	+	-	-	+	+	?	?
Kasper 2008	+	+	+	+	+	+	+
Köpke 2009	+	+	-	-	+	?	?
Köpke 2014	+	+	+	+	+	+	?
Kos 2007	+	?	-	+	-	?	?
O'Hara 2002	+	+	-	+	+	?	?
Prunty 2008a	+	+	-	+	-	?	?
Rahn 2018	+	?	?	?	-	+	?
Shinto 2008	+	+	-	+	+	?	?
Solari 2010a	+	+	-	+	+	+	?
Young 1986	+	?	-	+	?	?	?

Allocation

Sequence generation was adequate in all studies. Allocation concealment was adequate in seven studies (Kasper 2008; Köpke 2009; Köpke 2014; O'Hara 2002; Prunty 2008a; Shinto 2008; Solari 2010a), inadequate in Ennis 2006, and unclear in Kos 2007, Rahn 2018, and Young 1986.

Blinding

Two studies performed blinding of participants (Kasper 2008; Köpke 2014). Regarding blinding of assessors, we considered as adequate those studies in which outcomes were patient-reported, that is by a questionnaire or (telephone) interview; we considered seven studies as adequate (Ennis 2006; Kasper 2008; Köpke 2014; Kos 2007; O'Hara 2002; Prunty 2008a; Shinto 2008; Solari 2010a).

Incomplete outcome data

Attrition bias was present in three studies with more than 20% of dropouts at follow-up (Kos 2007; Prunty 2008a; Rahn 2018).

Selective reporting

Four studies had adequate reporting (Kasper 2008; Köpke 2014; Rahn 2018; Solari 2010a). Reported data from Köpke 2009 differed to some extent from the data in the trial registration. No protocol was available for the remaining studies (Ennis 2006; Kos 2007; O'Hara 2002; Prunty 2008a; Shinto 2008; Young 1986).

Other potential sources of bias

In seven studies (Ennis 2006; Köpke 2009; Kos 2007; Shinto 2008; Solari 2010a; Rahn 2018; Young 1986), there was a potential contamination between groups.

Effects of interventions

See: [Summary of findings for the main comparison](#) Information provision compared to (optimised) standard care for people with multiple sclerosis

See [Summary of findings for the main comparison](#).

Primary outcome measures

Knowledge

Five studies assessed the first prespecified primary endpoint using different instruments (Table 3) (Köpke 2014; Prunty 2008a; Rahn 2018; Solari 2010a; Young 1986). All reported significant differences between groups in favour of the intervention group (IG) (505 participants; moderate-certainty evidence). In Köpke 2014, there was a significant difference between groups two weeks after the intervention. Scores for "good knowledge", defined as more than 11 questions of a possible 19 answered correctly, were reported for 57/88 (64.8%) participants in the IG and 23/90 (25.6%) in the control group (CG) ($P < 0.001$). Mean knowledge was 12.3 ± 2.5 in the IG and 10.2 ± 2.3 in the CG ($P < 0.001$). In Prunty 2008a, there was a significant difference between groups for mean knowledge after the intervention (6.3 ± 2.2 in the IG versus 4.6 ± 1.9 in the CG of 10 possible points; mean difference 1.7; $P = 0.01$). In Solari 2010a, there was a significant difference between groups at one month. Scores within the highest tertile were reported for 36/60 (60%) participants in the IG and 15/60 (25%) in the CG (odds ratio 4.5, 95% confidence interval (CI) 2.1 to 9.8; $P < 0.001$). In Rahn 2018, both groups improved over time: in the IG from 8.3 (standard deviation (SD) 3.4) to 10.2 (3.2) after 3 months and 10.1 (4.1) after 6 months, and in the CG from 8.1 (SD 3.1) to 9.1 (3.8) after 3 months and 10.3 (3.4) after 6 months. In Young 1986, a significant difference was reported for knowledge about steroid therapy after the intervention (14.5 ± 2.5 versus 10.9 ± 2.6 of 17 possible points; mean difference 3.6; $P < 0.015$).

Decision making

Five studies assessed our second prespecified primary endpoint using different measures and instruments (793 participants; low-certainty evidence) (Table 3) (Kasper 2008; Köpke 2009; Köpke 2014; Prunty 2008a; Rahn 2018). In Kasper 2008, no changes were found between groups for "realised role preferences", assessed as congruency of role preferences at baseline compared to the decision roles used within the consultations, assessed with the Control Preference Scale (CPS). No differences between groups were found, with approximately 50% of participants in both groups showing congruency between preferred and expressed roles. In both groups participants reported that they were significantly more decided after the intervention with no differences between groups ($P = 0.42$, no numbers reported). In Köpke 2009, more participants in the IG reported an active role in decision making after the intervention: IG 93 (69%), CG 74 (42%); difference 27% (95% CI 16% to 37%; $P < 0.001$), assessed as a secondary outcome measure. In Köpke 2014, decisional conflict did not differ between groups or within groups for the two measurement points (before the intervention and after 12 months) for all subscales. Overall, more than two-thirds of the participants preferred more active than collaborative roles without significant differences between groups and between time points. Overall, 70 (IG) and 72 (CG) decisions on DMDs were reported during the 12 months of follow-up. In both groups most decisions were reported to be solely or mostly

driven by the participant or were shared between participants and physicians, with no differences between groups. In Prunty 2008a, there were no significant differences between groups for decisional conflict, decision self efficacy, and decision certainty at follow-up. However, mean changes between baseline and follow-up differed significantly between groups for all three measures: decisional conflict ($P = 0.001$), decision self efficacy ($P = 0.002$), and decision certainty ($P = 0.047$). Rahn 2018 assessed the CPS and the Decisional Conflict Scale (DCS) as secondary outcomes and detected no differences between groups.

Secondary outcome measures

Quality of life

Six studies reported results on quality of life, three using the 36-item Short Form Health Survey (SF-36) (Ennis 2006; O'Hara 2002; Shinto 2008), and three using the Hamburg Quality of Life Questionnaire in Multiple Sclerosis (HAQUAMS) (671 participants; low-certainty evidence) (Köpke 2009; Köpke 2014; Rahn 2018). In Shinto 2008, the SF-36 was the primary endpoint, whereas in Ennis 2006 and O'Hara 2002 it was assessed as a secondary endpoint. In Köpke 2009 and Köpke 2014, the HAQUAMS questionnaire was used to control for adverse events of the intervention. In Ennis 2006, significant differences between groups were reported for changes from baseline to eight weeks after the programme for the SF-36 subscales for physical health (IG $+8.1 \pm 14.8$ versus CG $+2.8 \pm 19.3$; $P = 0.03$), mental health (IG $+5.7 \pm 22.9$ versus CG -8.6 ± 13.0 ; $P < 0.01$), and general health (IG $+10.1$ (SD not reported) versus CG -1.2 ± 18.0 ; $P < 0.01$). No significant changes were observed for the other five subscales of the SF-36. In O'Hara 2002, significant changes between baseline and six months follow-up were reported for two subscales of the SF-36: mental health (IG $+3.7$, 95% CI 0.4 to 7.0 versus CG -1.2 , 95% CI -4.3 to 1.9; $P = 0.04$) and vitality (IG $+1.5$, 95% CI -2.7 to 5.7 versus CG -4.21 , 95% CI -7.92 to -0.51), with no significant differences for the other subscales. In Shinto 2008, there were no significant differences between the IG (education group) and the CG for mean changes between baseline and follow-up in all scales of the SF-36. In Köpke 2009, a slight improvement in both groups was reported for the HAQUAMS total score, with no significant difference between groups for changes in quality of life between baseline and two years of follow-up. Also, in Köpke 2014 and in Rahn 2018 there were no differences in changes in quality of life between groups.

Informed choice

Only Köpke 2014 and Rahn 2018 assessed informed choice, using the Multidimensional Measure of Informed Choice (MMIC) (Marteau 2001). Both studies indicated differences between groups in favour of the intervention group. Köpke 2014 showed significant differences between groups with 50 of 85 (58.8%) participants in the IG compared to 18 of 89 (20.2%) in the CG showing informed choice (difference 38.6%, 95% CI 24.1% to 53.1%; odds ratio 0.18, 95% CI 0.09 to 0.35; $P < 0.001$). In Rahn 2018, 15 of 31 (48%) participants in the IG compared to 6 of 20 (30%) participants in the CG achieved informed choice. As this was a pilot study, no statistical tests were performed.

Anxiety and depressive symptoms

Seven studies assessed anxiety or depressive symptoms using different instruments, none of them as a primary endpoint (Köpke 2014; Kos 2007; Prunty 2008a; Rahn 2018; Shinto 2008; Solari 2010a). In Köpke 2014, using the Hospital Anxiety and Depression

Scale (HADS) as a measure of adverse events, subscale mean scores for anxiety and depression were low with no significant differences found between groups and between time points. [Kos 2007](#) reported "no significant changes [...] in both groups" for the Mental Health Inventory (MHI) without providing data ([Ritvo 1997](#)). In [Prunty 2008a](#), there were no differences between groups after the intervention for anxiety (State-Trait Anxiety Inventory (STAI)) or depression (Center for Epidemiologic Studies Depression scale (CESD)) ([Radloff 1977](#)). [Rahn 2018](#) reported no differences in HADS scores between groups at follow-up. In [Shinto 2008](#), no significant difference was reported between groups for the Beck Depression Inventory (BDI) ($P = 0.76$). In [Solari 2010a](#), anxiety and depression, measured using the HADS, were comparable in both groups at baseline and follow-up.

Treatment choices and adherence

Six studies reported treatment choices ([Kasper 2008](#); [Köpke 2009](#); [Köpke 2014](#); [Rahn 2018](#); [Solari 2010a](#)). In [Kasper 2008](#), there were no significant differences between the IG and the CG for participants starting, changing, or stopping DMDs during follow-up for groups of participants with and without a DMD at baseline. In [Köpke 2009](#), relapse therapies, assessed as a primary endpoint, differed significantly between groups. In the IG, relapse therapies were less invasive, with 78% of relapses treated with oral corticosteroids or without corticosteroids compared to 56% in the CG (difference 22%, 95% CI 11% to 31%). In [Köpke 2014](#) and [Rahn 2018](#), there were no significant differences for participants with a DMD. [Kos 2007](#) reported "no significant changes in medication use occurred during the study", without providing data. In [Solari 2010a](#), there were no differences between groups for participants who continued (CG 86.5% versus IG 88.9%), switched (CG 5% versus IG 2.8%), or stopped DMD (CG 8% versus IG 8%). [Young 1986](#) assessed treatment adherence (termed "compliance") by asking participants about "how each patient was taking the medication", finding that all participants in both groups reported taking the medication correctly.

Other outcome measures

Satisfaction

Four studies assessed satisfaction with the information and the decisional process ([Kasper 2008](#); [Köpke 2009](#); [Köpke 2014](#); [Rahn 2018](#)). All studies reported no difference between groups after the intervention for this outcome.

Resource use

Only three studies reported resource use, hospital admissions, and use of healthcare service. In [Köpke 2009](#), the median numbers of visits to physicians and mean numbers of telephone calls to physicians significantly differed between groups, with fewer calls and visits reported for the IG. In [Köpke 2014](#) and [Solari 2010a](#), the groups did not differ with regard to physician contacts, hospital admissions, and other resource use. Furthermore, [Köpke 2009](#) and [Köpke 2014](#) reported that a detailed economic evaluation was to be published separately, with no publication available at present.

Activities of daily living

Only [O'Hara 2002](#) reported measures of ADL, assessed by the Barthel Index, finding no significant differences between groups for changes from baseline to follow-up, although in the CG a significant

(within-group) deterioration was found, whereas in the IG ADL levels remained stable.

Coping

[Kos 2007](#) assessed self efficacy using the Multiple Sclerosis Self-Efficacy Scale (MSSE), finding "no significant changes [...] in both groups", but without providing data. [Rahn 2018](#) used the "coping self-efficacy" scale ([Chesney 2006](#)), reporting no differences between groups.

Disability

See [Characteristics of included studies](#) for levels of disability at baseline. In [Köpke 2009](#) and [Köpke 2014](#), disability (assessed with the United Kingdom Neurological Disability Scale (UNDS)) was used as a safety measure. The studies reported no difference between groups at any time point ([Heesen 2007b](#)).

Role preferences

In [Kasper 2008](#), [Köpke 2014](#), [Rahn 2018](#), and [Solari 2010a](#), no differences were reported between groups at baseline and postintervention for role preferences, using the CPS.

Adverse events

Seven studies (751 participants) assessed adverse events. In [Ennis 2006](#), [Prunty 2008a](#), [Rahn 2018](#), and [Shinto 2008](#), no adverse events were detected. [Köpke 2009](#) and [Köpke 2014](#) found no differences in changes in health-related quality of life or disability status between groups, suggesting that the programmes had no negative side effects. In [Solari 2010a](#), no serious adverse events (admission to psychiatric ward, suicide attempt, or death) were recorded by the Independent Data and Safety Monitoring Committee.

Process-related results

Reporting (CREDECI 2)

Findings for the reporting of process-related results using the CREDECI 2 checklist are described in [Table 4](#) ([Möhler 2015](#)). In summary, almost all studies provided information about the development stage of the interventions. [Shinto 2008](#) reported only one of the six possible items included in this domain (item 2: Description of all components of the intervention). Only five studies reported information on the feasibility and piloting stage ([Kasper 2008](#); [Köpke 2014](#); [Kos 2007](#); [Prunty 2008a](#); [Rahn 2018](#)). For the evaluation stage, only three studies reported information on at least half of the items ([Kasper 2008](#); [Rahn 2018](#); [Solari 2010a](#)). Overall, most studies reported insufficient information on processes.

Consumer involvement

In seven studies consumers were involved in the development and provision of the intervention. [Kasper 2008](#), [Köpke 2009](#), and [Köpke 2014](#) referred to the same two pre-studies that investigated patients' needs and provided feasibility testing of intervention components ([Heesen 2004](#); [Kasper 2006](#)). In [Köpke 2009](#), people with MS were involved in the development of the programme and also as educators, providing the educational programme together with a health professional. In [Kasper 2008](#), people with MS were involved in the development of the information brochure. In [O'Hara 2002](#), consumers were involved in a pre-study and in the development of the educational booklet ([O'Hara 2000](#); [Robinson](#)

1996). Prunty 2008a involved consumers in a pre-study (Prunty 2008b); also, the decision aid was piloted in 20 women with MS who commented on its readability, balance, and usefulness and gave feedback on its content. Rahn 2018 reported involvement of consumers in the development and feasibility testing of the information platform. In Solari 2010a, people with MS (and health professionals) were involved in qualitative studies conducted before the trial to inform intervention contents (Solari 2007). In addition, the experiences of patients and health professionals were assessed at the end of the trial to identify "active" components and trial challenges (Borreani 2014).

Perception of the intervention

Four studies assessed how patients or health professionals, or both, perceived the intervention (Köpke 2014; Prunty 2008a; Solari 2010a; Young 1986). Using their own instruments, Kasper 2008 found that IG participants rated the information as significantly more helpful for decision making than CG participants, who received standard information ($P < 0.001$). Intervention group participants also reported that they felt better informed ($P < 0.001$), got important questions more adequately answered ($P < 0.01$), and were better supported in finding their preferred role ($P < 0.05$) compared to CG participants. In Köpke 2014, two in-depth interviews and two focus group meetings were conducted with participants from both groups at one study centre 15 to 18 months after the intervention. It emerged from the interviews that both IG and CG participants were satisfied with the intervention, but they were only able to recall parts of the intervention content and the main goal. Participants from both groups described the group situation as particularly helpful to discuss the programme's content and to learn about other participants' experiences. The relevance of dealing with uncertainty and the of the programme to support decision making were particularly emphasised by the IG participants. In Prunty 2008a, 20 people with MS and 15 neurologists who were involved in the piloting of the decision aid provided generally positive feedback (Prunty 2008b). Solari 2010a performed a qualitative study after the trial to assess the experiences of trial participants (Borreani 2014), using semi-structured interviews with participants and focus group meetings with physicians who delivered the intervention. Experiences with the intervention of people with MS were positive, as they felt that it enhanced their understanding of their disease. Physicians were also positive in their overall evaluation but noted initial difficulties in using the information CD. All participants considered the combination of personal interview, CD navigation, and take-home booklet essential, but urged a more flexible scheduling of the personal interview. In a subsequent prospective, open-label, non-randomised controlled trial study (Giordano 2014), the aims were to assess the effectiveness of the intervention in clinical practice and to compare the whole information aid (personal interview with navigation through the website plus take-home materials) with the take-home booklet and website component alone. The results (21 centres, 159 enrolled participants) showed that the entire information aid was not superior to the booklet and website alone, and that both were comparable in efficacy to the IG of the previous RCT (Solari 2010a). In Rahn 2018, acceptance of the intervention was assessed as part of the process evaluation using qualitative and quantitative methods, showing high acceptance rates of both the information platform and the decision coaching, which was assessed as most helpful for decision making.

DISCUSSION

In this review update we summarised 11 RCTs investigating the effectiveness of information provision for people with MS aimed at enhancing informed choice. As in the previous review, we detected marked clinical heterogeneity between the included studies and were therefore unable to perform meta-analyses. Although originally planned in the study protocol, we also refrained from categorising interventions.

Summary of main results

We included one new study in this updated review, bringing the total to 11 trials involving 1387 participants with MS. The interventions differed in many aspects. Although all of the interventions included information provision as at least one of the main intervention components, the interventions' main goals differed between studies. Whereas most trials were aimed at increasing knowledge, informed choice, or decision making, others were concerned with increasing treatment adherence, Young 1986, or uptake of a certain behaviour (Ennis 2006; Kos 2007; O'Hara 2002). The control interventions also differed between studies, ranging from 'usual care' to control interventions comparable in size to the active intervention. In one trial assessing the effectiveness of a naturopathic intervention (Shinto 2008), information was only provided as a "time and attention" control group. All of the interventions were complex interventions, but the number and extent of the intervention components differed markedly between studies (Figure 2). Furthermore, endpoints were inconsistent between trials (Table 3), with only five trials assessing the predefined primary endpoints of knowledge, decision making, or both. Four of five studies reporting knowledge detected significant differences between groups as a result of the intervention (Köpke 2014; Prunty 2008a; Solari 2010a; Young 1986), whereas the descriptive analysis in Rahn 2018 indicated only small differences in favour of the IG, which was not present at six months follow-up. Although these results indicate that information may successfully increase participants' knowledge, it is not possible to judge the overall magnitude of the effect as different instruments were used and knowledge was mostly assessed in the short term only. Also, the relevance of the knowledge gained could not be quantified. For the five trials assessing decision making (Kasper 2008; Köpke 2009; Köpke 2014; Prunty 2008a; Rahn 2018), the picture was even less clear, as only Köpke 2009 found significant differences between groups for active roles in decision making, whereas the other studies found no significant differences for "expressed role preferences" (Kasper 2008), decision self efficacy and decision certainty (Prunty 2008a), or decisional conflict (Köpke 2009; Prunty 2008a; Rahn 2018). As different instruments were used at different time points, interpretation was difficult, and based on these results we were unable to determine a general impact on the quality of decision making. There was no consistent effect concerning quality of life, which was assessed in six studies (Ennis 2006; Köpke 2009; Köpke 2014; O'Hara 2002; Rahn 2018; Shinto 2008). Of these studies, only one assessed this outcome as a primary outcome measure (Shinto 2008), whereas in two studies it was used as one of various outcome measures (Ennis 2006; O'Hara 2002), with all trials using the SF-36. Three trials used the HAQUAMS as a safety measure (Köpke 2009; Köpke 2014; Rahn 2018). Three trials showed no differences between groups at follow-up, but O'Hara 2002 and Ennis 2006 showed significant differences in favour of the intervention for different subscales of the SF-36, again

providing inconclusive results. The same applies for all of the other outcomes. The results must therefore be interpreted carefully, as there were few studies reporting on each outcome category, and most of the outcomes were assessed as secondary endpoints. For most outcomes, including satisfaction and ADL, no differences were detected. Two further results should be noted. First, Köpke 2014 found a highly significant effect on "informed choice" as a primary outcome, although this result was based mainly on the marked between-group difference concerning disease-related knowledge, which was also shown in Rahn 2018. Second, the primary endpoint in Köpke 2009 addressing the application mode of corticoid relapse therapies showed a significant difference towards less invasive therapy choices, which could be interpreted as 'hard' indicator for increased patient choice as a result of information provision, which is lacking in all other trials. Due to the lack of sufficient data, we could not make assumptions about cost comparisons or cost-effectiveness. The in-depth analysis of the complex interventions used (Table 4) revealed generally poor and inconsistent reporting of relevant criteria to permit intervention comparison, although the newly included study, Rahn 2018, was comparatively well reported with regard to these issues. As most interventions that aim to provide information to patients will mostly be complex interventions, the syntheses will always present important methodological challenges, which should be acknowledged by authors of the primary studies and systematic reviews.

Overall completeness and applicability of evidence

Taking into account the needs of people with MS for adequate patient information and the multitude of available information programmes and materials, the number of studies included in this review was small, and we added only one small pilot study for this update. As noted above, we found marked variation between studies concerning the content and delivery format of the interventions, which might be seen as an indicator for the diversity of programmes currently offered to people with MS. We were unable to retrieve sufficient data to make meaningful statements about the primary and key secondary endpoints, as less than half of the studies addressed these endpoints, and those that did used different instruments. The generalisability and applicability of the results to different countries and healthcare systems seems limited, as the studies were conducted in only six different countries, predominantly in Europe. Although there is obviously a need for rigorously developed and conducted studies on patient information in MS, there is currently no ongoing RCT evaluating any patient information intervention in MS. Moreover, there is clearly a lack of interventions addressing people with progressive MS, as most studies have solely or mainly addressed people with relapsing MS.

Quality of the evidence

The methodological quality of the studies varied, with only two studies having an overall low risk of bias (Kasper 2008; Köpke 2014). All trials used adequate sequence generation for randomisation. Concerning allocation concealment, risk of bias was unclear in three studies, Kos 2007; Rahn 2018; Young 1986, and inadequate in one study (Ennis 2006). As could be expected from interventions based on (group) provision of patient information, blinding of participants and staff was not achieved in most studies, with only Kasper 2008 and Köpke 2014 succeeding in blinding participants by the use of comparable control interventions. However, all but

one study, Köpke 2009, applied blinded outcome assessment. We detected no important attrition rates in all but three studies (Kos 2007; Prunty 2008a; Rahn 2018). We were unable to assess the possibility of selective outcome reporting in six trials due to missing pre-published study protocols or study registrations (Ennis 2006; Kos 2007; O'Hara 2002; Prunty 2008a; Shinto 2008; Young 1986). Of the remaining five studies, only Köpke 2009 had an unclear risk of bias in this domain due to missing results for three pre-planned outcome measures. Apart from Kasper 2008, we could not rule out risk of contamination between groups for all other studies.

Validity of outcome measures

Apart from the problem of different outcome measures for primary and key secondary endpoints, validity of the measures was not always reported or had not been assessed, especially for knowledge and decision-making measures. There were almost as many instruments assessing knowledge as there were studies. Only Solari 2010a and Rahn 2018 used a formally validated instrument, the Multiple Sclerosis Knowledge Questionnaire (MSKQ) (Giordano 2010), validated in Italian MS patients, and the Risk Knowledge in Relapsing Multiple Sclerosis (RIKNO) questionnaire (Heesen 2015), validated in German MS patients, respectively. Validity was most consistently present for measures of quality of life. In Ennis 2006, O'Hara 2002, and Shinto 2008, the quality of life instrument used was the well-established SF-36, whereas Köpke 2009, Köpke 2014, and Rahn 2018 used the HAQUAMS, which has been validated in German MS patients (Gold 2001).

Potential biases in the review process

Due to our comprehensive search strategy, we are confident that publication bias is unlikely. Two review authors independently performed selection of studies and data extraction, and analyses were undertaken and differences were resolved by consensus or by consulting a third person when necessary. A major point of concern could be that five of the 11 studies were from our own groups. To minimise bias, all results from these studies were checked by a third review author who was not involved in the primary study. We therefore believe that bias within the review process has been avoided.

Agreements and disagreements with other studies or reviews

So far, there is no other systematic review of controlled studies assessing the effectiveness of information provision in people with MS. The suggested positive effect on knowledge has been shown before for other diseases, for example stroke (Forster 2012), diabetic kidney disease (Li 2011), and rheumatoid arthritis (Riemsma 2003). A recent Cochrane Review on information provision for stroke patients found that effects on some psychological outcomes as well as on quality of life were more likely if the information was provided actively as opposed to passive information provision, that is if the intervention did not include a "subsequent systematic follow-up or reinforcement procedure" (Forster 2012). In our review, due to the narrative synthesis of results, we refrained from such a subgroup analysis, with only two studies likely using 'passive' approaches (Kasper 2008; Young 1986). There are three recently published reviews with some overlap with our study, all targeting people with MS. Demaille-Wlodyka 2011 performed a non-systematic review on MS treatment education including 11 studies. Plow 2011 summarised

27 interventions reported in 34 papers in a scoping review on self management interventions. [Reen 2017b](#) performed a systematic review of interventions to improve understanding of DMD risks and benefits that included 15 studies. These three reviews found that the interventions were diverse and often poorly described, and the study quality was rated as poor in most instances, particularly as the reviews were liberal in their inclusion criteria regarding study design. As a result, in no instance was quantitative synthesis of findings possible, even in the two reviews focusing on MS DMDs ([Plow 2011](#); [Reen 2017b](#)). Although our review used stricter and more focused inclusion criteria, we were not able to perform a quantitative synthesis due to the marked heterogeneity of the included interventions, with as many intervention approaches as there were studies. We therefore, as already concluded by [Plow 2011](#), emphasise the need for a standardised description of studies to be able to compare and delineate intervention approaches. We have used the CREDECI 2 checklist ([Möhler 2015](#)), which showed poor reporting for most of the elements ([Table 4](#)). Finally, it is worth mentioning that patients frequently overestimate DMD benefits in spite of intervention exposure ([Reen 2017b](#)).

AUTHORS' CONCLUSIONS

Implications for practice

Our results provide some evidence that information provision for people with multiple sclerosis can increase disease-related knowledge and may have a positive impact on decision making and quality of life. The studies included in this review reported no negative side effects from informing patients. Effects on health behaviour, resource use, and quality of care were rarely addressed as endpoints, and a clear effect on these outcomes was only demonstrated in [Köpke 2009](#), who found a marked decrease in the number and invasiveness of steroid therapies as a result of the intervention. Still, due to the marked heterogeneity of the interventions and outcome measures, it is not possible to make clear recommendations for specific methods of information provision. Information provision is an ethical requirement to enable patients to make informed decisions.

Implications for research

As our review leaves most questions unanswered, there are important implications for research. The development and evaluation of future interventions should be based on recent methodological requirements, for example those provided by the Medical Research Council (MRC) framework ([Craig 2008](#); [Moore 2015](#)). This includes rigorous planning and pre-studying of the intervention, which should also be clearly theory-based. There should be a pre-planned and transparently reported evaluation of the process to allow for better understanding and replication of interventions. Furthermore, outcomes should be clearly linked to the aim of the interventions with surrogate outcomes and including knowledge as well as outcomes that are important to patients, such as improved decision making and adequate disease-related measures, for example relapse rates, disability, or disease progression. Outcome measures should be assessed using instruments with proven validity for the actual study population. In view of our results, this seems especially important for the assessment of disease-related knowledge. There should be more discussion about what would be the most relevant and feasible outcome measures for patient-important outcomes. Information should be understandable to those with low education and those with symptoms that can impair decision-making capacity, as these patients may experience more difficulty in accessing and interpreting available information. In the presence of severe cognitive compromise, provision of information to people with multiple sclerosis and their surrogate decision makers is a further challenge and ethical priority.

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CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

Ennis 2006

Methods	<p>Randomised controlled trial</p> <p>Study period: "Over a period of two years", dates not reported</p>
Participants	<p>Country: UK</p> <p>Location: MS clinic at a regional "neuroscience centre"</p> <p>Number of participants: 64</p> <p>Age, mean (SD), years: 45 (9) in IG, 46 (8) in CG</p> <p>Female: 63% in both groups</p> <p>Level of disability: EDSS 0 to 3: 22% in IG, 23% in CG; EDSS 3.5 to 6: 69% in IG, 74% in CG; EDSS 6.5 to 7: 9% in IG, 3% in CG</p> <p>Education: not reported</p> <p>Inclusion criteria: confirmed diagnosis of MS (Poser criteria (Poser 1983)) with at least 6 months disease duration; EDSS 1.0 to 7.0; age 18 to 65; "Desire for health promotion education"</p> <p>Exclusion criteria: "Clinically significant cognitive deficit"</p>
Interventions	<p>Intervention group</p> <p>"OPTIMISE programme" aiming to provide knowledge, skills, and confidence to undertake health-promoting activities</p> <p><u>Structure</u>: 8 weekly 3-hour education sessions in small groups of approximately 8 participants per group held within the hospital</p> <p><u>Content</u>: education addressed "participants' individual needs" in supporting informed decision making regarding health-promoting activities including 5 subjects based on published work (Marge 1988; Pender 1987).</p> <ol style="list-style-type: none"> Exercise and physical activity Lifestyle adjustment/fatigue management Stress management Nutritional awareness Responsible health practices <p>Each participant was provided with a theory session ("outlining the rationale for undertaking the health promotion activity and the interaction between the activity and living with multiple sclerosis") and its "practical implications to consider" together with "practical sessions" to increase self efficacy (Bandura 1977).</p> <p>The 8 sessions were: 1. introductory session; 2.-6. the five subjects; 7. exercise and physical activity; 8. a final session "which summarises the course for spouses/family members/ friends and focuses on planning longer term goals".</p>

Ennis 2006 (Continued)

The sessions were delivered by "relevant health care professionals (occupational therapist, physiotherapist, dietician and multiple sclerosis nurse specialist)" supplemented with written material.

Co-intervention: All participants in the intervention group received a "general health check" at the beginning of the study with physical examination and routine blood tests followed by "discussion regarding the use of screening services and a review of family and social history" with 19 (59%) receiving subsequent "medical interventions".

Control group

Usual care (no description given)

Outcomes	<p>Primary outcome</p> <ol style="list-style-type: none"> 1. Health Promoting Lifestyle Profile II (HPLP) (Walker 1987), administered at baseline and postintervention (2 months afterwards) <p>Secondary outcomes</p> <ol style="list-style-type: none"> 1. Self-Rated Abilities for Health Practices Scale (SRAHP) (Becker 1993), administered at baseline and postintervention (2 months afterwards) 2. SF-36 administered at baseline and postintervention (2 months afterwards) <p>Adverse events</p> <ol style="list-style-type: none"> 1. Reported ("No adverse incidents were recorded for the duration of the study"), but assessment method unclear
Notes	Number and training of providers was not reported.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"The procedure involved placing 40 small pieces of paper with the letter A printed on them and 40 pieces with the letter B into a large envelope. Following a thorough shake of the envelope, and under the observation of an independent colleague, pieces were picked out individually and the sequence recorded."
Allocation concealment (selection bias)	High risk	Randomisation list known to receptionist who performed randomisation.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and personnel were not blinded to group allocation.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	"At the point of data entry the researcher was blinded to a subject's group"
Incomplete outcome data (attrition bias) All outcomes	Low risk	3 dropouts in the intervention group (8.8%), none in the control group
Selective reporting (reporting bias)	Unclear risk	No protocol found.
Other bias	Unclear risk	Possible contamination between groups

Kasper 2008

Methods	<p>Randomised controlled trial</p> <p>Study period: October 2004 to February 2006</p>
Participants	<p>Country: Germany</p> <p>Location: Multiple locations including primary and hospital care</p> <p>Number of participants: 297</p> <p>Age, mean (SD), years: 43 (12) in IG; 43 (10) in CG</p> <p>Female: 69% in IG; 78% in CG</p> <p>Level of disability: Mean UNDS score (SD): 10 (7.0) in IG, 9.2 (5.8) in CG</p> <p>Education: > 11 years: 53% in IG; 52% in CG</p> <p>Inclusion criteria: confirmed diagnosis of MS (self reported) or clinical isolated syndrome (self reported) (information provided by authors on request), considering a decision on immunotherapy, age ≥ 18</p> <p>Exclusion criteria: "Patients with cognitive impairment having problems in following a telephone conversation"; "patients who had already participated in studies on informed decision making"</p>
Interventions	<p>Intervention group</p> <p>Provision of "comprehensive evidence-based MS patient information booklet about immunotherapy options and an interactive worksheet". Not stated how the booklet was provided. On request, authors reported that it was sent by postal mail.</p> <p><u>Basis:</u></p> <ol style="list-style-type: none"> 1. "International standards for the development of evidence-based decision support tools" (Coulter 1999; Elwyn 2006) 2. "Preliminary studies investigating patients' needs and the feasibility of the methods" (Heesen 2004; Kasper 2006) 3. UK Medical Research Council framework for development and evaluation of complex interventions (Campbell 2000) <p><u>Content of the booklet:</u></p> <ol style="list-style-type: none"> 1. Basics on risk communication and MS 2. Discussion of benefits and adverse effects of "all available immunotherapy options giving numerical data if possible" using "pictograms of 100 human stick figures" 3. Information structured for disease courses on 3 difficulty levels 4. Additional worksheet providing decision criteria "for each aspect of the decision" with the possibility to "allocate weights to the different criteria out of a given limited amount" <p>Control group</p> <p>Standard information material on immunotherapy as supplied by the German MS self help organisation Deutschen Multiple Sklerose Gesellschaft (DMSG), comparable in size to the information booklet (80 pages), without a worksheet. On request, authors reported provision of CG material also by postal mail.</p>
Outcomes	<p>Primary outcome</p> <ol style="list-style-type: none"> 1. "Achievement of role preferences" defined as consistency between role preference at baseline and reported role after the consultation with physician. Assessment via telephone interviews using the CPS (Degner 1997)

Kasper 2008 (Continued)

Secondary outcomes

1. Treatment choice, i.e. immunotherapy 6 months after randomisation (self reported during telephone interview)
2. Measures of the decision process
 - a. Participants' attitude towards immunotherapy assessed at baseline, after the intervention, and after the decision encounter using a 10-point Likert scale ranging from -5 (in no case immunotherapy) to +5 (in any case immunotherapy)
 - b. Stage of progress in the decision assessed at baseline, after the intervention, and after the decision encounter using a scale ranging from 0% ("I am still completely undecided") to 100% ("I have made my decision")
3. Participants' evaluation of interventions and decision making assessed using 5-point Likert scales

Adverse events

1. Not assessed

Notes

1. We contacted the authors about inclusion criteria, who replied that there had been a reporting error as not only people with a "a confirmed diagnosis of MS" were included (as stated in the inclusion criteria), but also people with a clinical isolated syndrome.
2. Adverse events discussed: "Previous findings indicate that MS patients are capable of coping with the uncertainty of scientific evidence without becoming emotionally distressed or experiencing therapeutic nihilism."

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Randomisation was carried out [...] using computer generated random numbers."
Allocation concealment (selection bias)	Low risk	"Randomisation was carried out by concealed allocation...". No further information Author information on request: External person had randomisation list and send out pre-packed envelopes with information material to IG and CG participants.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	"Participants [...] were not told whether the information they received was standard information or the newly developed DA."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	"To preserve blinding assessors explicitly asked patients not to refer to details of the information material."
Incomplete outcome data (attrition bias) All outcomes	Low risk	14 (9.4%) dropouts in the intervention group, 5 (3.4%) in the control group
Selective reporting (reporting bias)	Low risk	Additional endpoints as stated in the study registration not reported in the publication (e.g. control beliefs).
Other bias	Low risk	

Kos 2007

Methods	<p>Randomised controlled trial</p> <p>Study period: not reported</p>
Participants	<p>Country: Belgium</p> <p>Location: community-based participants recruited "by flyers and personal invitation through the Belgian National MS Society and on referral by the treating neurologist"</p> <p>Number of participants: 51</p> <p>Age, mean (SD), years: 43 (9) in IG; 45 (10) in CG</p> <p>Female: 71% in IG; 65% in CG</p> <p>Level of disability: mean (SD) Multiple Sclerosis Functional Composite (MSFC) score: 0.13 (0.6) in IG; -0.16 (0.7) in CG</p> <p>Education, mean (SD), years: 13.4 (2.8) in IG; 13.6 (2.9) in CG</p> <p>Inclusion criteria: MS diagnosis, living in community, high impact of fatigue (score ≥ 3 on the fatigue subscale of the Guy's Neurological Disability Scale (Sharrack 1999)), able to walk ≥ 100 m, no rehabilitation programme within the last 2 years, no energy management programme in the past, not under psychiatric treatment for depression</p> <p>Exclusion criteria: cognitive impairment defined as PASAT score adjusted for education lower than the 10th percentile (PASAT score of 35)</p>
Interventions	<p>Intervention group</p> <p>Participation in "Multidisciplinary fatigue management programme (MFMP)"</p> <p><u>Basis:</u> Multiple Sclerosis Council for Clinical Practice Guidelines on management strategies for fatigue (MS Council for Clinical Practice Guidelines 1998)</p> <p><u>Structure:</u> "Each session started with information provided by the instructor, followed by an interactive part, in which participants discussed the strategies they used and planned in the near future." "The MFMP was instructed by four different therapists, who stimulated participants to try out the discussed strategies" (no more information on instructors provided).</p> <p><u>Content:</u> information and interactive parts on pharmacological treatment, diet, informing and involving the social environment, regular sleep, exercise, relaxation, cooling, assistive devices, adaptation of home or work environment, and energy saving methods. "No structured homework was planned in the sessions."</p> <p>Control group</p> <p>"Placebo intervention" programme of same frequency and duration with topics "[...] that were interesting enough to avoid dropouts and did not concern themes directly related to fatigue (i.e., car adaptations and driving abilities, communication skills, lift techniques for back protection and general information about MS)."</p>
Outcomes	<p>Primary outcome</p> <ol style="list-style-type: none"> 1. Fatigue impact: Modified Fatigue Impact Scale (MFIS) administered at baseline, 3 weeks, and 6 months after the intervention (MS Council for Clinical Practice Guidelines 1998) <p>Secondary outcomes</p> <ol style="list-style-type: none"> 1. Fatigue severity: Fatigue Severity Scale (FSS) administered at baseline, 3 weeks and 6 months after the intervention (Krupp 1989) 2. Self efficacy: Multiple Sclerosis Self-Efficacy Scale (MSSE) administered at baseline, 3 weeks, and 6 months after the intervention (Schwartz 1996)

Kos 2007 (Continued)

3. Perceived disease impact: Impact on Participation and Autonomy (IPA) Scale administered at baseline, 3 weeks, and 6 months after the intervention ([Cardol 1999](#))
4. Depression, anxiety, behavioural control, positive affect: Mental Health Inventory (MHI) administered at baseline, 3 weeks, and 6 months after the intervention ([Ritvo 1997](#))

Adverse events

1. Not assessed

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Matched pairs were composed [...]. The identity number of every subject was written down on a paper and put in an envelope together with the other pair member. An independent research assistant separated each pair and divided the individuals over two groups (group A or group B) by random draw."
Allocation concealment (selection bias)	Unclear risk	Although described as "random draw" between matched pairs, it remains unclear how this could result in different group sizes (IG n = 28, CG n = 23).
Blinding of participants and personnel (performance bias) All outcomes	High risk	"Due to the nature of the intervention, blinding of participants was not possible."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	"Group allocation was kept concealed for data analysis."
Incomplete outcome data (attrition bias) All outcomes	High risk	4 (14.3%) dropouts in the intervention group; 7 (30.4%) in the control group. Intention-to-treat analysis only for primary outcome (MFIS)
Selective reporting (reporting bias)	Unclear risk	No protocol available
Other bias	Unclear risk	Possible contamination between groups

Köpke 2009

Methods	Randomised controlled trial Study period: May 2003 to June 2004
Participants	Country: Germany Location: 2 MS clinics located at a University Hospital (Hamburg) and a General Hospital (Osnabrück), and 1 neurologist's practice (Herborn) Number of participants: 150 Age, mean (SD), years: 37 (7) in IG; 39 (8) in CG Female: 82% in IG; 73% in CG Level of disability: Mean UNDS score (SD): 7.2 (5.9) in IG; 8.6 (6.4) in CG

Köpke 2009 (Continued)

Education: > 11 years: 49% in IG; 58% in CG

Inclusion criteria: physician-confirmed diagnosis of MS (self reported) with at least 1 relapse during the past 12 months or at least 2 relapses during the past 24 months; no major cognitive deficit; age ≥ 18

Exclusion criteria: "History of steroid sensitivity and/or pregnancy"

Interventions
Intervention group
Education programme on relapse management

Basis: protection motivation model applied to decisional autonomy (Boer 1996; Rogers 1975). Curriculum based on the practical oriented approach of education (Meyer 1983).

Content: structured 4-hour education programme. Topics included personal experiences, relapses, relapse therapy, oral corticosteroid therapy, relapse management options, and reflection. Methods used were PowerPoint presentations, worksheets, individual and group work, and guided discussions.

Structure: 10 participants with their partners or close relatives were invited per session. 2 educators held the programme: a nurse and a specially trained person with MS. At 1 centre (Herborn), the MS practice nurse carried out the training alone. After the programme, treating physicians of participants were sent a fax informing them about their patients' inclusion in the study together with brief study information.

Educational booklet

2 weeks before the programme, participants received a 40-page educational booklet summarising the evidence on relapses and relapse management, based on the principles of evidence-based patient information (Steckelberg 2005). It was not stated how the booklet was provided. On request, authors reported that it was sent by postal mail.

Corticosteroid prescription

Participants were offered a prescription of 30 tablets of 100 mg methylprednisolone, which was given to participants after the programme if requested.

Control group

Control group participants received a 2-page standard information leaflet on relapse treatment including information about the option of oral corticosteroid therapy.

Outcomes
Primary outcome

Proportion of relapses with oral corticosteroid therapy or without corticosteroid therapy within 2 years of follow-up

Secondary outcomes

Time to initiation of corticosteroid treatment, location and invasiveness of corticosteroid treatment, and costs

Further outcomes comprised perceived decision autonomy, quality of life, and disability status assessed at baseline and at 2-year follow-up.

Adverse events

Adverse events of corticosteroid treatment and of the overall intervention including changes in quality of life and disability status over 2 years

Notes

Accuracy of primary endpoint unclear as self reported by participants. Blinded neurologists rated relapses after follow-up from case report files.

Risk of bias

Köpke 2009 (Continued)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Computer generated randomisation lists"
Allocation concealment (selection bias)	Low risk	"By external central telephone. Participants were stratified by study centre and drawn consecutively using three separate randomisation lists"
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and educators were not blinded.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Assessors were not blind to participants' allocation. In order to minimise bias, assessment was carried out using standardised questionnaires. 1 author regularly supervised assessors.
Incomplete outcome data (attrition bias) All outcomes	Low risk	6 (7.8%) dropouts in the intervention group; 7 (9.5%) in the control group
Selective reporting (reporting bias)	Unclear risk	3 secondary endpoints were not reported: time to initiation of corticosteroid treatment ("not able"), cost ("will be published separately", although not yet published), and protection motivation (not mentioned in the publication).
Other bias	Unclear risk	Possible contamination between groups; self reporting of MS relapses by participants; participants in the IG were older than those in the CG (63 versus 53 years)

Köpke 2014

Methods	Randomised controlled trial Study period: May 2009 to October 2010
Participants	Country: Germany Location: 6 academic MS centres Number of participants: 192 Age, mean (SD), years: 37 (10) in IG; 37 (10) in CG Female: 74% in IG; 75% in CG Mean UNDS score (SD): 4.1 (3.9) in IG; 5.1 (4.7) in CG Education: > 11 years: 57% in IG; 47% in CG Inclusion criteria: self reported confirmed or possible relapsing-remitting MS within the last 2 years; age between 18 and 60 Exclusion criteria: major cognitive deficit; primary or secondary progressive MS
Interventions	Intervention group <i>Education programme on diagnosis, prognosis, and early therapy</i>

Köpke 2014 (Continued)

Basis: the 4-hour programme was based on preparatory work and pre-studies, and followed the MRC framework on complex interventions (Craig 2008), as well as principles of risk communication and evidence-based patient information (Bunge 2010).

Content: the curriculum followed the "theory of planned behavior" (Ajzen 1985). The programme comprised the presentation of knowledge on MS, on relevant aspects of clinical epidemiology (e.g. study designs of prognostic studies, measures of diagnostic accuracy, etc.). The best available evidence regarding diagnostic testing in MS, prognosis of MS, and early MS DMD was presented using PowerPoint presentations, exercises, decision trees, group work, and guided discussions.

Structure: 10 participants with their partners or close relatives were invited per session. The programme was led by 1 "non-medical" person from the study centre based on structured presentation materials and moderation cards.

Educational booklet

2 weeks before the education programme, IG participants received a 57-page educational booklet containing relevant methodological information and information on the recent evidence on diagnosis, prognosis, and early therapies in MS. Presentation followed the principles of evidence-based patient information (Bunge 2010).

Control group

MS-specific stress management programme

Participants in the CG took part in a 4-hour MS-specific stress management programme led by a specially trained psychologist. The programme was based on an existing programme focusing on "patients' experience with management of stress and anxieties", aiming to "enhance participants' resources as well as stress coping strategies".

Standard information

2 weeks before the programme, a 5-page information leaflet with information on diagnosis, prognosis, and early therapy as provided on the website of the German MS Society was sent to participants.

Outcomes

Primary outcome

Informed choice using the Multidimensional Measure of Informed Choice (MMIC) assessed at 6-month follow-up (Marteau 2001)

Secondary outcomes

1. Control beliefs using the German version of the Control Beliefs Questionnaire assessed 2 weeks before the intervention and after 12 months (Lohaus 1989; Otto 2011)
2. Autonomy preferences (using the CPS) assessed 2 weeks before and 2 weeks and 12 months after the intervention
3. Decision autonomy and satisfaction with the decision assessed during the 3 months preceding the telephone interviews at 3, 6, 9, and 12 months
4. Decisional conflict administering the German version of the Decisional Conflict Scale 2 weeks before the intervention and after 12 months (Buchholz 2011)
5. Anxiety and depression administering HADS before randomisation and 2 weeks and 12 months after the intervention
6. DMD status assessed before randomisation and at 3, 6, 9, and 12 months
7. Disease-related resource use assessed during the telephone interviews at 3, 6, 9, and 12 months

Adverse events

Disease progression and health-related quality of life

Notes

Risk of bias

Köpke 2014 (Continued)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Computer-generated randomisation lists."
Allocation concealment (selection bias)	Low risk	"Concealed allocation of participants by external central telephone."
Blinding of participants and personnel (performance bias) All outcomes	Low risk	"Participants were blinded to study groups as they were not informed about the 'active' intervention." Trainers could not be blinded, but "had no role in data assessment or management".
Blinding of outcome assessment (detection bias) All outcomes	Low risk	"Outcomes were assessed via blinded telephone calls and mailed questionnaires."
Incomplete outcome data (attrition bias) All outcomes	Low risk	2 (2%) dropouts in the intervention group, 5 (5%) in the control group
Selective reporting (reporting bias)	Low risk	Outcomes as reported in the study registration.
Other bias	Unclear risk	Possible contamination between groups

O'Hara 2002

Methods	Randomised controlled trial Study period: June 1996 to February 1999
Participants	Country: UK, London Location: Centre for Research and Rehabilitation at Brunel University's Osterley Campus in West London Number of participants: 183 Age, mean (SD), years, range: 52 (11), 28 to 79 in IG; 50 (10), 30 to 81 in CG Female: 71% in IG; 68% in CG Level of disability (%): not reported Education: at least secondary: 79% in IG; 78% in CG Inclusion criteria: diagnosis of MS confirmed by general practitioner Exclusion criteria: none
Interventions	Intervention group Basis: no theoretical basis mentioned. "Pragmatic approach", O'Hara 2000, based on previous publications of patients' needs, Robinson 1996, and own pre-studies (O'Hara 2000). The self care programme was primarily comprised of a discussion of self care strategies supported by an information booklet developed for the study in line with consumer priorities (Robinson 1996). Structure: participants were contacted by telephone by a health professional and an appointment was made to discuss individual self care strategies and to introduce the information booklet. The health

Information provision for people with multiple sclerosis (Review)

O'Hara 2002 (Continued)

professional assigned participants to either group or 1-to-1 sessions. Sessions were conducted either at participants' homes or in local therapy centres. The discussions lasted between 1 and 2 hours and were conducted on 2 occasions, over a 1-month period. The format of the discussions focused on "individuals' interests and concerns rather than on covering all the information contained in the booklet".

Content: topics in the booklet covered physical, social, and psychological (e.g. strategies to cope with stress) "domains of life".

Control group:

Participants were under the care of their family doctor (general practitioner); some were receiving advice or information from MS Society branches (or other charities) on how to deal with their MS. None of those entering the research study were receiving regular input from a healthcare practitioner (information provided by Dr De Souza on request).

Outcomes	Primary endpoints 1. Mobility scale assessed at baseline and follow-up (De Souza 1999) 2. Standard Day Dependency Record (SDDR) administered at baseline and follow-up (Lawson 1985) 3. SF-36 administered at baseline and follow-up 4. Barthel Index assessed at baseline and follow-up Adverse events Not assessed	
Notes		
Risk of bias		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"An independent person not involved in the study randomised each participant using random number tables, with odd/even number allocation to intervention/control group, with random draw"
Allocation concealment (selection bias)	Low risk	"Each random number was written on paper and sealed in an opaque envelope prior to the start of the study. An independent person held the envelopes and had no contact with the assessors. The health professionals administering the intervention received the sealed envelopes from the independent person, in groups of ten, following the baseline assessments. Names of participants were written on the outside of the envelopes and then the envelopes were opened to reveal their assignment to control or intervention. Information concerning the intervention and the assessments were stored separately. The blind code was broken after the final follow-up assessments had occurred. Evidence for the success of the blinding was not gathered"
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants not blinded, personnel unclear
Blinding of outcome assessment (detection bias) All outcomes	Low risk	No blinding of outcome assessment reported, but as self administered questionnaires were used, outcome measurement was not likely to be influenced by lack of blinding.
Incomplete outcome data (attrition bias) All outcomes	Low risk	7 (8.7%) withdraw participation and were lost to follow-up in the intervention group; 7 (6.8%) withdraw participation and were lost to follow-up in the control group.

O'Hara 2002 (Continued)

Selective reporting (reporting bias)	Unclear risk	No protocol available. Information provided by Dr De Souza on request: The protocol (PCD/A2/27) was held for the duration of the study until 3 years after by the NHS R&D committee and was available in the public domain, however this repository is no longer active.
Other bias	Unclear risk	Probable selection bias due to recruitment via "voluntary group members" Unexplained difference in number of participants between groups (difference of 23 although randomisation in blocks of 10)

Prunty 2008a

Methods	Randomised controlled trial Study period: March to November 2005
Participants	Country: Australia Location: community-based women with MS in New South Wales and Victoria Number of participants: 194 Age, mean (SD), years: 32 (4) in IG; 31 (6) in CG Female: 100% Level of disability: not reported Education: not reported Inclusion criteria: women with MS; ages 20 to 40; currently undecided about motherhood; literate in English Exclusion criteria: not reported
Interventions	<p>Intervention group</p> <p>Printed decision aid (DA) called "Motherhood choice".</p> <p><u>Basis</u>: no theoretical basis given. Content and structure based on literature search and Ottawa Decision Support Framework and the CREDIBLE criteria (Stacey 2017).</p> <p><u>Content</u>: general background information about MS; psychosocial impact of MS regarding parenting; effect of MS on fertility, pregnancy, labour, delivery, miscarriage, childrearing, pregnancy, and course of MS; evidence about the safety of different medications during conception and pregnancy; MS in the postnatal period; breastfeeding; commonly asked questions, etc.</p> <p>The DA included patient stories, options that women may consider, and exercises to consider personal values.</p> <p>Co-intervention</p> <p>Participants in the IG were telephoned 2 weeks after receiving the DA to "ensure they had read and understood the DA, to answer questions and to screen for distress". Telephone conversations did not exceed 20 min.</p> <p>Control group</p> <p>There is no standard care in terms of information provided to people with MS about having children. People with MS receive information differently, from different health professionals, whether that be their neurologist, general practitioner, support centre (e.g. MS Society), or by gathering information online. Some do not know to ask questions about this issue either, and the information received will vary</p>

Prunty 2008a (Continued)

based on from where it has come and the individual's own bias (information provided by Dr Prunty on request).

Outcomes	Primary outcomes 1. Knowledge assessed before and after the intervention 2. Decisional conflict before and after the intervention (O'Connor 1995a) 3. Decision self efficacy before and after the intervention (O'Connor 1995b) 4. Decision certainty before and after the intervention Secondary outcomes 1. Depression (Center for Epidemiologic Studies Depression Scale (CESD)) and anxiety (State-Trait Anxiety Inventory (STAI)) before and after the intervention (Radloff 1977) 2. Direction of the decision ("balance") before and after the intervention Adverse events None reported.	
Notes	Reported results for balance not interpretable.	
Risk of bias		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Random numbers corresponding to intervention versus control were generated using the Excel Bernoulli function and linked to participant identification numbers."
Allocation concealment (selection bias)	Low risk	"[...] These numbers were linked to a series of consecutive participation numbers (1, 2, 3, 4, 5, etc) by an independent researcher (LS) who was not involved in the recruitment of patients. The randomisation numbers were concealed electronically (akin to opaque envelopes). Once participants had returned their assessment and their consent form, they were assigned the next available subject number; and then the allocation code was broken to determine which group they had been allocated to" (information provided by Dr Prunty on request)
Blinding of participants and personnel (performance bias) All outcomes	High risk	Patients and personnel obviously not blinded.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Blinding of outcome assessment not reported, but as self administered questionnaires were used, outcome measurement not likely to be influenced by lack of blinding.
Incomplete outcome data (attrition bias) All outcomes	High risk	27 (25.7%) dropouts in the intervention group; 28 (31.4%) in the control group
Selective reporting (reporting bias)	Unclear risk	No protocol found.
Other bias	Unclear risk	Probable selection bias due to exclusive recruitment through MS societies

Rahn 2018

Methods	<p>Randomised controlled trial</p> <p>Study period: May 2014 to March 2016</p>
Participants	<p>Country: Germany</p> <p>Location: 2 German MS university centres</p> <p>Number of participants: 73</p> <p>Age, mean (SD), years: 38 (9) in IG; 36 (11) in CG</p> <p>Female: 68% in IG; 80% in CG</p> <p>Level of disability: EDSS mean score (SD) 2.0 (0 to 5.0) in IG; 2.0 (0 to 6.0) in CG</p> <p>Education: higher education (at least 12 years): 51% in IG; 69% in CG</p> <p>Inclusion criteria: "People with suspected or relapsing-remitting MS facing immune-treatment decisions on first line drugs"</p> <p>Exclusion criteria: "Secondary-progressive or primary-progressive MS as well as any other suspected central nervous system disease, facing a decision on escalation immune-treatment or on symptomatic treatment, and severe cognitive deficit or major psychiatric illness affecting information uptake"</p>
Interventions	<p>Intervention group</p> <p>Decision-coaching sessions</p> <p><u>Basis</u>: the concept of the "decision coaching programme" is described in the study protocol (Rahn 2015).</p> <p><u>Content</u>: the intervention consists of up to 3 coaching sessions, access to the DECIMS-Wiki, and up to 2 physician consultations.</p> <p><u>Structure</u>: the decision-coaching sessions are structured following the 6 steps of shared decision making:</p> <ol style="list-style-type: none"> 1. reviewing the problem; 2. key message; 3. information about pros and cons of each option; 4. expectations of the patient; 5. decision; and 6. arrangements (Elwyn 2001). <p>Patient workbooks, 1 on first-line treatment and 1 for people with MS considering a treatment change, as well as a coaching guide were developed to support and guide the decision coaching. Both workbooks and the coaching guide were pre-tested for feasibility.</p> <p>Control group</p> <p><i>DECIMS-Wiki and treatment as usual</i></p> <p>The DECIMS-Wiki aims to provide information on several relevant topics on MS, but focuses mainly on treatment options. The content was built on previously developed evidence-based patient information brochures and literature searches (Rahn 2015). Information on benefits and side effects on all available drugs are provided. Bar charts on disability progression and relapses were therefore developed to display the absolute risk reduction for each immunotreatment option. The comprehension of the bar charts was evaluated in a randomised controlled trial (Kasper 2017).</p> <p>For feasibility testing, feedback on the DECIMS-Wiki was obtained from 2 consumer representatives from a self help initiative, nurses, and people with MS. 1 consumer representative worked regularly on the development of the DECIMS-Wiki for over a year and discussed the content with the researchers.</p>

Rahn 2018 (Continued)

Participants received login details and a user guide after they filled in the baseline questionnaires. The DECIMS-Wiki was also used during coaching sessions (see above).

Outcomes

Primary outcome

1. Informed choice using the Multidimensional Measure of Informed Choice (MMIC) assessed at 6-month follow-up ([Marteau 2001](#))

This measure includes the subdimensions risk knowledge measured by the RIKNO (assessed after 14 days) ([Heesen 2015](#)), attitude concerning immunotreatment (1 question assessed after physician consultation), and immunotreatment uptake (survey after 6 months).

Secondary outcomes

1. Decisional Conflict Scale supplemented by a version for health professionals to achieve dyadic measurement, assessed after last decision coaching, and directly after final physician decision encounter ([Buchholz 2011](#))
2. Analyses of videotaped coaching sessions assessing SDM as well as MS patients', physicians', and coaches' evaluation of SDM by the MAPPIN'SDM questionnaire ([Kasper 2012a](#))
3. CPS assessed 2 weeks and 6 months after final physician encounter ([Degner 1997](#))
4. Coping Self-Efficacy assessed at baseline, 2 weeks, and 6 months after final physician encounter ([Chesney 2006](#))
5. Trust in physicians and decision coaches assessed after last decision coaching and directly after final physician decision encounter ([Bova 2012](#))

The Planned Behaviour in MS (PBMS) questionnaire was not analysed as a new scaling format was applied ([Kasper 2012b](#)).

Adverse events

1. HADS assessed at baseline, 2 weeks, and 6 months after final physician encounter
2. HAQUAMS assessed at baseline, 2 weeks, and 6 months after final physician encounter ([Gold 2001](#))

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated randomisation (information provided by author on request)
Allocation concealment (selection bias)	Unclear risk	"Lists with randomised recruitment days were generated by an external statistician (EV) for both centres and one of two researchers (IB or AR) informed the nurses in the afternoon before recruitment days. Therefore, allocation concealment of the nurses was assured."
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	"Decision coaches were not blinded to group assignment, while the MS patients and physicians were." We considered risk of bias to be low, although decision coaches were part of the team.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Self reported outcomes: "Data were collected at baseline, after the final coaching session, after the physician consultation as well as two weeks, three and six months after the physician consultation." "Nurses, patients and physicians filled in questionnaires online. After six months, some data were collected by blinded research assistants via phone via a standardised questionnaire (see suppl. material 3, Rahn 2015)."

Rahn 2018 (Continued)

Incomplete outcome data (attrition bias) All outcomes	High risk	There was a considerable amount of missing data despite email reminders, telephone calls, and the option to receive the questionnaire via postal mail. Importantly, there were more missing data in the CG than in the IG.
Selective reporting (reporting bias)	Low risk	Primary outcome reported as planned in the study protocol (Rahn 2015). Secondary outcome "Planned behaviour in MS (PBMS)" not reported. Message from AR: "We did not analyse PBMS as a new scaling format was applied. Therefore, results will be analysed separately." We considered this to be low risk of bias.
Other bias	Unclear risk	Possible contamination between groups

Shinto 2008

Methods	Randomised controlled trial Study period: not reported
Participants	Country: USA, Portland (Oregon) Location: MS Center of Oregon at Oregon Health & Science University Number of participants: 45 Age, mean (SD), years: 43 (9) in education group; 39 (10) in naturopathic group; 46 (8) in CG Female: 86% in education group; 93% in naturopathic group; 81% in CG Mean EDSS score (SD): 2.6 (1.2) in education group; 2.6 (1.1) in naturopathic group; 2.6 (1.2) in CG Education: college diploma or degree: 50% in education group; 40% in naturopathic group; 64% in CG Inclusion criteria: definite MS (Poser criteria) (Poser 1983); relapsing–remitting course of MS; EDSS ≤ 6 Exclusion criteria: corticosteroids or relapse within 30 days of enrolment; "serious medical problems" (e.g. cancer, uncontrolled diabetes mellitus, congestive heart failure, severe psychiatric disorder); pregnancy; or "recent visits to a complementary and alternative medicine practitioner"
Interventions	Participants were randomised to 1 of the following 3 groups. Education sessions (note: this group was implemented as a "time and attention" control, the number of visits and time spent with the nurse matched the "active" naturopathic intervention. There was no overlap with the information provided in the naturopathic intervention.) <u>Basis</u> : no theoretical basis given. <u>Content</u> : educational pamphlets published by the National MS Society on fatigue; mood; cognitive problems; bowel and bladder problems; exercise; stress; nutrition; vitamins, minerals, and herbs <u>Structure</u> : 8 visits over a period of 6 months with a nurse that specialised in MS care plus usual care. At each visit, the participant received an educational pamphlet published by the National MS Society containing information about MS. The nurse instructed each participant that the intent of the session was to focus on the information contained within the pamphlets. If participants had questions about other aspects of their care, such as advice on medications, specific interventions for MS-related symptoms, or alternative therapies, the nurse instructed the participants to contact their physicians for answers to such questions. Naturopathic intervention (note: this group was the "active" intervention to be assessed by this study.)

Shinto 2008 (Continued)

Basis: no theoretical basis given. Pre-study applying a survey and a delphi panel to determine "the best naturopathic treatment model" (Shinto 2004)

Structure: 8 visits with a naturopath over a period of 6 months plus usual care

Content: the naturopathic intervention included oral dietary supplement, intramuscular vitamin B₁₂ once a week based on 4 diet levels. 4-day "Diet Recall" documentation was completed prior to each visit to the naturopath.

Control group

Usual care (no description given). Participants in all arms were allowed to continue their conventional treatment for MS, including disease-modifying therapies and prescription symptomatic therapy.

Outcomes

Primary outcome

1. Quality of life (SF-36) assessed at baseline and 6-month follow-up

Secondary outcomes

1. Fatigue (Modified Fatigue Impact Scale) assessed at baseline and 6-month follow-up (Fisk 1994)
2. Depression (Beck Depression Inventory) assessed at baseline and 6-month follow-up (Beck 1961)
3. Cognition (Stroop test, Perret 1974, and PASAT-3, Gronwall 1977) assessed at baseline and 6-month follow-up
4. Neurologic impairment (EDSS plus Multiple Sclerosis Functional Composite (MSFC)) assessed at baseline and 6-month follow-up (Rudick 2002)

Adverse events

Safety was measured by "comprehensive metabolic panel, complete blood count with differential, and adverse event reports". Unclear if assessed for all participants

Notes

We considered only the education and the control groups for this review.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated randomisation schedule (information provided by Dr Shinto on request)
Allocation concealment (selection bias)	Low risk	Allocation by external centre after inclusion of participants (information provided by Dr Shinto on request)
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and personnel were not blinded.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	"Patients were instructed not to disclose their treatment intervention to the neurologists and research assistants performing end-of-study assessments." An evaluation at the end of the study suggested successful blinding (93%).
Incomplete outcome data (attrition bias) All outcomes	Low risk	No dropouts in intervention or control group
Selective reporting (reporting bias)	Unclear risk	No protocol or further information other than in the publication (information provided by Dr Shinto on request)

Shinto 2008 (Continued)

Other bias	Unclear risk	Possible contamination between groups
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Solari 2010a

Methods	<p>Randomised controlled trial</p> <p>Study period March 2008 to June 2009</p>
Participants	<p>Country: Italy</p> <p>Location: 5 Italian tertiary MS care centres</p> <p>Number of participants: 120</p> <p>Age, mean (SD), years, range: 34 (9), 17 to 60 in IG; 36 (9), 22 to 56 in CG</p> <p>Female: 73.3% in IG; 63.3% in CG</p> <p>Median EDSS score (range): 2 (0 to 5) in IG; 2 (0 to 6) in CG</p> <p>Education: college diploma or degree: 13.3% in IG; 25.0% in CG</p> <p>Inclusion criteria: all patients aged 18 years or above referred for possible MS diagnosis</p> <p>Exclusion criteria: "Prior MS diagnosis disclosure, overt cognitive impairment, history of overt psychiatric disease, and substance abuse"</p>
Interventions	<p>Intervention group</p> <p>The study intervention consisted of a personal interview with a physician using a navigable CD, and presentation of a take-home booklet at the end of the interview.</p> <p><u>Basis:</u> no theoretical basis given. Authors reported on request that they had followed the MRC framework on complex interventions (Craig 2008). Content and structure based on "comprehensive literature review" and pre-study ("focus groups with patients and clinicians") (Solari 2007). The CD and booklet were developed in Italian "by a multidisciplinary panel through an iterative process of review and revision in collaboration with patients with MS."</p> <p><u>Structure:</u> the interview was scheduled 1 to 15 days after diagnosis disclosure (mean time between disclosure and interview 11.6 days (SD 7.3)). Participants' significant other were also invited if requested by the participant. The interviewing physician (not the person who communicated the diagnosis or followed the patient) was a neurologist or trainee neurologist experienced in MS. 5 physicians (1 at each centre) were trained during 1 day in the personal interview and CD navigation. Physician and participant went through the topics of the CD guided by participant preferences. Topics raised by the participant were discussed. "At the end of the interview the interviewing physician completed an interview report which was included in the patient case report form."</p> <p><u>Content:</u></p> <ol style="list-style-type: none"> 1. CD: the CD has 8 sections: MS basics, diagnosis, time after diagnosis, therapies, emotions, having a child, FAQs, and glossary. The CD contains animations, visual aids, and a background comment explaining the text and illustrations. The Emotions section contains a link to an 8-minute movie. 2. Interview: see above. 3. Booklet: the 90-page take-home booklet had 8 chapters, a glossary (36 pages), and a section for patient notes with the first 7 chapters matching the CD sections in title and content. Chapter 8 reports findings of a preliminary study. Selected references/links are given at the end of each chapter. <p>Control group</p> <p>Usual practice (no description given)</p>

Solari 2010a (Continued)

Outcomes

Primary outcome

1. Composite of disease knowledge (MS Knowledge Questionnaire (MSKQ) ([Giordano 2010](#))) and satisfaction with care (section 2 of COSM-R (Comunicazione medico-paziente nella Sclerosi Multipla, revised version) ([Solari 2010b](#))) assessed at 1-month postal follow-up and 6-month follow-up

Secondary outcomes

1. MSKQ assessed at 1-month postal follow-up and 6-month follow-up
2. COSM-R section 2 assessed at 1-month postal follow-up and 6-month follow-up
3. HADS assessed at baseline, 1-month postal follow-up, and 6-month follow-up
4. CPS assessed at baseline and 6-month follow-up
5. Physician consultations (over 6 months)
6. Disease-modifying therapies (over 6 months)
7. Switching care centre (over 6 months)

Serious adverse events ("monitored by an Independent Data and Safety Monitoring Committee")

1. Admission to psychiatric ward
2. Suicide attempt
3. Death

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Allocation sequences (1:1 ratio) were computer-generated in permuted blocks of four, stratified by centre."
Allocation concealment (selection bias)	Low risk	At baseline, after MS diagnosis disclosure, the investigator faxed patient eligibility characteristics to the randomisation unit. The allocation was faxed back to the investigator who informed the patient, who also received a contact diary.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and personnel were not blinded.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Blinding of outcome assessment not reported, but as self administered questionnaires were used, outcome measurement was not likely to be influenced by lack of blinding.
Incomplete outcome data (attrition bias) All outcomes	Low risk	5 (8.4%) dropouts in the intervention group; 3 (5%) in the control group
Selective reporting (reporting bias)	Low risk	"Switching care centre" not included in the study registration
Other bias	Unclear risk	Possible contamination between groups

Young 1986

Methods	Randomised controlled trial Study period: not reported
Participants	Country: USA; Baltimore (Maryland) Location: Johns Hopkins University Hospital, Baltimore Number of participants: 18 participants were enrolled, but it is unclear how many were randomised Age, mean (SD), years, range: 39 (8), 28 to 52 in IG; 39 (7), 28 to 50 in CG Female: 75% in IG; 62.5% in CG Level of disability: not reported Education: not reported Inclusion criteria: people with MS beginning steroid therapy Exclusion criteria: not reported
Interventions	Intervention group 1. Physician and nurse led oral presentation 2. Patient information booklet <u>Basis</u> : no information provided on theoretical background. Intervention based on clinical experience. <u>Structure</u> : no information given, training of educators not reported. <u>Content</u> : information on methylprednisolone (drug action, usage, side effects, danger signs) Control group Physician- and nurse-led oral presentation Co-interventions Review of correct answers after baseline test Methylprednisolone prescribed at 2 mg/kg and given on alternate days.
Outcomes	Primary outcome Knowledge on steroid therapy assessed before and after the intervention Secondary outcome Compliance Adverse events Not mentioned
Notes	
Risk of bias	
Bias	Authors' judgement Support for judgement
Random sequence generation (selection bias)	Low risk "Randomisation was done per patient via coin flip program on a computer" (information provided by Dr Brooks on request)

Young 1986 (Continued)

Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Information provided by Dr Brooks on request: participants were given information booklet per randomisation above after the pre-test. Pre-test done by nurse specialist or nurse assistant postdiscussion by MD with participant. At 1-month clinic visit, due to the business of the clinic, the staff were assumed not to know who had information booklet and who did not.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Information provided by Dr Brooks on request: post-test was part of intake during triage before full chart review for that encounter. Pre-test and post-test were completed by each participant without registered nurse or nurse assistant input.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Unclear how many participants were randomised, results given for 18 participants
Selective reporting (reporting bias)	Unclear risk	No protocol found.
Other bias	Unclear risk	Possible contamination between groups

CG: control group

CPS: Control Preference Scale

DECIMS: DEcision Coaching In persons with relapsing-remitting Multiple Sclerosis

DMD: disease-modifying drug

EDSS: Expanded Disability Status Scale

HADS: Hospital Anxiety and Depression Scale

HAQUAMS: Hamburg Quality of Life Questionnaire in Multiple Sclerosis

IG: intervention group

MAPPIN'SDM: Multifocal Approach to Sharing in Shared Decision Making

MRC: Medical Research Council

MS: multiple sclerosis

RIKNO: Risk Knowledge in Relapsing Multiple Sclerosis

PASAT: Paced Auditory Serial Addition Test

SD: standard deviation

SDM: shared decision making

SF-36: 36-item Short Form Health Survey

UNDS: United Kingdom Neurological Disability Scale

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Berger 2005	Not primarily information provision

Study	Reason for exclusion
Bombardier 2008	Information provision only optional
Bombardier 2013	Information provision only optional
Burgess 2012	Participants with chronic fatigue syndrome, not multiple sclerosis
Christopherson 2006	Information provision only optional
Cosio 2011	Not information provision
Dlugonski 2012	Not primarily information provision
Ehde 2017	Not information provision
Feicke 2014	No randomised controlled trial
Finlayson 2011	Not information provision
Forman 2010	Not primarily information provision
Garber 2002	Only 2 participants of 41 with multiple sclerosis, no separate data for participants with multiple sclerosis available
Ghahari 2010	Only 78% of participants with multiple sclerosis, no separate data for participants with multiple sclerosis available
Hill 2012	Not a randomised controlled trial
Kalina 2017	Not information provision
Köpke 2017	Not a randomised controlled trial
Lutz 2017	Not primarily information provision
Mattioli 2012	Not primarily information provision
McAuley 2007	Not primarily information provision
McClurg 2011	Main intervention abdominal massage, both groups received "advice"
Miller 2011	Information provision concerning only individual disease status and appointment planning
Mohamadirizi 2017	Both intervention and control received information provision intervention with different formats.
Moss-Morris 2012	Not primarily information provision
Motl 2017	Not primarily information provision
Möller 2010	Not primarily information provision
Rigby 2008	Not primarily information provision
Turner 2016	Not information provision
Van Kessel 2015	Not information provision

Study	Reason for exclusion
Ward 2004	Only 40% of participants with multiple sclerosis, no separate data for participants with multiple sclerosis available
Wassem 2003	Information provision only optional

ADDITIONAL TABLES

Table 1. Search results

Source	Date searched	Records re-trieved (excluding dupli- cates)
Cochrane Multiple Sclerosis and Rare Diseases of the Central Nervous System Group Trials Register	Searched 29 November 2017	441
PsycINFO	Searched 29 November 2017	193
metaRegister of Controlled Trials	Searched 29 November 2017	22
World Health Organization International Clinical Trials Registry Platform (WHO ICTRP) (apps.who.int/trialsearch/)	Searched 29 November 2017	1
Forward and backward tracking of included articles and relevant system- atic reviews	Searched 29 November 2017	0
TOTAL after rejecting duplications		657

Table 2. Intervention components

	Disease information	Drug therapies	Non-drug therapies	General information
Ennis 2006	n.r.	n.r.	n.r.	Sessions on “Health pro- moting activities” 1. Exercise and physical ac- tivity 2. Lifestyle adjustment/fa- tigue management 3. Stress management 4. Nutritional awareness 5. Responsible health prac- tices
Kasper 2008	MS basics	Immunotherapy options	Very shortly addressed	No

Table 2. Intervention components (Continued)

Köpke 2009	Evidence on relapses	Relapse therapy (corticosteroids)	CAM discussed during educational session	No
Köpke 2014	MS basics: pathology, relapses, progression, disease courses, natural course, prognosis	Therapy options for early MS focusing on immunotherapy, but also on other options including CAM	CAM included in the brochure (information provided by author on request)	No
Kos 2007	n.r.	Pharmacological treatment	Diet, cooling, assistive devices, and energy saving methods	Regular sleep, exercise, relaxation, adaptation of home or work environment
O'Hara 2002	An introduction to MS (included in the information booklet; information provided by Dr De Souza on request)	Medication, therapists and therapies (included in the information booklet; information provided by Dr De Souza on request)	Diet (included in the information booklet; information provided by Dr De Souza on request)	Coping with the emotional impact of MS; support from friends and family; rest; working (included in the information booklet; information provided by Dr De Souza on request)
Prunty 2008	General background information about MS; psychosocial impact of MS regarding parenting; effect of MS on fertility, pregnancy, labour, delivery, miscarriage, childrearing, pregnancy and course of MS; MS in the post-natal period	Evidence about the safety of different medications during conception and pregnancy	n.r.	n.r.
Rahn 2018	MS basics, pathology, relapses, progression, disease courses, natural course, diagnosis, prognosis, symptoms	Immunotherapy options and relapse therapy (corticosteroids)	CAM, vitamins, physical activity, and other options (briefly)	Background information on clinical studies including information on risk reduction and confidence intervals
Shinto 2008	n.r.	Therapies for fatigue, mood, cognitive problems, bowel and bladder problems	Nutrition; vitamins, minerals, and herbs	Exercise, stress
Solari 2010	MS basics, diagnosis, time after diagnosis, emotions, having a child	Relapse therapies and disease-modifying drugs	Definition of CAM reported only in the glossary (information provided by author on request)	n.r.
Young 1986	n.r.	Information on methylprednisolone (drug action, usage, side effects, danger signs)	n.r.	n.r.

n.r.: not reported

CAM: complementary and alternative medicine; MS: multiple sclerosis

Table 3. Summary of outcomes assessed

Knowledge	Decision making	Quality of life
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Table 3. Summary of outcomes assessed (Continued)

Ennis 2006	Not assessed	Not assessed	SF-36 (SO)
Kasper 2008	Not assessed	Realised role preferences (CPS) (PO) Degree of decision progress (self developed questionnaire) (SO)	Not assessed
Köpke 2009	Not assessed	Active role in decision on relapse treatment (self developed questionnaire) (SO) Satisfaction with the decision (self developed questionnaire) (SO)	HAQUAMS (SO)
Köpke 2014	Self developed questionnaire (part of the PO)	Informed choice (MMIC) (PO) Autonomy preferences (CPS) (SO) Decision autonomy (self-developed questionnaire based on CPS) (SO) Decisional conflict (DCS) (SO) Satisfaction with the decision (self developed questionnaire) (SO) Decision process (PBMS) (SO)	HAQUAMS (SO)
Kos 2007	Not assessed	Not assessed	Not assessed
O'Hara 2002	Not assessed	Not assessed	SF-36 (SO)
Prunty 2008	Self developed questionnaire (PO)	Decisional conflict (DCS) (PO) Decision self efficacy (DSES) (PO) Decision certainty (self developed questionnaire) (PO)	Not assessed
Rahn 2018	RIKNO (part of the PO)	Decisional conflict (DCS) (SO) Analyses of videotaped coaching sessions assessing SDM as well as MS patients', physicians', and coaches' evaluation of SDM by the MAPPIN'SDM questionnaire (SO) CPS (SO)	HAQUAMS (SO)
Shinto 2008	Not assessed	Not assessed	SF-36 (PO)
Solari 2010	MSKQ (part of PO)	Not assessed	Not assessed
Young 1986	Self developed questionnaire (PO)	Not assessed	Not assessed

PO: primary outcome measure; SO: secondary outcome measure

CPS: Control Preference Scale; DCS: Decisional Conflict Scale; DSES: Decision Self-Efficacy Scale; MMIC: Multidimensional Measure of Informed Choice; HAQUAMS: Hamburg Quality of Life Questionnaire in Multiple Sclerosis; MAPPIN'SDM: Multifocal Approach to Sharing in Shared Decision Making; MSKQ: Multiple Sclerosis Knowledge Questionnaire; PBMS: Planned Behaviour in MS questionnaire; RIKNO: Risk Knowledge in Relapsing Multiple Sclerosis questionnaire; SDM: shared decision making; SF-36: 36-item Short Form Health Survey

Table 4. Evaluation of the included studies using the CReDECI 2 checklist

(A)

Table 4. Evaluation of the included studies using the CReDECI 2 checklist *(Continued)*

	Ennis 2006	Kasper 2008	Köpke 2009	Köpke 2014	Kos 2007	O'Hara 2002
Development						
Item 1	Yes, p.786: Self-efficacy Theory	(Yes), p.1347	Yes, p.97: Protection Motivation Theory	Yes, p.412, Theory of Planned Behaviour	No	Yes, "self-care", p.121 (Ref. 6)
Item 2	Yes, p.786, (Refs. 2, 5)	Yes, p.1347, table 1	Yes, p.97-98, table 1	Yes, p.412, table 1	(Yes), p.997	Yes, p.121/122
Item 3	No	Yes, table 1	Yes, p.97-98	Yes, p.412, table 1	(Yes), p.997	No
Item 4	No	No	(Yes), p.97-98: oral corticosteroid prescription fitted to Germany	No	No	(Yes), p.121
Feasibility and piloting						
Item 5	No	Yes, p.1347 (Refs. 12, 13)	No	(Yes), p.412-413	Yes (Ref. 23)	No
Evaluation						
Item 6	No, p.785: control group continued with their present level of care	Yes, p.1347	Yes, p.98	Yes, p. 412	Yes, p.997	No
Item 7	(Yes), p.786	NA	No	(Yes), p.412	No	No
Item 8	(Yes), p.786	Yes, table 1	Yes, p.97, table 1	Yes, p.412, table 1	No	No
Item 9	No	No	No	No	No	No
Item 10	No	No	No	No	No	No
Item 11	No	No	No	No	No	No
Item 12	No	No	No	No	No	No
Item 13	No	No	(Yes), p.99 (planned)	No	No	No
(B)						
	Prunty 2008	Rahn 2018	Shinto 2008	Solari 2010	Young 1986	
Development						
Item 1	(Yes), p.109/10	Yes, (Rahn 2015, p.16)	No	(Yes), p.1394	No	

Table 4. Evaluation of the included studies using the CReDECI 2 checklist *(Continued)*

Item 2	Yes, p.110	Yes, e.g. p.3 and table S1 (see also Rahn 2015)	Yes, p.491-492	Yes, p.1394-1396	Yes, p.27
Item 3	No	(Yes), e.g. p.9	No	No	No
Item 4	No	Yes, (e.g. Rahn 2015 , p.10)	No	No	No
Feasibility and piloting					
Item 5	Yes, p.110	Yes	No	(Yes), p.1394	No
Evaluation					
Item 6	No	Yes, (Rahn 2015 , p.6)	No	No, p.1404: "usual care regarding MS diagnosis disclosure"	Yes, p.27
Item 7	No	(Yes)	Yes, p.492	No	No
Item 8	Yes, p.109-110	Yes	Yes, p.492	Yes, p.1394-1395	No
Item 9	No	Yes, p.7f	No	Yes, p.1397/98	No
Item 10	No	Yes, (Rahn 2015 , p.15)	No	Yes, p.1399: ongoing study mentioned (Ref. 15, Borreani 2014 published)	No
Item 11	No	Yes, p.7f	No	(Yes), p.1399: ongoing study mentioned (Ref. 15, Borreani 2014)	No
Item 12	No	No	No	No	No
Item 13	No	No	No	(Yes), p.1399-1401	No

NA: not applicable

APPENDICES

Appendix 1. Keywords used to search Cochrane Multiple Sclerosis and Rare Diseases of the Central Nervous System Group Register

education OR "patient education" OR "education* method*" OR "education* material*" OR "education* program*" OR (information AND coping) OR "patient information*" OR "health information*" OR "information* method*" OR leaflet* OR lecture* OR "communications media" OR "information sheet*" OR "patient guidance" OR brochure* OR pamphlet* OR counselling OR "patient counselling" OR "telephone call*" OR "web site*" OR website* OR (teaching AND computer*) OR (audiovisual AND information) OR "decision making" OR "shared decision making" OR "informed choice" OR "decision support" OR advice OR "Health Education" OR "Consumer Health Information" OR "Decision Making" OR "Decision Support Techniques" OR "Informed Consent" OR "Communication" OR "Patient Participation" OR "Self Care" OR "Health Status Indicator*" OR "Drug Information Services" OR "Information Dissemination" OR "Access to Information"

Appendix 2. PsycINFO (Ovid-SP)

multiple sclerosis.mp. OR exp Multiple Sclerosis/ OR optic neurit*.mp. OR acute disseminated encephalomyelitis.mp. OR exp Encephalomyelitis/ OR myelo optic neuropathy.mp. OR myelitis.mp. OR exp Myelitis/ OR neuromyelitis optica.mp. OR Encephalomyelitis.mp. OR clinically isolated syndrome.mp. OR transverse myelitis.mp. OR devic disease.mp. OR devics.mp. OR demyelinating disease.mp. OR demyelinating disorder.mp. OR adem.mp.

AND

patient participation.mp. OR client participation.mp. OR exp Client Participation/ OR decision making.mp. OR exp Decision Making/ OR communication.mp. OR exp Communication/ OR exp Counseling/ OR counseling.mp. OR decision support technique*.mp. OR decision support systems.mp. OR exp Decision Support Systems/ OR informed consent.mp. OR exp Informed Consent/ OR health education.mp. OR exp Health Education/ OR consumer education.mp. OR exp Consumer Education/ OR client education.mp. OR exp Client Education/ OR patient education.mp. OR consumer health information.mp. OR health education.mp. OR exp Health Education/ OR drug information.mp. OR drug education.mp. OR exp Drug Education/ OR information dissemination.mp. OR exp Information Dissemination/ OR access to information.mp. OR patient information.mp. OR information method.mp. OR leaflet*.mp. OR lecture*.mp. OR communications media.mp. OR exp Communications Media/ OR information sheet.mp. OR 2 teaching.mp. OR exp Education/ OR education.mp.

AND

exp Clinical Trials/ OR clinical trial*.mp. OR controlled clinical trial*.mp. OR crossover procedure.mp. OR cross over stud*.mp. OR crossover design.mp. OR double blind.mp. OR single blind.mp. OR exp Random Sampling/ OR random*.mp.

mp. [mp=title, abstract, heading word, table of contents, key concepts]

Appendix 3. List of trial and dissertation registers

1. metaRegister of Controlled Trials (www.controlled-trials.com/mrct) (includes ISRCTN register; Action Medical Research; Medical Research Council (UK); National Health Service Research and Development Health Technology Assessment Programme (HTA); National Institutes of Health (NIH) - randomised trial records held on NIH ClinicalTrials.gov website; The Wellcome Trust; UK Clinical Trials Gateway)
2. UMIN Japan Trial Register (www.umin.ac.jp/ctr/)
3. Australian Digital Theses Program (adt.caul.edu.au/)
4. Canadian Theses and Dissertations (www.collectionscanada.ca/thesescanada/index-e.html)

WHAT'S NEW

Date	Event	Description
29 November 2017	New search has been performed	First update of the review initially published in 2014
29 November 2017	New citation required but conclusions have not changed	We have included 1 new study with 73 participants in the review (Rahn 2018).

HISTORY

Protocol first published: Issue 10, 2010

Review first published: Issue 4, 2014

Date	Event	Description
10 September 2010	Amended	We have updated the Declarations of interest section.

CONTRIBUTIONS OF AUTHORS

SK and CH initially planned the review. SK and AG extracted and interpreted the data and wrote the review. AS, FK, AR, and CH contributed to data analysis and commented substantially on draft versions.

DECLARATIONS OF INTEREST

SK was involved in four of the 11 included studies.

AS was a board member for Biogen Idec and Novartis. She has received speaker honoraria from Almirall, EXCEMED, Genzyme, Merck Serono, and Teva. In addition, she was involved in one of the 11 included studies.

FK has nothing to declare.

AR was involved in one of the 11 included studies.

CH has received speaker honoraria, travel reimbursements, and research grants from Bayer HealthCare, Biogen Idec, Merck Serono, Genzyme, Sanofi-Aventis, Teva, and Novartis. In addition, he was involved in four of the 11 included studies.

AG was involved in one of the 11 included studies.

SOURCES OF SUPPORT

Internal sources

- University of Lübeck, Institute of Social Medicine and Epidemiology, Germany.
- Neurological Institute Carlo Besta, Milan, Italy.
- University Medical Centre Hamburg, Institute of Neuroimmunology and and Multiple Sclerosis (INIMS), Hamburg, Germany.
- University of Hamburg, Unit of Health Sciences and Education, Germany.

External sources

- No sources of support supplied

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

As in the previous version of this review, we have mostly adhered to the protocol in this update with the main difference being that we did not perform meta-analyses due to marked clinical heterogeneity. For the same reason, we did not categorise interventions, as initially planned, and did not perform subgroup analyses. Instead of using the planned category 'counselling methods' as a possible intervention component, we used 'personal information', as this seemed a more appropriate term. For the current version of the review, we made major adaptations to the [Background](#), updated the search strategy, and amended the [Results](#) section and the [Discussion](#) as a result of the newly included trial.

INDEX TERMS

Medical Subject Headings (MeSH)

*Patient Education as Topic; Consumer Health Information; Decision Making; Health Knowledge, Attitudes, Practice; Multiple Sclerosis [*therapy]; Multiple Sclerosis, Relapsing-Remitting [therapy]; Quality of Life; Randomized Controlled Trials as Topic

MeSH check words

Adult; Female; Humans; Male; Middle Aged