

Information provision for persons with multiple sclerosis (Protocol)

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[Intervention Protocol]

Information provision for persons with multiple sclerosis

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ABSTRACT

This is the protocol for a review and there is no abstract. The objectives are as follows:

1. To evaluate the effectiveness of different information strategies provided to persons with MS with the intention to promote informed choice and thereby improve relevant outcomes.
2. To evaluate the components and the developmental process of the complex interventions used.
3. To highlight the quality and quantity of research evidence available and to set an agenda for future research.

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 of life (Compston 2008). Prevalence rates vary between geographical areas with highest rates of 120-180 per 100,000 people in Northern Europe, North America and Australia (Multiple Sclerosis International Federation 2010), although figures might be slightly exaggerated (Poser 2007). The early disease course is characterised by inflammation causing relapses i.e. episodes of neurological dysfunction that usually recover. However, over time neurodegeneration seems to be more important than inflammation leading to progression of disability. As cause and mechanisms of the disease remain mostly unexplained (Compston 2008), uncertainty remains a constant feature of the disease (NCC-CC 2004). Individual patients' disease courses and prognoses are variable and hard to predict. The disease is commonly characterised by periodic relapses with a number of presentations from mild sensory dysfunctions to severe symptoms (e.g. loss of vision or paraplegia). However, one third of people with a diagnosis of MS seem to remain relatively unaffected by the disease (Ramsarasing 2006). A number of so called 'disease-modifying' drugs (DMDs) e.g. interferons, glatiramer acetate, and natalizumab are licensed to reduce relapses and slow down disease progression. However, long term effects remain unclear (Freedman 2008). DMDs are expensive and have regular adverse effects (Fillipini 2003).

The effectiveness of DMDs in progressive disease courses is unknown. For patients with primary progressive disease course, so far there are no disease modifying therapies available. As MS disease courses can differ in patients, their need for information also varies, depending on the disease course. With complexity of treatment options rapidly increasing, the availability of well-developed, unbiased up-to-date information is increasingly necessary to enable informed treatment choices. Despite a lack of strong evidence, many symptomatic therapies may be provided e.g. high-dose intravenous steroids for relapse therapy (Köpke 2004).

Also, there is uncertainty concerning diagnostic tests. Diagnostic criteria for MS are based mostly on experts' consensus. A gold standard to evaluate new diagnostic tests is lacking. Despite the limited specificity of diagnostic tests in MS, a 'hit hard and early' treatment approach is increasingly promoted by experts and pharmaceutical stakeholders (Freedman 2009). This is likely to result in over-diagnosis and over-treatment (Whiting 2006).

In 2007 the European Union has 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 patients to self-manage their disease as much as possible. In practice, most people with MS claim autonomous roles in decision making although there may be cultural differences (Giordano 2008; Solari 2007). This contrasts with

poor disease related knowledge (Giordano 2010; Heesen 2004). Several studies have outlined communication and information deficits in the care of patients with MS (Heesen 2003; Solari 2007; Vickrey 2000; Wollin 2000). Therefore, MS management guidelines have acknowledged the need for balanced information and patient participation in MS decision making (NCC-CC 2004). Recently, a number of decision aids for people with MS have been developed, some being evaluated in clinical trials (Kasper 2008; Köpke 2009; Prunty 2008).

Description of the intervention

Various patient information tools for MS have been developed. Despite a large amount of information available for example on the Internet, the comprehensibility, up-to-dateness, relevance, validity, and efficacy of this information have not been studied. Available education and information materials include patient information handouts and booklets provided by pharmaceutical companies, charities, and/or self-help groups. Other forms of information provision frequently provided via IT (CDs, Websites) are becoming more and more important. Furthermore information technologies commonly referred to as 'Web 2.0'-systems (podcasts, blogs and social networks) or smart phones and pocket PC technologies might be used to provide the intervention to MS patients. For this review we will include studies with interventions aimed at providing information about MS to persons with MS. The information may be provided in different formats such as printed materials, educational programmes, lectures, audiovisual aids, computer programmes or web sites, decision support tools, direct counselling or combination of any of these.

How the intervention might work

Accurate and unbiased information may help to prevent patients from unrealistic expectations about disease course and effects of therapies. In order to express preferences, patients need sufficient and appropriate information (Coulter 1999). Balanced and relevant information allow patients to participate in making informed decisions together with their physicians (Kasper 2006). Therefore, information provision may not only directly influence patients' knowledge, but also positively affect psychological outcomes, quality of life, sense of control, and health services utilization. Treatment choices, adherence or discontinuation of treatment may become more rational economical. Also positive effects on the disease course could be expected if information provision leads to more effective disease management strategies (Heesen 2007).

Why it is important to do this review

With increased availability of various treatment options for MS care, it is important that patients have access to adequate information in order to make informed choices. In this context, it is imperative to evaluate which information strategies are most effective to enhance informed choice. The best evidence for the efficacy of interventions aiming to provide patients with information should be formed from large, well-conducted (randomised) controlled trials or from meta-analyses. A systematic review is therefore required to identify all trials in this area and to summarise the existing evidence. Potentially, there are several kinds of interventions providing information to people with MS using different strategies and also aiming at different outcome measures. Despite the wide range of information provision, a systematic review summarising the findings of relevant studies has not been conducted so far and is therefore urgently warranted. A number of systematic reviews address different forms of information provision for patients, health-professionals and/or caregivers. One review (Smith 2008) indicated that information provision may have positive effects on knowledge, patient satisfaction, and depression. Active information compared with passive information provision seemed to have a greater benefit at least in some outcome measures. Another review (O'Connor 2009) included 55 trials that showed that decision aids are effective in increasing knowledge and also positively influence decision making, however this review did not include studies addressing MS patients.

OBJECTIVES

1. To evaluate the effectiveness of different information strategies provided to persons with MS with the intention to promote informed choice and thereby improve relevant outcomes.
2. To evaluate the components and the developmental process of the complex interventions used.
3. 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

Randomised, cluster-randomised, or quasi-randomised of information provision interventions compared to standard care will be included. Also, trials comparing two different kinds of information provision will be included.

Types of participants

Patients of all ages with a diagnosis of MS or in the diagnostic process will be included. Criteria of diagnosis will be any established diagnostic criteria (e.g. Schumacher (Schumacher 1965), Poser (Poser 1983), or McDonald (Polman 2005) classification) as used in the original studies.

Types of interventions

Any intervention or group of interventions where subjects or clusters are assigned to either information provision or standard usual care; and studies comparing two types of information programmes will be included.

Interventions will be grouped into the following categories:

1. Disease information, e.g.
 - aetiology,
 - diagnosis,
 - natural course, and/or
 - prognosis of MS.
2. Drug therapies, e.g.
 - immunotherapy,
 - relapse therapy, and/or
 - symptomatic therapies.
3. Other (non-drug) therapies e.g.
 - unidisciplinary interventions (e.g. physiotherapy) and/or
 - multidisciplinary interventions (e.g. rehabilitation programmes with multiple therapies)
4. General information e.g.
 - general health issues
5. Comprehensive information
These may be:
 - websites or
 - comprehensive information programmes

Trials may have used one or a combination of the following types of information provision:

1. information leaflets, booklets, manuals, or pamphlets,
2. educational programmes or lectures,
3. audiovisual aids like videos, tape recordings, or computer programmes/web sites,
4. "web 2.0 systems" as podcasts, social networks (Facebook and Twitter) or other information technologies such as smart phone
5. decision support tools, and /or
6. counselling methods (house visit or phone call).

It seems likely that some interventions e.g. educational programmes were designed as complex interventions i.e. comprise 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 or ineffective components of the interventions. Therefore, supplementary (e.g. qualitative) data produced from the included studies (if available) will be described to allow deeper understanding of the complex interventions and its components. In case of missing information, we will contact authors of primary studies.

Types of outcome measures

Primary outcomes

Primary outcomes will be

- disease related (risk) knowledge measured by any type of validated instruments used in the included studies (e.g. questionnaire or interview), and/or
- 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 1995).

Secondary outcomes

Further outcomes will be

- measures of Informed choice e.g. the Multimodal Measure of Informed Choice (MMIC) (Marteau 2001)
- quality of life measure e.g. MSQOL-54 (e.g. Vickrey 1997) or HAQUAMS (Gold 2001),
- psychological status measures e.g. Hospital Anxiety and Depression Scale (e.g. Airlie 2001),
- treatment choices (e.g. invasive, less invasive, or no treatment), and
- treatment compliance.

Also we will consider

- satisfaction with the information received and with the decisional process,
- hospital admissions and use of health care services
- measures of activities of daily living (ADLs),
- coping e.g. Coping Orientation for Problem Experienced (Goretti 2009),
- disability e.g. EDSS (Kurtzke 1983),
- realisation of role preferences (e.g. Kasper 2008), and
- adverse events as suggested by the Cochrane Consumers & Communication Review Group (CCCRG 2008)

Furthermore, process-related outcomes (e.g. qualitative data) will be described to allow analysis and deeper understanding of the complex interventions used.

Search methods for identification of studies

No language restrictions will be applied to the search.

Electronic searches

The Trials Search Co-ordinator will search the Cochrane Multiple Sclerosis Group's Specialised Register.

Keywords are listed in (Appendix 1).

Information on the Cochrane Multiple Sclerosis Group's Trials Register, and details of search strategies used to identify trials can be found in the 'Specialized Register' section within the Cochrane Multiple Sclerosis Group's module.

Additional databases to be searched by the authors (SK, AG):

1. PsycINFO (Ovid SP) (1967 -) (Appendix 2)

Searching other resources

1. Trial and dissertation registers (Appendix 3) will be checked for unpublished or ongoing trials.
2. Reference lists of published reviews and retrieved articles will be checked for additional trials.
3. Experts in the field will be contacted to identify unpublished or ongoing studies.

Data collection and analysis

Selection of studies

Two authors (SK, AG) will independently examine titles and abstracts of citations obtained from the search and will independently assess articles for inclusion according to the above criteria. Disagreements will be resolved by discussion or, if necessary, referred to a third author (CH).

Data extraction and management

We will design and pilot a data extraction form using a standardised data collection form based on the Consumers & Communication Group's data extraction template and enter data in the current version of RevMan 5 (Review Manager (RevMan)). Data from included studies will be extracted independently by two authors, using the standardised form and checked for accuracy. Data extraction for primary studies in which authors of the review are involved, will be checked by one author not involved in the primary study. We will extract data for: characteristics of participants, baseline data, interventions, duration of intervention, length of follow-up, outcome measures, and adverse events. For dichotomous data, we will extract the number in each treatment group and the numbers experiencing the outcome of interest. For each outcome measure, data will be extracted on every person assessed. To allow for an intention-to-treat (ITT) analysis, we will extract the data irrespective of compliance, whether or not the person was subsequently deemed ineligible, or otherwise excluded from treatment or follow-up. If intention-to-treat data are not available in the publications, "on-treatment" or data of those who completed

the trial will be sought and indicated as such. Study names will not be masked. In case of disagreement, they will consult a third author to reach consensus.

Assessment of risk of bias in included studies

Quality assessment will follow the Cochrane Handbook for Systematic Reviews of Interventions, version 5.0.2 (Higgins 2009). Two authors (SK, AG) will independently assess and score the studies' methodological quality in order to identify any potential sources of systematic bias. Criteria for appraisal of studies will be internal validity and low risk of bias through selection bias, performance bias, attrition bias, and detection bias. We will determine study validity by categorising individual studies into low or high risk of bias. As recommended in the Cochrane Handbook, we will use a two-part tool, addressing six domains (sequence generation, allocation concealment, blinding, incomplete outcome data, selective outcome reporting, and other issues). The first part describes what has been reported in the study. In the second part a judgement concerning the related risk of bias is assigned for each entry, by asking for the adequacy of the study in relation to the entry, such that "Yes" indicates low risk of bias, "No" indicates high risk of bias, and "Unclear" indicates unclear or unknown risk of bias. The domains of sequence generation, allocation concealment (avoidance of selection bias) and selective outcome reporting (avoidance of reporting bias) will be 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) will be considered separately for objective outcomes and subjective outcomes. Incomplete outcome data (avoidance of attrition bias) will be considered separately for different length of follow up (shorter and longer follow up).

Measures of treatment effect

Data extraction will follow the Cochrane Handbook. Summary statistics will be required for each trial and each outcome. For dichotomous data (e.g. informed choice) the effect measure will be odds ratio (OR). The absolute numbers in each group and the numbers experiencing the outcome of interest will be sought and recorded. For continuous data (e.g. risk knowledge) the effect measure will be the mean difference if the same instrument is used or the standardised mean difference if different instruments are used for the same outcome measure. The mean change from baseline, the standard deviation of the mean change, and the number of patients for each treatment group at each assessment will be extracted. Where changes from baseline are not reported, we will extract the mean, standard deviation and the number of participants for each group at each time point, if available.

Unit of analysis issues

We will assess for each study 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

Missing data will be reported. Non-missing random data will be dealt with by replacing the missing data with proxy values (i.e. last observation carried forward). The amount and kind of missing data related to participants' dropout that cannot be retrieved from the original authors will be reported and described in the 'Characteristics of Included Studies' table and the impact will be discussed. The potential impact of the missing data on the results will depend on the extent of missing data, the pooled estimate of the treatment effect and the variability of the outcomes. Variation in the degree of missing data may also be considered as a potential source of heterogeneity. If possible, we will conduct intention-to-treat analyses by imputing outcomes for the missing participants using the last observation carried forward approach. Recognizing that statistical analysis cannot reliably compensate for missing data (Unnebrink 2001), the impact of any assumption will be assessed by trying more than one method as a sensitivity analysis. For example, for dichotomous data, we will first assume that all missing participants in the first group incurred the event and those in the second group did not, after which the opposite will be assumed. When missing data are common, these worst-case/best-case scenarios will cover a very wide range of possible treatment effects and thus the analysis will not be very informative. However, when missing data are not common and this procedure is done across all trials in the review with little impact on the results, it can be concluded that the missing data will not affect the outcome of the review.

Assessment of heterogeneity

Studies will be analysed and presented separately. We will only perform meta-analysis, when studies are sufficiently homogeneous in terms of participants, interventions and outcomes. We will consider both clinical heterogeneity and statistical heterogeneity. Statistical heterogeneity between trials included in each analysis will be tested using I^2 with 95% confidence intervals (CIs) (Ioannidis 2007). In case of evidence for statistical heterogeneity, we will explore this by identifying any results with non-overlapping 95% CIs, creating a subgroup analysis, and seeking to confirm any statistically significant differences between subgroups by comparing the ratio of the difference in the natural logarithm of the relative risks and the standard error of the difference in log relative risks to the standard normal distribution (test for interaction).

Assessment of reporting biases

In order to minimise the risk of publication bias, we will perform a comprehensive search in multiple databases, including searching for unpublished studies. Data from all identified trials for each analysis will be entered into a funnel plot to investigate the likelihood of overt publication bias. If appropriate, other statistical methods e.g. Egger's regression method or Begg's rank correlation method will be used to estimate publication bias (Sterne 2005).

Data synthesis

Meta-analysis will be conducted for interventions of the same category (as outlined above). It is likely that some interventions will include elements of more than one category. In this case comparable interventions (e.g. including information about diagnosis and early drug therapy) will be considered for meta-analysis. Outcomes will be examined as mentioned in the types of outcomes section. Data will be analysed and will be reported in the table of comparisons. Meta-analysis for ordinal or continuous data may require the combination of data from trials using different instruments to assess an outcome. The measure of the treatment difference for any outcome is the mean difference when the pooled trials use the same instrument. The standardized mean difference, which is the absolute mean difference divided by the pooled standard deviation, is calculated when different instruments are used. The duration of follow-up in trials may vary considerably. If the range of follow-up is considered too large to pool all trials into one meta-analysis, the data will be divided into smaller time periods and separate meta-analyses will be conducted for each period. Some trials may contribute data to more than one time period if multiple assessments have been made. For binary outcomes, such as informed choice or no informed choice, the odds ratio will be used to measure treatment effect. Peto odds ratios will be calculated using RevMan 5 Software. 95% Confidence intervals will be calculated for each of the pooled estimates. Presentation of meta-analysis will be carried out in forest plots. If it is not possible to

pool the data, results will be presented in a descriptive review of different interventions and effects.

Subgroup analysis and investigation of heterogeneity

Depending on availability of sufficient data, we will categorize and analyze interventions separately according to:

- patients' disease courses (i.e. Clinical Isolated Syndrome, Relapsing Remitting MS, and Secondary and Primary Progressive MS),
- type of intervention (e.g. active information (e.g. educational programme with participants active involvement or counselling interventions) vs. passive information (e.g. written information only and/or provision of audiovisual material),
- cultural area or cultural group (e.g. North vs. South Europe),
- method of group allocation (i.e. randomised vs. non-randomised),
- "dosage" of intervention (i.e. number of educational sessions, time period of information provision etc.), and
- blinding (i.e. blinded vs. unblinded outcome assessment).

Sensitivity analysis

To incorporate assessment of risk of bias in the review process, we will first plot intervention effects estimates stratified for risk of bias for each relevant domain. If differences in results will be presents among studies at different risk of bias, we will perform sensitivity analysis excluding from the analysis studies with high risk of bias.

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* Indicates the major publication for the study

APPENDICES

Appendix 1. Keywords used to search MS 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. PsychINFO (Ovid SP)

multiple sclerosis.mp. OR exp Multiple Sclerosis/ OR optic neurit*.mp. OR acute disseminated encephalomyelitis.mp. OR exp Encephalomyelitis/ OR myeloptic 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. 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 patient guidance.mp. OR brochure*.mp. OR pamphlet*.mp. OR exp Counseling/ OR counselling.mp. OR telephone call*.mp. OR website*.mp. OR exp Internet/ OR exp Websites/ OR exp Teaching/ or 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. Meta Register of Controlled Trials (<http://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. WHO International Clinical Trials Registry Platform Search Portal (<http://apps.who.int/trialsearch/>) (includes Australian New Zealand Clinical Trials Registry; Chinese Clinical Trial Register (ChiCTR); Clinical Trials Registry - India (CTRI); German Clinical Trials Register (DRKS); Iranian Registry of Clinical Trials (IRCT); ISRCTN Register; Japan Primary Registries Network; The Netherlands National Trial Register (NTR); Pan African Clinical Trial Registry (PACTRI); Sri Lanka Clinical Trials Registry (SLCTR))

3. ISI Web of Science with ISTP Conference Proceedings (<http://apps.isiknowledge.com/>)

4. UMIN Japan Trial Register (<http://www.umin.ac.jp/ctr/>)

5. Australian Digital Theses Program (<http://adt.caul.edu.au/>)

6. Canadian Theses and Dissertations (<http://www.collectionscanada.ca/thesescanada/index-e.htm>)

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CONTRIBUTIONS OF AUTHORS

SK and CH initially planned the study. SK has written the study protocol. AS, FK, AG and CH have substantially commented on draft versions.

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SK, AS, FK, and AG have nothing to declare.

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