Psychosocial adjustment to multiple sclerosis diagnosis: A meta-review of systematic reviews

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Abstract

This meta-review aimed to synthesise evidence on psychosocial adjustment to multiple sclerosis, to identify available treatment models and services for recently diagnosed individuals, and to explore their effectiveness. MEDLINE, CINAHL, EMBASE, PsycINFO, Web of Science, Cochrane Database of Systematic Reviews and grey literature were searched to include systematic reviews on psychosocial adjustment in multiple sclerosis. Two reviewers independently screened and assessed the quality of the selected reviews. Data were synthesised using narrative approach. Overall, thirty systematic reviews were included (with ~131,813 people with multiple sclerosis). A variety of psychosocial factors were identified in relation to adjustment to multiple sclerosis. Seven theoretical models that underpinned the available services and ten different intervention categories (e.g. cognitive behavioural approaches, mindfulness) for adjustment to multiple sclerosis were identified. There was some evidence that these interventions improved quality of life and coping, however, the difference they could make to people's adjustment was inconclusive. It was also difficult to conclude whether these interventions were particularly effective with the newly diagnosed. There is some support for the effectiveness of adjustment interventions. However, there is a need to design and rigorously evaluate support programmes for newly diagnosed people with multiple sclerosis, specifically focusing on information and adjustment support.

Keywords: Multiple sclerosis, adjustment, diagnosis, meta-review

Highlights

- Acceptance is one of the strongest predictors of coping with multiple sclerosis.
- Interventions are needed to provide support and advice for the newly diagnosed.
- Effective interventions tend to be based on theoretical models.
- Theoretical models that focus on psychoeducation and acceptance might be useful.

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Introduction

Diagnosing multiple sclerosis can be a lengthy, complicated and a challenging process due to the lack of a single diagnostic test and the unpredictable nature of the disease. This can cause distress, confusion, dissatisfaction and frustration among individuals at the time around diagnosis (Dennison, Yardley, Devereux, & Moss-Morris, 2011; Edwards, Barlow, & Turner, 2008; Giordano et al., 2011; Solari et al., 2007). Difficulties faced during this period may influence people's views about multiple sclerosis and their future relationships with healthcare teams, leading to problems in adjusting to the diagnosis and disease, and affecting the treatment outcomes (Edwards et al., 2008; Johnson, 2003). Therefore, providing support to individuals around the point of multiple sclerosis diagnosis is important. The provision of support might also have implications in terms of costs to the health services and the society, as well-adjusted individuals have better emotional wellbeing and use services more appropriately and keep their jobs for longer compared to those less well-adjusted (Dennison, 2011; Sweetland, Howse, & Playford, 2012).

However, currently, the support and information people receive around the point of diagnosis is poor (Köpke, Solari, Khan, Heesen, & Giordano, 2014; Methley, Chew-Graham, Campbell, & Cheraghi-Sohi, 2015; Strickland, Worth, & Kennedy, 2017). There is also a limited understanding of which intervention strategies and services are most effective in supporting those newly diagnosed with multiple sclerosis. Psychosocial adjustment interventions may be helpful in terms of supporting people during diagnosis. However, the evidence is lacking on whether such strategies can be successfully implemented and are effective within the diagnostic period in supporting individuals. Therefore, there is a need to

understand the factors associated with psychosocial adjustment and to document the services and support programmes available.

Our initial scoping exercise of the literature revealed that there were several systematic reviews related to adjustment in multiple sclerosis. These reviews had some elements of emotional support around multiple sclerosis that may be useful in consolidating our understanding of this topic. However, each review focussed on a specific aspect of adjustment, therefore, we conducted a systematic review of these reviews (i.e., a meta-review), with the aim of bringing together all the available evidence on psychosocial adjustment in multiple sclerosis, with a specific focus on the period around diagnosis.

The aims of our meta-review of systematic reviews were to identify the: (i) factors related to psychosocial adjustment in multiple sclerosis; (ii) models that underpin interventions and services to facilitate psychosocial adjustment around multiple sclerosis diagnosis; (iii) interventions and services available for psychosocial adjustment around multiple sclerosis diagnosis, (iv) to explore the extent to which these services/interventions are effective.

Methods

We followed Smith, Devane, Begley, and Clarke's (2011) guidelines for conducting meta-reviews. To ensure accountability, integrity and transparency of the completed review, we followed the PRISMA-P guidelines for designing the meta-review protocol (Moher et al., 2015). The meta-review protocol was prospectively registered on PROSPERO (Registration number: CRD42017067697, 10.07.2017).

The search strategy was formulated using the CHIP (Context, How, Issues of Interest and Population) tool (Shaw, 2010). A health sciences librarian, with expertise in systematic review searching, and our Patient and Public Involvement Lead (CB) were also consulted.

Six electronic databases were searched for relevant literature published in the English language: the Cochrane Database of Systematic Reviews, MEDLINE, EMBASE, CINAHL, PsycINFO, and Web of Science. Searches were from the inception of each database to September 2018. The final search strategy was adapted to the syntax and subject headings of each of the databases. The MeSH explode function was used in databases where possible, and the final search terms were combined using Boolean operators ('AND' and 'OR') (See Appendix A for the final search strategy for MEDLINE).

To maximise the potential to identify reports or grey literature not retrieved by the database searches, searches of national and local government and charity websites (e.g., the MS Society, MS Trust, and the Department of Health) and grey literature resources (OpenGrey, PsycEXTRA, and the British Library's EThOS database) were also conducted. Our Patient and Public Involvement team was also consulted to identify additional sources of grey literature. Reference lists of the reviews we included were also searched.

Reviews were included if they: (1) were systematic reviews (reviews were considered to be systematic if the authors defined a strategy to search for studies, appraised their quality and to synthesised their findings); (2) focussed on factors relating to psychosocial adjustment in multiple sclerosis, and the services and interventions available for those at the point of diagnosis, or for those newly diagnosed with multiple sclerosis. Reviews including studies that included people who were diagnosed longer than five years ago were also considered eligible only if the review included data on the diagnosis experiences and psychosocial adjustment. If a review did not provide information on disease duration, but included data on diagnosis experiences and/or psychosocial adjustment, it was included. Reviews focusing on families and carers were also considered eligible, but only if the review included data on the impact of caregiving or family-related factors on psychosocial adjustment of the person with multiple sclerosis at the point of diagnosis. We excluded reviews if they were: (1) in

languages other than English; (2) on conditions other than multiple sclerosis, (3) people under the age of 18 years; (4) about the transition and adjustment to secondary progressive multiple sclerosis; and (5) about the transition from paediatric to adult services. If a review did not provide information on disease duration, and did not include data on diagnosis experiences and/or psychosocial adjustment, we excluded it. We kept our search criteria broad (including 'neurological diseases' as a search term) to be inclusive and in order not to miss any important reviews.

To facilitate screening, all references identified through the searches were imported to an EndNote bibliographic library. The initial screening was undertaken by two reviewers (HG and GT) independently, who scanned the titles and abstracts of all identified references to determine their eligibility for the meta-review. Reviews where there were any uncertainties were screened as full texts, and discrepancies were arbitrated by the review team (led by RdN). Reviews identified as being potentially relevant for inclusion were screened independently by two reviewers (HG and GT) as full texts, using a study selection checklist developed based on our selection criteria. Any disagreements were resolved through discussion with the wider review team. The selection and screening process were recorded step-by-step on a PRISMA flowchart (Moher, Liberati, Tetzlaff, Altman, & The PRISMA Group, 2009) (see Figure 1).

A structured data extraction form was developed and used independently by at least two research team members (ET, KJP, HG or GT) to extract relevant data from the included reviews. Any disagreements were dealt with through discussion with or, if necessary, by arbitration with wider review team. The reviews deemed eligible for inclusion were assessed independently by at least two reviewers (EM, KJP, HG or GT) for methodological quality and risk of bias using the Assessment of Multiple Systematic Reviews checklist (AMSTAR) (Shea et al., 2007). This is a validated quality assessment tool developed for the assessment

of the quality of systematic reviews. Disagreements over quality assessment were resolved by discussion, or arbitrated, if necessary, by the wider review team. No reviews were excluded on the basis of quality appraisal, however more emphasis was given to 'high quality' reviews with an AMSTAR score ≥8 (Pieper, Koensgen, Breuing, Ge, & Wegewitz, 2018) during the synthesis process.

As the articles varied considerably in terms of the review methods and analyses used (e.g., systematic reviews, meta-analyses, meta-syntheses, scoping reviews, etc.) and the outcomes assessed, we opted to conduct a narrative synthesis, which facilitated the exploration of the relationships and findings both within and between the included reviews.

Results

In total, 30 systematic reviews were included in this meta-review (with approximately 131,813 people with multiple sclerosis). Please see Appendix B for the list of included review papers and the assigned reference number for each review paper. The reviews were published between 2003 and 2018. The majority of the individual studies reported in the reviews were conducted in Europe and North America. There were four meta-syntheses (Review 2, 22, 25, 27) and two meta-analyses (Reviews 8 & 9). Fourteen reviews (Reviews 1, 4-7, 11, 13, 15, 18, 20, 24 28, 29) conducted a narrative, integrative or qualitative synthesis (i.e., a form of narrative synthesis to synthesise both quantitative and qualitative papers). Ten reviews (Reviews 3, 10, 12, 14, 16, 17, 19, 21, 23, 26, 30) did not report the type of synthesis they used to synthesise the findings, however they reported their findings using a narrative approach. See Appendix C for characteristics of individual reviews.

Quality ratings for each review can be found in Appendix C. The overall quality of the reviews based on AMSTAR criteria was 'moderate', but varied widely (Mean score = 7.6;

range 2-11 of total possible score of 11). Main weaknesses in the reviews were lack of assessment of the likelihood of publication bias and lack of incorporation of study quality in the conclusions.

Factors relating to psychosocial adjustment in multiple sclerosis

We identified several factors associated with psychosocial adjustment in multiple sclerosis. These were divided into two inter-linked factors, one relating to internal processes (i.e., self) and the other relating to external stressors and resources. Figure 2 summarises both the internal and external factors that this meta-review found were linked to adjustment to multiple sclerosis, and also presents the temporal relationships between the identified factors and adjustment. Negative and positive emotional responses, personal attributes and daily life stressors people with multiple sclerosis experience were found to be associated with the management techniques people used and how people adjust to the multiple sclerosis diagnosis. In addition, external stressors and resources, such as the formal and informal support provision and the diagnostic process were found to play a mediating and moderating role in the relationship between the internal processes and the adjustment. Table 1 lists all the predictors identified in the meta-review.

Negative emotional responses

Reviews identified various negative emotions and behaviours as relevant to patients' psychosocial adjustment. Negative thoughts and emotions that played an important role in poor adjustment included: low mood, distress, fear, anxiety, depression, stress, negative appraisal/interpretation of multiple sclerosis, loss, devastation, learned helplessness, shock, anger, frustration, denial and suicidal thoughts. Poor adjustment was also linked with reduced quality of life (Reviews 3 & 14), poor social functioning, isolation and withdrawal (Reviews 7, 16, 20, 27), poor family life and relationships (Reviews 4, 6, 7, 12, 28), loss of

employment and financial difficulties (Reviews 2, 20, 21, 23), lack of information about multiple sclerosis and services (Review 18), poor coping (e.g., using avoidant emotion-focused coping strategies) (Reviews 7, 16, 22), increased illness severity, uncertainty and unpredictability of the disease (Reviews 2, 4, 5, 7, 9, 20-22, 24, 27-29), lower acceptance of multiple sclerosis diagnosis (Reviews 5, 22, 29), and increased cognitive errors (Review 7).

Several of the high-quality reviews included in this meta-review (AMSTAR ratings ≥8) described illness uncertainty and unpredictability as a significant predictor of mood and adjustment (e.g., Reviews 9, 18, 22, 27). The sense of uncertainty was described as the 'fear of the unknown' in some reviews and found to be at its highest at two time points of individuals' multiple sclerosis journey (i.e., diagnosis and relapse) (Review 27). It was evident in multiple studies that people experienced uncertainty before and after the diagnosis, and it resulted in various negative emotional responses in relation to their symptoms and treatment, affecting adjustment to their diagnosis (Reviews 18, 27). Uncertainty was associated with unpleasant emotions (e.g., loneliness) and depressed mood in several papers, and was found to affect sense of control and ability to make decisions negatively (Reviews 9, 22, 27). The type of multiple sclerosis and the severity of the illness also appeared to be linked to uncertainty and adjustment. For instance, people with moderately severe multiple sclerosis experienced loss of purpose due to uncertainties surrounding their future (Review 27). For people with relapsing remitting forms of multiple sclerosis, the unpredictability of day-to-day health seemed to adversely affect their quality of life (Review 24).

Another significant predictor of mood and adjustment that frequently appeared in the high quality reviews was 'acceptance' (e.g., Reviews 4, 5, 22, 25, 27). It was evident that most people struggled to accept their diagnosis, current or future functional limitations, and their changed identities. One review found that the 'inability to accept' related to the perceived threat that multiple sclerosis represented, and the perception that acknowledging the illness

would limit their self-expression and impact on their self-worth (Review 22). Anxiety and other negative emotional responses, such as shock, anger and frustration were consistently associated with low levels of acceptance and high levels of defiance, denial and resistance (Reviews 5, 22). A meta-synthesis found that the main source of psychosocial problems identified by both the individual and the family were mainly originated from an inability to accept and adapt to the changed identity (Review 2). People who struggled to accept and adapt to their new identities and focused on retaining their previous identities were more likely to experience negative emotional responses (Reviews 2, 5, 22), whereas people who came to terms with their multiple sclerosis diagnosis did not feel the need to deny their diagnosis and new identity, and experienced less unpleasant emotions (Review 22). Acceptance and uncertainty were also found to have a significant relationship, suggesting that the unpredictable nature of multiple sclerosis could make it particularly difficult to accept the multiple sclerosis diagnosis (Review 19) and that accepting the uncertainties could potentially cause fear to subside (Review 27).

Positive emotional responses

Reviews reported that positive emotional responses to multiple sclerosis such as positive mood, optimism, hope and relief aided people's adjustment to multiple sclerosis. In particular, feeling optimistic about the future (Review 7), being hopeful for a cure for multiple sclerosis, and feeling relief that the illness has been identified and that it was not a fatal illness, were associated with positive emotional responses and positive adjustment (Reviews 11, 18, 22). In particular, feelings of relief after diagnosis that the illness has been identified and that it was not a fatal illness were consistently reported and were associated with positive emotional responses and acceptance, resulting in better adjustment (Reviews 11, 18, 22). Feeling optimistic about the future and being hopeful for a cure for multiple sclerosis or for a sense of normality in life were found to have a direct link with acceptance

and better adjustment (Reviews 7, 22). Better adjustment was also linked to better quality of life (Review 3), improved return to work (Review 17), increased access to information about multiple sclerosis and available services and healthcare support (Review 18), and improvement to family life and relationships (Reviews 4, 7, 25, 28). In addition, good two-way communication with health professionals, and being accepted and understood, led to feeling reassured, listened to and taken seriously, and was accompanied by a sense of relief, which in turn resulted in better adjustment (Review 28).

Impact on day-to-day life

There were several reviews that explored what aspects of daily living impacted on adjustment. Worse adjustment was linked to poorer health-related quality of life (Reviews 7, 9, 13, 23, 24), fatigue (Reviews 15, 22, 23), and disrupted engagement in activities (Reviews 7, 9, 21, 22, 24). Conversely, increased levels of positive social functioning (Reviews 7, 9, 11), support-seeking behaviour (Reviews 2 & 7), and remaining in employment (Reviews 16, 17, 23) were linked to better adjustment. More specifically, these reviews found that the loss of valued activities and interests due to multiple sclerosis diagnosis resulted in strong feelings of depression (Review 9), which was mediated and moderated by the inability to accept the diagnosis (Review 22). Another significant predictor of quality of life and adjustment was fatigue (Reviews 15, 22, 23). It was evident that fatigue influenced day-to-day life by negatively impacting on the ability to work and engage in activities (Reviews 15, 23). Fatigue was also associated with feelings of resignation to their own situation and low levels of acceptance, resulting in worse adjustment (Review 22).

The Impact of family on adjustment

Several papers explored how family and relationships were affected by the diagnosis and how this in turn impacted on the person with multiple sclerosis. Studies have suggested that

people who had low quality relationships were more likely to experience depression and poorer health outcomes (Review 4). The family's reaction to and understanding of multiple sclerosis, and their ability to support the patient were linked to adjustment. Family members' mood, level of depression and distress also appeared to be affected by the diagnosis of multiple sclerosis and impacted on the adjustment of person with multiple sclerosis. Typically, the more support and positive interactions by family and carers (e.g., having accepting and supportive relationship, and adopting reciprocal relationship patterns), the better the person with multiple sclerosis will adjust (Reviews 2, 4, 7, 26, 28). Family conflict, negative reactions from significant others, disrupted relationships, lack of communication and understanding, and high levels of carer stress and depression were linked to worse patient adjustment (Reviews 6, 7, 28). One high-quality review that examined the psychosocial correlates of depression in multiple sclerosis found that support provided by family members was a significant predictor of mental health in individuals, with effects sizes ranging from moderate to very large, suggesting that interpersonal relationships play an important role in adjustment to multiple sclerosis (Review 9). However, some reviews also found that receiving a diagnosis resulted in disruptions in interpersonal relationships with family members and friends (Review 24).

Personal attributes

Some reviews found that certain characteristics of the person with multiple sclerosis were associated to their level of adjustment, such as levels of self-esteem (Reviews 4, 9, 12, 15, 29), self-efficacy (Reviews 5, 7, 9, 17), self-confidence (Review 27). In particular, some reviews described changes to identity (loss of pre-diagnosis identity and/or difficulty in accepting new identity) as one of the significant predictors of how people cope with and adjust to multiple sclerosis (Reviews 2, 4, 16, 19, 21, 22, 27). Those who attempted to retain a pre-diagnosis identity which was not compatible with the changed circumstances were more

likely to use avoidance and bracketing coping styles, which were often associated with negative psychosocial outcomes (e.g. social withdrawal, relationship problems and loss of self-worth) (Reviews 2, 19, 27).

Management techniques

Many reviews reported several adjustment techniques and coping strategies (e.g., information seeking, planning, control and self-regulation) that people with multiple sclerosis adopted to manage their situation. Typically, worse adjustment was related to unhelpful cognitive beliefs and behavioural responses (e.g., learned helplessness, diagnosis concealment) (Reviews 2, 7, 9, 22), and avoidance strategies (e.g., avoiding emotions, activities and situations threatening an individual's identity) (Reviews 4, 5, 7, 9, 22, 27). More specifically, at the time of the diagnosis, people with multiple sclerosis often used denial or avoidance coping to bracket the illness in an attempt to maintain normality and preserve pre-diagnosis identities (Reviews 2, 4, 5, 22, 27). However, avoiding emotions or situations that challenge one's identity were found to be maladaptive, resulting in poor adjustment to multiple sclerosis (Reviews 4, 27). Conversely, adaptive and problem-focused strategies appeared to be associated with positive outcomes (e.g., increased social activity, lowered depressive feelings) and this relationship was found to be mediated by certain disease-specific factors (i.e., multiple sclerosis and symptom representations) (Reviews 2, 9). It was also evident that coping with and adjusting to multiple sclerosis was a constant and dynamic process, as people had to re-evaluate and re-appraise their illness and coping strategies as new symptoms emerge or as the disease progresses (Review 2). Positive adjustment was also linked to accepting the diagnosis of multiple sclerosis (Reviews 4, 22, 25, 28, 29), 'cooperative attitude' of patients (i.e., proactive choice to 'take part' in life to maintain a positive outlook, asking and letting others help), accepting assistance from formal support resources (e.g., respite care) (Reviews 25, 26, 28, 29), engaging in psychological interventions (e.g., interventions focusing on cognition,

self-efficacy, coping and self-management) (Review 17), benefit finding (Review 7), spirituality and religion (Reviews 7 & 29), and better self-efficacy strategies (Review 17).

The diagnostic process

Some individual papers identified how the process of being diagnosed affected people's adjustment. Better adjustment was linked with timely support and information provision from health services (Reviews 13, 16, 18, 26, 29), formal support from and access to healthcare professionals (Reviews 4, 9, 10, 12, 17, 18, 29), peer support (Review 29), prior awareness that something was wrong (Reviews 8 & 22), access to early treatment (Review 10), access to healthcare services (Review 18), continuity of care (Review 18), learning empowerment strategies (Review 17), and support-seeking behaviour (Reviews 2 & 7). Worse adjustment was associated with a prolonged investigative diagnostic process (Reviews 18 & 27) and lack of information about diagnosis from professionals (Review 12). In particular, a lack of timely information and difficulty in accessing support services were consistently found to have a direct link to negative emotional responses (e.g., fear, anxiety and distress) (Reviews 9, 18). Timely provision of information and access to support and services were described as necessary for individuals to understand their multiple sclerosis and adopt appropriate coping strategies, mediating emotional reactions and improving adjustment to multiple sclerosis (Reviews 9, 13, 18).

Models of psychosocial adjustment

We were interested in how researchers explained how people with multiple sclerosis made sense of their psychosocial adjustment, and what theory or models underpinned the interventions that aided people's adjustment to multiple sclerosis. These models helped predict outcomes of interventions, explained the mechanisms that made the intervention

work, or assessed the overall utility of the interventions. The models identified from 18 of the included reviews were:

(1) Working model of adjustment to multiple sclerosis (Dennison, 2011), incorporating helpful/unhelpful factors, behaviours, beliefs, personality, values and goals;

(2) Coping theories and models, and health psychology models of health behaviour and belief;

(3) Model of emotional adjustment and hope (Soundy, Roskell, Elder, Collett, & Dawes, 2016), representing the combination of an emotional response, the ability to integrate and adjust to multiple sclerosis and the expression of a patient's hope;

(4) Model of the psychological impact of the unpredictability of multiple sclerosis (Wilkinson & das Nair, 2013), explaining the psychosocial impact of unpredictability over the course of multiple sclerosis;

(5) Protection motivation model (Rogers, 1975), incorporating perceived severity of a threatening event, vulnerability, the efficacy of the recommended preventive behaviour, and the perceived self-efficacy;

(6) Social cognitive theory (Bandura, 1989), suggesting that an individual's knowledge acquisition can be directly related to observing others through social interactions and experiences; and

(7) Cognitive Analytic Framework informed sequential diagrammatic reformulation of reciprocal roles (Jones, Walsh, & Isaac, 2017), explaining the key relational themes in multiple sclerosis and demonstrating how reciprocal roles can be linked with adjustment.

We also identified the following six approaches to psychotherapy that were used as models when designing interventions: (1) Cognitive Behavioural Therapy, (2) Mindfulness, (3)

Acceptance and Commitment Therapy, (4) Motivational interviewing, (5) Psychoeducation, and (6) Supportive counselling/psychotherapy.

Table 2 provides the list of models and the reviews the models were extracted from.

The following frameworks (i.e., foundational underpinnings that guide development of conceptual and theoretical models (Polit & Beck, 2017)) and guidelines (i.e., a set of recommendations resulting from research and 'best' practice) were also identified as relevant to psychosocial adjustment in multiple sclerosis:

(1) The European Multiple Sclerosis Platform (European Multiple Sclerosis Platform, 2008) code of practice on provision of clear, concise and high quality interventions was used to highlight the need for information provision for people with multiple sclerosis to empower them to self-manage their condition to the greatest degree possible (Review 13);

(2) The International Classification of Functioning, Disability and Health (ICF) (World Health Organization, 2002) was utilised as a framework to classify the spectrum of psychosocial and functional difficulties experienced by people with multiple sclerosis with an aim to provide a person-centred and holistic approach to healthcare and treatment (Reviews 9 & 23);

(3) The National Institute for Health and Clinical Excellence (NICE) multiple sclerosis guidelines (National Institute for Health and Clinical Excellence, 2004) were used to emphasise the provision of support (including emotional) for newly diagnosed people with multiple sclerosis and those caring for people with multiple sclerosis (Reviews 4, 17, 21); and

(4) The National Service Framework for Long-Term Conditions (Department of Health, 2005) was used to highlight the utilisation of appropriate expertise for assessing and managing emotional impairments (Review 21).

Some of these models or frameworks were either developed directly as a result of the review to explain the relationships between factors related to adjustment, or used as the theoretical basis to support the provision of information and support for newly diagnosed people with multiple sclerosis and their families/carers.

Interventions for psychosocial adjustment around multiple sclerosis diagnosis

Eleven reviews identified the use of 64 different types of interventions for adjustment to multiple sclerosis, or for those newly diagnosed with multiple sclerosis, which fell within 10 broad intervention categories. Interventions included cognitive behavioural approaches (Reviews 8, 10, 17, 19, 21, 24), relaxation activities (Reviews 10, 17, 19, 24), physical activities (Reviews 3, 10, 17, 19, 30), educational programmes (Reviews 1, 13, 19), mindfulness (Reviews 10, 19, 30), counselling (Reviews 1, 17), and social support groups (Reviews 10 & 17). There were also coping-based, self-management and symptom management interventions (Reviews 1, 3, 10, 13, 17, 19, 24). Other interventions included Acceptance and Commitment Therapy (Review 10), combined (multi-modal) wellness-based interventions (Review 30), and supportive psychotherapy (Review 24). See Table 3 for the full list of interventions identified.

Interventions were delivered in different formats, such as groups (Reviews 3, 8, 19, 21, 24, 30), one-to-one (Reviews 3, 8, 19, 24, 30), via information booklets (Reviews 13, 19, 24), worksheets (Review 13), informational CD (Review 13), supplementary audio and video content (Review 30), over the telephone (Reviews 1, 8, 19, 24), over the internet (Skype™ and videoconferencing) (Reviews 1 & 30), and using virtual reality (Review 1). Interventions were typically led by nurses (Reviews 1, 8, 13, 17, 19, 21, 24), psychologists (Reviews 8 & 21), occupational therapists (Review 1), social workers (Review 8), physicians (Review 13), or self-directed by the person with multiple sclerosis (Review 10). The duration of

interventions varied widely, with the shortest lasting 4 weeks (Review 1, 19, 30) and the longest lasting 60 months (Review 3). The frequency of sessions also varied, with the most frequent being daily sessions (Review 1, 24, 30) and the least frequent being monthly (Review 1).

Effectiveness of Interventions

Detailed information about effectiveness of the interventions (including effect sizes, where this was available) for all the included reviews can be found in Appendix D. Interventions that were found to be effective included cognitive behavioural techniques, coping skills training, self-management and symptom management, relaxation activities and educational programmes. With these interventions, improvements were found on quality of life (Reviews 1, 3, 10, 13, 19, 24, 30), coping (Reviews 8, 10, 19, 24, 30), self-management (Review 17), community integration (Review 8), depression (Reviews 1, 8, 10, 24, 30), anxiety (Reviews 1, 10, 19, 24, 30), fatigue (Reviews 1, 8, 10, 17, 30), psychosocial adjustment (Review 17), self-efficacy (Reviews 10 & 17), knowledge gain (Review 13 & 17), and job satisfaction (Review 23). Overall, there was conflicting and inconclusive evidence regarding whether or not these improvements were statistically significant and/or clinically important. It was also unclear how effective these interventions were in improving individual's *adjustment to multiple sclerosis*. In addition, as most of these interventions were administered to and tested with mixed groups of people with multiple sclerosis (i.e., newly diagnosed and people diagnosed longer than 5 years), it was difficult to conclude whether these interventions were particularly effective with a newly diagnosed patient group. Table 4 presents a summary of the intervention categories (and specific interventions) that were found to improve outcomes from the included reviews with an AMSTAR score of ≥8. However, on the basis of evidence from the high-quality reviews (AMSTAR score of ≥8 and included RCT studies), educational programmes (Review 8), cognitive behavioural interventions, relaxation activities, and self-

management and symptom management interventions (Review 24) significantly improved knowledge gain, anxiety, depression and problem-focused coping. Only one meta-analysis (Review 8) reported the effectiveness of interventions (but received an AMSTAR quality score of 7), and found significant improvements with cognitive behavioural interventions and counselling for depression (dw = 1.34) and fatigue (dw = 0.42).

Recommendations for future interventions/services

Thirteen reviews discussed what services or service improvements should be made available for those diagnosed with multiple sclerosis. Recommendations to health services included: more multi-disciplinary team involvement (Reviews 9 & 15), more effective communication from healthcare professionals (Review 18), and better access to professionals (Review 16). To improve information provision, more and/or better information from MS Society (Review 18), and more reliable and clear information (Reviews 16 & 17) were recommended. Recommendations were also made with regards to the specific types and formats of interventions for people with multiple sclerosis. These included: tele-rehabilitation (Review 1), practical support (Review 9), peer support (Review 9), self-management (Review 9 & 22), and group treatments (Review 21). Interventions highlighting 'acceptance' (Review 28) and/or services that includes or works with the family (Reviews 4, 6, 26, 28) were also recommended for improving adjustment to multiple sclerosis. Other recommendations included providing employment specialists (Review 23) and vocational psychological services for younger people and those with recent diagnosis (Reviews 11 & 16). Detailed recommendations extracted from included reviews can be found in Appendix E.

Discussion

Several factors have consistently been shown to be associated with psychosocial adjustment to multiple sclerosis. Of these, the strongest evidence was for the link between mood and

adjustment, which is in line with the adjustment literature for other chronic illnesses (Johansson, Rydén, & Finizia, 2011; Taylor, Todman, & Broomfield, 2011). While low levels of anxiety and depression were consistently linked with poor adjustment, having a positive mood and positive attitude led to better adjustment outcomes. Another factor that was consistently associated with low levels of adjustment was the degree of perceived illness uncertainty and unpredictability. The perception of unpredictability is associated with a sense of curability and controllability (Cameron & Moss-Morris, 2010), and high levels of perceived unpredictability may decrease the perceived control people can have on multiple sclerosis (Topcu, Buchanan, Aubeeluck, & Garip, 2016), causing further anxiety (Armfield, 2006), which may lead to poor adjustment.

Furthermore, our review suggests that many people with multiple sclerosis experience psychological stress in relation to worries about diagnosis and prognosis, challenges faced during the diagnostic process, and disruption of everyday life functions and roles. Some evidence was also found for links between adjustment and variables concerned with social functioning, relationships with family and friends, employment and financial situation, and personal attributes (e.g., self-efficacy, self-esteem, and self-identity).

Management techniques and strategies that are used to cope with multiple sclerosis were important factors that had a mediating and moderating effect in the relationship between perceived stress and adjustment. There were several techniques that people with multiple sclerosis adopted to manage their situation. In line with the adjustment literature for other chronic illnesses (Kvillemo & Bränström, 2014; Shakeri et al., 2015), worse adjustment was related to certain avoidant emotion-focused coping strategies, whereas better adjustment was linked to engaging in problem-focused coping styles.

We found that stress and coping models of adjustment might be useful in explaining adjustment to multiple sclerosis. The majority of studies in the general adjustment literature are based on Lazarus and Folkman (1984) Stress and Coping Model, in which stress response is defined as the result of a transaction between an individual and his/her environment where a set of cognitive, affective and coping factors mediate this transaction. According to this model, it is the individual's appraisal of the significance of a situation, rather than its objective characteristics, and his/her ability to cope with the situation that determine the coping response (Lazarus & Folkman, 1984). Previous research has supported the utility of the stress and coping model in explaining adjustment to multiple sclerosis (Pakenham, 1999). In line with this model, interventions targeting an individual's appraisals, coping resources and coping strategies should moderate the negative effects of being diagnosed with multiple sclerosis. However, many researchers have argued that this model could potentially underestimate the complexity of associations between stressors, appraisals and coping (Goldsworthy & Knowles, 2008; Zarit, 1989). It also places emphasis on the individual to reappraise the illness process as 'non-threatening' (Folkman & Lazarus, 1988). However, in the context of multiple sclerosis, it is not always possible to achieve this reappraisal due to the unstable, unpredictable and incurable nature of the disease. Indeed, it is likely that the demands of multiple sclerosis will increase and intensify as the disease progresses, making reappraising the situation as 'benign' and 'non-threatening' a challenging process. Therefore, more comprehensive and disease-specific models could be more useful in fully understanding the adjustment process to multiple sclerosis diagnosis, as generic models of stress and coping do not consider the unique aspects of the diagnosis (e.g., the unpredictable nature of disease).

Our meta-review identified other models that could be useful in explaining adjustment to multiple sclerosis. Of these models, some were developed as a result of the individual reviews to specifically understand adjustment to multiple sclerosis (e.g., the working model

of adjustment to multiple sclerosis (Dennison, 2011), model of emotional adjustment and hope (Soundy et al., 2016), model of the psychological impact of the unpredictability of multiple sclerosis (Wilkinson & das Nair, 2013)). Although these models were postulated to be important in explaining adjustment to multiple sclerosis *in general*, it is unclear whether they are useful in explaining adjustment to the *process of being diagnosed* to multiple sclerosis, as none of them specifically targeted the challenges faced during the period around diagnosis. Therefore, there is a need for a comprehensive theoretical framework that focuses on the period surrounding the multiple sclerosis diagnosis.

Moreover, although we have identified interventions that had some evidence showing improvements in coping with MS, mood and quality of life, how effective they were for newly diagnosed patient groups was uncertain. This was because most of the interventions were delivered to and tested with mixed groups of people with multiple sclerosis (including people diagnosed longer than five years). It was also difficult to definitively uncover what interventions work, for whom and why from the available evidence.

Strengths and limitations

The use of meta-review methodology enabled us to synthesise the available evidence relating to a broad range of different approaches addressing psychosocial adjustment in multiple sclerosis. This provides a comprehensive overview for researchers, clinicians, policy makers and commissioners of healthcare services, to inform policy and practice. As strengths, we adhered to Smith et al.'s (2011) respected meta-review guidelines to conduct the meta-review and followed the PRISMA guidelines (Moher et al., 2015) to consolidate consistency in conducting and reporting the review, and to ensure its accountability, integrity and transparency. Each stage of the review was conducted by at least two reviewers independently, and discussed with the wider review team to ensure rigour and trustworthiness

of the findings. Any discrepancies were discussed with the review team until a consensus was reached. Another strength was the involvement of our patient-partner (CB) and our Patient and Public Involvement Group in the meta-review process (to identify and formulate the research question, design the protocol, search grey literature, screen and synthesise data), which helped strengthen the quality and relevance of our review, offering a patient perspective on the whole process.

Nevertheless, this meta-review also has limitations. Our meta-review relied on the quality of the included systematic reviews (e.g., their search strategies, accurate data extraction, synthesis and reporting). There might be considerable overlap in terms of primary studies included in the reviews which may result in unwarranted emphasis on findings of commonly cited primary studies. However, due to poor reporting, we were unable to investigate the level of overlap in primary studies across the included reviews. According to Pinnock et al. (2017), "*resynthesizing materials that have already been synthesised risks further loss of detail and has the potential for erroneous assumptions, especially if the primary focus of the review did not directly align with the questions of the meta-review*" (p. 28). This meta-review is open to the same risk. Therefore, we acknowledge that conducting a systematic review of systematic reviews distances us (the reviewers) from the primary data, causing a possible loss of depth and reflexivity at the primary level (Pearce et al., 2015). However, the involvement of our patient-partner provided further confidence that our conclusions are firmly rooted in the best available evidence and centred on experiences of people with multiple sclerosis.

Although we have conducted a comprehensive search of both published and grey literature, we acknowledge that the risk of publication bias remains as primary studies with negative results are less likely to be published. Additionally, for practical reasons, we excluded reviews published in languages other than English which might have introduced further bias or missed key literature. Furthermore, the heterogeneity of individual primary studies limited

or prevented many reviewers to perform meta-analysis or meta-synthesis. Of the 30 included reviews, there were only four meta-syntheses and two meta-analyses. This presented challenges for our meta-review and limited the conclusions we could draw. Another intrinsic limitation to meta-reviews is that they can only report on studies that has previously been captured in published or grey literature (Harvey et al., 2017; Pinnock et al., 2017), meaning recently published primary study findings not yet included in a review were not included in this meta-review. In addition, it was not possible to make a more nuanced assessment of how different types of multiple sclerosis (e.g., relapsing-remitting, primary progressive) relate to adjustment, as different types may pose different challenges for the individuals. However, neither the included reviews nor the primary studies appeared to make this distinction between multiple sclerosis types. Future research should therefore outline outcomes based on multiple sclerosis types and other clinical characteristics (e.g., comorbidities).

Conclusion

The results of this meta-review indicate that there is need to design and test a support programme, structured using theoretical frameworks, that specifically targets newly diagnosed people with multiple sclerosis to provide effective support and advice around the point of diagnosis. This could facilitate the adjustment to and coping with multiple sclerosis diagnosis, and enhance patients' health and wellbeing. Our review highlights that adjustment can be established by balancing both internal and external stressors by using the appropriate coping and support resources. Early information and support provision may also consolidate patients' future relationships with healthcare teams, leading to better outcomes from treatment and more positive adjustment.

Our meta-review has also highlighted some important determinants of psychosocial adjustment, which could be targeted when designing support interventions for newly

diagnosed people. For instance, acceptance of multiple sclerosis (i.e., diagnosis, current or future functional limitations and changed identities) consistently emerged as one of the strongest predictors of coping with multiple sclerosis, and has been found to be inversely related to depression and poor adjustment, and positively linked to better adjustment outcomes such as life satisfaction. As such, psychological interventions targeting acceptance might be beneficial in alleviating psychological distress among newly diagnosed people with multiple sclerosis. This review also highlighted that certain MS symptoms (e.g. fatigue) play an important role in adjusting to the illness. Therefore, it is important not only to support individuals to manage symptoms that are debilitating and directly or indirectly impacting on adjustment, but also tailor interventions around these symptoms so that individuals may benefit more from them.

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Authors' contributions

GT, AD, NE, CB, DF & RdN designed the protocol. GT and HG performed searches and screened the retrieved papers. GT, HG, ET and KJP extracted data and appraised the included reviews. GT, HG, SC, JMM and RdN synthesised the extracted data. GT, HG and RdN drafted the manuscript. CB provided patient and public involvement input to the key stages of the review process. All authors were involved in the interpretation of the data and critically revised the work, and all have approved the final version to be published.

Conflict of interest

RdN is an author in two reviews that were included in this meta-review. GT is an author in one review that was included in this meta-review. All other authors declare that they have no conflicts of interest.

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Figures

Figure 1. PRISMA flow diagram describing the literature search and screening process. Adapted from Moher et al., 2009.

Figure 2. A conceptual map of adjustment to multiple sclerosis, representing the temporal relationships between the identified psychosocial factors and adjustment

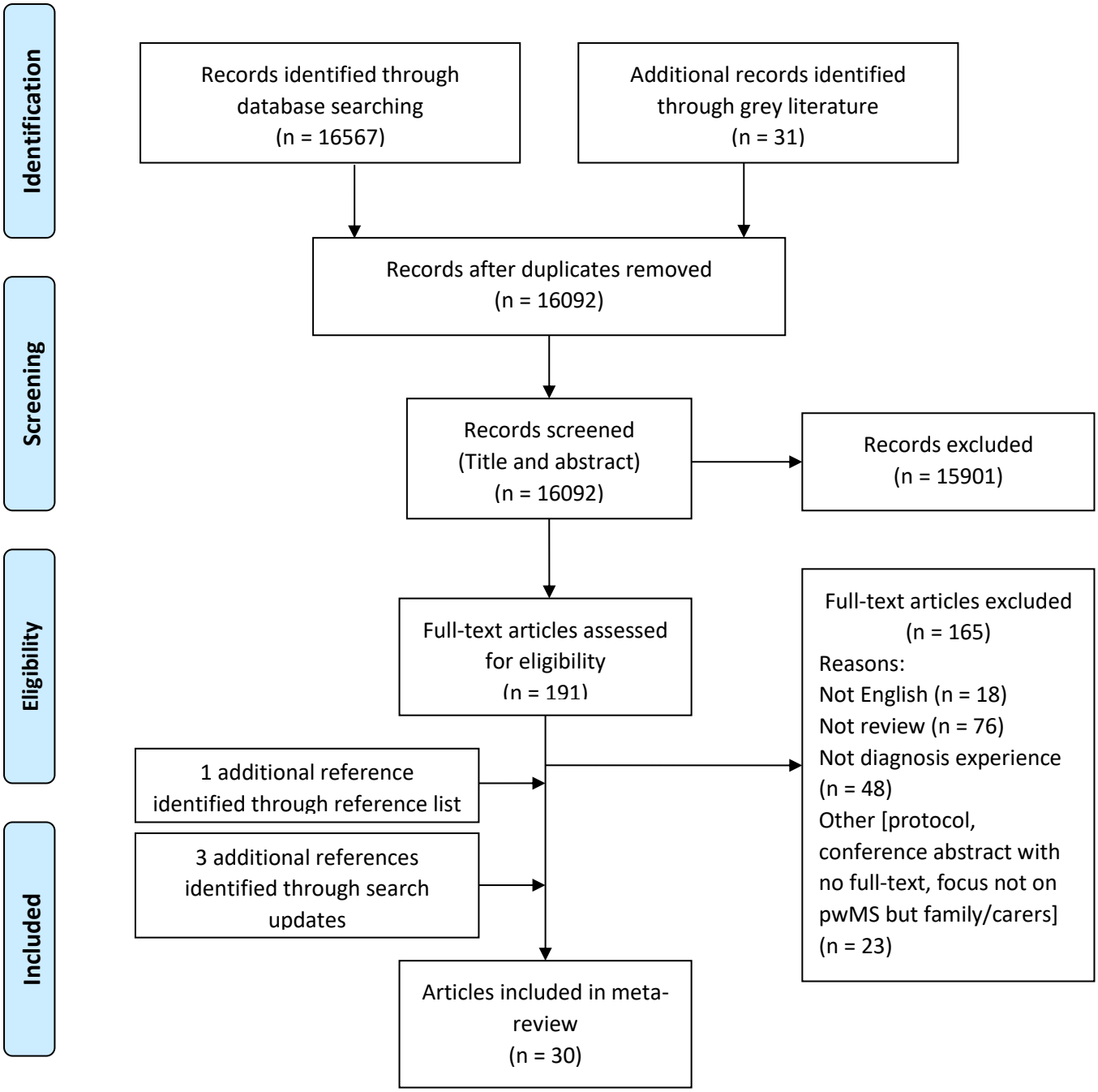

Figure 1. PRISMA flow diagram describing the literature search and screening process. Adapted from Moher et al., 2009.

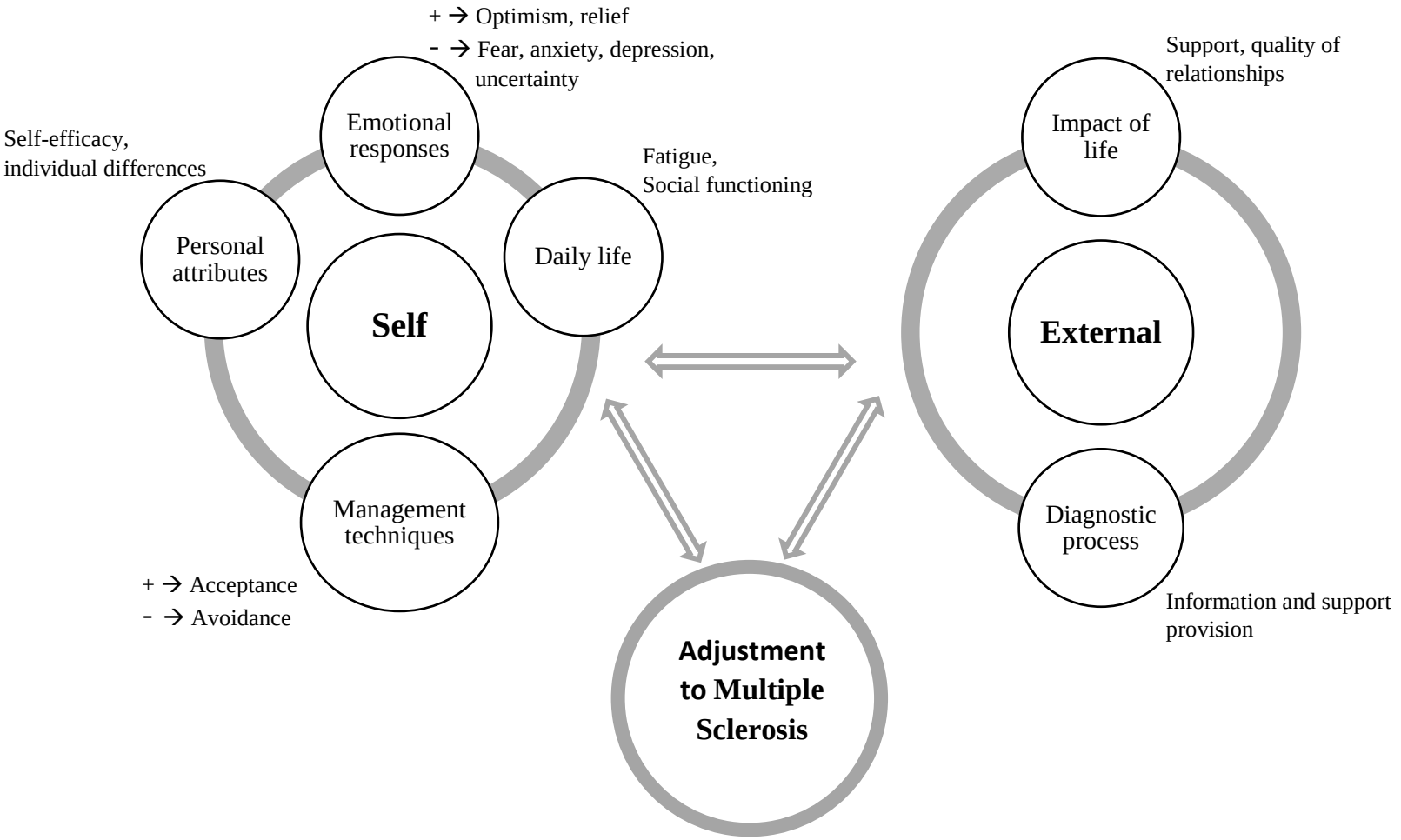

Figure 2. A conceptual map of adjustment to multiple sclerosis, representing the temporal relationships between the identified psychosocial factors and adjustment.

Tables

Table 1. List of factors relating to psychosocial adjustment in multiple sclerosis.

Category	Factor	N Studies (/30)	Review reference numbers
Positive emotional response	Positive mood/emotions	8	4, 7, 9, 16, 17, 18, 22, 25
	Relief	4	11, 18, 22, 28
	Hope	2	7, 22
	Optimism	1	7
	Positive attitude	1	29
Negative emotional response	Illness uncertainty/unpredictability	12	2, 4, 5, 7, 9, 18, 19, 21, 22, 24, 27, 28
	Illness Acceptance	11	2, 4, 5, 7, 9, 11, 19, 22 25, 26, 29
	Anxiety	9	5, 6, 7, 9, 16, 18, 22, 23, 27
	Depression	9	3, 4, 7, 9, 14, 16, 17, 20, 23
	Low mood/negative emotions	8	3, 4, 7, 12, 14, 21, 22, 27

Category	Factor	N Studies (/30)	Review reference numbers
	Stress	4	2, 3, 7, 23
	Distress	3	4, 7, 18
	Fear	3	18, 22, 27
	Shock	3	18, 19, 22
	Denial	2	7, 22
	Suicide/suicidal thoughts	2	7, 20
	Loss	1	27
	Devastation	1	18
	Negative appraisal/interpretation of multiple sclerosis	1	7
	Anger	1	22
	Frustration	1	22
Impact on day to day life	Social functioning	13	2, 7, 9, 11, 12, 16, 17, 20, 21, 23, 24, 26, 27

Category	Factor	N Studies (/30)	Review reference numbers
	Health-related quality of life	12	3, 7, 9, 11, 12, 13, 14, 15, 16, 17, 23, 24
	Employment and financial situation	9	2, 3, 7, 16, 17, 20, 21, 24, 23
	Activities and Interests	8	7, 9, 11, 12, 15, 21, 22, 24
	Fatigue	3	15, 22, 23
The impact of family on adjustment	Family/friends	9	2, 4, 7, 12, 15, 24, 26, 28, 29
	Relationships (spouse)	5	2, 4, 7, 26, 28
	Carer's mood/emotions	2	4, 25
	Carer's depression	2	6, 7
	Carer's distress	2	3, 6
	Carer's response to multiple sclerosis	1	7
	Carer's/partner understanding of multiple scleorisus	1	4
	Carer/partner support to patient	1	4

Category	Factor	N Studies (/30)	Review reference numbers
Personal Attributes	Identity	7	2, 4, 16, 19, 21, 22, 27
	Self-esteem	5	4, 9, 12, 15, 29
	Self-efficacy	4	5, 7, 9, 17
	Individual Differences	2	3, 7
	Age of patient	2	20, 26
	Gender of patient	2	4, 20
	Self-confidence	1	27
Management Techniques	Coping	9	2, 4, 7, 9, 16, 22, 26, 27, 29
	Control and self-regulation	6	7, 9, 11, 22, 27, 29
	Avoidance	6	4, 5, 7, 9, 22, 27
	Acceptance	5	4, 22, 25, 28, 29
	Benefit finding	4	2, 4, 7, 22
	Cooperation	4	25, 26, 28, 29
	Symptom management	4	2, 4, 7, 29

Category	Factor	N Studies (/30)	Review reference numbers
	Learned Helplessness	3	2, 7, 9
	Planning	3	2, 11, 29
	Symptom/diagnosis concealment	2	2, 22
	Sense of curability	2	9, 22
	Spirituality/religion	2	7, 29
	Diagnosis disclosure	1	2
	Engagement in Rehabilitation	1	3
	Other strategies	6	2, 7, 15, 17, 22, 29
The Diagnostic Process	Professional Support	8	4, 9, 10, 12, 17, 18, 29
	Information provision	5	13, 16, 18, 26, 29
	Support seeking behaviour	2	2, 7
	Awareness that something is wrong	2	18, 22
	Experience of the diagnostic process	2	18, 27
	Access to treatment	1	10

Category	Factor	N Studies (/30)	Review reference numbers
	Access to services	1	18
	Continuity of care	1	18
	Interventions	1	17
	Peer support	1	29

Note. Please see Appendix B for the list of included reviews and their corresponding reference numbers.

Table 2. List of models and frameworks for psychosocial adjustment and/or newly diagnosed people with multiple sclerosis.

Model	Number of reviews	Review reference numbers
Cognitive behavioural therapy	6	8, 10, 17, 19, 21, 24
The National Institute for Health and Clinical Excellence guidelines (NICE, 2004)	3	4, 17, 21
Mindfulness	3	10, 19, 30
Working model of adjustment (Dennison, 2011)	2	5, 7
Coping theories and models	2	24, 29
Psychoeducation	2	8, 21
Supportive counselling/psychotherapy	2	8, 24
The International Classification of Functioning, Disability and Health	2	9, 23
Health psychology model of health behaviour and belief	1	24
Social cognitive theory	2	1, 24
Model of emotional adjustment and hope (Soundy et al., 2016)	1	22

Model	Number of reviews	Review reference numbers
Model of the psychological impact of the unpredictability of multiple sclerosis (Wilkinson et al., 2013)	1	27
Protection motivation model	1	13
Cognitive Analytic Framework informed sequential diagrammatic reformulation of reciprocal roles	1	28
The European Multiple Sclerosis Platform (EMSP, 2007) code of practise	1	13
The National Service Framework for Long-Term Conditions (Department of Health, 2005)	1	21
Acceptance and commitment therapy	1	10
Motivational interviewing	1	8

Table 3. List of interventions for psychosocial adjustment in multiple sclerosis.

Intervention		Number of reviews	Review reference numbers
Cognitive behavioural interventions	Cognitive behavioural therapy group	3	10, 21, 24
	Cognitive behavioural therapy for adjustment	1	21
	Cognitive behavioural therapy for fatigue	1	19
	Cognitive behavioural therapy one-to-one and psychotherapy in group	1	19
	Cognitive behavioural therapy with relaxation and exercise	1	10
	Cognitive behavioural strategies and body exercises	1	19
	Cognitive behavioural therapy one-to-one	1	8
	Stress reduction training including cognitive behavioural therapy and relaxation	1	24
Relaxation activities	Relaxation training	3	10, 17, 19
	Biological-oriented imagery treatment with relaxation	1	24
	Stress reduction training including Cognitive behavioural therapy and relaxation	1	24

Intervention		Number of reviews	Review reference numbers
Physical activities	Aerobic training	2	3, 30
	Cognitive behavioural strategies and body exercises	1	19
	Internet exercise programme	1	1
	Internet fatigue management group	1	1
	"OPTIMISE" group programme for skills, knowledge and confidence to seek health promoting activities	1	13
	Exercise training (assisted-cycling, body weight support treadmill training, total-body recumbent stepper training, aquatic exercise)	1	30
	Other physiotherapy interventions	1	17
	Tai chi programme	1	3
Educational programmes	Educational group and Information booklet about MS	1	13
	Educational programme	1	19
	Educational interview with informational CD and booklet	1	13
	Information booklet about multiple sclerosis and interactive worksheet	1	13

Intervention		Number of reviews	Review reference numbers
	Oral informational presentation	1	13
	Printed decision aid about fertility and MS	1	13
	Telephone based education + counselling	1	1
Coping skills training	Coping skills group	3	10, 19, 24
	Coping strategies/skills	1	17
	Self-efficacy training	1	17
Counselling	Counselling	2	8, 17
	Motivational interviewing	1	8
	Telephone based education + counselling	1	1
Social support groups	Supportive expressive group	2	10, 17
	Insight oriented group	1	10, 17
	Psychodrama group	1	10
	Relationship enrichment workshop	1	19
Mindfulness	Mindfulness	2	10, 30

Intervention		Number of reviews	Review reference numbers
	Modified Mindfulness Based Stress Reduction intervention	1	19
	Mindfulness based cognitive therapy	1	30
Self-management and	Energy conservation/fatigue management course	3	3, 13, 19
symptom management	Adjustment and symptom management group	2	10, 19
	Self-care strategy programme and Information booklet	2	13, 19
	Assistive technology	1	17
	Autogenic training	1	19
	Cognitive rehabilitation	1	24
	Dietary interventions	1	17
	Disease modifying drug intervention	1	3
	Modified Mindfulness Based Stress Reduction intervention	1	19
	Neurological compensatory training	1	24
	Self-management course	1	19
	Self-management group	1	10

Intervention		Number of reviews	Review reference numbers
	Speech and language interventions	1	17
	Symptom treatment drug intervention	1	3
Others	Adjustment group	2	19, 24
	Unspecified rehabilitation programme	2	3, 19
	Acceptance and commitment therapy	1	10
	Expert rehabilitation nursing interventions	1	17
	Lifestyle change class	1	19
	Meditation	1	19
	Mood and self-efficacy group	1	10
	Occupational therapy interventions	1	17
	Social work interventions	1	17
	Supportive psychotherapy	1	24
	Vocational rehabilitation	1	17
	Dietary interventions	1	30

Intervention	Number of reviews	Review reference numbers
Combined (multi-modal) wellness based interventions	1	30

Table 4. Interventions reported to be effective, for systematic reviews with an AMSTAR score of ≥8

Intervention category	Intervention	Outcome
Cognitive behavioural interventions	Stress reduction training including cognitive behavioural therapy and relaxation (Review 24)	Anxiety Depression Perceived distress Problem-focused coping
Relaxation activities	Relaxation training (Review 10)	Body image Depression Disease coping
	Biological-oriented imagery treatment with relaxation (Review 24)	Anxiety
	Stress reduction training including Cognitive behavioural therapy and relaxation (Review 24)	Anxiety

Intervention category	Intervention	Outcome
		Depression
		Perceived distress
		Problem-focused coping
Physical activities	"OPTIMISE" group programme for skills, knowledge and confidence to seek health promoting activities (Review 13)	Quality of life
Educational programmes	Educational interview with informational CD and booklet (Review 13)	Knowledge gain
	Oral informational presentation (Review 13)	
	Printed decision aid about fertility and MS (Review 13)	
Coping skills training	Coping skills group (Review 10)	Improved adaptability
	Coping strategies/skills (Review 19)	Coping behaviour and well-being

Intervention category	Intervention	Outcome
		Gains in psychosocial role performance
Counselling	Telephone based education + counselling (Review 1)	Fatigue
Social support groups	Supportive expressive group (Review 10)	Depression
	Insight oriented group (Review 10)	Depression
	Psychodrama group (Review 10)	Improved relationships
		Positive behaviour changes
Self-management and symptom management	Adjustment and symptom management group (Review 10)	Depression,
	Self-care strategy programme and Information booklet (Review 13)	Quality of life
	Cognitive rehabilitation (Review 24)	'Mental health subscale'
		Depression

Intervention category	Intervention	Outcome
	Self-management group (Review 10)	Disease impact
Others	Mood and self-efficacy group (Review 10)	Anxiety
		Resilience
		Self-efficacy

Appendices

Appendix A. Meta-review MEDLINE Search Strategy (Ovid MEDLINE(R) 1946-present).

1. exp Multiple Sclerosis/
2. (MS or "multiple sclerosis" or ((neurodegenerat* or autoimmun* or demyelinat* or neuro-degenerat* or auto-immun* or de-myelinat*) adj3 (disease* or disorder* or condition* or dysfunction*))).mp.
3. exp Neurodegenerative Diseases/
4. exp Autoimmune Diseases/
5. exp Demyelinating Diseases/
6. or/1-5
7. ((newly or recently or currently) ADJ3 diagnos*).mp.
8. exp Patients/
9. pwMS.mp.
10. MSer*.mp.
11. exp Caregivers/ or exp Carer/
12. ((informal* or spous* or partner* or wife or wives or husband* or "significant other*" or famil* or relation* or relative* or parent* or father* or mother* or sibling* or brother* or sister* or child* or son* or daughter* or neighbo*) adj2 (support or care*)).mp.
13. exp Family/
14. exp Spouses/
15. 7 OR 8 OR 11 OR 12 OR 13 OR 14
16. exp Diagnosis/ or exp Delayed diagnosis/ or exp Diagnosis, Differential/ or exp Early diagnosis/
17. ((diagnos*) or ((early or delayed or late or differential) ADJ2 diagnos*)).mp.
18. exp “Health services needs and demand”/
19. ((need* or problem* or well-being or wellbeing or “well being”) adj2 (unmet or unaddressed or unreali?ed or emotional* or physical* or psychological* or information*)).mp.
20. exp Depression/
21. exp Anxiety/ or exp Anxiety Disorders/
22. exp Mental health/
23. exp Stress, psychological/
24. exp adaptation, psychological/
25. exp Social support/
26. exp Social Adjustment/
27. exp Emotional Adjustment/
28. (depress* or anxiety or stress or distress).mp
29. (coping or cope*).mp.
30. ((emotional* or early or social*) ADJ3 (support or adjust*)).mp.
31. exp Self Efficacy/
32. (self-efficacy or “self efficacy”).mp.
33. exp Interpersonal Relations/
34. ((interpersonal or social) ADJ (relation* or interaction*)).mp.

35. (“benefit finding” or ((benefit* or valu* or worth*) adj2 (find* or identif* or establish* or feel*))).mp.
36. Exp “Quality of life”/
37. (“quality of life” or QoL or HRQoL or life quality).mp.
38. (“life satisfaction” or “satisfaction with life”).mp.
39. ((life or lives or living) adj2 satisf*).mp.
40. Or/16-39
41. systematic review*.mp.
42. exp meta-analysis/ or exp meta-analysis as Topic/
43. (meta-analy* or metaanaly* or meta analy*).mp.
44. exp "Review Literature as Topic"/ or exp "Review"/
45. (meta-synthes* or metasynthes* or meta synthes*).mp.
46. Cochrane.mp.
47. ((research or evidence) ADJ3 synthes*).mp.
48. (metaethnograph* or meta-ethnograph* or meta ethnograph*).mp.
49. ((scoping or mapping) ADJ2 review*).mp.
50. ((narrative or realist or critical or thematic literature or meta-narrative or state-of-the-art) ADJ2 (synthes* or review*)).mp.
51. (Meta-summary or meta summary or metasummary).mp.
52. ((mixed or multi* or cross) adj1 (method* or design* or research or strategy)) adj2 (synthes* or review*).mp.
53. ((mixed-method* or multi-method* or mixed-design or multi-design or multiple-methods or multi-strategy or cross-design) adj2 (synthes* or review*)).mp.
54. Or/41-53
55. ((6 AND 15) OR 9 OR 10) AND 40 AND 54

Note. mp = title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms

Appendix B. List of included review papers and their assigned review numbers.

1. Amatya, B., Galea, M. P., Kesselring, J., & Khan, F. (2015). Effectiveness of telerehabilitation interventions in persons with multiple sclerosis: A systematic review. *Multiple Sclerosis and Related Disorders, 4*(4), 358-369. doi:https://doi.org/10.1016/j.msard.2015.06.011

2. Barker, A. B. (2015). *Social identity change in people with multiple sclerosis: a social identity approach to the role of the family in identity reconstruction.* (PhD Thesis), University of Nottingham, Nottingham, UK.

3. Benito-León, J., Manuel Morales, J., Rivera-Navarro, J., & Mitchell, A. J. (2003). A review about the impact of multiple sclerosis on health-related quality of life. *Disability and Rehabilitation, 25*(23), 1291-1303. doi:10.1080/09638280310001608591

4. Broome, H. (2012). *The association between cognition, social functioning, physical impairment, and relationship factors in individuals with multiple sclerosis.* (Clinical Doctorate Thesis), The University of Hull, Hull, UK.

5. Butler, E., Matcham, F., & Chalder, T. (2016). A systematic review of anxiety amongst people with Multiple Sclerosis. *Multiple Sclerosis and Related Disorders, 10*, 145-168. doi:https://doi.org/10.1016/j.msard.2016.10.003

6. Corry, M., & While, A. (2009). The needs of carers of people with multiple sclerosis: a literature review. *Scandinavian Journal of Caring Sciences, 23*, 569-588.

7. Dennison, L. (2011). *Factors and Processes involved in Adjustment to Multiple Sclerosis.* (PhD Thesis), University of Southampton, Southampton, UK.

8. Dorstyn, D., Mathias, J., & Denson, L. (2011). Psychosocial outcomes of telephone-based counseling for adults with an acquired physical disability: A meta-analysis. *Rehabilitation Psychology, 56*(1), 1-14.

9. Dorstyn, D., Black, R., Mpofu, E., & Kneebone, I. (2017). Utilizing the ICF to understand depressive symptomology in multiple sclerosis: An exploratory systematic review. *Rehabilitation Psychology, 62*(2), 143-164.

10. Firth, N. (2013). Effectiveness of psychologically focused group interventions for multiple sclerosis: A review of the experimental literature. *Journal of Health Psychology, 19*(6), 789-801. doi:10.1177/1359105313479630

11. Gruenewald, D. A., Higginson, I. J., Vivat, B., Edmonds, P., & Burman, R. E. (2004). Quality of life measures for the palliative care of people severely affected by multiple sclerosis: a systematic review. *Multiple Sclerosis Journal, 10*(6), 690-725. doi:10.1191/1352458504ms1116rr

12. Kefaliakos, A., Pliakos, I., & Diomidous, M. (2016). Managing the Quality of Life in Patients with Multiple Sclerosis: A Literature Review. In J. Mantas, A. Hasman, P. Gallos, A. Kolokathi,

& M. S. Househ (Eds.), *Unifying the Applications and Foundations of Biomedical and Health Informatics* (Vol. 226, pp. 220-221). Amsterdam: IOS Press.

13. Köpke, S., Solari, A., Khan, F., Heesen, C., & Giordano, A. (2014). Information provision for people with multiple sclerosis. *Cochrane Database of Systematic Reviews, 4* (CD008757), 1-59. doi:10.1002/14651858.CD008757.pub2

14. Krokavcova, M., Van Dijk, J. P., Nagyova, I., Rosenberger, J., Gavelova, M., Gdovinova, Z., & Groothoff, J. W. (2009). Perceived health status as measured by the SF-36 in patients with multiple sclerosis: a review. *Scandinavian Journal of Caring Sciences, 23*(3), 529-538. doi:10.1111/j.1471-6712.2008.00633.x

15. Baixinho, C. L., Duarte, A. F., Teixeira, F. M., Quental, I. A., Martins, S. S., & Mertens, J. M. (2016). Nursing interventions promoting functionality among adults with multiple sclerosis: integrative review. *Journal of Nursing UFPE, 10*(2), 838-847.

16. Martinez-Assucena, A., Marnetoft, S.-U., Rovira, T. R., Hernandez-San-Miguel, J., Bernabeu, M., & Martinell-Gispert-Sauch, M. (2010a). Rehabilitation for Multiple Sclerosis in Adults (I); Impairment and Impact on Functioning and Quality of Life: An Overview. *Critical Reviews in Physical & Rehabilitation Medicine, 22*(1-4), 103-177.

17. Martinez-Assucena, A., Marnetoft, S.-U., Rovira, T. R., Hernandez-San-Miguel, J., Bernabeu, M., & Martinell-Gispert-Sauch, M. (2010b). Rehabilitation for Multiple Sclerosis, in Adults (II); Management and Impact on Impairment, Functioning, and Quality of Life: An Overview. *Critical Reviews in Physical & Rehabilitation Medicine, 22*(1-4), 179-240.

18. Methley, A. M., Chew-Graham, C., Campbell, S., & Cheraghi-Sohi, S. (2015). Experiences of UK health-care services for people with Multiple Sclerosis: a systematic narrative review. *Health Expectations, 18*(6), 1844-1855. doi:10.1111/hex.12228

19. Pagnini, F., Bosma, C. M., Phillips, D., & Langer, E. (2014). Symptom changes in multiple sclerosis following psychological interventions: a systematic review. *BMC Neurology, 14*(1), 222. doi:10.1186/s12883-014-0222-z

20. Pompili, M., Forte, A., Palermo, M., Stefani, H., Lamis, D. A., Serafini, G., . . . Girardi, P. (2012). Suicide risk in multiple sclerosis: A systematic review of current literature. *Journal of Psychosomatic Research, 73*(6), 411-417. doi:https://doi.org/10.1016/j.jpsychores.2012.09.011

21. Sevilla Guerra, S. (2013). Management of psychosocial adjustment among people with multiple sclerosis: a critical analysis. *British Journal of Neuroscience Nursing, 9*(2), 89-92. doi:10.12968/bjnn.2013.9.2.89

22. Soundy, A., Roskell, C., Elder, T., Collett, J., & Dawes, H. (2016). The Psychological Processes of Adaptation and Hope in Patients with Multiple Sclerosis: A Thematic Synthesis. *Open Journal of Therapy and Rehabilitation, 4*, 22-47.

23. Sweetland, J., Howse, E., & Playford, E. D. (2012). A systematic review of research undertaken in vocational rehabilitation for people with multiple sclerosis. *Disability and Rehabilitation, 34*(24), 2031-2038.

24. Thomas, P. W., Thomas, S., Hillier, C., Galvin, K., & Baker, R. (2006). Psychological interventions for multiple sclerosis. *Cochrane Database of Systematic Reviews, 1* (CD004431), 1-54. doi:10.1002/14651858.CD004431.pub2

25. Topcu, G., Buchanan, H., Aubeeluck, A., & Garip, G. (2016). Caregiving in multiple sclerosis and quality of life: A meta-synthesis of qualitative research. *Psychology & Health, 31*(6), 693-710. doi:10.1080/08870446.2016.1139112

26. Uccelli, M. M. (2014). The impact of multiple sclerosis on family members: a review of the literature. *Neurodegenerative Disease Management, 4*(2), 177-185.

27. Wilkinson, H. R., & das Nair, R. (2013). The psychological impact of the unpredictability of multiple sclerosis: a qualitative literature meta-synthesis. *British Journal of Neuroscience Nursing, 9*(4), 172-178.

28. Jones, J. B., Walsh, S., & Isaac, C. (2017). The relational impact of multiple sclerosis: an integrative review of the literature using a cognitive analytic framework. *Journal of Clinical Psychology in Medical Settings, 24*(3-4), 316-340.

29. Dehghani, A., Keshavarzi, A., Jahromi, M. F., Shahsavari isfahani, S., & Keshavarzi, S. (2018). Concept analysis of coping with multiple sclerosis. *International Journal of Nursing Sciences, 5*(2), 168-173. doi:https://doi.org/10.1016/j.ijnss.2018.04.009

30. Venasse, M., Edwards, T., & Pilutti, L. A. (2018). Exploring Wellness Interventions in Progressive Multiple Sclerosis: an Evidence-Based Review. *Current Treatment Options in Neurology, 20*(5), 13. doi:10.1007/s11940-018-0497-2

Appendix C. Characteristics and AMSTAR ratings of the systematic reviews included in the meta-review.

Review reference number	Author (year)	Type of review / synthesis	Review aim(s)	Number of papers included	Publication years of included papers	Countries studies undertaken	Total sample size of included studies	Age of included participants (Mean range in years)	Disease duration of participants in included studies (Mean range in years)	Research designs of included studies	AMSTAR Rating
1	Amatya (2015)	Systematic Review using qualitative analysis (best evidence synthesis)	Assess effectiveness, safety and cost-efficiency of tele-rehabilitation interventions for PwMS	12	2003-2015	USA, Germany, Spain, Italy Belgium, Scotland	564 pwMS	41-52 years (M=47)	7- 19 years (M=12)	RCT, Cohort studies	10
2	Barker (2016)	Meta-synthesis using meta-ethnographic analytic approach	Explore identity reconstruction following a diagnosis of MS by reviewing qualitative studies of the changes to a person's family identity in pwMS	16	1980-2012	Majority from Europe and North America	Not reported	Not reported	Not reported	Qualitative studies	8
3	Benito-Leon (2003)	Systematic Review (synthesis type not reported)	Review the impact of MS on Health-related quality of life	89	1981-2002	Not reported	Not reported	Not reported	Not reported	Not reported	6
4	Broome (2012)	Systematic review using narrative approach and a critical analysis	Review the different aspects of the couple's relationship which may impact on the physical and	11	1988-2011	Not reported	551 dyads, 605 PwMS	Range 46-54 years old	Range 6-20+ years	Qualitative, cross-sectional, longitudinal	9

Review reference number	Author (year)	Type of review / synthesis	Review aim(s)	Number of papers included	Publication years of included papers	Countries studies undertaken	Total sample size of included studies	Age of included participants (Mean range in years)	Disease duration of participants in included studies (Mean range in years)	Research designs of included studies	AMSTAR Rating
		of the included studies	psychological well-being of the partner diagnosed with MS								
5	Butler (2016)	Systematic review using narrative synthesis	Gain an overview of the strength of evidence for factors associated with anxiety in the context of MS & identify methodological problems, gaps within the literature and directions for future research	131	1994-2016	Not reported	32108 pwMS	Mean range 15.7-67.6 years	Not reported	Cross-sectional, Prospective	11
6	Corry & While (2009)	Systematic review using Thematic Content Analysis	Review the research addressing the experiences of carers of pwMS	33	2002-2007	UK, Ireland, USA, Australia, Italy, Belgium, Canada, Netherlands, Norway, Sweden, Spain	3459 carers/family; 62 non-carers; 161 pwMS	Not reported	7-9.5 years (only three studies reported)	Cross-sectional, qualitative and longitudinal	7
7	Dennison (2011)	Systematic review using narrative synthesis	1) identify psychological factors 2) explore the strength of	110	1980-2011	USA, Australia, Canada (not	19527 pwMS	Mean range 41-50 reported for 53 studies	Average of 7-11 years in most papers, very few	Cross-sectional, longitudinal	7

Review reference number	Author (year)	Type of review / synthesis	Review aim(s)	Number of papers included	Publication years of included papers	Countries studies undertaken	Total sample size of included studies	Age of included participants (Mean range in years)	Disease duration of participants in included studies (Mean range in years)	Research designs of included studies	AMSTAR Rating
			evidence for relationships between a range of psychological variables and adjustment outcomes in MS 3) Identify common methodological weaknesses in the research, gaps within the literature, and directions for future research			reported in 38 studies)			study samples had a mean diagnosis of less than five years or more than fifteen years previously.		
8	Dorstyn (2011)	Meta-analysis	Evaluate the impact of telephone-administered psychological interventions on the psychosocial functioning of adults with an acquired physical disability caused by spinal cord injury, limb amputation, severe burn MS	8	1985-2010	Not reported	Mixed group -449 reported as MS only (one paper with mixed diagnosis n=38 but not clear how many MS)	Range 33-55 years (mixed diagnoses, MS only not reported)	M=8.7 years (6.1-13)	RCT, longitudinal	7

Review reference number	Author (year)	Type of review / synthesis	Review aim(s)	Number of papers included	Publication years of included papers	Countries studies undertaken	Total sample size of included studies	Age of included participants (Mean range in years)	Disease duration of participants in included studies (Mean range in years)	Research designs of included studies	AMSTAR Rating
9	Dorstyn (2017)	Exploratory systematic review (meta-analysis)	To profile the available summary evidence from the extant empirical literature on MS and depression symptomology and maps identified psychosocial correlates onto ICF domains	49	1984-2015	Majority from Europe & United States	7548 pwMS	Range 18-90 years old (mean= 43.86)	9.76 years (range= <1-60)	Cross-sectional, Longitudinal	10
10	Firth (2013)	Systematic review (synthesis type not reported)	Assess evidence for the effectiveness of psychologically-focused group interventions for pwMS	14	1884-2012	Not reported	1099 pwMS	Mean range 36-51 years	Average 3-17 years (Not reported for all studies)	Controlled trials with comparison groups	10
11	Gruenewald (2004)	Systematic review using meta-synthesis [qualitative narrative synthesis?]	Identify multidimensional health-related quality of life measures, the domains relevant to PwMS and how well these are	166	Search performed for 1991-2003	Not reported	Not reported	Not reported	Not reported but review includes studies with pwMS diagnosed earlier than 5 years	Qualitative and questionnaire-based	5

Review reference number	Author (year)	Type of review / synthesis	Review aim(s)	Number of papers included	Publication years of included papers	Countries studies undertaken	Total sample size of included studies	Age of included participants (Mean range in years)	Disease duration of participants in included studies (Mean range in years)	Research designs of included studies	AMSTAR Rating
			addressed by the measures								
12	Kefaliakos (2016)	Systematic review (synthesis type not reported)	To investigate the quality of life for MS patients and the possibility of reconstruction activities	~20	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	2
13	Köpke (2014)	Systematic review using qualitative synthesis (narrative form)	1. Evaluate effectiveness of information provision interventions for pwMS that aim to promote informed choice and improve patient-relevant outcomes 2. Evaluate components and developmental processes of complex interventions 3. Highlight quality and quantity of available research evidence and set an agenda for future research	10	1986- 2013	UK, Germany, Belgium, Australia, USA, Italy	1314 pwMS	Mean range 31-51 years	Not reported but review includes studies with newly diagnosed pwMS or people who referred for possible MS diagnosis	RCTs	11

Review reference number	Author (year)	Type of review / synthesis	Review aim(s)	Number of papers included	Publication years of included papers	Countries studies undertaken	Total sample size of included studies	Age of included participants (Mean range in years)	Disease duration of participants in included studies (Mean range in years)	Research designs of included studies	AMSTAR Rating
14	Krokavcova (2009)	Literature review (Synthesis type not reported)	Review the literature focusing on the associations between disease duration, disability and perceived health status as measured by the SF-36, and the psychological well-being related to perceived health status in pwMS	8	1997-2005	Europe, USA	1158 pwMS, 261 respondent (general population), 44 spouses	Not reported	Includes studies with <6 years, 6-10 years, >10 years	Cross-sectional, longitudinal	6
15	Baixinho (2016)	Integrative literature review (organising data into a priori categories)	Identify nursing interventions that impact on the functionality of adult pwMS; Analyse nursing interventions that impact on functionality of adult pwMS	28	Search performed for 2009-2014	Not reported	Not reported	Not reported	Not reported	Not reported (21 primary studies/descriptive papers, 2 reference books, 3 theses, 2 websites)	5
16	Martinez-Assucena (2010) a	Literature review (synthesis type not reported – summary of results)	Evaluate health problems and impact on HRQoL and QoL of PwMS; assess perceived and main body function, body	Not reported	Search performed for 1995-2011	Not reported	Not reported	Not reported	Not reported	Not reported	4

Review reference number	Author (year)	Type of review / synthesis	Review aim(s)	Number of papers included	Publication years of included papers	Countries studies undertaken	Total sample size of included studies	Age of included participants (Mean range in years)	Disease duration of participants in included studies (Mean range in years)	Research designs of included studies	AMSTAR Rating
			structure, activities and participation problems, and needs arising for pwMS; measure the impact of body function and body structure impairment on activities, participation, and QoL of PwMS; assess effects of being significant other or carer of PwMS.								
17	Martinez-Assucena (2010) b	Literature review (synthesis type not reported – summary of results)	Report the effectiveness of rehabilitation planning and global interdisciplinary rehabilitation interventions, paramedical rehabilitation packages of comprehensive care components for pwMS; Report	Not reported	Search performed for 1995-2011	Not reported	Not reported	Not reported	Not reported	Not reported	4

Review reference number	Author (year)	Type of review / synthesis	Review aim(s)	Number of papers included	Publication years of included papers	Countries studies undertaken	Total sample size of included studies	Age of included participants (Mean range in years)	Disease duration of participants in included studies (Mean range in years)	Research designs of included studies	AMSTAR Rating
			the impact of MS information and education for pwMS, their significant others and carers; describe the main features of case management; report the impact of interdisciplinary rehabilitation interventions and paramedical rehabilitation packages of comprehensive care components on pwMS; and describe the accessibility and use of rehabilitation services in different countries								
18	Methley (2015)	Systematic review using narrative summary approach	Critically review qualitative studies reporting patients' experiences of health-care services in the UK	6 papers (5 studies)	2003-2009	England & Northern Ireland	78 pwMS	Range 35-72 years old	Range 0.4 years to 37 years	Qualitative Studies	10

Review reference number	Author (year)	Type of review / synthesis	Review aim(s)	Number of papers included	Publication years of included papers	Countries studies undertaken	Total sample size of included studies	Age of included participants (Mean range in years)	Disease duration of participants in included studies (Mean range in years)	Research designs of included studies	AMSTAR Rating
19	Pagnini (2014)	Systematic review (synthesis type not reported)	Evaluate impact of psychological interventions on the physiological symptoms in pwMS	22	1996-2013	Not reported	5705 pwMS	Mean range 31.5 years to 51.5 years	Mean 8 years (range 2-15 years)	RCTs	8
20	Pompili (2012)	Systematic review using qualitative synthesis	Investigate relationship between MS and suicidal behaviour/ attempted suicide/ suicide ideation	12	1971-2012	Canada, Denmark, Sweden (not all reported)	53917 pwMS	Not reported	Not reported (some papers included retrospective data around diagnosis)	Cohort, Retrospective, Observational	10
21	Sevilla (2013)	Systematic review (synthesis type not reported - critical analysis)	Highlight the effectiveness of psychological interventions and adjustment management that can be carried out by nurses	2	2010-2012	UK	Not reported in review [134 pwMS]	Not reported in review [Mean range 41.7-48.6 years]	Not reported in review [0.8-49 years (Mean range 3-9.7)]	RCTs	5
22	Soundy (2016)	Thematic meta-synthesis using framework analysis	Illustrate processes of psychological adaptation following events that relate to MS which include symptoms of MS which impact on	47	1990-2013	UK, USA, Sweden, Canada, Australia	1146 pwMS	Aggregated mean age 49.3 years	Aggregated mean time with illness 12.3 years	Qualitative (interviews, case study, phenomenological, qualitative mixed-methods, naturalistic paradigm,	10

Review reference number	Author (year)	Type of review / synthesis	Review aim(s)	Number of papers included	Publication years of included papers	Countries studies undertaken	Total sample size of included studies	Age of included participants (Mean range in years)	Disease duration of participants in included studies (Mean range in years)	Research designs of included studies	AMSTAR Rating
			the individual's mental well-being both pre- and post- diagnosis							naturalistic case study, action research, focus group, grounded theory, ethnography, internet survey, narrative, interpretative)	
23	Sweetland (2012)	Systematic review (synthesis type not reported)	Identify the factors that lead to unemployment for people with MS and to describe the vocational rehabilitation (VR) interventions that are of bene t to this population	89	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	7
24	Thomas (2006)	Systematic review (4 mini-reviews - only two similar studies in one mini-review for a meta-analysis)	Assess the effect of psychological interventions on mental and physical wellbeing in people with multiple sclerosis	17 (16 studies)	1984-2004	Not reported	1006 pwMS	Mean range 39-47 years	Range 0.3 years to 40 years	RCTs	10
25	Topcu (2016)	Meta-synthesis using meta-ethnorgaphy	Identify factors that may affect the QoL of MS	17	1992-2013	USA, Australia, Netherlands,	1023 carers	Range 17-84 years	Not reported	Qualitative (interviews, focus groups, interview	10

Review reference number	Author (year)	Type of review / synthesis	Review aim(s)	Number of papers included	Publication years of included papers	Countries studies undertaken	Total sample size of included studies	Age of included participants (Mean range in years)	Disease duration of participants in included studies (Mean range in years)	Research designs of included studies	AMSTAR Rating
			carers, and derive a new conceptual understanding of the views and experiences of carers of pwMS			Belgium, Ireland, UK				questionnaire) & mixed-methods (open questions)	
26	Uccelli (2014)	Literature review (synthesis type not reported)	Explore repercussions of MS on family, the impact of MS on each component of the family	30	2008-2013	Not reported	2545 pwMS and 4092 carers/ relatives; 36072 controls	Not reported	Not reported	Cross-sectional, correlational, retrospective, exploratory, longitudinal, prospective cohort, quantitative and qualitative	6
27	Wilkinson (2013)	Meta-synthesis using critical realist epistemological position	Explore the psychological impact of unpredictability in MS	6	1997-2008	Ireland, Sweden, USA (3 not reported)	59 pwMS	Range 20-60 years	Range 6 months- 39 years	Qualitative (Interviews, focus groups)	9
28	Jones (2017)	Integrative review using a Cognitive Analytic Therapy framework	Develop understanding of how MS influences relational functioning and wellbeing	38	1985-2014	Not reported	1851 pwMS and 663 Family/ carer	Not reported	Not reported	Qualitative (inductive thematic analysis, constant comparative analysis, IPA, hermeneutic phenomenology, grounded theory), Quantitative (cross-sectional, comparison), Other	9

Review reference number	Author (year)	Type of review / synthesis	Review aim(s)	Number of papers included	Publication years of included papers	Countries studies undertaken	Total sample size of included studies	Age of included participants (Mean range in years)	Disease duration of participants in included studies (Mean range in years)	Research designs of included studies	AMSTAR Rating
29	Dehghani (2018)	Systematic review (thematic analysis with Rodgers' Evolutionary method of concept analysis	Clarify 'coping' concept, identify factors relevant to coping in MS	55	1995-2017	Not reported	Not reported	Not reported	Not reported	Not reported	7
30	Venasse (2018)	Systematic review (synthesis type not reported)	Examine the role of wellness based interventions in patients with progressive MS	21	2000-2017	Not reported	288 people with progressive MS	Mean range 47-62 years	Mean range 11.2-21.6 years (7 studies not reported)	RCT, pre-post	7

Key. MS = Multiple Sclerosis; pwMS = People with Multiple Sclerosis; RCT = Randomised Controlled Trial.

Appendix D. Effectiveness information for specific interventions.

Review reference number	Interventions	Effectiveness information
1	12 widely varying telerehabilitation programs: 1. Social cognitive theory based behavioural intervention with web video coaching, internet delivered, 12 weeks, 4 sessions in first months, 2 in second month, 1 in third month 2. Same as 1 3. Structured education and counselling by rehabilitation nurse, delivered in home by telephone or video, 30-40min sessions, weekly for 5 weeks then fortnightly for a month 4. Group fatigue management programme facilitated by occupational therapist, internet delivered, 12 weeks, 4 sessions in first months, 2 in second month, 1 in third month 5. Home Automated Telemanagement – individualised exercise programmes, internet delivered, daily sessions over 12 weeks 6. Balance, postural control and strength training programme, internet delivered, two 45 minute training sessions weekly for 12 weeks 7. Experimental group programme using gaming protocol, visual and proprioceptive exercises, delivered using virtual reality gaming system and videoconference, 40 sessions, 4 per week 8. Home Care Activity Desk intervention for hand/arm function, delivered using videoconference, 1 session 5 days a week for a month 9. Same as 1 10. Individualised physiotherapy programme, internet delivered, 2 sessions a week for 12 weeks 11. Same as 1 with addition of a pedometer, log book and goal tracker software, 15 sessions over 6 months	• Improvements in functional activity (Interventions #1, #2, #5-12), fatigue (Interventions #3, #4, #11), pain and sleep (Intervention #3), spasticity (Intervention #5), depression (Interventions #3, #11) and anxiety (Intervention #11) • No significant difference in quality of life in most (Interventions #2, #3, #5, #10, #11), but improvement in most subscales of quality of life in one study (Intervention #4) Note. See review #1 for the list of effect sizes for each included studies.

	12. Same as 1, with addition of online materials becoming available at timed intervals, skype delivered, weekly sessions for 6 months	
3	19 interventions where health-related quality of life measure was used: 1. Aerobic training, 15 weeks 2. Rehabilitation programme, duration not specified 3. Outpatient rehabilitation programme, 12 months 4. Interferon beta, 12 months 5. Rehabilitation programme 6. Baclofen for spasticity, 12 months 7. Interferon trial, 12 months 8. Tai Chi programme, 8months 9. Inpatient rehabilitation, 15 weeks 10. Inpatient rehabilitation, 12 moths 11. Interferon beta, 60 months 12. Interferon beta, 12 months 13. Interferon beta, 6 moths 14. Interferon beta, 36 months 15. Methylprednisolone, 3 months 16. Energy convservation course, 19 weeks 17. Intramuscular interferon, 24 months 18. Outpatient rehabilitation programme, 6 weeks 19. Intramuscular interferon beta, 12 months	• Improvements in health-related quality of life were found using exercise training, physical rehabilitation, tai chi and some drug trials (Interventions #1-3, #5, #8, #9 on mental domains, #11, #12, #13 and #14 on physical domain, #15-18) • Health-related quality of life decreased in one pharmacological study (Intervention #7)
8	8 telephone based counselling programs: 1. For SCI, delivered by nurse, 1:1, psychoeducation and supportive counselling model, 9 sessions over 9 weeks 2. For SCI, stroke and multiple sclerosis, by social worker, group and 1:1, psychoeducation and supportive counselling model, 8 sessions over 8 weeks 3. For SCI, by psychologist, group and 1:1, Cognitive Behavioural Therapy and supportive counselling model, 7 sessions over 24 weeks 4. For multiple sclerosis, by psychologist, 1:1, Cognitive Behavioural Therapy model, 8 sessions over 8 weeks	• Significant improvement in coping strategies (d = 0.57) (Intervention #5) • Significant improvements in disability impairment (d = 0.49) (Intervention #5) • Significant improvement in community integration (dw = 0.45) (Interventions #2, #3, #7) • Significant improvement in depression (dw = 0.44) (Interventions #4, #3, #5) and even stronger effect in the multiple sclerosis study (dw = 1.34) (Intervention #4) • Improvements in effects of fatigue (dw = 0.42) (Interventions #5, #7)

	5. For multiple sclerosis, by psychologist, 1:1, Cognitive Behavioural Therapy model, 16 sessions over 16 weeks 6. For multiple sclerosis, by nurse, psychoeducation and supportive counselling model, 9 sessions over 9 weeks 7. For multiple sclerosis, by psychologist, motivational interviewing model, 6 sessions over 12 weeks 8. For multiple sclerosis, by nurse, psychoeducation and supportive counselling model, 6 sessions over 12 weeks	• Non-significant improvement in physical and psychological aspects of health care (dw = 0.32) (Interventions #3, #7, #8) • Very small improvement in quality of life (dw = 0.08) (Interventions #7, #8) • Very small negative effect on social support (dw = -0.03) (Interventions #3, #8)
10	14 psychological group interventions: 1. CBT group, 6 sessions overs 6 weeks 2. Insight oriented group, 50 sessions over 25 weeks 3. Coping skills group, 8 sessions over 8 weekly 4. Psychodrama group, 52 sessions over 52 weeks 5. Supportive expressive group vs 1:1 Cognitive Behavioural Therapy, 16 sessions over 16 weeks 6. CBT, relaxation and exercise group, 7 sessions over 7 weeks 7. Adjustment and symptom management group, 4 sessions over 4 weeks 8. Same as 5 9. Mood and self-efficacy group, 3 sessions over 3 weeks 10. Lay-led generic self-management group, 6 sessions over 6 weeks 11. CBT adjustment group, 6 sessions over 12 weeks 12. Mindfulness group, 8 sessions over 8 weeks 13. Same as 11 14. Acceptance and commitment therapy vs relaxation training, 5 sessions over 14 weeks	• Significant improvement in: o Depression (Interventions #1, #2, #5, #6, #11, #12, #13, #14), o anxiety (Interventions #9, #12, #13), o mood (Intervention #1) o psychiatric disorders (Interventions #13), o quality of life (Interventions #8, #12, #13), o fatigue (Intervention #12), o locus of control (Intervention #2), o adaptability (Intervention #3), o neuropsychological composite (Intervention #3), o role performance (Intervention #3), o wellbeing (Interventions #3, #8), o behaviour changes (Intervention #4), o relationships (Intervention #4), o body image (Intervention #6), o disease coping (Intervention #6), o symptom severity (Intervention #7), o resilience (Intervention #9), o self-efficacy (Interventions #9, #14), o disease impact (Interventions #10, #13), o acceptance and action (Intervention #14) • Some benefits may be from group participation itself rather than the intervention
13	10 educational and multiple sclerosis information provision programmes:	• Significantly increased “knowledge” (Interventions #5, #7, #9, #10)

	1. "OPTIMISE" group programme providing knowledge, skills and confidence to undertake health promoting activities, 8 weekly sessions 2. Information booklet and interactive worksheet about immunotherapy options 3. Multidisciplinary fatigue management programme 4. Educational group programme on relapse management including educational booklet and corticosteroid prescription 5. Educational group program on diagnosis, prognosis, and early therapy with educational booklet 6. Self-care strategy programme with information booklet, 2 sessions over 1 month 7. "Motherhood choice" printed decision aid about multiple sclerosis and fertility etc. 8. 1:1 information from nurse with aid of National Multiple Sclerosis Society leaflets symptoms etc., 8 sessions over 6 months 9. Interview with physician with informational CD and take-home information booklet 10. Physician and nurse led oral presentation and patient information booklet	• Higher roles in decision making in one study (Intervention #4), and three studies found no sig difference (Interventions #2, #5, #7) • Increased quality of life (Interventions #1, #6) on some and three studies showed no significant difference (Interventions #4, #5, #8) • No effects on satisfaction (Interventions #2, #4, #5), coping (Intervention #3) , mood (Interventions #3, #5, #7, #8, #9) or activities of daily living (Interventions #6)
15	Interventions promoting functionality	• Evidence available to implement in clinical practice
17	Covers wide range of rehabilitation: • Physiotherapy • Occupational therapy • Neuropsychological and psychological interventions: cognitive behavioural interventions, coping strategies, insight-oriented group therapy, a supportive-expressive group therapy, supportive-emotion-focused therapy, relaxation techniques, self-efficacy training and counselling • Speech and swallowing therapy • Dietary interventions • Expert rehabilitation nursing interventions • Assistive technology	• Psychological interventions to increase self-efficacy have been useful for psychosocial adjustment and promising results for fatigue management • Therapeutic exercise, short-term physiotherapy programs, and hydrotherapy have shown some benefit for mood • Self-management education interventions improved self-efficacy leading to better adjustment • Information aid added into multiple sclerosis diagnosis practise produced good disease knowledge and satisfaction

	• Social work interventions • Vocational rehabilitation interventions	
19	22 psychological interventions 1. Chronic Disease Self Management Course teaching range of skills and strategies, 6 weeks duration 2. lifestyle-change classes and telephone follow-up, 8 weeks 3. Progressive Muscle Relaxation Technique, 63 sessions over 2 months 4. Psychological program with cognitive behavioural strategies for coping with stress and body exercises, 7 weeks 5. Intervention group programme for adjustment to multiple sclerosis, 6 weeks 6. Self-care intervention using information booklet, two 1-2hour discussions over 1 month 7. Telephone Cognitive Behavioural Therapy, 16 weeks 8. Relationship enrichment workshop/teleconference, in person duration 1–2 days or teleconference 4–6 weeks 9. Individualised rehabilitation programme, 12 months 10. AT (autogenic training), 10 weeks 11. Relaxation training, 6 days 12. Energy Conservation course, 6 weeks 13. A modified version of the Mindfulness-Based Stress Reduction (MBSR), 8 weeks 14. Meditation, 2 months 15. CBT based on model of fatigue, 8 weeks 16. Coping skills group, 8 weeks 17. Individual stress management program, 20-24 weeks 18. individual Cognitive Behavioural Therapy, group psychotherapy, 16 weeks 19. Coping skills group, 18 weeks 20. Nursing intervention in promoting adjustment and symptom management, 4 weeks 21. Same as 17	• Psychological treatments = improved quality of life and wellbeing, reduced depressive symptoms, anxiety and perceived stress • coping skills intervention (Intervention #16) yielded gains in psychosocial role performance, coping behaviour and well-being • Most psychological treatments had positive effects

	Patient education program to enhance decision autonomy, 4 hours	
21	Two Cognitive Behavioural Therapy based interventions: 1. Psychological group intervention based on Cognitive Behavioural Therapy, delivered by assistant psychologist, covering topics such as problem-solving, worry (anxiety), gloom (depression), relationships and the future 2. CBT for adjusting to multiple sclerosis (the saMS trial), delivered by general nurses, 8 weekly sessions	• Fewer depressive symptoms (Intervention #1) • No significant effect on anxiety, self-efficacy or quality of life (Intervention #1) • Less functional impairment and distress, and more accepting of the limitations their illness created than supportive listening group (Intervention #2) however, the gains were lost by 12 months
24	16 interventions: 1. Individualised neurological compensatory training vs supportive psychotherapy 2. Individual cognitive rehabilitation and goal directed neuro-psychotherapy 3. Computer aided retraining of memory and attention 4. Group-based insight-oriented psychotherapy 5. Social skills training aimed at easing interaction strain 6. Cognitive remediation strategy involving daily interviews with nursing staff and memory notebook 7. Individual stress inoculation training involving Cognitive Behavioural Therapy and relaxation 8. Group-based coping-focussed Cognitive Behavioural Therapy 9. Programme aimed at increasing self-efficacy for adjustment 10. Cognitive assessment and targeted cognitive rehabilitation 11. Group-based biologically-oriented imagery treatment with relaxation 12. Group-based directive coping skills sessions with peer telephone support 13. Group-based wellness programme for women based on health psychology models of health behaviour and belief 14. Group-based Cognitive Behavioural Therapy 15. Telephone-based individual Cognitive Behavioural Therapy 16. Group based Cognitive Behavioural Therapy	All results compare changes pre and post intervention vs other intervention arm or control group: • Significant improvement in depression in some studies (Intervention #2 $p=0.04$, Intervention #5 $p<0.05$, Intervention #7 $p=0.001$, 14 $p<0.01$, Intervention #15 $p=0.01$) but no significant difference found in others (Intervention #1, Intervention #3 $p=0.67$, Intervention #8 $p>0.05$, Intervention #16) • Significant improvement in anxiety in some studies (Intervention #7 $p=0.015$, Intervention #11 $p<0.05$) but no significant difference found in others (Intervention #2 $p=0.42$ for current anxiety and $p=0.75$ for general anxiety, Intervention #5 $p>0.05$, Intervention #8 $p>0.05$) • Significant improvement on mental health subscale (Intervention #3 $p=0.04$, Intervention #13) and pain subscale (Intervention #13) of quality of life but no differences in overall quality of life in one study (Intervention #10 $p>0.05$) • Significant improvement in perceived distress (Intervention #7 $p=0.02$) • Significant improvements in problem-focussed coping (Intervention #7 $p=0.01$) • No significant difference in self-efficacy (Intervention #6, Intervention #8 $p>0.05$) except one study which found a significant improvement (Intervention #13)

		• No differences in mood (Intervention #10 p>0.05, Intervention #11 p>0.05), cognitive outcomes (Intervention #1 p=0.53, Intervention #2 p=0.09, Intervention #10 p>0.05), locus of control (Intervention #5 p>0.05, Intervention #7 p=>0.05), self-esteem (Intervention #5 p>0.05, Intervention #6), social distress, social avoidance or social anxiety (Intervention #6), dispositional resiliency (Intervention #8), fatigue (Intervention #9) or pain (Intervention #9) • CBT evidence "look encouraging" – but could be due to group format rather than therapy itself, and sample sizes small
30	Four different wellness based interventions: 1. Individual or group-based exercise training, 4 – 24 weeks (e.g. Aerobic exercise training, assisted-cycling, body weight support treadmill training, total-body recumbent stepper training, aquatic exercise) 2. Individual or group-based emotional wellness interventions (interventions primarily included mindfulness therapy, e.g. group-based mindfulness, mindfulness-based cognitive therapy), 8-10 weeks 3. Dietary interventions (low fat diet, calorie restricted modified Mediterranean diet, supplementation), 42 days – 6 months 4. Combined (multi-modal) intervention (inc. exercise training, mediation, dietary modifications), 12 months	• Significant improvements in depressive symptoms, fatigue (intervention #1 – aerobic training) • Non-significant improvements in fatigue, quality of life (intervention #1) • Conflicting findings – no change in some quality of life scales (intervention #1) • Significantly lower psychological distress, reduced depression, anxiety, and improved psychological quality of life immediately after the intervention, at 3-month follow-up (Intervention #2). • Significant reduction in fatigue, depression, anxiety and cognitive symptoms and improvements in coping and mindfulness (Intervention #2 – mindfulness-based cognitive therapy) • Improved outcomes of balance and symptom management (Intervention #2) • Level B classification (i.e., probably effective) on psycholofical distress, depression, anxiety, pain, and quality of life (Intervention #2) • Significant improvement in fatigue, quality of life, depression, anxiety, cognitive performance (Intervention #4)

Key. d=effect size; dw=combined effect size weighted according to sample size.

Appendix E. Recommendations for future interventions/services

Review reference number	Recommendations
1	• Tele-rehabilitation and similar are recommended as is a timely, cost-effective, patient-centred and transparent service
3	• Patients should be encouraged to exercise regularly and those have significant disability should be offered rehabilitation programmes
4	• Clinician should focus on positive aspects of couple, their strengths, future expectations, hopes and resiliency • Aim to work collaboratively to decrease helplessness/increase acceptance • Should assess quality and supportive nature of patients' relationships and clinician jointly decides whether to include partner in support • Offer preventative family and couple therapy also to increase emotional wellbeing for pwMS and partner • Give opportunity to couple to discuss difficult emotions and topics within a safe, therapeutic environment • Signpost other services if support cannot be offered to couple
7	Recommends cognitive behavioural therapy as potentially useful framework to use with factors in the model including: • Consider social supports and include family members • Stress management techniques • Dealing with control and uncertainty • Encouraging health behaviours, e.g. goal setting, addressing barriers, pacing techniques • Tackling maladaptive cognitions
9	• Cognitive behavioural therapy-based treatments as implications for treatment • Should be multidisciplinary program such as Can Do MS • More interventions that promote positive social networks • Include practical support, professionally guided peer support, a supportive multidisciplinary team, and promote autonomy and self-management
11	• Vocational and psychological services needed for young people and those with recent MS diagnosis
15	Review results give recommendations for nursing interventions across categories. Those relevant to diagnosis/adjustment: <u>Health management/ perception:</u> • Run interventions aimed at teaching and education with a view to health promotion • Encourage health seeking behaviours • Refer to other associations that support pwMS • Planning of info and rehab strategies should be done by multidisciplinary teams • Validate what person already knows about MS • Include teaching and education in strategies to manage symptoms, especially fatigue • Teach both pwMS and family about medicines and side effects

	• Non-pharmacological therapy should focus on supplementary treatment, e.g., muscle relaxation • Identifying individual coping strategies <u>Self-awareness and self-concept :</u> • Evaluating mood, signs of depression and provide counselling if needed • Evaluate motivation for self-care, self-concept, self-image, self-esteem, difficulties in fulfilling everyday activities, decision-making capacity and independence in order to find coping strategies • Nurse should provide emotional support and answer questions to reduce fear • Provide group discussion time for externalisation of feelings and verbalisation of difficulties <u>Role and relationship:</u> • Nurse must include family members <u>Coping:</u> • Identifying individual coping factors and strategies • Promote adaptation and seek to change dysfunctional behaviours • Nurse should inform, educate and encourage caregiver to be present during hospitalisation, take periods of rest, etc. • Identify persons support network and encourage social support <u>Beliefs and values:</u> • Nurse should identify beliefs and values, and advise on adaptations needed to facilitate acceptance of disease and maintenance of quality of life
16	• Better accessibility to physicians, nurses, occupational therapists, and information on social insurance/vocational rehabilitation • Informational needs **for early post-diagnosis MS sample** re: optic neuritis, education sessions, and sources of reliable information among general practitioners, ophthalmologists, and neurologists
17	• For depression in MS – cognitive behavioural therapy-based adjustment intervention • Teach coping strategies to deal with MS and related disability • Self-efficacy strategies recommended to adjust to changing health status • Nurse's roles includes support, information and education re: disease course, treatment, etc. shortly after diagnosis and throughout for pwMS and caregivers • Information may not be understood on initial delivery, especially in peri-diagnostic period, which can cause negative effects psychologically and on disease management • Early delivery information should be provided
18	• More effective communication from professionals • Provide information on MS Society at time of diagnosis • Need for further research into NHS structure • Increase continuity of care from diagnosis to subsequent care
21	• Nursing practise could shape existing interventions or new ones to introduce pwMS to cognitive behavioural principles. Aiming to learn new skills, means of managing emotions, behavioural techniques to improve mood disorders and adjust to MS • Lack of availability of group therapy in clinical practise

22	• Help patients self-manage and empower with knowledge by providing choice, respecting their identity and privacy
23	• Provide recommendations regarding rehabilitation for work-based support
24	• Individual psychological therapy may help develop skills to cope with emotions, thoughts and adjustment to MS diagnosis and symptoms
28	• Interventions needed that approach families as dynamic units, and that supports them to improve communication, work through and minimise unhelpful relational patterns, to re-find mutuality and to move towards accepting-supported relation pattern. • MS care needs to be holistic • Services highlighting acceptance and adjustment and re-acceptance, and facilitating understanding and supportive relationships are needed.
30	• Lifestyle modification within the current continuum of patient care

Key. MS = Multiple Sclerosis; pwMS = people with Multiple Sclerosis.