Associations between Self-Efficacy and Multiple Sclerosis Symptoms

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Declaration

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Abstract

Multiple Sclerosis (MS) is a demyelinating neurodegenerative condition that can have devastating physical, psychological and cognitive consequences. With no current cure, perceived self-efficacy, or self-confidence, has been identified as a critical factor in MS symptom management and adjustment. However, literature examining the relationship between self-efficacy and MS symptomology has revealed mixed results. This may, in part, be due to discrepancies in how self-efficacy is operationalised. Potential moderators - namely gender, age and time since diagnosis, also need to be considered. Greater understanding of the self-efficacy-MS symptom relationship is important in order to develop effective self-management interventions for this cohort.

Literature Review

Overview

Multiple sclerosis (MS) is a chronic, degenerative neurological disorder and the primary cause of non-traumatic, permanent disability in young adults (Ramagopalan & Sadovnick, 2011). MS is characterised by variable patterns of motor, sensory and cognitive impairments that can be detrimental and disruptive to many aspects of daily life (Rigby, Domenech, Thornton, Tedman, & Young, 2003). The complex symptom profile in MS results in high healthcare utilisation and lower quality of life (Ke et al., 2016; Williams, Vietri, Isherwood, & Flor, 2014). With no known cure, it is important that patients are informed and educated about symptom management (Kraft et al., 2008). To this end, a vast body of research has examined the psychosocial factors which contribute to effective MS symptom management. A construct that is critical to optimising symptom self-management behaviours is self-efficacy (SE): the perception of one's ability to produce desired effects or outcomes (Bandura, 1997).

This review will examine the role of SE in the self-management of MS symptoms and sequalae. To provide a context to this research, the nature of MS – including its disease course, epidemiology, symptoms, and management – will first be discussed. The concept of SE will then be introduced and its association with physical, psychological and cognitive symptoms examined and critiqued. Important insight into the role of SE in the incidence and burden of symptoms in people living with MS will be provided.

Multiple Sclerosis

Definition. MS is a chronic, demyelinating disease of the central nervous system (Dendrou, Fugger, & Friese, 2015; Ramagopalan & Sadovnick, 2011). The cause of MS remains unknown but is suspected to begin as an inflammatory autoimmune process

characterised by autoreactive lymphocytes (Files, Jausurawong, Katrajian, & Danoff, 2015; Roach, 2004). A combination of environmental (e.g. lifestyle, diet, sun exposure) and genetic factors have been implicated in this process (Abdollahpour, Nedjat, Mansournia, Sahraian, & van der Mei, 2018; Nielsen et al., 2005). Later, as the disease progresses it is believed to be dominated by microglial activation and chronic neurodegeneration (Pérez-Cerdá, Sánchez-Gómez, & Matute, 2016).

Subtypes. There are four clinical phenotypes of MS, based on the disease pattern and trajectory: *clinically isolated syndrome (CIS), relapsing-remitting MS (RRMS), primary progressive MS (PPMS)* and *secondary progressive MS (SPMS)* (Lublin et al., 2014). *CIS* represents the first suspected episode of MS. This subtype is characterised by acute (i.e., lasting at least 24 hours) signs and symptoms indicative of inflammatory demyelination, but not yet meeting criteria for a diagnosis of MS (i.e., no previous episodes of demyelination and/or no MS specific MRI findings). *RRMS* is the most common disease course, accounting for 85-90% of cases (Weinshenker, 1994). It is characterised by distinct attacks (i.e., relapses or exacerbations) followed by a period of partial or complete recovery (i.e., remissions). During remission there is no apparent disease progression, however sequelae and permanent residual deficits may result from the relapse (Lublin et al., 2014). *SPMS* follows an initial relapsing-remitting course, with the majority of individuals initially diagnosed with RRMS transitioning to SPMS 10 to 20 years following disease onset (Eriksson, Andersen, & Runmarker, 2003). In SPMS there is a progressive decline in neurological functioning, with or without occasional relapses, minor remissions, and plateaus (Lublin et al., 2014). Lastly, *PPMS* - the least common subtype (diagnosed in approximately 10-15% of those with MS), is characterised by progressive accumulation of disability from onset, with the absence of early relapses, remissions or plateaus (Koch, Kingwell, Rieckmann, & Tremlett, 2009). Dependant on the stability of the disease, RRMS is further classified as *active* (i.e., clinical relapse

and/or MRI evidence) or *not active*, as well as *worsening* (i.e., incomplete recovery from relapse) or *not worsening* (Lublin et al., 2014).

Epidemiology. Gender differences in MS are noted, with women more likely than men to develop the disease at a 2-3:1, female-to-male ratio (Ahlgren, Oden, & Lycke, 2011; Alonso & Hernan, 2008). Recent studies indicate that the incidence of MS in females is increasing, suggesting the possible influence of sex chromosomes in pathology (Dunn & Steinman, 2013; Koch-Henriksen, Thygesen, Stenager, Laursen, & Magyari, 2018). MS is also common, affecting approximately 25,600 people in Australia (Ahmad, Palmer, Campbell, van der Mei, & Taylor, 2018) and 2.5 million worldwide (Koriem, 2016). Geographically there is variability in the incidence and prevalence of MS. It is widely believed that there is an association between latitude and risk of MS, with the risk increasing from south to north (Alonso & Hernan, 2008). However, meta-analytic findings do not support a universal latitudinal gradient of MS prevalence (Koch-Henriksen & Sorensen, 2010).

The reported mean age of onset of MS ranges from 28 to 31 years, with clinical symptoms typically presenting between the ages of 15 and 45 years. However, cases as early as the first years of life have been identified (Goodin, 2014). MS symptoms can also present later in life – with some cases not developing until the seventh decade of life and then progressing rapidly (Goodin, 2014). The age of onset is somewhat dependent on gender and MS subtype; the peak age of onset being approximately 5 years earlier for women (Ramagopalan & Sadovnick, 2011) and RRMS typically presenting earlier than PPMS (i.e., mean 25 to 29 years vs. mean 39 to 41 years; Goodin, 2014). Advances in disease-modifying treatments and MS care in the last few decades have considerably improved the life expectancy of diagnosed persons. Most people diagnosed with MS can expect to live 95% of

the normal life expectancy; approximately 7 years less compared with the general, healthy population (Lunde, Assmus, Myhr, Bo, & Grytten, 2017).

Symptoms and sequelae. The broad spectrum of MS symptomology arises primarily from the variability of lesion location and severity within the CNS. Symptoms and sequelae of MS impact on three main areas of functioning: *physical* abilities, *psychological* wellbeing, and *cognition*.

Physical symptoms. Sensory and motor disturbances (e.g., spasticity, gait disturbance, dysphagia), bowel, bladder and sexual dysfunction, visual disturbances (e.g., nystagmus, optic neuritis), fatigue, pain and paroxysmal symptoms (e.g., Lhermitte's sign) (Boissy & Cohen, 2007; Richards, Sampson, Beard, & Tappenden, 2002) are common in MS. Among these symptoms, fatigue is frequently reported as the most disabling (Trojan et al., 2007), with up to 65% of individuals experiencing chronic fatigue on a daily basis (Cook et al., 2013). While there appears to be a central nervous system component to the development of MS-related fatigue (Tartaglia et al., 2004), studies examining the association between disability or disease activity and fatigue have reported mixed findings (Kroencke, Lynch, & Denney, 2000; Patrick, Christodoulou, & Krupp, 2009). Chronic pain, or pain lasting longer than 12 weeks, is another common symptom of MS, with a recent review reporting a point prevalence estimate of 63% (Jawahar, Oh, Yang, & Lapane, 2013). Notably, current biomedical treatments for pain have demonstrated limited efficacy for this cohort. Rather, psychosocial factors have been found to explain 30% of the variance in pain severity, after controlling for demographic and disease variables (Harrison, Silber, McCracken, & Moss-Morris, 2015). As a disabling disease, MS also impacts negatively on mobility and physical activity levels (Motl et al., 2005; Sinnakaruppan, Macdonald, McCafferty, & Mattison, 2010). This is concerning given that physical activity is associated with a reduction in MS-

related symptoms and, in turn, improved health-related quality of life (Pardo & Fjeldstad, 2011).

Psychological symptoms. Persons with MS appear to have higher prevalence of psychiatric symptoms and disorders. Among the most common are depression and anxiety. A recent systematic review and meta-analysis identified a pooled prevalence rate of 35% for clinically significant depressive or anxiety symptoms, with a lower rate for diagnosed disorders: 21% for depression and 10% for anxiety (Boeschoten et al., 2017; Haussleiter, Brune, & Juckel, 2009). These rates are substantially higher than those reported in the general population (range: 3.6-8% for depression diagnosis and 2.6 -7.7% for anxiety diagnosis; World Health Organisation, 2017), but also other chronic diseases, such as cancer (depression diagnosis 22%; Krebber et al., 2014) and Parkinson's disease (depression 17%; Reijnders, Ehrt, Weber, Aarsland, & Leentjens, 2008).

MS is also associated with an increase in several other psychological difficulties, notably low self-esteem (McCabe, 2005), worry (Bruce & Arnett, 2009) and hopelessness (Patten & Metz, 2002a). Of concern is the heightened risk of suicide in this cohort (Feinstein & Pavisian, 2017; Fredrikson, Cheng, Jiang, & Wasserman, 2003), although this finding is not supported by all studies (e.g., Sumelahti, Tienari, Wikstrom, Salminen, & Hakama, 2002). Whether these psychological symptoms are a direct consequence of the biological processes that occur as a result of the MS disease process (i.e., changes in brain structure, inflammation; Feinstein, 2011), a side effect of interferon-beta therapy – a disease modifying treatment (Klapper, 1994), or dependent on level of disability and duration of disease (Lester, Stepleman, & Hughes, 2007) remains unclear.

Cognitive symptoms. Over 70% of persons with MS will experience some form of cognitive impairment over the course of the disease (Chiaravalloti & DeLuca, 2008).

Deficits most commonly occur in the domains of information processing speed, short-term memory and executive functioning (Chiaravalloti & DeLuca, 2008; Deloire et al., 2005). The deficits are detrimental to many aspects of daily living - including independent living, maintenance of employment, and societal and recreational engagement (Chiaravalloti & DeLuca, 2008). Disease duration and subtype, both of which can determine degree of inflammation, neuronal degeneration and lesion formation, in addition to cognitive reserve (as determined by educational level and intelligence), all play a role in the aetiology of cognitive impairment (Hughes et al., 2015). In addition, physical disability and depression can impair cognitive performance, although the causal nature of this relationship remains unclear – that is, whether a decline in cognitive function increases risk of developing mood symptoms, thus compromising physical ability, or whether cognitive impairment makes a person more likely to become depressed (Lester et al., 2007).

In sum, MS is a complex disease with high variability in presenting physical, psychological and cognitive symptoms. These symptoms may occur because of demyelination within the central nervous system or in response to countless psychosocial stressors experienced, including disruptions to family, work and social life. Given there is no cure for MS, the management of MS must revolve around symptom management: the primary goal being the prevention of long-term physical disability and enhancement of quality of life (Toosy, Ciccarelli, & Thompson, 2014). A person's ability to manage symptoms is primarily determined by their self-efficacy, or perceived self-competence (Bandura, 1997). Indeed, the ability to monitor and self-manage symptoms and disability is fundamental for those living with a chronic condition such as MS.

Self-Efficacy

Self-efficacy (SE) refers to an individual's belief in his or her ability to implement behaviour to achieve a desired outcome, goal, or expectation, across a variety of situations (Bandura, 1986). It is a core concept of Bandura's (1977) social cognitive theory – which posits that people learn by observing others. This theory has been extensively analysed and applied to many areas of human functioning, particularly health behaviour. Self-efficacy has been implicated in the perceived impact of, adjustment to, and management of numerous acute and chronic health conditions, and is recognised as a determining factor in performing self-care (Martos-Méndez, 2015). Furthermore, it is well established that SE is a modifiable treatment target, with enhancement in SE beliefs associated with improvements in both physical and psychological health outcomes (Bishop, Frain, & Tschopp, 2008; Hoffman, 2013).

Self-efficacy beliefs impact on an individual's behaviour in two major ways. First, SE determines how much effort and persistence individuals exhibit in the face of challenges or adversity (Bandura, 1977). That is, individuals with higher SE are said to have greater confidence in their ability to complete a task and persist longer in those efforts whereas those who endorse low levels of SE perceive themselves as not being able to cope. This contributes to poor planning and higher levels of psychological distress (Airlie, Baker, Smith, & Young, 2001; Shnek et al., 1997). Second, an individual's perceived SE influences decision making and goal setting: those with lower SE likely to avoid difficult tasks and have low aspirations (Shnek et al., 1997).

Bandura (1977) posits that there are four sources of information that contribute to the development of SE beliefs: direct mastery experiences, vicarious experiences, social/verbal persuasion, and physiological or affective states. Mastery experiences or successful task completion through sustained effort are the most effective way of developing a strong sense

of SE. Vicarious experiences - observing others similar to oneself succeed through perseverant effort – also raises ones' belief that they, too, possess the skills to succeed with a similar task. Social/verbal persuasion, in which respected others (e.g., health professional) provide positive feedback and encouragement regarding capabilities to achieve a goal, promotes SE beliefs, although it is argued that the effects are only transitory (Rajati et al., 2014). Finally, an individual's mood and interpretation of their stress reactions (both physical and psychological) can influence judgements regarding SE.

Self-efficacy is also conceptualised at two levels: general and task-specific SE. General SE focuses on a broad sense of personal competence. It refers to an individual's confidence in his or her ability to cope effectively with a variety of demanding situations (Chen, Gully, & Eden, 2001; Sherbaum, Cohen-Charash, & Kern, 2006). General SE has been studied widely in relation to chronic illness with many measures adapted for use in various disease populations (e.g., Arthritis SE Scale, MS SE scale). Measures of general SE assess perceived ability to perform the broad range of behaviours and skills required in chronic illness management (Mohebi, Azadbakht, Feizi, Sharifirad, & Kargar, 2013). Conversely, some researchers have perceived general SE in a task-specific manner. In this context, SE refers to an individual's level of self-confidence to manage and successfully engage in an activity specific to a situation (Banik, Schwarzer, Knoll, Czekierda, & Luszczynska, 2018). However, the degree of specificity varies with the context. For instance, if a researcher is interested in exercise SE, or an individual's beliefs in their ability to engage in physical activity (e.g. Dlugonski, Wojcicki, McAuley, & Motl, 2011; Ferrier, Dunlop, & Blanchard, 2010), or self-confidence and efficacy in the job search process (Dorstyn et al., 2018), the wording of SE items will be quite narrow and specific.

There is argument that SE is dependent upon context, situational demands and one's prior experience with a given task, thus emphasising the importance of measuring task-

specific SE. Indeed, some researchers have argued that task-specific SE provides an accurate picture of an individual's perception of their ability to perform a task or skill (Keefer, Kiebles, & Taft, 2011). However, whilst the high specificity of task-specific SE measures is important in some contexts, they only allow prediction of a limited range of behaviours or outcomes, and therefore cannot be generalised to general tasks/domains, such as the multi-task health-care regimens that are associated with the successful self-management of chronic disease such as MS (Banik et al., 2018; Luszczynska & Schwarzer, 2015). For individuals with MS, common challenges are not limited to a specific task or area of functioning, instead they experience a constellation of symptoms that are unpredictable and vary as the disease progresses. For this population, then, general rather than task-specific SE is more appropriate.

Self-Efficacy and MS Symptoms

The relationship between SE and MS symptoms is of interest in MS rehabilitation, with SE representing an important target for psychological intervention for diagnosed individuals. MS researchers have demonstrated the impact of SE beliefs in the occurrence and severity of a range physical, psychological and cognitive MS disease symptoms. These symptoms are discussed in more detail below.

Physical symptoms.

Fatigue. The relationship between fatigue and SE in persons with MS remains unclear, with studies reporting varied findings. For instance, a 6-week intervention program designed to build perceived SE through education and support from others living with MS, noted significant pre- to post-improvement in the perceived impact of fatigue on daily functioning (Mulligan et al., 2016). Furthermore, Trojan et al. (2007) found that reduced MS-specific SE was a predictor of general, physical and mental fatigue in a small, cross-sectional study of 53 individuals with relapsing-remitting and progressive forms of MS.

Conversely, while Nedeljkovic et al. (2016) found no change in self-reported fatigue severity immediately following a 3-week multidisciplinary rehabilitation program, significant improvement in MS-related SE was reported at 1- and 3-months follow-up. When interpreting the above findings consideration must be given to patient demographics. For example, Mulligan et al.'s (2016) intervention study focussed exclusively on females. It is widely accepted that gender differences exist in SE (Bandura, 1997). Within the MS literature, women have also been found to have a significantly greater belief in their ability to function with MS compared to men (Fraser & Polito, 2007). Thus, gender represents an important moderating factor on SE beliefs and requires examination.

Pain. Within the wider chronic disease literature, the relationship between pain and SE has been well established. Meta-analytic data of chronic pain samples ($N_{participants}$ = 15, 161) confirms a large and significant correlation: high SE is a strong correlate, and potentially important risk/protective factor, for adjustment to chronic pain (Jackson, Wang, Wang, & Fan, 2014). In comparison, the relationship between pain and SE beliefs in individuals with MS is not yet established, although preliminary evidence suggests there may be a negative relationship. In their study of 292 adults with predominately (84%) relapsing-remitting MS, Motl et al. (2009) reported a large, significant relationship between pain levels and illness-related SE beliefs: those reporting sensory (i.e., pain location, intensity, sensation) and affective aspects of pain (i.e., overall appraisal of pain) reported low SE.

Mobility. Research indicates that higher levels of SE are significantly correlated with increased function, including mobility. For instance, Sinnakaruppan et al. (2010) reported that higher SE expectations were associated with higher ratings of physical functioning among 115 outpatients with MS. In contrast, Shnek et al. (1997) found no significant relationship between SE and mobility. This variation may, however, be attributed to the use

of a disease-specific measure of SE which was originally designed for use in individuals with arthritis, hence may not capture specific issues for MS.

Physical activity. A number of studies have examined self-efficacy's reciprocal relationship with physical activity. Those with a higher sense of exercise SE are more likely to engage in physical activity (Motl, Snook, McAuley, & Gliottoni, 2006). Moreover, successful exercise routines can contribute to strong SE (Motl et al., 2006). Whether this same relationship exists in regard to general SE is, however, unknown. For instance, in their sample of 292 individuals with chronic MS (average 10 years post-diagnosis), Motl et al. (2009) reported a significant positive correlation between scores on the MS Self-Efficacy Scale (MSSE; Schwartz, Coulthard-Morris, Zeng, & Retzlaff, 1996), and time spent engaging in physical activity: the higher the level of SE, the more reported time spent physically active. However, Ng et al. (2013) found no such relationship in their sample of 129 individuals who had lived with a diagnosis of MS for an average of 4 years. Given the significant difference in mean time since diagnosis between samples, this may represent a possible moderating factor. Indeed, Fraser and Polito (2007) argue that the increasing disability and psychosocial changes (e.g., employment status, losses in social roles) which individuals with MS typically experience over time can impact negatively on perceived SE beliefs. Conversely, others contend that time since diagnosis may enhance an individual's ability to adapt to living with MS and, therefore, lead to higher levels of SE (Devins & Seland, 1987).

Psychological symptoms.

Depression. Self-efficacy has been widely established as an important mediating factor in relation to depressive symptoms in MS. For instance, a study of 292 community-dwelling individuals recruited from the US-based National Multiple Sclerosis Registry found that two self-report measures – MSSE and the Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith, 1983) were strongly and inversely correlated (r = -.62; Motl,

McAuley, Snook, & Gliottoni, 2009). However, it is important to consider the generalisability of these findings. In particular, Motl et al. (2009) recruited their sample through MS societies and support groups. As such, their sample included participants already engaged with MS services and, potentially, more receptive to such support. A smaller study of outpatients (N = 93) recruited from two outpatient clinics in the UK also found a significant association between depressive symptoms and perceived SE (r = -.56; Airlie et al., 2001). Integration of these findings, in the form of a quantitative review, would perhaps widen the generalisability of the findings to the broader MS population.

Anxiety. As with depression, the relationship between MS-related anxiety symptoms and SE beliefs has been widely studied, although this literature is characterised by substantial heterogeneity. For instance, an Australian-based cross-sectional study reported a moderate significant relationship between SE and anxiety symptoms in individuals who were newly diagnosed with MS (average time since diagnosis = 2 years), as measured by the HADS (Tan-Kristanto & Kiropoulos, 2015). A similar relationship was identified in a UK-based sample of adults with chronic MS: low SE was implicated as a possible psychosocial risk factor for the development of anxiety symptoms (Garfield & Lincoln, 2012). However, this latter study excluded individuals with deficits in cognitive functioning (Garfield & Lincoln, 2012). This limits the generalisability of findings given that over 50% of individuals with MS experience severe cognitive deficits (Chiaravalloti & DeLuca, 2008). Furthermore, the range of disability experienced by individuals with MS was limited, with participants across both studies screened based on their ability to walk independently without a mobility aid (i.e., Expanded Disability Scale Score < 6.5; Garfield & Lincoln, 2012).

Self-esteem. Self-esteem, a judgment of one's self-worth (Rosenberg, 1989), is an evaluation often based on important life domains such as physical and psychological health. Uccelli, Traversa, and Ponzio (2016) examined the relationship between self-esteem and SE

in community-dwelling young adults (age range 18-35) with MS and found that individuals reporting high self-esteem also endorsed higher SE. The limited age range of the sample, however, may limit the generalisability of the findings to the broader MS population. Indeed, a negative association between general SE and age has been reported amongst other chronic disease populations (e.g., diabetes; Dehghan et al., 2017). Fraser (2005) also reported strong relationships between both the control and function subscales of the MSSE and self-esteem (as measured by the Rosenberg Self-Esteem Scale) among their sample of 550 individuals with MS. Notably, this study provided limited methodological and procedural detail, possibly as the results were presented in a conference proceeding, bringing the validity of these findings into question.

Worry. Within the general population, higher levels of worry have been associated with lower levels of SE (Tahmassian & Jalali Moghadam, 2011). Within the MS literature, Thornton, Tedman, Rigby, Bashforth, and Young (2006) found that individuals endorsing higher levels of worry, as measured by the Penn State Worry Questionnaire - a common screening tool for Generalised Anxiety Disorder (Meyer, Miller, Metzger, and Borkovec, 1990), also reported a decreased sense of MS-specific SE. However, this finding was based on a small (N = 39) cross-sectional study of individuals with MS.

Hopelessness. Reduced SE contributes to negative self-statements including hopelessness, or negative expectations about the future. The role of hopelessness has been explored in chronic illness populations, such as amyotrophic lateral sclerosis and lung cancer (Akechi et al., 1998; Plahuta et al., 2002), but less so in MS. Sinnakaruppan et al. (2010) reports limited evidence to suggest that hopelessness and MS-related SE are inversely related. More specifically, those who perceived poor control over the ability to cope with their illness (MSSE Control subscale) also reported increased feelings of hopelessness about the future in addition to reduced motivation and expectations. This same study provided limited

information regarding key sample parameters - such as marital status, employment status, and number of comorbidities, all of which have been shown to influence perceived SE in those with a chronic illness (Buck, Poole & Mendelson, 2010; Wade et al., 2013). In sum, the impact of potential sample confounds needs to be considered when examining the role of SE in MS symptom management (Calandri et al., 2018; Plow et al., 2015).

Cognitive symptoms. Less is understood about the relationship between cognitive functioning and SE beliefs. For instance, in their large longitudinal study of community-dwelling individuals with MS, Hughes et al. (2015) identified SE as a significant predictor of general cognitive functioning and executive functioning, independent of the effects of depression and fatigue. However, Middleton, Denney, Lynch and Parmenter (2006) found no significant relationship between perceptions of global cognitive and objective performance, as measured by the Neuropsychological Screening for MS. Furthermore, self-reported depression and fatigue have been found to influence cognition, although these results have not been replicated with clinician-based neuropsychological assessments (Kinsinger et al., 2010; Middleton et al., 2006).

Preliminary evidence of the relationship between cognitive performance and illness-related SE was provided by Jongen et al. (2015) based on a select sample of adults recently diagnosed (i.e., < 2 years) with clinically isolating syndrome or relapsing-remitting MS. Various types of attention, reaction time and memory were assessed using a battery of computerised cognitive tests from the Cognitive Drug Research system (CDR; Wesnes et al., 1987). Those who reported high SE demonstrated poorer performance on tasks of immediate and delayed word recall, word recognition and picture recognition (episodic memory), and complex information processing speed (speed of memory). Notably, these findings were based on a sample of 33 employed individuals. This may limit the generalisability of findings, given that a recent international study found that 39% of individuals with MS were

unemployed (MS International Federation, 2016). As such, employment status may represent a key confound when examining SE beliefs, as has been demonstrated in the general population (Lunenburg, 2011).

Summary

MS is a common and debilitating neurological disorder characterised by an unpredictable and chronic course. This symptom course involves physical, psychological and cognitive impairments of varying severity. With no current cure, SE has been recognised as an important contributing factor in MS symptom management. However, questions remain as to the magnitude of these relationships. Future research examining the relationship between SE and MS symptoms must consider the operationalisation of SE in addition to potential demographic and illness moderators. This research can then help to inform the development of efficacy enhancing interventions for use in MS care and, in turn, reduce the symptom burden associated with this chronic disease.

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Associations between Self-Efficacy and Multiple Sclerosis Symptoms: A Systematic Review and Meta-Analysis

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Abstract

Background: Perceived self-efficacy (SE), or belief in one's own abilities, can enhance symptom self-management in adults with multiple sclerosis (MS). To date, a quantitative review of this literature is missing. **Methods:** Twenty-two independent studies ($N_{participants}$ = 2846) were identified from the Pubmed, PsycINFO, Embase, CINAHL and Scopus databases. Data were categorised according to three symptom domains: physical, psychological and cognitive. Study reporting quality was evaluated using the *QualSyst* tool. Correlation *r* was the primary effect size index. Associated 95% confidence intervals (Cls), *p*-values and Fail-safe *N*s in addition to between-study heterogeneity (tau squared and I^2) were calculated using a random effects model. **Results:** Medium-to-large pooled correlations were noted across physical and psychological symptom domains. That is, higher SE was associated with reduced fatigue (r_w = -.57; 95% CI [-.64, -.49]), improved mobility (r_w= .39; 95% CI [.25, .52]), and self-esteem (r_w= .58; 95% CI [.38, .67]), alongside reduced depression (r_w= -.49; 95% CI [-.56, -.41]) and anxiety (r_w= -.44; 95% CI [-.48, -.39]). An individual study identified significant associations between greater SE and improved cognitive performance. The observed effects were similar, regardless of whether studies utilised general or disease-specific SE measures. **Conclusions:** Rehabilitation interventions for adults living with MS should incorporate SE concepts in order to teach techniques that can enhance fatigue management in addition to mobility, self-perception and psychological wellbeing. Further longitudinal research is necessary to clarify the casual pathways between SE and MS symptom development in addition to temporal changes in these pathways in response to the MS clinical course.

Keywords: multiple sclerosis, self-efficacy, symptom, meta-analysis

Impact and Implications

- This work is the first to systematically and quantitatively review the available literature on the relationship between self-efficacy (SE) and the burden of the physical, psychological and cognitive symptoms of multiple sclerosis (MS).
- Pooled findings from 22 studies identified consistent patterns: higher SE was significantly and positively associated with physical functioning (i.e., reduced fatigue, improved mobility) and psychological wellbeing (i.e., higher self-esteem, reduced anxiety and depression). There was limited evidence in relation to the role of SE in cognitive performance.
- Self-efficacy represents an important early intervention target for MS. Routine assessment of SE beliefs, from the time of diagnosis and throughout the MS symptom course, supplemented with psychoeducational interventions to improve knowledge, skills and abilities in self-care can help to reduce the symptom burden of MS.

Introduction

Multiple sclerosis (MS) is a chronic, degenerative neurological disorder and the primary cause of non-traumatic, permanent disability in young adults (Ramagopalan & Sadovnick, 2011), affecting 2.5 million worldwide (Koriem, 2016). The disorder is characterised by variable patterns of sensory, motor, psychological and cognitive impairments that can be detrimental and disruptive to many aspects of daily life (Rigby, Domenech, Thorton, Tedman, & Young, 2003). Physical impairments commonly include fatigue (65% of individuals experience daily) and pain (prevalence of 63%); considered to be the most common and disabling symptoms of MS (Trojan et al., 2007). MS also impedes mobility and activity levels (Motl et al., 2005; Sinnakaruppan, Macdonald, McCafferty, & Mattison, 2010). This is concerning given that physical activity is associated with a reduction in MS-related symptoms and, in turn, improved health-related quality of life (Pardo &

Fjeldstad, 2011). Psychological disorders frequently experienced by individuals living with MS include depression and anxiety, with point prevalence estimates of 21% and 10%, respectively. These rates are substantially higher than those reported in the general population (range: 3.6-8% for depression diagnosis, and 2.6 -7.7% for anxiety diagnosis; World Health Organisation, 2017), as well as other chronic disease populations (Krebber et al., 2014; Williams & Murray, 2015). Other psychological difficulties commonly experienced by this cohort include low self-esteem (McCabe, 2005), worry (Bruce & Arnett, 2009) and hopelessness (Patten & Metz, 2002a). Cognitive function can also be affected. Indeed, over 70% of persons with MS experiencing some form of cognitive impairment over the course of the disease (Chiaravalloti & DeLuca, 2008).

The complex symptom profile in MS results in high healthcare utilisation and lower quality of life (Ke et al., 2016; Williams, Vietri, Isherwood, & Flor, 2014). With no known cure, it is important that patients are informed and educated about symptom management (Kraft et al., 2008). To this end, a vast body of research has examined the psychosocial factors which contribute to effective MS symptom management. A construct that is critical to optimising symptom self-management behaviours is self-efficacy (SE), identified as a significant predictor of disease management and adjustment in MS (Eccles & Simpson, 2011; Hoffman, 2013).

Self-efficacy refers to an individual's belief in his or her ability to implement behaviour to achieve a desired outcome, goal, or expectation, across a variety of situations (Bandura, 1986). It is a core concept of Bandura's (1977) social cognitive theory – which posits that people learn by observing others. Self-efficacy is conceptualised at two different levels: general and task-specific SE. General SE focuses on a broad sense of personal competence and refers to an individual's confidence in his or her ability to cope effectively with a variety of demanding situations. General SE has been studied widely in relation to

chronic illness with many measures adapted for use in various disease populations (e.g. Arthritis SE Scale, MS SE scale). Measures of general SE assess perceived ability to perform the broad range of behaviours and skills required in chronic illness management (Mohebi, Azadbakht, Feizi, Sharifirad, & Kargar, 2013). Conversely, some researchers have perceived general SE in a task-specific manner. In this context, SE refers to an individual's level of self-confidence to manage and successfully engage in an activity specific to a situation (Banik, Schwarzer, Knoll, Czekierda, & Luszczynska, 2018). However, the degree of specificity varies with the context. For instance, if a researcher is interested in exercise SE, or an individual's beliefs in their ability to engage in physical activity (e.g., Dlugonski, Wojcicki, McAuley, & Motl, 2011; Ferrier, Dunlop, & Blanchard, 2010), or even self-confidence and efficacy in the job search process (Dorstyn et al., 2018), the wording of SE items will be quite narrow and specific.

There is argument that SE is dependent upon context, situational demands and one's prior experience with a given task, thus emphasising the importance of measuring task-specific SE. Indeed, some researchers have argued that task-specific SE provides an accurate picture of an individual's perception of their ability to perform a task or skill (Keefer, Kiebles, & Taft, 2011). However, whilst the high specificity of task-specific SE measures is important in some contexts, they only allow prediction of a limited range of behaviours or outcomes, and therefore cannot be generalised to general tasks/domains, such as the multi-task health-care regimens that are associated with the successful self-management of chronic disease such as MS (Banik et al., 2018; Luszczynska & Schwarzer, 2015). For individuals with MS, common challenges are not limited to a specific task or area of functioning, instead they experience a constellation of symptoms that are unpredictable and vary as the disease progresses. For this population, then, general rather than task-specific SE is more appropriate.

SE represents an important target for rehabilitation intervention for persons diagnosed with MS. However, the relationship between SE and symptom impairment remains unclear. For example, some studies have reported a significant association between fatigue severity and reduced SE (Mulligan et al., 2016; Trojan et al, 2007), whereas others have not (Nedeljkovic et al., 2016). Mixed findings have also been noted in relation to the role of SE in promoting mobility (Sinnakaruppan et al., 2010; Shnek, 1997) or even physical activity levels (Motl et al., 2009; Ng et al., 2013). Conversely, SE has been widely established as an important mediating factor in relation to depressive (e.g., Airlie et al., 2001; Motl et al., 2009) and anxiety symptoms (e.g., Tan-Kristiano & Kiropoulos, 2015; Garfield & Lincoln, 2012) in MS, although this literature is also characterised by methodology heterogeneity. For example, studies have, excluded participants based on their level of disability (i.e., Expanded Disability Scale Score > 6.5; Tan-Kristanto & Kiropoulos, 2015) and level of cognitive functioning (Garfield & Lincoln, 2012). Consequently the generalisability of these findings to individuals with other clinical courses of MS and those who are more severely impacted by the disease may be limited.

The assessment of SE beliefs within the MS literature also varies greatly, with some studies utilising general SE measures while others rely upon MS-specific measures. Whether SE-symptom associations differ depending on the measure of SE remains unknown. Variation in method of symptom data collection (i.e., self-report vs. clinician-administered tools) represents another possible source of heterogeneity, with self-report measures prone to under-reporting and over-reporting of symptoms (Brenner & DeLamater, 2016; Hunt, Auriemma, & Cashaw, 2003).

Sociodemographic characteristics of MS samples may also contribute to between-study differences. For instance, it is widely accepted that gender differences exist in SE (Bandura, 1997), with women found to have a significantly greater belief in their ability to

function with MS compared to men (Fraser & Polito, 2007). However, MS studies are typically biased towards females, due to the predominance of MS in women (Ahlgren, Oden, & Lycke, 2011). Substantial fluctation in mean time since diagnosis among studies represents another possible moderator. Indeed there is argument that the increasing disability and psychosocial changes (e.g., vocational status, losses in social roles) typically experienced by individuals with MS have a detrimental, additive impact on perceived SE beliefs over time (Fraser & Polito, 2007).

In summary, the relationship between SE and the occurrence and severity of MS symptoms has been examined, however, methodological inconsistences and limitations characterise this literature. The current study provides a systematic and quantitative review of the literature in an attempt to answer the following research questions: *What is the magnitude of the association between SE beliefs and the various MS symptoms that have been examined in the existing literature? Which symptoms have the strongest individual association with SE? And, to what extent is the strength of this association moderated by (a) SE measurement used and (b) sample characteristics, namely sociodemographics (e.g., gender, age) and illness details (e.g. time since diagnosis)?* By synthesising this evidence, I aim to identify gaps in the research but also help to inform the development of self-management programs for individuals with MS.

Method

Literature Search

Five electronic databases (PubMed, PsycINFO, Scopus, Embase, and CINAHL) were searched for publications between January 1970 (i.e., database inception) and September 2018. The search strategy, developed in consultation with a research librarian, included a broad list of keywords and phrases related to the population (e.g., multiple sclerosis, disseminating sclerosis), the psychological construct of interest (i.e., self-efficacy, self-

concept) and common MS symptoms and sequelae (i.e., psychological, physical, cognitive - as described by DasGupta & Fowler, 2003; Goldenberg, 2012; Williams, Vietri, Isherwood, & Flor, 2014) (see Appendix A for example logic grid). Reference-checking of all included studies and relevant reviews (Arnett, Barwick, & Beeney, 2008; DasGupta & Fowler, 2003; Dorstyn, Black, Mpofu, & Kneebone, 2017; Young & Edwards, 2014) was conducted to ensure that all relevant articles were included. As a countercheck, international peer-reviewed journals covering the clinical neurology and rehabilitation of MS (*Multiple Sclerosis Journal, International Journal of MS Care, Multiple Sclerosis International, Multiple Sclerosis and Related Disorders, Multiple Sclerosis from BMJ)* were electronically searched using, 'self-efficacy' and 'symptoms' as keywords. This review is registered on the PROSPERO database for systematic reviews (protocol no. CRD42018102103).

Eligibility Criteria

Studies which targeted adults (aged ≥ 18 years) diagnosed, or reported having been diagnosed, with MS (McDonald et al., 2001; Polman et al., 2011; Thompson et al., 2018) and which incorporated a multi-item, standardised measure of self-efficacy (SE) were eligible for inclusion. For the purpose of this review, Bandura's (1977) conceptualisation of general SE, which emphasises an individual's perception of his or her ability to perform across a variety of situations, was adopted. Studies which adopted extensions of a generalised SE measure for use with persons with MS (e.g., MS Self-Efficacy Scale [MSSE]) were eligible. Studies also had to report a relationship between SE and MS symptom severity, that is physical (e.g., fatigue, pain), psychological (e.g., depression, anxiety), and/or cognitive (e.g., attention) impairments or sequelae experienced as a direct or indirect consequence of the disease process. In addition, studies had to provide parametric data to enable the calculation of an effect size *r* (i.e., means, SDs, correlations, one-way ANOVA statistic, *t*-tests, exact *p*

values). To ensure methodological rigour, only journal articles in English were eligible (Jüni, Holenstein, Sterne, Bartlett, & Egger, 2002).

Studies that adopted the SE construct to explain specific behaviours or skills (e.g., self-efficacy for physical activity) were ineligible. Studies that did not separate the data for individuals with MS from those with other diagnoses (e.g., brain injury, spinal cord injury, cancer) were also excluded. Additionally, studies which reported multivariate data (e.g., regression R^2, ß coefficients) were not eligible – this ensured that effect estimates were equivalent, by exclusively examining the bivariate relationship between SE and a given MS symptom.

Reliability of the article selection process was checked, with a second reviewer (post-graduate psychology student, P.T) screening the titles and abstracts of 50 potentially eligible articles randomly selected by the author (K.P). Inter-rater reliability was high, with agreement achieved on 94% of occasions, $\kappa = 0.88$, 95% CI [0.75, 1.0] (McHugh, 2012). Any discrepancies were subsequently discussed and resolved by consensus.

The initial literature search returned 1,766 articles, which reduced to 1,133 after removal of duplicates. The titles and abstracts of each article were subsequently reviewed against the eligibility criteria, further narrowing the pool of potentially relevant articles to 418. The full-text versions of these studies were obtained, and eligibility once again assessed. An additional primary study was found by manual inspection of the reference lists of available MS review papers, resulting in a total of 24 eligible studies. These studies were further examined to ensure independence of samples. Sample overlap was suspected in four studies: two led by Motl (Motl, McAuley, Snook, & Gliottoni, 2009; Motl & Snook, 2008) and two by Shnek (Shnek et al., 1997; Shnek, Foley, LaRocca, Smith, & Halper, 1995). Attempts to contact the corresponding or lead authors of these studies were not successful. As sample overlap remained a possibility, these four studies were combined and treated as

two independent studies. The final sample comprised of 22 independent studies (see Figure 1).

Risk of Bias Assessment

The reporting quality of the overall evidence was assessed using the *QualSyst* tool (Kmet, Lee, & Cook, 2004). This scale critically appraises study design, sample selection and sample size – aspects which can contribute to methodological bias. Three criteria specific to intervention studies (i.e., *random allocation, blinding of investigators, blinding of subjects*) were not applicable to the cross-sectional data analysed and so were excluded (Kmet et al., 2004). Each study was therefore rated against 11 quality criteria ('Yes'= 2, 'Partial'= 1, 'No'= 0), with a summary score calculated for each by summing the relevant item score and dividing by the total possible sum (score range from 0.0 to 1.0). The percentage of studies receiving scores of 2, 1 and 0, for each item was additionally calculated.

Data Extraction, Organisation and Preparation

In line with evidence-based recommendations for the reporting of meta-analysis (PRISMA; Moher, Liberati, Tetzlaff, & Altman, 2009), summary data was extracted from each study using a purposely designed Microsoft excel sheet. This data included: (1) sample demographics (e.g., mean age, gender, education, marital status), (2) illness variables (e.g., MS subtype, disease duration - standardised, in years), (3) study characteristics (e.g., study design, sample *N*), (4) outcome measurement and (5) effect-size data in the form of Pearson's correlation *r*. This metric quantifies the direction and strength of the relationship between SE and MS symptom severity. The lead author of one study (Henneghan et al., 2017) provided this additional data on request. Publications were subsequently checked for

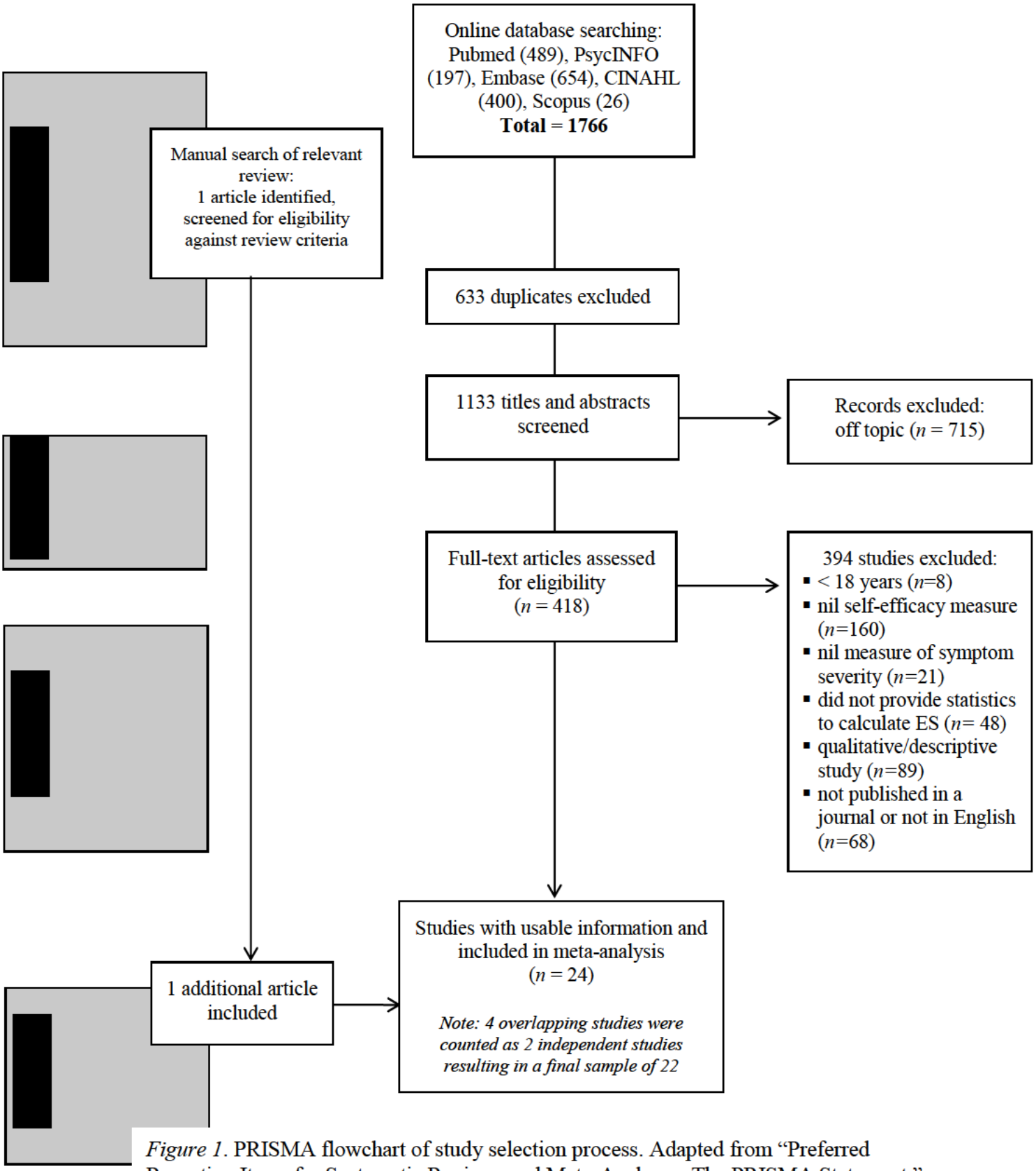

Figure 1. PRISMA flowchart of study selection process. Adapted from "Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement," by D. Moher, A. Liberati, J. Tetzlaff, D. G. Altman, The PRISMA Group, 2009, *PLoS Medicine,* 6(7): e1000097.

coding of scales. For one domain, mobility, data were standardised so that higher scores on a given measure (e.g., Patient Determined Disease Steps) represented greater levels of impairment. Overall, thirteen MS symptoms were identified and classified according to three broad impairment types or domains: physical (i.e., mobility, physical activity, fatigue, pain) psychological (i.e., depression, anxiety, self-esteem, worry, hopelessness), and cognitive (i.e., memory, attention, reaction time).

Data Analysis

Comprehensive Meta-Analysis Software was utilised for the data analysis (Version 3, 2014 Biostat, Englewood, NJ, USA). Effect sizes were interpreted according to Cohen's (1992) guidelines, with correlations of 0.10, 0.30 and 0.50 representing small, medium and large associations, respectively. Pooled effect sizes were calculated for each symptom category following methods described by Lipsey and Wilson (2001). First, to ensure no issues of dependency within the data, each study contributed only one bivariate association (SE-MS symptom *r*) to each symptom. If a study reported *r*s on multiple aspects of SE (e.g., MSSE subscale scores), an average *r* was calculated. This involved transforming individual *r's* to Fisher's *Z* (thereby avoiding bias towards underestimation of the effect size in simple *r* averaging procedures; Corey, Dunlap & Burke, 1998), computing the average Fisher's *Z* and then back-transforming *Z* to the original *r* metric (Borenstein, Hedges, Higgins & Rothstein, 2011). Third, effect sizes from different studies that utilised the same combination of SE and symptom measurement, were pooled. Finally, an average *r* was obtained for each broad symptom category (i.e., physical, psychological, cognitive) using the same procedure. As the reliability of individual effect sizes is somewhat dependent on their underlying sample size (e.g., larger samples represent less sampling error), study *rs* for each symptom domain were weighted by their inverse variance before being pooled (mean r_w; Cohen, 1992). Given the clinical and methodological heterogeneity present in the MS literature (Disanto et al., 2011;

Ziemssen, Medin, Couto, & Mitchell, 2017), weighting was based on a random-effects model (Borenstein et al., 2011). The model assumes that variation between observed effect sizes is due to subject-level sampling error as well as differences within individual study designs (Lipsey & Wilson, 2001).

To determine the accuracy of individual and pooled effect sizes, 95% confidence intervals (CIs) and exact *p*-values were calculated. Effect sizes were considered statistically significant if the CI did not span zero and the associated *p*-value was < 0.05 (Stratford, 2010). To account for a potential validity threat - publication bias, Orwin's (1983) fail-safe *N*s (N_{fs}) was calculated for both individual and pooled *r*s (Zakzanis, Leach, & Kaplan, 1999). N_{fs} represents the hypothetical number of unpublished or unidentified studies reporting no effect required to render a calculated effect size as meaningless (i.e., $r < 0.1$). The higher the N_{fs} value, the more robust the effect estimate. A N_{fs} was considered adequate if its value exceeded the number of studies contributing to an *r* (i.e., $N_{fs} > N_{studies}$). This provided a more conservative estimate than other formulas where *N* refers to the total number of studies that are undergoing a meta-analysis (Lipsey & Wilson, 2001).

Between-study heterogeneity was evaluated using tau squared (τ^2) and I^2 statistics. τ^2 reflects the between-studies variance (with τ analogous to a standard deviation for the overall r_w; Borenstein et al., 2011, p. 116). I^2 is a proportional estimate of true effect variance over sampling error observed, expressed as a percentage from 0 (low) to 100% (high) heterogeneity (Borenstein, Higgins, Hedges, & Rothstein, 2017; Higgins, Thompson, Deeks, & Altman, 2003).

For the purposes of interpretation, SE was considered to have important personal and clinical implications in symptom management for persons with MS, if it was: (a) found to have at least a medium ($r \geq .30$) association that was (b) statistically significant (i.e., 95% CI

did not contain 0), and was (c) robust to publication bias (i.e., $N_{fs} > N$ studies included for a given analysis).

Moderator analyses. The potential moderating effects of measurement characteristics (i.e., general vs. illness-related SE); were evaluated for the depression symptom category. This domain was associated with moderate to substantial heterogeneity ($I^2 \geq 50\%$) and had sufficient statistical power for subgroup analysis (i.e., $N_{studies \geq} 10$ or average pooled sample size $N > 80$; Fu et al., 2011; Huedo-Medina, Sánchez-Meca, Marín-Martínez, & Botella, 2006). Group mean differences were examined using the *Q*-test of homogeneity and a mixed-effects model: thereby assuming some within-group variation of the true effects estimates (Borenstein et al., 2011). In addition, data from six individual studies which specifically evaluated the relationship between SE and potentially important contextual variables were examined: medical comorbidities (number of), age, gender, relationship status, education level, MS duration and subtype.

Results

Study Characteristics

The characteristics of the 22 studies included in this meta-analysis are presented in Table 1. Twenty studies were observational in design (i.e., cross-sectional, cohort, case control) with two intervention trials included (providing baseline data only). Publication dates ranged from 1995 to 2018. Data originated from Europe ($N_{studies} = 10$) and North America ($N_{studies} = 9$), followed by Canada ($N_{studies} = 2$), with a single study from Australia contributing. Recruitment sources included outpatient rehabilitation clinics, MS data registries, primarily the National MS Society and MS Research Australia databases, community support and advocacy groups, and a clinical trial unit.

Table 1

Study Characteristics

First author (year)	Country	*N* (m:f)	Mean age (*SD*)	Mean years since diagnosis (*SD*)	Recruitment source	SE measure (s)	Study design
Airlie (2001)	UK	93 (20:73)	45 (11.2)	10 (8.3)	Outpatient; community	LSSS	Cross-sectional
Calandri (2018)	Italy	90 (35:55)	37 (12)	-	Outpatient	SEMS	Cross-sectional
Fournier (2002)	Netherlands	98 (39:59)	45 (9.3)	4 (3.4)	Outpatient	GSE	Cross-sectional
Garfield (2012)	UK	157 (47:110)	50 (10.15)	11.42 (7.7)	Community	MSSS	Cohort
Goodworth (2016)	USA	199 (36:163)	46.24 (10.83)	8.3 (6.84)	Outpatient	MSSE	Cross-sectional
Henneghan (2017)	USA	183 (23:160)	49.35 (7.95)	12.64 (7.97)	Outpatient; community	Sherer SE	Cross-sectional
Jongen (2015)	Netherlands	33 (3:25)	39.8 (8.5)	1.125 (.4)	Outpatient	MSSE	Cross-sectional
Lester (2007)	USA	82 (18:64)	44 (11.08)	7 (6.73)	Outpatient	SEMCD	Cross-sectional
Motl (2008; 2009)^	USA	292 (47:245)	48 (10.3)	10.3 (7.9)	Community	MSSE	Cross-sectional
Motl (2013)	USA	269 (46:223)	45.9 (9.6)	8.8 (7)	Community	MSSE-C; MSSE-F	Cohort
Motl (2017)	USA	69 (21:48)	50.5 (8.9)	14.4 (10.5)	Community	MSSE-C; MSSE-F	Cross-sectional
Ng (2013)	USA	129 (30:99)	49 (11)	4 (2)	Community	MSSE-C	Intervention
Plow (2015)	Canada	335 (68:267)	53 (10.2)	15 (8.3)	Community	CDSE	Cross-sectional
Riazi (2004)	UK	89 (26:63)	43.6 (12.1)	-	Outpatient	MSSE-C; MSSE-F	Intervention
Rigby (2003)	UK	142 (46:96)	44.7 (9.67)	9 (7.08)	Outpatient; community	MSSE; SESMS	Cross-sectional
Schmitt (2014)	USA	81 (20:61)	48.6 (9.3)	14.34 (10.17)	Outpatient; community	MSSE	Cross-sectional
Shnek (1995; 1997)^	USA	80 (28:52)	44.1 (10.1)	9.2 (5.7)	Outpatient	MSBS; ABS (adapted)	Cross-sectional
Sinnakaruppan (2010)	Scotland	115 (44:71)	45.56 (10.43)	8.74 (8.44)	Outpatient	MSSE-C; MSSE-F	Cohort
Tan-Kristanto (2015)	Australia	129 (12:117)	38.41 (9.18)	2.04 (1.45)	Community	MSSE	Cross-sectional
Thornton (2006)	UK	39 (12:27)	48.3 (9.34)	-	Community	SESMS	Cross-sectional
Trojan (2006)	Canada	53 (19:34)	47 (9.6)	15.1 (8.41)	Outpatient	ASES (adapted)	Cross-sectional
Uccelli	Italy	89 (14:75)	24.2 (2.8)	5.3 (3.2)	Community	GSE	Case-control

^Studies with overlapping samples were combined and treated as one independent study. *Measure Abbreviations:* ABS = Arthritis Belief Scale; ASES = Arthritis Self-Efficacy Scale; CDSE = Chronic Diseases Self-efficacy questionnaire; GSE = General Self-Efficacy Scale; LSSS = Liverpool Self-efficacy Scale; MSBS = MS Beliefs Scale; MSSE = Multiple Sclerosis Self-Efficacy Scale; MSSE-C = Multiple Sclerosis Self-Efficacy Scale – Control subscale; MSSE-F = Multiple Sclerosis Self-Efficacy Scale –Function subscale; MSSS = Multiple Sclerosis Self-efficacy Scale; SEMCD = Self-Efficacy for Managing Chronic Disease; SEMS = Self-Efficacy in Multiple Sclerosis scale; SESMS = MS Self-efficacy Scale; Sherer SE = Sherer Self-Efficacy scale.

A total of three standardised, self-report measures of general self-efficacy (e.g., General Self-efficacy Scale [GSE]) and eleven illness-related SE measures were utilised across studies. Some studies incorporated SE subscales. This commonly included the MSSE (Schwartz et a., 1996), which is partly based on Bandura's (1977) self-efficacy framework. The MSSE provides a total scale score in addition to subscale scores covering Function (i.e., confidence in one's ability to perform daily activities) and Control (i.e., confidence in managing disease symptoms and limitations). Studies relied on self-report rating scales to assess symptom severity, with few utilising the same combination of SE and symptom measurement.

Risk of Bias Assessment

The average quality assessment summary score was 0.91 (*SD* = 0.06, range = 0.82-1.0; see Appendix B). All studies therefore met the conservative threshold for inclusion (i.e., met more than 75% of items), as proposed by Kmet et al. (2004). More specifically, studies generally provided a clear description of their *objectives*, *study design* and *subject selection* (Criterion 1-3: 74% fulfilled). Key *subject characteristics*, such as age and gender, were also sufficiently reported (Criterion 4: 93% fulfilled), as were *outcomes.* This included clear definitions and justification for their use of SE and symptom measures (Criterion 5: 95% fulfilled). All studies were sufficiently powered (Criterion 6: 100% fulfilled) to detect a significant association between SE and symptom severity (i.e., $N = 26$, power at 0.80, $\alpha = 0.05$, $r = 0.50$; Cohen, 1992) and statistical *analyses* were pre-specified (Criterion 7: 93% fulfilled). *Estimates of variance* (e.g., confidence intervals, standard errors, range) were not routinely reported (Criterion 8: 68% fulfilled), however studies typically controlled for potential *confounders* (e.g. gender, ethnicity, level of education) by adjusting for covariates (Criterion 9: 95% fulfilled). Finally, significant and non-significant *results* were sufficiently explained (Criterion 10: 93% fulfilled), and *conclusions supported* (Criterion 11: 100%

fulfilled). In sum, studies included in this review provided sufficient information in relation to potential sources of methodological bias and none were excluded based on quality scores.

Participant Characteristics

The total, pooled sample comprised of 2846 individuals living with relapsing-remitting or progressive forms of MS (see Table 2). Both newly diagnosed and individuals with 2 to 51-year disease duration were represented. Disease severity (as measured by the

Table 2

Sample Characteristics ($N_{participants}$ = 2846)

Variable	$N_{studies}$	$N_{participants}$ (%)	*M*	*SD*	Range
Sample size	22	2846 (100)	129.37	81.11	39-335
Age	22	2846 (100)	46.12	11.33	18-90
Time since diagnosis (years)	19	2628 (92)	9.63	8.07	<1-51
MS severity (EDSS)	6	438 (15)	3.02	2.03	1-9
Gender					
Females	22	2187 (77)			
Males	22	659 (23)			
Marital Status					
Married/partnered	11	989 (73)			
Single/Widowed	9	443 (36)			
Employment status					
Employed	14	912 (49)			
Unemployed	13	914 (50)			
Education status					
> high school	7	755 (63)			
MS type					
RRMS	15	1545 (72)			
PPMS	10	163 (10)			
SPMS	11	336 (21)			
PRMS	3	67 (14)			
CIS	1	14 (42)			
Benign	1	3 (2)			
Unsure	4	60 (12)			

Note. MS = multiple sclerosis; CIS = Clinically Isolated Syndrome; EDSS = Expanded Disability Status Scale; RRMS = relapsing-remitting multiple sclerosis; PPMS = primary progressive multiple sclerosis; SPMS = secondary progressive multiple sclerosis; PRMS = progressive relapsing multiple sclerosis.

Expanded Disability Status Scale [EDSS], Kurtzke, 1983) varied: some participants were able to walk without any aid (EDSS score < 5) whilst others had significant impairment (EDSS score 5-9). The ratio of female to males was 3:1, consistent with the epidemiological profile of MS reported in the literature (Ahlgren, Oden, & Lycke, 2011; Milo & Miller, 2014). Employment rates ranged from as low as 25% (Rigby et al., 2003) to 100%, with Jongen et al. (2015) exclusively recruiting those in full-time employment. Additional socio-demographic details were not consistently reported ($N_{studies} < 12$).

Effect Size Estimates

Effect estimates for the 13 symptoms identified in this meta-analysis are grouped according to their impairment type (physical, psychological, cognitive) and presented, rank ordered by size, in Tables 3 to 5. Each MS symptom is reviewed in detail in the following sections.

Physical Symptoms

Fatigue. Motl et al. (2009) and Trojan et al. (2007) reported a large and significant relationship between fatigue symptom severity and illness SE among adults who had been living with MS for over a decade (see Table 3). That is, individuals reporting low SE for managing their MS also experienced severe fatigue, in terms of both physical and psychological (mental) exhaustion, which negatively impacted on their activities and lifestyle. Although the N_{fs} value exceeded the number of studies included in this analysis, suggesting that these results withstood publication bias, this finding was still based on limited data ($N_{studies} = 2$).

Pain. Motl et al. (2009) was the only study to assess pain levels in relation to illness-related SE beliefs in a sample of 292 adults with predominately (84%) relapsing-remitting MS (see Table 3). A highly significant and large effect size was noted: those reporting

sensory (i.e., pain location, intensity, sensation) and affective aspects of pain (i.e., overall appraisal of pain) reported low SE.

Mobility. Seven studies assessed the relationship between level of mobility and SE, commonly assessed with the MSSE (see Table 3). Both walking speed in everyday life, as measured by clinician-based assessment (e.g., Timed 25-Foot Walk test [T25-FW]; Fischer, Rudick, Cutter, & Reingold, 1999), and self-reported walking ability (e.g., Patient Determined Disease Steps [PDDS]; Hohol, Orav, & Weiner, 1995), were examined (see Table 4). Some dispersion was, however, evident amongst individual and pooled effect size estimates (i.e., wider CI) for this category (*r* range: -.48 to .14). The overall weighted effect was moderate and highly significant: higher SE expectations were associated with higher ratings of physical functioning. The large N_{fs} suggests that a substantial number of unpublished findings would be needed to overturn this result. Between-study variance was, however, noted, with small to very large individual effect estimates reported across the seven studies. In particular, Shnek et al. (1997) reported the only non-significant relationship (r =.14, 95% CI [-.08, .35], p = .22). Notably, this study utilised a composite index of physical functioning (Sickness Impact Profile [SIP] – Physical subscale; Bergner, Bobbitt, Carter, & Gilson, 1981) rather than an individual subscale score. Removing this study from the overall analysis increased the pooled effect estimate marginally (r_w = .43, 95% CI [.28, .55], p < .001, τ^2 = .01, I^2 = 83.34%).

Physical activity. Three independent studies each identified the significant role of weekly physical activity in illness-related SE (see Table 3): higher levels of SE were associated with greater activity frequency and intensity (as measured by the Godin Leisure-Time Exercise Questionnaire [GLTEQ]; Godin & Shephard, 1997). Significant, albeit smaller, associations were noted when various dimensions of physical activity were examined, including household, sport and recreation and work-related activity (as assessed by

Table 3

Correlations between Self-Efficacy and Physical Symptoms

Symptom	First author (Year)	SE Measure	Symptom Measure		$N_{studies}$	$N_{participants}$	r	r_w	95% CIs		N_{fs}	τ^2	I^2
									LL	*UL*			
Fatigue	Motl (2009)	MSSE	FSS		1	292	**-.58**		-.65	-.50	6		
	Trojan (2007)	ASES (adapted)	MFI-GF		1	53	**-.52**		-.69	-.29	5		
	Trojan (2007)	ASES (adapted)	MFI-PF		1	53	**-.52**		-.69	-.29	5		
	Trojan (2007)	ASES (adapted)	FSS		1	53	**-.50**		-.68	-.27	5		
	Trojan (2007)	ASES (adapted)	MFI-MF		1	53	**-.38**		-.59	-.12	3		
				Total	2	345		**-.57**	-.64	-.49	12	.00	0.00
Pain	Motl (2009)	MSSE	SF-MPQ	Total	1	292	**-.48**		-.56	-.39	4		
Mobility	Motl (2017)	MSSE-F	6MW (adapted)		1	69	**.67**		.52	.78	8		
	Motl (2009)	MSSE	PDDS		1	292	**.55**		.47	.63	6		
	Motl (2017)	MSSE-F	T25-FW		1	69	**.55**		.36	.70	6		
	Sinnakaruppan (2010)	MSSE-F	EDSS		1	115	**.54**		.40	.66	5		
	Motl (2017)	MSSE-C	6MW (adapted)		1	69	**.53**		.34	.68	5		
	Riazi (2004)	MSSE-C	MSWS-12		1	89	.44		.26	.59	4		
	Riazi (2004)	MSSE-F	MSWS-12		1	89	.43		.24	.59	4		
	Motl (2017)	MSSE-C	T25-FW		1	69	.40		.18	.58	3		
	Schmitt (2014)	MSSE	AI		1	81	**.38**		.18	.55	3		
	Sinnakaruppan (2010)	MSSE–C	EDSS		1	115	**.34**		.17	.49	3		
	Plow (2015)	CDSE	MSWS-12		1	335	.20		.10	.30	1		
	Shnek (1997)	ABS (adapted)	SIP- P		1	80	.14		-.08	.35	0		
				Total	7			**.39**	.25	.52	23	.03	83.26
Physical Activity	Motl (2009)	MSSE	GLTEQ		1	292	**.41**		.31	.50	3		
	Motl (2013)	MSSE-C	GLTEQ		1	269	.24		.12	.35	1		
	Motl (2013)	MSSE-F	GLTEQ		1	269	.22		.10	.33	1		
	Ng (2013)	MSSE-C	PASIPD		1	129	.18		.01	.34	1		
				Total	3	690		.28	.14	.38	5	.01	78.38

Note: $N_{studies}$ = number of studies providing data; $N_{participants}$ = number of participants providing this data; r_w = weighted mean correlation; 95% CI = confidence interval with lower (*LL*) and upper (*UL*) limits; N_{fs} = Fail-safe *N*; τ^2 = between-study variation; I^2 = percentage of between-study heterogeneity. *Measure Abbreviations:* 6MW = Six Minute Walk test; ABS = Arthritis Belief Scale; AI = Ambulation Index; ASES = Arthritis Self-Efficacy Scale; CDSE = Chronic Diseases Self-efficacy questionnaire; EDSS = Expanded Disability Status Scale; FSS = Fatigue Severity Scale; GLTEQ = Godin Leisure-Time Exercise Questionnaire; MFI-GF = Multidimensional Fatigue Inventory-General Fatigue; MFI-MF = Multidimensional Fatigue Inventory – Mental Fatigue; MFI-PF = Multidimensional Fatigue Inventory – Physical Fatigue; MSSE = Multiple Sclerosis Self-Efficacy Scale; MSSE-C = Multiple Sclerosis Self-Efficacy Scale – Control subscale; MSSE-F = Multiple Sclerosis Self-Efficacy Scale –Function subscale; MSWS-12 = 12-Item MS Walking Scale; PASIPD = Physical Activity Scale for Persons with Physical Disabilities; PDDS = Patient Determine Disease Steps; SF-MPQ = Short Form-McGill Pain Questionnaire; SIP-P = Sickness Impact Profile; T25-FW = Time 25-Foot Walk. Values in bold indicate significant effect: $r \geq .30$; 95% CI $\neq 0$, $p < .05$.

the Physical Activity Scale for Individuals with Physical Disabilities [PASIPD]; Washburn et al., 2002). Again, these findings need to be interpreted cautiously as they were based on single studies.

Psychological Symptoms

Self-esteem. Two studies, involving a combined sample of 182 outpatients and community-dwelling individuals with MS, examined the relationship between general SE and self-esteem (Dlugonski & Motl, 2012; McCabe, 2005) (see Table 4). The pooled, weighted effect size was large and highly significant: individuals reporting high levels of self-esteem also endorsed higher SE. Although the associated N_{fs} value suggests that this finding is robust, few studies assessed this vital psychological resource.

Worry. A single study (Thornton, Tedman, Rigby, Bashforth, & Young, 2006) examined the relationship between pathological worry, assessed using the Penn State Worry Questionnaire - a common screening tool for Generalised Anxiety Disorder (Meyer, Miller, Metzger, and Borkovec, 1990), and MS-specific SE (see Table 4). The resulting effect size was large and highly significant: persons with MS reporting low SE also reported persistent intrusion of negative thoughts regarding the future and constant awareness of possible future danger. However, given that a single small-scale study (n = 39) contributed to this finding, this result is not conclusive.

Depression. Thirteen studies examined the relationship between SE and depressed mood. Studies used a combination of five self-report scales, most commonly the Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith) ($N_{studies}$ = 8; see Table 4). The overall weighted effect was large and highly significant: lower levels of SE were associated with increased depressive symptoms. The associated N_{fs} value suggests that a substantial number of unpublished studies with non-significant results would need to exist to call this

Table 4

Correlations between Self-Efficacy and Psychological Symptoms

Symptom	First author (Year)	SE Measure	Symptom Measure		$N_{studies}$	$N_{participants}$	r	r_w	95% CIs		N_{fs}	τ^2	I^2
									LL	*UL*			
Self-esteem	Uccelli (2016)	GSE	RSES		1	89	**.62**		.47	.73	7		
	Airlie (2001)	LSSS	RSES		1	93	**.54**		.38	.67	5		
				Total	2	182		**.58**	.47	.67	12	.00	0.00
Worry	Thornton (2006)	SESMS	PSW	Total	1	39	**-.53**		-.72	-.26	5		
Depression	Rigby (2003); Thornton (2006)	SESMS	HADS-D		2	181		**-.70**	-.77	-.62	18	.00	0.00
	Motl (2009); Rigby (2003)	MSSE	HADS-D		2	434		**-.60**	-.66	-.54	13	.00	0.00
	Airlie (2001)	LSSS	HADS-D		1	93	**-.56**		-.67	-.40	6		
	Lester (2007)	SEMCD	HADS–D		1	82	**-.56**		-.69	-.39	6		
	Goodworth (2016)	MSSE	BDI-II		1	199	**-.55**		-.64	-.45	6		
	Shnek (1997)	ABS (adapted)	CES-D		1	80	**-.47**		-.63	-.28	4		
	Henneghan (2017)	Sherer SE	CES-D		1	183	**-.41**		-.52	-.28	3		
	Calandri (2018)	SEMS	CES-D-10		1	90	**-.40**		-.56	-.21	3		
	Schmitt (2014)	MSSE	CMDI		1	81	**-.39**		-.56	.19	3		
	Tan-Kristanto (2015)	MSSE	DASS-D		1	129	**-.37**		-.51	-.21	3		
	Shnek (1995)	MSBS	CES-D		1	80	**-.33**		-.51	-.12	2		
	Fournier (2002); Uccelli (2016)	GSE	HADS-D		2	187		**-.31**	-.53	-.05	5	.02	71.32
				Total	13	1597		**-.49**	-.56	-.41	60	.02	75.91
Anxiety	Airlie (2001)	LSSS	HADS-A		1	93	**-.50**		-.64	-.33	5		
	Rigby (2003); Thornton (2006)	SESMS	HADS-A		2	181		**-.49**	-.59	-.37	9	.00	0.00
	Garfield (2012)	MSSS	HADS-A		1	157	**-.49**		-.60	-.36	5		
	Lester (2007)	SEMCD	HADS-A		1	82	**-.46**		-.62	-.27	4		
	Motl (2009); Rigby (2003)	MSSE	HADS-A		2	434		**-.43**	-.52	-.33	8	.00	23.09

Table 4 *(continued)*

Symptom	First author (Year)	SE Measure	Symptom Measure		$N_{studies}$	$N_{participants}$	r	r_w	95% CIs		N_{fs}	τ^2	I^2
									LL	*UL*			
Anxiety	Tan-Kristanto (2015)	MSSE	DASS-A		1	129	**-.41**		-.54	-.26	3		
	Fournier (2002); Uccelli (2016)	GSE	HADS-A		2	187		**-.35**	-.47	-.22	5	.00	0.00
				Total	9	1121		**-.44**	-.48	-.39	34	.00	0.00
Hopelessness	Sinnakaruppan (2010)	MSSE – C	BHS			115	**-.50**		-.63	-.35	5		
	Sinnakaruppan (2010)	MSSE - F	BHS			115	-.16		-.33	.02	1		
				Total	1	115		**-.34**	-.49	-.17	2		

Note: $N_{studies}$ = number of studies providing data; $N_{participants}$ = number of participants providing this data; r_w = weighted mean correlation; 95% CI = confidence interval with lower (*LL*) and upper (*UL*) limits; N_{fs} = Fail-safe *N*; τ^2 = between-study variation; I^2 = percentage of between-study heterogeneity. *Measure Abbreviations:* ABS = Arthritis Belief Scale; BDI = Beck's Depression Inventory; BHS= Beck Hopelessness Scale; CES-D = Center for Epidemiological Studies Depression Scale; CMDI = Chicago Multiscale Depression Inventory; DASS-A = Depression Anxiety Stress Scale – Anxiety subscale; DASS-D = (Depression Anxiety Stress Scale – Depression subscale; GSE = General Self-Efficacy Scale; HADS-A = Hospital Anxiety and Depression Scale – Anxiety Subscale; HADS-D = Hospital Anxiety and Depression Scale –Depression Subscale; LSSS = Liverpool Self-efficacy Scale; MSBS = MS Beliefs Scale; MSSE = Multiple Sclerosis Self-Efficacy Scale; MSSE-C = Multiple Sclerosis Self-Efficacy Scale – Control subscale; MSSE-F = Multiple Sclerosis Self-Efficacy Scale –Function subscale; MSSS = Multiple Sclerosis Self-efficacy Scale; PSW = Penn State Worry; RSES = Rosenberg Self-Esteem Scale; SEMCD = Self-Efficacy for Managing Chronic Disease; SEMS = Self-Efficacy in Multiple Sclerosis scale; SESMS = MS Self-efficacy Scale; Sherer SE = Sherer Self-Efficacy scale.
Values in bold indicate significant effect: $r \geq .30$; 95% CI $\neq 0$, $p < .05$.

finding into question. Individual effect sizes were medium-to-large in magnitude, although Fournier et al. (2002) reported the only small and non-significant association (r = -.18, 95% CI [-.37, .02], p = .08) among their Dutch outpatient sample. In comparison, Uccelli et al. (2016), utilising the same general SE and depression measures (HADS), reported a strong correlation (r = -.43, 95% CI [-.56, -.24], p < .001). Indeed, participants in this latter study reported significantly higher average HADS scores (M = 7, SD = 4) in comparison to Fournier et al.'s (2002) sample (M = 3.7, SD = 3.4; t (185) = 6.10, p < .001). Removing the Fournier et al. (2002) study from the overall analysis resulted in a small increase in the overall pooled r (r_w = .51, 95% CI [-.57, -.44], p < .001, τ^2 = .01, I^2 = 62.05%).

Anxiety. Nine independent studies explored the relationship between anxiety symptom severity, commonly operationalised by the HADS, and perceived SE – conceptualised as MS-specific ($N_{studies}$ = 7) or general efficacy ($N_{studies}$ = 2) (see Table 4). Studies consistently reported medium-to-large and significant associations (r range: -.35 to -.50): lower levels of SE were associated with heightened anxiety. The associated N_{fs} value suggests that the findings are not influenced by potential publication bias.

Hopelessness. Sinnakaruppan et al. (2010) found some evidence to suggest that hopelessness and illness-related SE are inversely related (see Table 4). More specifically, those who perceived poor control over the ability to cope with MS (MSSE Control subscale) also reported increased feelings of hopelessness about the future in addition to reduced motivation and expectations. Again, this finding can only be considered tentative as it was based on a single study.

Cognitive Symptoms

Jongen et al. (2015) provided preliminary evidence of the relationship between cognitive performance and illness-related SE in a select sample of adults recently diagnosed

Table 5

Correlations between Self-Efficacy and Cognitive Symptoms

Symptom	First author (Year)	SE Measure	Symptom Measure		$N_{studies}$	$N_{participants}$	r	95% CIs		N_{fs}
								LL	*UL*	
Episodic memory	Jongen (2015)	MSSE	CDR	Total	1	33	**.36**	.02	.63	3
Continuity of attention	Jongen (2015)	MSSE	CDR	Total	1	33	**.36**	.02	.63	3
Working memory	Jongen (2015)	MSSE	CDR	Total	1	33	.23	-.12	.53	1
Cognitive reaction time	Jongen (2015)	MSSE	CDR	Total	1	33	-.25	-.55	.10	2
Speed of memory	Jongen (2015)	MSSE	CDR	Total	1	33	**-.53**	-.74	-.23	5
Reaction time variability	Jongen (2015)	MSSE	CDR	Total	1	33	**-.57**	-.76	-.28	6
Power of attention	Jongen (2015)	MSSE	CDR	Total	1	33	**-.65**	-.81	-.40	8

Note: $N_{studies}$ = number of studies providing data; $N_{participants}$ = number of participants providing this data; r_w = weighted mean correlation; 95% CI = confidence interval with lower (*LL*) and upper (*UL*) limits; N_{fs} = Fail-safe *N*; I^2 = percentage of between-study heterogeneity. *Measure Abbreviations:* CDR = Cognitive Drug Research computerised system; MSSE = Multiple Sclerosis Self-Efficacy Scale.
Values in bold indicate significant effect: $r \geq .30$; 95% CI $\neq 0$, $p < .05$.

(i.e., < 2 years) with clinically isolating syndrome (CIS) or relapsing-remitting MS (see Table 5). Different types of attention, reaction time and memory were assessed using a battery of computerised cognitive tests from the Cognitive Drug Research system (CDR; Wesnes et al., 1987). Total MSSE scores significantly correlated with performance accuracy on tasks of sustained attention (continuity of attention) and timed tasks of focussed attention (i.e., power of attention; reaction time variability). Those who reported high SE also demonstrated better performance on tasks of immediate and delayed word recall, word recognition and picture recognition (episodic memory), and complex information processing speed (speed of memory). These findings were, however, based on a small sample – as reflected in the wide confidence intervals for each individual *r*.

Moderator Analyses

Sub-group analyses for depression, as a symptom category, revealed no significant differences in effect estimates between studies which utilised a generic SE measure (e.g., r_w = -.40, $p < .001$, 95% CI [-.53, -.26], $N_{studies} = 4$) and those which utilised measures specific to MS (e.g., r_w = -.52, $p < .001$, 95% CI [-.60, -.44], $N_{studies} = 9$; Q_B (1) = 2.35, $p = .13$).

Six studies examined the relationship between socio-contextual and disease variables on general and illness-related SE (see Table 6). Both Fournier et al. (2002) and Plow et al. (2015) reported significant correlations between SE and number and severity of symptoms (e.g. bladder and bowel difficulties, spasticity) as measured by the MS-related symptoms checklist (Gulick, 1987) and Symptoms of MS Scale (McMillan & Moore, 2006), respectively. Plow et al. (2015) also found a significant and moderate association with number of physical comorbidities (e.g. arthritis, diabetes, CVD). Schmitt et al. (2014) reported a significant negative correlation between SE and disease type (relapsing-remitting, primary progressive, secondary progressive), whilst Jongen et al. (2015) found no significant

relationship, although this latter study did not include progressive types of MS in their examination. In comparison, age, gender, relationship status and education level were not identified as significant moderators of SE (Calandri et al., 2018; Jongen et al., 2015; Shnek et al., 1995). Similarly, correlations between disease duration (Calandri et al., 2018; Schmitt et al., 2014) and disease severity (Shnek, 1997), and SE were small and not significant.

Table 6

Correlations Between Self-Efficacy and Socio-Demographic and Disease Variables.

Variable	SE Measure		$N_{studies}$	$N_{participants}$	r	r_w	95% CIs		N_{fs}
							LL	*UL*	
Gender	SEMS	Total	1	90	.14		-.07	.34	0
	SEMS		1	90	.06		-.15	.26	0
Age	MSBS		1	80	.09		-.13	.30	0
		Total	2	170		.08	-.33	.46	0
	SEMS	Total	1	90	-.02		-.23	.19	0
Disease duration	MSSE	Total	1	81	-.06		-.28	.16	0
Education	ABS (adapted)	Total	1	80	.16		-.06	.37	1
Marital Status	MSBS	Total	1	80	.05		-.17	.27	0
Employment	ABS (adapted)	Total	1	80	.27*		.05	.46	2
EDSS	ABS (adapted)	Total	1	80	-.15		-.35	.07	0
Symptoms	GSE		1	98	-.21*		-.39	-.01	1
	CDSE		1	335	-.44***		-.52	-.35	4
		Total	2	433		-.35***	-.52	-.15	5
Comorbidities (no. of)	CDSE	Total	1	335	-.27***		-.37	-.17	2
MS type	MSSE	Total	1	81	-.30**		-.49	-.09	2

Note: $N_{studies}$ = number of studies providing data; $N_{participants}$ = number of participants providing this data; r_w = weighted mean correlation; 95% CI = confidence interval with lower (*LL*) and upper (*UL*) limits; N_{fs} = Fail-safe *N*. *Measure Abbreviations:* ABS = Arthritis Belief Scale; CDSE = Chronic Diseases Self-efficacy questionnaire; GSE = General Self-Efficacy Scale; MSBS = MS Beliefs Scale; MSSE = Multiple Sclerosis Self-Efficacy Scale, SEMS = Self-Efficacy in Multiple Sclerosis scale.
*$p < .05$. ** $p < .01$. *** $p < .001$.

Discussion

This meta-analytical review examined the association between SE and various symptoms in people living with MS. The pooled findings from 22 independent studies, involving 2846 adults with MS, indicate strong correlations between perceived SE and the incidence and burden of physical and psychological symptoms of MS. There was less evidence in relation to the role of SE on cognitive functioning. Importantly, the findings were based on studies which were relatively robust to potential sources of methodological bias, thus contributing to the reliability of these results.

The strong, positive association between SE and self-reported physical activity is consistent with findings in the general population (Feltz & Payment, 2005). However, whether higher SE is also associated with reduced fatigue, pain and improved physical activity levels, remains to be determined given that few studies examined these relationships. Indeed, the current systematic review highlighted the dearth of MS studies examining the relationship between general SE beliefs and a number of frequently reported physical symptoms, such as bladder and bowel dysfunction and visual disturbances (e.g., nystagmus, optic neuritis; Giannantoni, Proietti, Gubbiotti, Rossi De Vermandois, & Porena, 2013), underlining the need for further research in this area.

Similarly, the strong negative correlations noted between SE with depression and anxiety are not unique to MS. These findings have also been demonstrated in other disability cohorts including spinal cord injury (van Diemen, Crul, van Nes, Geertzen, & Post, 2017) and people with chronic pain (Jackson et al., 2015). SE has been recognised as a significant mediator between stressful life events (e.g., death of a spouse, life-threatening illness or injury) and depressive symptoms. This is supported by longitudinal data: individuals with low SE are at risk of developing severe symptoms of depression (Maciejewski, Prigerson & Mazure, 2000). Additionally, high SE has been implicated as a protective factor against the

development of distress (Bandura, 1997). The suggestion is that SE indirectly effects depressive or anxiety symptoms via appraisals; a person with low SE may perceive that their disability is overwhelming and that they cannot cope which, in turn, can exacerbate depressive symptoms (van Leeuwen et al., 2012). Improved self-esteem - or a general belief in one's own self-worth - was also associated with higher SE. This finding is not surprising given that it is widely recognised that people often attach value to their capabilities (Bandura, 1997; Kavanagh & Bower, 1985).

The relationship between SE and cognitive symptoms of MS remains to be determined. Preliminary findings from this review suggest that high SE is associated with improved cognitive functioning - particularly in the domains of attention, episodic memory and processing speed (Jongen et al., 2015). Indeed, there is evidence that SE as a significant predictor of subjective general cognitive functioning and executive functioning in individuals with MS (Hughes et al., 2015). However, whether SE is predictive of objective cognitive impairment in persons with MS, requires further evaluation.

Implications for Practice

The current study highlights the influence of SE on the severity and burden of physical and psychological symptoms of MS. Whilst SE has been recognised as a key contributing factor in the self-management of chronic disease (Martos-Méndez, 2015), which includes psychological interventions such as cognitive-behavioural therapy (CBT) (National Institute for Health and Care Excellence, 2014), such interventions are generally only considered in response to the treatment of psychological symptoms.

Screening of SE beliefs and severity of MS symptoms at time of diagnosis of MS - and throughout the course of disorder, represents a quick and easy system for identifying potentially vulnerable patients who would benefit from interventions to increase SE (French,

Moore, Pohlig, & Reisman, 2016). The scope of possible psychological interventions for SE is vast, with SE beliefs modifiable through four main sources of efficacy information – direct experience, modelling (e.g., group therapy sessions), social persuasion (e.g., support from treating psychologists and allied health professionals), and affective state (Bandura, 1977, 1997). The social-cognitive program; *Can Do MS*, for instance, utilises all these pathways. Preliminary evidence suggests that this brief (3-4 day) program contributes to improvements in SE which are maintained in the longer term (i.e., up to 6 months post-intervention; Jongen et al., 2014; Ng et al., 2012). Established CBT treatments have also demonstrated impact on SE (Nash, Ponto, Townsend, Nelson, & Bretz, 2013). Importantly, technological advancements have allowed the delivery of CBT via telephone and online platforms, minimising the burden of accessibility issues, such as distance and time (Brenes, Danhauer, Lyles, Hogan, & Miller, 2015). Online and live video chat platforms also provide a space for community engagement, providing an opportunity to influence SE through modelling and social persuasion. For instance, Jaglal et al. (2013) identified significant gains in general SE among individuals with chronic health conditions when delivering an established intervention program - *Chronic Disease Self-Management Program* (CDSMP) via telehealth. Based on Bandura's (1997) SE theory, CDSMP is 6-week program aimed at building participants' confidence in managing their health and keeping them active and engaged in their lives (Lorig, 2014). Finally, psychological interventions aimed at improving adherence to disease modifying therapies by increasing SE have been identified as another important rehabilitation target (Csillik et al., 2016). Future research should focus on the development of such programs for individuals with MS.

Limitations

A number of methodological limitations encountered during this review need to be considered. First, the operational definition of SE as a general construct may have failed to

capture all relevant studies. In an attempt to minimise this limitation, the database search strategy utilised a broad list of relevant keywords and phrases, and a manual search of reference lists of included studies and relevant reviews was conducted (which accounted for one additional study included in the systematic review). Whilst N_{fs} statistics were calculated, it is acknowledged that this statistic does not fully alleviate the problem of publication bias (Orwin, 1983).

Second, the tendency for MS studies to rely on registry data (e.g., National MS Society and MS Research Australia databases) presents statistical difficulties for meta-analytic methods. Careful screening of studies and contact with authors was necessary to ensure data independence. Although this resulted in a reduced sample, none of the observations overlapped, and no single study provided a disproportionate amount of data to the calculation of a pooled effect size *r*. To ensure transparency of data, it is nonetheless important for MS sub-studies to cite any primary publication.

Third, the examination of potential moderators to explain the substantial heterogeneity for the pooled correlations of mobility and depression, was limited due to the infrequent reporting of sociodemographic and illness-related sample parameters. Indeed, the possible mediating role of employment status and disease duration have been noted (Fraser & Polito, 2007). The unexplained between-study variability in effect estimates identified in the current review, highlight the need for future MS research to provide information regarding key sample parameters, such as employment status and disease duration, to allow for appropriate examination of possible moderators. Additionally, disease modifying therapies - which may indirectly influence SE beliefs through symptom improvement (which in turn positively impact on SE), should be explored further (Higuera, Carlin & Anderson, 2016).

Fourth, the primary reliance on cross-sectional data precluded conclusions and inferences regarding the causal and directional relationships among variables. For example, it is not known whether higher SE results in physical activity, or whether increased physical activity promotes SE (Motl et al., 2009). Future research should consider longitudinal and prospective designs.

Finally, the review revealed the limited generalisability of findings, given the frequent exclusion of individuals based on a range of disease factors such as level of cognitive functioning (Garfield & Lincoln, 2012), mobility (Tan-Kristanto & Kiropoulos, 2015), and employment status (Jongen et al., 2015), and a tendency to overlook individuals who are not actively engaged treatment, with studies recruiting participants primarily though MS societies and outpatient clinics (Patten, Beck, Williams, Barbui, & Metz, 2003). Future studies should attempt to minimise potential sources of bias in sampling and selection - such as those mentioned above - through the use of more diverse sample populations and recruiting through a range of different sources. Additionally, a more consistent operationalisation of the term SE in MS literature would aid in the comparison of findings across studies.

Conclusion

This systematic review highlights the importance of SE as a key target for rehabilitation interventions for adults living with MS. This includes a need to incorporate SE concepts in order to teach techniques that can enhance fatigue management in addition to mobility and psychological wellbeing. Further longitudinal research will help to clarify the reciprocal relationship between SE with physical and mental health symptoms in this cohort. This includes the stability of general SE over time in response to the changing symptom and disease pattern of MS.

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Appendices

Appendix A

Example of logic grid with Boolen operators - PubMed

	AND	AND	AND
OR	self-efficac*[tiab] OR “self-efficacy”[mh] OR personal efficacy[tiab] OR selfefficac*[tiab] OR “self concept”[mh noexp] OR self concept*[tiab] OR Self-perception*[tiab] OR Self-assessment*[tiab] OR “self-assessment”[mh] OR selfassessment[tiab] OR mastery[tiab] OR social cognitive theory[tw] OR self-esteem*[tiab] OR "internal-external control"[tiab] OR "internal-external control"[mh] OR "locus of control"[tiab] OR "control locus"[tiab] OR self-criticism*[tiab] OR Bandura[tiab] OR Perceived control[tiab]	“multiple sclerosis”[mh] OR multiple scleros*[tw] OR “multiplesclerosis”[tiab] OR "disseminated sclerosis"[tiab]	secondary health condition*[tw] OR secondary condition*[tiab] OR complex symptom*[tiab] OR symptom*[tiab] OR comorbid*[tiab] OR comorbid[tiab] OR “comorbidity”[mh] OR multimorbid*[tiab] OR “primary dysautonomias”[mh] OR Dysautonomia*[tiab] OR autonomic dysfunction*[tiab] OR Orthostatic intolerance*[tiab] OR “hypotension”[mh] OR Hypotensi*[tiab] OR blood pressure[tiab] OR “vertigo”[mh] OR vertigo*[tiab] OR “dizziness”[mh] OR Dizziness[tiab] OR Dizzyness[tiab] OR Orthostasis[tiab] OR Lightheaded*[tiab] OR Light-headed*[tiab] OR “headache”[mh] OR Headache*[tiab] OR Head-pain*[tiab] OR Cranial pain*[tiab] OR Cephalalgia*[tiab] OR Cephalgia*[tiab] OR Hemicrania[tiab] OR “migraine disorders”[mh] OR Migraine*[tiab] OR Status Migrainosus[tiab] OR Thermoregulation*[tiab] OR Body temperature regulation*[tiab] OR “body temperature regulation”[mh:noexp] OR heat sensitiv*[tiab] OR “fatigue”[mh] OR fatigue*[tiab] OR lassitude[tiab]OR Asthenia*[tiab] OR Tiredness[tiab] OR energy[tiab] OR “Sleep wake disorders”[mh] OR Dyssomnia*[tiab] OR Sleep Initiation and Maintenance Disorder*[tiab] OR

Appendix B

Individual risk of bias assessment

	Criteria											
First Author (Year)	Question/ Objective	Study Design	Subject selection	Subject characteristics	Outcome measure	Sample size	Analytic methods	Estimate of variance	Confounding	Results	Conclusions	Overall Score
Airlie (2001)	2	2	2	2	2	2	2	2	2	2	2	1
Calandri (2016)	2	2	1	2	2	2	2	1	2	2	2	0.91
Fournier (2002)	2	2	2	2	2	2	2	1	2	2	2	0.95
Garfield (2012)	2	2	1	2	2	2	2	2	2	2	2	0.95
Goodworth (2016)	2	1	1	2	2	2	2	1	2	2	2	0.86
Henneghan (2017)	2	2	2	2	2	2	2	1	2	2	2	0.95
Jongen (2015)	2	2	1	2	2	2	2	1	2	2	2	0.91
Lester (2007)	2	2	1	2	2	2	1	2	2	2	2	0.91
Motl (2009a)	2	2	1	2	2	2	2	2	2	2	2	0.95
Motl (2013)	2	2	2	2	2	2	2	1	2	2	2	0.95
Motl (2017)	2	2	2	2	2	2	2	1	2	2	2	0.95
Ng (2013)	2	2	1	2	1	2	2	1	1	2	2	0.82
Plow (2015)	2	2	1	2	2	2	2	1	2	2	2	0.91
Riazi (2004)	2	2	1	2	1	2	2	2	2	1	2	0.86
Rigby (2003)	2	2	1	2	2	2	2	2	2	2	2	0.95
Schmitt (2014)	2	2	1	2	2	2	1	2	2	2	2	0.91
Shnek (1997)	2	2	1	1	2	2	2	1	2	1	2	0.82
Sinnakaruppan (2010)	2	2	1	2	2	2	1	1	1	2	2	0.82
Tan-Kristanto (2015)	2	2	1	1	2	2	2	1	2	2	2	0.86
Thorton (2006)	2	2	1	2	2	2	2	1	2	2	2	0.91
Trojan (2007)	2	2	2	2	2	2	2	2	2	2	2	1
Uccelli (2016)	2	2	2	2	2	2	2	2	2	2	2	0.86
										Overall Mean Score:		0.91