

# The effects of psychological interventions for mood in people living with multiple sclerosis: Evidence snapshot

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The logo for the National Disability Insurance Scheme (NDIS) is displayed in white lowercase letters. The letter 'i' has a small green dot above it. The logo is set against a dark purple rounded square background.

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This evidence snapshot is designed to contribute to the knowledge base by providing an overview of the evidence on the effect of psychological interventions for mood in people living with multiple sclerosis (MS). Some supports described in this evidence snapshot might be funded outside the National Disability Insurance Scheme (NDIS). Therefore, this evidence snapshot should be used to empower participants and early intervention partners to advocate for evidence-based supports through their engagement with mainstream and community supports from other government funded services, like health and mental health.

Views and recommendations of third parties in this report, do not necessarily reflect the views of the NDIA, or indicate a commitment to a particular course of action.

## Acknowledgements

The NDIA acknowledges the Traditional Owners and Custodians throughout Australia and their continuing connection to the many lands, seas, and communities. The NDIA pays respect to Elders past and present and extends that respect to any Aboriginal and Torres Strait Islander people who may be reading this Report.

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# Abbreviations

ACT	Acceptance and commitment therapy
CBT	Cognitive behavior therapy
MS	Multiple sclerosis
NDIA	National Disability Insurance Agency
NDIS	National Disability Insurance Scheme
NS	Non-statistically significant
RRMS	Relapsing-remitting multiple sclerosis

## Executive summary

Mood disorders are common in people with multiple sclerosis (MS). Psychological interventions have been shown to be safe and efficacious in various clinical populations. We selected 10 systematic reviews and meta-analyses to identify the best available quantitative evidence on the topic. Based on cumulative data from over 30 randomised controlled trials in people with MS, we conclude that:

- Cognitive behaviour therapy (CBT) is associated with moderate reductions in pain and fatigue in people with MS, but there is not enough evidence to determine its efficacy on depression, anxiety, and quality of life.
- Mindfulness interventions are associated with moderate reductions in symptoms of depression, anxiety, stress, and fatigue, as well as better coping and quality of life in people with MS.
- Stress management interventions are associated with moderate reductions in symptoms of depression, anxiety, and stress in people with MS.
- Despite some evidence to support acceptance and commitment therapy and relaxation therapy, the evidence base is small and inconclusive in people with MS.

The evidence presented in this evidence review is based on clinical studies which have focused on quite different psychological interventions, delivered in different formats, doses, settings and with different comparator groups. Although the number of studies included in many of the reported systematic reviews and meta-analyses enabled some further analyses to investigate if differences in these factors influences the effectiveness of the intervention, further work is still needed to understand the benefit of psychological interventions in people with MS. That said, given these interventions are inherently safe, scalable and have a strong evidence base in other populations, it is likely that more evidence in this field will augment rather than reverse the current conclusions, and in the meanwhile can be used by people with MS for mood management.

This evidence snapshot is designed to contribute to the knowledge base by providing an overview of the evidence on the effect of psychological interventions for mood in people living with multiple sclerosis. Some supports described in this evidence snapshot might be funded outside the NDIS. Therefore, this evidence snapshot should be used to empower participants and early intervention partners to advocate for evidence-based supports through their engagement with mainstream and community supports from other government funded services, like health and mental health.

# 1. Background and NDIS context

Multiple sclerosis (MS) is an incurable chronic neurological disease, in which the body's own immune system attacks and damages the myelin sheath– the protective layer around nerves. Due to this damage, the nerves cannot send and receive messages as they should, resulting in a range of debilitating symptoms in people with MS. These may include physical symptoms such as muscle pain, lack of coordination fatigue, dizziness and vertigo, tremor, bladder and bowel issues, visual disturbances as well as psychological symptoms including depression, anxiety, and cognitive impairment.

The prevalence of people living with MS in Australia in 2021 was 33,335 (MS Australia). As of September 2022, there were 9,375 NDIS participants with a diagnosis of MS as a primary disability and 334 participants with MS listed as a secondary disability. Of those with a primary disability of MS, approximately 5-7% present with a psychosocial disorder, anxiety, or depression as a secondary disability, making these one of the leading non-primary disabilities in NDIS participants with MS.

Many people with MS experience high levels of depression and anxiety, significantly more than the general population (Marrie et al., 2013). A recent meta-analysis of observational studies estimated the prevalence of depression among people with MS to be 27% and the prevalence of anxiety among people with MS to be 35%, whilst a recent study of an Australian MS patient cohort found that up to 60% of people with MS suffer from anxiety and depression, remarkably higher than the reported prevalence among NDIS participants (Peres et al., 2022; Ribbons et al., 2017). Depression is related to other non-motor symptoms of MS, most notably fatigue and cognitive impairment, and may contribute to a range of adverse life outcomes in MS such as lower quality of life and community participation, increased risk of suicide and difficulties following medical care (Siegert & Abernethy, 2005).

Psychological interventions that can effectively reduce depressive symptoms have the potential to improve the ongoing quality of life, social participation, and overall functioning of people with MS. This evidence snapshot summarises the most recent evidence of the effectiveness of these psychological interventions for people with MS.

## 1.1 What are psychological interventions?

Psychological interventions generally refer to a range of non-pharmacological therapies and techniques aimed at addressing psychological problems and disorders through the use of psychological principles and techniques (Ho et al., 2022). The psychological interventions covered in this evidence snapshot were selected on the basis of their specific focus; these include:

### **Cognitive behaviour therapy**

Cognitive behaviour therapy (CBT) is a type of psychotherapy ('talking therapy') based on the idea that how you think, and act affects how you feel. Cognitive behaviour therapy works

by helping you to recognise patterns of thinking and behaviour that cause problems and teaching you practical ways to learn or re-learn more helpful habits (Ost, 2008). Cognitive behaviour therapy is a multicomponent intervention and mindfulness, relaxation, and stress management interventions (described below) may also be components of CBT.

### **Acceptance and commitment therapy**

Acceptance and commitment therapy (ACT) is a behavioural therapy that incorporates acceptance and mindfulness-based strategies to help patients in overcoming negative thoughts and feelings (Thompson et al., 2022). It focusses on targeting an individual's relationship to psychological events by improving 'psychological flexibility,' rather than seeking to change or challenge thoughts or feelings (Hayes, 2019). ACT is a multicomponent intervention and mindfulness, relaxation, and stress management interventions (described below) may also be components of ACT.

### **Mindfulness interventions**

Mindfulness interventions are based on the idea that mindfulness (the state of being aware of one's emotions, thoughts, or body) is being present and fully engaged in the present moment, without interpretation or judgement. Mindfulness interventions can include breathing methods, guided imagery, and other practices to relax the body and mind and reduce stress. Mindfulness can promote coping strategies and resources that can address psychological challenges (Carletto et al., 2020; Simpson et al., 2020).

### **Relaxation therapy**

Relaxation therapy is an evidence based psychological focused therapy, focused on releasing tension. It can include a range of relaxation techniques which may involve tensing and relaxing muscles throughout the body, visualization (positive images), or meditation (focusing thoughts) (Carletto et al., 2016). Although relaxation therapy sounds similar to mindfulness-based interventions, mindfulness is focussed on becoming aware of how you are feeling physically, emotionally or mentally, whereas relaxation is focussed on releasing tension, either physically or mentally (Luberto et al., 2020).

### **Stress management interventions**

Stress management interventions refer to a range of techniques and approaches that collectively aim to prevent, reduce, and cope with stress. The techniques used can include problem solving, relaxation, time management techniques and lifestyle improvement. Commonly included components of a stress management intervention can include: challenging and confronting negative or pessimistic thoughts, mindfulness acceptance (e.g. mindfulness-based stress reduction) to train self-awareness and coping ability, or behavioural techniques to relieve stress including progressive muscle relaxation and controlled breathing (Taylor et al., 2020).

## 1.2 How are they typically delivered?

Psychological interventions are typically delivered by mental health professionals such as psychologists, psychiatrists, some GPs with training in mental health, mental health nurses, some counsellors and other therapists, but may also be delivered by other health care professionals or facilitators with no formal training (Sesel et al., 2018; Taylor et al., 2020).

The interventions can be delivered either individually, or in group-based sessions, across a number of channels including in person, face-to-face, via telephone/teleconference, or online course, or as a self-guided delivery. In some instances, in-session learning, can be supplemented with daily practice, for example to reinforce relaxation skills or techniques taught. The number of sessions and duration of the session for each intervention can also vary considerably, from a few brief sessions to sessions delivered over months or even years. In many cases, interventions may also be delivered in a combination of delivery methods, content, or clinical targets.

## 1.3 What is the evidence base?

The number of clinical trials investigating the efficacy of psychological interventions on psychological and functional outcomes for people with MS is expanding. These trials were summarized in several systematic reviews and meta-analyses which have examined the benefits relating to psychological and functional outcomes in people with MS.

The NDIA Evidence Synthesis & Innovation Research team carried out a scoping review of the scientific literature to find relevant systematic reviews and meta-analyses. We screened 801 articles and from a collection of 22 systematic reviews and meta-analyses, selected 10, identified for providing the most recent and accurate information relatively to other reviews on the topic. In the current report, we present the key results from these 10 recent systematic reviews and meta-analyses that synthesised the research evidence. The key results include the effect sizes (Hedges'  $g$  and 95% confidence intervals) of the psychological and functional outcomes in people with MS from the individual systematic review and meta-analysis.

## 1.4 What did we find?

[Table 1](#) provides the key results from these 10 systematic reviews and meta-analyses that synthesised the research evidence. Results are organised by intervention categories and psychological and functional outcomes.

**Table 1. Effect sizes [Hedges' g (95% confidence interval)] of psychological and functional outcomes in people with MS**

**Note:** \*Cognitive behaviour therapy (CBT) and acceptance and commitment therapy (ACT) are multicomponent interventions and mindfulness, relaxation, and stress management interventions may also be components of CBT and ACT. †Mindfulness interventions includes mindfulness-based stress reduction, mindfulness-based cognitive therapy, and other mindfulness-based interventions. ‡Stress management interventions includes mindfulness-based stress reduction, mindfulness integrated CBT, progressive muscle relaxation, and CBT. + = Sufficient evidence to indicate benefit. NS = Non-statistically significant. Implies that there was not enough information to determine whether the intervention is efficacious with sufficient statistical precision. k = Number of clinical trials included in the meta-analysis.

Interventions	Depression (Psychological outcome)	Anxiety (Psychological outcome)	Stress (Psychological outcome)	Coping (Psychological outcome)	Pain (Functional outcome)	Quality of life (Functional outcome)	Fatigue (Functional outcome)
<b>Cognitive behaviour therapy (CBT)*</b>	NS 0.14 (-0.20, 0.48) k=5 (Sesel et al., 2018)	NS 0.34 (-0.15, 0.84) k=3 (Fiest et al., 2016)	No data	No data	+ Moderate effect size: 0.42 (0.12, 0.73) k=5 (Hadoush et al., 2022)	NS 0.16 (-0.05, 0.77) k=3 (Sesel et al., 2018)	+ Moderate effect size: 0.32 (0.01, 0.63) k=5 (Phyo et al., 2018)
<b>Acceptance and commitment therapy (ACT)*</b>	NS 0.92 (-0.06, 1.91) k=5 (Thompson et al., 2022)	NS 0.41 (-0.11, 0.93) k=4 (Thompson et al., 2022)	+ Moderate effect size: 0.49 (0.08, 0.89) k=2 (Thompson et al., 2022)	No data	No data	NS 0.39 (-0.08, 0.85) k=3 (Thompson et al., 2022)	No data
<b>Mindfulness interventions†</b>	+ Large effect size: 0.77 (0.41, 1.12) k=9 (Carletto et al., 2020)	+ Large effect size: 0.63 (0.25, 1.00) k=8 (Carletto et al., 2020)	+ Large effect size: 1.07 (0.48, 1.65) k=5 (Carletto et al., 2020)	+ Moderate effect size: 0.47 (0.10, 0.84) k=5 (Han, 2022)	NS 0.16 (-0.46, 0.79) k=3 (Simpson et al., 2020)	+ Moderate effect size: 0.40 (0.18, 0.61) k=14 (R. Simpson et al., 2022)	+ Moderate effect size: 0.49 (0.21, 0.77) k=8 (Carletto et al., 2020)
<b>Relaxation therapy</b>	No data	No data	No data	No data	No data	No data	+ Large effect size: 0.90 (0.51, 1.30) k=2 (Phyo et al., 2018)
<b>Stress management interventions‡</b>	+ Large effect size: 1.08 (0.44, 1.73) k=5 (Taylor et al., 2020)	+ Large effect size: 0.99 (0.32, 1.67) k=5 (Taylor et al., 2020)	+ Large effect size: 0.83 (0.38, 1.29) k=8 (Taylor et al., 2020)	No data	No data	No data	No data

## **Cognitive behaviour therapy**

Three recent meta-analyses investigated the efficacy of cognitive behaviour therapy (CBT) on different psychological and functional outcomes in people with MS, collectively summarising the results of thirteen clinical trials (Hadoush et al., 2022; Phyo et al., 2018; Sesel et al., 2018). These included:

**Depression:** In our view, the most comprehensive review of evidence for the efficacy of CBT for depression and quality of life outcomes is provided by an Australian meta-analysis published in 2018 by Sesel and colleagues (Sesel et al., 2018). They synthesised the results from five studies including 497 people with MS. Meta-analyses revealed small effects of CBT interventions on depression and quality of life, which were not statistically significant. This means that we do not have enough information from the studies to determine whether CBT is efficacious for these outcomes. The quality of this evidence was low, meaning that our confidence in the effect estimates is low and further larger studies are likely to change these results.

**Anxiety:** Only 2 studies included in the systematic review by Sesel and colleagues provided data on the effect of CBT on anxiety, and therefore a meta-analysis was not conducted (Sesel et al., 2018). However, an earlier meta-analysis from 2016 reported a moderate but statistically non-significant effect of CBT on anxiety in pooled results from 3 studies (Fiest et al., 2016).

**Pain:** A meta-analysis published in 2022, synthesised results from 5 clinical trials focused on pain, including a total of 168 people living with MS (Hadoush et al., 2022). This meta-analysis revealed moderate reduction in pain intensity among people living with MS in favour of CBT.

**Fatigue:** The best available evidence for the efficacy of CBT on fatigue is provided by a meta-analysis from 2018 by Phyo and colleagues (Phyo et al., 2018). In a meta-analysis of 5 studies with 429 people with MS, CBT was found to reduce fatigue. The UK National Institute for Health and Care Excellence (NICE) 2022, evaluated the evidence from four studies on the effect of CBT on fatigue in people with MS (National Institute for Health and Care Excellence, 2022b). Although there was some evidence that CBT is beneficial for fatigue, the evidence was not sufficient due to limitations in the studies. Of the outcomes reported, there was uncertainty in the direction and/or size of the effect based on the confidence intervals. However, despite the current shortage of evidence for fatigue, NICE do recommend CBT for treatment of depression in neurological conditions more generally (National Institute for Health and Care Excellence, 2022a).

## **Acceptance and commitment therapy**

In our view, the most comprehensive review of evidence for the efficacy of acceptance and commitment therapy (ACT) for a range of outcomes is provided by a meta-analysis published in 2022 by Thompson and colleagues, summarising the results of 6 studies (Thompson et al., 2022).

**Depression:** A meta-analysis of 5 studies revealed large effects of ACT interventions on depression, which were not statistically significant (Thompson et al., 2022). This means that we do not have enough information from the studies to determine whether ACT is efficacious for depression. The quality of evidence was low, meaning that our confidence in these results is low.

**Anxiety:** A meta-analysis of 4 studies revealed moderate effects of ACT interventions on anxiety, which was not statistically significant (Thompson et al., 2022). This means that we do not have enough information from the studies to determine whether ACT is efficacious for anxiety. The quality of evidence was also low, meaning that our confidence in these results is low as well.

**Stress:** Only 2 studies included in the systematic review by Thompson and colleagues provided data on the effect of ACT on stress (Thompson et al., 2022). A meta-analysis of these 2 studies revealed a moderate effect of ACT interventions on stress. The quality of evidence was low, meaning that our confidence in these results is low.

**Quality of life:** A meta-analysis of 3 studies revealed a moderate effect of ACT interventions on quality of life, which was not statistically significant (Thompson et al., 2022). The quality of evidence was low, meaning that our confidence in these results is low.

### **Mindfulness interventions**

Three recent meta-analyses investigated the efficacy of mindfulness interventions on different psychological and functional outcomes in people with MS, collectively summarising the results of 20 clinical trials (Carletto et al., 2020; R. Simpson et al., 2022; Simpson et al., 2020).

**Depression:** In our view, the most comprehensive review of evidence for the efficacy of mindfulness interventions for depression is provided by a meta-analysis published in 2020 by Carletto and colleagues (Carletto et al., 2020). Meta-analyses of 9 studies revealed large effects of mindfulness interventions on depression. However, although most of the studies were judged to have a minimal risk of bias, most of the studies had a limited sample size meaning that our confidence in the effect estimates is low.

**Anxiety:** Carletto and colleagues conducted a meta-analysis on the efficacy of mindfulness interventions for anxiety (Carletto et al., 2020). Meta-analysis of 8 studies revealed large effects of mindfulness interventions on anxiety. However, as most of the studies has limited sample size, our confidence in the effect estimates is low.

**Stress:** Carletto and colleagues conducted a meta-analysis on the efficacy of mindfulness interventions for stress (Carletto et al., 2020). Meta-analysis of 5 studies revealed large effects of mindfulness interventions on stress. However, our confidence in the effect estimates is low due to the limited sample size in most of the studies.

**Fatigue:** Carletto and colleagues conducted a meta-analysis on the efficacy of mindfulness interventions for fatigue (Carletto et al., 2020). Meta-analysis of 8 studies revealed moderate effects of mindfulness interventions on fatigue. However, as most of the studies has limited sample size, our confidence in the effect estimates is low.

**Quality of life:** A 2022 meta-analysis by Simpson and colleagues explored the effect of mindfulness interventions on quality of life among 937 individuals with MS (R. Simpson et al., 2022). In meta-analysis of 14 studies, mindfulness interventions positively improved overall quality of life in people with MS, with the greatest benefits seen on mental health related quality of life. Moderate heterogeneity was observed in the meta-analysis and only half of the included studies were judged to have a minimal risk of bias meaning that our confidence in the effect estimates is low.

**Pain:** A meta-analysis published in 2020, synthesised results of 3 studies on the efficacy of mindfulness interventions on pain (Simpson et al., 2020). This meta-analysis revealed small effects of mindfulness interventions on pain which was not statistically significant (Simpson et al., 2020). This means that there is not enough information from the studies to determine whether mindfulness interventions are efficacious for this outcome.

**Coping:** A meta-analysis by Han 2022, synthesised results of 5 studies focused on coping (Han, 2022). This meta-analysis revealed moderate improvement in coping among people living with MS in favour of mindfulness interventions. However, the quality of the evidence was low, meaning that our confidence in these results is low, and further larger studies are likely to change the results.

Two other recent meta-analyses of mindfulness and acceptance-based interventions by Han 2021 and Han 2022 summarising results from 23 clinical trials reported generally large positive effects on depression, anxiety, stress, pain, quality of life and fatigue in people with MS (Han, 2021, 2022). However, significant heterogeneity was found in the meta-analyses, related to several methodological flaws such as inclusion of outliers and the author's method of calculating effect sizes, which was likely to overestimate benefits. Also, the quality of the evidence was low, meaning that our confidence in these results is low and further larger studies or more robust meta-analysis methods are likely to change these results.

### **Relaxation therapy**

**Fatigue:** Only 1 recent meta-analysis from 2018 by Phyo and colleagues investigated the efficacy of relaxation therapy on fatigue (Phyo et al., 2018). They summarised the results of 2 clinical trials, and, revealed large effects of relaxation therapy on fatigue meaning that relaxation therapy decreased fatigue levels in people with MS. However, only 2 studies, including 110 people with MS were included in the meta-analysis and the quality of both studies was only moderate, meaning that our confidence in the effect estimates is low, and further large studies may change these results.

### **Stress management interventions**

A recent Australian meta-analysis, published in 2020 examined the effects of stress management interventions in people with MS across 8 clinical trials (Taylor et al., 2020). This meta-analysis reported large effect sizes in favour of stress management interventions for depression, anxiety, and stress outcomes (see [Table 1](#)). However, these effect sizes were confounded by substantial heterogeneity, which was related to small-study effect ('publication bias') as well as well the inclusion of a range of stress management interventions (including mindfulness-based stress reduction, mindfulness-integrated CBT,

progressive muscle relaxation or CBT) and delivery settings. This means that the effect size of the intervention on the specific outcomes in the individual studies was very diverse. Also, the quality of the evidence was low, meaning that our confidence in the effect estimates is low and further large studies may change these results.

## 1.5 Factors to consider that may influence the effectiveness of the interventions

The evidence presented in this evidence snapshot is based on clinical trials which have focused on different psychological interventions, delivered in different formats, doses, settings and compared to different comparators. Although the number of studies included in many of the reported systematic reviews and meta-analyses was small, some systematic reviews conducted further analyses to investigate if differences in intervention design factors are related to the 'effectiveness' or strength of the benefit. Key findings are summarised below.

### Intervention types

While the reviews included in this report have examined specific interventions for people with MS (as shown in the rows in [Table 1](#)), many of the individual studies included in these reviews used different components for the intervention or combined them with various approaches. For example, the meta-analysis by Carletto et al evaluated the effect of mindfulness interventions on depression, anxiety, stress, and fatigue, pooling results from 14 studies (Carletto et al., 2020). Although most of the mindfulness interventions included in the studies were mindfulness-based stress reduction (n = 12), 2 studies investigated the effect of mindfulness-based cognitive therapy and 3 studies used other mindfulness-based approaches. Given the limited number of studies with different components of mindfulness interventions, most studies did not evaluate differences by specific intervention component. Therefore, based on the current evidence, there is still some uncertainty about the specific type of intervention that may be more beneficial for people with MS. Further studies should investigate which components of the interventions could be more beneficial for people with MS.

### Intervention setting

The studies included in this report have focused on psychological interventions delivered in a range of settings, including group-based settings, or delivered individually, and delivered in a range of ways, including face-to-face, via telephone/teleconference, online, or as a self-guided delivery. Given the limited number of studies included in the systematic reviews for the specific interventions, it was often not possible to evaluate differences by delivery setting or mode. However, some systematic reviews were able to investigate whether some delivery settings or mode of delivery works better than others by comparing results across different designs for all interventions pooled together. For example, Sesel and colleagues (Sesel et al., 2018) conducted analyses to investigate whether psychological interventions (all pooled, including CBT and other non-CBT interventions) were efficacious when the therapy was face-to-face vs via telephone or teleconference, and individual therapy vs group therapy. These analyses did not find evidence for differences between the different modes. However,

there were not enough studies (only 8 studies included) to make reliable comparisons, and it cannot be determined from this work whether differences are likely.

### **Intervention dose**

There was a large variability in the dose of therapy (number of therapy hours and weeks of intervention) offered in the included studies and sometimes it was not reported.

**Cognitive behaviour therapy:** The number of therapy hours in the CBT studies ranged from 45 minutes to 2 hours for 6 to 20 weeks, for a total of 3 to 24 hours (Hadoush et al., 2022; Phyo et al., 2018; Sesel et al., 2018).

**Mindfulness interventions:** The number of hours of mindfulness interventions varied from 1 to 3 hours, over a period of 6 to 24 weeks, with most interventions lasting 8 weeks (Carletto et al., 2020; Simpson et al., 2020). Some studies also included daily home practice; in one study it was reported to be 45 minutes, whilst other studies did not report the duration (Han, 2022).

**Acceptance and commitment therapy:** The number of sessions ranged from 4 to 8, with the sessions ranging from 14 minutes to 2.5 hours, for a total of 2 to 20 hours (Thompson et al., 2022). 2 studies also included a one-off “booster” session up to 3 months post-intervention (Thompson et al., 2022).

**Relaxation therapy:** The number of sessions ranged from 8 to 12 with 2 sessions per week lasting approximately 40 minutes each, for a total of 5 to 8 hours (Phyo et al., 2018).

**Stress management interventions:** Stress management interventions were time-limited, averaging 8 sessions (range: 4 to 16) delivered over 9 weeks (range 3 to 24 weeks), with a mean session duration of 90 minutes (range 50 minutes to 2 hours) (Taylor et al., 2020).

Due to the limited number of studies included in the systematic reviews, most did not evaluate whether there is a dose response relationship. Sesel and colleagues investigated a dose response effect for all interventions pooled together (both CBT and non-CBT interventions), and tentatively found that the number of therapy hours was significantly related to great improvements in mental, physical and overall quality of life after treatment. (Sesel et al., 2018). However, it is currently unknown what the minimal number of hours needed to achieve clinically meaningful benefits is, based on the current body of systematic reviews.

### **Comparator (control) group**

The effect sizes provided in [Table 1](#) represent the magnitude of benefits in the intervention groups over and above their respective control groups (the group receiving no intervention /standard care). It is possible that these results are impacted when comparing the interventions with a passive control group (i.e., standard care) which shows greater effects than when compared to active control (i.e., other potentially efficacious intervention).

For example, the meta-analysis by Phyo and colleagues investigating the efficacy of CBT for fatigue conducted separate analyses of CBT compared with non-active controls (i.e., telephone delivered education intervention, waitlist, and standard care) versus CBT

compared with active controls (relaxation therapy and supportive-expressive group psychotherapy) (Phyo et al., 2018). Although CBT was more efficacious for fatigue than both control conditions, effect sizes were larger when CBT was compared to active (alternative treatment) groups than to non-active comparators. Conversely, Simpson and colleagues' 2022 meta-analysis of mindfulness interventions (Robert Simpson et al., 2022) found that the effect estimates on quality of life were smaller when mindfulness is compared to active controls than when compared to non-active control conditions. In summary, we suspect that the effects found in these meta-analyses are overstated. However, the evidence regarding whether the effects are over- or understated or reliable across meta-analyses is mixed.

### **Study participants**

The characteristics of the people living with MS, included in the available studies was heterogeneous. There was heterogeneity in the severity of disease, duration of time living with MS, and MS subtype. However, in most studies, all MS phenotypes were included, with the majority having relapsing-remitting multiple sclerosis (RRMS) and a substantial proportion being female. All studies included only adults >18 years. Yet, except for Sesel and colleagues, who found some evidence that a higher proportion of RRMS in the sample (indicative of less severe participants) is associated with better quality of life outcomes, no meta-analysis compared the effects of the interventions across strata of disease severity or disability level.

### **Cognitive impairment**

Cognitive impairment in MS is common (DeLuca et al., 2020) and can be potentially managed by other interventions such as cognitive training (Lampit et al., 2019). Evidence from other populations suggests that cognitive impairment is associated with reduced response to psychological interventions and specifically CBT (Carroll et al., 2011). Moreover, there is also some evidence to suggest an association between cognitive impairment and depressive symptoms in people with MS (Chan et al., 2021; Feinstein et al., 2014). Yet only few of the studies included in the systematic reviews stated whether those with cognitive impairment were included or whether it was assessed. The meta-analysis by Simpson and colleagues reported that of 13 studies, 9 studies explicitly excluded those with cognitive impairment, while the other studies did not mention cognitive impairment in the eligibility criteria (R. Simpson et al., 2022).

Sesel and colleagues have suggested that since cognitive impairment in MS is common, CBT may be less well suited to people with MS, due to the nature of this intervention (Sesel et al., 2018). One key component of CBT is the ability to recognise patterns of thinking and the ability to learn new skills or strategies that will help, which may be more difficult to comply with for people with MS with cognitive impairment (Sesel et al., 2018). Sesel and colleagues further suggested that interventions which focus on single skills such as mindfulness or relaxation, and which require fewer cognitive demands, may have greater potential benefit in people with MS (Sesel et al., 2018). Furthermore, Thompson and colleagues have also suggested that since MS is a chronic, persistent disease, and CBT focuses on 'challenging negative thoughts,' which are likely to be 'real' for people with MS, other types of psychological interventions may be better suited to people with MS (Thompson et al., 2022).

However, given the limited evidence in this area, and the limited number of studies including those with cognitive impairment, it cannot be determined from this work whether differences are likely for people with MS with cognitive impairment.

## 2. Discussion

### 2.1 Summary

Mood disorders such as depression and anxiety are common in people with MS, significantly more than in the general population. There is evidence to suggest that fluctuations in mood, for example depression, anxiety, and stress may be associated with an increased risk of MS disease relapse which can substantially impair day to day functioning and quality of life. Effective early interventions for mood disorders that have the potential to maintain functioning and improve the quality of life in people with MS are important in reducing the debilitating impacts of the condition and to maintain social and economic independence.

There is some evidence from recent systematic reviews of randomised clinical trials in people with MS that psychological interventions could be beneficial. Moreover, there are some indications that effects of these interventions could extend to improvements in pain, fatigue, and quality of life. Based on data from over 30 randomised control trials it's important to ensure that treatment received responds to specific symptoms to maximise outcomes, for example:

- Cognitive behaviour therapy moderately reduces pain and fatigue, but there is not enough evidence for its efficacy on depression, anxiety, and quality of life.
- Mindfulness interventions moderately reduce symptoms of depression, anxiety, stress, and fatigue, as well as better coping and quality of life.
- Stress management interventions moderately reduce symptoms of depression, anxiety, and stress.
- Despite some evidence to support acceptance and commitment therapy and relaxation therapy, the evidence base is small and inconclusive.

Therefore, it is important that people with MS are educated about the different types of interventions available and which ones are most appropriate for their particular needs. By being educated about their options, people with MS can make informed decisions about their treatment and choose the intervention that is most likely to be effective for them. This may help them to better manage their symptoms, maintain functioning, and improve their overall quality of life.

The evidence presented in this evidence review is based on clinical studies which have focused on quite different psychological interventions, delivered in different formats, doses, settings and with different comparator groups. Although the number of studies included in many of the reported systematic reviews and meta-analyses enabled some further analyses to investigate if differences in these factors influences the effectiveness of the intervention, further work is still needed to understand the benefit of psychological interventions in people with MS. That said, given these interventions are inherently safe, scalable and have a strong evidence base in other populations, it is likely that more evidence in this field will augment rather than reverse the current conclusions, and in the meanwhile can be used by people with MS for mood management.

## 2.2 Current evidence gaps

We can further improve our understanding of the effectiveness of psychological interventions for people with MS by closing several evidence gaps:

- Intervention types: Which exact type of intervention may be best for people with MS? What is the effectiveness of one specific type of psychological intervention compared to another? (e.g., CBT vs relaxation alone)?
- Intervention setting: Are psychological interventions delivered in a range of settings (i.e., group-based settings, or individually) or delivered in a range of ways (face-to-face, via telephone/teleconference, online, or as a self-guided delivery) as effective?
- Dose response: What is the treatment “dose” (i.e., session number, duration) required to achieve benefit?
- Time scale: What is the long-term effect? Is the benefit sustained over time?
- Types of MS: Are all psychological interventions effective for all phenotypes of MS, and across the course of the disease?
- Are psychological interventions useful in children and adolescents with MS?
- Are psychological interventions useful in people with MS with cognitive impairment?

While the evidence gaps mentioned above require more trials and of better quality as well as more comprehensive evidence synthesis work, several research directions could assist to provide better supports to people living with MS.

First, build an understanding of the assessments and supports currently provided to people with MS as a secondary prevention strategy to support mood and other psychological outcomes of particular interest, to better understand their impact on, cognition and supports (e.g., employment), and the availabilities of these services in the community.

Second, an examination of the broader psychological intervention literature might offer insights on how such interventions could be better utilised. Critical factors include the most efficacious intervention components, alternative delivery methods (e.g., remote interventions in thin markets), dose, timing, responder characteristics, as well as combined therapies. Similarly, it would be beneficial to know how these interventions interact with other common supports.

Finally, and perhaps most importantly is to examine the real-life outcomes of using mood interventions as early interventions. These may include everyday functioning, social and community participation and employment, considering individual needs and goals. Further work could also explore whether these and other interventions, when provided as early intervention, can delay, or prevent the need for supports as the diseases progresses.

## 2.3 Limitations of this report

This report is informed by recent systematic reviews and meta-analyses identified in a scoping review. This is not a systematic umbrella review, but a summary of key findings from recent systematic reviews with meta-analyses, which were judged by authors of the original reviews as the best available evidence. It therefore cannot be ruled out that a primary review using different methodology would lead to different conclusions or close some of the evidence gaps mentioned in the previous section. Moreover, other psychological interventions may have beneficial effects on mood, quality of life and functioning, but were out of scope of this evidence snapshot.

The results presented in this report are based upon the small size of the current reviews (2 to 14 studies), imprecise estimates of the benefit of the interventions, the statistical heterogeneity, and the low methodological quality of most of the included studies. Moreover, most of the current reviews were not able to conduct subgroup analyses to identify which intervention features might be more effective in improving outcomes, due to the limited number of included studies for each outcome and for each type of intervention.

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