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## Third wave cognitive behavioural therapies for people with multiple sclerosis: a scoping review

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### ABSTRACT

**Purpose:** Multiple sclerosis (MS) is a chronic condition linked to a wide range of psychological difficulties. While traditional cognitive behavioural therapy has been studied extensively with people with MS, much less is known about more recent “third wave” approaches.

**Methods:** A scoping review was carried out by performing a systematic search across MEDLINE Complete, PsycINFO, CINAHL, Academic Search Ultimate, and Cochrane Library up to January 2022.

**Results:** From an initial return of 8306 citations, 35 studies were included, 20 of which were randomised controlled trials (RCTs). These showed that four third wave approaches have been investigated with people with MS to date: acceptance and commitment therapy (ACT), dialectical behaviour therapy (DBT), mindfulness-based stress reduction (MBSR), and mindfulness-based cognitive therapy (MBCT). MBSR and MBCT may be helpful to address a range of psychological difficulties up to three months post-intervention. However, MS-specific adaptations may be required, and more evidence is needed on longer-term effectiveness. Limited evidence is also available for DBT and ACT, but additional research is warranted before any recommendation can be made.

**Conclusions:** As third wave approaches keep being refined, further more rigorous investigations are needed to implement them to the benefit of people with MS.

### ARTICLE HISTORY

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### KEYWORDS

Multiple sclerosis; third wave cognitive behavioural therapies; dialectical behaviour therapy; acceptance commitment therapy; mindfulness-based stress reduction

### ► IMPLICATIONS FOR REHABILITATION

- Multiple sclerosis is linked to a wide range of psychological difficulties in adults.
- Little is currently known on third wave psychotherapies for people with MS.
- Mindfulness-based stress reduction and mindfulness-based cognitive therapy may be helpful to address a wide range of difficulties in MS.
- Specific adaptations may be needed to deliver suitable therapies to people with MS.
- Additional research is warranted to build on preliminary findings for DBT and ACT.

## Introduction

Multiple sclerosis (MS) is a chronic autoimmune neurodegenerative condition affecting myelinated axons in the central nervous system [1]. Its main symptoms include sensory deficits, motor weakness, optic neuritis, cognitive impairment, pain, and chronic fatigue, and can vary significantly based on the location of lesions and auto-inflammatory processes, making the course of the disease often unpredictable [2]. Most people are initially diagnosed with MS between 20 and 40 years of age [3] – a period which coincides with important life events, such as trying to establish a career or start a family. As such, the effects of the condition can be wide-reaching, impacting employment and financial stability, family relationships, life-goals, and well-being [4–6]. At present, MS is treatable but not curable, and continues to represent one of the most common causes of physical impairments in younger adults.

While MS is often conceptualised as a unitary condition, different types of MS with varying clinical courses are recognised [1]. Relapsing-remitting MS (RRMS) is the most common presentation, affecting up to 85–90% of individuals [7] and characterised by periods of remission alternated with unpredictable relapses, which cause the onset of acute symptoms [8–10]. As RRMS develops over time it can transition into secondary progressive MS (SPMS), individuals will experience a gradual increase in symptoms over time [11] affecting both their physical and cognitive function [1,12]. Primary progressive MS (PPMS) is another variant which follows a progressive course from the time of diagnosis with no relapsing-remitting phase [13], and affects approximately 10–15% of people diagnosed with MS [14]. Lastly, progressive-relapsing multiple sclerosis (PRMS), which is characterised by the occurrence of relapses within a progressive course of MS, represents the least common subtype of MS and affects approximately 5% of people diagnosed with MS [1].

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In addition to physical symptoms, people with MS often report a lower quality of life [15] and increased psychological distress, even when compared to other neurological conditions [16,17]. Indeed, psychological stress has been found to be associated with exacerbation of MS symptoms [18], and interpersonal stress has been positively associated with brain lesions on magnetic resonance imaging (MRI; [19,20]), in what appears to be a complex interplay between psychological and physiological factors. As MS progresses, new symptoms can emerge that may have a significant impact on daily life and cause psychological difficulties, resulting in a process of continual adaptation [21]. The unique and wide-ranging uncertainties associated with MS can impact on how well a person adjusts to their diagnosis [5,21], with people who experience higher levels of physical impairments, shorter-lasting symptoms, and greater uncertainty showing poorer adjustment to their illness [22,23]. For similar reasons, while present across the whole spectrum of the condition [24–27], manifestations of psychological distress tend to vary across the different subtypes of MS – e.g., secondary progressive MS (SPMS) being linked with higher rates of depression compared to people living with remitting relapsing MS (RRMS; [28,29]).

Among psychological difficulties, depression and anxiety are the most common in individuals with MS, showing a higher level compared to the general population [28,29] and frequently experienced together [30,31]. However, while depression has been widely studied in MS since the 1940s [32,33], anxiety has comparatively been less well researched [30] – even though its occurrence with the former has been linked to increased risk of suicide [34]. Other less common psychological difficulties may include bipolar disorder, dysphoria, pathological laughing or crying, and behavioural changes [34,35]. In addition, not dissimilarly to other motor neurodegenerative conditions (e.g., Huntington’s disease, Parkinson’s, amyotrophic lateral sclerosis; [36–38]), many manifestations of psychological distress in people with MS also appear to revolve around loss of perceived control, certainty, and emotion regulation [35,39], particularly due to the unpredictability of its course [40].

Given the high prevalence of psychological difficulties in people affected by MS, a number of psychological interventions have been explored and implemented with this population, often as a complement to pharmacological treatments [41]. Among these, the most frequently adopted approach is cognitive behavioural therapy (CBT), which has shown to be effective for the treatment of anxiety [42,43], depression [41,44], fatigue [45], stress [42,46], and sleep difficulties [47]. Arising from a combination of cognitive therapy and behaviourist principles, CBT holds that how events are thought about or interpreted affects subsequent emotional, behavioural, and physical reactions [48]. As a consequence, the therapy focuses on changing maladaptive or unhelpful thoughts and behaviours [49].

Since the early 2000s, however, a new approach to this type of therapy, known as the “third wave” of CBT, has started gaining momentum [50]. Unlike early behaviour therapies (“first” wave) and CBT (“second” wave), third wave therapies are characterised by “contextual concepts focused more on the person’s relationship to thought and emotion than on their content” ([51] p.245). In particular, their novel emphasis on concepts such as acceptance, mindfulness, and compassion has been seen as particularly helpful within the context of chronic conditions [52,53], and especially neurodegenerative diseases [54–57]. This also includes MS, where there is evidence of increasing interest in third wave approaches for a wide range of psychological difficulties [41,58,59].

However, unlike CBT, which has been the subject of several systematic reviews and meta-analyses (e.g., [45,60–63]), no review currently exists on third wave therapies with this population. This represents a considerable limitation, as evidence has linked some of the components of third wave therapies to increased psychological well-being in young adults (e.g., mindfulness; [64,65]) and third wave therapies generally have shown promising results in people with other chronic and neurodegenerative conditions [53,57,66–69].

Thus, the overarching aim of this paper was to provide a comprehensive review of the types of third wave cognitive behavioural therapies adopted in individuals affected by MS and their effectiveness for different psychological outcomes. To our knowledge, this is the first review of this kind in this population.

## Methods

### *Methodological approach*

Upon planning the methodological approach to adopt for the present review, a preliminary search was run to explore the current diversity of the literature. This showed a significant heterogeneity involving not only different methods (e.g., quantitative, qualitative, mixed), but also a wide breadth of methodologies (e.g., randomised control trials, quasi-experiments, pretest-posttest designs, case series) as well as MS-specific therapeutic applications and adaptations.

As a consequence, a scoping review was carried out, following the guidelines from the Joanna Briggs Institute [70]. This methodology was chosen to allow for the exploration of a broad research question based on a diverse range of methods and approaches while still retaining a systematic and replicable search strategy [71,72].

### *Inclusion criteria*

To be included in the present review, studies had to: a) relate to people with any form of MS; b) include people aged 18 or above; and c) outline the delivery of any third wave cognitive behavioural intervention to address psychological outcomes in MS. To identify a CBT approach as third wave, the definition provided in the latest Cochrane review on the topic (“intervention focused on modifying the function of thoughts rather than on modifying their content.”; [73], p.8) was adopted as a key criterion. Based on this, studies focused on any implementation of the following approaches were considered eligible for inclusion: acceptance and commitment therapy (ACT), compassion focused therapy (CFT), dialectical behaviour therapy (DBT), metacognitive therapy, mindfulness-based cognitive therapy (MBCT), mindfulness-based stress reduction (MBSR). Qualitative studies were included whenever related to psychological interventions.

Exclusion criteria included not being related to the delivery of third wave interventions for individuals with MS, being based mainly on animal models, not being published in the English language, involving individuals below age 18, lacking sufficient details around the psychological intervention (e.g., specific methods), involving only carers and focusing mainly on cognition or neuroimaging. Reviews (whether narrative or systematic), commentaries, editorials, conference proceedings and letters were also excluded.

**Table 1.** Logic grid for search strategy.

Population	Interventions
Multiple sclerosis	Acceptance and commitment therapy Behavio* therapy Cognitive analytic therapy Cognitive behavio* therapy Cognitive therapy Compassion* focused therapy Counsel* Couple* therapy Dialectical behavioral therapy Emotion focused therapy Emotive behavio* therapy Eye movement desensiti* and reprocessing Family therapy Gestalt therapy Group* therapy Integrative therapy Interpersonal therapy Meditat* Metacognitive therapy Mindfulness Mindfulness-based cognitive therapy Mindfulness-based stress reduction
	Motivational interviewing Narrative therapy Person cent* therapy Psychoanal* Psychodynamic therapy Psychoeducati* Psychological intervention Psychotherap* Rational emotive behavio* therapy Schema therapy Self-management Solution focused therapy Systemic therapy

### Quality assessment

Based on the current guidelines on scoping reviews, quality assessments are not considered appropriate for this methodology [70,74,75]. As a consequence, a formal quality assessment of the included citations was not performed in the present study. However, any methodological or clinical limitations, as well as more robust designs such as randomised control trials (RCTs), were highlighted whenever possible in the results.

### Procedure

#### Search strategies

A systematic search based on a combination of free text terms was performed across five major databases (MEDLINE Complete, PsycINFO, CINAHL, Academic Search Ultimate, Cochrane Library) up until January 2022. The list of keywords was discussed with experts in the field and agreed with the research team through consultation. Hand-searches were also performed across the reference lists of included citations and key reviews to identify further relevant studies. While the present review focused on third wave cognitive behavioural therapies for individuals with MS, a comprehensive set of search terms covering most psychotherapeutic approaches was adopted to ensure that no studies were overlooked based on terminological issues. Table 1 illustrates the logic grid for the search strategy, while Table 2 outlines the specific search terms.

#### Study selection

First, the raw results from the searches were filtered for duplicate citations and studies not fully in English. Following this, all titles and abstracts were screened by one reviewer (NZ) against the abovementioned inclusion criteria. In a second phase, all remaining full-text articles were screened for eligibility by three reviewers (NZ, FE, AB) and confirmed by three more (CL, AM, JS). The PRISMA flow diagram for the study selection is illustrated in Figure 1.

### Data extraction

Data were extracted independently by three reviewers (NZ, AM, CL) and double-checked for accuracy by further three (FE, JS, AB). The data extraction file was developed and piloted through consultation with the research team.

### Data synthesis

Following their extraction, data were synthesised by one reviewer (NZ) and checked by the rest of the research team. The findings of the included studies are reported below, categorised by therapeutic approach. RCTs are highlighted for each category, and details on the samples' MS types are indicated in each study when available.

### Results

The database searches identified a total of 8306 citations, reduced to 4958 following the initial filtering for duplicates and articles not in English. From these, the screening of titles and abstracts led to the exclusion of 4912 studies, leaving a total of 46 full-text articles to consider for inclusion. A total of 35 studies were eventually included, whose key characteristics and results are showed in Table 3. Table 4 lists the 11 excluded full-texts and the respective reasons for exclusion.

#### Acceptance and commitment therapy (ACT)

ACT is a third wave cognitive behavioural therapy which focuses on improving individuals' acceptance of distressing thoughts, beliefs, sensations, and emotions, with the aim to stimulate behavioural change and improve quality of life [50]. Particular emphasis is placed on identifying and acting towards key goals and values that are most important to the person, which then become the target for behavioural changes. A total of nine studies that adopted ACT were identified by this review, five of which were RCTs [76–80].

Proctor and colleagues [77] carried out a pilot RCT which recruited 14 people with RRMS, PPMS, or SPMS for an 8-week telephone intervention based on an ACT self-help book (*Get out*

Table 2. Overview of adopted search terms and identified items per database.

## Search terms

(Multiple sclerosis AND Acceptance and commitment therapy) OR (Multiple sclerosis AND Behavio\* therapy) OR (Multiple sclerosis AND Cognitive analytic therapy) OR (Multiple sclerosis AND Cognitive behavio\* therapy) OR (Multiple sclerosis AND Cognitive therapy) OR (Multiple sclerosis AND Compassion\* focused therapy) OR (Multiple sclerosis AND Counsel\*) OR (Multiple sclerosis AND Couple\* therapy) OR (Multiple sclerosis AND Dialectical behavioral therapy) OR (Multiple sclerosis AND Emotion focused therapy) OR (Multiple sclerosis AND Emotive behavio\* therapy) OR (Multiple sclerosis AND Eye movement desensiti\* and reprocessing) OR (Multiple sclerosis AND Family therapy) OR (Multiple sclerosis AND Gestalt therapy) OR (Multiple sclerosis AND Group\* therapy) OR (Multiple sclerosis AND Integrative therapy) OR (Multiple sclerosis AND Interpersonal therapy) OR (Multiple sclerosis AND Meditat\*) OR (Multiple sclerosis AND Metacognitive therapy) OR (Multiple sclerosis AND Mindfulness) OR (Multiple sclerosis AND Mindfulness-based cognitive therapy) OR (Multiple sclerosis AND Mindfulness-based stress reduction) OR (Multiple sclerosis AND Motivational interviewing) OR (Multiple sclerosis AND Narrative therapy) OR (Multiple sclerosis AND Person cent\* therapy) OR (Multiple sclerosis AND Psychoanal\*) OR (Multiple sclerosis AND Psychodynamic therapy) OR (Multiple sclerosis AND Psychoeducati\*) OR (Multiple sclerosis AND Psychological intervention) OR (Multiple sclerosis AND Psychotherap\*) OR (Multiple sclerosis AND Rational emotive behavio\* therapy) OR (Multiple sclerosis AND Schema therapy) OR (Multiple sclerosis AND Self-management) OR (Multiple sclerosis AND Solution focused therapy) OR (Multiple sclerosis AND Systemic therapy)

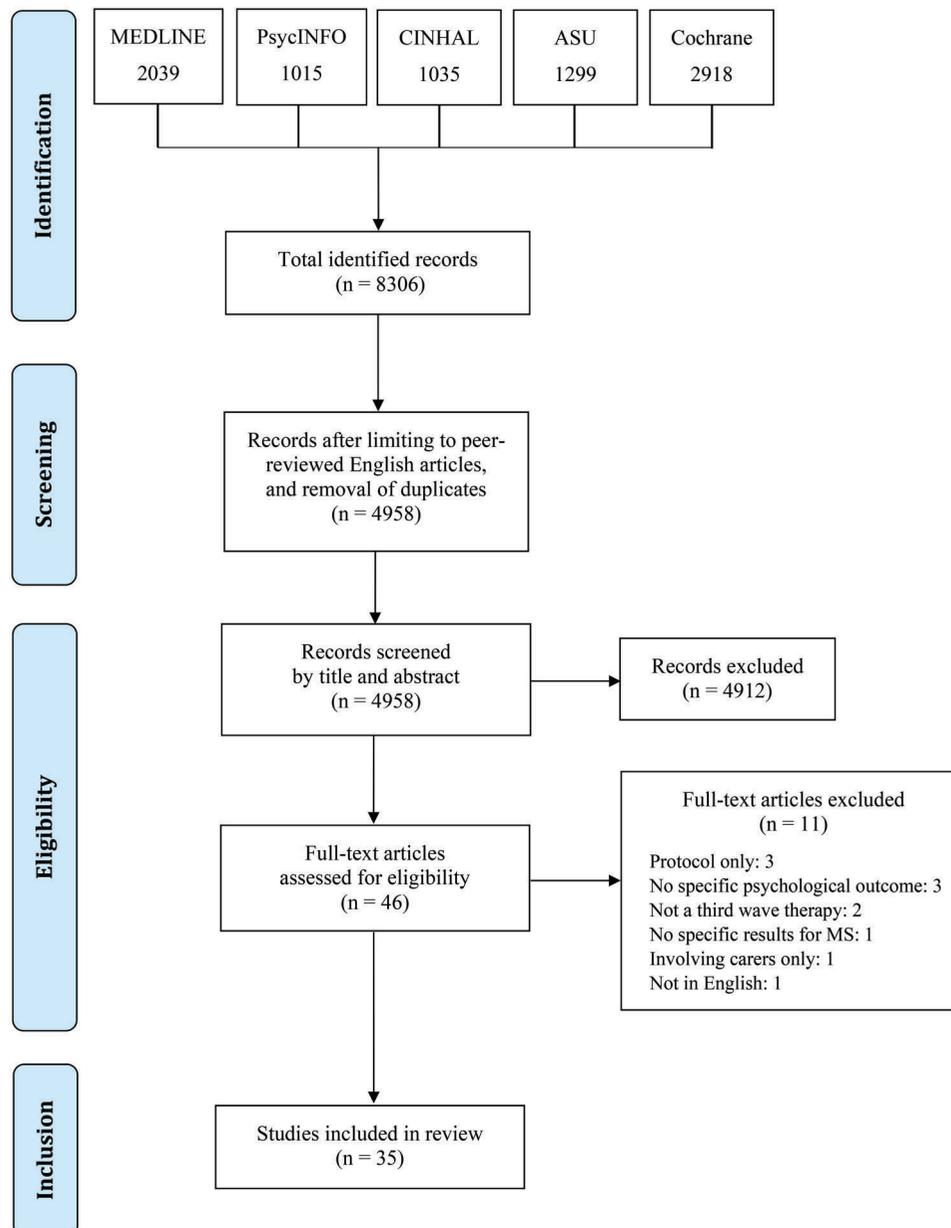


Figure 1. PRISMA diagram for selection of studies.

of your mind and into your life; [122]). A matched group of individuals with MS only receiving treatment as usual (TAU) was enrolled as control. The results showed a significant effect of treatment on anxiety at post-intervention. However, the treatment group

suffered from very high levels of attrition (33%), meaning that only five participants eventually completed the intervention.

Lotfifar and colleagues [76] enrolled a sample of 48 women with MS to test the effectiveness of ACT (12 2-h sessions),

Table 3. Key characteristics of included studies.

Citation	Approach	Design	Sample	MS types	Relevant outcomes	Key results
[76]	ACT	RCT	I: 16 C1: 16	N/S	Death anxiety	Significantly greater reductions in death anxiety in both the ACT and LT (C2) groups compared to controls (C1). No significant differences were between ACT and LT interventions.
[77]	ACT	RCT	I: 14 C: 13	RRMS PPMS SPMS	Anxiety Depression	Significant effect of treatment on anxiety at post-intervention. 33% drop-out rate.
[78]	ACT	RCT	I: 11 C: 10	RRMS SPMS	Anxiety Depression	Significantly greater decrease in depression in control group (relaxation) at post-intervention. No significant between-group differences for anxiety.
[79]	ACT	RCT	I: 20 C: 19	RRMS PPMS SPMS	Quality of life Anxiety Depression Resilience Perceived stress	No statistically significant differences between groups in health-related quality of life, mood, resilience, and psychological flexibility.
[80]	ACT	RCT	I: 7 C: 7	SPMS	Anxiety Depression Self-efficacy	Recruitment strategy not feasible. No significant changes between baseline and 8-week or 12-week follow up on any measures. Interview feedback suggesting positive outcomes not captured through self-report measures.
[81]	ACT	Uncontrolled pretest-posttest	I: 37	RRMS	Psychological flexibility Resilience	Significant improvements for resilience, physical health quality of life, mental health quality of life, depression, stress, defusion, values, and acceptance.
[82]	ACT	Uncontrolled pretest-posttest	I: 237	PPMS SPMS RRMS PPMS SPMS	Quality of life Distress Resilience Quality of life Distress Anxiety Depression Stress	Significant improvements on all outcomes at post-intervention or 3-month follow-up, but small effect sizes. Qualitative data suggesting participation in intervention was associated with wide range of personal improvements.
[83]	ACT	Uncontrolled pretest-posttest	I: 15	N/S	Psychological flexibility Quality of life	Significant improvements on depression, extent of thought suppression, impact of pain on behaviour, and quality of life.
[84]	ACT	Case series	I: 7	PPMS	Psychological distress Pain Illness perceptions	No differences for mindfulness or impact of physical symptoms. Three participants showed significant improvements in pain outcomes, two showed no change, and two worsened. Five participants showed significant change on pain catastrophizing, negative emotional representations of pain, beliefs about chronicity and negative consequences, avoidance of social activities and, to a lesser extent, pain acceptance.

(continued)

Table 3. Continued.

Citation	Approach	Design	Sample	MS types	Relevant outcomes	Key results
[85]	DBT	RCT	I: 10	N/S	Depression	Significantly greater decrease in depression for the treatment group at post-intervention.
[86]	DBT	Controlled pretest-posttest	C: 10 I: 10	RRMS	Depression	No follow-up assessment. Significant improvement in depression, anxiety, and quality of life at post-treatment, with benefits maintained at the 6-month follow-up. The same not observed for TAU.
[87]	MBSR	RCT	C: 10 I: 15	PPMS N/S	Anxiety Stress	No post-intervention between-group analysis. Stress and fatigue improved in intervention group
[88]	MBSR	RCT	C: 15 I: 54	RRMS	Fatigue Quality of life	Significantly higher quality of life and significantly lower depression, anxiety, and sleep problems in intervention group at post-intervention.
[89]	MBSR	RCT	C: 67 I: 76	SPMS RRMS	Anxiety Depression Sleep Fatigue Quality of life	No significant group differences at 6 months. Significant differences between groups for all primary outcomes at both timepoints.
[90]	MBSR	RCT	C: 74 I: 20	SPMS N/S	Depression	Benefits for health-related quality of life and depression reduced at 6-month follow-up. Significant decrease in depression, anxiety, and stress in the intervention group both post-treatment and at follow-up.
[91]	MBSR	RCT	C: 20 I: 12	N/S	Fatigue	Significant improvement in scores of emotional well-being, health distress, health perception, overall quality of life, and fatigue severity.
[92]	MBSR	RCT	C: 12 I: 20	RRMS	Emotion regulation	No change in pain, social performance, and health change. Significantly greater reductions in emotion dysregulation, rumination, and worry.
[93]	MBSR	RCT	C1: 20 C2: 21 I: 33 C: 29	PPMS RRMS PPMS	Quality of life Perceived stress Anxiety	No between-group differences in quality of life. No follow-up assessment. Improved in all emotional well-being outcomes for both intervention and control groups.
[94]	MBSR	Secondary qualitative analysis of Simpson <i>et al.</i> (2017)	I: 23	SPMS RRMS PPMS	Depression Fatigue Pain Resilience N/A	No significant difference between groups. Good level of acceptability for people with MS. Optimisation needed for some components to avoid causing discomfort (e.g., mindful movement).
[95]	MBSR	RCT	I: 16 C: 9	SPMS N/S	Perceived stress Fatigue Quality of life	Significant improvements in depression, coping, and perceived stress at post-intervention. No differences between groups at 6-month follow-up.

(continued)

Table 3. Continued.

Citation	Approach	Design	Sample	MS types	Relevant outcomes	Key results
[96]	MBSR	RCT	I: 25	RRMS	Perceived stress	Significantly greater improvements with large effect sizes in perceived stress, depression, positive affect, and self-compassion.
			C: 25	PPMS SPMS	Quality of life	Small beneficial effects for quality of life. Effects on perceived stress and depression considerably reduced at 3-month follow-up.
[97]	MBSR	Quasi-experiment	I: 15	SPMS	Anxiety	Significant increase in character traits reflecting the maturity of the self in self-directedness and cooperativeness.
			C: 13	PPMS	Depression	Significant increase of mindfulness and conscientiousness and decrease in trait anxiety.
[98]	MBSR	Quasi-experiment	I: 22	N/S	Personality Sleep	Within-group moderate to large effect sizes on measures of sleep efficiency and total sleep time.
			C: 12		Fatigue Depression Quality of life N/A	No between-group differences.
[99]	MBSR	Secondary qualitative analysis of [98]	I: 14	N/S	N/A	Participants generally found the intervention to be acceptable and beneficial.
[100]	MBSR	Uncontrolled pretest-posttest	I: 25	N/S	Depression	Significant improvements in depressive symptoms, quality of life, fatigue, mindfulness skills, and self-compassion. Largest effect on quality of life.
[101]	MBCT	RCT	I: 19	PPMS	Quality of Life Stress Fatigue Distress	Significant distress improvement in intervention group at postintervention and follow-up (medium to large effect size).
			C: 21	SPMS	Depression	Reduced mean scores for pain, fatigue, anxiety, depression and, impact of MS in intervention group at postintervention and follow-up.
[102]	MBCT	RCT	I: 10	RRMS	Anxiety Pain Fatigue Anxiety	Significantly greater improvements for the intervention group in anxiety, depression, and hope.
[103]	MBCT	RCT	C: 10		Depression Hope	No significant reduction of stress.
			I: 50	PPMS	Perceived stress	Significant improvement of quality of life.
[104]	MBCT	RCT	C: 50	SPMS	Quality of life	Any effect of the intervention reduced over the 6-month contact period with the study team.
			I: 45	RRMS	Depression Anxiety Fatigue	Intervention significantly more effective in reducing depressive symptoms, but not anxiety or perceived stress, in per-protocol-analysis.
			C: 45	PPMS	Depression	Main effect of group became non-significant in intention-to-treat analysis.
				SPMS PRMS	Anxiety Stress Illness perception Quality of life	

(continued)

Table 3. Continued.

Citation	Approach	Design	Sample	MS types	Relevant outcomes	Key results
[105]	MBCT	Controlled pretest-posttest	I: 30	RRMS	Anxiety	Within-group significant improvement in anxiety and depression at post-intervention. No between-group comparisons.
[106]	MBCT	Uncontrolled pretest-posttest	C: 30 I: 39	RRMS  PPMS	Depression Fatigue  Anxiety Depression Sleep Coping Quality of life	Improvements in all outcomes except life satisfaction and sleep at post-intervention and maintained at 3 month follow up. 29% drop-out rate.
[107]	MBCT	Uncontrolled pretest-posttest	I: 23	RRMS	Quality of life	Significant improvements in psychological distress, perceived stress, mental health quality of life, mindfulness, self-compassion, and acceptance.
[108]	MBCT	Uncontrolled pretest-posttest	I: 126	PPMS SPMS RRMS	Psychological distress Fatigue Distress	Significant improvements in psychological distress, perceived stress, mental health quality of life, mindfulness, self-compassion, acceptance, and physical health quality of life.
[109]	MBCT	RCT	I: 18	N/S	Perceived stress Quality of life Fatigue Emotional well-being	No between-group differences on measures of efficacy, including emotional well-being, pain, quality of life, and health perceptions.
			C1: 18 C2: 19		Pain Quality of life Health perceptions	Qualitative analysis showed good feasibility and acceptability.
[110]	MBCT	Uncontrolled pretest-posttest	I: 30	RRMS	Depression	Significant increase in trait mindfulness and decrease in depression and fatigue following the intervention.
				PPMS	Fatigue	Increased trait mindfulness associated with decreased MS symptoms.
				SPMS	Rumination Mindfulness	No significant change in trait rumination.

Note. ACT: Acceptance and Commitment Therapy; C: control; DBT: Dialectical Behaviour Therapy; I: intervention; MBCT: Mindfulness Based Cognitive Therapy; MBSR: Mindfulness Based Stress Reduction; MS: multiple sclerosis; N/A: Not applicable; N/S: Not specified; PPMS: primary progressive MS; PRMS: progressive-relapsing MS; RCT: Randomised Controlled Trial; RRMS : relapsing-remitting MS; SPMS: secondary progressive MS.

logotherapy (LT), and a 3-h workshop (control) in reducing death anxiety. While both the ACT and LT groups showed significantly greater reductions in death anxiety compared to controls, no significant differences were observed between the two interventions. Similar results were reported for the adoption of ACT when compared to relaxation training (RT) in a small RCT enrolling 20 people with RRMS and SPMS, which found a significantly greater decrease in depression in the RT group at post-intervention, and no significant between-group differences for anxiety [78].

Pakenham *et al.* [81] carried out an uncontrolled pretest-posttest study to evaluate the MS adaptation of a group resilience training programme based on ACT principles (REsilience for Adults EverydaY, READY) in a group of 37 individuals with RRMS, PPMS, or SPMS. The findings looked promising, showing significant improvements at post-intervention in measures of resilience, physical and mental quality of life (QoL), depression, stress, as well as ACT principles such as defusion, values, and acceptance. These were confirmed when READY was delivered by frontline

services in Italy in an uncontrolled pretest-posttest with 237 people with MS, which found positive results post-intervention on most psychological outcomes (e.g., anxiety, depression, stress), and psychological flexibility [82]. However, effect sizes on all included outcomes were small. Moreover, when a pilot RCT was carried out to test the same programme against group relaxation in a pilot RCT [79], the results showed no statistically significant differences between groups on measures of health-related quality of life (HRQoL), mood, resilience, and psychological flexibility. In all these studies, READY was generally found feasible and acceptable by participants.

A feasibility RCT examined the efficacy of a 6-week ACT-based telephone supported bibliotherapy intervention (Acceptance Based Support, ABS) against TAU in people who had just transitioned from PPMS to SPMS [80]. The results – based on only seven participants per group due to recruitment difficulties – showed no significant changes between baseline and 8-week or 12-week follow-up on measures of anxiety, depression, self-efficacy, and

Table 4. Articles excluded following full-text review.

Citation	Approach	Reason for exclusion
[111]	MBSR	Protocol only
[112]	Mindfulness	No specific psychological outcome
[113]	ACT	No specific psychological outcome
[114]	MBCT	Protocol only
[115]	Yoga, meditation, mindfulness	Not a third wave therapy
[116]	Psychoeducation	No specific results for MS
[117]	ACT	Not in English
[118]	Mindfulness of movement	No specific psychological outcome
[119]	Mindfulness-based art therapy (MBAT)	Not a third wave therapy
[120]	ACT	Involving carers only
[121]	Mindfulness	Protocol only

Note. ACT: acceptance and commitment therapy; MBCT: mindfulness based cognitive therapy; MBSR: mindfulness based stress reduction; MS: multiple sclerosis.

psychological flexibility. However, positive participants' feedback from individual interviews suggested that some favourable outcomes may have not been captured through self-report measures (e.g., "talking to [a therapist] that's impartial and knows exactly what you're talking about, it just helps people").

Sheppard and colleagues [83] asked 15 individuals with MS to attend a 5-h ACT-based workshop, during which they also underwent measures of psychological distress, QoL, and MS-related impairments. When assessed again after 12 weeks, the participants showed mixed results, with significant improvements in depression, thought suppression, QoL, and impact of pain on behaviour, but no differences in terms of mindfulness or impact of physical symptoms. Similar mixed findings were observed specifically for MS-related pain in a case series which evaluated the effectiveness of a guided self-management hybrid ACT and CBT intervention and showed significant improvements for three participants, while two showed no difference and further two even worsened [84].

### Dialectic behavioural therapy (DBT)

Initially developed to treat people with borderline personality disorder [123], DBT has since been adopted with people with a number of different difficulties, including people with chronic or life-limiting conditions [124]. While retaining CBT's focus on changing unhelpful cognitions and behaviours to improve well-being, DBT places additional emphasis on emotion regulation, distress tolerance, self-acceptance, and validation of experiences. So far, only two studies have assessed DBT with within the context of MS, with only one RCT [85].

Blair and colleagues [86] administered 16 biweekly sessions of DBT to 10 people with either RRMS or SPMS. The intervention proved feasible and the results showed a significant improvement in depression, anxiety, and quality of life at post-treatment, with benefits maintained at the 6-month follow-up. The same was not observed in a similar group of individuals with MS which received TAU during the same period. However, no post-intervention between-group analysis was carried out.

Sepehri and colleagues [85] carried out a small RCT comparing 10 women with MS receiving 12 weeks of DBT with matched controls receiving TAU. At post-intervention, the DBT group showed a significantly greater decrease in depression compared to TAU. No information was provided on the participants' MS type.

### Mindfulness-based stress reduction (MBSR)

As the name suggests, MBSR is an approach based on mindfulness, a quality of consciousness which focuses on bringing the attention to the present moment, accepting experiences, feelings,

sensations, and emotions non-judgementally [125]. When applied within the context of neurodegenerative diseases such as MS, this may emphasise the acceptance of pain, discomfort, and physical impairments by promoting a renewed focus on relaxation techniques and appreciation of the abilities and resources that are maintained [126]. Traditionally, MBSR is delivered in groups and consists of eight weeks of training in mindful body postures ("mindful movement") as well as breath and body awareness [127]. A total of 14 studies have investigated the effectiveness of MBSR, nine of which were RCTs [87–95].

Kolahkaj and Zargar [90] compared the effectiveness of MBSR on anxiety, depression, and stress in a sample of 48 women with MS compared to TAU, and found significantly greater improvements on all outcomes at post-intervention and 1-month follow-up. Similarly, a larger RCT ( $N = 150$ ) which compared the effectiveness of MBSR on depression, anxiety, fatigue, and HRQoL with TAU showed a significant effect of MBSR on all outcome measures at post-intervention [89]. However, benefits for HRQoL and depression appeared to reduce after eight months.

Cavalera and colleagues [88] enrolled a large sample ( $N = 121$ ) of people with RRMS or SPMS and randomly assigned them to MBSR or psychoeducation *via* telemedicine (control). At post-intervention, the results showed significantly greater improvements for QoL, depression, anxiety, and sleep problems in the MBSR group. However, the differences were no longer significant after six months. Similarly, a recent pilot RCT compared the Mindfulness Ambassador Program (MAP) – an MBSR-inspired 10-week intervention – to TAU and found significant improvements in depression, coping, and perceived stress at post-intervention [95], but no differences between groups at the 6-month follow-up.

Another RCT by Simpson et al. [94] found that, when compared to waitlist controls, MBSR led to significantly greater improvements with large effect sizes in perceived stress, depression, positive affect, and self-compassion, while small beneficial effects were also reported for QoL. However, at 3-month follow-up the effects on perceived stress and depression had considerably reduced. A secondary qualitative analysis of the trial carried out by the same authors [96] highlighted that, although MBSR had shown a good level of acceptability for individuals with MS, a number of components would need to be optimised with this population to avoid causing discomfort (e.g., mindful movement).

Two small RCTs ( $N \leq 30$ ) tested the effectiveness of MBSR alone or in combination with Consciousness Yoga at improving QoL, stress, and fatigue in women with MS [87,91]. The results showed significantly greater improvements on all outcomes at post-intervention when compared to TAU. However, no follow-up assessment was carried out in either study.

Schirda et al. [92] found that a 4-week adaptation of MBSR led to significant reductions in emotion dysregulation, rumination, and worry in 20 people with RRMS or PPMS when compared to adaptive cognitive training or waitlist controls. However, no between-group differences were observed for QoL measures, nor was any follow-up assessment performed after post-intervention. Less promising results were instead reported by a larger trial with 180 people with RRMS, SPMS, or PPMS which compared MBSR to simple education around MS and found within-group improvements for perceived stress, emotional well-being, depression, anxiety, fatigue, and resilience, but no between-group differences at either post-intervention or 12-month follow-up [93].

A small quasi-experiment ( $N = 28$ ) found a number of improvements in character traits and trait anxiety of people with RRMS, SPMS, or PPMS following the administration of MBSR compared to TAU [97]. However, no follow-up data was provided. A similarly

designed study [98] investigated the effectiveness of an MBSR-inspired sleep education intervention ("SleepWell") to reduce sleep difficulties in people with MS compared to waitlist controls. The results showed within-group moderate to large effect sizes on measures of sleep efficiency and total sleep time, but no between-group differences. A secondary qualitative analysis of part of the same sample later showed that the participants found the intervention acceptable and beneficial [99].

Finally, Blankespoor and colleagues [100] carried out an uncontrolled pretest-post-test study to pilot the adoption of MBSR in 25 individuals with RRMS, SPMS, or PPMS. The results showed significant improvements on depressive symptoms, QoL, fatigue, mindfulness skills, and self-compassion at post-intervention, but no follow-up assessments were carried out.

### **Mindfulness-based cognitive therapy (MBCT)**

Also rooted in mindfulness principles, MBCT as a type of therapy originated from the integration of MBSR with components of CBT for depression [128], retaining the 8-week duration and activities of MBSR while adding a series of cognitive exercises. This review identified a total of ten studies that explored MBCT, five of which were RCTs [101–104].

Bogosian and colleagues [101] administered MBCT online to 19 people with PPMS and found significantly greater improvements in mean scores for anxiety, depression, pain, fatigue, and impact of MS at post-intervention and 3-month follow-up compared to controls placed on a wait list. Similar positive results were observed for anxiety, depression, and hope in people with RRMS enrolled in a similarly sized RCT [102]. A larger trial ( $N = 100$ ) comparing MBCT along with meditation and progressive muscle relaxation to waitlist controls instead reported no significant effect of treatment on stress at post-intervention or follow-up, and only a significant effect on quality of life in a secondary analysis based on median scores [103].

De la Torre et al. [105] randomly assigned 60 people with RRMS to either MBCT or TAU. At post-intervention, both groups showed significant improvement in measures of anxiety and depression compared to baseline. No information was provided on any between-group comparisons at post-intervention. Positive results were instead reported by a multiple baseline waitlist controlled study which administered group MBCT to 39 individuals with severely fatigued RRMS or PPMS and found significant improvements at post-intervention for fatigue, anxiety, depression, catastrophising, and emotion-oriented coping [106]. All improvements were maintained at 3-month follow-up, and high levels of satisfactions were reported by most participants. However, the study also reported a 29% drop-out rate.

Spitzer and Pakenham [107] carried out an uncontrolled pretest-posttest study with 23 people with RRMS, SPMS, or PPMS to explore the adoption of "Mindfulness for MS", a community-based mindfulness programme adapted from both MBSR and MBCT protocols. The results at post-intervention, based on univariate analyses, showed significant improvements in psychological distress, perceived stress, the mental health QoL dimension, mindfulness, self-compassion, and acceptance. Data from qualitative interviews also showed that participants benefitted in terms of awareness, coping skills, self-compassion, acceptance, support, and changed perspectives. A subsequent update study, based on the administration of the same programme to 126 participants with MS over five years, later confirmed improvements in the same outcomes with the addition of physical health QoL [108].

A 3-arm mixed methods RCT tested the feasibility, acceptability, and effectiveness of Mindfulness for Multiple Sclerosis (M4MS), an online 8-week MS-specific intervention based on the MBCT protocol, against Chair Yoga and waitlist controls [109]. The qualitative results, based on a total sample of 55 participants with MS, showed that the online delivery of the intervention was feasible and acceptable. However, the quantitative analyses failed to find any between-group differences on measures of effectiveness, including emotional well-being, pain, QoL, and health perceptions.

A further investigation adopted an uncontrolled pretest-posttest design to evaluate a 1-week mindfulness programme adapted from MBCT in 30 individuals with MS facing a short-term acute hospital stay [110]. The assessment at post-intervention showed significant decrease in depression and fatigue, as well as a significant increase in trait mindfulness, which was negatively correlated with MS symptoms. However, no significant changes were observed in trait rumination.

Finally, Carletto and colleagues [104] enrolled 90 individuals with RRMS, PPMS, SPMS, or PRMS to compare Body-Affective Mindfulness (BAM) – an 8-week group intervention combining mindfulness with principles of cognitive and sensorimotor therapy – against education around MS. The per-protocol-analysis showed that BAM was more effective in reducing depressive symptoms, but not anxiety or perceived stress. Moreover, when an intention-to-treat analysis was carried out including the 19 participants who dropped out of either arm, the main effect of group became non-significant, thus weakening the evidence in favour of the greater effectiveness of the intervention.

## **Discussion**

### **Summary of main findings**

The present study aimed to scope the current literature on the implementation of third wave cognitive behavioural therapies in individuals affected by MS. To our knowledge, this is the first comprehensive review of which third wave interventions have been adopted with this population and their effectiveness for specific psychological outcomes. From an initial return of 8306 citations, 35 studies were eventually found eligible for inclusion, 20 of which were RCTs. The main findings showed that, among all third wave approaches, four have been implemented in people with MS to date, namely acceptance and commitment therapy (ACT), dialectical behaviour therapy (DBT), mindfulness-based stress reduction (MBSR), and mindfulness-based cognitive therapy (MBCT).

The current evidence for the use of ACT with individuals with MS, based on nine studies, appears to be mixed. While some preliminary positive results are reported for anxiety, depression, stress, and QoL [77,81–84], other investigations reported no differences when ACT interventions were compared to TAU or logotherapy [76,79,80], or even lower effectiveness when compared to relaxation training [78]. Therefore, further evidence based on larger samples is currently needed to shed light on the effectiveness of ACT for people with MS.

The adoption of DBT was explored only by two studies, both showing promising results for the treatment of depression, anxiety and QoL [85,86]. Nonetheless, it should be noted that no between-group comparison was available in one case [86]. Thus, further larger studies are warranted to investigate the use of DBT individuals affected by MS.

MBSR was the most adopted third wave approach within the context of MS, with almost half of the included studies (14 out of

35) exploring it in one of its variations. The current findings, also supported by nine RCTs, appear to suggest that MBSR is an effective short-term intervention for a wide range of outcomes in people with MS, including anxiety, depression, fatigue, QoL, sleep problems, perceived stress, and emotion dysregulation. However, the longitudinal effect is less convincing, with the treatment effects tending to reduce significantly after three to six months [88,89,95,129], while other investigations did not include any follow-up assessments [87,91,92,97,100] or between-group analyses [98]. Moreover, the largest RCT currently available for the use of MBSR with participants with MS ( $N = 180$ ) did not observe any significant between-group differences in depression, anxiety, perceived stress, emotional well-being, and fatigue when compared to simple education around MS [93]. Thus, more longitudinal research is needed to clarify the long-term effectiveness of MBSR for psychological outcomes in this population.

Finally, MBCT was adopted by 10 studies, including five RCTs. The current evidence from uncontrolled or small- to mid-scale (i.e.,  $N < 50$ ) investigations appears to suggest that MBCT can be effective to improve outcomes such as anxiety, depression, hope, pain, and fatigue [101,102,106,107,110]. However, the results from RCTs including larger samples painted a different picture, reporting either smaller effects (Carletto et al., 2016) or no between-group differences at all [103,109]. As a consequence, further large-scale studies are warranted to clarify the extent to which MBCT may be an effective therapy for people with MS.

### **Clinical implications and future directions**

While less conclusive than reviews focusing on CBT, this current review on third wave therapies in individuals with MS has a number of important implications, particularly due to the recognised role played by psychological issues in the successful implementation of rehabilitation programmes [130]. More specifically, our findings suggest that standardised and time-limited mindfulness-based interventions such as MBSR and MBCT may reduce the level of psychological difficulties, with the former showing to be especially effective in the short term (i.e., up to three months). However, these may need to undergo a number of MS-specific adaptations to increase acceptability – such as modifying the mindful movement components in order to account for motor impairments, chronic fatigue, and pain [96] – and more data are needed on their mid- to long-term effectiveness. Limited preliminary evidence also showed promising results for the adoption of DBT – in particular for depression, anxiety, and QoL – but further research is warranted before any recommendation can be made. Similarly, although less limited, the current evidence on the use of ACT with people with MS appears to be inconclusive, thus calling for more rigorous and conclusive investigations. These future research endeavours should also attempt to address or avoid the methodological limitations observed in some of the studies outlined above by including follow-up evaluations, enrolling larger and/or sufficiently powered samples, and implementing qualitative components in clinical trials when feasible.

Besides the need for additional research on the therapies identified by the present review, future studies should also explore the adoption of third wave approaches currently neglected in the MS literature. One of these is compassion focused therapy (CFT), an integrative psychotherapeutic approach which combines principles drawn from cognitive therapy, evolutionary psychology, Buddhist philosophy, and neurobiology to reduce shaming through compassion [131], which has shown promising results in people with dementia [132] and other chronic conditions [66]. In

addition, while most of the included citations specified the MS types included in their samples, none of them reported any detailed results for specific types or explored differences between them. Since we know that different forms of MS can have different psychological impacts – e.g., transitioning from RRMS and SPMS can be particularly challenging [133] and SPMS is associated with higher levels of depression compared to RRMS; [134,135] – this represents a limitation in our understanding of how to target the condition effectively with psychological approaches and should be addressed by future investigations.

### **Conclusion**

The reviewed studies suggest that a number of third wave cognitive behavioural therapies may be viable and effective to treat a wide range of psychological difficulties linked with MS. However, additional, more rigorous and conclusive evidence is needed on how to best implement them to the benefit of affected individuals.

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