

Table S1. Search Strategies

Embase.com

((('exercise'/exp OR 'kinesiotherapy'/exp OR 'exercise therap*':ti,ab,kw) OR (cognit* NEAR/3 (therap* OR intervention* OR therap*)):ti,ab,kw OR ('alternative medicine'/exp OR 'mind-body therap*':ti,ab,kw) OR ('psychotherapy'/exp OR 'positive psychotherap*':ti,ab,kw OR 'positive psychology intervention':ti,ab,kw) OR ('muscle relaxation'/exp OR 'progressive muscle relaxation':ti,ab,kw) OR ('qigong'/exp OR qigong:ti,ab,kw) OR ('meditation'/exp OR meditat*:ti,ab,kw) OR ('non pharmacological*':ti,ab,kw OR 'non pharmaceutical*':ti,ab,kw OR 'non drug':ti,ab,kw)) AND (('multiple sclerosis'/exp OR 'multiple sclerosis':ti,ab,kw OR ms:ti,ab,kw) AND ('sleep'/exp OR insomnia*:ti,ab,kw OR sleep*:ti,ab,kw OR asleep:ti,ab,kw OR circadian*:ti,ab,kw))

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1 exp multiple sclerosis/ or multiple sclerosis.ti,ab,kw. or MS.ti,ab. (413212)

2 exp Sleep/ or exp Sleep Wake Disorders/ or (insomnia\$ or sleep\$ or asleep or circadian\$).ti,ab,kw. (291875)

3 exp Exercise Therapy/ or exercis\$.ti,ab,kw. or "physical therap\$.ti,ab,kw. or physiotherap\$.ti,ab,kw. or "physical activit\$.ti,ab,kw. (566127)
 4 exp Behavior Therapy/ or (cognit\$ adj3 (therap\$ or intervention\$)).ti,ab,kw. (98252)
 5 exp Complementary Therapies/ or "mind-body therap\$.ti,ab,kw. (242234)
 6 exp Psychotherapy/ or positive psycholog\$.ti,ab,kw. (210946)
 7 Muscle Relaxation/ or "Progressive muscle relaxation".kw,ti,ab. or (muscle adj3 relax\$.ti,ab,kw. (27016)
 8 (qigong or mindfulness or meditation).ti,ab,tw. (13800)
 9 1 and 2 (3171)
 10 or/3-8 (994806)

Web of Science

#3 AND #4


TI=(exercis* or "behavior therap*" or "complimentary therap*" or "mind-body therap*" or psychotherap* or "positive psycholog*" or relaxation or "progressive muscle relaxation" or qigong or yoga or mindfulness or meditat* or non-pharmacologic* or non-pharmaceutic* or non-drug) OR AB=(exercis* or "behavior therap*" or "complimentary therap*" or "mind-body therap*" or psychotherap* or "positive psycholog*" or relaxation or "progressive muscle relaxation" or qigong or yoga or mindfulness or meditat* or non-pharmacologic* or non-pharmaceutic* or non-drug)

#2 AND #1

Sleep* or insomnia* or sleep* or asleep or circadian* (Title) or Sleep* or insomnia* or sleep* or asleep or circadian* (Abstract)
 multiple sclerosis (Title) or multiple sclerosis (Abstract) or MS (All Fields)


Table S2. Study Summaries

First author	Year	Country	Study design	Enrolled (dropout), No.	Intervention type	Outcomes			Impact on sleep
						Was sleep primary outcome?	Primary outcome	Sleep outcome	
<i>Physical Activity</i>									
Pilutti	2014	US	RCT	82 (6)	Internet-delivered lifestyle physical activity intervention	Unclear	Unclear	PSQI	
Sadeghi Bahmani	2019 b	Iran	RCT	92 (21)	Group aerobic exercise or coordinative training	Yes	ISI	ISI	+
Sadeghi Bahmani	2020	Iran	RCT	62 (2)	Aquatic exercise	No	Sexual dysfunction	ISI	
Al-Sharman	2019	Jordan	Pilot RCT	40 (10)	Moderate-intensity aerobic exercise	Unclear	Unclear	PSQI, ISI, actigraphy (in subsample), biomarkers	+

Cederberg	2021	US	Pilot RCT	15 (1)	Physical activity	Unclear	Unclear	IRLS, PSQI, Seven-Day Diary, actigraphy, ESS	+
Grubic-Kezele	2021	Croatia	Pilot RCT	24 (0)	Exercise	Unclear	Unclear	PSQI, ISI	+
Siengskon	2016	US	Pilot RCT	28 (6)	Aerobic exercise	Yes	PSQI, ESS	PSQI, ESS	+
Andreu-Caravaca	2021	Spain	Single-group pre-post test	18 (0)	Resistance training	Yes	Subject sleep quality (Karolinska sleep diary) and actigraphic sleep quality	Actigraphy and Karolinska sleep diary	+
Jeong	2020	US	Single-group pre-post test	17 (0)	Exercise telerehabilitation	Yes	PSQI	PSQI	-
Kozlowski	2017	US	Single-group pre-post test	13 (8)	Exoskeleton-assisted walking	No	Feasibility and safety	Neuro-QOL sleep disturbance section	-
Mehrabani	2021	Canada	Single-group pre-post test	41 (5)	Physical activity intervention	Unclear	Unclear	PSQI	+ [immediate] - [7 weeks]
Sadeghi Bahmani	2019a	Switzerland	Single-group pre-post test	51 (5)	Aerobic exercise and physiotherapy	Yes	Main outcomes: changes in objective and subjective sleep, depression, fatigue, and paresthesia	EEG, ISI	+
Vasudevan	2021	India	Single-group pre-post test	10 (0)	Personalized yoga therapy	Unclear	Unclear	PSQI	
CBT-I									
Siengskon	2021	US	Pilot RCT	41 (21)	Web-based CBT-I	No	Feasibility	ISI, PSQI, SSES, MCSB	+
Siengskon	2020	US	Pilot RCT	33 (3)	CBT-I	No	Feasibility	ISI, PSQI, SSE	+
Williams-Cooke	2021	US	Pilot RCT (secondary analysis of Siengskon 2020)	25 (3)	CBT-I	Yes	Actigraphy, sleep log	Actigraphy, sleep log	+
Clancy	2015	US	Case series	11 (unclear)	Individual or group CBT-I	Unclear	Unclear	ISI, TST	+
Loveless	2019	US	Case study	1 (n/a)	CBT-I	Unclear	Unclear	Self-report sleep quality, sleep log, ISI, ESS	+
Majendie	2017	UK	Case study	1 (n/a)	CBT-I	Unclear	Unclear	PSQI, sleep diary	+
CBT/Psychotherapy									
Abbasi	2016	Iran	RCT	72 (6)	CBT	Yes	PSQI	PSQI	+ [immediate] + [1 mo]
Baron	2011	US	RCT (secondary analysis)	127 (7)	Telephone psychotherapy for depression	Yes	3 items on the Hamilton	3 items on Hamilton	+

							Depression Rating Scale	Depression Rating Scale	
Kiropoulos	2016	Australia	RCT	30 (0)	CBT	No	Depression	PSQI	+ [immediate] + [20 weeks]
Mindfulness/Relaxation									
Cavalera	2019	Italy	RCT	139 (49)	Online mindfulness meditation	No	Multiple Sclerosis Quality of Life-54	Medical Outcomes Study Sleep scale	+ [immediate] - [6 mo]
Lorenz	2021	US	Quasi-experimental	34 (16)	Mindfulness-based stress reduction plus sleep retraining	No	Feasibility of intervention	Actigraphy, PSQI, FOSQ-10, Sleep Behavior Self-Rating Scale-Revised	[immediate] [3 mo]
Sessanna	2021	US	Qualitative (secondary analysis of Lorenz)	14 (0)	Mindfulness-based stress reduction plus sleep retraining	No	Acceptability	Qualitative reports	+
Dayapoglu	2012	Turkey	Single-group pre-post test	35 (3)	Progressive muscle relaxation	Unclear	Unclear	PSQI	+
Hoogwerf	2017	The Netherlands	Single-group pre-post test	59 (20)	Mindfulness-based cognitive therapy	No	CIS-20-Fatigue	Sleep subscale of the SCL-90	[immediate] [3 mo]
Simpson	2018	Scotland	Qualitative (secondary analysis)	33 (0)	Mindfulness-based stress reduction	No	Unclear	Qualitative reports	+
Education/Self-management Support									
Hugos	2019	US	RCT	218 (14)	Multicomponent fatigue management program	No	MFIS	PSQI	- [immediate, 3 mo] + [6 mo]
Akbarfahimi	2020	Iran	Pilot RCT	22 (2)	Occupational therapy-based sleep intervention	Yes	PSQI	PSQI	+
Munger	2021	US	Quasi-experimental Retrospective chart review	21 (0)	Cognitive rehabilitation	No	Neuro-QoL	Sleep disturbance domain on Neuro-QoL measure	+
Sauter	2008	Austria	Single-group pre-post test	32 (5)	Fatigue management	Unclear	Not stated	PSQI	+ [immediate] + [7-9 mo]
Complementary and Alternative Interventions									
Sajadi	2020	Iran	RCT	70 (7)	Foot reflexology	Unclear	Unclear	PSQI	+
Sgoifo	2017	Italy	RCT	48 (0)	Integrated imaginative distention	No	MFIS	ISI	-
Jensen	2018	US	Pilot RCT	35 (3)	NF+HYP or MM+HYP	No	Average pain intensity/fatigue severity	PROMIS Sleep Disturbance Short Form 8-item Version B	NF+HYP + [immediate] + [1 mo] MM+HYP [immediate]

									- [1 mo]
Becker	2016	US	Single-group pre-post test	14 (0)	Acupuncture + health promotion education	Unclear	Not stated	PROMIS sleep disturbance	+
Lynning	2021	Denmark	Single-group pre-post test	9 (2)	Trauma-releasing exercises	Unclear	Unclear	5-point numeric rating scale in newly developed patient-reported outcome tool	+

+ = improvement in sleep; – = worsening, no improvement in sleep, or mixed results;  = improvement not statistically significant.

CBT, cognitive behavioral therapy; CBT-I, cognitive behavioral therapy-insomnia; CIS-20, Checklist of Individual Strength-20-subscale fatigue; EEG, electroencephalogram; ESS, Epworth Sleepiness Scale; FOSQ-10, Functional Outcomes of Sleep Questionnaire; ISI, Insomnia Severity Index; MCSB, motivation to change sleep behavior; MFIS, Modified Fatigue Impact Scale; MM+HYP, mindfulness meditation + hypnosis; n/a, not applicable; NF+HYP, neurofeedback + hypnosis; PROMIS, Patient-Reported Outcomes Measurement Information System; PSQI, Pittsburgh Sleep Quality Index; RCT, randomized controlled trial; SCL-90, Symptom Checklist-90; SSE, Sleep Self-Efficacy; TST, total sleep time; UK, United Kingdom; US, United States.

Table S3. Study Details

Author year	Sample Demographics				Intervention Details			Major Sleep Findings
	No. enrolled (dropouts) Age, y mean (SD)	MS type	Severity, mean (SD)	Disease duration, mean (SD), y	Intervention type (dose)	Interventionist	Setting	
<i>Physical Activity</i>								
Al-Sharma n 2019	n = 40 (10) Intervention: 38.7 (13); control: 31.9 (10)	Not reported	EDSS intervention : 2.1 (1.8); control: 1.9 (1.03)	Intervention: 9.6 (8.49); control: 5.43 (4.2)	Moderate-intensity aerobic exercise (3x/week; 50-60 min/session; 6 weeks)	Not reported	Intervention: n: supervised; control: home	Compared with HEP, MAE group had significant improvement on the PSQI ($P = .004$), ISI ($P = .04$), sleep efficiency ($P = .04$), and WASO ($P = .003$) (assessed via actigraphy) and increase in serotonin ($P = .002$).
Andreu- Caravaca 2021	n = 18 (0) 44.88 (10.62)	16 PPMS, 2 RRMS	EDSS: 3.12 (1.74)	Not reported	Resistance training (3x/week for 10 weeks)	Supervised by researcher	Sports center	Sleep quality and comfort, ease of falling asleep, and feeling of rest (sleep diary, $P < .05$) improved after 10 weeks of resistance training (RN week 1 vs RN week 10).
Cederberg 2021	n = 15 (1) Intervention: 55.6 (9.5); control: 57.4 (13.0)	Intervention: n: 7 (100%) RRMS Control: 6 (85.7%) RRMS, 1 (14.3%) PPMS	EDSS score median (IQR): Intervention 4.0 (.5); control: 4.0 (1.0)	Intervention: 22.0 (4.4); control: 20.0 (7.3)	Physical activity (16-week program with 12 one-on-one video chats)	Behavioral coach	Home	Significant positive effect of the intervention on RLS symptom severity ($P = .01$, $\eta^2 = .43$), RLS severity during the night ($P = .03$, $\eta^2 = .35$), during the day while resting ($P = .01$, $\eta^2 = .44$), during the day while active ($P < .01$, $\eta^2 = .61$), and on sleep satisfaction ($P = .01$, $\eta^2 = .49$). Intervention has significant effect on self-reported TIB ($P = .03$, $\eta^2 = .37$) and TST ($P = .03$, $\eta^2 = .36$).
Grubic- Kezele 2021	n = 24 (0) Intervention: 50.0 (9.3);	Intervention: n: 53.8% RRMS, 15.4%	Intervention (EDSS median [range],	Not reported	Exercise (2x/week, 60 min/session for 8 weeks)	Physiotherapist	MS society center	Statistically significant group-by-time interaction for insomnia severity ($P = .023$, $\eta^2 = .213$) and daytime sleep dysfunction ($P = .031$, $\eta^2 = 0.195$).

	control: 53.8 (11.8)	PPMS, 30.8% SPMS Control: 36.3% RRMS, 9.1% PPMS, 54.5% SPMS	mean [SD]: 3.0 (1.0-7.5), 3.8 (1.8); control: 5.0 (1.0-7.0), 4.0 (2.0)					
Jeong 2020	n = 17 (0) 60.1 (11.4)	Self-report: progressing 5 (29.4%), stable 11 (64.7%), improving 1 (5.9%)	Self-assessed: 5 mild (29.4%), 10 moderate (59.8%), 2 severe (11.2%)	26.0 (13.5), range: 2.5-50.8 (since diagnosis)	Exercise telerehabilitation (individualized plan; asked to perform daily for 3 months [mean (SD) total time over 3 mo: 30.7 (19.8) hours])	Physiotherapist	Home	Average changes between baseline and 3M for PSQI sleep efficiency, PSQI sleep disturbances, PSQI daytime disturbances, and PSQI total score were -0.1 (84.7 at BL to 84.5 at 3M), 0.9 (6.4 at BL to 7.3 at 3M), 0.5 (1.0 at BL to 1.5 at 3M) and 0.2 (6.7 at BL to 6.9 at 3M), respectively (indicating a slight worsening of sleep from BL to 3M).
Kozlowski 2017	n = 13 (8) Median: 47; range: 38-62	92% progressive MS	EDSS: 6.5 (5.5-7)	Not reported	Exoskeleton-assisted walking (3x/week; 30-90 min/session; for 8 weeks)	“Research personnel who completed the device manufacturer’s training program”	Outpatient MS clinic/tertiary care hospital	1 participant had improved sleep disturbance; 1 had worse sleep disturbance; 6 did not exceed the conditional MDC threshold. (Note: only 5 completed >20 walking sessions.)
Mehrabani 2021	n = 41 (5) 50 (10.3)	26 RRMS (63.4%)	(EDSS < 4) 18 (43.9%); (4 < /= EDSS < /= 6.5) 23 (56.1%) (PDDS = 0) 2 (4.8%); (PDDS < 3) 10 (24.3%); (3 < /= PDDS < /= 6) 29 (70.7%)	14.3 (11.3)	Physical activity intervention (1x/week; 15-30 min/session; for two 7-week stages)	“Intervention coach”	Home	Significant change from baseline to postintervention for sleep quality ($P = .034$, effect size = 0.35) but was not sustained at long-term follow-up.
Pilutti 2014	n = 82 (6) Intervention: 48.4 (9.1); control: 49.5 (9.2)	Intervention: 31 RRMS, 8 SPMS, 2 PPMS; control: 34 RRMS, 2 SPMS, 5 PPMS	PDDS median (IQR): Intervention: 2.0 (4.0); control: 3.0 (3.0)	Intervention: 10.6 (7.1); control: 13.0 (9.1)	Online lifestyle physical activity intervention (15 online video coaching sessions; 7 in the first 2 months, 6 in the second 2 months, and 2 in the final 2 months. New content uploaded throughout intervention; daily pedometer log.)	Behavioral coaches: “highly trained doctoral students or a postdoctoral fellow”	Real-world; online video sessions	Favorable nonsignificant effect of the intervention on sleep quality post-trial ($P = .06$, $\eta^2 = .05$, Cohen $d = .45$).
Sadeghi Bahmani 2019a	n = 51 (5) 50.74 (11.28)	Not reported	EDSS: 5.3; women: 5.49 (1.11); men: 4.89 (1.27)	Not reported	Endurance exercise (30 min/session; 5 sessions/week) and 2 physiotherapy interventions/da	Sport scientist for exercise intervention; intervention	Inpatient rehabilitation center	Significant reduction in insomnia severity ($P = .048$), sleep-onset latency ($P < .01$), and wake time after sleep onset ($P = .04$); sleep efficacy improved ($P = .04$).

					y (consisting of progressive resistance training for 45 min and low-intensity physiotherapeutic session for 30 min) for 3 weeks	onist for physiotherapy not reported.		
Sadeghi Bahmani 2019b	n = 92 (21) Coordination training: 39.17 (8.66) Endurance training: 37.96 (8.69) Active control: 37.90 (9.91)	Not reported	EDDS Coordination training: 3.38 (1.87) Endurance training: 2.46 (1.50) Active control: 2.02 (1.84)	Groups Coordination: 8.13 (6.37) Workout: 6.92 (6.81) Active control: 7.21 (6.57)	Group aerobic exercise or coordinative training (3x/week; 30-45 min/session; 8 weeks)	“Professional instructors” monitored the intervention; clinical psychologist monitored control	Hospital setting	Sleep complaints decreased over time (time x group interaction, $P = <.05$, effect size = 0.32). Cohen d for change in ISI from baseline to week 8: endurance group = .53 (medium); coordination group = .62 (medium); and active control group = .11 (small). P values not provided for within group change from baseline to week 8.
Sadeghi Bahmani 2020	n = 62 (2) AE 2x/week: 39.35 (7.10); AE 3x/week: 40.61 (8.97); ACC: 33.77 (6.56)	Not reported	EDSS median (range): Intervention: AE 2x/week: 3.00 (5.00); AE 3x/week: 1.5 (4.00); active control: 1.50 (6.00)	AE 2x/wk: 8.87 (3.60); AE 3x/wk: 6.58 (3.92); active control: 6.34 (4.34)	Aquatic exercise (2x/week OR 3x/week; 60 min/session; 8 weeks)	“Certified instructor” organized and supervised aerobic exercise Control: clinical psychologist	Rehabilitation center of hospital	Nonsignificant intervention effect on sleep ($P = .079$, $\eta^2 = 0.09$). (Sleep complaint data provided in pretrial Table 1 is same as in posttrial Table 2, which makes interpretation of results difficult.)
Siengsukon 2016	n = 33 (3) Intervention: 48.9 (13.6); control: 50.9 (12.2)	Intervention: 10 RRMS, 2 SPMS; control: 9 RRMS, 1 SPMS	MSFC AE: 0.395 (0.89); WS: 0.868 (0.68)	AE: 10.8 (8.4); WS: 9 (5.6)	Aerobic exercise (3x/week; 60 min/session; 12 weeks)	Not reported	Not reported	Both groups improved on PSQI (main effect sleep $P = .006$; $\eta^2 = 0.336$) but no significant between group difference ($P = .447$; $\eta^2 = 0.031$); there was a significant between-group difference on Epworth Sleepiness Scale ($P = .018$; $\eta^2 = 0.263$).
Vasudevan 2021	n = 10 (0) Not reported	Not reported	Not reported	First MS attack: <10 y ago = 3 11-19 y ago = 5 20+ y ago = 2	Personalized yoga therapy (12 private [1 therapist: 2 patients] sessions; 1 hour/week; 3 months then three 90- to 100-min group education sessions)	Certified yoga therapists	Private setting	Nonsignificant ($P = .061$) improvement in sleep quality.
CBT-I								
Clancy 2015	n = 11 (unclear) 52 (11)	8 RRMS, 3 progressive MS	Not reported	Not reported	Individual or group CBT-I (2-16 sessions; mean [SD]: 8 [4.8])	“Clinician”	Not reported	86% reported improvement in insomnia with average ISI score 21 before CBT-I and average ISI score of 17 after treatment. [ISI scores recorded for only 7 of 11 participants because ISI not used by clinic until 2010.] 73% reported an increase in TST (average improvement 1.5 hrs).
Loveless 2019	n = 1 (n/a) 55	RRMS	Not reported	“Started in early 1990s”	CBT-I (biweekly, 13 total sessions)	Postdoctoral fellow and a practicum student	University health system behavioral	Patient reported improvement in self-report sleep quality; sleep log demonstrated an increase in sleep efficiency (from 29.0% to 74.49%) and TST (from 2.69 hrs to 5.86 hrs) and

						supervised by an attending licensed clinical psychologist	medicine clinic	decrease in sleep latency (from 145 min to 60 min), WASO (from 240 min to 60 min), and early morning awakenings (from 110 min to 0 min). At posttreatment, scored 6/28 on ISI and 2/24 on Epworth Sleepiness Scale.
Majendie 2017	n = 1 (n/a) 40	SPMS	“Wheelchair bound” (no measure explicitly reported)	“At least 9 years”	CBT-I (1x/week; 60 min/session; 8 weeks) plus homework	Psychologist	Local community neuro service clinic	Improvement in PSQI global score from 10 at start to 5 at end of treatment and to 1 at 7 months posttreatment; overall improvements in sleep log outcomes.
Siengskun 2021	n = 41 (21) Intervention: 50.1 (11.8); control: 53.8 (6.9)	wCBTi: 10 RRMS wCBTi + calls: 9 RRMS, 1 SPMS	PDDS wCBTi: 1.3 (1.5) wCBTi + calls: 2.4 (1.3)	Not reported	Web-based CBT-I (41 total daily lessons over 6 weeks; with or without one-on-one telephone calls)	Research personnel trained in motivational interviewing	Not reported	Both groups demonstrated significant improvement in ISI (wCBTi: $P < .001$; wCBTi + calls: $P = .005$) but no significant difference between groups ($P = .068$); both groups showed significant improvements in PSQI (wCBTi: $P < .001$; wCBTi + calls: $P = .028$).
Siengskun 2020	n = 33 (3) CBTi: 51.1 (7.9); ACC: 50.4 (12.4); BE: 56.9 (10.1)	CBTi: 8 RRMS, 2 SPMS ACC: 10 RRMS BE: 9 RRMS, 1 SPMS	PDDS CBTi: 1.3 (2.21) ACC 1.7 (2.3) BE 2.0 (2.1)	CBTi: 17.3 (8.5) ACC: 9.1 (8.9) BE: 18.3 (11.4)	CBTi (1x/week; 45-60 min/session [one-on-one] for 6 weeks)	Trained CBTi specialist/PT	Not reported	All 3 groups showed a significant large reduction on ISI (CBTi: $P < .001$, ES = 2.729; ACC: $P = .002$, ES = 1.018; BE: $P < .001$; ES = 2.570) with the CBTi showing the largest change (-13.8); CBTi and BE showed a significant large improvement on PSQI (CBTi-I: $P < .001$, ES = 2.314; BE: $P < .001$, 1.672) with CBTi having largest magnitude in change (-6.7); CBTi and BE group showed significant increase in SSE (CBTi: $P < .001$; BE: $P = .044$) but only CBTi showed a large effect (ES = 1.221).
Williams-Cooke 2021 (secondary analysis of Siengskun 2020)	n = 25 (3) CBTi: 49.25 (7.72); ACC: 50.38 (13.96); BE: 58.78 (8.66)	CBTi: 7RRMS, 1 SPMS ACC: 8 RRMS, 0 SPMS BE: 8 RRMS, 1 SPMS	Not reported	CBTi: 13.88 (5.14) ACC: 8.88 (10.02) BE: 19.22 (11.72)	CBTi (1x/week; 45-60 min/session; [one-on-one]; 6 weeks)	Trained CBTi specialist/PT	Not reported	For the sleep log outcomes, CBTi group showed significant increase in SE ($P = .006$, ES = 1.203) and reduction in TIB ($P = .001$, ES = 0.993) and variability in SE ($p = 0.026$, ES = 0.657). For the actigraphy outcomes, CBTi group demonstrated significant reduction in TIB ($P = .005$, ES = 0.925) and TST ($P = .004$, ES = 0.893). ACC group showed a significant increase in variability in SE ($P = .035$, ES = 0.463).
<i>CBT/Psychotherapy</i>								
Abbasi 2016	n = 72 (6) Intervention: 35.3 (5.3); control: 33.2 (8.9)	Intervention: 85.2% RRMS Control: 88.3% RRMS	Not reported	Intervention: 5.6 (5.8) Control: 6.1 (6.5)	CBT (1x/wk; 90 min/session; 8 total group sessions)	Psychiatric nurse (the researcher)	Not reported	Significant difference in sleep quality control vs intervention groups at postintervention and 1-month follow-up ($P < .001$). Sleep quality for intervention group had significant difference ($P < .001$) across baseline, post, follow-up, but there was no significant change over time for controls.
Baron 2011 (secondary analysis)	n = 127 (7) CBT: 48.9 (9.6); SEFT: 47.6 (10.1)	89% RRMS, PPMS 10%, 1 did not report type	Guy's Neurologic Disability Scale: CBT: 23.9 (5.8) SEFT: 22.9 (6.7)	Not reported	Telephone psychotherapy for depression (1x/wk; 50 min/session; 16 weeks)	Doctoral-level psychologists with 1-5 years of postdegree experience	Telephone	78% (n = 98) reported insomnia of any type ≥ 3 times/week at baseline, which declined to 43% (n = 53) at posttreatment. [Did not report within-group change in insomnia or between-group comparison in results.]
Kiropoulos 2016	n = 30 (0) CBT: 34.60 (9.06); TAU: 39.27 (9.93)	RRMS	100% “able to walk independently without aid”	Since diagnosis/since first symptoms (mo): intervention: 26.20	CBT (1x/week; 60 min/session; 8 weeks [first session was 90 min])	Senior clinical psychologist and provisional clinical	Outpatient hospital clinic	Significant group differences on the PSQI score postintervention ($P < .001$) and at 20-week follow-up ($P < .01$). Cohen d for PSQI pre to post was 1.31 and pre to 20-week follow-up was 1.06.

				(15.58)/35.54 (16.47); control: 23.53 (16.06)/30.57 (18.68)		psychologist		
<i>Mindfulness/Relaxation</i>								
Cavale ra 2019	n = 139 (49) Intervention: 42.26 (8.35); control: 43.19 (9.02)	Intervention: 94% RRMS, 6% SPMS; control: 92% RRMS, 8% SPMS	EDSS Intervention median: 3; control median: 3	Since MS diagnosis (mean [SD]): intervention: 12.64 (8.15); control: 14.24 (7.27)	Online mindfulness meditation (1x/week group sessions; 8 weeks)	Expert MBSR trainer	Skype	Strong effect found on sleep at the postintervention evaluation ($P < .001$, $\eta^2 = 0.130$), but no statistical difference between groups after 6 months ($P = .202$, $\eta^2 = 0.017$).
Dayapo glu 2012	n = 35 (3) 38.15 (9.48)	Not reported	Not reported	<2 y = 43.8% 3-5 y = 18.8% 6-8 y = 15.5% >8 y = 21.9%	Progressive muscle relaxation (one 60-min patient education session about PMRT under supervision of instructor. After education exercises performed at home 1x/day for 6 weeks. Two weeks after education, participants come to clinic and perform PMRT under instructor's supervision.)	Researcher; no details provided on who provides education	Neurology polyclinic; home	PSQI global score decreased from before PMRT to after ($P < .001$); there was a significant improvement in PSQI subscale scores of subjective sleep quality ($P < .001$), sleep latency ($P < .001$), sleep duration ($P < .05$), sleep efficiency ($P < .05$), sleep disorder ($P < .001$), and daytime dysfunction ($P < .001$).
Hooger werf 2017	n = 59 (20) 48.2 (8.5)	67% RRMS 33% SPMS	EDSS: 3.9 (1.7) (range: 1- 7.5)	11.2 (7.9) (range: 1- 32)	MBCT (1x/wk group meetings; 150 min/session; 8 weeks over period of 10 weeks with homework and exercises of up to 60 min/day; 6x/week]	Certified MBCT trainers (minimum 2-y experienc e with MBCT and working with patients with MS)	Not reported	For SCL-90 Sleep, the effect size was small (partial $\eta^2 = .08$) and not significant at different assessment time points ($P = .030$; $\alpha = .01$).
Lorenz 2021	n = 34 (16) 47.1 (10.9)	Not reported	EDSS: 1.6 (1.1)	Since diagnosis: 11.2 (6.5) Since symptom onset: 14.5 (9.0)	MBSR plus sleep retraining (1 orientation session followed by 60 min/week of training for 8 weeks)	Certified MBSR instructor and sleep expert	Primarily virtual but comparator group was in-clinic	Both videoconference and control groups had reduced number of awakenings ($P = .039$ and $P = .032$, respectively). In videoconference group, Cohen d effect sizes suggested moderate to large pre to post effect on sleep behaviors ($P = .145$; $d = .36$), sleep efficiency ($P = .042$; $d = .78$), and TST ($P = .156$; $d = .54$). No statistically significant differences between groups on sleep outcomes at postintervention but small effect on TST ($P = .522$; $d = .35$) and sleep behavior ($P = .458$; $d = .33$) seen. One-way repeated-measures ANOVA, including baseline, postintervention, 3M postintervention for

								videoconference group suggested small to medium effect on self-reported sleep quality ($P = .415$; partial $\eta^2 = 0.278$) and sleep behaviors ($P = .069$; partial $\eta^2 = 0.257$).
Sessanna 2021 (secondary analysis of Lorenz)	n = 14 (0) Range: 30-70	Not reported	EDSS: < 7	Not reported	MBSR plus sleep retraining (1 orientation session followed by 60 min/week training for 8 weeks)	Certified MBSR instructor and sleep expert	Mainly virtual but in-clinic comparator	Both formats proved to be acceptable and provided effective mode of delivery to a variety of adults with MS who experience wide variety of symptoms and levels of disability.
Simpson 2018 (secondary analysis)	n=33 (0) Range: 21-66	Mixed, but mostly RRMS	EDSS: 4.5 (range: 1-7)	Not reported	MBSR (1x/week for 8 weeks)	Certified MBSR instructors	NHS center for integrated care	Improved sleep was commonly reported.
<i>Education and Self-Management Support</i>								
Akbarfahimi 2020	n = 22 (2) Intervention: 37.5 (8.89); control: 39.7 (7.90)	Not reported	EDSS Intervention: 1.6 (0.97) Control: 1.2 (1.03)	Not reported	Occupational therapy-based sleep intervention (1x/wk; 30-45 min/session; 8 weeks; also 2-3 sessions/week by telephone)	Occupational therapist	Occupational therapy clinic	Sleep quality for intervention group significantly improved from baseline to reassessment ($P < .001$) but not control group. (Not clear what P value set for significance because states "level of significance was $P = .05$ and was adjusted familywise for multiple comparisons.")
Hugos 2019	n = 218 (14) Intervention (FTC): 53.9 (9.8); control (MSTC): 53.6 (10.5)	Intervention (FTC): 62.6% RRMS, 14.0% SPMS, 24.3% PPMS Control (MSTC): 55.6% RRMS, 19.4% SPMS, 24.1% PPMS	EDSS mean (SD, range): Intervention (FTC): 5.1 (1.1, 3.5-6.5) Control (MSTC): 5.3 (1.1, 3.0-6.5)	Intervention (FTC): 12.3 (7.6) (range: 1.59-34.96); control (MSTC): 12.7, (9.3) (range: 0.25-41.78) (from diagnosis)	Multicomponent fatigue management program (1x/week group sessions; 120 min/session; 6 weeks)	"MS professionals"	Outpatient MS clinic	No significant change in PSQI either at program completion ($P = .09$) or at the 3M in FTC ($P = .83$). Sleep quality improved in FTC group at 6 months ($P < .0001$) and there was significant difference between groups by this time point ($P = .004$).
Munger 2021	n = 21 (0) Intervention: 47.9 (4) Comparator: 48.9 (4.4)	Intervention: 75% RRMS Comparator: 67% RRMS	Not reported	Not reported	Cognitive rehabilitation (varied and individualized; average of 3-4 sessions total)	Occupational therapist and SLP	Real-world clinic	Sleep disturbance scores improved after ICRP participation ($P = .005$); no significant change in sleep disturbance in comparison group. (No between-group difference provided.)
Sauter 2008	n=32 (5) Not reported	53% RRMS, 47% progressive MS (13.3% PPMS, 33.3% SPMS)	EDSS: 4.0 (1.9)	11.8 (7.2); range: 2.5-27.3	Fatigue management (1x/week group sessions; 120 min/session; 6 weeks)	Not reported	Not reported	PSQI score significantly improved after course and remained improved after 7-9 months ($P = .004$); SE component score significantly reduced at 7-9 months ($P = .047$).
<i>Complementary and Alternative Interventions</i>								
Becker 2016	n = 14 (0) 54.14 (9.65)	1 benign sensory, 6 RRMS, 2 PPMS, 2 SPMS, 3 unclear	Not reported	13.64 (7.99) (from diagnosis)	Acupuncture + health promotion education (8 sessions; 90 min; plus with 30 min of	Classes delivered by certified MS nurse; acupuncture	Not reported	Pre to post PROMIS sleep disturbance scores improved ($P = .009$).

					acupuncture before or after each class)	delivered by licensed and national board-certified acupuncturist (third author) or one of her clinical colleagues		
Jensen 2018	n = 35 (3) 57.53 (10.63)	MS onset course: 23 (72%) RRMS, 8 (25%) progressive MS, 1 (3%) not reported Current disease course: 17 (53%) RRMS, 6 (19%) SPMS, 3 (9%) PPMS, 6 (19%) unclear	Not reported	Since diagnosis: 20.09 (10.00) Since symptoms began: 28.52 (13.63)	NF + HYP or MM + HYP (3 weeks; 2x/week of either (a) NF or (b) MM followed by 1 face-to-face HYP session and then 4 sessions of NF/MM occurring before 4 prerecorded self-hypnosis training sessions or (c) 3 weeks; 2x/week of waiting period followed by a 1 face-to-face HYP session and then 4 prerecorded self-hypnosis training sessions)	MM-HYP: 1 of 3 bachelor-level research staff trained and supervised by clinical psychologist expert in mindfulness-based treatments NF: staff In-person HYP: clinical psychologist experienced with hypnosis	Outpatient medical center or MS clinic	Large nonsignificant time multiplied by condition effect for sleep disturbance ($P = .17$; $\eta^2p = 0.15$); large significant time effect for NF-HYP ($P = .03$; $\eta^2p = 0.61$) and large nonsignificant time effect for MM-HYP ($P = .40$; $\eta^2p = 0.33$). Improvement was maintained at 1-month reassessment for the NF-HYP but not for MM-HYP.
Lynnig 2021	n = 9 (2) 51.6	6 RRMS, 1 SPMS, 2 PPMS	Not reported	12.7 (from diagnosis)	TRE (1x/week ;30-45 min/session; 9 weeks with instructor and daily at-home after second session)	TRE instructor + home	Home; info about sessions with instructor not reported	Sleep quality significantly increased ($P < .05$).
Sajadi 2020 Iran	n = 70 (7) Range: 18-50	100% RRMS	EDSS ≤ 4	Not reported	Foot reflexology (2x/week; 30-40 min/session; 4 weeks)	Certified foot reflexologist (first author)	Private room	Significant difference between groups' PSQI scores at baseline ($P = .04$). Difference in sleep quality between reflexology and control group was statistically significant after intervention ($P = .001$). PSQI scores statistically improved from before to after intervention in reflexology group ($P = .003$).
Sgoifo 2017 Italy	n = 48 (0) Not reported	Intervention: 83.3% RRMS, 0% PPMS, 16.7% SPMS Control: 91.7% RRMS, 4.2% PPMS,	EDDS mean (SD, range): Intervention: 3.15 (1.97, 1-6.5) Control: 3.44, (2.01, 0-7.5)	Since symptoms mean (SD, range): intervention: 10.5 (8.2, 0-27); control: 16.1, (11.1, 3-43)	Integrated imaginative distention (8 weekly training group sessions in 2 months; 60 min/session)	Single skilled psychotherapist	Not reported	No significant improvement in ISI between intervention group and control group ($P = .146$).

		4.2% SPMS	Combined mean: 3.29 (1.97)	Since diagnosis mean (SD, range): interventi on: 8.2 (7.3, 0-27; control: 10.5, (8.5, 0-33)										
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3M, 3-month reassessment; ACC, active control condition; AE, aquatic/aerobic exercise; ANOVA, analysis of variance; BE, basic education; BL, baseline; CBTi, cognitive behavioral therapy for insomnia; EDSS, Expanded Disease Status Scale; FTC, Fatigue: Take Control; HEP, home exercise program; HYP, hypnosis; IAYT, International Association of Yoga Therapists; ICRP, integrated cognitive rehabilitation program; ISI, Insomnia Severity Index; MAE, moderate-intensity aerobic exercise program; MBCT, mindfulness-based cognitive therapy; MBSR, mindfulness-based stress reduction; MDC, minimal detectable change; MCID, minimal clinically important difference; MFIS, Modified Fatigue Impact Scale; MM, mindfulness meditation; MS, multiple sclerosis; MSFC, Multiple Sclerosis Functional Composite; MSTC, Multiple Sclerosis: Take Control; n/a, not applicable; NF, neurofeedback; NHS, National Health Service; PDDS, Patient-Determined Disease Steps; PHQ-9, Patient Health Questionnaire; PMRT, progressive muscle relaxation technique; PPMS, primary progressive multiple sclerosis; PROMIS, Patient-Reported Outcomes Measurement Information System; PSQI, Pittsburgh Sleep Quality Index; PT, physical therapist; RLS, restless legs syndrome; RN, rest night; RRMS, relapse-remitting multiple sclerosis; SCL-90, Symptom Checklist-90; SE, sleep efficiency; SEFT, supportive emotion-focused therapy; SLP, speech-language pathologist; SPMS, secondary progressive multiple sclerosis; SSE, sleep self-efficacy; TAU, treatment as usual; TIB, time in bed; TN, training night; TRE, trauma-releasing exercise; TST, total sleep time; WASO, wakefulness after sleep onset; wCBTi, web-based cognitive behavioral therapy for insomnia; WS, walking and stretching program.

Table S4. Quality Appraisal

First author														Quality score, %
RCT	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13	
Abbasi	Yes	NR	Yes	NR	No	NR	No	No	No	Yes	NR	U	Yes	35
Akbarfahimi	Yes	Yes	No	No	Yes	Yes	Yes	Yes	No	Yes	NR	U	Yes	65
Al-Sharman	Yes	U	Yes	No	No	Yes	Yes	No	No	Yes	Yes	Yes	Yes	65
Baron	U	NR	Yes	NR	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	73
Cavalera	Yes	NR	Yes	No	NR	NR	Yes	Yes	Yes	Yes	Yes	Yes	Yes	62
Hugos	Yes	NR	Yes	Yes	No	NR	No	No	Yes	Yes	NR	Yes	Yes	54
Kiropoulos	Yes	Yes	Yes	No	No	NR	Yes	Yes	No	Yes	NR	No	Yes	54
Pilutti	Yes	NR	Yes	NR	NR	NR	Yes	Yes	No	Yes	NR	No	Yes	46
Sadeghi Bahmani 2019a	Yes	Yes	No	NR	No	NR	Yes	Yes	No	Yes	NR	No	Yes	46
Sadeghi Bahmani 2020	Yes	Yes	Yes	NR	NR	NR	Yes	Yes	No	Yes	NR	No	Yes	54
Sajadi	Yes	Yes	No	Yes	NR	Yes	Yes	No	No	Yes	NR	No	Yes	54
Sgoifo	Yes	NR	Yes	No	NR	NA	Yes	No	Yes	Yes	NR	Yes	Yes	54

Pilot RCT	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13	
Cederberg	U	NR	Yes	No	No	U	Yes	Yes	No	Yes	No	Yes	Yes	54
Grubic Kezele	NR	NR	NR	NR	NR	Yes	Yes	No	No	Yes	NR	No	Yes	31
Jensen	U	NR	NR	NR	NR	NR	Yes	Yes	No	Yes	NR	Yes	Yes	42
Siengsukon 2016	U	NR	Yes	NR	NR	Yes	Yes	No	No	Yes	NR	No	Yes	42
Siengsukon 2020	U	NR	No	NR	NR	Yes	Yes	No	No	Yes	NR	No	Yes	35
Williams-Cooke	U	NR	No	NR	NR	Yes	Yes	No	No	Yes	NR	No	Yes	35
Siengsukon 2021	U	NR	Yes	NR	NR	NR	Yes	Yes	No	Yes	NR	No	Yes	42
Quasi-experimental	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9					
Lorenz	Yes	Yes	Yes	Yes	No	No	Yes	No	Yes					67
Munger	Yes	No	Yes	Yes	No	NA	Yes	No	No					50
Single-group pre-post	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12		
Andreu-Caravaca	Yes	Yes	Yes	NR	No	Yes	Yes	NR	Yes	Yes	No	NA		64
Becker	Yes	Yes	Yes	CD	No	CD	Yes	NR	NR	Yes	No	NA		55
Dayapoglu	Yes	Yes	Yes	NR	No	NR	Yes	NR	No	Yes	No	NA		45
Hoogerwerf	Yes	No	Yes	No	No	Yes	Yes	No	No	Yes	Yes	NA		55
Jeong	Yes	No	Yes	NR	No	No	Yes	NR	Yes	No	No	NA		36
Kozlowski	Yes	Yes	Yes	NR	No	No	yes	NR	No	No	No	NA		36
Lynning	Yes	Yes	Yes	NR	No	No	Yes	NR	No	Yes	No	NA		45
Mehrabani	Yes	Yes	Yes	NR	Yes	Yes	Yes	NR	NR	Yes	No	NA		64
Sadhegi Bahmani 2019b	Yes	Yes	Yes	CD	No	No	Yes	NR	No	Yes	No	NA		50
Sauter	No	No	Yes	NR	No	NR	Yes	NR	No	Yes	No	NA		27
Vasudevan	Yes	No	Yes	No	No	No	No	No	Yes	Yes	No	NA		36
Case series	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10				
Clancy	Yes	Yes	U	NA	NA	Yes	No	Yes	Yes	Yes				81
Case report	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8						
Loveless	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes						88
Majendie	No	No	No	Yes	Yes	Yes	No	Yes						50
Qualitative research	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10				
Simpson	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes				80
Sessanna	No	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes				70

CD, cannot determine; NA, not applicable; NR, not reported; RCT, randomized controlled trial; U, unclear.