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Quality of life in adults with multiple sclerosis: a systematic review

Irene Gil-González ![ORCID],[1] Agustín Martín-Rodríguez,[1] Rupert Conrad,[2] María Ángeles Pérez-San-Gregorio[1]

[1]Personality, Assessment, and Psychological Treatment, University of Seville, Seville, Spain
[2]Department of Psychosomatic Medicine and Psychotherapy, University Hospital Bonn, Bonn, Germany

Correspondence to
Irene Gil-González; igil2@us.es

ABSTRACT

Objective In recent years, quality of life (QoL) in multiple sclerosis (MS) has been gaining considerable importance in clinical research and practice. Against this backdrop, this systematic review aimed to provide a broad overview of clinical, sociodemographic and psychosocial risk and protective factors for QoL in adults with MS and analyse psychological interventions for improving QoL.

Method The literature search was conducted in the Scopus, Web of Science and ProQuest electronic databases. Document type was limited to articles written in English, published from January 1, 2014, to January 31, 2019. Information from the selected articles was extracted using a coding sheet and then qualitatively synthesised.

Results The search identified 4886 records. After duplicate removal and screening, 106 articles met the inclusion and exclusion criteria for qualitative synthesis and were assessed for study quality. Disability, fatigue, depression, cognitive impairment and unemployment were consistently identified as QoL risk factors, whereas higher self-esteem, self-efficacy, resilience and social support proved to be protective. The review analysed a wide spectrum of approaches for QoL psychological intervention, such as mindfulness, cognitive behavioural therapy, self-help groups and self-management. The majority of interventions were successful in improving various aspects of QoL.

Conclusion Adequate biopsychosocial assessment is of vital importance to treat risk and promote protective factors to improve QoL in patients with MS in general care practice.

INTRODUCTION

The Constitution of the WHO declares health to be '…a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity'.[1] Quality of life (QoL) is a multidimensional concept that encompasses the domains included in this definition of health.[2 3] Its introduction in medical literature dates back to 1960,[4] with its importance continuously growing to date.[5]

Multiple sclerosis (MS) is a chronic neurodegenerative condition characterised by a wide range of symptoms and a highly unpredictable prognosis, which can severely affect patient QoL.[6–8] Patients with MS tend to report lower QoL than the general

Strengths and limitations of this study

► This is the first systematic review of risk factors and psychological intervention for quality of life in multiple sclerosis for over a decade.
► A comprehensive and robust search strategy and strict inclusion criteria were employed to cover all the relevant evidence.
► Careful standardised risk of bias was assessed in all 106 studies included.
► Due to heterogeneity of the studies, only qualitative synthesis of results was possible.
► The huge number of publications made it necessary to limit the time span to the 5-year period from January 1, 2014, to January 31, 2019.

population.[9–12] This diminished QoL may be due to their impaired functioning in daily living, more so if the help of caregivers is required, impeding family relations, work and social dynamics.[13 14] The impact of MS on QoL can be affected by numerous disease-related factors, such as disability level or MS type, and individual factors such as social support, education, age or employment.[15–18]

Identification of risk and protective factors is a key point in implementing strategies to improve patient's QoL.[7] In this context, all influences must be considered to contribute to QoL in MS.[7 19] In addition to providing practitioners with useful information on the impact of symptoms and therapy on the patient's life, QoL is also an indicator of treatment success and a predictor of disease progression.[20–22]

In view of its relevance in healthcare research, the need to compile and condense available scientific evidence on the subject is urgent. Against this backdrop, this systematic review gives a comprehensive overview of risk and protective factors related to QoL in MS as well as relevant psychological interventions. The growing number of studies on this subject[2 22] provides a vast amount of data, which due to the inconsistency of findings needs careful assessment to come to evidence-based conclusions.

METHODOLOGY

This systematic review was performed following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[23] As a review of prior publications, ethical approval (or informed consent) was unnecessary. A review protocol is available from the corresponding author on request.

Search strategy

The systematic search focused on journal articles published between January 1, 2014, and January 31, 2019. The Scopus, Web of Science and ProQuest databases were searched in February and March 2019. The key words used were ('multiple sclerosis') AND ('quality of life' OR 'health-related quality of life' OR 'well-being' OR 'well-being' OR 'life satisfaction'). The search terms were intentionally broad to ensure wide coverage of the literature. The search field was limited to 'title/abstract' and language was limited to 'English'. The complete research string is reported under online supplemental file 1.

There is no published systematic review on this topic in the Cochrane Library.

Study selection

First, title and abstract were screened to identify suitable articles for full text review. The screening process was performed independently by two researchers. Any disagreement about study selection was resolved by consensus with a third reviewer.

Inclusion criteria were the following:

1. Studies primarily focusing on QoL determinants and psychological intervention to improve it.
2. Study participants aged over 18 years with a confirmed MS diagnosis.

The following exclusion criteria were applied:

1. Non-psychological intervention.
2. Not primary research studies (systematic reviews, meta-analyses, protocols and clinical guidelines were excluded).
3. Studies on the development and validation of QoL measurement instruments.
4. QoL risk or intervention studies for healthy behaviour, cognitive rehabilitation, physical activity or pharmacological treatment.
5. Studies on comorbidity with another illness or mental health diagnosis.
6. Sample selection based on a special condition (eg, only employees or patients with MS under certain pharmacological treatment).
7. Studies not using a validated QoL measurement tool.

Quality assessment

The methodological quality of the studies was appraised with a well-established standardised 12-item checklist,[24] in which every item represents a methodological feature: inclusion/exclusion criteria, methodology/design, attrition rate, attrition between-groups, exclusions after, follow-up, occasion of measurements, pre/post measures, dependent variables, control techniques, construct definition and imputing missing data. The codification criteria proposed by the checklist authors was used. No article was excluded from quality appraisal.

Data abstraction

Data were extracted from selected articles based on a previously designed coding sheet. The pilot study was approved by consensus. The information extracted included: title, authors and publication year, country (city), design, sample characteristics, study variables and measurement tools, main results and conclusions. After extraction, the information was independently reviewed by two authors to avoid errors or omitting data.

A meta-analysis was not possible due to the heterogeneity of study designs and outcomes, so a narrative synthesis was undertaken.

RESULTS

Literature screening

A total of 4886 articles were initially identified from Scopus, Web of Science and ProQuest. After removal of duplicates and abstract analysis, 188 studies were eligible for full text review. Finally, 106 were selected for the narrative analysis. The selection process is detailed below in a PRISMA flow diagram (figure 1).

Methodological quality

Methodological quality scores using the 12-item checklist are summarised in table 1.

Study characteristics

The articles included were analysed by their primary and secondary outcomes. Seventy studies analysed QoL risk and protective factors (table 2), 11 focused on the development of QoL at different ages and times in the disease (table 3) and 25 studied the effect of psychological intervention on QoL in MS (table 4).

All the articles included employed standardised and validated QoL measurement instruments; 64 studies evaluated QoL with a generic measure and 50 studies made use of a disease-specific measure. The Short Form Health Survey 36 (SF-36) was mainly used (n=29) as a generic measure and Multiple Sclerosis Quality of Life-54 (MSQoL-54) (n=28) as a disease-specific measure. Finally, 11 studies used more than one measure to evaluate QoL. The study designs were mostly cross-sectional (n=74), and sample sizes ranged from 7 to 74 451 participants.

The main findings of the articles are summarised below.

Risk and protective MS QoL factors

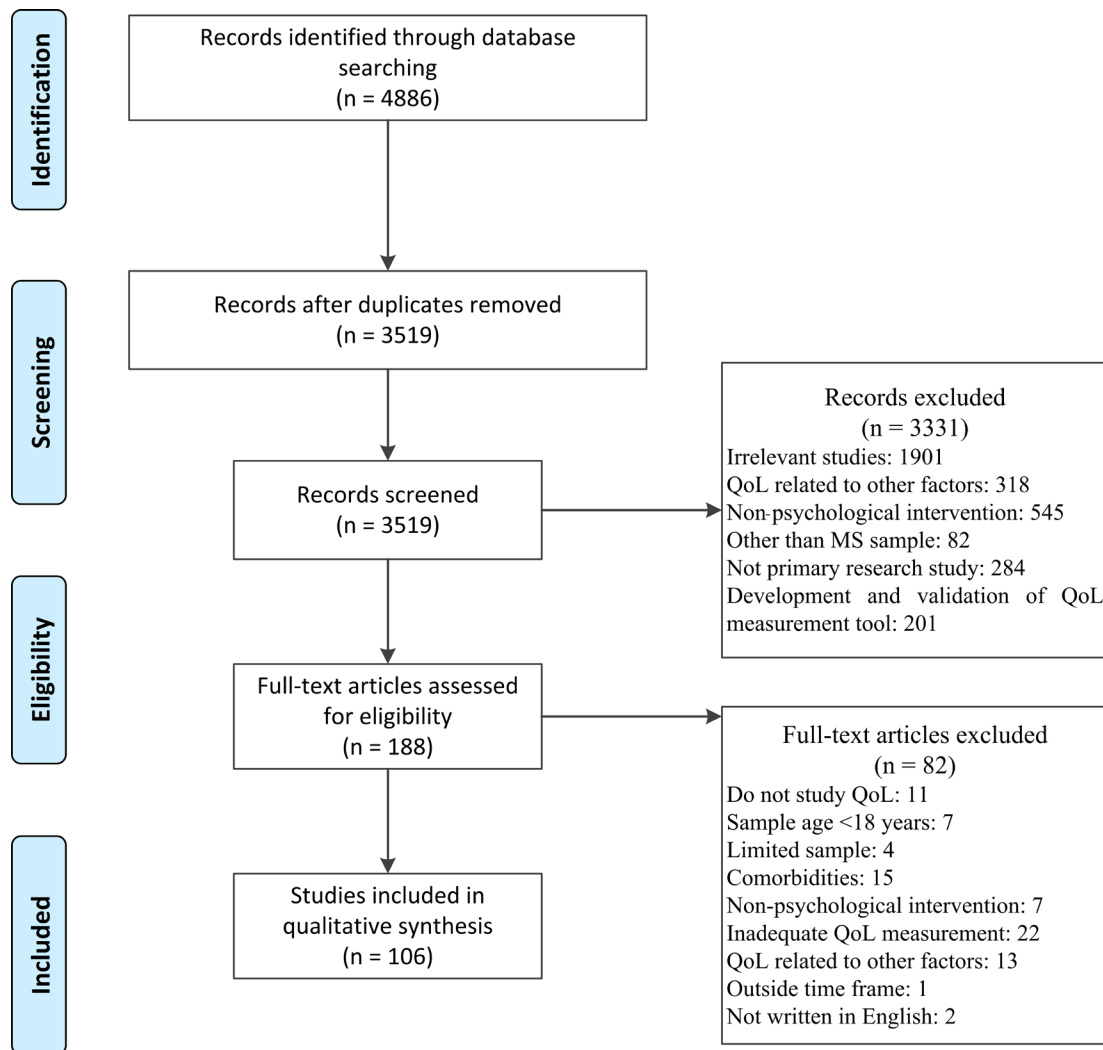Factors influencing MS patient's QoL are summarised in table 2.

Figure 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram of selection process. MS, multiple sclerosis; QoL, quality of life.

Clinical factors

Functional impairment as assessed by the Expanded Disability Status Scale (EDSS) level was one of the leading causes of diminished QoL.[25–35] Disease duration,[30 31] progressive type,[26 36 37] progressive MS onset[38] and relapses in the last 3 months were further relevant factors negatively affecting QoL.[26]

Several studies found a significant association between the severity and number of symptoms and the decline of QoL in MS.[33 37–41] Fatigue was identified as a main risk factor.[28 29 39 40 42–52]

A number of articles stated the importance of sensory[53 54] and motor[49 52 54 55] dysfunction on QoL, including paralysis, walking difficulties, balance, stiffness and spasms as motor problems, specifically emphasising pain[34 39 50 51 55 56] and spasticity,[49 57 58] and low sensory sensitivity and sensation avoidance as sensory problems.

Bladder dysfunction,[34 59 60] bowel dysfunction,[34] sexual,[60–62] and sleeping[34 39 48 63 64] problems contributed to deterioration of QoL.

A diversity of cognitive impairments, for instance, cognitive fatigue, memory loss and planning/organisational dysfunction, were recognised as risk factors by a number of studies.[39 50 52 53 65–67] Sgaramella *et al*[68] showed that maintaining executive functioning was a protective factor of QoL. This was also the only study on the important subject of cognitive reserve and QoL.

Psychosocial factors
Emotional symptoms

Some studies reported the beneficial effect of emotional stability on QoL[69] and the harmful effect of emotional problems.[52 70] The emotional symptom studied most was depression[28 29 32 34 35 39 40 51 55 65 69 71–75] followed by anxiety.[39 40 51 69 71–74 76] Both symptoms were confirmed as risk factors for QoL in MS. Similarly, high levels of perceived stress,[37 40 41] anger expression-in[74] and apathy[29] were identified as factors related to emotional regulation negatively affecting QoL in MS.

Table 1 Methodological quality of articles (n=106)

Item	Category	%
Inclusion criteria	Yes	99
	No or N/A*	1
Design	Pre-experimental	7.7
	Quasi experimental	33.7
	Experimental	58.7
Attrition	Yes	48.1
	No or N/A*	51.9
Attrition between groups	Yes	28.9
	No or N/A*	62.9
Exclusion after	Yes	22.1
	No or N/A*	77.9
Follow-up period	Yes	32.7
	No or N/A*	67.3
Occasion of measurement	One	70.2
	Two or more	29.8
Same pre-post measurement	Yes	70.2
	No or N/A*	29.8
Normalisation of DV measurement	Yes	100
Control techniques	Yes	70.2
	No or N/A*	29.8
Construct definition	Yes	100
Imputing missing data	Yes	19.2
	No or N/A*	80.8

*No or N/A=the item is not proceeded or does not appear.

Personality domains

The role of personality domains was explored in several studies. Cyclothymic and depressive temperament were associated with a lower QoL in MS, in contrast to hyperthymic temperament, which was associated with higher QoL.[77] Another study recognised extraversion as a personality trait related to higher QoL levels.[69] Cioncoloni *et al*[34] recognised introverted personality as a risk factor for QoL in MS, and finally, type D personality was another relevant factor.[78]

Coping strategies

Results with regard to coping strategies were consistent. Active coping, problem resolution, planning problem solving, cognitive positive restructuring, emotional and instrumental social support, emotional expression, acceptance and growth were related to a higher QoL in MS.[51 71 79–82] In addition, Grech *et al*[80] found a similar connection with restrained coping, Strober[51] with humour and Mikula *et al*[82] with stopping unpleasant emotion coping strategies. On the contrary, problem avoidance,[71 81] behavioural disengagement,[51 80] distancing,[81] self-distraction,[79] denial,[51 79] emotion-focused and venting coping strategies,[80] social withdrawal,[71] wishful thinking,[71] self-criticism,[71 81] suppression[80] and self-controlling coping[70] were associated with lower QoL.

Coping strategies were also identified as relevant mediator variables. Problem-focused, emotion-focused and stopping unpleasant emotion coping strategies were partial mediators between fatigue[83] or type D personality[84] and QoL as measured by the Mental Composite Score (MCS).

Other psychological factors

According to Van Damme *et al*,[85] acceptance of the illness is a protective factor for QoL. The role of flexible adjustment and tenacious goal pursuit in achieving personally blocked goals was not as clear, although their findings showed a trend towards a positive relationship.

Resilience was confirmed as a protective factor of QoL in MS.[27 86] Moreover, Koelmel *et al*[87] highlighted its role as a mediator variable in the relationship between social support and MCS.

High levels of self-efficacy,[51 88] self-esteem,[88] illness identity[88] and sense of coherence[89] correlated with higher QoL, and self-esteem mediated in the relationship of social support with MCS.[90] Ultimately, cognitive fusion, the extent to which people feel fused with or attached to their thoughts, mediated the relationship between stigma and QoL in MS.[91]

Social factors

Social support[92] and participation[93] were positively related with QoL. Several mediators in this relationship were mentioned above.

Demographic factors

Employment was found to be the leading sociodemographic factor influencing QoL. Several studies

Table 2 Characteristics of included articles

Authors, publication year	Study design	Quality of life measurement	Sample size (N) Age (mean) Sex (female %)	Main results		
				Risk factors	Protective factors
Clinical variables					
Gupta *et al* (2014)[25]	Cross-sectional	Short Form Health Survey 12 (SF-12)	N=74 451 47.9 years 51.3%	EDSS (PCS)	
Gross *et al* (2017)[36]	Cross-sectional	Short Form Health Survey 36 (SF-36)	N=810 RRMS 48.9 years SPMS 55.7 years RRMS 71.6% SPMS 56.2%	Progressive MS type (PCS)	
Zhang *et al* (2019)[38]	Cross-sectional	EuroQol 5-Dimensions (EQ-5D)	N=1958 55.3 years 78.1%	Progressive MS type onset	
Rezapour *et al* (2017)[26]	Cross-sectional	Multiple Sclerosis Quality of Life-54 (MSQoL-54)	N=171 35.7 years 76.6%	Relapses in the last 3 months	Mild EDSS RRMS type
Marck *et al* (2017)[56]	Cross-sectional	Multiple Sclerosis Quality of Life-54 (MSQoL-54)	N=2296 45.5 years 82.2%	Pain	
Milinis *et al* (2016)[57]	Cross-sectional	Leeds MS Quality of Life Scale (MSQoL)	N=701 48.8 years 72%	Spasticity	
Zettl *et al* (2014)[58]	Cross-sectional	EuroQol 5-Dimensions (EQ-5D) Multiple Sclerosis Quality of Life-54 (MSQoL-54)	N=414 48.6 years 64.3%	Spasticity	
Leonavicius *et al* (2016)[42]	Cross-sectional	Short Form Health Survey 36 (SF-36)	N=137 44.7 years 72.3%	Fatigue (MCS)	
Garg *et al* (2016)[43]	Cross-sectional	Multiple Sclerosis Quality of Life-54 (MSQoL-54)	N=89 54.26 years 66%	Fatigue	
Fernández-Muñoz *et al* (2015)[44]	Cross-sectional	Short Form Health Survey 36 (SF-36)	N=108 44 years 55%	Fatigue	
Weiland *et al* (2015)[45]	Cross-sectional	Multiple Sclerosis Quality of Life-54 (MSQoL-54)	N=2738 45.5 years 82.3%	Fatigue	
Aygünoğlu *et al* (2015)[46]	Cross-sectional	Multiple Sclerosis Quality of Life-54 (MSQoL-54)	N=120 34.24 years 70%	Fatigue	

Continued

Table 2 Continued

Authors, publication year	Study design	Quality of life measurement	Sample size (N) Age (mean) Sex (female %)	Main results	
				Risk factors	**Protective factors**
Vister et al (2015)[47]	Cross-sectional	WHO Disability Assessment Schedule (WHODAS) 2.0	N=210 50.8 years 72.4%	Fatigue	
Tabrizi et al (2015)[48]	Cross-sectional	Multiple Sclerosis Quality of Life-54 (MSQoL-54)	N=217 36.2 years 79%	Fatigue Poor sleep quality Low MCS (PCS)	
White et al (2019)[64]	Cross-sectional	EuroQol 5-Dimensions (EQ-5D)	N=531 51.60 years 70.1%	Sleep disorder	
Barin et al (2018)[49]	Cross-sectional	EuroQol 5-Dimensions (EQ-5D) EuroQol Visual Analogue Scale (EQ-VAS)	N=855 48 years 72.7%	Fatigue Balance Spasticity Paralysis Walking difficulties	
Kratz et al (2016)[50]	Cross-sectional	Short Form Health Survey 36 (SF-36)	N=180 50.5 years 78%	Fatigue (MCS) Pain (MCS) Memory loss (MCS)	
Colbeck et al (2018)[53]	Cross-sectional	RAND-36 Health Item Survey (RAND-36)	N=30 – 73.33%	Cognitive fatigue Low sensory sensitivity Sensation avoiding	
Grech et al (2015)[65]	Cross-sectional	Multiple Sclerosis Quality of Life-54 (MSQoL-54)	N=107 48.8 years 77.6%	Cognitive inflexibility	
Sgaramella et al (2014)[68]	Cross-sectional	Quality of life questionnaire (QoL)	N=39 42.2 years 71.8%		Executive function
Khalaf et al (2016)[59]	Cross-sectional	Short Form Health Survey 36 (SF-36)	N=1048 47.8 years 81%	Lower urinary tract symptoms	
Vitkova et al (2014)[60]	Cross-sectional	Short Form Health Survey 36 (SF-36)	N=223 38.4 years 67.3%	Bladder dysfunction (PCS) Sexual dysfunction (MCS)	
Qaderi et al (2014)[61]	Cross-sectional	Multiple Sclerosis Quality of Life-54 (MSQoL-54)	N=132 36.9 years 100%	Sexual problems (PCS and MCS)	
Schairer et al (2014)[62]	Cross-sectional	Short Form Health Survey 12 (SF-12)	N=6138 50.6 years 74.7%	Sexual dysfunction	
Ma et al (2017)[63]	Cross-sectional	Multiple Sclerosis Impact Scale (MSIS-29)	N=231 40.2 years 58.4%	Sleep disorders	

Continued

Table 2 Continued

Psychosocial variables

Authors, publication year	Study design	Quality of life measurement	Sample size (N) Age (mean) Sex (female%)	Main results	
				Risk factors	**Protective factors**
Hernández-Ledesma et al (2018)[71]	Cross-sectional	WHO Quality of Life Questionnaire (WHOQoL-BREF)	N=26 39.2 years 57.5%	Problem avoidance Social withdrawal Wishful thinking Self-criticism Anxiety Depression	Problem resolution Cognitive restructuring Emotional social and instrumental support Emotional expression
Grech et al (2018)[80]	Cross-sectional	Multiple Sclerosis Quality of Life-54 (MSQoL-54)	N=107 48.8 years 77.57%	Behavioural disengagement Suppression and self-control Emotional venting	Acceptance Growth Restrain
Zengin et al (2017)[79]	Cross-sectional	WHO Quality of Life Questionnaire (WHOQoL-BREF)	N=214 36–46 years 53.2%	Self-distraction Denial Substance use	Planning Active coping Acceptance Positive reinterpretation Social support
Farran et al (2016)[81]	Cross-sectional	Multiple Sclerosis International Quality of Life Questionnaire (MusiQoL)	N=34 36 years 56%	Self-criticism Escape avoidance Distancing Self-controlling	Emotional social support Instrumental social support Planful problem solving Positive reappraisal
Mikula et al (2014)[82]	Cross-sectional	Short Form Health Survey 36 (SF-36)	N=113 40.8 years 77%		Problem focused coping Stopping unpleasant emotion Getting support
Van Damme et al (2016)[85]	Cross-sectional	Short Form Health Survey 36 (SF-36)	N=117 41 years 70.2%		Acceptance (PCS and MCS) tenacious goal pursuit (PCS) flexible goal adjustment (MCS)
Wilski et al (2016)[88]	Cross-sectional	Multiple Sclerosis Impact Scale (MSIS-29)	N=257 47.9 years 69.93%		Self-efficacy Self-esteem Illness identity
Nery-Hurwit et al (2018)[86]	Cross-sectional	Function Neutral Health-Related Quality of Life Short Form (FuNHRQoL-SF)	N=259 48.6 years 84.23%		Resilience Self-compassion
Calandri et al (2018)[89]	Cross-sectional	Short Form Health Survey 12 (SF-12)	N=90 37 years 61.1%		Sense of coherence
Fernández-Muñoz et al (2018)[75]	Cross-sectional	Short Form Health Survey 36 (SF-36)	N=108 44 years 55%	Depression	
Pham et al (2018)[76]	Cross-sectional	Short Form Health Survey 12 (SF-12)	N=310 49 years 73.6%	Anxiety	

Continued

Table 2 Continued

Authors, publication year	Study design	Quality of life measurement	Sample size (N) Age (mean) Sex (female%)	Main results — Risk factors	Main results — Protective factors
Prisnie et al (2018)[72]	Longitudinal (T1=basal level/ T2=2 weeks later)	Short Form Health Survey 12 (SF-12)	N=139 40 years 70.5%	Anxiety Depression	
Alsaadi et al (2018)[73]	Cross- sectional	WHO Quality of Life Questionnaire (WHOQoL-BREF)	N=80 35.1 years 65%	Anxiety Depression	
Labiano-Fontcuberta et al (2015)[74]	Cross- sectional	Functional Assessment of Multiple Sclerosis (FAMS)	N=157 41.7 years 66.9%	Depression Anxiety Anger expression-in	
Paziuc et al (2018)[69]	Cross- sectional	Short Form Health Survey 36 (SF-36)	N=60 46 years 85%	Trait anxiety State anxiety Depression	Extraversion Emotional Stability
Phillips et al (2014)[70]	Cross-seccional	WHO Quality of Life Questionnaire (WHOQoL-BREF)	N=32 44.0 years 75%	Emotional problems	
Salhofer-Polanyi et al (2018)[77]	Cross-sectional	Multiple Sclerosis Quality of Life-54 (MSQoL-54)	N=139 40.0 years 70.5%	Depressive temperament Cyclothymic temperament	Hyperthymic temperament
Demirci et al (2017)[78]	Cross-sectional	Short Form Health Survey 36 (SF-36)	N=74 35.3 years 65.51%	Type D personality	
Mikula et al (2015)[93]	Cross-sectional	Short Form Health Survey 36 (SF-36)	N=116 40.4 years 72.4%		Social participation (MCS y PCS)
Costa et al (2017)[92]	Cross-sectional	Short Form Health Survey 36 (SF-36)	N=150 41.7 years 70.7%		Social support
Nakazawa et al (2018)[27]	Cross-sectional	Multiple Sclerosis Quality of Life-54 (MSQoL-54)	N=63 41.7 years 66.67%	EDSS level	Resilience
Ciampi et al (2018)[28]	Cross-sectional	Multiple Sclerosis Impact Scale (MSIS-29)	N=43 57.2 years 65.1%	EDSS level Fatigue Depression	
Fernández-Jiménez et al (2015)[32]	Cross-sectional	Functional Assessment of Multiple Sclerosis (FAMS)	N=97 47.3 years 82.5%	EDSS level Depression	
Klevan et al (2014)[29]	Cross-sectional	Short Form Health Survey 36 (SF-36)	N=93 41.8 years 69%	EDSS (PCS) Fatigue Depression Apathy	

Continued

Table 2 Continued

Authors, publication year	Study design	Quality of life measurement	Sample size (N) Age (mean) Sex (female%)	Main results Risk factors	Protective factors
Williams et al (2014)[55]	Cross-sectional	Short Form Health Survey 36 (SF-36) Short Form Health Survey 12 (SF-12)	N=447 49.3 years 70.02%	Pain (PCS) Muscle spasms (PCS) Stiffness (PCS) Depression (MCS)	
Hyncicova et al (2018)[40]	Cross-sectional	Short Form Health Survey 36 (SF-36)	N=67 32.3 years 53.7%	Number and severity of symptoms Fatigue Stress Depression Anxiety	
Shahrbanian et al (2015)[39]	Cross-sectional	Person Generated Index (PGI)	N=188 43 years 74%	Pain Fatigue Irritability Anxiety Depression Sleep disorder Cognitive deficit	
Strober et al (2018)[51]	Cross-sectional	Short Form Health Survey 36 (SF-36)	N=69 40.4 years 89.5%	Pain Fatigue Behavioural disengagement Denial Depression Anxiety High neuroticism Low extroversion Low self-efficacy	Acceptance Growth Emotional social and instrumental support Planning Active coping Positive reinterpretation Humour
Dymecka et al (2018)[52]	Cross-sectional	Multiple Sclerosis Impact Scale (MSIS-29)	N=137 46.5 years 53.3%	Fatigue Upper limb disability Lower limb disability Cognitive disorders Emotional problems	
Samartzis et al (2014)[66]	Cross-sectional	Short Form Health Survey 36 (SF-36)	N=100 40.5 years 64%	Perceived planning/ organisation dysfunction Perceived retrospective memory dysfunction Depression	
Brola et al (2016)[31]	Cross-sectional	EuroQol 5-Dimensions (EQ-5D) EuroQol Visual Analogue Scale (EQ-VAS) Multiple Sclerosis Impact Scale (MSIS-29)	N=2385 37.8 years 69.7%	EDSS level MS duration Lack of DMD treatment Age	

Continued

Table 2 Continued

Authors, publication year	Study design	Quality of life measurement	Sample size (N) Age (mean) Sex (female%)	Main results	
				Risk factors	Protective factors
Brola et al (2017)[30]	Cross-sectional	EuroQol 5-Dimensions (EQ-5D) EuroQol Visual Analogue Scale (EQ-VAS) Multiple Sclerosis Impact Scale (MSIS-29)	N=765 44.9 years 67.7%	EDSS MS duration Be unemployed Age No immunomodulatory therapy	
Abdullah et al (2018)[54]	Cross-sectional	Multiple Sclerosis Quality of Life-54 (MSQoL-54)	N=200 35.1 years 68%	Motor symptoms Low resistance Sensory symptoms Low income Be unemployed	
Nickel et al (2018)[33]	Cross-sectional	Multiple Sclerosis International Quality of Life (MusiQoL)	N=1220 47.8 years 76%	EDSS Comorbidity	High educational level High employment status
Campbell et al (2017)[67]	Cross-sectional	Functional assessment of multiple sclerosis (FAMS) EuroQol 5-Dimensions (EQ-5D)	N=62 49.4 years 69.35%	Cognitive deficit Be unemployed	
Chiu et al (2015)[94]	Cross-sectional	Short Form Health Survey 12 (SF-12)	N=157 43.8 years 86%	Be unemployed	Disability adjusted employment
Boogar et al (2018)[35]	Cross-sectional	Multiple Sclerosis Quality of Life-54 (MSQoL-54)	N=193 38.1 years 64.8%	High disability Depression Low socioeconomic status	Positive story treatment
Bishop et al (2015)[41]	Cross-sectional	Quality of Life Scale (QoLS)	N=1839 54 years 78.1%	Number and severity of symptoms Perceived stress	High educational level High employment status Job satisfaction Job match
Cioncoloni et al (2014)[34]	Cross-sectional	Short Form Health Survey 36 (SF-36)	N=57 41.7 years 68.42%	EDSS level Fatigue Pain Bladder dysfunction Bowel dysfunction Depressive manifestations Sleeping problems Introverted personality Be unemployed	

Continued

Table 2 Continued

Authors, publication year	Study design	Quality of life measurement	Sample size (N) Age (mean) Sex (female%)	Main results	
				Risk factors	Protective factors
Cichy et al (2016)[37]	Cross-sectional	Quality of Life Scale (QoLS)	N=703 63 years 76%	Progressive MS Progressive diagnosis Number and severity of symptoms Perceived stress Be male Not married/not living with significant other Unable to meet living expenses	
Mediational variables				*Mediator variable*	*Mediated relation*
Mikula et al (2018)[84]	Cross-sectional	Short Form Health Survey 36 (SF-36)	N=156 40 years 75%	Coping strategies Problem focused Emotional focused Stopping	Personality type D and MCS
Mikula et al (2015)[83]	Cross-sectional	Short Form Health Survey 36 (SF-36)	N=154 40.05 years 76%	Coping strategies	Fatigue and MCS and PCS
Mikula et al (2017)[90]	Cross-sectional	Short Form Health Survey 36 (SF-36)	N=74 35.3 years 65.51%	Self-esteem	Social participation and MCS
Koelmel et al (2017)[87]	Longitudinal (T1=basal level/ T2=10 weeks later/T3=26 weeks later/T4=52 weeks later)	Short Form Health Survey 8 (SF-8)	N=163 52.2 years 87.1%	Resilience	Social support and MCS
Valvano et al (2016)[91]	Cross-sectional	Leeds MS Quality of Life Scale (MSQoL)	N=128 45.5 years 85%	Cognitive fusion	Stigma and QoL

DMD, disease modifying drug; EDSS, expanded disability status scale; MCS, Mental Composite Score; MS, multiple sclerosis; PCS, physical composite; QoL, quality of life; RRMS, remittent remitting; SPMS, secondary progressive.

Table 3 Characteristics of included studies

Authors, publication year	Study design (T1:/T2:…)	Quality of life measurement	Sample size (N) Age (median) Sex (female%)	Main results
Years of diagnosis				
Possa et al (2017)[95]	Cross-sectional	Multiple Sclerosis Quality of Life-54 Instrument (MSQoL–54)	N=38 32.9 years 58%	Decrease in MCS (38%) and PCS (19%) in the first year after diagnosis.
Calandri et al (2017)[97]	Cross-sectional	Short Form Health Survey 12 (SF-12)	N=102 35.8 years 61.8%	Problem solving (β=0.28) and avoidance (β=0.25) was related to a higher MCS in the first 3 years of diagnosis.
Nourbakhsh et al (2016)[98]	Longitudinal (T1=basal level/ T2=3 months after diagnosis/ T3=6 months after diagnosis/ T4=12 months after diagnosis/ T5=18 months after diagnosis/ T6=24 months after diagnosis/ T6=36 months after diagnosis)	Short Form Health Survey 36 (SF-36)	N=43 36 years 72%	Baseline severity of fatigue and depression predicts PCS and cognitive function and fatigue MCS in the first 3 years of diagnosis.
MS progression				
Kinkel et al (2015)[100]	Longitudinal (T1=CIS diagnosis/ T2=5 years after diagnosis/ T3=10 years after diagnosis)	Short Form Health Survey 36 (SF-36) Multiple Sclerosis Quality of Life Inventory (MSQLI)	N=127 34.1 years 74%	A second clinic event consistent with CDMS, higher EDSS at the diagnosis and an earlier onset CDMS predicts a decrease in PCS.
Bueno et al (2014)[101]	Cross-sectional (25–30 years after diagnosis)	Multiple Sclerosis Quality of Life-54 Instrument (MSQoL–54)	N=61 54.9 years 83.6%	Patient changing from benign (EDSS<3) to non-benign (EDSS>3) decreases PCS.
Years of MS duration				
Baumstarck et al (2015)[102]	Longitudinal (T1=basal level/ T2=24 months later)	Multiple Sclerosis International Quality of Life questionnaire (MusiQol) Short Form Health Survey 36 (SF-36)	N=526 40.0 years 74.3%	Low levels of QoL, higher MS duration and higher EDSS level at T1 predicted worse QoL at T2.
Tepavcevic et al (2014)[103]	Longitudinal (T1=basal level/ T2=3 years later/T3=6 years later)	Multiple Sclerosis Quality of Life-54 Instrument (MSQoL–54)	N=93 41.5 years 71%	Higher EDSS and depression at basal level predicted a decrease of QoL at T1 and T2.
Young et al (2017)[105]	Longitudinal (T1=basal level/ T2=7 years later/T3=10 years later)	Assessment of Quality of life (AQoL)	N=70 59.8 years 71.6%	Higher pain predicts a decrease in QoL.
Chruzander et al (2014)[104]	Longitudinal (T1=basal level/ T2=10 years later)	EuroQol 5-Dimensions (EQ-5D) EuroQol Visual Analogue Scale (EQ-VAS) Sickness Impact Profile (SIP)	N=118 49 years 72%	Cognitive impairment, depressive symptoms and EDSS predicted a decrease in QoL at T2.
Group age				

Continued

Table 3 Continued

Authors, publication year	Study design (T1:/T2:....)	Quality of life measurement	Sample size (N) Age (median) Sex (female%)	Main results
Stern et al (2018)[96]	Cross-sectional	Multiple Sclerosis Quality of Life Instrument (MSQoL–54)	N=57 50 years 73.7%	The youngest group (35–44) presents worst PCS vs the oldest (55–65).
Buhse et al (2014)[99]	Cross-sectional	Multiple Sclerosis Quality of Life-54 (MSQoL–54)	N=211 65.5 years 80%	Risk of neurologic impairment, physical disability, depression and the comorbidity of thyroid disease was associated with decrease in PCS. Being widowed and employed was associated with increase in PCS.

CDMS, clinical defined multiple sclerosis; CIS, clinical isolated syndrome; EDSS, Expanded Disability Status Scale; MCS, Mental Composite Score; MS, multiple sclerosis; PCS, Physical Composite Score; QoL, quality of life.

displayed an association between unemployment and lower QoL.[30 34 54 67 94] Others showed a positive correlation between jobs adapted to disability,[94] job match and job satisfaction,[41] high employment status[33 41] and QoL in MS. Low socioeconomic status[35] and financial straits[37] were also risk factors for lower QoL.

Brola et al[30 31] noted that not having access to an adequate pharmacological treatment put QoL in danger. Congruent with this finding, Boogar et al[35] found a positive treatment experience to be a protective factor.

Other sociodemographic variables related to poorer QoL in MS were male sex,[37] old age,[30 31] unmarried or living with significant others,[37] whereas a higher education was a protective factor.[33]

Disease history

Some of the selected studies examined QoL in MS in its early years. According to Possa et al,[95] QoL decreased in the first year of diagnosis, as assessed by the MCS and Physical Composite Score (PCS). Stern et al[96] found the worst QoL in the youngest group of patients with MS.

Calandri et al[97] found that during the first 3 years from diagnosis, problem solving and avoidance coping strategies had a positive effect on QoL. Nourbakhsh et al[98] also studied factors influencing the development of QoL in the first 3 years. Their results showed that higher baseline levels of fatigue and depression predicted worse QoL as assessed by the PCS, whereas lower cognitive functioning and higher fatigue predicted a worse MCS.

Another study on QoL in MS by Buhse et al[99] focused on old age. These authors identified neurological impairment, physical disability, depression and comorbidity with thyroid disease as risk factors for worse QoL as assessed by the PCS in a sample of elderly patients with MS. On the contrary, being widowed and employed were identified as protective PCS factors.

In a longitudinal study, Kinkel et al[100] showed that a second clinical event consistent with clinically defined MS, higher EDSS at the time of diagnosis and an earlier MS onset predicted a decrease in PCS 10 years after diagnosis. Bueno et al[101] also showed that progression from benign MS to non-benign MS predicted a decrease in PCS 25–30 years after diagnosis.

Some longitudinal predictors of QoL identified have been: longer MS duration predicted worse QoL 2 years later,[102] and worse EDSS predicted worse QoL 2,[102] 6,[103] and 10[104] years later. Depression predicted worse QoL 6[103] and 10[104] years later, and stronger pain[105] and cognitive impairment[104] predicted worse QoL 10 years later.

Interventions

Details of the selected articles on psychological intervention are presented in table 4.

Mindfulness-based therapies

All mindfulness-based therapy intervention programmes showed improvement in QoL at some evaluation point and at least in some QoL domains. Body-affective

Table 4 Characteristics of the included articles

Authors, publication year	Programme name	Study design	Quality of life measurement	Sample size (N) Age (median) Sex (female%)	Main results
Mindfulness-based therapies					
Carletto et al (2017)[106]	Body-affective mindfulness (BAM)	Longitudinal (T1=basal level/T2=post-treatment/T3=6 months later)	Functional Assessment of Multiple Sclerosis (FAMS)	N=45 44.1 years 71.1%	Increase in general score FAMS from T1 to T2 (p<0.001) and from T2 to T3 (p=1).
Besharat et al (2017)[107]	Mindfulness-based stress reduction (MBSR)	Longitudinal (T1=pre-treatment/T2=post-treatment)	Short Form Health Survey 36 (SF-36)	N intervention/control=12/11 35 years 100%	Increase in general QoL score in the intervention group (p<0.05).
Blankespoor et al (2017)[108]	Mindfulness-based Stress Reduction (MBSR)	Longitudinal (T1=pre-treatment/T2=post-treatment)	Multiple Sclerosis Quality of Life-54 (MSQoL-54)	N=25 52.6 years 84%	Increase PCS (p<0.001).
Simpson et al (2017)[109]	Mindfulness-based Stress Reduction (MBSR)	Longitudinal (T1=pre-treatment/T2=post-treatment/T3=3 months later)	Multiple Sclerosis Quality of Life Inventory (MSQLI)	N=25 43.6 years 92%	Small and insignificant increase QoL from T1 to T2 (p=0.48) and insignificant increase from T2 to T3 (p=0.71).
Spitzer et al (2018)[110]	Community-based group mindfulness	Longitudinal (T1=pre-treatment/T2=post-treatment/T3=8 weeks later)	Short Form Health Survey 36 (SF-36)	N=23 48.4 years 91.3%	Increase MCS from T1 to T2 (p=0.008).
Ghodspour et al (2018)[111]	Mindfulness-based Cognitive Therapy (MBCT)	Longitudinal (T1=pre-treatment/T2=post-treatment)	Multiple Sclerosis Quality of Life-54 Instrument (MSQoL-54)	N intervention/control=15/15 36 years 100%	Increase in health distress (p=0.032), mental well-being (p=0.001), role limitation due to emotional problems (p=0.005) and cognitive performance (p=0.04) subscales.
Cognitive behavioural					
Case et al (2018)[112]	Trial of healing light guided imagery (HLGI)	Longitudinal (T1=pre-treatment/T2=post-treatment)	Multiple Sclerosis Quality of Life-54 Instrument (MSQoL-54)	N intervention/control=9/8 49.1 years –	Increase in PCS (p=0.01) and MCS (p<0.01) in the intervention group.
Blair et al (2017)[113]	Dialectical Behaviour Group Therapy (TCD)	Longitudinal (T1=pre-treatment/T2=post-treatment/T3=6 months later)	Multiple Sclerosis Quality of Life-54 Instrument (MSQoL-54)	N intervention/control=10/10 40.4 years 90%	Increase in MSQoL-54 from T1 to T3 (p=0.01).
Calandri et al (2017)[114]	Group-based cognitive behavioural therapy (CBT)	Longitudinal (T1=pre-treatment/T2=6 month post-treatment/T3=1 year post-treatment)	Short Form Health Survey 12 (SF-12)	N intervention/control=54/31 38 years 61%	Increase in MCS T2 in the CBT group vs control (p=0.036). Increase in MCS T3 in the CBT group vs control (p=0.049).

Continued

Table 4 Continued

Authors, publication year	Programme name	Study design	Quality of life measurement	Sample size (N) Age (median) Sex (female%)	Main results
Graziano et al (2014)[115]	Group-based cognitive behavioural therapy (CBT)	Longitudinal (T1=pre-treatment/T2=post-treatment/ T3=6 months later)	Multiple Sclerosis Quality of Life-54 Instrument (MSQoL-54)	N intervention/control=41/41 42.3 years 66%	Increase in MSQoL-54 at T3 in the CBT group vs control group (p<0.05).
Kiropoulos et al (2016)[116]	Cognitive behavioural therapy (CBT) for depressive symptoms	Longitudinal (T1=pre-treatment/T2=post-treatment/ T3=20 weeks later)	Multiple Sclerosis Quality of Life-54 Instrument (MSQoL-54)	N intervention/control=15/15 34.6 years 86.7%	Differences between control and CBT group MCS and PCS in T2 and T3 (p<0.001).
Chruzander et al (2016)[117]	Cognitive behavioural therapy (CBT) focused on depressive symptoms	Longitudinal (T1=basal level/ T2=3 weeks post-treatment/ T3=3 months post-treatment)	Multiple Sclerosis Impact Scale (MSIS-29) EuroQol 5-Dimensions (EQ-5D) EuroQol Visual Analogue Scale (EQ-VAS)	N=15 38 years 80%	Improvement in QoL from MSIS-29 and EQ-5D in T2 and T3 (p<0.05).
Kikuchi et al (2019)[118]	Cognitive behavioural therapy (CBT) on depression	Longitudinal (T1=pre-treatment/T2=mind-treatment/ T3=post-treatment)	Functional Assessment of Multiple Sclerosis (FAMS)	N=7 46.1 years 71.4%	Positive but not significant increase in FAMS (p>0.05).
Pakenham et al (2018)[119]	Resilience Training Programme (ACT)	Longitudinal (T1=pre-treatment/T2=post-treatment/ T3=3 months later)	Multiple Sclerosis Quality of Life-54 Instrument (MSQoL-54)	N=37 39.4 years 73%	Increase in PCS (p<0.001) and MCS (p<0.006) from T1 to T2, maintained at T3, without significant changes.
Proctor et al (2018)[120]	Telephone-supported acceptance and commitment bibliotherapy (ACT)	Longitudinal (T1=pre-randomisation/T2=12 weeks after randomisation)	EuroQol 5-Dimensions (EQ-5D)	N intervention/control=14/13 45.8 years 78%	No significant increase in QoL (p=0.62).
Social and group support					
Liu (2017)[125]	Hope-Based Group Therapy (HBGT)	Longitudinal (T1=pre-treatment/T2=post-treatment)	Multiple Sclerosis Impact Scale (MSIS-29)	N intervention/control=18/14 35.1 years 100%	Physical and psychological QoL increase in HBT group (p<0.05).
Abolghasemi et al (2016)[121]	Supportive-Expressive Therapy (SE)	Longitudinal (T1=pre-treatment/T2=post-treatment	WHO Quality of Life questionnaire (WHOQoL-BREF)	N intervention/control=16/16 31.8 years 41.7%	Increase QoL from T1 to T2 (p<0.001).
Jongen et al (2016)[123]	Intensive social cognitive treatment (can do treatment) with participation of support partners	Longitudinal (T1=basal level/ T2=12 months post-treatment)	Multiple Sclerosis Quality of Life Instrument (MSQoL-54)	N=38 – 65.8%	PCS increase (p=0.032) and MCS (p=0.087) in the RR group.
Jongen et al (2014)[122]	Intensive social cognitive wellness programme with participation of support partners	Longitudinal (T1=basal level/ T2=1 months post-treatment/ T3=3 months post-treatment T4=6 months post-treatment	Multiple Sclerosis Quality of Life Instrument (MSQoL-54)	N=44 45.7 years 79.5%	MCS increase at T2, T3 and T4 and PCS at T4 (p<0.05).

Continued

Table 4 Continued

Authors, publication year	Programme name	Study design	Quality of life measurement	Sample size (N) Age (median) Sex (female%)	Main results
Eliášová et al (2015)[124]	Self-Help group (SH)	Cross-sectional (T1=after the treatment)	WHO Quality of Life questionnaire (WHOQoL-BREF)	N intervention/control=46/35 42.2 years 59%	Increase in physical (p<0.001), psychological (p<0.001) and social relationships (p<0.001) in the SH group.
Symptom and self-management-based therapies					
Mulligan et al (2016)[126]	Fatigue self-management programme 'Minimise Fatigue, Maximise Life: Creating Balance with Multiple Sclerosis (MFML)'	Longitudinal (T1=1 month pre-treatment/T2=pre-treatment/ T3=post-treatment).	Short Form Health Survey 12 (SF-12)	N=24 49.3 years 100%	Positive but not significant changes in SF-12 (p>0.05).
Thomas et al (2014)[127]	Group-based fatigue management (FACETS)	Longitudinal (T1=1 week before treatment/T2=1 month post-treatment/T3=4 month post-treatment/T4=12 month post-treatment)	Multiple Sclerosis Impact Scale (MSIS-29) Short Form Health Survey 36 (SF-36)	N intervention/control=84/80 48 years 73%	Changes in physical health MSIS-29 (p=0.046) and vitality SF-36 (p=0.03) at T4.
Ehde et al (2015)[128]	Telephone-Delivered Self-Management (SM)	Longitudinal (T1=before group randomisation/T2=post-treatment/T3=6 month post-treatment/T4=12 month post-treatment)	Short Form Health Survey 8 (SF-8)	N intervention/control=75/88 51 years 89.3%	MCS and PCS increase at T2, T3 and T4 (p<0.05).
Feicke et al (2014)[129]	Education programme for self-management competencies (S.MS)	Longitudinal (T1=1 basal level/T2=post-treatment/ T3=6 month post-treatment)	Hamburg quality of life questionnaire in multiple sclerosis (Sclerosis Quality)	N intervention/control=31/33 41.9 years 87.1%	Stable positive changes in QoL (p=0.007).
Other psychological intervention					
LeClaire et al (2018)[130]	Group Positive Psychology	Longitudinal (T1=basal level/ T2=post-treatment)	Short Form Health Survey 36 (SF-36)	N=11 53.5 years 100%	Increase in SF-36 vitality subscale score (p=0.016). Increase in mental health SF-36 subscale (p=0.098) that did not reach statistical significance.

HBT, hope-based group therapy; MCS, mental component score; PCS, physical component score; QoL, quality of life; RR, relapsing–remitting.

mindfulness intervention increased the general QoL score up to 6 months after treatment.[106]

Of the three studies on mindfulness-based stress reduction programmes, two showed a significant increase in QoL after treatment.[107–109] One study[109] only produced a small, insignificant increase after treatment and at the 3-month follow-up.

A community-based mindfulness programme resulted in a significant increase in MCS.[110]

Finally, mindfulness-based cognitive therapy did not show any significant difference in general QoL between the control and the experimental group; however, it did show significant differences in QoL: in health distress, mental well-being, role limitation due to emotional problems and cognitive performance.[111]

Cognitive behavioural
A wide spectrum of cognitive behavioural interventions was analysed.

In a study by Case et al,[112] the experimental group attended 10 1-hour weekly sessions of healing light guided imagery. They found a greater increase in QoL in this group than with 10 hours of positive journaling in the active control group.

Blair et al[113] focused intervention on emotion regulation. The design consisted of 16 1.5-hour biweekly sessions for 8 weeks. The intervention resulted in a significant increase in QoL 6 months after treatment.

Interventions by Calandri et al[114] and Graziano et al[115] had a comparable design. Participants were divided into two subgroups by age. Intervention comprised four to five 2-hour sessions over the course of 2 months, and one follow-up session 6 months after treatment. Calandri et al[114] also included one follow-up session 12 months after treatment. At follow-up, the intervention groups in both studies had experienced an increase in QoL.

Three studies[116–118] focused intervention on depressive symptoms. Kiropoulos et al[116] and Chruzander et al[117] found improvement in QoL at post-treatment and follow-up assessments. Kikuchi et al[118] also found a post-treatment improvement, but not significant.

Two of the studies based intervention on acceptance and commitment therapy (ACT). Pakenham et al[119] implemented an 8-week programme aimed at training in resilience. QoL increased at treatment end and at 3-month follow-up. Proctor et al[120] implemented an 8-week intervention comprising telephone calls and self-help ACT books. No significant increase in QoL was observed.

Social and group support
The following social support and group interventions had an impact on QoL in MS.

Abolghasemi et al[121] implemented a 12-session supportive–expressive therapy programme, which improved QoL.

Jongen et al[122] tested an intensive social-cognitive wellness programme involving the partner or other significant informal caregiver. The results showed an increase in the MCS at 1, 3 and 6 months from treatment and in the PCS

6 months after treatment. The results of the programme were evaluated again 12 months after treatment. The relapsing–remitting MS group showed an increase in PCS and MCS.[123]

Eliášová et al[124] found more improvement across several QoL domains in patients with MS after self-help group sessions than in patients who did not attend the self-help groups. Liu[125] detected an increase in physical and psychological QoL in women with MS after participating in a hope-based group therapy programme for 1 hour twice a week for 8 weeks.

Symptom and self-management-based therapies
Two studies analysed a fatigue self-management group therapy. Mulligan et al[126] reported positive, but not significant, changes in QoL after their treatment. Thomas et al[127] reported significant positive changes in physical health assessed by the Multiple Sclerosis Impact Scale (MSIS-29) and vitality as measured by the SF-36 in the intervention group 12 months after the treatment.

In addition to fatigue self-management, Ehde et al[128] focused in their intervention on pain and depression self-management. The results were compared with an educational programme. There was a higher QoL post-treatment and 12-month follow-up score in the self-management group. Feicke et al[129] implemented a programme focused on MS self-management. As in Ehde et al,[128] improvements in QoL were still maintained at 6-month follow-up.

Other psychological intervention
LeClaire et al[130] implemented a 5-week positive psychology programme. The results showed only a significant improvement in the SF-36 vitality subscale.

DISCUSSION
First, the present systematic review was intended to identify risk and QoL protective factors in MS. The results showed that the EDSS was most employed for assessment of functional impairment.[25–35] As expected, the number and severity of symptoms and associated impairment appeared to play a crucial role in QoL. Fatigue,[28 29 39 40 42–52] cognitive impairment,[39 50 52 53 63 66 67] and pain,[35 39 50 51 55 56] in particular, were the focus of a large number of studies and were confirmed as important risk factors. Longitudinal studies suggested that greater fatigue,[98] pain[105] and cognitive impairment[98 104] also predicted worse QoL up to 10 years later. This has important clinical implications, as treatment of the abovementioned symptoms should be prioritised. In general, functional impairment,[102–104] as well as longer duration of illness,[102] was predictor of QoL 2 to 10 years later, whereas disease progression[101] from benign to non-benign MS predicted QoL as measured by the PCS up to 30 years later.

Among the emotional symptoms, there was convincing evidence that depression,[28 29 32 34 35 39 40 51 55 66 69 71–75] along with depressive temperament[77] and anxiety,[38 40 51 69 71–74 76]

were associated with lower QoL and that depression also predicted QoL up to 10 years later.[104]

The coping strategies applied obviously influenced QoL in MS, however their effect depended on the specific circumstances of the disease history. For example, problem solving and avoidance coping, normally classified as opposite strategies, both seemed to have a positive effect on the MCS in the first 3 years of diagnosis.[97] However, in general, strategies associated with denial[51 79] and avoidance of the challenges of the disease, such as problem avoidance,[71 81] behavioural disengagement,[51 80] distancing,[81] self-distraction,[79] social withdrawal[71] and wishful thinking,[71] were associated with a lower QoL. On the contrary, strategies based on acceptance and active commitment, such as active coping, humour, problem resolution, cognitive positive restructuring and emotional expression, led to higher QoL in MS.[51 71 79–82] Obviously, there is a close connection between the active confrontation of the challenges of illness and specific personality-based convictions, such as a high self-efficacy. Thus, higher self-efficacy,[51 88] self-esteem[88] and sense of coherence[89] improved QoL in MS.

Regarding sociodemographic influences on QoL, not surprisingly, unemployment, a low socioeconomic status[35] and financial difficulties[37] proved to be major risk factors.[30 34 54 67 94] In keeping with the negative influence of the scarcity of resources, lack of access to therapy was also identified as a risk factor.[30 31]

The second aim of this systematic review was to study QoL in patients with MS at different times during their disease history. Two studies showed diminishing QoL in patients with MS in its early stage.[95 96] This might have to do with the fact that patients being diagnosed with a severe chronic disease need a certain time to come to terms with this emotional shock. Oscillation between avoidance and problem solving, which both have a positive influence in the first 3 years after diagnosis,[97] may be behind this inner struggle. In older patients, neurological impairment and physical disability,[97] which represent the age-associated increase in physical impairment, were identified as risk factors for QoL in MS.

Finally, the third aim of this review was to analyse psychological interventions for the improvement of QoL in MS. Symptomatic improvement of psychopathology usually at the centre of psychotherapy outcome studies was not the primary focus of our review.[131] Eight of the intervention studies specifically treated depressive symptomatology,[106 110–112 115 117 118] either with mindfulness-based or cognitive behavioural approaches, both of which proved to be successful.

Three studies were specifically directed towards the treatment of fatigue[112 126 127] by light guided imagery or self-management programmes. Both the imagery and self-management group intervention approaches were successful, whereas the individual self-management programme did not show significant improvement.

A variety of mindfulness-based approaches[107–109] and a community-based intervention were directed at stress reduction.[110] Three of the four studies showed some kind of improvement in QoL, including the only study with a control group.

Several of the interventions were designed to reinforce protective factors in patients with MS. Graziano et al[115] focused on identity redefinition, sense of coherence and self-efficacy. Pakenham et al[119] implemented a programme based on resilience training, and the programme by Blair et al[113] focused on the improvement of emotional regulation. All of them were successful in improving QoL, confirming the alternative focus on protective factors instead of risk factors.

A wide spectrum of interventions based on social support concentrated on reinforcement of the social network of patients with MS, for example, self-help groups,[124] hope-based group therapy,[125] supportive–expressive therapy[121] and social cognitive training with support partners.[122 123] All interventions aimed at helping people overcome MS barriers in daily living by strengthening their social support, improving some aspects of QoL. This is consistent with the studies mentioned above[92 93] and emphasises the importance of social support and participation as a protective factor for QoL.

Limitations

The main limitation of this study was the impossibility of carrying out a quantitative synthesis of the results, due to the heterogeneity of methodologies and designs in the articles included. Due to the vast number of topics and limited resources, our search was restricted to a 5-year period through January 2019.

CONCLUSIONS

This review was intended to give a broad overview of QoL in MS. The findings show the importance of clinical, psychosocial and demographic variables as QoL risk and protective factors. A variety of psychological interventions ranging from mindfulness-based and cognitive behavioural approaches to self-help groups addressing these factors were identified as promising options for improving QoL. These findings have important clinical implications. A sound biopsychosocial assessment of patients with MS in daily clinical practice is necessary to ensure the possibility of early identification of QoL risk factors and evidence-based psychological intervention is recommended to improve or stabilise QoL.

ORCID iD
Irene Gil-González http://orcid.org/0000-0002-1810-3687

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