Review article

Illness perceptions and outcome in multiple sclerosis: A systematic review of the literature

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ABSTRACT

According to Leventhal's self-regulation model, ill people construct personal representations of their disease, namely *illness perceptions*, which impact their coping strategies and the emotional response to their condition. Since these representations develop in the social environment, the individuals' perceptions may also be related to the opinions of their caregivers. This systematic review aims at synthesising and critically appraising literature pertaining the relationship between illness perceptions and outcome in persons with multiple sclerosis and their caregivers. A literature search was conducted in MEDLINE, PsycINFO, and CINAHL. Only papers with the following characteristics were included: quantitative studies; written in English or Italian; published from 1992; investigating the relationship between illness perceptions and any outcome in persons with multiple sclerosis and/or their caregivers; using validated scales assessing illness perceptions. Twenty papers were included and appraised through the 16-item Quality Assessment Tool for Studies with Diverse Designs. The quality of the papers was acceptable. Eighteen out of 20 papers reported the existence of a moderate effect size when analysing the relationship between illness perceptions and outcome, whereby "positive" perceptions (e.g. stronger beliefs of control) related to better outcomes, while "negative" ones (e.g. attribution of negative consequences to the disease) related to worse outcome.

1. Introduction

Multiple sclerosis (MS) is the most common cause of neurological impairment in young adults and is estimated to affect more than 2 million people worldwide (Kingwell et al., 2013). MS frequently presents a relapsing-remitting course but can also lead to a progressive worsening. Across all MS types the symptoms can affect different functions (movement, sight, sexual function, cognition, etc.), lifelong treatment with medication is required and clinical outcome is unpredictable (Simmons, 2010). MS can impair life in several domains, such as psychological wellbeing, physical health and social functioning. As a result, persons with MS (PwMS) deal with uncertainty about their future and are at high risk of experiencing poor quality of life (Simmons, 2010).

According to Leventhal's self-regulation model (SRM), ill people construct personal representations of their disease ("illness perceptions"), which ultimately impact their coping strategies and the emotional response to their condition (Leventhal et al., 1992, 2003). These representations refer to the label attached to the disease and its symptoms (*identity*), the assumptions regarding its course (*timeline*) and determinants (*causes*), the beliefs concerning the illness's impact on everyday life (*consequences*) and the possibility to control it (*control*) (Leventhal et al., 2003, 1992). Other dimensions (Broadbent et al., 2006; Moss-Morris et al., 2002) include the understanding of the illness (*coherence*) and the emotional effect of the disease (*emotional representations*). Considering medical conditions in general, negative illness perceptions typically relate to higher rates of worrying thoughts (persisting even after a negative diagnostic test), reduced satisfaction after a consultation, poor compliance, impaired coping and worse psycho-physical well-being (Petrie et al., 2007).

Previous reviews have reported an association between negative illness perceptions and a variety of negative outcomes such as low quality of life, high levels of depression, anxiety, functional impairment, and pain. These findings have been replicated in the context of several medical conditions, such as cardiovascular and pulmonary disease, hip/knee arthroplasty, cancer, alopecia and epilepsy (Dempster et al., 2015; Sawyer et al., 2019), but have not included MS.

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A previous review addressing the psychological correlates of adjustment (conceptualized as encompassing depression, quality of life, relationship satisfaction, etc.) in PwMS mentioned illness perceptions as possible predictors (Dennison et al., 2009).

However, the paper focused on the relationship between a specific outcome (psychological adjustment) and a variety of possible determinants (e.g., self-efficacy, social support, psychopathology), with only limited information on illness perceptions. In addition, due to its year of publication (2009), the review did not include the bulk of literature, which has been produced after 2009. Since data suggest that illness appraisals show moderate-to-strong relationships with coping and a variety of outcomes (e.g., psychological well-being, distress, role and social functioning, vitality) across all studies addressing this topic (Hagger and Orbell, 2003), we performed a review specifically addressing the relationship between illness perceptions and outcome not only among individuals with MS, but also among their caregivers.

Indeed, since "every component of the self-regulation system will be shaped and re-shaped by the social environment" (Leventhal et al., 2003, p. 55), it is plausible that the individuals' perceptions may be somewhat related to the opinions of other relevant people, such as their caregivers, namely family members, friends or partners taking care of them. In addition, caregivers are affected by MS, albeit indirectly, in terms of physical, psychological and financial consequences (McKeown et al., 2003), making their illness perceptions worthy of consideration. Building on this, some studies are starting to focus on the role of illness perceptions of significant others (e.g. partners) on the outcome of persons affected by chronic conditions, including MS, suggesting a possible association (Bassi et al., 2016; Sterba et al., 2008; Wu et al., 2013).

To the best of our knowledge no systematic review has specifically addressed the possible relationship between illness perceptions and outcome in MS. However, one cannot be sure that the findings obtained by previous reviews addressing other chronic conditions may be transferable to MS, considering its peculiar nature (high unpredictability and prevalence among younger people).

Consequently, this systematic review addresses this gap in the literature, aiming to synthesize and critically appraise quantitative evidence answering the following question: "Do illness perceptions affect outcome in persons with multiple sclerosis and their caregivers?" This review considered a broad range of outcomes, thus including psychological, physical and social ones.

2. Materials and methods

This review was registered on Prospero (record CRD42021255459). The formulation of the review question was informed by the PICOS framework (Centre for Reviews and Dissemination, 2006) even though not all components of the framework were operationalized in the search strategy, so as not to restrict the results (see the section "Database searching" below).

More specifically, the **P**opulation of interest consists of *persons* (18+ years) *with MS (any phenotype) and/or their caregivers* and the **I**ndicators are represented by *validated questionnaires addressing illness perceptions (see the inclusion criteria below)*. No specific **C**omparator was chosen for this review. Regarding **O**utcome, no specific terms were used, so as not to restrict the results, not only because "outcome" itself can refer to different aspects, but also because it can potentially differ according to the considered population. For instance, depression may be an outcome applicable to both PwMS and caregivers, while MS-related fatigue is an outcome only applicable to PwMS. The **S**tudy designs included in this review were *quantitative studies* (all types).

2.1. Inclusion criteria

Only papers with the following characteristics were included in this review: quantitative studies (all types); written in English or Italian; published from 1992 (date when a complete theorization of illness perceptions was published (Leventhal et al., 1992); investigating the relationship between illness perceptions (of the affected persons and/or their caregivers) and any outcome in the PwMS and/or their caregivers (e.g. severity of fatigue, compliance, psychological adjustment, depressive symptoms, quality of life, coping, etc.), even if the main focus of the research was not illness representations; any gender, age, ethnicity; using validated scales (administered by researchers or self-administered) assessing the different dimensions of illness perceptions as theorized by Leventhal et al. (1992), as stated above.

2.2. Exclusion criteria

Papers with the following characteristics were excluded by this review: studies with no specific focus on the relationship between illness perceptions and outcome (e.g. studies assessing illness perceptions in persons with worse outcome without investigating the relationship between perceptions and outcome); studies failing to address the varying dimensions of illness perceptions (e.g. studies focusing *only* on the perception of uncertainty or the perception of treatment efficacy in MS).

The review only included primary research articles, and excluded review papers and materials available outside traditional academic publishing (gray literature).

2.3. Database searching

The search was finalised with advice from academic librarians of Lancaster University (UK) and performed separately in MEDLINE, PsycINFO, and CINAHL (lastly accessed in September 2021).

The search was consistent in all databases. Title and abstract searches were performed. Two main concepts were searched for: "MS" and "illness perceptions". For MS both free terms and subject headings (those considered as being relevant to the review) were used and combined with the Boolean operator "OR". No subject headings were deemed appropriate for operationalising illness perceptions. The separate searches for "MS" and "illness perceptions" (and related terms), were combined with "AND". Proximity searches and asterisk operators were also applied.

The following search terms were used:

1) "multiple sclerosis"; "MS"; "demyelinating disease"; "relapsing remitting" (and relevant subject headings. For Medline: MH "Multiple Sclerosis+" OR MH "Multiple Sclerosis Chronic Progressive" OR MH "Multiple Sclerosis Relapsing Remitting". For PsycINFO: DE "Multiple Sclerosis". For CINAHL: MH "Multiple Sclerosis+")
2) "illness"; "disease"; "sickness"; "condition"; "disability"; "health issue" N3 "perception*"; "representation*"; "belief*"; "opinion*"; "appraisal*"; "attitude*"

The finalised literature search was successfully tested on Medline, in order to ensure that 10 papers, deemed as certainly relevant for the review and previously retrieved from Google Scholar, could be found.

In order to maximize the retrieving of papers, three additional search strategies were adopted:

- searching the reference list of the papers included in the review;
- searching for papers by key authors in the field, identified as the most prolific ones in relation to the final number of selected papers;
- searching for papers citing those included in the review (on Google scholar).

2.4. Selection of the relevant papers

All the papers meeting the inclusion criteria were considered as *relevant* to the review. A first screening of eligibility involved the selection of papers whose titles were broadly or specifically referring to the review topics. Then, the revision of the abstracts and the revision of

the full-texts, the latter performed when the former was not sufficient, allowed us to reach a definite decision of inclusion/exclusion. For a visual presentation of the review stages (identification of the papers, screening, eligibility, included articles), based upon the PRISMA 2020 (Page et al., 2021) statement and flow diagram, see Fig. 1.

The papers to be screened were managed through the Endnote 8x software. More specifically, after the exclusion of papers deemed as certainly irrelevant from each database, the potentially relevant records ($n = 65$) were saved on Endnote. Then, once the duplicate references were eliminated (through Endnote and double-checked manually) the remaining papers were analysed for exclusion/inclusion.

2.5. Data extraction

All the relevant papers were thoroughly assessed in order to extract the information to answer the review question. To serve this purpose, a data extraction form was customized for the specific needs of this review, using the data extraction form of the Joanna Briggs Institute for experimental/observational studies (freely adapted for this review) and the Joanna Briggs Institute guidelines for extracting data (Godfrey and Harrison, 2015; The Joanna Briggs Institute, 2020). The data extraction tool contains specific information including: study design, sample characteristics, clinical outcome measures, relationship between illness perceptions and outcome and considerations regarding any confounding variables. In order to facilitate the recording of relevant information,

outcomes were divided into the following broad categories, informed by the literature: psychological aspects (e.g. adjustment, depression), physical condition (e.g. fatigue, pain), illness management (e.g. adherence, service use), and socioeconomic aspects (e.g. work, social isolation). The form offered the possibility to specify the outcomes and add any missing ones.

2.6. Critical appraisal

The quality of the selected papers was assessed using the 16-item Quality Assessment Tool for Studies with Diverse Designs-QATSDD (Sirriyeh et al., 2012). The tool, reliable and valid when assessing papers adopting different designs, considers several aspects of studies, such as explicit reference to a theoretical framework, representativeness of the sample, description of the research setting, fit between research question and methods of analysis, etc. Each aspect can be evaluated with a score ranging from 0 (not at all) to 3 (complete), whereby higher numbers indicate higher quality. The maximum total score is 42 and it is possible to calculate, for each paper, the percentage obtained in relation to the maximum total score, in order to obtain a quality ranking useful to compare studies (Sirriyeh et al., 2012).

2.7. Synthesis and analysis

The findings regarding the relationship between illness perceptions
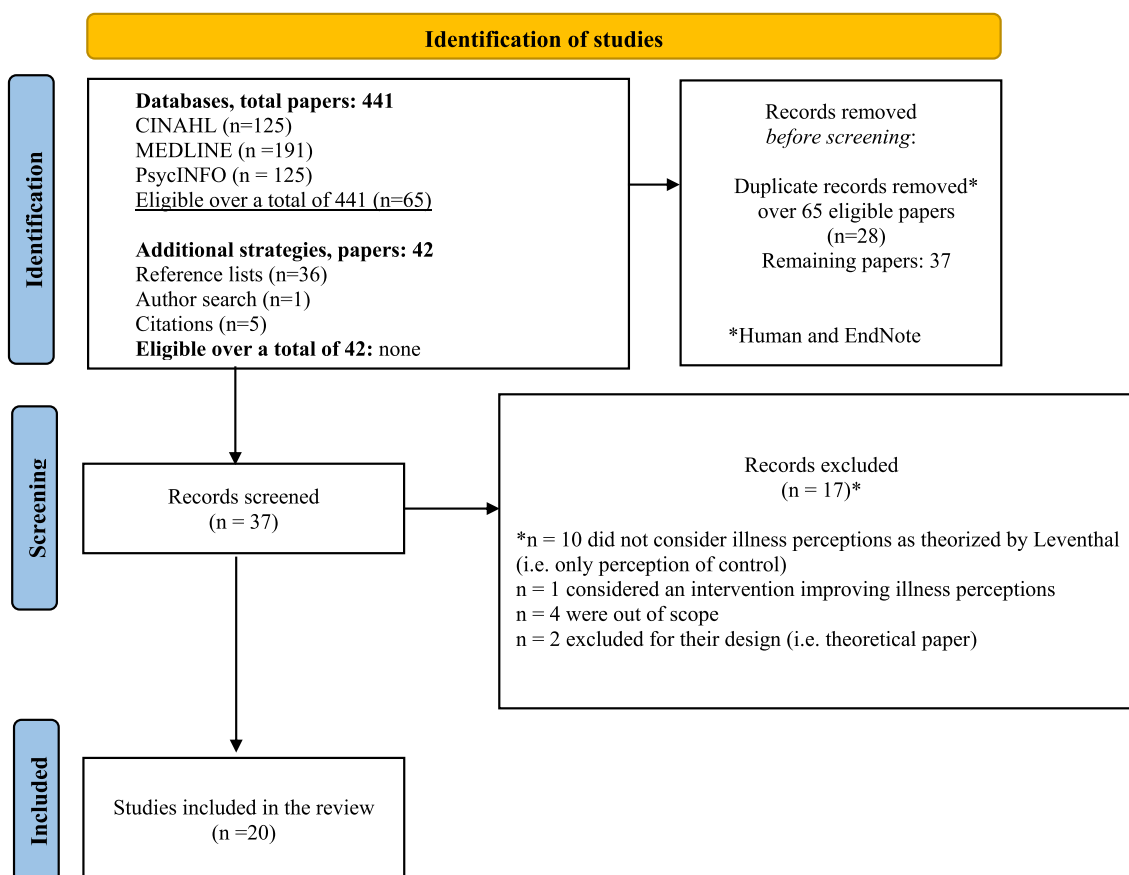
From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71. For more information, visit: http://www.prisma-statement.org/

Fig. 1. PRISMA flowchart.
From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71. For more information, visit: http://www.prisma-statement.org/.

and outcome, derived from the relevant papers, were subjected to a descriptive synthesis. The latter was performed considering the main findings of the studies, similar patterns, disconfirming cases and overall interpretation of the findings. The overall (based on the range of values) effect size (ES) of the relationship between illness representations and outcome were evaluated for each paper, considering the ES reported by the authors, or the findings referring to the relationship between variables. The latter were interpreted in accordance with the following criteria (Cohen, 1992; Sullivan and Feinn, 2012):

Odds ratios 1.5 (small ES), 2 (medium ES), 3 (large ES);

Pearson's correlation 0.10 (small ES), 0.30 (medium ES), and 0.50 (large ES).

In particular, the size and direction of every correlation were recorded in the data extraction form. Then, the ES was grossly inferred for each paper, considering the range of values as a whole (the most represented ones dictating the final ES). For example, in the case of a paper reporting a total of 8 correlations, 5 of them showing an ES <0.30 and 3 of them showing an ES >0.30, the overall ES was considered as being small.

Findings other than correlations, such as the impact of illness perceptions on the percentage of explained variance, as investigated through regression analyses, were also reported.

2.8. Quality control of the review process

In order to improve the quality of the review process, the selection, data extraction and quality appraisal phases were independently performed by the first author and a senior colleague (last author), using a list of 10 papers selected randomly from the databases. The quality evaluation phase highlighted negligible disagreements (difference of no more than 1 point in the total score) for the critical appraisal and

therefore the rest of the data extraction and critical appraisal was entirely performed by the first author.

3. Results

3.1. Retrieved papers

The literature search returned a total of 418 records (125 from PsycINFO, 191 from Medline, 102 from CINAHL). A first screening was performed, in order to eliminate the papers whose titles clearly referred to topics irrelevant to this review. Sixty-five papers remained after this screening. After the deletion of 28 duplicate references, a total of 37 papers were analysed in more depth. Twelve papers were eliminated through abstract evaluation, five papers required full-text access and were then excluded (see Fig. 1 for the reasons of exclusion). A total of 20 papers remained and were considered as relevant for this review, in accordance with the previously mentioned inclusion criteria (see Table 1 for an overview of the selected papers). The revision of the reference lists of these papers allowed the identification of 36 possibly relevant articles (according to the title), that were eliminated after abstract/full-text analysis. The search for the most prolific authors in the field returned just 1 paper, that was excluded because it did not consider illness perceptions. The search for papers citations (total 1185) yielded only 5 more possibly relevant records, excluded because they did not meet the inclusion criteria (see Fig. 1 for a visual presentation of the selection process).

3.2. General characteristics of the selected papers

The relevant papers refer to research conducted in different geographical areas (Europe, Australia, New Zealand, USA, Israel). The

Table 1
Overview of the selected papers.

First author	Year	Location and setting	MS type	Sample size	Mean age	Is the relationship between illness perceptions and outcome the main focus of the paper?
Ackroyd	2011	UK, CL	**R-R**, S-P	72 PwMS 72 caregivers	47.5 48.6	Yes
Bassi	2016	Italy, CL	**R-R**, P-P, S-P	68 PwMS 68 caregivers	39.6 46.0	Yes
Bassi	2020	Italy, CL	**R-R**, P-P, S-P	680 PwMS	40.1	Yes
Bassi	2021	Italy, CL	**R-R**, P-P, S-P	680 PwMS	40.1	Yes
Dennison	2010	UK, CL	**R-R**, P-P, S-P	94 PwMS	41.7	No
Glattacker	2018	Germany, CO	**R-R**, P-P, S-P	590 PwMS	45.6	Yes
Heffer-Rahn	2018	UK, CO	**R-R**, P-P, S-P, P-R	132 PwMS	43.3	No
Jopson	2003	NZ, CO	R-R, **P-P**, S-P	168 PwMS	50.6	Yes
Neter	2009	Israel, CL	Not specified	101 PwMS	41.2	No
Neter	2021	Israel, CL	R-R	186 PwMS	40.6	No
Santos	2019	Portugal, CL	**R-R**, S-P	100 PwMS 72 caregivers	39.4 42.4	No
Schiaffino	1998	USA, CL	Not specified	66 PwMS	42.0	Yes
Spain	2007	Australia, CL, CO	**R-R**, P-P, S-P, ?	580 PwMS	46.7	Yes
Timkova	2021	Slovakia, CL	Not specified	162 PwMS	40.9	Yes
Vaughan	2003	UK, CL	Not specified	99 PwMS	44.8	Yes
Wilski	2016	Poland, CL, CO	**R-R**, P-P, S-P, P-R, ?	185 PwMS (only F)	48.8	No
Wilski	2016a	Poland, CL, CO	**R-R**, P-P, S-P, P-R, ?	257 PwMS	47.9	Yes
Wilski	2016b	Poland, CL	**R-R**, P-P, S-P, P-R	210 PwMS	47.0	Yes
Wilski	2017	Poland, CL, CO	**R-R**, P-P, S-P, P-R, ?	264 PwMS	49.3	No
Wilski	2019	Poland, CL, CO	**R-R**, P-P, S-P, P-R, ?	278 PwMS	48.0	Yes

The Table provides an overview of the selected papers. CL: clinic; CO: community F: females; MS: multiple sclerosis; R-R: relapsing-remitting MS; P-P: primary progressive; PwMS: persons with MS; P-R: progressive-relapsing; S-P: secondary-progressive; ?: indeterminate/unknown; NZ: New Zealand. In bold the most frequent MS type.

majority of studies were cross-sectional, with 2 out of 20 adopting a longitudinal design (Neter et al., 2021; Schiaffino et al., 1998). Despite 3 articles enrolling both caregivers (mainly spouses) and PwMS (Ackroyd et al., 2011; Bassi et al., 2016; Santos et al., 2019), only two of them analysed illness perceptions among caregivers, too (Ackroyd et al., 2011; Bassi et al., 2016). Considering the whole body of literature (20 selected papers), the sample size for PwMS ranged from a minimum of 66 (Schiaffino et al., 1998) to a maximum of 680 (Bassi et al., 2020, 2021), resulting in a total sample size of 4972 participants, of whom 1419 were males and 3542 were females [11 participants had missing data from one study (Glattacker et al., 2018)]. One paper focused only on female PwMS (Wilski et al., 2016), providing data on the relationship between illness perceptions and body esteem. Considering the 20 papers as a whole, the most represented MS phenotype was the relapsing-remitting one, while mean disease duration was higher than 5 years in almost all studies, ranging from a minimum of <3 years (Santos et al., 2019) to a maximum of 13.8 years (Wilski et al., 2016). Disease severity was, overall, mild-moderate. Regarding the caregivers where illness perceptions were assessed, the sample size ranged from 68 (Bassi et al., 2016) to 72 (Ackroyd et al., 2011), resulting in a total sample size of 140.

3.3. Critical appraisal

The quality of the papers ranged from 64% to 83% of the possible total QATSDD score. These values are indicative of an overall acceptable quality of the analysed literature, as for previous reviews (Harrison et al., 2021). The main limitations leading to a lower score were the lack of a clear theoretical framework, a poor description of procedure for data collection, the absence of a statistical assessment of reliability and validity of the measurement tools, or no consideration of sample size during study design. Virtually all papers did not clearly state the rationale for the choice of data collection tools (apart from the expected reference to previously conducted validation studies). See Table 2 for the critical appraisal of all papers.

Table 2
Critical appraisal of the selected papers.

Paper	Quality score	Percentage% (of the possible total score)
Ackroyd et al., 2011	28/42	67
Bassi et al., 2016	32/42	76
Bassi et al., 2020	29/42	69
Bassi et al., 2021	30/42	71
Dennison et al., 2010	31/42	74
Glattacker et al., 2018	27/42	64
Heffer-Rahn et al., 2018	31/42	74
Jopson et al., 2003	34/42	81
Neter et al., 2009	32/42	76
Neter et al., 2021	30/42	71
Santos et al., 2019	33/42	78
Schiaffino et al., 1998	31/42	74
Spain et al., 2007	30/42	71
Timkova et al., 2021	32/42	76
Vaughan et al., 2003	32/42	76
Wilski et al., 2016 (body esteem)	29/42	69
Wilski et al., 2016 (self-management)	32/42	76
Wilski et al., 2016 (health-related QoL)	31/42	74
Wilski et al., 2017	33/42	78
Wilski et al., 2019	35/42	83

The Table shows the quality ranking of the papers included in the review. The total score and the percentage in relation to the maximum possible score are reported.

3.4. Assessment of illness perceptions among the selected papers

Most of the papers analysed illness perceptions through the Illness Perception Questionnaire (IPQ), classical or revised version. Eight papers (Glattacker et al., 2018; Wilski et al., 2016; Harrison et al., 2021; Dennison et al., 2010; Timkova et al., 2021; Wilski and Tasiemski, 2016a, 2016b; Wilski and Tomczak, 2017; Wilski et al., 2019) used the brief illness perception questionnaire (B-IPQ). One paper (Schiaffino et al., 1998) used the Implicit Models of Illness Questionnaire (IMIQ), but was included since it explicitly referred to Leventhal's theoretical framework. In addition, the IMIQ items have some overlap with Leventhal's dimensions (e.g. variability, cyclic timeline, curability, control). Adopting a longitudinal design, the paper addressed the relationship between illness perceptions, illness severity, and current and future depression.

3.5. Illness perceptions and outcome among PWMS and their caregivers

Regarding the relationship between illness perceptions and outcome, only two papers did not find any significant statistical association, as detailed below (Heffer-Rahn and Fisher, 2018; Neter et al., 2021). All the remaining papers reported that illness perceptions predicted outcome, even after controlling for potentially confounding variables (see below). For a visual presentation of the relationship between illness perceptions and outcome in the remaining 18 papers, see Tables 3 and 4.

Adversar.: adversarial; chr.: chronic; B-IPQ (brief illness perception questionnaire); emot. rep: emotional representations; IPs: illness perceptions; diseng.: disengagement; impair.: impairment; re-eng.: re-engagement; phys.: physical; psych.: psychological; QoL: quality of life.

The term "dimensions" refer to the use of a variety of tests addressing different aspects of the studied outcome. *in this paper, high coherence related to low mental health

The final list of studies included papers addressing the following "outcomes": psychological (e.g. depression, anxiety, life satisfaction, self-esteem), physical (e.g. physical function, fatigue, pain management), illness management (e.g. adherence, service use) and socioeconomic aspects (functional impairment from a work and social perspective). Most of the papers addressed psychological outcomes or a combination of psycho-physical aspects. The illness perception dimensions most reported as related to the PwMS' outcome measures were identity (label attached to the disease and symptoms attributed to it), consequences and control (personal and treatment); see Tables 3 and 4.

Overall, a stronger beliefs of control (either personal or treatment-related), clear understanding of the disease (coherence), attribution of the disease to external causes (e.g. virus) or bad luck were related to better outcomes (Bassi et al., 2016; Wilski et al., 2016; Spain et al., 2007; Vaughan et al., 2003). Conversely, higher emotional representations (emotional impact of the disease), illness attribution to psychological causes (thinking that MS might be related to stress), identity (number of symptoms attributed to MS) and consequences (limitations posed by MS) related to worse outcome (Bassi et al., 2020; Jopson and Moss-Morris, 2003; Timkova et al., 2021; Neter et al., 2009). In contrast to several papers reporting a correlation between high coherence and better outcome (Bassi et al., 2016; Spain et al., 2007; Vaughan et al., 2003; Wilski et al., 2016), one study (Santos et al., 2019) reported high illness coherence as related to lower mental health.

Regarding timeline, the results were inconsistent. Some papers reported that cyclic and chronic attributions were linked to worse outcome (Bassi et al., 2020, 2021; Jopson and Moss-Morris, 2003; Schiaffino et al., 1998), while others reported that cyclical (Ackroyd et al., 2011) and chronic (Jopson and Moss-Morris, 2003) timeline perceptions related to better outcome. Inconsistent findings were also observed when using the IPQ and B-IPQ, which analysed timeline as a unique construct, without the "cyclic" specifier (Spain et al., 2007; Vaughan et al., 2003; Wilski et al., 2016; Wilski and Tasiemski, 2016b). A paper focusing on past use of rehabilitation and intention to use rehabilitation

Table 3
Illness perceptions and outcome in the selected papers (part 1).

IPs	Ackroyd et al., 2011 adversar. growth	Bassi et al., 2016 well-being (dimensions)	Bassi et al., 2020 psych. adjust.	Bassi 2021 phys. health; fatigue	Dennison et al., 2010 functional impairm.; psych. distress	Glattacker et al., 2018 rehabilit. use (past-future)	Jopson 2003 adjustment (dimensions)	Neter et al., 2009 goal diseng; goal re-eng; well-being	Santos et al., 2019 mental QoL physical QoL
Timeline Acute/Chronic				X (chr.)			X (chr.)		
Cyclical	X		X	X			X		X
Consequences			X	X		X	X	X	X
Emot. rep.		X	X	X	X				X
Identity	X	X	X	X	X		X	X	X
Concerns (B-IPQ)					X				
Coherence		X	X	X	X		X		X*
Control								X	
Treatment			X	X		X	X		X
Personal	X		X	X			X		
Causes			X	X			X		

The Table offers an overview of the illness perceptions (first left column) found to be related with outcome (first top row). Each X indicates that at least one statistically significant association has been found.

Table 4
Illness perceptions and outcome in the selected papers (part 2).

IPs	Schiaffino et al., 1998 psych. adjust.	Spain et al., 2007 health-related QoL	Timkova et al., 2021 psychol. distress	Vaughan et al., 2003 psycho-physical outcome (dimensions)	Wilski et al., 2016 body esteem	Wilski et al., 2016a health-related QoL	Wilski et al., 2016b self-manag.	Wilski 2017 estimated MS impact	Wilski et al., 2019 perceived MS impact; treatment beliefs
Timeline Acute/Chronic		X		X	X		X	IPs (general) are worse in overestimators intermediate in realists low in underestimators	Negative IPs (general) positively relate with perceived MS impact and negatively with treatment beliefs.
Cyclical	X (variability)								
Consequences	X	X		X	X	X			
Emot. rep.			X		X				
Identity		X		X	X	X			
Concerns (B-IPQ)			X		X				
Coherence					X				
Control	X (curability)	X		X					
Treatment					X	X	X		
Personal					X	X			
Causes		X							

The Table offers an overview of the illness perceptions (first left column) found to be related with outcome (first top row). Each X indicates that at least one statistically significant association has been found. Adjust.: adjustment; B-IPQ (brief illness perception questionnaire); emot. rep: emotional representations; IPs: illness perceptions; manag.: management; MS: multiple sclerosis; psych./psychol.: psychological; QoL: quality of life. The term "dimensions" refer to the use of a variety of tests addressing different aspects of the studied outcome.

in the future reported that PwMS with stronger beliefs regarding both the consequences of MS and its controllability through treatment were more likely to have used and to use rehabilitation in the future (Glattacker et al., 2018). A longitudinal study (Schiaffino et al., 1998) related "consequences" and "curability" (control) to higher and lower concurrent perceived illness severity respectively, while "variability" (beliefs regarding the cyclic nature of the disease) correlated with higher depression over time.

The two papers analysing illness perceptions among caregivers (Ackroyd et al., 2011; Bassi et al., 2016) were consistent in reporting that caregivers with higher emotional representations reported worse psychological health. Both papers also reported inter-dyadic influences, such as the link between PwMS's identity and consequences with partner's adversarial growth (Ackroyd et al., 2011) and the correlation between low coherence in the couple and lower positive affect among the PwMS (Bassi et al., 2016).

3.6. Illness perceptions as predictors of outcome variance

In addition to bivariate analyses (correlations), some papers used hierarchical multiple regressions, reporting illness perceptions as potential predictors of outcome. For example, Dennison et al. (2010), observed that the addition of PwMS' cognitive-behavioural responses to their symptoms and illness perceptions to a model including disease severity and phenotype explained 22.6% of the variance in functional impairment ($p < 0.01$), with the strongest predictors being unhelpful behavioural responses (such as avoidance) and "identity". The addition, to the same model (disease severity and phenotype), of other variables (e.g. acceptance, symptom responses) raised the percentage of total variance explained to 37% along with illness perception "coherence" accounted for a 37.1% of variance in distress ($p < 0.05$).

In the paper by Jopson et al. (2003) the illness perception dimensions (identity and consequences in particular) accounted for 29% of the variance in psychosocial dysfunction, 32% of the variance in anxiety ($p < 0.01$) and 32% of the variance in physical fatigue ($p < 0.01$).

In a multi-step model applied by Bassi et al. (2016), after controlling

for demographic variables, the introduction of each dimension of illness perceptions determined significant contributions to variance in: 1) psychological well-being due to PwMS' identity (6%, lower well-being), coherence (7%, higher well-being) and emotional representations (14%, lower well-being); 2) life satisfaction due to identity (7%, lower life satisfaction), coherence (10%, higher life satisfaction) and emotional representations (12%, lower life satisfaction); 3) positive affect due to coherence (11%, higher positive affect) and emotional representations (26%, higher positive affect).

Spain et al. (2007), after adding the illness perception dimension "identity" to a model containing other variables (such as illness measures, physical impairment, anxiety and depression), reported a significant contribution of 38% to variance regarding bodily pain and of 71% to variance pertaining physical functioning.

Vaughan et al. (2003) recorded a contribution of illness representations to explain 66% of variance in illness intrusiveness. In particular, stronger beliefs regarding the consequences of MS and the attribution to the disease to psychological causes predicted higher intrusiveness, while chronic timeline predicted lower intrusiveness. Identity was reported as a significant predictor of both the psychological and physical components of health-related quality of life in a model including disease severity, age and self-efficacy (Wilski and Tasiemski, 2016a).

3.7. Illness perceptions and outcome: mediation models

A small number of papers explored mediating mechanisms in the relationship between illness representations and outcome or alternatively described how the illness representations themselves acted as mediators (i.e. influenced the relationship between other variables and outcome).

Bassi et al. (2020, 2021), using multiple mediation models, focused on the possible mediators (coping and social support) of the relationship between illness perceptions and a variety of outcome measures (mental health, depression, satisfaction with life, psychological well-being, perceived physical health). The reported findings suggested that illness perceptions (consequences, identity, psychological causes, illness attribution to bad luck, emotional representations, coherence) may show mixed positive and negative effects, depending on the mediational effect of coping strategies (e.g. avoidance as a detrimental factor, problem-focused strategies as protective factors) and social support (protective factor). For example, stronger MS-related emotional representations related to lower physical health through higher use of avoidance and lower perceived social support (Bassi et al., 2021). Moreover, while stronger identity (number of symptoms attributed to the disease) directly related to worse outcome, it contributed to better outcome whenever coping strategies focusing on meaning were mobilized (Bassi et al., 2020).

Timkova et al. (2021) reported that self-esteem partially mediated the relationship between illness appraisals and well-being. More specifically, the adjusted models showed that the direct relationships between both "consequences" and "treatment control" and psychological well-being lost their statistical significance when self-esteem was added to the model as a mediator, while the direct relationships between both "emotional representations" and "concern" and psychological well-being persisted. In addition, positive illness perceptions and self-esteem jointly reduced the impact of other variables (e.g. low income, poor sleep quality, fatigue) on psychological well-being.

Regarding the possible mediational role of illness perceptions, Santos et al. (2019) demonstrated that identity and consequences mediated the relationship between PwMS' depression and worse quality of life (mental and physical, respectively). Wilski et al. (2019) reported that negative illness perceptions (overall) mediated the relationship between worse perceptions of MS-related physical condition and distrust towards treatment efficacy.

3.8. Effect size of the relationship between illness perceptions and outcome

Twelve out of 20 papers were analysed in terms of ES for the direct relationship between illness perceptions and outcomes (correlations). Two papers did not report correlations between illness perceptions and outcome (Neter et al., 2021; Heffer-Rahn and Fisher, 2018) and six papers did not report data from correlation analyses (Bassi et al., 2020; Jopson and Moss-Morris, 2003; Schiaffino et al., 1998; Spain et al., 2007; Wilski and Tomczak, 2017; Wilski et al., 2019). One study contained a direct reference to ES (Spain et al., 2007) and all the remaining 11 reported correlation coefficients or Odd Ratios.

The correlation coefficients suggested a medium ES (evaluated as detailed in the "Materials and methods" section; most frequent range: 0.30–0.40) for the relationship between illness perceptions and the variety of studied outcomes, with negative illness perceptions relating to worse outcome, regardless of its typology (physical, psychological, socioeconomic, etc.). Despite the papers reporting some differences in results, the overall ES of the relationship between illness perceptions and outcome was similar across studies, with the most represented values suggesting medium strength.

3.9. Disconfirming cases

Two out of the 20 papers included in this review did not support the relationship between illness perceptions and outcome. More specifically, one longitudinal study (Neter et al., 2021), the only one of this review focusing on the possible predictors of PwMS's adherence to and persistence in treatment, reported illness perceptions as uninfluential over these variables. In addition, a cross-sectional study reported a significant correlation between "consequences" (positive correlation: worse outcome), "treatment control", "personal control" (negative correlation: better outcome) and distress ($p < 0.01$). However, after controlling for demographic and clinical variables, illness perceptions did not account for additional variance in distress (Heffer-Rahn and Fisher, 2018).

4. Discussion

This review aimed to synthesize and critically appraise quantitative evidence regarding the relationship between illness perceptions (among PwMS and their caregivers) and outcome measures, including psychological, physical, illness management and socioeconomic aspects.

Only two out of 20 papers did not find an association between illness perceptions and outcome (Neter et al., 2021; Heffer-Rahn and Fisher, 2018).

All the other papers included in this review reported the existence of a moderate effect size when analysing the relationship between illness perceptions and outcome, whereby the perceptions entailing stronger beliefs of control, disease understanding, and attribution of the disease to external causes were related to better outcomes, while higher emotional representations and number of symptoms, illness attribution to psychological causes and stronger beliefs about the negative consequences of MS related to worse outcome.

Overall, the direction of the association (better or worse outcome) reflects the specific meaning of each perception. For instance, stronger beliefs regarding MS as causing a great number of symptoms (identity), serious repercussions on one's own life (consequences) and psychological distress (emotional representations), can be easily interpreted as perceptions that may relate to worse outcome (psychological, physical, social). Similarly, beliefs regarding a psychological cause of the disease (e.g. stress) may elicit feelings of guilt and hopelessness (since the person may feel himself/herself as irreparably "weak", being sensitive to stress), while the attribution to external causes or even bad luck may free the person from any responsibility, thus resulting in better health-related well-being (Bassi et al., 2020).

Considering positive beliefs, building upon Bandura's theory of self-efficacy (1977), it can be anticipated that the perceptions implying a

higher sense of mastery, such as personal and treatment control, as well as the belief of having a clear understanding of the illness (coherence), may prompt a more effective management of MS and reduce the level of distress.

As previously stated, the findings regarding timeline are inconsistent. However, it should be noted that despite cyclicality representing the core feature of MS (thus cyclical timeline actually represents an accurate depiction of its course), beliefs regarding this rather uncontrollable characteristic of the disease may not prompt specific coping efforts, thus limiting the importance of timeline on adjustment (Bassi et al., 2020).

The few studies addressing mediators highlight how illness perceptions do not exert their role in a vacuum, so that apparently "negative" beliefs may result in positive outcome. For example, the attribution of MS to psychological causes (i.e. life stressors), albeit theoretically negative (burdening the affected person with feelings of guilt and hopelessness, in relation to the perceived vulnerability of one's self), may potentially determine a positive change, prompting the PwMS to take better care of themselves, or modify their lifestyle, in order to reduce everyday stress. The different outcome, in such cases, may depend on both the coping strategies adopted by the PwMS and their perceived social support, as reported by Bassi et al. (2020, 2021). More specifically, the attribution of MS to psychological causes seems to determine worse or better psychological outcome when accompanied by avoidant or meaning/problem-focused coping, respectively (Bassi et al., 2020).

Similarly, perceived social support seems to be another important mediator of the relationship between illness representations and outcome. Indeed, more intense emotional representations and negative beliefs about the consequences of MS may be associated with lower physical health through lower perceived social support (Bassi et al., 2021).

These findings highlight that illness perceptions are deeply influenced by context and are strictly linked to coping, as acknowledged by Leventhal et al. (2003). Indeed, it is easy to envision that both the environment and the specific beliefs held by a person may elicit coping efforts that seem to be congruent with the person's opinions. In this context, even the unexpected, and apparently paradoxical, relationship between increased coherence and lower mental health, reported in one paper, may be explained (Santos et al., 2019). On the one hand, less information may protect the person from the psychological burden related to "knowing too much" (as commented by the authors themselves). On the other hand, this finding might be related to specific coping strategies or contextual factors, that were not considered in the paper.

Building on this influence of other factors, the caregivers' perceptions may also represent significant contributors to outcome. Unfortunately, the paucity of the papers covering caregivers' perceptions does not allow us to draw conclusions. However, promising results arose from the analysed papers: PwMS' illness representations may influence partners' adjustment and, vice versa, shared negative perceptions may negatively influence PwMS' outcome (Ackroyd et al., 2011; Bassi et al., 2016).

Despite the quality of the papers being acceptable overall, some specific limitations arose, that should be addressed in future studies focusing on the relationship between illness perceptions and outcome. In particular, the most common flaws identified across the papers related to theoretical (lack of a clear framework) and methodological aspects, such as failure to address the measurement tools' validity within the analysed sample, lack of explanation pertaining the rationale for use of specific tools, limited information on how primary data were collected, absence of considerations regarding sample size when designing the research. These limitations led to the attribution of a lower score at the QATSDD during the critical appraisal phase. For the sake of completeness, it should be noted that some papers included in this review may have been "penalised" (e.g. papers considering aspects, such as service use, that do not require validated questionnaires) over others scoring high on quality but showing a poor presentation of the results (an aspect not considered by the tool).

Our findings are consistent with those of other reviews (Pai et al., 2019; Richardson et al., 2017). In particular, Pai et al. (2019), focusing on the link between illness perceptions and psychological adjustment in stroke, reported that identity, consequences and emotional representations were related to higher distress, while coherence was associated with lower distress.

Richardson et al. (2017) focusing on persons with cancer, reported moderate to large effect sizes between illness representations (in particular, identity, emotional representations, consequences) and psychological distress.

4.1. Strengths and limitations of this review

This review has some limitations. Firstly, despite the quality of papers being addressed, all studies were granted the same weight when interpreting the results. Moreover, the reported ES has been grossly inferred from the studies, considering each paper overall, without specifying the ES of every single correlation. However, it should be noted that this is a narrative review of heterogeneous papers, aiming at offering an overview of the topic of interest. Considering the limitations of the included papers themselves, the cross-sectional nature of almost all them does not allow us to infer causation. Nonetheless, the overall sample size and quality of the papers was acceptable which enabled us to draw conclusions.

The inclusion of qualitative studies may have added value to this review, but the specific review question, implying the search for associations, demanded the selection of quantitative ones.

The main strength of this paper is that of considering outcome from a broad perspective. Indeed, no specific outcomes to be included were considered *a priori,* so that this review not only contributes to answer the main question but also allows identification of the topics that have been investigated when considering outcome among the specific population of PwMS and can highlight what has been overlooked. In particular, our findings highlight the paucity of studies involving caregivers (mostly partners). This gap in the literature could prompt research specifically focusing on illness perceptions within the PwMS-partner dyads and the variables influencing such perceptions.

4.2. Clinical implications and future work

The findings of this review may inform psychological interventions aimed at reducing negative representations, ultimately improving couples' adaptation to MS. For example, a paper (Chiong-Rivero et al., 2021), focusing on the efficacy of an educational intervention (watching a short narrative film) in improving illness perceptions, reported more positive appraisals regarding treatment and understanding of the disease in exposed versus not exposed PwMS. However, research in this area is limited and future studies with longitudinal design and which address the complex nature of illness perceptions and their development (e.g., quality of PwMS-caregiver relationship, personality characteristics, etc.) may further inform tailored psychological approaches.

Ethics

Not applicable.

Authors' contributions

ML: research conduction and writing of the paper; FE and GPA:

supervision and critical revision of the paper; FP: quality control of the review process and critical revision of the paper.

Declaration of Competing Interest

None.

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