

# The experience of fatigue in neurological patients with multiple sclerosis

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## Accepted Manuscript

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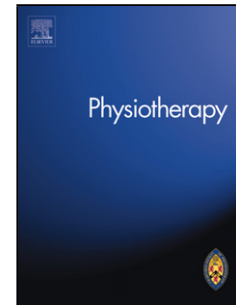
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Title Page

**Title: The Experience of Fatigue in Neurological Patients with Multiple Sclerosis: A Thematic Synthesis**

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**Contribution of the Paper**

- To the best of our knowledge, this is the first qualitative synthesis considering the common experiences of multiple sclerosis related fatigue (MSRF).
- This synthesis has provided a consensus of understanding around common experiences of MSRF and theoretically saturated themes, a feature lacking within empirical studies.
- MSRF management strategies used by patients most commonly were planning and prioritising activities and interactions, accepting the different and varied impact and meaning of MSRF and using rest and sleep for recovery. Physiotherapists could remember this by using the acronym “PAR” (Planning, Acceptance, Rest).
- MSRF is influenced by psychological and environmental factors that relate to the experiences of secondary fatigue. We provide evidence of how physiotherapists could limit the impact of such factors on patients.

## **ABSTRACT**

### **Objectives**

To identify the experiences that result from MS-related fatigue (MSRF) through a systematic review and thematic synthesis of qualitative literature.

### **Design**

The thematic synthesis was undertaken in three stages: (1) a systematic review of the literature, searching relevant databases from their inception to March 2016. (2) A critical appraisal of included studies, and (3) a double blind 2-phase synthesis of results was undertaken.

### **Setting**

Participants were included from articles using primary and secondary care settings.

### **Participants**

The synthesis included nine articles that incorporated a total of one hundred and fifty two participants (103 females and 49 males) were included in the review.

### **Results**

No articles were excluded following critical appraisal. Two major themes were synthesised: (1) biopsychosocial experiences of fatigue, which illustrated the physical, cognitive and social challenges patients experience (2) experiences that alter the impact of fatigue including the strategies individual employ to help manage fatigue. These major themes were further split into five subthemes.

### **Limitations**

Only the most common experiences of MSRF were identified. Findings did not break down results by key demographics e.g. disease type. Only English language studies were included.

### **Conclusion**

Physiotherapists are able to support the management by: (a) having a greater understanding of MSRF and (b) being able to help patients manage the factors that influence it.

**Key Words:** Fatigue, Multiple Sclerosis, Qualitative, Synthesis, Experience

## INTRODUCTION

Multiple Sclerosis (MS) is an autoimmune inflammatory condition, affecting the central nervous system, including the brain and the spinal cord. MS is characterised by an unpredictable course, which often results in substantial disability [1]. Three primary types exist including; relapsing remitting MS (exacerbation of symptoms through distinct attacks which fade after a time; 85% of people), primary or secondary progressive (a build up of disability and symptoms that is sustained) and Benign (limited disability and symptoms over an extended period of time). Around 2.1 million people have MS worldwide [1]. MS is the most common neurological disorder in young adults in the UK; it affects around 0.2% of people in Scotland [3], is often less prevalent in countries that near the equator [3] and is more common in women than men [2,3]. MS patients experience a wide range of clinical symptoms, fatigue being one of the most common [4] and disabling [5]. For instance, fatigue is regarded as the most important factor which influences decisions about continuing or stopping work [6].

MS-related fatigue (MSRF) has been defined as a reversible, motor and cognitive impairment, which can occur spontaneously or can be brought on by mental or physical activity [7]. MSRF can be subtyped into primary and secondary fatigue. Primary fatigue is defined as direct damage to the CNS (e.g. demyelination, heat sensitivity or cognitive fatigue). Secondary fatigue is associated with symptoms of MS e.g. side effects from medication or sleep problems. The causes of secondary fatigue are usually more amenable to treatment [8].

MSRF is different to from normal fatigue due to its increased severity and ability to effect daily activities. MSRF is identified as complex and subjective and influences the bio-psychosocial and emotional aspects of the patient's life [5, 9]. Due to the complexity of

MSRF and its multi-dimensional nature it is poorly understood [10]. The main reasons for this lack of understanding include that; (a) the pathogenesis is unknown (we do not consider this in more detail in this paper) [2,3,4], (b) the experience of fatigue for individuals with MS is different to that experienced by the healthy population [11], (c) the subjective experience of fatigue does not correlate to objective physical signs, and (d) two of the most utilised scales that measure fatigue (Fatigue Severity Scale; FSS and Modified Fatigue Impact Scale; MFIS) have been identified as insensitive and unresponsive to changes in a patients fatigue level [12]. MSRF is therefore known as an invisible symptom [13].

Physiotherapists often as part of a multi-disciplinary team, identify a specific rehabilitation programme for patients, aid and manage long term symptoms and functional abilities and promote self-management and co-ordinate care for patients [14]. Poor understanding of MSRF makes the clinical management challenging. Physiotherapists generally do not understand, and consequently underestimate, an individual's experience of MSRF and its detrimental impact on daily life, this can negatively impact on the treatment provided [5]. Creating a consensus of common experiences identified from qualitative research of MSRF would aid the physiotherapists treatment and clinical practice.

A number of reasons may explain the lack of understanding by physiotherapists of MSRF including; (a) a reliance on quantitative self-report measures that are often not effective in identifying MSRF despite individuals subjectively reporting it [4], (b) a use of broader scales of fatigue (e.g. FSS and MFIS) that are limited to the impact of fatigue rather than considering how or why fatigue affects a patient and (c) quantitative review based evidence that focuses on the effect or association between symptoms and experiences [15,16], e.g., association between embarrassment about symptoms and remission status [15] rather than understanding how or why that is experienced by the individual and what factors influence

this experience. Qualitative syntheses are required in order to provide details on the experiences of MSRF [16]. The purpose of the current review is to gain an in-depth understanding of the wide range of common subjective experiences of MSRF.

## 2.0. METHODS

### 2.1. Methodology

A 'subtle realist' position<sup>1</sup> was adopted, it has been utilised in other qualitative reviews that consider the experience of patients with MS [1]. The thematic synthesis [17], was undertaken in three stages: 1) a systematic review of the literature, 2) a critical appraisal of the included studies and 3) a two phase thematic synthesis of qualitative results from the included studies.

### 2.2. Systematic Search of Included Studies

Details of the systematic search can be found in the Supplementary file.

#### Eligibility criteria

The eligibility criteria were based on the SPIDER (sample, phenomenon of interest, design, evaluation, results type) tool [18]. Studies were included if:

- **Sample:** studies identified that patients had a medical diagnosis of MS and who experience fatigue as one of their symptoms.
- **Phenomenon of interest:** articles needed to focus on patient's recollections of what fatigue felt like for them and no other stakeholder's view was deemed appropriate, for instance, MSRF is often invisible and rarely understood by others [5].

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<sup>1</sup> The supplementary file provides further consideration and a defence of this position.



- **Design:** all qualitative designs were deemed appropriate for inclusion. Mixed method studies were included if they obtained a clear qualitative results section. Reviews, books, fictional writing and conference proceedings were excluded.
- **Evaluation:** articles were included if they involved interviews or focus groups, investigating experiences and opinions of fatigue. The topic of MSRF had to be included within the interview schedule and be represented by a theme within the results.
- **Results type:** qualitative and mixed methods results were included. Articles must be published in English.

### 2.3. Critical Appraisal of the Included Studies

An adapted 13-item version of the Consolidated Criteria for Reporting Qualitative Studies (COREQ) was used as it has been identified as sensitive to assessing qualitative studies in MS [1]. The 13-item tool (scoring out of 13; one point for covering the question correctly) consisted of 3 domains; 1) 'research team and reflexivity' (5 items) focusing on both personal characteristics and relationship with participants; 2) 'study design' (5 items) analysing the theoretical framework and data collection; 3) 'analysis and findings' (3 items) examining both data analysis methods and the reporting of information. Authors GN and AG conducted a blind critical appraisal of the methodological aspects of studies, disputes were identified and resolved with the author AS.

### 2.4. Thematic Synthesis

A 2-phase approach to synthesis was undertaken. During phase 1 authors GN and AG undertook blind data driven synthesis. The steps included 1) coding the text 'line-by-line', 2) development of descriptive themes and 3) the subsequent generation of 'analytical

themes'. The themes were generated by 'idea webbing' to understanding how concepts, themes and subthemes link together [18] and 'concept mapping' to allow exploration of ideas [19,20]. Both authors removed concepts that didn't have at least 2 articles supporting them. During phase 2 author AS considered both thematic frameworks and integrated the blind analyses. Full details are available from the corresponding author.

### **3.0. RESULTS**

#### **3.1. The Systematic Search**

Nine articles met the inclusion criteria [5, 7, 21-27]. One hundred and fifty two individuals (103 females and 49 males) participated in the nine studies. All participants were clinically diagnosed with MS and experienced fatigue as a symptom. Of the 152 participants, 18 had primary progressive MS, 43 had secondary progressive, 44 had relapsing remitting and 47 remained unknown. The aggregated mean age (across 8/9 studies) was 47.8 years. The aggregated mean time post diagnosis of MS (across 7/9 studies) was 13.9 years. Studies originating from six countries, the most common were Sweden (n=2), America (n=2) and New Zealand (n=2). The supplementary file shows a PRISMA diagram and checklist [28] demonstrating the full search process. Table 1 provides full demographic information.

#### **3.2. Critical Appraisal of the Included Studies**

The COREQ scores range between 6 and 8 and no fatal flaws (methodological weaknesses that compromised the study) were identified and all studies were included in the synthesis. See supplementary file for a summary table.

Within COREQ tool analysis

Domain one was the lowest scoring domain with an average of 1.8/5. Within this domain, experience and training of the interviewer, participation knowledge of the interviewer and interviewer characteristics with reference to minimising bias were rarely reported or considered. Domain three, achieved the highest score with an average of 2.7/3. Occasionally within domain three, clarity of minor themes were not included within the studies. Finally domain two scored relatively high with an average of 3.2/5. Detail within this domain was often given about interview guides; however, data saturation and non-participation were rarely stated.

### **3.3. Thematic Synthesis**

The synthesis of the included articles generated two main themes:

- (1) Biopsychosocial experiences of fatigue; and
- (2) Factors that influence fatigue.

A summary of the thematic synthesis with verbatim quotations is provided in Table 2. The text identified below provides an analytical summary of the thematic content.

#### **3.3.1. Theme 1: Biopsychosocial Experiences of Fatigue**

The impact of MSRF existed across physical and functional experiences, psychological (cognitive and emotional) experiences and social experiences. Accordingly four subthemes illustrate this range of impact.

##### **3.3.1.1 Subtheme 1: Physical descriptions and experiences of fatigue**

This sub-theme had four codes: (a) a lack and loss of energy; participants described the lack, loss and reduction of energy within the entire body. They identified feelings of being both empty of energy and drained of energy and strength during tasks. (b) The experience of heavy limbs; fatigue caused an inability to move and perform physical functions. Most often

with the lower limbs feeling heavy e.g. had to drag a foot during walking. (c) The inability and restriction of movement; individuals identified experiences where they felt unable to move and feelings that they were paralyzed. This often occurred once energy had run out where individuals felt overwhelmed and like their body was shut down. (d) (in)ability to perform activities and utilisation of aids; individuals identified limitations in physical functioning and an inability to perform activities of daily living; this included specific functions e.g. not being able to drive or the need for mobility scooters and aids.

#### 3.3.1.2 Subtheme 2: Cognitive experiences of fatigue

This subtheme had two codes: (a) Restrictions in thinking; individuals experienced moments when they were unable to think clearly, this included experiences where they felt as if they were in a dream or not fully aware of being present in the moment or situation. The environment could influence this e.g., noisy environments could interfere with the ability to think. (b) difficulties concentrating and memorising; individuals experienced difficulties in concentration on topics during conversations and expressed an inability to absorb information and remember information subsequently. Greater effort and time was needed to take on information and remember it. This directly impacted on meaningful activities and interactions.

#### 3.3.1.3 Subtheme 3: Emotional experiences of fatigue

This subtheme had two codes related to emotions that were associated with fatigue: (a) Sorrow, shame, depression and isolation; individuals could express feeling worthless and disappointed, as well as feeling shame and being embarrassed about the impact the MS had in their lives (e.g., falling or inability to walk) and the function of their bodies. This could have a negative impact on their social identity due to being isolated from others. (b) Fear, worry and anxiety; Fear and worries were generated regarding the ability to complete

activities (e.g. walking). Individuals worried about how difficult it would be to complete an activity or how others perceive them. The meta-perception about how their activities were performed could generate shame and embarrassment.

#### 3.3.1.3 Subtheme 4: Social experiences of fatigue

This subtheme had two codes associated with MSRF: (a) Losses of autonomy and dependency; individuals' expressed a reduction in autonomy and ability to be independent when attempting to complete activities of daily living. This was associated with feelings of dependency on others, helpless and also included an inability to engage in interactions. (b) Not being understood by others because of MSRF; it was identified that others (family, health care professionals, friends) could lack insight to the symptoms and not be able to understand the experiences of MSRF. Further, health care professionals could dismiss the symptoms and therefore failed to provide helpful advice.

### 3.3.2. Theme 2: Factors that Influence Fatigue

This theme was divided into four subthemes but no codes were identified: (a) Variation of fatigue by season and weather; warm and hot weather that could make individuals feel sluggish and increase fatigue. Alternatively cold weather could increase the experience of spasticity, a symptom with possible association with fatigue. (b) Accepting the impact and uncertainty of fatigue; being able to accept the fatigue and what it meant within their lives (e.g., tasks would take longer, it can be unpredictable as a symptom, or that activities may not be possible or there would be limits to them) could help patients' feel more empowered and enhance their perceived ability to cope and manage the MSRF. (c) Managing fatigue through planning and prioritising activities and interactions; Being able to plan and prioritise activities, plan rest and become good at self-regulating activities helped patients' manage

MSRF. The value in planning was that it helped individuals maintain strength and conserve energy so the potential for activity participation could be reached. (d) Using rest to manage fatigue; individuals identified the important and need for rest. This included immediate rest (e.g., needing to lie down immediately) because of the fast onset of MSRF, as well as rest in preparation for an event. Short periods of rest (10-30 mins) could aid energy levels and provide relief to fatigue.

#### **4.0. DISCUSSION**

To the best of the author's knowledge, the current review is the first to bring together existing qualitative studies that examine the experience of MSRF. The critical appraisal identified that the methodological quality of the studies was good. The theoretical saturation of themes can provide direction for future qualitative research to be conducted. The results identified a clear association between the secondary causes of fatigue and behavior. These results are able to identify how clinicians can respond to and help patients with their experiences of MSRF.

##### **4.1. Experiences of MSRF**

###### The need to manage losses of energy and low energy

The review highlighted a clear impact on the energy levels of patients and the reduction of strength as well as the impairment of function. In agreement with past research [29] the current results identified the importance of managing secondary fatigue (e.g., a lack of physical activity and physical deconditioning, sleep disorders, and psychological factors like depression). Physiotherapists should consider three principle aspects of MSRF management reported by patients within this review: (1) the importance of planning and prioritising

activities and interactions in order to conserve energy, (2) the potential benefits of being able to accept MSRF and (3) the benefit of rest and sleep to maintain and regain energy. These strategies should be supplemented with a combination of exercise or behavioral and psychological approaches [30]. The implications section considered this further.

### Psychosocial Experiences of Fatigue

Psychological experiences included both cognitive and emotional experiences of fatigue. The current review identified the impact of cognitive experiences including; decreased concentration, the inability to think clearly and poor memory. These illustrative personal accounts are supported by previous quantitative research [4, 31]. Emotional experiences were portrayed when participants perceived not being able to manage compared to the healthy population. It is likely that emotions including worry and fear are associated with undertaking less social activities. Future research should consider the association between MSRF and emotions, psychological adaptation and behaviour.

Previous research e.g. [8, 32] has identified that fatigue limits social activities, e.g., during a relapse of MS the impact of this is greater [14]. It is also apparent that a lack of understanding [33] or disinterest from others could prevent social engagement.

Physiotherapists should help patients consider the dependency on others which may arise and ensure that carers and family are informed of the influence of MSRF on the patient

### The importance of acceptance and managing MSRF

Participants within this review stated that acceptance decreased the impact of fatigue. Recent research has highlighted the importance of acceptance, in that it can enhance an individual's quality of life and their mental well being [34]. The current review identified

that the implementation of other patient centered management strategies are important including: (a) relieving factors like reducing temperature. (b) Planning and prioritizing, studies from this review identified that planning and prioritising are of vast importance to managing fatigue. Previous research supports this [1], but also highlights the importance of adaptable goals [35]. Finally, (c) It was found to be essential to incorporate adequate rest and sleep within patient's daily lives. Indeed, short rests throughout the day or one longer rest is found to help reduce fatigue [30].

### **4.3. Implications for Practice**

Fatigue in MS is subjectively experienced and may be misunderstood and misinterpreted by family members, friends, work colleagues and healthcare professionals [31]. Patients require physiotherapists to have more knowledge, be more empathetic and become better at information provision regarding MSRF [36,37]. Greater understanding of MSRF is required to stop physiotherapists relating their own experiences of fatigue to how the patients are feeling [25]. Educating both family members or carers will allow patients to work in a partnership with someone else which can promote coping [35]. Physiotherapists need to manage psychological factors like a sense of control or depression and mood [29]. Physiotherapists should consider using educational programs that incorporate mindfulness, energy conservation and fatigue management strategies [29, 30, 38]. The clinical assessment of MSRF must be undertaken with a measure that is of most relevance to the fatigue experience by the individual and must include broader factors, which are associated with secondary fatigue (e.g., mood and sleep) [39]. Theory based research may be well placed to support this [40]. One recent theory focuses research towards, supporting and measuring hope, psychological adaptation, emotions and encouraging patients with MS to



identify the choices they have and to act on those choices [41]. The core elements of the theory can be assessed very simply and quickly by Physiotherapists [42].

#### **4.2. Limitations**

Unique findings may have been lost during this type of synthesis that focuses on the most common experiences. This review may reflect themes and interests generated by the authors. Findings may be difficult to generalise to the entire MS population due to the inability to break down results by disease type, status or time since diagnosis and gender or country. Only English language studies were included which will have limited the results.

#### **4.5. Conclusion**

Physiotherapists should consider the most consistent MSRF management strategies used by patients as well as understanding the biopsychosocial experiences of MSRF identified by patients. Physiotherapists can utilise this information in practice to ensure that patients receive the highest quality of care possible.

#### **Conflict of Interest:**

None

#### **Acknowledgement:**

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Table 1: Summary data extraction table of included studies.

Authors	Aim	Methodology and Methods	Participants	Main themes around MS related fatigue and recommendations
Coenen et al <sup>21</sup>	To consider the patients perspective of functioning and disability	Methodology: Framework used for analysis.  Methods: Focus groups	<u>Number of participants</u> : 27 (19 females and 8 males). <u>Recruitment source</u> : Individuals who attended an MS centre in Germany. <u>Sampling method</u> : Maximum variation and purposive. <u>Diagnosis</u> : Clinically diagnosed MS. RR: 11. PP: 5. SP: 11. <u>Years since diagnosis</u> : Mean: 13 years (range 1-48 years). <u>Age</u> : Mean: 50 years (range 28-73 years). <u>Country</u> : Germany.	1327 concepts identified linked to 171 ICF categories.  Qualitative analysis identified the problems related to fatigue.  Recommendations: The development of international standards for comprehensively describing functioning and disability in individuals with MS.
Flensner et al <sup>5</sup>	To describe MS-related fatigue as lived by a group of MS patients.	Methodology: Phenomenology  Methods: Qualitative semi-structured Interviews	<u>Number of participants</u> : 9 (5 females and 4 males) <u>Recruitment source</u> : MS-group within a branch of Swedish Association of Neurological Disability. <u>Sampling method</u> : Purposive. <u>Diagnosis</u> : Clinically diagnosed MS. No sub-type given. <u>Years since diagnosis</u> : Mean: 22 years (range 3-46 years) <u>Age</u> : Mean: 56 years (range 25-88 years). <u>Country</u> : Sweden.	9 themes: Non-constructive themes: <ul style="list-style-type: none"> <li>- Time consuming and all absorbing</li> <li>- Involvement of the body</li> <li>- Energy loss</li> <li>- Emotional perception</li> <li>- Dependency</li> <li>- Restrictions of life</li> </ul> Constructive themes: <ul style="list-style-type: none"> <li>- Desire for acceptance of life</li> <li>- Desire for a structured daily living</li> <li>- Means of assistance</li> </ul> Recommendations: To investigate connections between conditioning factors for self-care and fatigue.
Johnson et al <sup>22</sup>	To gain a better understanding of the	Methodology: Phenomenology	<u>Number of participants</u> : 16 (14 females and 2 males) <u>Recruitment sources</u> : (1) A newsletter by the MS	5 themes: <ul style="list-style-type: none"> <li>- Profound</li> </ul>

	benefits and barriers by persons with MS in the workplace.	Methods: Qualitative semi-structured interviews.	Association of King County, (2) medical centre rehabilitation counsellors and (3) outpatient clinic MS nurses and by word of mouth. <u>Sampling method</u> : Purposive. <u>Diagnosis</u> : Clinically diagnosed MS. Types not identified. <u>Years since diagnosis</u> : Mean: 8.9 years (range: 4-16 years). <u>Age</u> : Mean: 43.7 years (range: 27-62 years). <u>Country</u> : USA.	<ul style="list-style-type: none"> <li>- Unpredictable</li> <li>- Invisible to others</li> <li>- Affects thinking</li> <li>- Cognitive change is frightening</li> </ul> <p>Recommendations: Consideration by HCPs regarding MS related fatigue and employment is needed. Decisions regarding employment should be made after symptoms/exacerbation is reduced.</p>
Kayes et al <sup>23</sup>	To gain understanding into facilitators and barriers to engagement in physical exercise for people with MS.	Methodology: Grounded Theory  Methods: Qualitative semi-structured interviews	<u>Number of participants</u> : 10 (7 females and 3 males) <u>Recruitment sources</u> : (1) Advertisement through local MS societies, (2) on district health board in New Zealand and (3) from on larger study. <u>Sampling method</u> : purposive sampling. <u>Diagnosis</u> : Clinically diagnosed MS. RR = 4 PP = 3 SP = 3 <u>Years since diagnosis</u> : Mean: 11.5 years (range 3-17 years) <u>Age</u> : Mean: 44.1 years (range 34-53 years). <u>Country</u> : New Zealand	3 themes: <ul style="list-style-type: none"> <li>- Beliefs about physical activity relating to fatigue.</li> <li>- Emotional response to physical activity and fatigue.</li> <li>- The experience of fatigue.</li> </ul> <p>Recommendations: To explore the barriers and facilitators to engagement in physical activity from the perspective of people with MS. Focusing on the role of fatigue in the decision to take up physical exercise.</p>
Mills and Young <sup>7</sup>	To define the symptoms of fatigue, as experienced by patients with MS.	Methodology: Mixed Methods  Methods: Qualitative semi-structured interviews.  Cross sectional	<u>Number of participants</u> : 40 (32 females and 8 males) <u>Recruitment source</u> : The Walton Centre outpatient clinic. <u>Sampling Method</u> : Purposive. <u>Diagnosis</u> : Clinically diagnosed MS RR: 19 PP: 5 SP: 16 <u>Years since diagnosis</u> : Mean: 16.3 years (range 1-41)	11 themes: <ul style="list-style-type: none"> <li>- Motor features</li> <li>- Cognitive impairment</li> <li>- Motivation, energy and need to rest</li> <li>- Behavioural response including sleep</li> <li>- Other (i.e. yawning)</li> <li>- Cadence</li> <li>- Chronicity</li> <li>- Precipitating/aggravating factors</li> </ul>

		questionnaire.	years). <u>Age</u> : Mean: 49 years (range: 34-78 years) <u>Country</u> : UK	<ul style="list-style-type: none"> <li>- Relieving factors</li> <li>- Severity</li> <li>- Associated factors.</li> </ul> <p>Recommendations: To utilise both quantitative and qualitative definitions of MS related fatigue in order to have a comprehensive understanding of it.</p>
Moriya and Kutsumi <sup>24</sup>	To gain descriptors of the experience of fatigue in MS patients, including experiences relating to their interpersonal relations and social life.	<p>Methodology: Exploratory approach.</p> <p>Methods: Qualitative semi-structured interviews.</p>	<p><u>Number of participants</u>: 9 (6 females and 3 males) <u>Recruitment source</u>: Publically advertised through support groups. <u>Sampling Method</u>: Purposive. <u>Diagnosis</u>: Clinically diagnosed MS. Type not given. <u>Years since diagnosis</u>: Mean: 9.2 years (range: 1-17 years). <u>Age</u>: Mean: 42.3 years (range: 31-57 years). <u>Country</u>: Japan.</p>	<p>7 themes:</p> <ul style="list-style-type: none"> <li>- Unique and novel experience</li> <li>- Self-analysis of factors that are associated with fatigue</li> <li>- Effects on living and the self</li> <li>- Unique measure of handling fatigue</li> <li>- Incompleteness of the measures for treating fatigue</li> <li>- Living with fatigue i.e. acceptance</li> <li>- Lack of understanding</li> </ul> <p>Recommendations: Conduct further studies to understand the overall picture of how people with MS experience fatigue.</p>
Olsson et al <sup>25</sup>	To elucidate the meaning of fatigue for women with MS.	<p>Methodology: Phenomenological hermeneutic method</p> <p>Methods: Qualitative semi-structured interview</p>	<p><u>Number of participants</u>: 10 females <u>Recruitment source</u>: Hospital rehabilitation clinic in the South of Sweden. <u>Sampling Method</u>: Purposive. <u>Diagnosis</u>: Clinically diagnosed with SP MS SP = 10. <u>Years since diagnosis</u>: not stated. <u>Age</u>: Mean: 49 years (range: 43-59 years) <u>Country</u>: Sweden.</p>	<p>5 themes:</p> <p>Experiencing the body as a barrier:</p> <ul style="list-style-type: none"> <li>- Heavy body</li> <li>- Having the will but not the ability</li> <li>- Saving strength and needing rest</li> </ul> <p>Experiencing a different absence:</p> <ul style="list-style-type: none"> <li>- Unusual and invisible feeling</li> <li>- Feeling of being absent</li> </ul> <p>Recommendations: For nurses and other HCP's to have an understanding of what MS fatigue is like and not to compare it to their own feelings of</p>

				tiredness. More research into possible interventions that will aid women in their everyday lives and maintain a sense of normality.
Smith, Fitzgerald, Whitehead <sup>26</sup>	To gain understanding of how MS related fatigue influences exercise participation in men.	Methodology: Interpretivism and a descriptive approach.  Methods: Qualitative semi-structured interviews	<u>Number of participants</u> : 18 males. <u>Years since diagnosis</u> : mean not given. <u>Recruitment sources</u> : (1) Advertisement in MS Society local branch newsletters in Otago, Canterbury and Southland regions and (2) on the Facebook page of the National New Zealand MS society. <u>Sampling Method</u> : Purposive <u>Diagnosis</u> : Clinically diagnosed with MS RR: 10 PP: 5 SP: 3 <u>Years since diagnosis</u> : Mean: not stated (range: 3-21 years) <u>Age</u> : Mean: not stated. (Range: 36-68 years) <u>Country</u> : New Zealand	3 themes: - Complex expressions of fatigue - Engaging in exercise and goal adjustment - Emotional responses to fatigue and exercise.  Recommendations: To explore the differences in framework of gender and health construction.
Stuifbergen and Rogers <sup>27</sup>	To elicit a description of the experience of fatigue within MS, its perceived antecedents and the self-care strategies used to manage fatigue.	Methodology: Exploratory  Methods: Qualitative semi-structured interviews.	<u>Number of participants</u> : 13 (10 females and 3 males) <u>Recruitment source</u> : Notices in a local newspaper for persons with MS. <u>Sampling Method</u> : Purposive <u>Diagnosis</u> : Clinically diagnosed MS. Type not stated. <u>Years since diagnosis</u> : Mean: 13.9 years (range 2-27 years) <u>Age</u> : Mean: 44.6 years(range: 35-63 years) <u>Country</u> :	5 themes: - Constant and ongoing experience - Vast impact on life - Exacerbation of symptoms - Paralyzing force - Extreme nature of fatigue  Recommendations: More research into the effect of exercise programs and specific interventions on fatigue in those with MS. Increasing knowledge and understanding of



				fatigue among healthcare professionals and readily issuing helpful tip sheets to manage fatigue.
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Note: PP = Primary progressive, RR = Relapsing remitting, SP = Secondary progressive, MS = Multiple Sclerosis, HCP = Health care professional.

Table 2: The thematic structure from the analysis

Primary author Theme	Primary author Sub-theme and code	Code (GN)	Blind Code(s) from AG	Agreed Code title definition and example units from studies
Biopsychosocial experiences of fatigue	Physical descriptions and experiences of fatigue	Reduction and loss of energy and strength	A physical lack and loss of energy	Agreed definition: A lack and loss of energy  Example units: "Loss of strength to low energy levels" (8). "Fatigue meant that they always seemed to have less energy and strength" (2).
		Lower limbs described as feeling 'heavy'	Metaphors and expressions that relate to feelings of heaviness	Agreed definition: The experience of heavy limbs  Example units: "heaviness in limbs or body" (5). "Legs as feeling like several tons" (7). "Wearing a trenchcoat that goes down to your ankles and it's made of lead". (8)
		A paralysing experience	Metaphors and expressions that relate to an inability to move and feelings of paralysis	Agreed definition: The inability and restriction of movement  Example units: "Overwhelming effects of fatigue and her experience of the paralyzing force" (9). "On some days fatigue means not being able to get out of bed" (3). "your body shuts down" (4)
		Abilities to perform activities of daily living and exercise	The impairment of activities and utilisation of mobility and functional aids	Agreed definition: (in)ability to perform activities and utilisation of aids.  Example units: "After exercise you feel sort of emptied out and your body's sort of empty." (8) wearing diapers due to extent of fatigue making getting to the bathroom impossible. (6)
	Cognitive experiences of fatigue	Inability to think clearly  Restrictions in engaging in social	Not being present in the moment	Agreed definition: Restrictions in thinking  Example units: "brain not totally clear" (7). "I don't think as clearly" (3).

		activities due to surroundings		<p>"Like being in a dream." (9)</p> <p>"Loss of judgment and/or perception." (9)</p> <p>You are there without being. That's probably the normal. I can't describe it." (7)</p>
		Poor memory, struggle to absorb and retain information	Difficulties in concentration and impairment	<p>Agreed definition: Difficulties concentrating and memorising</p> <p>Example units:</p> <p>"I have trouble concentrating on what people are saying" (3).</p> <p>"I can't remember anything and I don't want to remember anything" (9).</p> <p>"I can't retain the information" (3).</p> <p>"I cannot concentrate as I did before due to fatigue. By the way, this is my major problem" (1)</p>
	Emotional experiences related to fatigue	Feeling worthless or disappointed in themselves	<p>Feelings of depression, sorrow, shame and embarrassment</p> <p>Being lonely and isolated and consequently depressed</p>	<p>Agreed definition: Sorrow, shame, depression and isolation</p> <p>Example units:</p> <p>"When failing or not managing, emotional perceptions of being worthless" (2)</p> <p>"I am often very disappointed in my body because it doesn't do what I want it to do"(1)</p>
		Fears and worries about the difficulty of activities Worry, fear and stress could increase fatigue.	Feelings of anxiety	<p>Agreed definition: Fear, worry and anxiety</p> <p>Example units:</p> <p>"worries and thoughts about how hard something was going to be could in themselves bring about the onset of fatigue" (2)</p> <p>"Fear of am I going to be able to handle a situation, if I get tired" (3)</p> <p>Anxiety toward challenges due to fatigue. (6)</p>

	(4) Social experience s of fatigue	Dependency on others to accomplish everyday taken for granted tasks	Loss of autonomy and independence when driving licenses were revoked  Feelings of dependency, helplessness and being a burden	Agreed definition: Losses of autonomy and dependency  Example units: “help from others consists of asking for, accepting, and/or receiving help from others to accomplish tasks of everyday living” (9). “trapped in the sense of needing help from other people” (2)
		Lack of understanding by others because it was an invisible symptom.	Frustration at lack of understanding among friends, family and health care professionals  Dismissive or poor attitude of health care professional	Agreed definition: Not being understood by others  Example units: “people had difficulty understanding their condition” and “an unusual and invisible feeling” (7) “When I went to an art museum, I got tired and became unable to walk. Because I looked so healthy, [others] didn’t quite understand. I said “Could you lend me a hand?” But, it took quite a bit [of time until I was understood]. I should have said “pain” rather than “fatigue”, but I wasn’t understood.” (6)  “It doesn’t always show on the outside that you’re fatigued. Instead it’s more here inside, so others can say, ‘What now, are you going to sit down?’ But I can’t manage.” (7)
Factors that influence fatigue		Fatigue could very greatly by season and weather	The effect of warm and cold weather	Agreed definition: Variation of fatigue by season and weather  Example units: “heat” and “intense sunlight” (9) increase fatigue. “Hot or humid environments could cause fatigue such as a warm room, hot shower or a car without air conditioning” (5).
		Acceptance of fatigue led to self-care strategy that helped manage	Acceptance of and adjustment to fatigue and its unpredictability	Agreed: Accepting the impact and uncertainty of fatigue  Example units: “facing up to the facts, accepting and living within ones limits and boundaries” (2) “focussed on what they could manage instead of what they could not and perceived a sense of happiness and contentment in managing small things” (2)

		<p>Planning and prioritising</p>	<p>Self regulation of energy expenditure by pacing activities and keeping activities as simple as possible</p> <p>Planning how to use the finite energy, activities were planned to enable coping.</p>	<p>Agreed definition: Managing fatigue through planning and prioritising activities and interactions</p> <p>Example units:  “everything planned in advance” and “prioritised their special interests” (2)  “plan their daily lives so that they would not lose too much energy and strength” (7)</p>
		<p>Rest and sleep, relief or recharging could be gained short periods</p>	<p>The need for immediate rest or sleep and fatigue avoidance</p>	<p>Agreed definition: Using rest to manage fatigue</p> <p>Example Units.  “refreshed or revitalised after such sleep” and “rest or inactivity to recover from fatigue” (5).  “relief itself was often rapid with only ten to thirty minutes of rest or sleep required” (5)  “I rested most of Saturday afternoon so I could enjoy the evening” (4)  “I lay down quite a lot really. When I get home about ten-ish, I lay down for half an hour and if I take a normal day, I put the wash in the machine, then I lay down while it is on the go – about an hour. Then I hang it up to dry, and then I rest again” (2)</p>

Note: (1) = Coenen et al (2011), (2) = Flesner et al (2003), (3) Johnson et al (2004), (4) = Kayes et al(2015), (5) = Mills and Young (2007), (6) = Moriya and Kutsumi (2010), (7) Olsson et al (2008), (8) = Smith et al (2015), (9) = Stuifbergen and Roger (1997).