Exploring the societal burden of multiple sclerosis

A study into the non-clinical impact of the disease, including changes with progression

Daniela Rodriguez-Rincon, Brandi Leach, Jack Pollard, Sarah Parkinson, Evangelos Gkousis, Catherine Lichten, Jon Sussex and Catriona Manville
This document presents the findings from a study sponsored by F. Hoffmann-La Roche on the topic of multiple sclerosis (MS). The study used a rapid but thorough review of relevant academic literature, as well as key informant interviews to explore the non-clinical impacts of MS and disease progression on individuals with MS, their carers and wider society. The study adopted an international view, with specific country focus on Australia, Canada, France, Germany, Italy, Spain, the United Kingdom and the United States.

This report is intended to be of interest to policymakers, healthcare professionals, patient advocates and others within the healthcare system. It aims to look at current policy and evidence, as well as opportunities for the future.

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For more information about this report or RAND Europe please contact:

Dr Catriona Manville
RAND Europe
Westbrook Centre
Milton Road
Cambridge CB4 1YG
UK
manville@rand.org
Multiple sclerosis (MS) is a chronic, progressive disease of the central nervous system that affects more than 2.2 million people worldwide and causes the loss of approximately 1,151,478 disability-adjusted life years globally\(^1\) (GBD Multiple Sclerosis Collaborators 2016). There are four types of MS: relapsing remitting MS, secondary progressive MS, primary progressive MS and progressive relapsing MS (Figure S.1), although clear distinction between disease categories is not always possible. In addition to the health burden on people affected by MS, it is a disease that is associated with high costs in terms of both medical costs and wider economic costs to society. It also requires a high amount of informal care provided at home by family and friends.

\(^1\) These values are from 2016 and calculated using the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD).
This study aimed to look beyond the physical symptoms of the disease and understand the non-clinical or psychosocial impacts of MS, with specific focus on disease progression. It addressed this question from the perspective of the individual, carers and broader society. A literature review and key informant interviews were used to address the following research questions:

- What are the psychosocial impacts of MS on individuals with MS and their carers?
- What is the societal cost associated with MS?
- Do the impacts of MS on individuals, their carers or wider society vary according to the stage of the disease?
- What support is available to individuals with MS and their carers?

The study aimed to look at the international context, with a specific country focus on Australia, Canada, France, Germany, Italy, Spain, the United Kingdom and the United States as these countries cover different continents and healthcare structures, and are high-income economies. Overall, 88 studies were included for the literature review, made up of 26 literature reviews and 62 primary research papers. For literature reporting on monetary values, costs were updated to 2018 values based on the latest country-specific gross domestic product (GDP) deflators from the World Bank (The World Bank, n.d.). For costs
that were averages from multiple European countries, the GDP deflator for the entire euro area was used. Further details on the literature review are provided in Section 2.1.

The literature review was complemented by interviews with representatives of patient advocacy groups and healthcare professionals in the countries of focus. These interviews furthered the themes reported in the literature by exploring the thoughts of experts on how MS impacts individuals, their network and wider society. The interviews also provided a more in-depth exploration of country-specific issues. A total of 18 interviews across seven countries were conducted. Further details on the interviews are provided in Section 2.2.

**What are the impacts of MS on patients and their carers?**

Individuals with MS experience fatigue, which impacts their daily lives. Although it is one of the first symptoms to appear, there is no evidence that fatigue intensity varies by disease severity. In addition to its direct impact on the person affected by MS, fatigue contributes to reduced capacity to work and decreased ability to participate in society. Other barriers to employment and social participation experienced by individuals with MS include reduced mobility, decreased cognitive functions, stigma as a result of physical symptoms, and unpredictability. However, despite these challenges, people with MS can, and increasingly do, stay in the workforce.

MS is associated with increased depression and anxiety, and reduced quality of life. Mental health challenges are related to uncertainty due to the unpredictability of MS and concerns over the future. Despair and depression levels seem to be highest around key disease progression stages, such as before needing a walking frame or before being unable to walk, due to patients being forced to think about their disease. Active and problem-focused coping strategies, as well as adequate social support, may improve mental health in individuals with MS.

Personal relationships may evolve following a diagnosis of MS. Some of these changes are driven by physical changes, while others are the result of changing circumstances. Relationships also face strains, such as personality changes resulting from MS-related cognitive changes, and mental health issues such as depression and anxiety that can be challenging for a partner or child to cope with.

There is less focus in the literature on the impact of MS on carers than on the individual with MS (just over 20 per cent is focused on carers compared to nearly 80 per cent on individuals with MS) (Figure S.2).
The families and wider network of individuals with MS are also impacted by the diagnosis. People with MS often require care outside that provided by the healthcare system, referred to as informal care, which generally falls on families. As the disease progresses, individuals with MS have decreased cognitive abilities and reduced mobility, which increase the requirements for care. This leads to caregiver burden, which may lead carers to experience career disruption and negatively impact their mental well-being. Additionally, taking on the role of a carer leads to a shift in the relationship with the individual with MS, and may impact other social relationships. Despite the impacts on carers of individuals with MS, there is a lack of support available to deal with caregiver burden. This study concludes that the impacts of MS are often shared between the patient and the carer, but lived in different ways.

**What are the impacts of MS on society?**

MS is associated with high economic costs to society. Estimates of the impacts of MS on society are mainly in the form of economic studies assessing the cost of informal care time, the costs to the healthcare system and lost productivity. However, there are further societal impacts of MS less commonly mentioned in the literature, including the disruption of education of young patients and lower levels of community engagement.

The literature estimates that almost half of MS patients receive informal care at an average of 30 hours per week globally. There is evidence that the average cost of informal caregiving related to MS in 2015 was
€13,092 per annum2 (Oliva-Moreno et al. 2017), although this varies considerably by country and disease severity.

MS is associated with high levels of healthcare utilisation and associated healthcare costs, with three-quarters of MS patients across Europe having at least one consultation with a healthcare professional over a three-month period (Kobelt, Thompson et al. 2017). Healthcare utilisation and healthcare costs vary by disease severity and progression, number and type of relapse, age, and gender.

Additionally, lost productivity accounts for a large amount of the total cost of MS to society through both absenteeism and presenteeism.3 The size of the productivity loss depends on disease characteristics such as severity, progression and relapse, although overall costs largely increase considerably as disease severity worsens.

**What is the impact of disease progression in MS on individuals, carers and society?**

There is limited evidence on the impact of disease progression on individuals with MS, their carers and society. The majority of studies selected through searches carried out as part of this study did not consider the impacts of MS according to the type or stage of the disease. Out of 88 papers from which data on the impact of MS were extracted, 21 focused on the impact of progression. The majority of data and tools available to assess disease progression use only the physical aspects of the disease (i.e. reduced mobility) as a proxy for disease stage, and do not consider mental functioning. A number of interviewees suggested that it would be helpful to gather more data on the psychosocial impacts of disease progression, along with the physical indicators, in order to broaden understanding of the disease and its implications.

The majority of individuals with MS will experience disease progression. As the disease progresses, individuals experience greater cognitive difficulties and reduced mobility, which affect their social and family life, as well as their ability to work. Individuals with MS will also become more dependent on external help, which increases caregiver burden. Interviewees mentioned that during the initial stages of the disease, where disability is not yet visible, there are ‘hidden symptoms’ such as fatigue that can profoundly affect the daily lives of people with MS, and their carers.

The economic impact of MS also increases with disease progression. For example, in Spain the cost per individual per annum of informal care ranges from €1,115 in mild MS to €19,120 in severe MS, the cost of healthcare ranges from €15,750 in mild MS to €24,962 in severe MS, and the cost of lost productivity ranges from €4,098 in mild MS to €17,067 in severe MS (Oreja-Guevara et al. 2017). This pattern is seen across all European countries for which evidence was available in the literature (further details can be found in Chapter 6).

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2 This, like all monetary values stated in this report unless otherwise indicated, has been converted into 2018 price terms.

3 Presenteeism is the act of attending work when unwell.
What support is available to individuals with MS and their carers?

In general, individuals with MS have access to medical support (e.g. diagnosis, medications and some therapy) and welfare benefits (e.g. for unemployment and disability), often through the public healthcare and welfare systems. Other services important for the care and management of MS include rehabilitation; psychologists; occupational therapists and speech therapists; and services to reduce social isolation, such as community and home adaptations and transportation. These are also often covered by the public healthcare system, although access and availability may be variable across a nation.

The public healthcare system is often supported by the informal care provided by relatives and others in the home, and by charitably funded patient associations. Interviewees reported that patient associations, for example, often provide rehabilitation and occupational therapy, as well as peer support groups for individuals with MS.

There is less information and support on offer for carers of individuals with MS. In some countries, there are public schemes available aimed at offering relief and support to carers in person and online, although availability and funding for these are limited.

What are the policy and research implications of the study findings?

The range of impacts that affect both the individual with MS and their carer are widespread, yet the literature focuses largely on the impacts on the individual with MS rather than on the impacts on the carer. It is important that the impacts both on individuals with MS and their carers are fully reflected in research, so that policy can be appropriately informed. Similarly, there is a need for additional research examining the psychosocial impact of disease progression to inform decision-making around policy and care choices. While the healthcare costs associated with MS are large, so too are wider costs such as those of providing informal care, the impact on the economy through loss of productivity and other negative impacts on individuals’ lives. It is important that policymakers are aware of and take into account the full range and magnitude of costs of all kinds. Going forwards, greater investment in supporting the needs of carers for individuals with MS could support the informal care they provide, as well as supporting the carer as an individual.
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<td>Disease modifying therapy</td>
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<td>EDSS</td>
<td>Expanded Disability Status Scale</td>
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<td>GBP</td>
<td>Pound sterling</td>
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<td>GDP</td>
<td>Gross domestic product</td>
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<td>HRQoL</td>
<td>Health related quality of life</td>
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<td>MS</td>
<td>Multiple sclerosis</td>
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<td>MSFC</td>
<td>Multiple Sclerosis Functional Composite</td>
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<td>PPMS</td>
<td>Primary progressive multiple sclerosis</td>
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<td>PRMS</td>
<td>Primary relapsing multiple sclerosis</td>
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<td>QoL</td>
<td>Quality of life</td>
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<td>RRMS</td>
<td>Relapsing remitting multiple sclerosis</td>
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1. Introduction

1.1. What is multiple sclerosis?

Multiple sclerosis (MS) is a chronic, progressive disease of the central nervous system that affects more than 2.2 million people worldwide and causes the loss of approximately 1,151,478 disability-adjusted life years globally⁴ (Collaborators 2019). The prevalence of MS varies – countries closer to the equator tend to have much lower rates of MS than countries further from the equator. For example, North America and Europe have prevalence rates of 140 and 108 respectively per 100,000 population, while Sub-Saharan Africa and East Asia have rates around 2 per 100,000 (Kanavos et al. 2016). Ethnicity also plays a role in the prevalence of MS. Studies show that certain ethnic groups, such as the First Nations in Canada (Marrie et al. 2018) or the Sami in Norway (Benjaminsen et al. 2014), have a lower prevalence of MS, despite living in countries where MS is common.

MS is considered a disease of ‘young adults’ and is the most common disease of the central nervous system in this demographic. Diagnosis of MS occurs generally between 20 and 40 years of age (Palace 2001), although onset may be earlier, including paediatric or childhood MS, defined as onset before the age of 16 years (Alroughani and Boyko 2018). MS affects more women than men: about twice as many women as men are diagnosed with MS, and the difference between genders has grown since 2008 (MS International Federation 2013).

MS is caused by damage to the myelin sheath⁵ around nerve cells. The loss of myelin results in disruption to the transmission of the nervous signal, leading to a wide array of physical and mental symptoms, including decreased coordination and mobility, muscle spasms, chronic pain, changes in cognition and speech, bladder issues, and extreme fatigue (MS International Federation 2018; National Institute of Neurological Disorders and Stroke 2018). As a result, MS is a disease associated with high costs in terms of disability-adjusted life years lost by individuals with MS, medical costs and wider economic costs to society.

Along with these symptoms, people with MS, as well as friends and family who provide informal care, may also suffer from psychosocial issues related to the MS diagnosis. These include depression and anxiety, difficulty working and associated productivity losses, changes in social functioning, and negative

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⁴ These values are from 2016 and calculated using the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD).
⁵ Myelin is a fatty material that insulates nerves and allows rapid transmission of a nervous impulse.
psychological effects associated with the unpredictability of not being able to plan ahead due to the uncertainty of how symptoms associated with MS will present on any given day (Roche 2017; Kanavos et al. 2016).

1.2. Types of MS and disease progression

There are four types of MS: relapsing remitting MS, secondary progressive MS, primary progressive MS and progressive relapsing MS (Figure 1.1), although clear distinction between disease categories is not always possible. Relapsing remitting MS (RRMS) is the most common form of MS, associated with patterns of relapse and remission with new or worsening symptoms. About 85 per cent of people diagnosed with MS will initially be diagnosed with RRMS, but roughly 80 per cent of these will eventually progress to secondary progressive MS (SPMS). Primary progressive MS (PPMS) is the most debilitating form of the disease, and affects approximately 10 per cent of people diagnosed with MS. PPMS is characterised by rapid disease progression without patterns of relapse and remission. The least common form of the disease is progressive relapsing MS (PRMS), which affects roughly 5 per cent of diagnosed individuals. This form of the disease is associated with steady neurological decline with clear patterns of relapse, which may or may not be followed by partial recovery (MS International Federation 2016; 2013). See Figure 1.1 for a graph charting the typical disease course of each type of MS.

Figure 1.1 Typical disease course of the different types of MS

![Graph charting the typical disease course of each type of MS](https://commons.wikimedia.org/wiki/File:Multiple_Sclerosis_Disease_Course.png)

Source: (Garcia-Lorenzo 2010)
Exploring the societal burden of multiple sclerosis

Disease severity and progression in MS is most commonly measured using the Expanded Disability Status Scale (EDSS) (Kurtzke 1983), a clinician-administered assessment scale that evaluates the degree of neurological impairment in MS. The EDSS is used to determine disease progression and to assess the effectiveness of therapeutic interventions in clinical trials. It consists of a scale that ranges from 0 to 10 in 0.5 unit increments, each representing a higher level of disability. The lower-scale values (EDSS<6) measure impairments based on neurological examination, whereas the upper-scale values (EDSS >6) measure handicaps. A one unit increase in the upper half of the scale represents a bigger impact on the life of a person with MS than a one unit increase in the lower half of the scale. For example, a person who goes from an EDSS score of 3 to 4 is still able to walk without an aid, whereas a person who goes from an EDSS score of 6 to 7 goes from being able to walk with a stick or crutch to being essentially restricted to a wheelchair. However, one of the main critiques of the EDSS is its reliance on walking as the main measure of disability (Multiple Sclerosis Trust 2018). It is also argued that it does not sufficiently assess some functional areas impacted by MS, such as cognitive function, levels of energy or quality of life (Multiple Sclerosis Trust 2018).

Another commonly used instrument to measure disease progression in MS is the Multiple Sclerosis Functional Composite (MSFC), developed by the MS Society’s Clinical Assessment Task Force (Cutter et al. 1999). The MSFC was developed with the aim of improving the standard measure of MS disability for clinical trials and developing a multidimensional metric of MS status, including an assessment of cognitive function (Fischer et al. 1999). It is a three-part performance scale that evaluates the level of impairment in MS by assessing leg function (Timed 25-Foot Walk), arm function (9-Hope Peg Test), and attention/concentration (Paced Auditory Serial Addition Test) (Fischer et al. 2001). Although the MSFC is more sensitive and reliable than the EDSS, its weaknesses include difficulty with the interpretation of the integrated score, the learning effects in relation to the Paced Auditory Serial Addition Test,7 and the lack of a visual dimension (Meyer-Moock et al. 2014).

Additional instruments exist to assess disease progression in MS. However, none are recognised for use in clinical trials without restrictions. These instruments include the Ambulation Index (Hauser et al. 1983), the Cambridge Multiple Sclerosis Basic Score (Mumford & Compston 1993), the Scripps Neurological Rating Scale (Sipe et al. 1984), the Illness Severity Scale (Mickey et al. 1984), Guy’s Neurological Disability Scale (Sharrack & Hughes 1999), the Functional Independence Measure (Hamilton et al. 1987), and the Multiple Sclerosis Impairment Scale (Ravnborg et al. 1997). There are also specific instruments to assess health-related quality of life for people with MS, such as the Multiple Sclerosis Quality of Life-54 (Vickrey et al. 1995) and the Multiple Sclerosis Quality of Life Inventory (National Multiple Sclerosis Society 2018).

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6 For a description of each unit in the scale see the Multiple Sclerosis Trust (2018).
7 A patient may learn to conduct the test and therefore their measured performance improves, making it difficult to detect deterioration over time.
1.3. Treatment of MS

There have been a number of relatively recent breakthroughs in MS treatment that are changing how the disease is managed. MS treatment can be divided into three types: (i) acute relapse management; (ii) symptomatic treatment; and (iii) disease modifying therapies (DMTs). An acute relapse is defined as an episode of neurological disturbance with duration of at least 24 hours with no other cause (e.g. fever) (McDonald et al. 2001). Treatment of an acute relapse mainly consists of corticosteroid therapy (NICE 2003). Although there is evidence that corticosteroid therapy accelerates the recovery from relapse, the exact mode of action in MS is unclear (Leary et al. 2005). During an acute relapse, symptomatic treatment for new symptoms may also be required, mainly when the relapse is prolonged. However, given the variety of symptoms of MS and the fact that multiple symptoms usually co-exist, there is no consistent symptomatic drug treatment model currently available (Thompson 2001).

In addition to treating acute relapses and associated symptoms, DMTs can be used to reduce the frequency of relapses. DMTs are medicines that can slow down the damage caused by relapsing MS by reducing both the number of relapses and the severity of relapses when they occur (Multiple Sclerosis Trust 2019). DMTs act on the immune system to reduce the inflammatory process that occurs on nervous cells during MS. However, they do not repair damage done to nervous cells and therefore do not reverse existing symptoms (Multiple Sclerosis Trust 2019).

Since the first DMTs became available in the 1990s, newer and more effective DMTs have been developed that can significantly improve disease courses and limit levels of disability, especially with early treatment (Giovannoni et al. 2016; Cross & Naismith 2014). Although significant progress has been made in terms of treatment options for MS, access to treatment remains an issue. World Health Organization (WHO) data suggest that only half of the treatment-eligible population worldwide actually receive a DMT (MS International Federation 2013).

Alongside advances with DMTs, there has also been research aimed at building a more comprehensive understanding of MS and how to improve outcomes. New survey evidence has expanded understanding of how MS affects patients and their carers (Roche 2017; Kanavos et al. 2016; Karampampa et al. 2012) and may be used to inform economic evaluations and improve services provided to individuals with MS. In addition, new research in clinical practice and policymaking has documented how the significant delays in diagnosis and treatment contribute to worse outcomes and higher costs (Wilsdon et al. 2014). This research has fuelled new consensus statements from clinicians that focus on the importance of early diagnosis and referral to specialists, access to newer DMTs sooner after diagnosis, rapid and efficient decision making when switching medications, and the importance of lifestyle changes to support brain health (Giovannoni et al. 2016; Scolding et al. 2015).

1.4. Rationale for the study

Costs associated with MS and its treatment can be broken down into direct medical costs (e.g. medication and treatment), direct non-medical costs (e.g. formal care in homes and care homes, informal care, devices and aids), indirect costs (e.g. productivity losses, early retirement), and intangible costs (e.g. anxiety, pain
Exploring the societal burden of multiple sclerosis and changes in social functioning) (Naci et al. 2010; Wundes et al. 2010). These costs are borne by the healthcare system, people with MS, their carers and wider society.

Estimates of the average cost of illness per person with MS vary, but range from around €28,265 (Karampampa et al. 2012)\(^8\) to around €41,529 per year (Kanavos et al. 2016),\(^9\) depending on the methodology used to estimate the costs and the cost categories captured in each model. Despite variability between studies, cost of illness and cost-effectiveness studies tend to agree that costs increase as MS progresses to higher disability levels, and that the balance of costs tends to shift from being mainly direct medical costs (primarily borne by the healthcare system) to larger indirect costs (primarily borne by people with MS, their carers and wider society) as the disease progresses (Naci et al. 2010; Karampampa et al. 2012; Kobelt, Thompson, et al. 2017; Ernstsson et al. 2016).

There are a number of challenges to estimating the societal burden of MS and of disease progression in MS. One challenge is that there is a lack of real-world data measuring the long term cost-effectiveness of newer DMTs, meaning that cost of illness and cost-effectiveness studies may fail to fully capture the societal benefits that these new therapies may confer by slowing disease progression and leading to fewer disabilities overall (Kobelt, Thompson, et al. 2017; Naci et al. 2010; Thompson et al. 2013). Additionally, many economic analyses, including those for health technology assessments (HTAs), fail to capture the wide range of costs associated with MS (Kobelt, Thompson, et al. 2017; Kwiatkowski et al. 2014), including some of the impacts that matter most to people with MS and their carers, such as depression, anxiety and fatigue (Kanavos et al. 2016). Thus, published studies do not always capture the costs borne outside the healthcare system, such as informal care costs, as well as productivity losses and the cost of early retirement that affect the economy and wider society (Giovannoni et al. 2016; Wundes et al. 2010).

There have nevertheless been a number of studies reported in academic and grey literature calculating the economic and wider societal costs of MS. This report synthesises that body of literature, with particular focus on the impact of disease progression in MS on the individual, their carers and network, and broader society. It is hoped that this will create a valuable resource for informing the policy debate around MS treatment.

### 1.5. Aims and objectives of the study

This study aimed to understand the impacts of MS (with specific interest in disease progression) on the individual, carers and broader society. A literature review and key informant interviews were undertaken to address the following research questions:

- What are the psychosocial impacts of MS to individuals with MS and their carers?

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\(^8\) Values were originally provided in GBP. These were adjusted to 2018 values using GDP deflators from the World Bank and then converting this value to Euros using 2018 exchange rates.

\(^9\) As the study referenced provided an average cost across multiple European countries, values were adjusted to 2018 values using the GDP deflator for the euro area.
• What is the societal cost associated with MS?
• Do the impacts of MS to individuals, their carers or wider society vary according to the stage of the disease?
• What support is available to individuals with MS and their carers?
2. Methods

To address the research questions, we undertook a rapid evidence assessment of the academic and grey literature, and conducted key informant interviews (Figure 2.1).

Figure 2.1 Project workflow

2.1. Literature review on the impact of disease progression in MS

The literature review was guided by a systematic approach and conducted following guidance published by the Centre for Reviews and Dissemination (2009) and the Cochrane Handbook (Higgins et al. 2019). We followed the five steps below:

- Step 1: Develop search terms.
- Step 2: Determine the eligibility criteria.
- Step 3: Identify relevant literature based on information presented in the title and abstract.
- Step 4: Extract data based on information presented in the full text of the selected articles.
- Step 5: Evidence synthesis and analysis.

2.1.1. Step 1: Develop search terms

We developed a search strategy to capture information relevant to the focus of the study (Table 2.1). As part of this development, we undertook rapid piloting of the search strategy to ensure that search terms
yielded sufficient and relevant results (‘hits’). Piloting also ensured that the terms were broad enough to include a range of relevant studies, but also narrow enough to ensure that the search was manageable.

An information specialist from RAND Knowledge Services performed a database search using the search sequences in Table 2.1 to identify the relevant literature. The literature review aimed to assess the international landscape, with a specific country focus on Australia, Canada, France, Germany, Italy, Spain, the United Kingdom and the United States, as these countries cover different continents and healthcare structures, and are high-income economies. The focus of the review was on academic publications. Searches were conducted on 27 March 2019 and performed in two databases: PubMed and Scopus. The search was limited to the period 2009–2019 and restricted to the English language. The search yielded 5,920 hits after duplicate articles were removed.
<table>
<thead>
<tr>
<th>Database searched</th>
<th>Search sequence</th>
<th>Results yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scopus</td>
<td>TITLE-ABS-KEY (&quot;Multiple sclerosis&quot;) AND (( TITLE (economic* OR qaly OR &quot;quality adjusted life year&quot; OR &quot;quality adjusted life years&quot; OR &quot;disability adjusted life year&quot; OR &quot;disability adjusted life years&quot; OR daly OR value) OR TITLE (cost-benefit OR out-of-pocket OR &quot;direct cost&quot; OR &quot;direct costs&quot; OR &quot;indirect cost&quot; OR &quot;indirect costs&quot; OR budget* OR financial)) OR ABS (economic* OR qaly OR &quot;quality adjusted life year&quot; OR &quot;quality adjusted life years&quot; OR daly OR value) OR ABS (cost-benefit OR out-of-pocket OR &quot;direct cost&quot; OR &quot;direct costs&quot; OR &quot;indirect cost&quot; OR &quot;indirect costs&quot; OR budget* OR financial)) OR (( TITLE (&quot;Social burden&quot; OR &quot;social burdens&quot; OR societal burden OR &quot;societal burdens&quot; OR &quot;social impact&quot; OR &quot;social impacts&quot; OR &quot;societal impact&quot; OR &quot;societal impacts&quot; OR &quot;social care&quot; OR &quot;economic burden&quot; OR carer* OR spouse* OR partner* OR friend*) OR TITLE (&quot;informal care&quot; OR psychosocial OR psychological OR nonclinical OR non-clinical OR nonmedical OR non-medical OR depression OR anxiety OR work OR employment OR productivity OR &quot;plan ahead&quot; OR unpredictability OR job OR employer) OR ABS (&quot;Social burden&quot; OR &quot;social burdens&quot; OR societal burden OR &quot;societal burdens&quot; OR &quot;social impact&quot; OR &quot;social impacts&quot; OR &quot;societal impact&quot; OR &quot;societal impacts&quot; OR &quot;social care&quot; OR &quot;economic burden&quot; OR carer* OR spouse* OR partner* OR friend*) OR ABS (&quot;informal care&quot; OR psychosocial OR psychological OR nonclinical OR non-clinical OR nonmedical OR non-medical OR depression OR anxiety OR work OR employment OR productivity OR &quot;plan ahead&quot; OR unpredictability OR job OR employer) OR TITLE (&quot;quality of life&quot;) OR ABS (&quot;quality of life&quot;)</td>
<td>2,798</td>
</tr>
<tr>
<td><strong>Total (de-duplicated)</strong></td>
<td><strong>5,920</strong></td>
<td></td>
</tr>
</tbody>
</table>
2.1.2. Step 2: Determine the eligibility criteria

During the study design phase, the eligibility inclusion and exclusion criteria for studies to include in the review was determined by looking at population, interventions, outcomes and study designs (Table 2.2). These inclusion and exclusion criteria were then refined following the literature search, based on an initial screening of titles and abstracts during which researchers identified key criteria that had been omitted from the initial eligibility criteria. The changes to the eligibility criteria that were made during the initial screening included the decision to exclude articles that assessed the validity and reliability of tools used for measuring quality of life outcomes, such as the Becks Depression Inventory, rather than assessing quality of life outcomes themselves.

Table 2.2 Inclusion and exclusion criteria for the literature review

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Inclusion</th>
<th>Exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population</td>
<td>• Patients who have experienced at least one episode of MS</td>
<td>• Patients who have predisposition to MS but have not developed the disease</td>
</tr>
<tr>
<td></td>
<td>• Patients that are in remission of MS</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Patients with disease progression in MS</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Carers of patients with MS</td>
<td></td>
</tr>
<tr>
<td>Intervention</td>
<td>• Effects of treatments (drug and non-drug) on psychosocial outcomes</td>
<td>• Effects of treatments (drug and non-drug treatments) on health outcomes</td>
</tr>
<tr>
<td>Comparison</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Outcome</td>
<td>Health outcomes:</td>
<td>Health outcomes:</td>
</tr>
<tr>
<td></td>
<td>• Survival</td>
<td>• Basic science studies documenting health changes with no link to wider outcomes</td>
</tr>
<tr>
<td></td>
<td>• Progression</td>
<td>• Assessments of tools measuring quality of life outcomes (e.g. depression scales, quality of life scales)</td>
</tr>
<tr>
<td></td>
<td>• Patient well-being and quality of life</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Psychological outcomes (e.g. depression, anxiety)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Health impacts on carers and families</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Economic outcomes:</td>
<td>Economic outcomes:</td>
</tr>
<tr>
<td></td>
<td>• Economic outcomes for patients (e.g. out of pocket expenses)</td>
<td>• Cost-effectiveness/cost-comparative studies on treatments</td>
</tr>
<tr>
<td></td>
<td>• Economic outcomes for carers (e.g. out of pocket expenses)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Economic outcomes for the wider health system (e.g. direct and indirect costs)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Economic outcomes for wider society (e.g. days lost from work/labour productivity)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Other economic impacts on carers and families</td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>• Primary research</td>
<td>• Protocol</td>
</tr>
<tr>
<td></td>
<td>• Literature review (systematic and non-systematic)</td>
<td>• Drug safety</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Commentary/letter</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Conference abstracts</td>
</tr>
</tbody>
</table>
2.1.3. Step 3: Identify relevant literature based on information presented in the title and abstract

After refining the eligibility criteria, the titles and abstracts for each study were screened against the eligibility criteria. The screening was split between two researchers (BL, DRR)\(^{10}\) and included double-screening of a subset of articles to help ensure consistency in screening. Using these criteria, a total of 460 studies were identified as eligible for inclusion in the review (270 from PubMed and 190 from Scopus).

2.1.4. Step 4: Extract data based on information presented in the full text of the selected articles

Given the high volume of studies considered relevant in the screening stage (n=460), we limited the initial round of data extraction to articles reporting literature reviews (systematic and non-systematic reviews). A total of 27 literature reviews were selected for full text review. The papers covered by the literature reviews included studies from 1980 to 2017. During full text review, information was extracted into an Excel template (Annex A). One article was excluded at this stage on the basis of relevance. Information was extracted from 26 literature reviews. Following full text review of the identified literature reviews we selected a subset of primary studies for full text review. These articles were selected through a mapping exercise that aimed to identify articles to fill in the gaps in information provided by the literature reviews. We approached the mapping exercise by first identifying the key topic areas covered by the 26 literature reviews. We then identified which outcomes were not covered in the literature reviews and used these as key words to search the titles and abstracts of the remaining articles. The topic areas were based on the outcomes of interest as identified in the eligibility criteria (e.g. survival, progression, quality of life, economic outcomes for patients). For the topic areas where gaps were identified,\(^{11}\) we selected additional primary research articles for full text review during a second stage of extraction, with the focus on more recent years not covered by the available literature reviews. A total of 62 research papers conducted between 2014 and 2019 were selected for the second stage of extraction. Data extraction was performed independently by four researchers (BL, DRR, JP, SP)\(^{12}\).

For literature reporting on monetary values, costs were updated to 2018 values based on the latest country-specific GDP deflators from the World Bank. For costs that were averages from multiple European countries, we used the GDP deflator for the entire Euro Area. For costs originally in GBP, we used UK deflators to inflate to 2018 and then converted to Euros using the mean exchange rate in 2018.

2.1.5. Step 5: Evidence synthesis and analysis

We conducted an internal workshop (BL, CM, DRR, JP, SP) to identify themes arising from the literature review and gaps in the evidence that could be further explored through the interviews. In this workshop, we classified the different outcomes described in the literature according to their impact on the person with MS, on the carer and support system of a person with MS, and on broader society.

\(^{10}\) BL: Brandi Leach, DRR: Daniela Rodriguez-Rincon

\(^{11}\) Identified gaps were employment, loss of productivity, quality of life, carers and disease progression.

\(^{12}\) BL: Brandi Leach, DRR: Daniela Rodriguez-Rincon, Jack Pollard, Sarah Parkinson
2.2. Key informant interviews

We conducted interviews with representatives of MS patient advocacy groups and healthcare professionals in the countries of focus. These interviews aimed to further the themes reported in the literature by exploring the thoughts of experts on how MS impacts individuals, their networks and wider society. The interviews also provided a more in-depth exploration of country-specific issues. In line with the country focus for the literature review, interviews focused on Australia, Canada, France, Germany, Italy, Spain, the United Kingdom and the United States. The initial approach was to send invitations in English; however, where the response rate was low the interview invitation email was translated into the country’s language, and participants were given alternatives such as conducting the interview in a language other than English or performing a written interview in their native language. As a result, one interview was conducted in French and one in Spanish. No interviews were secured from Germany.

We conducted 19 interviews with healthcare professionals (MS clinicians, MS nurses and MS physiotherapists) and representatives from patient advocacy groups in the selected countries (Table 2.3). Given their role in delivering care and support services, the members of these stakeholder groups were especially well-placed to provide information on the types of support available to individuals with MS and to their carers, within specific country contexts, while also offering broader insights into the impacts of MS on individuals with MS, their carers and wider society.

Table 2.3 Number of expert interviews conducted

<table>
<thead>
<tr>
<th>Country</th>
<th>Healthcare professional</th>
<th>Patient advocacy group</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Australia</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Canada</td>
<td>2</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>France</td>
<td>2</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Italy</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Spain</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>2</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>United States</td>
<td>2</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>9</strong></td>
<td><strong>10</strong></td>
<td><strong>19</strong></td>
</tr>
</tbody>
</table>

The findings from the literature review were used to develop an interview protocol (Annex B), as well as to identify interviewees and better guide discussions with country experts. Interviews were conducted over the telephone, lasting 45–60 minutes, and used a semi-structured format that allowed consistent information to be captured, while retaining flexibility to explore issues in more detail as appropriate, reflecting the background and expertise of the respondent.

Informed consent was sought from all participants for their participation. Prior to each interview, participants were provided with an information sheet (Annex C) that detailed what their participation in the study would involve and their right to refuse. Participants were given the option of signing and returning a consent form prior to the interview or to have consent taken verbally during the interview and audio recorded. With the participants’ permission, interviews were audio recorded for the purposes of
Exploring the societal burden of multiple sclerosis

accurate note taking. References to identifiable names and places were removed and interviews were anonymised by assigning an interview code (i.e. INTXX) to each interviewee (Annex D).

An Excel template (Annex E) was used to extract information from the interview notes and to facilitate analysis within and across countries. Following country-specific analysis, which summarised the findings from the extraction template, we held an internal workshop to identify cross-cutting themes. This workshop focused on the different impacts of MS, the data collected in the different countries regarding disease progression in MS, and differences in the delivery of care for MS in the different countries. The study team determined that due to the limited availability in the literature of country-specific data on the impacts of MS to support findings from the interviews, analysis would be carried out on a cross-country and global, rather than individual country, scale.

2.3. Caveats and limitations

The research conducted for this study faces several limitations; however, by using a multimethod approach, we hope to build on some of the strengths of each individual method and limit the impact of the weaknesses of the study. Literature reviews are always limited by the quality and availability of existing research. In the case of this study, the availability of research is also limited by the selection of two bibliographic, albeit major, databases (PubMed and Scopus) to the exclusion of other potential sources. Additionally, by pre-specifying the broad categories of outcome types of relevance in the search (in order to ensure a manageable number and sufficient focus for the scope of the review) it is possible that the study may not have captured all possible outcomes. However, the diversity of outcomes captured within the broad overarching categories is reassuring. The title and abstract screening process also presents the potential for reviewer selection bias in identifying studies for inclusion. We undertook double-screening of a subset of titles and abstracts in order to mitigate this bias and improve consistency in screening across reviewers.

When considering the interviews it is important to note the potential for bias arising from interviewee selection and acceptance, and that the information obtained from the interviews could represent an individual’s perspective rather than a broader view on the impact of MS in a given country. Also, by not interviewing people with MS or their carers directly, the study relies on second-hand accounts of the impacts of MS as reported by interviewees and within the literature. It is important to note, however, that some of the studies included within the research are based on first-person interviews with individuals with MS and their carers, and that taken together these studies reach a greater sample of people with direct experience of the impacts of MS than would have been possible to interview given the scope of this study.

As a final note, this study sought to recruit three interviewees from each country, which would allow for an exploration of the main impacts of disease progression in MS in a wide range of countries. In three countries, this number was not achieved. However, the authors of this study believe that any impact on the findings from this is minimal because the analysis is focused at a supranational/global level, and the study does not rely on interview data as the sole source for any country-specific findings.
3. What is the evidence in the peer-reviewed literature on the impact of disease progression in MS?

This chapter presents a brief mapping review of the available literature on the impact of disease progression in MS and explores the psychosocial, physical and societal outcomes that may impact an individual with MS, their carers and wider society.

The key findings are:

- The existing literature covers the three areas of interest for this project: impact on the individual, impact on carers and impact on wider society.

- The majority of the literature focuses on the impact of MS on the individual with MS.

- The outcomes that impact individuals with MS, their carers or wider society can be grouped into three categories: psychosocial, physical and societal.

- Of the literature we reviewed, the impact of psychosocial outcomes is the most widely reported, with impacts on both the individual with MS and their carers.

- Societal impacts are generally measured as the economic impact of the disease.

- The majority of studies do not consider the impacts of MS according to the type or stage of the disease.

Of the 88 papers from which data were extracted, 26 were literature reviews and 62 were primary studies. Among these papers, 70 (79.5 per cent) described impacts on the individual with MS, 20 (22.7 per cent) described impacts on the carer of an individual with MS, and 18 (20.5 per cent) described impacts on wider society (Figure 3.1). The number of studies in the different categories do not add up to 88 as studies were not mutually exclusive (i.e. one study might report simultaneously on impacts to the individual with MS, their carer and society).
Figure 3.1 Number of studies describing the impact of MS on the individual with MS, their carer and wider society (n=88)

Note: The number of studies in the different categories do not add up to n=88 as studies were not mutually exclusive (i.e. one study can report simultaneously on impacts to the individual with MS, their carer and society).

Only 21 studies (23.9 per cent) of the 88 included in the review reported on changes to the impacts on the individual with MS, their carer or wider society as the disease progresses (Figure 3.2). Of these 21 studies, 16 (76.2 per cent) assessed how disease progression in MS affects individuals with the disease, 4 (19 per cent) considered the impacts of disease progression in MS for carers, and 14 (66.7 per cent) assessed the impacts on society.
We further broke down the data available in the literature according to type of outcome, in order to synthesise the evidence on how the different outcomes impact the individual with MS, their carers and wider society. We grouped the outcomes into psychosocial, societal and physical outcomes (Figure 3.3). Psychosocial outcomes (78 studies) were the most widely reported outcomes to have an impact on both the individual (61 studies) and carers (17 studies) (Figure 3.3). Psychosocial outcomes described in the literature include fatigue, mental health issues (e.g. depression, anxiety and mood), quality of life, body image, social functioning and changes to social relationships. The studies describing societal outcomes (38 studies) were mainly focused on their impact on the individual with MS (35 studies), referring both to the ability of an individual to actively participate in society (e.g. employment) and the impact that having MS has on broader society (e.g. healthcare costs, healthcare utilisation, burden of informal care and loss of productivity); the latter were generally measured as the economic impact of the disease. Societal outcomes focused on the carer (3 studies) looked mainly at the impact that caring for a person with MS has on the carer’s employment. Additionally, 35 studies reported physical outcomes of MS on the patients. However, given that the search strategy focused on the psychosocial and economic impacts of MS, studies that looked at physical outcomes were only included in the review if they made reference to their psychosocial or societal impacts. Physical outcomes include pain, mobility and cognitive changes.
Figure 3.3 Types of outcome of MS described in the literature (n=88)

Note: The number of studies in the different categories do not add up to n=88 as studies were not mutually exclusive (i.e. one study can report simultaneously on impacts to the individual with MS, their carer and society).

The 21 studies that assessed the impacts of disease progression in MS looked at both psychosocial and societal outcomes (Figure 3.4). Of these, the majority (17 studies, 80.9 per cent) focused on psychosocial outcomes, and 14 (66.7 per cent) focused on societal outcomes.

Figure 3.4 Number of studies that focus on the impact of disease progression in MS according to the type of outcome (n=21)

Note: The number of studies in the different categories do not add up to n=21 as studies were not mutually exclusive (i.e. one study can report on both psychosocial and societal impacts of disease progression in MS).
4. Impacts of MS on the individual

As described in Chapter 3, the majority of the literature around MS is focused on the impacts of the different outcomes on the individual with MS. This chapter presents the findings on such impacts identified in the literature, complemented with findings from the interviews.

The key findings are:

- The impacts of fatigue on the daily lives of people with MS are widespread.
- MS is associated with increased depression and anxiety.
- People with MS experience a decline in their quality of life as the disease progresses.
- Social support can improve the mental well-being of people with MS.
- People with MS experience barriers to social participation.
- Relationships change after a diagnosis of MS.
- Despite challenges, people with MS can (and increasingly do) stay in the workforce.
- Positive employment experiences contribute to retaining people with MS in the workforce.

These findings are described in further detail below.

4.1. The impacts of fatigue on the daily lives of people with MS are widespread

Fatigue is the most frequently reported difficulty related to MS (Carrié et al. 2014), with 55 per cent of people with MS reporting it as one of their worst symptoms (Langeskov-Christensen et al. 2017; Newland et al. 2016). It is one of the first symptoms to appear (Kobelt, Thompson, et al. 2017) (INT05, INT14, INT016) and affects up to 90 per cent of people with MS (Bishop et al. 2016; Langeskov-Christensen et al. 2017; Penner & Paul 2017). Research suggests that fatigue intensity does not vary by disease severity (Kobelt, Eriksson, et al. 2017).

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13 This result was reported in two of the literature reviews included in this study. However, the data referred to is from the same original article in both reviews (Fisk et al. 1994).
14 As measured by self-reported scales such as the Visual Analogue Scale (VAS).
Interviewees confirmed that the impacts of fatigue are widespread and affect people’s social lives, home lives and ability to work (INT09, INT16, INT18). For example, research finds that fatigue contributes to a reduced capacity to work, including reduced work hours, taking more sick leave and changing work type to accommodate fatigue (Raggi et al. 2016; Kobelt, Thompson, et al. 2017), findings that were backed up by interviewees (INT06, INT09, INT16, INT20). Fatigue, together with mobility impairments and diminished stamina and physical strength, has been found to be a strong predictor of employment status in individuals with MS, with greater levels of fatigue linked to a higher likelihood of job loss or unemployment (Li et al. 2015). A study looking at the burden of MS in Europe found that fatigue was reported by 70 per cent of participants as the main reason for reduced work productivity, followed by cognitive difficulties (34 per cent), mobility (28 per cent), pain (21 per cent) and low mood (18 per cent) (Kobelt, Thompson, et al. 2017). Furthermore, lessening of fatigue is associated with improved ability to work, working more hours and taking fewer days of sick leave (Raggi et al. 2016). This study expands further on the economic impact of MS due to diminished workforce participation in Section 4.7.

Interviewees described fatigue as a ‘hidden symptom’ of MS as it causes no visible disability yet profoundly affects the lives of people with MS (INT05, INT09, INT10, INT12, INT15, INT16). The hidden nature of fatigue presents challenges. Several interviewees highlighted the difficulty of measuring fatigue (INT15, INT22) and how this could negatively affect people’s ability to qualify for benefits such as disability support payments (INT15). Invisible symptoms such as fatigue can also contribute to misunderstandings or even mistreatment when people with MS engage with members of the general public who are unaware of their disability and might not understand, for example, why the person with MS requires special accommodations such as a disabled parking space (INT16).

Among children and adolescents with MS, fatigue presents additional challenges. For example, fatigued children and adolescents with MS report significantly greater catastrophising (i.e. exhibiting an exaggerated negativity or interpreting minor problems as major problems) and all-or-nothing behaviour than healthy children and adolescents (Carroll et al. 2019). Children and adolescents with MS also have lower school attendance, with one study showing an average attendance rate of 0.76 for children and adolescents with MS who are fatigued compared to 0.95 for children and adolescents with MS who are non-fatigued and 0.97 for healthy children and adolescents (Carroll et al. 2019). Parents of children and adolescents with MS stressed that their children’s learning was disrupted by absences from school (Carroll et al. 2016). Children and adolescents with MS described their fatigue symptoms as ‘like wearing a giant sandbag’ or ‘like looking through a haze’, with some reporting that these feelings led them to lose motivation to do things, finding that resting was the ‘easier option’ (Carroll et al. 2016).

4.2. MS is associated with increased depression and anxiety

Depression and anxiety are more common among adults with MS than the general population (Bishop et al. 2016). A systematic review on anxiety among people with MS found that all 216 studies included in the review reported higher rates of anxiety among patients with MS compared with control groups (Butler et al. 2016). People with MS are also more likely to experience major depression, with research showing that 50 per cent of people with MS will experience major depression at some point in their life (lifetime prevalence), and approximately 20 per cent will have a diagnosis of major depression in any given year.
Exploring the societal burden of multiple sclerosis (annual prevalence) (Loffler et al. 2016). This is in comparison to worldwide lifetime prevalence estimates ranging from 1.5 per cent in Taiwan to 19 per cent in Beirut (Kessler & Bromet 2013). MS is also associated with suicidal ideation and an increased risk of suicide, as mentioned both in the literature and in interviews (Loffler et al. 2016; Jetté et al. 2017) (INT05). People with progressive MS generally report higher rates of anxiety and depression than people with other forms of the disease, and these differences are most pronounced early in the disease course (Zhang et al. 2019).

Loss of mobility and physical disability are associated with mental health challenges (Buhse 2015), and research has shown that depression levels\(^{15}\) are moderately associated with disability,\(^{16}\) with the highest levels of depression observed around key disease progression stages such as before needing a walking frame or assistance to walk (4.5 on the EDSS scale) and before being unable to walk (5.5 on the EDSS scale) (Rommer et al. 2017). The authors of this research suggest that these are periods when patients are forced to engage more intensively with their disease because of the need to adapt to increasing levels of impairment.

Interviewees suggested that mental health is intimately linked with uncertainty due to the unpredictability of MS and concerns over the future (INT12, INT17, INT20, INT22). One study found that despair is most prevalent during periods of relapse because, as reported by one study participant, this is the period when they are forced to think about their disease, and during periods of remission they are able to ‘put it out of [their] head’ (Kirk and Hinton 2019). For people living with MS, interviewees stressed that there is no way to know when a relapse and new symptoms will appear, and it may be difficult for some of them to accept new symptoms when they do arise after an extended period of remission (INT12, INT21). Interviewees felt that this unpredictability can make it difficult for people with MS to cope with their disease and to plan for the future, which contributes to anxiety and depression (INT12, INT17, INT20). One interviewee commented that for progressive types of MS, the uncertainty decreases with disease progression, but only over many years and after a relatively severe level of disability has been reached (INT17). Another interviewee said that mental health concerns may be greatest at time of diagnosis (INT01). There is evidence that anxiety disorders are associated with receiving an MS diagnosis and not just with the existence of MS symptoms. This was demonstrated by a systematic review which found that the prevalence of diagnosed anxiety disorders rose from 2.7 per cent at symptom onset to 6.2 per cent at the time of receiving an MS diagnosis (Marrie et al. 2015).

Physical functioning is not the sole determinant of mental health for MS patients. Research finds that coping styles mediate the relationship between disease progression and mental health. For example, Rommer et al. (2017) found that although depression was moderately associated with disability, patients who adopted ‘active and problem-focused coping’ styles had lower levels of depression compared with patients adopting other coping styles. Furthermore, research shows that patients’ ability to regulate their mood is better explained by individual coping styles than by disease progression (Loffler et al. 2016), and

\(^{15}\) As measured by the Beck Depression Inventory (BDI).

\(^{16}\) As measured by the Expanded Disability Status Scale (EDSS).
that individual resilience\textsuperscript{17} moderates the impact of depression and anxiety on quality of life (Rainone et al. 2017). Additionally, research on older people with MS shows that despite greater physical limitations, older people are no more likely than younger people, and may even be less likely, to have mental health issues such as depression (Buhse 2015).

4.3. People with MS experience a decrease in their quality of life as the disease progresses

People with MS report a host of factors negatively affecting their quality of life (QoL). An analysis of the burden of MS in Europe found that 70 per cent of study participants (N=16,808) reported negative impacts on their QoL, including problems in mobility, issues with self-care or in completing their usual activities, or pain or discomfort (Kobelt, Thompson, et al. 2017). Furthermore, the authors found that the negative impact of MS on QoL increased along with disease progression and severity of symptoms, a finding also reported in other research (Lanzillo et al. 2016). Additional research found an association between loss of mobility, physical disability and QoL (Buhse 2015), with studies specifically finding that higher disability scores on the EDSS and having had a relapse are associated with poorer health related quality of life (HRQoL) and perceived QoL, respectively (Jones et al. 2016).

The speed of disease progression may also affect QoL. For example, a study on QoL in early-onset MS found that QoL was not related to how long a person had had MS (i.e. disease duration), but rather the rapidity of disease progression (Lanzillo et al. 2016). The authors hypothesised that a more rapid accumulation of disability disrupts people’s ability to adapt to and cope with MS. Additional research shows that fear of disease progression is a real issue among people with MS, and that fear contributes to a lower QoL (Nickel et al. 2018). One of the key fears around disease progression cited by the study authors was becoming dependent on external help. Interviewees echo this point, saying that one cause of psychological distress for people with MS is the fear of becoming a burden to their loved ones (INT01, INT10).

4.4. Social support can improve the mental well-being of people with MS

Evidence shows that anxiety among individuals with MS may be affected by levels of social support (e.g. personal and family relationships, peer support networks), with research suggesting that lower levels of social support may be associated with increased risk of anxiety (Butler et al. 2016). Other factors mentioned in the literature that can impact anxiety levels include having more relapses, which can

\textsuperscript{17} Specifically, resilience defined as ‘competence to manage resources’ rather than resilience defined as an individual personality trait.
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significantly increase anxiety, and having more information about the disease, which may improve anxiety levels (Butler et al. 2016).

One interviewee mentioned that having appropriate mental health support, especially for those newly diagnosed with MS, can improve the mental well-being of people with MS (INT01). A study in Australia found that two-thirds of individuals with MS desired a greater variety of peer support groups to meet their needs, such as groups for newly diagnosed individuals (McCabe et al. 2015). The authors of the study on the unmet needs of people with MS in Australia also found that satisfaction with the level of peer support received varied according to age and disease severity, for example, the older group was more likely than the younger group to be less satisfied with the availability of counselling and psychological assistance when first diagnosed.

The importance of social participation for the QoL of people with MS was a recurrent finding in the literature. For example, one study on the economic burden of MS demonstrated that having reduced social participation negatively affected QoL, and that social participation was more strongly associated with QoL than physical impairment (Kwiatkowski et al. 2014). However, the authors noted that social participation appeared to be related to physical impairment, as study participants' social participation scores seemed to shift along with their ability to walk. A literature review on MS in older people found that social isolation also appeared to be one of their main concerns (Buhse 2015), and that being widowed may increase isolation and make it more difficult for people with MS to complete daily living activities that they may once have shared with their partner. The authors suggest that appropriate transportation and assistive devices to improve mobility and independence could potentially reduce social isolation and improve the QoL of this population (Buhse 2015).

4.5. People with MS experience barriers to social participation

Interviewees highlighted the many barriers to social participation faced by people with MS, and described how mobility issues present an increasing obstacle to social participation as the disease progresses (INT05, INT18, INT22). Interviewees also commented on how fatigue can interfere with a person’s ability to socialise (INT16, INT18), and how cognitive issues can affect social relationships (INT20). Additionally, one interviewee mentioned that physical symptoms such as incontinence can be stigmatising and make a person experiencing them reluctant to go out (INT05). Another interviewee found that uncertainty associated with MS can limit people’s ability to make plans, meaning that people with MS may fall into a pattern of not making plans and become isolated as a consequence (INT12).

Evidence in the literature supports the findings from the interviews that feelings of isolation and burden are common among people with MS (Borreani et al. 2014). A systematic literature review found that some people with MS feel that they are physically restricted in where they can go and reliant on others to assist them due to a lack of appropriate assistive devices such as powered wheelchairs. This contributes to a sense of isolation (Hartley et al. 2014). People with MS may also have lower social participation on the

18 N=16,808. The study authors recruited participants until they had at least 50 respondents in each of the 11 EDSS score categories for each of the 16 European countries included in the study.
days they experience higher levels of pain (Kratz et al. 2017). However, a qualitative study from Germany found that although people with MS experienced a decrease in the size of their network of friends as their disease progressed, social integration became less important to them as their basic physical needs became unmet (Galushko et al. 2014). The authors found that overall, social integration was identified as very important more by patients at lower levels of disability than by those at higher levels of disability. As one interviewee put it, ‘When your house is on fire, you have little time or attention to be paid to your social networks.’ (INT17)

4.6. Relationships change after a diagnosis of MS

Personal relationships may evolve following a diagnosis of MS. This section focuses on relationships from the perspective of the person with MS, and is complemented by Section 5.5 below that addresses relationship effects from the perspective of carers and family members. Research suggests that some of the changes to personal relationships are driven by physical changes, some reflect changing circumstances, and some represent a shift in focus. There is a substantial body of literature examining the effects of MS on sexual functioning and its implications for personal relationships. In general, it finds that MS impairs physical functioning related to sex directly (e.g. impaired genital sensation, decreased sexual desire, erectile dysfunction) and indirectly (e.g. fatigue, muscle weakness/spasticity), but that psychosocial issues around relationships are also a key concern (Cordeau & Courtois 2014; Delaney & Donovan 2017; Pottgen et al. 2018). The literature suggests that physical sexual functioning in MS is linked directly with a person’s level of disability as measured by their EDSS score, as well as with the duration of their disease, with physical sexual functioning progressively declining as the disease progresses (Cordeau & Courtois 2014). However, research suggests that the level of physical sexual dysfunction does not differ based on the type of MS (Delaney & Donovan 2017). Beyond the physical changes, people with MS report changes in body image or feelings of attractiveness that negatively impact their sexual functioning, worries about sexually satisfying their partner, and difficulty communicating with their partner about sex, which may negatively affect their relationship (Cordeau & Courtois 2014). One interviewee noted that sexual dysfunctions can lead some people with MS to feel like ‘no one wants them’ except for other people with MS (INT12). Circumstances can also negatively affect sexual activity and romantic relationships when having to depend on others for care results in a lack of privacy that negatively affects sexual activity (Delaney & Donovan 2017).

The literature and interviews highlighted that relationships face additional strains, including personality changes resulting from MS-related cognitive changes (INT05), and mental health issues such as depression and anxiety (Bishop et al. 2016) that can be challenging for a partner to cope with (INT16). One interviewee mentioned that relationships might also be impacted by the limited ability of the person with MS to socialise due to issues such as fatigue and limited mobility (INT22). This can potentially lead to frustration on the part of the partner without MS if they routinely have to cancel plans (INT22).

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19 This is in agreement with Maslow’s hierarchy of needs, a five-tier model of human needs in which needs lower down in the pyramid structure must be satisfied before individuals can attend to needs higher up.
Another interviewee noted that changes in relationships could be positive or negative, but that relationships always experience an element of change (INT21).

A diagnosis of MS can also impact the relationship between a parent and a child. A systematic review found that symptoms of MS such as fatigue interfere with parental functioning, ranging from being involved with daily activities to lack of patience (Razaz et al. 2014). One study looking at Italian women with MS found that women who were not aware of their diagnosis when they had children used their role as a mother to focus on how their children would respond to the diagnosis and on ensuring that their children’s needs were met, rather than on their own response to the disease (Willson et al. 2018). These women were more likely to say that they found strength in their children than women who chose to have children after their diagnosis. However, this study also found that some women felt a sense of loss that they were not always able to fulfil their roles as mothers as they were unable to participate in all of their children’s activities. This, alongside their children seeing them managing the symptoms of their disease, created a sense of loss and feelings of regret in some women (Willson et al. 2018).

4.7. Despite challenges, people with MS can (and increasingly do) stay in the workforce

MS is frequently diagnosed between the ages of 20–40 years (Palace 2001). As such, the disease often affects people during their prime working years. Researchers consistently find that workforce participation rates for people with MS are lower than that of the general population (Van Dijk et al. 2017). One study from 2006 found that exact workforce participation rates of people with MS vary by country, with estimates ranging from 26 per cent in Spain to 42 per cent in Italy (Kobelt et al. 2006) (Figure 4.1). A systematic review of papers published between 1993 and 2013 found that men with MS have workforce participation rates between 4 and 26 per cent lower than that of women (Raggi et al. 2016). One study hypothesised that this difference was potentially due to factors such as men being more likely to have physically demanding jobs or being less likely to ask for accommodations at work in a timely fashion (Van Dijk et al. 2017).
Many factors affect the ability of people with MS to continue working after their diagnosis. These include disease severity and physical functioning, mental health, social support and an employer’s willingness to make accommodations. For example, there is evidence that disability severity, mobility, and hand functioning are key factors in a person’s ability to continue working, with higher EDSS scores and reduced mobility and hand function associated with people reducing the amount they work, changing their type of work, or leaving work altogether (Raggi et al. 2016; Salter et al. 2017). Difficulties walking are particularly closely associated with work-related difficulties such as increased unemployment and sick leave (Raggi et al. 2016; Li et al. 2015). Issues with cognition, memory, and information-processing ability are also associated with work performance, with lower functioning in these outcomes linked to lower work performance and difficulties remaining in the same job role (Raggi et al. 2016; Salter et al. 2017). Fatigue is also linked with absenteeism and unemployment (Salter et al. 2017; Kobelt, Thompson, et al. 2017; Li et al. 2015), a point supported by comments from interviewees (INT06, INT009, INT15). Interviewees noted that different types of job may present different challenges for people with MS, for example, the mobility issues associated with MS may present the greatest barrier to remaining in the workforce for physical labourers, whereas for workers in the knowledge economy, cognitive issues or vision problems might be the largest barriers (INT01, INT05).

The relationship between work and mental well-being is complex, with depression, anxiety and mood influencing employment outcomes and job productivity, and vice versa with work affecting mental well-being. Research finds that for people with MS, psychosocial factors such as having a low mood or being depressed are linked with workplace difficulties, with workers who exhibit these disorders being more likely to reduce their working hours or to leave the workforce. However, research also finds that unemployment is a risk factor for depression (Raggi et al. 2016). Research indicates a similar pattern with
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anxiety and stress, where work is both influenced by and a cause of anxiety and stress for people with MS. For example, a 2015 study of people with MS in Italy found that factors such as feeling overwhelmed, anxious, or stressed, as well as experiencing a lack of motivation, made it difficult for people with MS to manage work (Ponzio, Brichetto, et al. 2015). Other research suggests that work can also be the cause of anxiety, with one systematic review finding that presenteeism, the act of attending work when unwell, was significantly associated with elevated levels of anxiety for people with MS (Butler et al. 2016).

In addition to the real economic losses that people with MS suffer when they are forced to reduce or stop working (see Section 6.3 for details), there are also issues of identity and social integration influenced by an individual’s relationships with work. People with MS report that they feel a loss of identity along with the loss of their job because their job comprises an important part of how they see themselves (Hartley et al. 2014). This is a point emphasised by interviewees who described how the loss of employment can leave people with MS feeling ‘useless’ (INT04) and questioning their self-worth (INT05). Additionally, social isolation may increase when people leave work (Hartley et al. 2014) (INT11). However, it should be noted that people with MS rate being effective in their job as becoming less important to their QoL as their disease progresses (Mattarozzi et al. 2016).

4.8. Positive employment experiences contribute to retaining people with MS in the workforce

Employment experiences of people with MS can be moderated by individual, social support and work-based factors (Ponzio, Gerzeli, et al. 2015). At the individual level, research suggests that positive individual attitudes towards work (described as being optimistic, being motivated and interested in the work, and being certain about one’s capabilities) is associated with maintaining employment. Individual coping styles might also affect employment status, with research finding that people with MS who adopt maladaptive coping mechanisms such as disengagement and substance abuse are more likely to leave the workforce than those who avoid these behaviours (Strober & Arnett 2016). Evidence also suggests that social support factors such as family support and help with household tasks could make it easier for people with MS to maintain their jobs (Ponzio, Brichetto, et al. 2015).

Work-based factors such as employer and co-worker support can enable people with MS to stay in the workforce for longer. Interviewees highlighted the necessity of employers supporting workers with MS by making necessary adaptations (INT01, INT17, INT18) and providing flexible schedules (INT15), while acknowledging that some people with MS may be reluctant to disclose their disease status out of a fear of negative repercussions, including losing their job (INT04). Research from Europe and Australia generally finds that employers are willing to make accommodations related to an employee’s job role, but that they may be less inclined to put in place needed environmental changes, such as making offices wheelchair accessible (Van Dijk et al. 2017; Carrié et al. 2014). Although environmental barriers of this type are reported less frequently by people with MS in research studies than task-related barriers (e.g. the pace or sequencing or work) or barriers resulting from company policies, one study from Italy found that 22 per cent of respondents cited the presence of stairs, 19 per cent the presence of unsuitable floors or floor coverings, and 16 per cent the lack of accessible parking as a barrier to work (Carrié et al. 2014). Research also shows that having supportive colleagues is important to people with MS (Ponzio, Brichetto,
et al. 2015); however, a study from Italy found that 56 per cent of workers with MS reported working with people they felt were hostile towards them due to their MS (Carrieri et al. 2014). Other perceived barriers to work typically include task-related barriers such as the pace or sequencing of work, reading written instructions, and working under stress or deadlines; or aspects of company policy such as inflexible sick or vacation leave policies, inflexible work schedules, or vague job descriptions (Carrieri et al. 2014). Carrieri et al. (2014) report that there is some evidence that these perceived barriers are weakly correlated with disease progression, with tasks requiring physical ability perceived as a greater barrier for people with reduced physical functioning, and people with higher cognitive functioning perceiving fewer barriers related to aspects of company policy.

Although research shows a greater likelihood of leaving the workforce over time following an MS diagnosis (Bishop et al. 2016; Van Dijk et al. 2017), recent research from Europe and Australia suggests that the prospects for long-term employment for people with MS are improving. For example, while a study from 2012 based in the United Kingdom estimated that ten years after diagnosis, 20 per cent of people with MS who had been employed at the time of diagnosis were still in the workforce (McFadden et al. 2012), recent studies from Europe have found that employment rates ten years post-diagnosis were as high as 68 per cent (Fantoni-Quinton et al. 2016, as referenced in Van Dijk et al. 2017). Furthermore, there is evidence that the number of people with MS living in Europe taking early retirement is decreasing leaving them in the workforce for longer, and a recent unrelated study found that workforce participation for people with MS in Australia increased from 48.8 per cent in 2010 to 57.8 per cent in 2013 (Van Dijk et al. 2017). Together, this evidence suggests that the ability of people with MS to remain in the workforce may be improving. In addition to the support of employers in making necessary modifications, Van Dijk et al. (2017) suggest that at least some of this improvement may be explained by the availability of DMTs, given their role in delaying disease progression and assisting with effective early symptom management.
5. Impacts of MS on carers and family

This chapter describes the impacts of MS on the carers and families of people with MS. Findings from the literature are supplemented with evidence from the key informant interviews.

The key findings are:

- MS is associated with a high level of informal care.
- Carers experience career disruption as a result of caregiver burden.
- Caregiver burden in MS negatively impacts the mental well-being of carers.
- The unpredictability and uncertainty of MS are important factors affecting the mental well-being of carers of individuals with MS.
- Taking on the role of a carer leads to a shift in the relationship with the individual with MS.
- There is lack of support available to deal with caregiver burden.

These findings are described in further detail below.

5.1. MS is associated with a high level of informal care, which increases as the disease progresses

People with MS often require informal care in addition to the care provided by the healthcare system. Informal care is defined as unpaid care provided by an individual within the social network of a patient, such as a spouse, parent, child, relative, friend or neighbour (Triantafillou et al. 2010). Interviewees from Australia, Canada, Spain and the United Kingdom mentioned that the families of individuals with MS had to take on the responsibility of providing care to individuals with MS as the healthcare systems of their countries would only cover the direct costs of the disease (e.g. hospital admittance and medication) (INT01, INT04, INT05, INT11). An interviewee from Spain commented on the importance of ‘family’ in Spain, and how if a family member develops MS it is the family’s responsibility to care for that person (INT04).

In MS, the requirements of care increase with disease progression (Kudra et al. 2017; Appleton et al. 2018). Interviewees mentioned that as the disease progresses, the symptoms also become more physical (e.g. reduced mobility), leading to increased dependency on others (INT04, INT05, INT13, INT16). Three interviewees commented that decreased cognitive abilities led carers to provide not only physical...
support but also support with, for example, managing appointments or making financial decisions (INT01, INT02, INT16).

5.2. Carers experience career disruption as a result of caregiver burden

Carers of people with MS are likely to experience career disruption as a result of caregiver burden, especially as the disease progresses. Two studies found that carers of people with MS were likely to stop working due to the burden associated with caring for a person with MS (Borreani et al. 2014; Kudra et al. 2017), mainly when caring for a person with severe MS (Borreani et al. 2014). This finding from the literature was echoed by interviewees who mentioned that as the disease progresses, the level of care and support required by individuals with MS increases, leading in many cases to carers taking a leave of absence from the workforce (INT02, INT05, INT10, INT12, INT14, INT15, INT20, INT21). Findings from the literature indicate that the likelihood of abandoning the workforce was even higher for female carers than male carers (Schofield et al. 2014),20 as well as for carers cohabiting with care recipients (Kudra et al. 2017). One interviewee mentioned that carers were less likely to abandon the workforce if there was flexibility in their working arrangements; however, this was currently not the norm for their country (INT15).

One study found that carers were likely to either leave work to provide informal care or conversely were likely to work more in order to make up for the loss of income experienced by the person with MS (Topcu et al. 2016). One interviewee mentioned that carers may work either less or more to accommodate the disease (INT09), and another commented that when an individual with MS is unable to work there is increased pressure on the carer to be both the primary carer and the primary source of income for the family (INT01). Two interviewees mentioned that although carers did not always remove themselves from the workforce, they did refuse professional promotions with increased time commitments (INT12, INT17).

Removal from the workforce for both people with MS and their carers can have an economic toll on families (INT05, INT22), especially considering the cost of home adaptation required at later stages of the disease (INT01, INT12, INT22). In some countries, such as Spain and Australia (as mentioned by interviewees), to enable carers to provide care without suffering economic detriment, individuals may register as a carer and receive some funding for the care they provide to their family members (INT21, INT22).21 However, given the bureaucratic burden of the process and the low amount of funding received, only a small proportion of people seek to do this (INT21).

20 This study did not look specifically at MS but rather grouped MS with ‘other diseases of the nervous system’, such as epilepsy, cerebral palsy, paralysis and chronic fatigue syndrome.

21 This statement is based on findings from the interviews and does not mean other countries do not provide this support, but rather we were unable to confirm this through the interviews.
5.3. Caregiver burden in MS negatively impacts the mental health of carers and family members

There are a number of psychosocial outcomes for carers reported in the literature, alongside reports of a lack of support for their psychosocial well-being. Studies have reported that carers of people with MS have high levels of distress, strain, and perceived burden, and lower health-related quality of life (Labiano-Fontcuberta et al. 2015; Topcu et al. 2016). One study found that one-third of carers of people with MS experience clinically significant symptoms of psychological distress (Bambara et al. 2014). A second study found that 44 per cent of carers report symptoms of anxiety and 24 per cent report symptoms related to depression (Kudra et al. 2017).

In a literature review measuring the burden on informal carers of patients with long-term conditions including MS, Kudra et al. (2017) found that as the level of dependency increases in a patient there are more caring tasks involved, which is associated with poorer health in carers. Topcu et al. (2016) found that carers suffer from distress as a result of the uncertainty and unpredictability of MS progression. A study focusing on armed forces veterans with MS found that greater disease severity of MS was associated with higher levels of depressive symptoms among carers, possibly due to an increase in the overall care requirements and medical complexities of the person with MS, which increases the caregiving demands in order to meet the care recipient needs (Bambara et al. 2014). The authors state that the availability of, and access to, social support (e.g. flexibility from an employer) may reduce general life stress as well as caregiver burden (Bambara et al. 2014).

Studies have assessed the impact of caring for a parent or a child with MS on the psychosocial well-being of the carer. A study by Uccelli (2014) concluded that across carers of people with MS, parent carers have the highest levels of clinical depression. This is complemented by a second study that assessed psychological distress in parents of children and adolescents with MS who suffered symptoms of fatigue (Carroll et al. 2019). Carroll et al. (2019) found that mean psychological distress scores were higher in parents of fatigued children and adolescents with MS than in parents of non-fatigued children and adolescents with MS (Carroll et al. 2019). The impact of fatigue on individuals with MS is described in further detail in Section 4.1.

One study looking at the impact of parental MS on the mental health of children found that children of parents with MS had a 34 per cent higher rate of psychiatric disorders than children whose parents did not have MS (Razaz, Tremlett, Marrie, et al. 2016). A second study from the same authors found that children of mothers with MS had a higher rate of mood or anxiety disorders than children of mothers without MS (Razaz, Tremlett, Boyce, et al. 2016). However, this difference was not observed between children of fathers with MS and children of fathers without MS (Razaz, Tremlett, Boyce, et al. 2016).

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22 This finding was mainly based on a cohort study of 79 carers of individuals with MS in Mexico (Lehan & Arango-Lasprilla 2012). Other categories of carers included in the study were: spouse/partner, sibling, son/daughter, and aunt/uncle.
5.4. The unpredictability of MS is an important factor affecting the mental well-being of carers of individuals with MS

The progressive, unstable and unpredictable nature of MS greatly affects the mental well-being of carers, as identified both in the literature and through the interviews. One study found that carers worry about future stress and about what will happen to their care recipient in the later stages of the disease and at times of exacerbations when people with MS become more dependent on others (Topcu et al. 2016). Further studies have reported that carers experience feelings of worry, fear, anger, and guilt (Strickland et al. 2015; Neate et al. 2018), as well as a sense of loss and grief (Neate et al. 2018). Carers also experience concerns about the future and what would happen if they are not around to care for the person with MS. One study found that an impact of this was that carers may not seek medical attention when they have medical issues for fear that there will be no one able to take care of the person with MS (Borreani et al. 2014).

Interviewees commented that the uncertainty of MS is a big concern for carers of people with MS (INT11, INT12, INT18, INT21). They mentioned that family members worry about how the disease will progress (INT12) and what their lives will be like once the disease progresses (INT10), how they will prepare financially for the long term (INT10, INT11), how the disease will affect their children (INT11) and whether their children will also have the disease (INT4, INT11), and how the diagnosis of MS will affect family planning (INT20). One interviewee said that carers also suffer from anxiety as a result of the uncertainty and unpredictability of the disease (INT22).

5.5. Taking on the role of a carer leads to a shift in the relationship with the individual with MS

As discussed in Section 4.6, personal relationships with carers, family members and the individual’s wider network may shift with a diagnosis of MS. One interviewee commented that ‘progressive MS affects families, not individuals’ and that the interviewee ‘always [tries] to talk about people affected by MS rather than people living with MS’ (INT17).

Caring for a partner with MS was found in much of the literature to have negative effects on the couple. One study found that spouses who provide care may be less likely than other carers, such as siblings, to embrace the caregiving role, which was attributed to a sense of duty and obligation (Topcu et al. 2016). This may also be due to the fact that spousal relationships are based on equality, and as the disease progresses the carer spouse takes on more familial responsibilities, as well as more of a carer role than a spousal role (INT13, INT20).

A more rapid onset of disease with fewer periods of remission, as well as situations where the partner has to adopt a clear carer role, have been associated with poor coping among couples (Uccelli 2014). One study found that difficulties in a relationship were associated with taking on certain chores that had previously been the domain of the person with MS (Strickland et al. 2015). Another study reported that MS can cause loss of companionship or intimacy, which can strain the relationship and lead to disagreements and conflicts (Topcu et al. 2016). Additionally, given the fact that the onset of MS generally occurs in early to mid-adulthood, becoming a carer of someone with MS often comes at a time
when there are conflicting demands between relationships, children and a career, which can lead to reduced employment, financial difficulties, separation and divorce (Appleton et al. 2018). A literature review that assessed the impact of MS on families found that 67 per cent of relationships in which one of the individuals had a diagnosis of MS had ended by 24 years after the onset of the disease, compared with 47 per cent in a control group where neither person in the relationship had a diagnosis of MS (Uccelli 2014). This study found that separation was more likely to occur in couples where the woman was diagnosed with MS and the male partner was healthy. However, being younger and having children was found to reduce the likelihood of separation (Uccelli 2014). The higher rate of divorce among couples where one person has MS was echoed by interviewees (INT05, INT16, INT20).

As mentioned in Section 4.6, a parental diagnosis of MS may change the relationship between a child and the parent. A literature review that assessed the impact of MS on family members found that children of parents with MS may feel more isolated than their peers as a result of caregiving responsibilities that impedes their involvement in other activities (Uccelli 2014). However, the author also found that children of parents with MS may be more independent and self-sufficient, and that some children reported feeling proud that they were relied on to provide care (Uccelli 2014).

All studies identified in this report that looked at the impact of MS on the carer were focused on the impact on family members. A survey conducted across 16 countries identified that nearly half of individuals with MS studied (46.3 per cent) were receiving informal care from family members (Kobelt, Thompson, et al. 2017). The paper did not say what proportion received informal care from people other than family members, nor what proportion received no informal care at all. The cost associated with informal care is described in Section 5.1. Although the majority of studies included in the literature review report on negative changes to social relationships of carers, one study looking at the psychological shift in partners of people with MS found that some carers felt the diagnosis of MS had led to positive changes, such as seeing life in a different way, re-evaluating and focussing on what was important in life, and a sense of empowerment (Neate et al. 2018).

5.6. There is lack of support available to deal with caregiver burden

One interviewee said that in a way, carers also live with MS (INT20). However, there is evidence that the psychosocial impacts on carers described above are not currently adequately catered for through support, the lack of which has been found to be associated with anxiety and depression in carers (Kudra et al. 2017). Interviewees agreed that overall there was lack of support offered to carers (INT01, INT04, INT05, INT09, INT11, INT12, INT15, INT22). Interviewees commented that although there are some government schemes aimed at offering relief to carers, these are generally underfunded and understaffed (INT01, INT04). Interviewees mentioned that most support provided to carers was organised by hospices, charities or patient associations (INT01, INT05, INT09, INT22).

The lack of support available may be due to the lack of understanding of caregiver burden. Studies have found that carers feel there is a lack of understanding of the challenges they face (Strickland et al. 2015; Vasileiou et al. 2017). Two studies using interviews to understand the experience of carers of people with MS (Strickland et al. 2015; Vasileiou et al. 2017) and a literature review on the impacts of MS on family members (Uccelli 2014) found that carers feel that they do not receive strong support, leading to feelings
of loneliness and isolation. Additionally, a literature review focused on the experiences of spousal or partner carers of people with MS found that carers may feel that they have lost their role in society and in relationships with friends and family, and that this need for social support is unmet (Appleton et al. 2018).

Evidence suggests that carers experience a lack of information on MS, as well as a lack of support and understanding, which may leave them feeling helpless (Vasileiou et al. 2017). For example, a phenomenological study based in the United Kingdom conducted through interviews found that carers are generally not included in key consultations with medical and nursing staff (Strickland et al. 2015). This study found that although the experience of the carer followed a similar trajectory to that of the person with MS, the carer experienced it from the perspective of a ‘concerned observer’. Lack of information on MS may affect family functioning and can contribute to anxiety in parents of children with MS (Ucelli 2014). Research also finds that children of parents with MS commonly report a lack of access to information about the disease and that they avoid talking to their ill parent about MS (Ucelli 2014). Additionally, adults who had been carers as children reported that they felt they had been constantly preparing for the death of a parent and were unprepared for disease progression (Ucelli 2014).

It is important to note that carers do not always actively seek the support they may require. One study found that carers of people with MS are unlikely to share their worries with the person with MS for fear of increasing the burden on the patient (Strickland et al. 2015). One interviewee from France mentioned that although there is respite care available for carers, people may not seek this opportunity due to feeling guilty about turning over caring responsibilities to a non-family member (INT12). However, another study found that carers seek support online, such as in the form of information about the disease and caring strategies, or by airing frustrations and creating a sense that they are not alone (Sillence et al. 2016).
6. Impacts of MS on society

This chapter describes the costs of MS to wider society, grouped by type of impact reported. The literature is supplemented with evidence from the key informant interviews.

The key findings are:

- Almost half of MS patients receive informal care at an average of 30 hours per week globally.
- MS is associated with high levels of healthcare utilisation and associated healthcare costs, with three-quarters of MS patients across Europe having at least one consultation with a healthcare professional over a three month period.
- Lost productivity accounts for a large amount of the total cost of MS to society through both absenteeism and presenteeism.
- The societal impacts of MS are varied and go beyond costs to the healthcare system and lost productivity, including disruption of education of young patients and community engagement.

These findings are described in further detail below.

6.1. Almost half of MS patients receive informal care at an average of 30 hours per week globally

As described in Section 5.1, MS is associated with high levels of informal care time. In a European-wide survey of 16,808 MS patients looking at the burden and costs of MS, Kobelt, Thompson, et al. (2017) found that 46 per cent of respondents received informal care from family members. A systematic review of the global literature found that the average caregiving time required for MS was 30 hours per week (Oliva-Moreno et al. 2017).

Table 6.1 summarises the proportion of MS patients receiving informal care from family members, and the amount of this care across Europe. The information in this table is based on country-specific analyses of the Kobelt, Thompson, et al. (2017) Europe-wide survey of MS patients.
Table 6.1 Proportion and amount of informal care received by MS patients across Europe

<table>
<thead>
<tr>
<th>Country</th>
<th>Percentage of patients</th>
<th>Amount of informal care</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>France</td>
<td>40</td>
<td>On average 16.7 days per month and 3.7 hours per day</td>
<td>Lebrun-Frenay et al. (2017)</td>
</tr>
<tr>
<td>Germany</td>
<td>46</td>
<td>On average 17.7 days per month and 3.8 hours per day</td>
<td>Flachenecker et al. (2017)</td>
</tr>
<tr>
<td>Italy</td>
<td>44</td>
<td>On average 16.8 days per month and 6.3 hours per day</td>
<td>Battaglia et al. (2017)</td>
</tr>
<tr>
<td>Spain</td>
<td>45</td>
<td>On average 16.6 days per month and 6.3 hours per day</td>
<td>Oreja-Guevara et al. (2017)</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>69</td>
<td>On average 19.3 days per month and 4.9 hours per day</td>
<td>Thompson et al. (2017)</td>
</tr>
</tbody>
</table>

Source: RAND Europe analysis

Such informal care time has substantial associated costs, which are absorbed by the informal caregiver (e.g. through lost personal income and leisure time) and society (e.g. through lost productivity). Oliva-Moreno et al. (2017) found through a systematic review that the average cost of informal caregiving was €13,092 per annum, although this varied considerably by country. In the context of Italy, a separate empirical study using a survey of 1,686 MS patients estimated that informal care costs amounted to €10,837 per year (Ponzio, Gerzeli, et al. 2015).

Kwiatkowski et al. (2014) used a mixed methods study of 41 MS patients receiving natalizumab\(^{23}\) to estimate that informal care makes up 4 per cent of the total annual cost of MS. However, Oliva-Moreno et al. (2017) found that, on average, the cost of informal care time accounted for 23 per cent of total societal costs associated with MS across all patients, considerably more than the 4 per cent associated with patients receiving natalizumab (Kwiatkowski et al. 2014). In their survey of patients with MS in Italy, Ponzio, Gerzeli, et al. (2015) estimated that informal care makes up 27 per cent of the overall annual costs associated with MS. These costs are found to vary by disease severity, and contribute to a notable proportion of the total costs associated with MS (Table 6.2).

\(^{23}\) Natalizumab is a DMT recommended for the treatment of highly active or severe MS (MS Society 2016).
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Table 6.2 Mean annual costs (in €2018) associated with informal care received by MS patients across Europe

<table>
<thead>
<tr>
<th>Country</th>
<th>Cost of informal care (per patient per year)</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mild MS</td>
<td>Moderate MS</td>
</tr>
<tr>
<td>France</td>
<td>€218</td>
<td>€1,351</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Germany</td>
<td>€756</td>
<td>€4,685</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Italy</td>
<td>€915</td>
<td>€5,235</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spain</td>
<td>€1,115</td>
<td>€7,631</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>United Kingdom</td>
<td>€703</td>
<td>€5,335</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note: Mild MS = EDSS score 0–3, Moderate MS = EDSS score 4–6.5, Severe MS = EDSS score 7–9.

Note: Values were inflated to 2018 values and then converted from pound sterling to euro based on the average exchange rate in 2018, £1.00 to €1.13, to ensure consistency with the rest of the table. Mild MS: £585; €703. Moderate MS: £4,441; €5,335. Severe MS: £11,337; €13,620.

Interviewees commented on the cost of informal care in their respective countries. In some countries, there may be assistance for informal carers to help compensate them for the services they provide outside of the formal market (INT01, INT09, INT21, INT22). One interviewee from Australia, for example, commented on a programme through which informal carers can register as official carers to receive financial assistance from the government (INT21). However, this interviewee reported that the programme is not used to its full potential because of difficulties in applying for and accessing these funds, which makes it an unattractive programme to many informal carers.

6.2. MS is associated with high levels of healthcare utilisation and associated healthcare costs

MS is associated with high levels of healthcare utilisation and healthcare costs, which vary by disease severity and progression, number and type of relapse, age, and gender. Healthcare utilisation refers to the healthcare services, diagnostics and medicines used by MS patients as a result of their condition, and healthcare costs are the costs associated with this utilisation. In their survey of MS patients across Europe, Kobelt, Thompson, et al. (2017) found that 75 per cent of respondents had had at least one consultation over the past three months, with 62 per cent seeing a neurologist, 28 per cent seeing a general practitioner (GP) and 12 per cent seeing an MS nurse. Table 6.3 provides a breakdown of the consultations that respondents received over the previous three months by country, based on country-level analyses of the Kobelt, Thompson, et al. (2017) European-wide survey. The table also presents information on the percentage of respondents having in-patient and day case admissions, as well as the average time and/or length of admissions, and the proportion of respondents attending a rehabilitation centre.
**Table 6.3 Proportion of MS patients receiving health services across Europe in the previous three months**

<table>
<thead>
<tr>
<th>Country</th>
<th>In-patient admissions</th>
<th>Day admissions</th>
<th>Patients attending rehabilitation centres</th>
<th>Consultations</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>France</td>
<td>8%</td>
<td>36%</td>
<td>10%</td>
<td>82% of which 61% with a neurologist, 41% with a physiotherapist &amp; 39% with a GP</td>
<td>Lebrun-Frenay et al. (2017)</td>
</tr>
<tr>
<td>Germany</td>
<td>10%</td>
<td>4%</td>
<td>5%</td>
<td>90% of which 81% with a neurologist, 45% with a physiotherapist &amp; 35% with a GP</td>
<td>Flachenecker et al. (2017)</td>
</tr>
<tr>
<td>Italy</td>
<td>5%</td>
<td>19%</td>
<td>9%</td>
<td>81% of which 71% with a neurologist, 21% with a physiotherapist &amp; 19% with a GP</td>
<td>Battaglia et al. (2017)</td>
</tr>
<tr>
<td>Spain</td>
<td>4%</td>
<td>27%</td>
<td>16%</td>
<td>75% of which 65% with a neurologist, 28% with a GP &amp; 16% with a physiotherapist</td>
<td>Oreja-Guevara et al. (2017)</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>4%</td>
<td>7%</td>
<td>2%</td>
<td>67% of which 34% with a GP, 27% with an MS nurse &amp; 25% with a neurologist</td>
<td>Thompson et al. (2017)</td>
</tr>
</tbody>
</table>

Source: RAND Europe analysis based on the sources named in the table.

These studies also present the use of diagnostics and medication in the previous month, which are other important determinants of healthcare utilisation (see Table 6.4).24

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24 These are measured through the percentage of patients undertaking ‘investigations and tests’, using ‘medication for MS and MS-related symptoms’, using ‘drugs other than disease modifying therapies (DMTs)’ and using ‘non-prescription drugs’ in the past month.
Table 6.4 Proportion of MS patients receiving diagnostics and medication care across Europe in the previous month

<table>
<thead>
<tr>
<th>Country</th>
<th>Patients receiving investigations and tests</th>
<th>Patients receiving medication for MS symptoms</th>
<th>Drugs other than DMTs</th>
<th>Patients receiving non-prescription drugs</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>France</td>
<td>66%</td>
<td>94%</td>
<td>47%; of which 32% for walking, spasticity and pain &amp; 16% for depression</td>
<td>38%</td>
<td>Lebrun-Frenay et al. (2017)</td>
</tr>
<tr>
<td>Germany</td>
<td>56%</td>
<td>89%</td>
<td>45%; of which 34% for walking, spasticity and pain</td>
<td>53%</td>
<td>Flachenecker et al. (2017)</td>
</tr>
<tr>
<td>Italy</td>
<td>63%</td>
<td>91%</td>
<td>53%; of which 22% for walking, spasticity and pain &amp; 11% for depression</td>
<td>64%</td>
<td>Battaglia et al. (2017)</td>
</tr>
<tr>
<td>Spain</td>
<td>33%</td>
<td>91%</td>
<td>37%; of which 27% for walking, spasticity and pain &amp; 10% for depression</td>
<td>40%</td>
<td>Oreja-Guevara et al. (2017)</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>15%</td>
<td>73%</td>
<td>37%; of which 26% for walking, spasticity and pain, 16% for incontinence &amp; 14% for depression</td>
<td>54%</td>
<td>Thompson et al. (2017)</td>
</tr>
</tbody>
</table>

Source: RAND Europe analysis based on the sources named in the table.

Although the information in Table 6.3 and Table 6.4 presents average healthcare utilisation across all MS patients, some evidence suggests that healthcare utilisation varies depending on the severity of the condition and the presence of relapse. Sicras-Mainar et al. (2017) analysed the electronic health record data of 222 MS patients in Asturias and Catalonia in Spain and concluded that patients with ‘severe disability’ (i.e. EDSS score 4–9.5) had significantly higher healthcare utilisation than patients with ‘no or moderate disability’ (i.e. EDSS score 0–3.5). Specifically, patients with ‘severe disability’ had more primary care medical visits (12.3 vs. 8.5), more specialised medical visits (3.0 vs. 2.3), more emergency room visits (2.0 vs. 1.2) and more hospitalisation days (5.6 vs. 1.3).25 In addition to the impact of disease severity, Jones et al. (2016) found that relapse was significantly associated with increased healthcare utilisation among a sample of 715 MS patients in the United States who responded to their survey.

The healthcare costs associated with the healthcare utilisation of MS patients have been found to contribute to a large proportion of the total costs associated with MS. One study estimated that healthcare costs accounted for half of the total annual costs of MS in 2014 (Kwiatkowski et al. 2014). In a systematic...

25 All of which is statistically significant at the 0.01 level.
review of the literature relevant to Spain, Fernandez et al. (2017) found that 30 to 50 per cent of the total cost of MS to the country was made up of healthcare costs (Fernandez et al. 2017). The authors found that MS resulted in annual direct healthcare costs of between €395 and €455 million nationally (Fernandez et al. 2017). When excluding the cost of DMT, this was estimated to be €3,583 per patient on average annually. A separate study of Italian MS patients estimated the annual healthcare costs associated with MS to be €13,707 on average, of which around half were attributable to DMT and 27 per cent were a result of admission to hospital (Ponzio, Gerzeli, et al. 2015).

Interviewees commented on the high costs of MS drugs and of DMTs in particular, as well as the high cost associated with specialised MS care and neurologists. Two interviewees – one from the United States and one from Canada – commented that DMTs have caused the societal costs of MS to increase, both because of the high cost of new DMTs and because DMTs may provide a viable treatment option for people with progressive or advanced MS, who previously did not access as many health services simply because there was not much that healthcare services could do for these patients.

Furthermore, after comparing healthcare cost data for MS patients to those without MS in the United States using routinely collected panel survey data, Campbell et al. (2014) estimated that costs were 5.1 times higher (i.e. $27,368 more) among the MS population after controlling for measured characteristics. For example, adjusted outpatient visit costs were $3,873 greater annually for the MS population.

Interviewees commented on the high costs of particular elements of health and social care in their country, although these high costs may also apply to other countries with similar healthcare systems. For example, an interviewee from Italy commented that the costs of MS become higher when the disease is not managed properly (INT14). Two interviewees from Australia and France commented on the high costs of equipment such as wheelchairs and home adaptations, and said that although the government covers part of this cost, people with MS and their families will often invest in better equipment/adaptations themselves (INT01, INT12). Similarly, an interviewee from Spain commented that although rehabilitation is partially covered by the government, people will often pay for extra rehabilitation services to cover the cost of rehabilitation outside of the specified interval the government covers (INT22).

Healthcare costs associated with MS differ depending on disease severity, relapse and progression, as well as the country in which the patient resides:

- In the United States, the total annual cost of healthcare was found to increase from $54,592 to $70,699 as EDSS scores increased from less than 3 to greater than 5 among MS patients (Jones et al. 2016). A relapse of MS was associated with a $4,624 increase in healthcare costs (Jones et al. 2016).  

- In Spain, healthcare costs have been found to vary substantially depending on disease severity. According to Fernandez et al. (2017), costs from a 2006 study, adjusted for inflation to 2018 values, were €9,056 for patients with an EDSS score of 0, €14,125 for an EDSS score between 3.5 and 5.5, €10,798 for an EDSS score between 6 and 7, and €7,028 for an EDSS score of more than 7, with DMT accounting for 80 to 90 per cent of these costs. The authors of a 2014 study found that a mild relapse costs on average €332 in healthcare costs, compared with €1,058 for a
Exploring the societal burden of multiple sclerosis moderate relapse and €3,686 for a severe relapse (Fernandez et al. 2017). Another study in Spain found that patients with ‘severe disability’ (i.e. an EDSS score of between 4 and 9.5) had healthcare costs of €11,828, compared to €9,403 for patients with ‘no moderate disability’ (i.e. an EDSS score of between 0 and 3.5) (Sicras-Mainar et al. 2017).

- In Italy, a cohort study of over 500 newly diagnosed relapsing remitting MS patients, who were followed up for ten years, found that a one-point higher EDSS score at the time of diagnosis was associated with a 13 per cent increase in annual healthcare costs (Moccia, Palladino, Lanzillo, Triassi, et al. 2017). Furthermore, milder disease evolution after ten years was associated with higher healthcare costs for treating MS in the cohort (Moccia, Palladino, Lanzillo, Carotenuto, et al. 2017).

Table 6.5 presents the annual costs associated with healthcare received by MS patients across Europe, based on country-level analyses of the Kobelt, Thompson, et al. (2017) European-wide survey. The costs vary significantly by disease severity.

**Table 6.5 Mean annual costs (€2018) associated with healthcare received by MS patients across Europe**

<table>
<thead>
<tr>
<th>Country</th>
<th>Cost of healthcare (per patient per year)</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mild MS</td>
<td>Moderate MS</td>
</tr>
<tr>
<td>France</td>
<td>€17,819</td>
<td>€22,664</td>
</tr>
<tr>
<td>Germany</td>
<td>€19,875</td>
<td>€20,108</td>
</tr>
<tr>
<td>Italy</td>
<td>€20,645</td>
<td>€24,213</td>
</tr>
<tr>
<td>Spain</td>
<td>€15,750</td>
<td>€22,472</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>€7,092</td>
<td>€6,621</td>
</tr>
</tbody>
</table>

Note: Mild MS = EDSS score 0–3, Moderate MS = EDSS score 4–6.5, Severe MS = EDSS score 7–9.

Note: Values were inflated to 2018 values and then converted from pound sterling to euro based on the average exchange rate in 2018, £1.00 to €1.13, to ensure consistency with the rest of the table. Mild MS: £5,903; €7,092. Moderate MS: £5,511; €6,621. Severe MS: £5,039; €6,054.

Source: RAND Europe analysis based on the sources named in the table.

Age and gender have been found to influence the healthcare costs associated with MS (Moccia, Palladino, Lanzillo, Triassi, et al. 2017), with each additional year of age at diagnosis associated with a 0.74 per cent decrease in the annual costs, while being female was associated with 12 per cent lower annual costs than being male.

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26 The publication year was used as the cost year for inflating values to 2018 values because the publication did not specify the year associated with the costs.
6.3. Lost productivity accounts for a large amount of the total cost of MS to society through both absenteeism and presenteeism

As described in Section 4.7, the physical and mental effects of MS result in lower labour force participation by patients with the disease, as well as by their carers and support network (Section 5.2). As well as MS having a direct impact on an individual’s ability to participate in the labour force, it also has an impact on an individual’s ability to produce work when participating in the labour force (i.e. presenteeism) (Ponzio, Gerzeli, et al. 2015; Kobelt, Langdon, and Jönsson 2019). This has a direct impact on a patient’s income from employment, as well as a wider impact at the macroeconomic level through lost productivity (Ponzio, Gerzeli, et al. 2015; Campbell et al. 2014; Fernandez et al. 2017; Palmer et al. 2019). The size of the productivity loss appears to depend on disease severity and progression, as well as relapse (Fernandez et al. 2017; Sicras-Mainar et al. 2017; Thompson et al. 2017; Lebrun-Frenay et al. 2017; Oreja-Guevara et al. 2017; Battaglia et al. 2017; Flachenecker et al. 2017). Ultimately, lost productivity appears to account for a large amount of the total cost of MS to society (Kwiatkowski et al. 2014; Fernandez et al. 2017).

At the individual level, the major components of lost productivity are absenteeism (i.e. lost working days) and presenteeism (i.e. reduced productivity when at work). In a survey of 1,686 Italian MS patients, 21 per cent experienced missing work due to their condition, and 20 per cent experienced a loss of working activity while at work (i.e. presenteeism) (Ponzio, Gerzeli, et al. 2015). Furthermore, based on additional analysis of the survey undertaken by Kobelt, Thompson, et al. (2017), Kobelt, Langdon, and Jönsson (2019) concluded that a 1-point increase in subjective cognitive impairment was associated with a 0.41-point increase in presenteeism as a result of MS, both measured on a self-reported 0 to 10 visual analogue scale. Similarly, a 1-point increase in fatigue was associated with a 0.28-point increase in presenteeism among MS patients, measured on the same scale. Both of these effects were statistically significant at the 0.01 level.

Unsurprisingly, such negative employment and productivity outcomes have been found to have a detrimental impact on employment income. In a survey of Italian MS patients by Ponzio, Gerzeli, et al. (2015), 63 per cent were employed, and among these, 34 per cent had experienced a reduction in income as a result of their condition. In an analysis of routinely collected data on MS patients in the United States, Campbell et al. (2014) found that total annual income was $7,613 lower for the MS population than for the non-MS population, after adjusting for measured characteristics. However, the adjusted annual income of the employed subpopulation was not statistically different for the MS population than for the non-MS population. In other words, the average income of employed individuals with MS was not significantly different from the average income of employed individuals without MS.

The costs associated with loss of productivity due to MS can be quantified financially using either the human capital method or the friction cost method. The human capital approach applies a patient perspective and counts any hour not worked by an individual as an hour of lost productivity, whereas the friction cost approach applies an employer perspective and only considers hours not worked until another
Individual takes over the work (van den Hout 2010). All of the studies reviewed for this study measured productivity losses using the human capital approach.

In Italy, mean annual productivity losses per patient were estimated to be €11,835 (Ponzio, Gerzeli, et al. 2015). A similar mean annual cost of €9,287 per patient was estimated for Spain (Fernandez et al. 2017). The authors of the study in Spain aggregated the individual cost of lost productivity to the patient population level, and found that MS was costing Spain between €212 million and €450 million per annum through productivity losses as a result of lost work hours and early retirement. In Australia, Palmer et al. (2019) found that mean productivity losses across the lifetime of patients resulted in productivity losses of AUD $580,279 in a health economic modelling of the lifetime costs of MS.

Thus far, the productivity impact of MS has been considered from the perspective of the average patient. However, evidence exists that suggests the size of the productivity loss depends on disease characteristics such as disease severity, progression and relapse. Overall, costs increase considerably as disease severity worsens. In a literature review focused on Spain, the total productivity loss per patient has been found to vary from €6,665 for patients with an EDSS score of 0 to €18,711 for patients with a score of greater than 7 (Fernandez et al. 2017). A relapse of MS was found to cost €1,677 in Spain due to lost work days (Fernandez et al. 2017). However, in their analysis of MS patients’ electronic health record data in Spain, Sicras-Mainar et al. (2017) found that even patients with ‘no or moderate disability’ had annual productivity costs of €14,463 after adjusting for measured characteristics, compared to costs of €18,310 for patients with ‘severe disability’. The annual productivity costs per patient with MS across five European countries, and by disease stage, are provided in Table 6.6. The information in this table is based on country-level analyses of the Kobelt, Thompson, et al. (2017) European-wide survey.

Table 6.6 Mean annual costs (€2018) associated with lost productivity from MS patients across Europe

<table>
<thead>
<tr>
<th>Country</th>
<th>Cost of lost productivity (per person per year)</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mild MS</td>
<td>Moderate MS</td>
</tr>
<tr>
<td>France</td>
<td>€4,463</td>
<td>€12,659</td>
</tr>
<tr>
<td>Germany</td>
<td>€8,586</td>
<td>€19,120</td>
</tr>
<tr>
<td>Italy</td>
<td>€1,761</td>
<td>€9,785</td>
</tr>
<tr>
<td>Spain</td>
<td>€4,098</td>
<td>€17,330</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>€5,382</td>
<td>€12,355</td>
</tr>
</tbody>
</table>

Note: Mild MS = EDSS score 0–3, Moderate MS = EDSS score 4–6.5, Severe MS = EDSS score 7–9.

28 For this value, the publication year of the study (2006) was assumed to be the year cost.
29 The difference in the cost was statistically significant at the 0.05 level.
Evidence suggests that lost productivity accounts for a significant proportion of the total cost of MS to society. In their mixed methods study of MS patients, Kwiatkowski et al. (2014) estimated that lost productivity made up 35 per cent of the total costs of MS. In Spain it has been predicted that productivity losses account for anywhere between 27 and 33 per cent of the total cost of MS in the country (Fernandez et al. 2017), whereas in Australia it has been estimated to comprise more than half of the total lifetime cost of MS.

6.4. The societal impacts of MS are varied and go beyond costs to the healthcare system and lost productivity

MS can disrupt the education of young patients, with school attendance in particular suffering as a result of the disease. One qualitative study undertook in-depth interviews with 21 young people diagnosed with MS in the United Kingdom, and found that physical and cognitive limitations as a result of their condition could disrupt not only their social lives, but also their education (Kirk & Hinton 2019). Furthermore, in an observational study of adolescent MS patients self-administering interferon-β1a in Italy, Ghezzi et al. (2017) found that the disease can affect school attendance and school dysfunction, with those with MS requiring supplementary educational services. A comparative study in the United Kingdom of 30 children and adolescents with MS (15 fatigued and 15 non-fatigued) vs. 30 healthy controls found that school attendance was high (97 per cent) among healthy controls and non-fatigued children and adolescents with MS, but considerably lower (76 per cent) in fatigued children and adolescents with MS.

Interviewees also commented on several other societal impacts associated with the progression of MS not captured in the review of the literature. Several interviewees commented on the costs to the exchequer associated with welfare benefit payments that people with MS access due to their illness, although these varied depending on the country. Welfare payments can take the form of transfer payments from taxpayers to welfare benefit recipients rather than resource costs to the economy, but they are nevertheless of interest to governments anxious to keep public spending under control. For example, an interviewee from Australia commented on the National Disability Insurance Scheme in Australia (INT21), and an interviewee from Spain commented on the disability pension that people with MS may collect (INT22). However, both interviewees commented that these schemes are not accessed by all people with MS (depending on their income), and that the funds provided through these programmes are often insufficient in covering the costs associated with disability due to MS. An interviewee from Canada commented on the costs of unemployment insurance for people with MS who are unable to work (INT11), and an interviewee from the United States commented on the cost of disability insurance and

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30 Interferon-β1a is a type of DMT, and one of five beta interferons used to treat inflammation associated with MS. (MS Society 2019).
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public healthcare insurance for people with MS (INT06). A patient representative from the United States also commented that the decreased income for people with MS and their carers may create a host of other social issues leading to societal costs, including poor nutrition and exercise, which may also be experienced by people with MS in other countries (INT17).

Along with these tangible societal costs, many interviewees also commented on the sense of people with MS and their carers that they are unable to contribute to and participate in society in the same way that they would have been able to without MS (INT05, INT12, INT16, INT18). Interviewees associated this intangible cost of MS with the increased social isolation that occurs in both patients and carers, which creates a wider societal impact. Some interviewees also commented on the higher divorce rate (INT05, INT16, INT20) and suicide rate among people with MS as a societal impact (INT20).

Although it was only mentioned by one interviewee in the United States, the public awareness of MS may cause a positive impact in society in terms of being aware of the importance of adaptations in public buildings, workplaces and homes for people with disabilities (INT13).
7. Implications for policy and research

This chapter draws together the findings from the literature and interviews to produce a number of reflections on the impacts of MS on the individual, their carers and wider society and draw out from these the implications of the findings for policy and research.

The key findings are that:

- MS has a range of impacts on individuals and their carers. However, the majority of the literature focuses on the impact on individuals with MS.
- MS is a shared experience between the individual with MS and their carers, but is lived in different ways.
- The societal impacts of MS are varied and go beyond costs to the healthcare system and lost productivity.
- There is limited literature exploring the range of impacts affected by disease progression. However, it is clear that the negative impacts of MS increase with disease progression.
- There is room for improvement in the services provided for individuals with MS and their carers.

7.1. MS has a range of impacts on individuals and their carers. However, the majority of the literature focuses on the impact on individuals with MS

MS is a disease with psychosocial impacts for the individual with MS, as well as for their carer and wider social network, although there is insufficient literature describing the impacts on carers. All interviewees described how MS affects both the person with MS and the people who care for them, yet the literature focuses largely on the impacts on the individual with MS (70 out of 88 papers included in the literature review) rather than on the impacts on the carer (20 out of 88 papers).

The range of impacts that affect both the individual with MS and their carer are widespread. This study found evidence in the literature, which was echoed in the interviews, of impacts on mental health such as increased depression and anxiety, shifts in personal relationships, reduced social participation, and career disruption for both the individual with MS and their carer. Additionally, there are physical symptoms experienced by the individual with MS (e.g. fatigue and reduced mobility) that have a psychosocial impact on both individuals with MS and their carers. However, as described in Section 7.2 below, the impact of these physical symptoms on the lives of individuals with MS and carers is different. Some impacts are
specific to individuals with MS (i.e. school attendance), and some impacts are specific to their carers (i.e. caregiver burden).

It is important that the impacts both on individuals with MS and their carers are fully reflected in research, so that policy can be appropriately informed.

7.2. **MS is a shared experience between the individual with MS and their carers, but is lived in different ways**

Receiving a diagnosis of MS is a ‘life changing’ experience not just for the individual with MS, but also for their carer and wider network. This study found that the uncertainty and unpredictability of MS affects both individuals with MS and their carers: both groups experience concerns about the future, about how the disease will progress and about how they will be able to cope with the disease as it progresses.

The relationships between people with MS and their carers and family will also change. Regarding their relationship with their partner, individuals with MS may experience sexual dysfunction, or may struggle with issues of body image that interfere with the couple’s sexual activities. On the carer side, MS may lead a spouse or child to take on more familial responsibilities, as well more of a carer role, which may impede their involvement in other activities.

Physical symptoms experienced by the individual with MS, such as fatigue and reduced mobility, have a psychosocial impact on both the individuals with MS and their carers. As described in Section 4.1, fatigue has a big impact on the lives of individuals with MS, including on an individual’s ability to participate in social activities and to work. These physical symptoms are experienced solely by the person with MS and have a profound effect on their quality of life, but although the carers do not experience fatigue themselves, it still impacts on their lives. For example, fatigue experienced by an individual with MS may lead carers to cancel social engagements or change plans at short notice so as to not leave the individual with MS alone. This is also the case with reduced mobility. However, as opposed to reduced mobility, fatigue is not necessarily a visible symptom, and therefore an individual with MS may find there is a lack of understanding from the carer when they are incapacitated due to fatigue, and carers may feel helpless as they do not know how to address this symptom.

7.3. **The societal impacts of MS are varied and go beyond costs to the healthcare system and lost productivity**

MS is a disease associated with a high economic cost to society, and this is broadly captured in the literature. As a chronic and progressive disease, MS has high healthcare costs, mainly associated with the cost of treatment and healthcare utilisation. However, as a debilitating disease MS also has costs associated with loss of productivity at work, both for the individual with MS and for their carer. Loss of productivity is due to both the reduced ability of a person with MS to participate in the labour force and to their reduced ability to produce work while participating in the labour force. In the case of severe MS, the cost
associated with loss of productivity ranges from €14,267 in the United Kingdom per individual per annum to €22,630 in Germany.

The burden of informal care also has economic impacts on society. This study found that family members commonly take on the responsibility of providing care to individuals with MS, in part because many healthcare systems do not provide support for in-home care, focusing instead on the direct costs of the disease. The literature estimates that almost half of individuals with MS receive informal care at an average of 30 hours per week globally. In Europe, the cost of providing informal care for severe MS ranges from €4,325 in France per individual per annum to €19,120 in Spain.

The impacts of MS on society extend beyond the costs to the healthcare system, the loss of productivity and the informal care required. Additional impacts include public spending on welfare benefits (e.g. disability and dependency pensions, unemployment benefits), reduced social participation and an increased divorce rate. Although this study found evidence in the literature relating to the impact on individuals with MS and their carers of reduced social participation, and how the disease is associated with an increased divorce rate, these outcomes were not assessed from the perspective of their impact on wider society.

While the healthcare costs associated with MS are large, so too are wider costs such as those of providing informal care, the impact on the economy through loss of productivity and other negative impacts on individuals’ lives. It is important that policymakers are aware of and take into account the full range and magnitude of costs of all kinds.

7.4. There is limited literature exploring the range of impacts affected by disease progression. However, it is clear that the negative impacts of MS increase with disease progression.

The majority of individuals with MS will experience disease progression. As the disease progresses, individuals experience greater cognitive difficulties and reduced mobility, which affect an individual’s social and family life, as well as their ability to work. Individuals with MS become more dependent on external help as their disease progresses, which increases caregiver burden. Interviewees mentioned that during the initial stages of the disease, where disability is not yet visible, there are ‘hidden symptoms’ such as fatigue that can profoundly affect the daily lives of people with MS, and their carers.

The economic impact of MS increases along with disease progression. For example, in Spain the cost per individual per annum of informal care ranges from €1,115 in mild MS to €19,120 in severe MS, the cost of healthcare ranges from €15,750 in mild MS to €24,962 in severe MS, and the cost of lost productivity ranges from €4,098 in mild MS to €17,067 in severe MS. This pattern is seen across all European countries for which evidence was available in the literature.

The value was inflated to 2018 values and then converted from pound sterling to euro based on the average 2018 exchange rate, £1.00 to €1.13.
Much of the literature on the impacts of disease progression in MS examines the issue from the perspective of economic impacts. There is little research assessing how the psychosocial impacts of MS vary according to disease progression. Out of the 88 papers from which data on the impact of MS were extracted, 21 focused on the impact of progression. The majority of data and tools available to assess disease progression use only the physical aspects of the disease (i.e. reduced mobility) as a proxy for disease stage, whereas a number of interviewees suggested that it would be helpful to gather more data on the psychosocial impacts of disease progression, along with the physical indicators, to broaden understanding of the disease and its implications.

7.5. There is room for improvement in the services provided for individuals with MS and their carers

Individuals with MS in all of the countries focused on in this study\textsuperscript{32} have access to medical support (e.g. diagnosis, medications and some therapy) and welfare benefits (e.g. unemployment and disability). In most cases, these services are provided by the public system. In some countries the public system may also cover the costs of other services important for the care and management of MS, such as rehabilitation, psychologists, occupational therapists and speech therapists; although, when available, these services are limited and may vary in available resources and capacity across countries and within a country. Additionally, support for community and home adaptations and transportation is available in some countries as a means of reducing social isolation. However, in countries such as Canada and the United States, the availability of these services is greatly dependent on the province or state.

In an effort to ensure patients are receiving proper care, interviewees mentioned that patient associations in each country provide individuals with MS with services not fully catered for by the public system. Besides rehabilitation and occupational therapy, patient associations offer peer support groups and interactive activities for individuals with MS. However, the perceived benefit of these varies, and design is key. For example, some evidence suggests that having a support group with individuals at different stages of the disease may be detrimental for individuals at an early stage as they ‘see their future with increased disability’.

Although MS is a shared experience between the individual with MS and their carer, there is a lack of information and support readily available to carers. More attention needs to be given to rectifying that lack. Some countries have public schemes aimed at offering relief to carers, mainly to reduce the amount of informal care they have to provide. However, these may not be sufficiently funded or easy to access. Additionally, feelings of guilt or of overburdening the individual with MS can act as a barrier to carers seeking the support they require. Online support and information may help alleviate the psychosocial impacts of caregiver burden, although more concrete forms of support to reduce caregiver burden, such as home adaptations and home nursing care, could also be of help.

\textsuperscript{32} These were: Australia, Canada, France, Germany, Italy, Spain, the United Kingdom and the United States.


McCabe, M., K.J. Ebacioni, R. Simmons, E. McDonald & L. Melton. 2015. ‘Satisfaction with Service Needs among People Living with Multiple Sclerosis.’ NeuroRehabilitation 36 (2): 167–73. doi: 10.3233/nre-151204


MS International Federation. 2018. ‘What is MS?’, Last Modified 2018. As of 14 September 2019: https://www.msif.org/about-ms/what-is-ms/


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National Multiple Sclerosis Society. Multiple Sclerosis Quality of Life Inventory (MSQOL). As of 18 October 2019: https://www.nationalmssociety.org/For-Professionals/Researchers/Resources-for-Researchers/Clinical-Study-Measures/Multiple-Sclerosis-Quality-of-Life-Inventory-(MSQOL)


Exploring the societal burden of multiple sclerosis


Annex A. Literature review data extraction template

Table A.1 Data extraction template for the literature review

<table>
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<tr>
<td>Information on psychosocial outcome</td>
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<td>Information on physical outcome</td>
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<td>Measure/Tool</td>
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<td>Societal outcome</td>
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<tr>
<td>Information on societal outcome</td>
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<td>Measure/Tool</td>
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<tr>
<td>Additional information</td>
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</table>
Annex B. Interview protocol

Societal burden of disease progression in multiple sclerosis: implications for future research, policy and practice

Preamble and background
RAND Europe (a not-for-profit research institute based in Cambridge UK) is undertaking an evidence synthesis on the impact on society of disease progression in multiple sclerosis (MS). This work has been commissioned by the pharmaceutical company Roche. However, RAND Europe has full independent of the analyses that will be performed of part of this study, as well as complete editorial control of the findings. This work will inform the public good and should not be taken as a commercial endorsement.

As part of this study we are conducting a review of the existing academic and grey literature calculating the economic and wider societal costs of MS, as well as that focusing on the psychosocial well-being of patients and their carers. This study seeks to synthesise that body of literature with particular focus on the impact of disease progression in MS on the individual, their carers and network, and broader society.

To complement what we have found in the literature, we are conducting a series of interviews with clinicians and representatives of patient advocacy groups to explore the implications of those findings in different country contexts, and explore what action can be recommended based on the findings.

The project will be written up as an independent RAND report. It will be subject to a peer review process and made publicly available on the RAND website. It should be completed by late 2019.

Do you have any questions for us before we begin?

Confirming consent
I would now like to switch on the recorder to confirm your consent to the items covered in the participant information sheet and consent form provided by RAND Europe, which you should have received prior to this interview (If they have already signed and returned their consent form by email, there is no need to take their consent again).

Are you happy for me to switch on the recorder?

I will now take your consent, and I need to go through each item one by one- I appreciate your patience as we do this. [Now go through each consent item, one by one].

Structure of the interview
The interview is divided into three main topics: understanding the burden of the disease, the data collected on a patient or carer’s journey with MS, and the delivery of care for MS in your country.

**Part 1 – Introduction**

*For clinicians only:*

1. How does your professional role fit into the wider healthcare delivery approach in MS in your country?

**Part 2 – Understanding of burden in general**

In this section, we are interested in the impact of MS on the daily life of patients and carers. Specifically, we are interested in psychological, social, economic or physical (e.g. mobility) impacts rather than clinical outcomes, so please refrain from providing information on any specific forms of medication in relation to MS.

2. How, in your opinion, does MS impact the daily lives of people with MS? *(Prompt if needed: this could be physically, psychologically, socially, economically or other types of impacts).*
   a. How does it impact their support network (carers and families)?
   b. How does it impact wider society? *(Prompt if needed: this could be about ability to work for instance).*

3. How do the impacts you have mentioned affect people’s lives more broadly? What are the main impacts?
   a. *Prompt if needed:* What are the wider impacts on carers and families?
   b. *Prompts if needed:* What are the wider impacts on society more broadly? Economic impacts?

4. Do these impacts vary by type of disease and stage of disease, and if so how? *(Types of disease are: progressive relapsing MS, secondary progressive MS, primary progressive MS and relapsing remitting MS. Stages of disease are: active, not active, worsening or not worsening)* *(Prompt for daily life impacts and wider impacts).*
   a. Are there other ways that these impacts vary across the patient population?
   b. To what extent does the disease type or stage reflect what the level of burden from these impacts is for the patient and those around them?

5. Of the various impacts we have discussed, which do you think are the most significant for patients and why?
   a. What about for their carers and families?
   b. What about for wider society?

**Part 3 - Data**

6. Are you aware of any data or studies that have been done in your country on how MS impacts those affected by the disease, beyond the direct physical effects?
   a. Are there particularly useful data sources or tools for measuring the impacts of MS? If so, what are they and why are they useful?

7. Are there any data that are not currently available but would be helpful to collect? Please explain what you think is needed and why, and how it could be used.

8. What types of data are available to show how MS progresses in individuals? Is this adequate?
Part 4 – Country-specific delivery of care for MS

9. In your country, what types of support, medical or non-medical, are available to people with MS and their carers? (Please provide specific examples) **Note: please refrain from providing information on any specific forms of medication in relation to MS**
   a. What types of support are most/least helpful and why?
   b. How does the level of support vary by disease stage?

10. Who provides this support? (please provide specific details)
   a. What is the role of patient groups in supporting care?

11. What costs related to having MS and caring for someone with MS are covered by the healthcare or insurance system(s)?
   a. What other costs are associated with MS and how do patients and their families cover them?

12. Do you feel the support given to people with MS in your country is adequate? Why or why not?
   a. Do you have any ideas about what the main obstacles are to providing adequate support?

13. Are there other types of support that should be made available in your country? Please explain what you think is needed and why.

Part 5 – Closing

14. Is there anything you would like to add that we did not cover in this interview? **Note: please refrain from providing information on any specific forms of medication in relation to MS**
Impact of disease progression in multiple sclerosis: participant information and consent

Participant information

RAND Europe has been sponsored by Roche to undertake an assessment of the societal burden of disease progression in multiple sclerosis (MS). As part of this study, we are aiming to understand the impacts of MS with specific interest in disease progression to the individual, carers and broader society. To carry out this task, we will be conducting interviews with stakeholders and experts on the topic, including patient advocates, healthcare professionals and policymakers. The interview will focus around psychological, social, economic and physical impacts rather than clinical outcomes (please refrain from providing information on any specific forms of medication). We will also ask questions on country-specific delivery of care for MS and data collected on the impacts of MS.

You have been invited to participate in an expert interview for this project due to your involvement in or knowledge of multiple sclerosis. The interview will take 45-60 minutes of your time. Your participation in this research is entirely voluntary, and you may choose to change your mind about participating at any time before, during or after the interview without giving a reason. During the interview you can also choose not to answer any questions. With your permission we would like to record this interview, and the recordings, along with any notes and transcripts, will be kept strictly confidential by RAND Europe and never be made available to any third party, including Roche.

The project will be written up as an independent RAND report. In the report, we will state the number of people we have interviewed and the country where they are based, and describe their professional roles in general terms (e.g. neurologist, nurse, or representative of a patient organisation). We will not refer to any interviewees by name or organisational affiliation in the report. With your permission, we might quote you in the report but will not explicitly identify you by name or include other directly identifying information. However, it may be that some comments could be identified as coming from you based on content and context.

All records will be kept in compliance with the General Data Protection Regulation (GDPR) 2018. This interview will be conducted by RAND Europe researchers, and the data will be recorded and stored in accordance with RAND Europe’s procedures. Further information about RAND Europe’s data security practices can be provided upon request.
Consent (to be obtained by phone prior to the start of the interview OR completed on paper, scanned and returned by email)

To provide RAND Europe with authority to use your information for this project we would like to ask you to confirm the following:

1. We would like to audio-record the interview so that we can refer to the recording later as part of the interview analysis process. Do you agree that the interview can be audio recorded?
   - Yes [ ] No [ ]

2. Do you agree that written notes can be taken during the interview?
   - Yes [ ] No [ ]

3. Do you agree that RAND Europe can store this interview data securely on password-protected computers and folders on its servers for the duration of the project?
   - Yes [ ] No [ ]

4. Do you agree that RAND Europe can destroy all notes and transcripts after the project has been completed?
   - Yes [ ] No [ ]

5. Do you agree that RAND Europe can securely use the data you have provided in their study on the impacts of multiple sclerosis and write reports on that?
   - Yes [ ] No [ ]

6. RAND Europe will not directly attribute any quotes explicitly to you by name or professional affiliation. It may be, however, that a reader could reasonably attribute some information or quotes to you based on content and context. Do you give us permission to quote you?
   - Yes [ ] No [ ]

7. Do you agree to be notified by email when the final report from the study is published?
   - Yes [ ] No [ ]

Should you change your mind on any of these points please contact us at redpo@rand.org using reference ‘Disease progression in multiple sclerosis’.

________________________________________  ________________________  ________________________
Interviewee name         Date     Researcher taking consent
### Annex D. Interview codes

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<tr>
<td>INT23</td>
<td>Patient group/healthcare professional</td>
<td>United Kingdom</td>
</tr>
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</table>

Note: Interviews corresponding to INT03, INT08 and INT19 were scheduled but not conducted due to last minute cancellations. The interviewee for INT07 conducted the interview but withdrew consent as they did not think they were the correct person within the organisation to be interviewed.
Annex E. Interview analysis template

Table A.3 Data extraction template for the interviews (part 1)

<table>
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<th>Interviewee code</th>
<th>Country</th>
<th>Stakeholder category</th>
<th>Fatigue</th>
<th>Mental health</th>
<th>Quality of life</th>
<th>Social functioning/participation</th>
<th>Support (e.g. peer support groups)</th>
<th>Workforce participation</th>
<th>Uncertainty</th>
<th>Relationships</th>
<th>Other types of impact</th>
<th>Lack of information</th>
<th>Lack of support and understanding</th>
<th>Isolation</th>
<th>Respite</th>
<th>Other types of impact</th>
<th>Impact on system/wider society</th>
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<td>How does MS impact the daily lives of people with MS?</td>
<td>How does MS impact the daily lives of carers and families of people with MS?</td>
<td>Impact on system/wider society</td>
<td>Informal care time</td>
<td>Healthcare utilisation and costs</td>
<td>Employment and school outcomes</td>
<td>Other impacts</td>
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Table A.4 Data extraction template for the interviews (part 2)

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<td>Wider impacts on society?</td>
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<td>Economic impacts?</td>
<td>Economic impacts?</td>
<td>Economic impacts?</td>
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<td>How do impacts vary by type of disease and stage of disease?</td>
<td>Other ways impacts vary across patient population</td>
<td>Other ways impacts vary across patient population</td>
</tr>
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<td>Extent to which disease type or stage reflects level of burden from impacts</td>
<td>Which impacts are most significant for individuals with MS?</td>
<td>Which impacts are most significant for individuals with MS?</td>
</tr>
<tr>
<td>Which impacts are most significant for carers and families?</td>
<td>Which impacts are most significant for carers and families?</td>
<td>Which impacts are most significant for carers and families?</td>
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<td>Which impacts are most significant for wider society?</td>
<td>Which impacts are most significant for wider society?</td>
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Table A.5 Data extraction template for the interviews (part 3)

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<td>Are there particularly useful data sources or tools for measuring the impacts of MS? If so, what are they and why are they useful?</td>
</tr>
<tr>
<td>Are there any data that are not currently available? Please explain what they would be and why it is needed and why it could be used.</td>
<td>Are there any data that are not currently available? Please explain what they would be and why it is needed and why it could be used.</td>
</tr>
<tr>
<td>What types of data are available to show how MS progresses in individuals? Is this adequate?</td>
<td>What types of data are available to show how MS progresses in individuals? Is this adequate?</td>
</tr>
<tr>
<td>In your country, what types of support, medical or non-medical, are available to people with MS and their carers?</td>
<td>What types of support are most/best helpful and why?</td>
</tr>
<tr>
<td>What is the role of patient groups in supporting care?</td>
<td>Who provides the support?</td>
</tr>
<tr>
<td>What costs related to having MS and caring for someone with MS are covered by the healthcare or insurance system?</td>
<td>What costs related to having MS and caring for someone with MS are covered by the healthcare or insurance system?</td>
</tr>
<tr>
<td>What other costs are associated with MS and how do patients and their families cover them?</td>
<td>What other costs are associated with MS and how do patients and their families cover them?</td>
</tr>
<tr>
<td>Is the support given to people with MS in your country adequate? Why or why not?</td>
<td>Is the support given to people with MS in your country adequate? Why or why not?</td>
</tr>
<tr>
<td>What are the main obstacles to providing adequate support?</td>
<td>What are the main obstacles to providing adequate support?</td>
</tr>
<tr>
<td>Are there other types of support that should be made available in your country? Please explain what you think is needed and why.</td>
<td>Additional comments</td>
</tr>
</tbody>
</table>