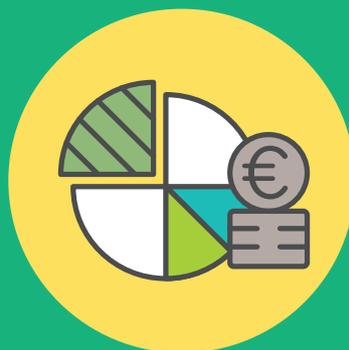
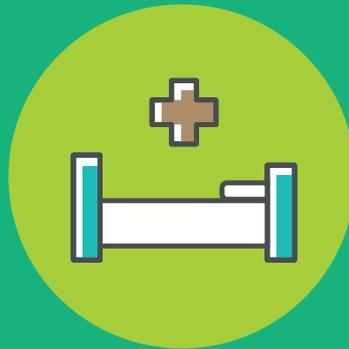


Societal Cost of **Multiple Sclerosis** in Ireland 2022



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in Ireland 2022

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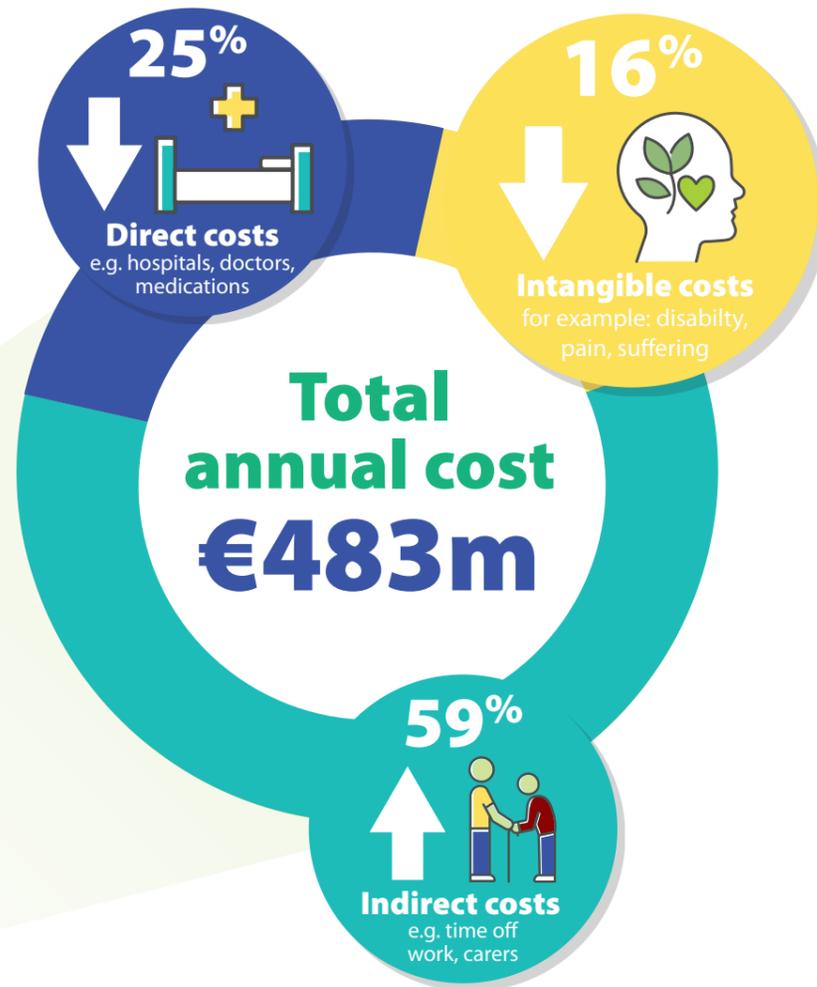
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Societal Cost of Multiple Sclerosis 2022

MS: A complex neurological condition affecting people in the prime of their life

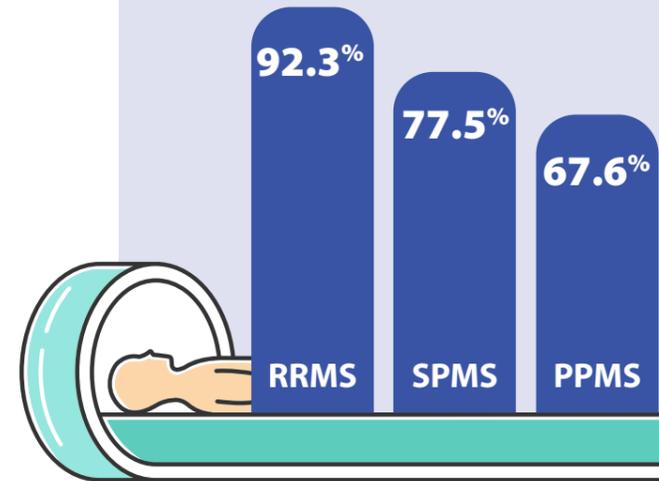
Over **9000** people living with **MS** in Ireland

The cost of MS has increased by **12%** since 2015

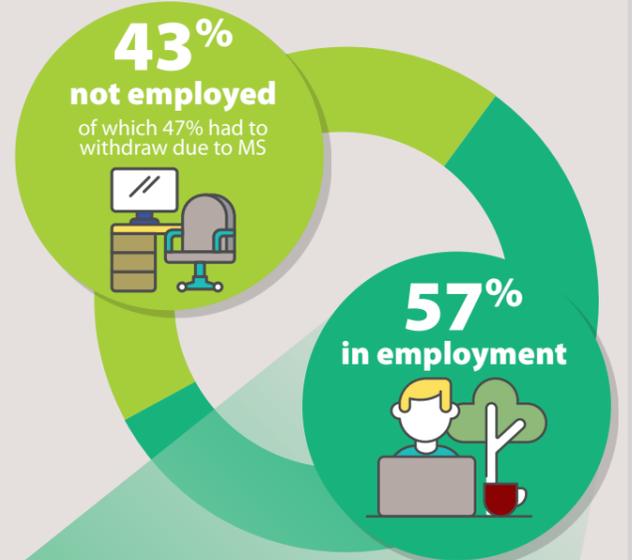


Good News!

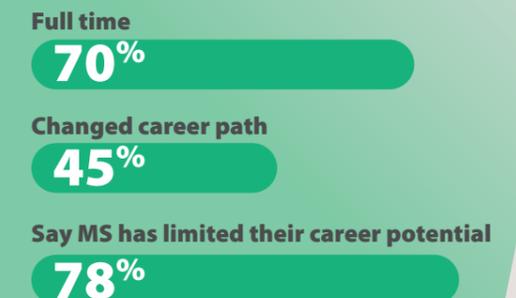
The study showed that the percentage of people undergoing MRI's has increased when compared to the 2015 data



Employment

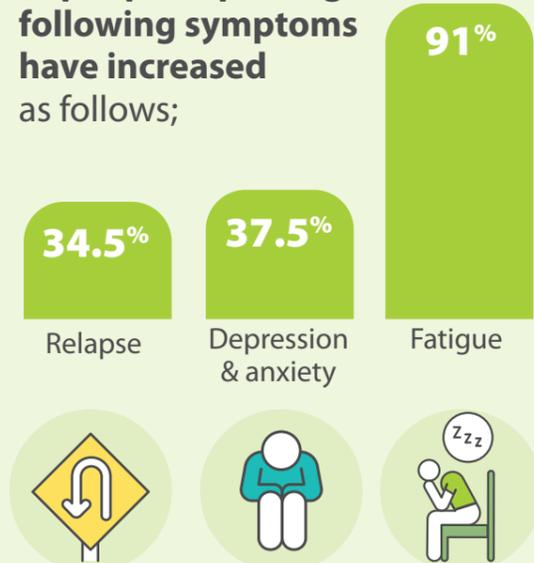


Of the 57% in employment:



Common Symptoms of MS

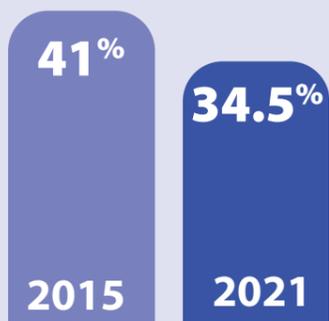
Since 2015, the percentage of people reporting the following symptoms have increased as follows;



Recommendations

- Access to interventions that reduce relapses and disability progression, and simultaneously support working and living independently.
- Improving employment opportunities for people with visible and invisible disabilities, such as MS.

Decrease* in self-reported relapses from 2015 to 2021



In this study there was a correlation between relapse and depression.



37.5% of those who had relapses also had depression

Informal care hours have increased since 2015 **2,956m** days of care provided by family and friends



The annual cost of relapse in 2021 was **€22.7m**

* More disease modifying treatments (DMTs) are available than in 2015 and more people with €22.7m MS are treated (data on file IMS)

References
1. Societal Cost of Multiple Sclerosis in Ireland 2022

1. Foreword



In 2015, together with our academic and industry partners, we undertook the first Societal Cost of MS study. It provided very valuable insights into the direct, indirect and intangible costs of MS as well as other self reported information from people with MS.

We have repeated the study – fieldwork undertaken late in 2021 – to see how the landscape has changed. There has been changes – as you will see and we must also keep in mind that the survey reflects the COVID experience of people with MS and that should be born in mind when reading the results.

I would like to thank the many people with MS who took the time to complete the Societal cost of MS questionnaire – without you this important report wouldnt be possible.

Ava Battles
CEO
MS Ireland

2. Introduction

Introduction and rationale for update to Societal Cost of MS

In 2015 the Societal Cost of Multiple Sclerosis in Ireland was published by MS Ireland in conjunction with Novartis. The aim of this update is to evaluate the cost of MS in Ireland in 2022 using the same methodology as the original report conducted in 2015 in order to draw comparison between the cost of MS in 2015 and 2022 and to determine if life has changed for patients with MS in Ireland.

While every effort was made to maintain consistency between the two years, the 2021 survey was conducted at a time when COVID-19 restrictions were in place and in a period where access to services for people living with MS had been limited or curtailed for up to 18 months. For this reason, we expect to see some variance in healthcare resource use associated with MS between the 2015 and 2021 surveys.

The number of people living with MS in Ireland was estimated to be 9,000 in 2015 and for comparability reasons this is the estimated number of people living with MS which was again used to calculate the cost of MS in 2021.

What is MS?

MS is the most common complex neurological disease of the CNS, the condition is characterised by denominational and axonal loss, resulting in neurological function impairment for many and leading to high levels of disability for some. Although the course of MS varies, 50% of people with the condition will need assistance with walking within 15 years after the onset of disease (Cottrell et al., 1999). In young adults, MS is the most common chronic disabling disease of the CNS, with the onset of the disease typically arising between 20 to 40 years of age (McDonald and Compston, 2006). Common symptoms of MS include functional impairment and disability, common symptoms of MS include visual disturbances, altered sensation and abnormal speech, swallowing disorders, fatigue, bladder and bowel problems, sexual dysfunction and mood impairment (Trisolini et al., 2010). Relapsing-remitting MS (RRMS) is the most common form of MS, with approximately 80-85% of all people with MS experiencing a relapsing–remitting (RR) onset of the disease, with around 65% of those, in time, entering the secondary progressive phase (SPMS) (Balk et al., 2014). RRMS is characterised by episodic exacerbations of neurological signs or symptoms which typically appear over a period of several days and stabilise, with complete or partial recovery. As the signs and symptoms of CNS dysfunction persist after relapses, or progression occurs between relapses, the diagnosis progresses to SPMS. A smaller proportion of people present with primary progressive MS (PPMS), for whom progressive neurological disability occurs from onset (Patwardhan et al., 2005). Details on the epidemiology of MS can be found in the 2015 publication, which can be accessed on www.ms-society.ie.

Due to the early onset of the condition and indeed its long duration, MS can impact heavily on the lives of those with the condition. As a consequence of relapses and symptoms of MS, hospitalisations are commonplace, resulting in the disruption of work, social and family life. The employment-related consequences of MS are well documented with very high levels of absenteeism, presenteeism and permanent withdrawal from the workforce due to MS, commonly being reported (Kobelt et al., 2006b, Karampampa et al., 2012a, Taylor et al., 2007). This restriction in professional activities allied with symptoms such as weakness, fatigue and cognitive impairment can lead to depression and isolation, further impinging on the quality of life (QoL) of those with the condition (L. Ford, 2001). Lifetime prevalence estimates of depression in people with MS are high, typically falling around 50% –more than twofold of that experienced in the general population (Arnett and Randolph, 2006, Horwath et al., 1992).

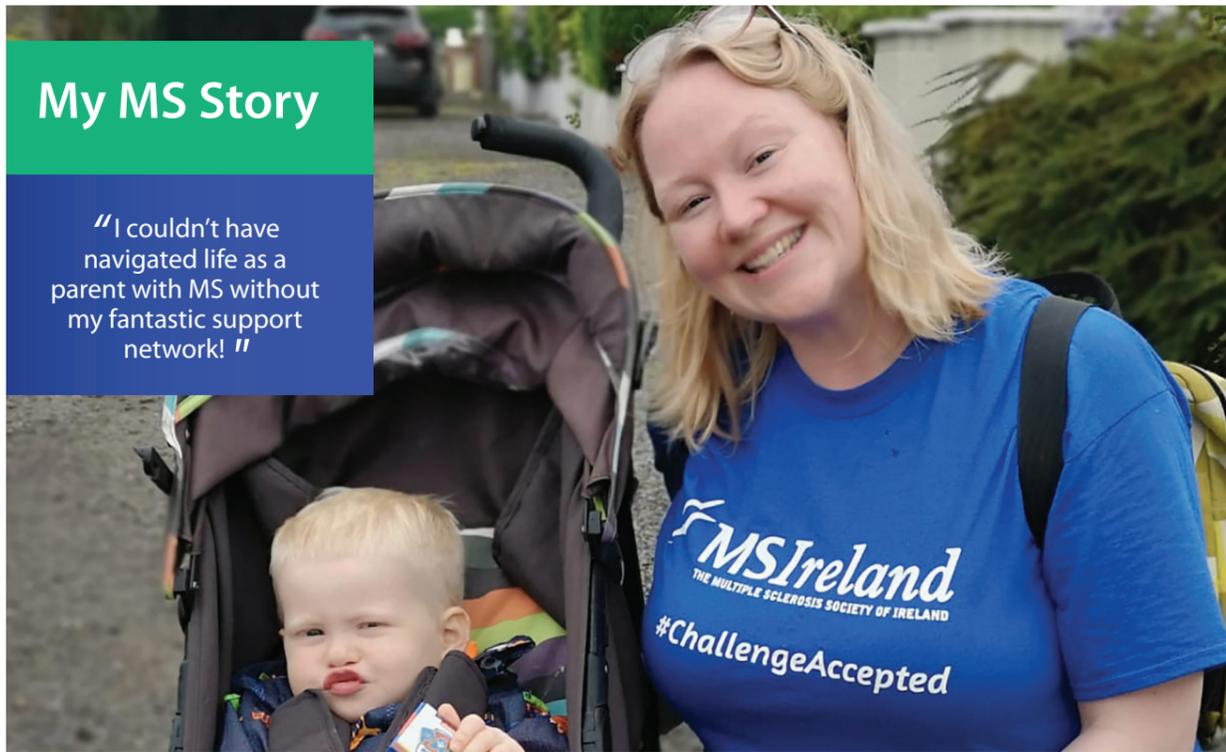
Societal Impact

While it is clear that MS can have a tremendous impact on the lives of those with the condition, the same is also true for their family members. During relapses and as the disease course progresses, a family member, in many cases a spouse, may be required to adapt their lives to cope with the caregiving responsibilities associated with MS. Reduced working weeks and indeed having to permanently withdraw from the workforce are also commonplace for those who care for people living with MS (Kobelt et al., 2006b, Karampampa et al., 2012a). Furthermore, the caregiving experience can be both physically and psychologically demanding and consequently may lead to a deterioration of physical and mental health, further increasing the caregiving burden (Brouwer, van Exel et al. 2005).

As the onset of MS typically occurs early in adult life, people are affected during their most productive years – this statement rings true for those with the condition and to a degree their family members. As a consequence of this and allied with the well documented large direct medical costs associated with the condition, MS has a considerable associated economic cost.

My MS Story

"I couldn't have navigated life as a parent with MS without my fantastic support network!"



Claire

In 2014, I was doing the Camino in Spain with my boyfriend, Ger. A week in, I developed pain at the back of my eyes and felt numb on my face and body. Within a few days, I had no vision from one eye. I later discovered this was optic neuritis and within a month I had my diagnosis of MS. My family and friends were a fantastic support and my MS nurse and MS Ireland gave me plenty of information, advice and even a meditation C.D.!

The first 3 years were very difficult; I had multiple relapses and could no longer work. At times, I couldn't make a coherent sentence or walk in a straight line. It's surreal when your body doesn't feel like your own and doesn't respond the way you want it to. In an effort to build my strength back up, I went to the pool every day, but I was just walking very slowly through the water, and most days, just floating. I did a fatigue management course with MS Ireland and met other people with MS.

Ger and I got married and I went back to full-time work. MS influenced every decision we made, what kind of house we could live in, career choices, whether or not to have children. I knew that I wouldn't let MS stop me from living my life. In 2020, a few months into a global pandemic, we welcomed our son, Sam to the world. He's now 2 years old and makes us laugh every single day. I couldn't have navigated life as a parent with MS without my fantastic support network! Thankfully my MS is stable and I can enjoy going to the beach and the park with Sam, but sometimes I have to explain that Mommy is very tired and doesn't have the energy for an adventure.

If I had let the fear of MS take over, I wouldn't have known the joy of motherhood. I still have moments of brain fog, I sometimes get visual flare-ups or brief muscle spasms. Sometimes I have reduced sensation in my arms and when running a bath, I can't tell how hot it is, so I need someone to double-check before putting Sam in. Life with MS, just like motherhood, is all about continually learning, evaluating and adapting. I don't know what tomorrow will bring, but with Ger and Sammy by my side, I'm excited to find out!

3. Methodology

3.1 Study Approach

This study represents a 2021 update to the Societal Cost of MS in Ireland published in 2015 (Carney et al, 2018) (Multiple Sclerosis Ireland, 2015). This update was undertaken because the cost of MS as with other chronic diseases are expected to change over this period. In order to provide a robust comparison of changes over the past six years, the updated analysis aligns itself with the methodology presented in the 2015 study, which in turn was based on several studies on the cost of MS in Europe and the US (Carney et al, 2018; Kobelt et al, 2006a; Kobelt et al, 2006c).

The cross-sectional web-based questionnaire approach used in the 2015 study was adopted in this 2021 study and is consistent with the methodology used by Karampampa (2012). This research is best categorised as a 'cost of illness' study using 'bottom-up' data collection strategies where costs are estimated in a sample of living with MS and extrapolated to the national level. In this case, people living with MS were invited to take part in a voluntary national survey relating to their disease and associated health care resource use and experiences in 2021.

Consistent with the 2015 study, the societal perspective was adopted. The societal perspective considers the cost of all those affected by MS including people living with MS, caregivers, family etc. The three typical cost categories that are considered are the direct costs (i.e., the medical costs directly related to an illness); the indirect costs (i.e., costs arising to the individual or society as a result of the illness –e.g., ability to work); and lastly intangible costs (i.e., the costs attributable to non-market 'goods'; they are considered intangible as there is no market price but these costs can be measured using 'willingness-to-pay' methodologies amongst others) (Wundes et al, 2010). Important examples in this context include disability, pain and suffering. In estimating these three cost categories, the aim of this research is to provide a comprehensive assessment of the societal costs of MS in Ireland.

This Chapter describes the national survey undertaken by people living with MS and the inputs required to estimate the societal cost of MS.



3.2 Participant Recruitment

MS Ireland invited all people living with MS, living in Ireland, to complete a questionnaire to capture the costs of MS. This cross-sectional, self-reported survey was hosted online for one month in 2021.

Respondents were included once they confirmed to have a clinical diagnosis of MS and were over the age of 18 and gave their informed consent to participate. A total of 724 participants entered the survey. Of these, the following responses were removed:

- 36 respondents did not reside in Ireland;
- 80 respondents did not fully indicate consent or were disqualified;
- and 280 respondents did not complete any information apart from some demographic questions.

In total, 328 individuals were included in the final sample; however, this sample included both fully completed questionnaires (n=284) and partially included questionnaires (n=44). Some partially completed questionnaires provided valuable information on resource use and were deemed relevant and included in the full analysis sample (n=328). All five domains of EuroQol EQ-5D-5L survey were completed by 304 respondents.

3.3 Survey Design

The survey was the same as the 2015 survey apart from the following exceptions:

- Mean age of respondents and mean age at onset of MS were not asked in the 2021 survey
- The questions on how MS affects a person's fatigue through the Modified Fatigue Impact Scale -5-Item Version (MFIS-5) were not included in the 2021 survey
- Questions on how MS affects a person's pain levels through the MOS Pain Effects Scale (PES) were not included in the 2021 survey

• There were fewer questions on the direct and indirect resources used associated with a relapse.

The structure of the survey can be divided into eight sections:

1. Background information
2. Disease information,
3. Medical cost of MS,
4. Care needs,
5. Productivity,
6. Health related quality of life (HRQoL),
7. Relapses,
8. MS disease progression

These sections are discussed in turn below. We also describe the unit cost inputs and sources that are applied to health-care utilisation to estimate costs.

3.4 Background Information

Respondents were asked the demographic questions; age, gender, location, nationality along with questions about whether they were in receipt of state benefits and/or approved for a long-term illness card.

3.5 Disability Information

Respondents were asked to report their form of MS; RRMS, PPMS, SPMS, benign disease or whether they did not know. They were also asked about how long since their diagnosis of MS and onset of MS symptoms before a formal diagnosis of MS.

The questionnaire also investigated severity of disease. One of the most common clinical instruments in the MS literature is the Expanded Disability Status Scale (EDSS). This is the main method of quantifying disability in MS and monitoring changes in the level of disability over time. The EDSS scale ranges from 0 to 10 in 0.5 unit increments that correspond to increasing levels of disability. Given the potential for 20 different levels of disability with the EDSS, a neurologist completes the scoring. In our study, in order to broadly stratify people with MS according to their EDSS score three classes of disability were considered: mild, moderate and severe MS. It was considered that ‘mild’ approximates to an EDSS of 0-3, ‘moderate’ to 3.5 to 7, and ‘severe’ to 7.5 to 10. Three statements (or symptom vignettes) were constructed based on the EDSS classification system and prior literature to reflect these three classes of disablement – mild, moderate, and severe. This question was reviewed and approved by two neurologists in the 2015 questionnaire. This question is provided below.

Figure 1. Questionnaire – MS Severity

The statement below shows three levels of disablement (mild; moderate; severe). Please tick the category which most closely reflects your general level of disability these days.		
Mild	Moderate	Severe
I am independently mobile with minimal disability	I have a moderate level of disability. My mobility is somewhat restricted and sometimes I depend on others to perform day-to-day activities.	I require a high level of assistance for all activities of daily living

Respondents were also asked about relapse and whether they experienced a relapse in the previous 12 months. They were provided with the definition of a relapse below.

Figure 2. Questionnaire – Relapse Definition

“The appearance of new symptoms related to your MS or very definite worsening of old symptoms, which lasted for at least 24 hours and occurred after you had been stable for at least a month and when you did not have a temperature, an infection or any other health trouble”

3.6 Medical Costs of MS and Care Needs

The 2021 survey is aligned with the 2015 survey and was designed to capture frequency information to inform the direct costs associated with MS in general and to those specific to MS relapses. Information on resource utilisation was collected through questions based on the Client Service Receipt Inventory (CSRI) and adapted to the setting of the study. The CSRI is a research instrument applied for the collection of information on costs and has been widely used in the cost of MS studies (Fogarty et al, 2014) (McCrone et al, 2008).

The length of the recall period varied depending on the expected frequency of resource use, e.g., for inpatient admissions, investigations and diagnostic tests a recall period of 12 months was given while for GP, Consultants, other healthcare professional and outpatient visits a six-month period of recall was applied; for home help a 1 week recall period was used. For non-routine items such as ‘mobility and other living aids’ (e.g., crutch, wheelchair, utensils) and ‘home modifications’ the full duration of the disease was used for recall. To reduce the burden on the survey respondents, detailed information regarding current medication for MS and anxiety/depression was not requested– as these can be imputed using alternative sources.

Respondents were also asked about what forms of care or assistance they received, due to their MS. This includes formal and informal care. The recall period for formal and informal care was one week.

The costs of informal care were estimated based on the hours of care provided and whether the caregiver had officially reduced their working week or given up their own job in order to provide care. Questions were also asked about whether the caregivers ever had to take extra unscheduled days off work to provide care duties.

Informal care was valued using the opportunity cost method, as earnings foregone as a result of time spent caregiving. Here earnings foregone up to a maximum of 40 hours per week were estimated and valued using the national gross mean hourly wage in Ireland (Central Statistics Office, 2020). Although it is the case that for many carers, the amount of care provided will be in excess of 40 hours, applying this cut-off point ensures a more conservative estimate. This approach mirrors that used in a recent Irish study (Fogarty et al, 2014).

3.7 Productivity

Productivity losses were estimated by loss of work and reduced productivity. With regards to work lost, questions were asked to measure the extent of labour force participation, unemployment, permanent withdrawal from the workforce, reduced working hours and sick leave related to MS. Questions were adapted from a validated survey instrument, the ‘Work Productivity and Activity Impairment – General Health’ questionnaire to assist in estimating the indirect costs resulting from reduced productivity (Reilly et al, 1993). These latter productivity-related questions asked participants to reflect upon the past seven days and state how much time was missed from work, how their work performance was affected, and whether MS affected one’s abilities to partake in regular daily activities outside of work.

Consistent with the 2015 study, productivity losses were measured using the human capital (HC) approach (Zhang & Anis, 2014). It assumes that the value to society of productivity loss should be measured as the present value of lost time according to the market wage, which in economic theory is supposed to equal the marginal revenue product (MRP) of labour in a competitive labour market¹³. Following this approach, productivity losses associated with reductions in working hours or sick leave and permanent withdrawal from the workforce, due to MS, were based on national gender-stratified average gross hourly and annual earnings, respectively.

Presenteeism relates to reduced productivity at work due to health problems. Presenteeism arises when a person attends for work but is not performing their duties as expected in terms of quality or quantity. The situation may arise when suffering ill-health. The costs associated with presenteeism can be substantial and may even outweigh those related to absenteeism (Krol & Brouwer, 2014).

Specifically, respondents in the study were asked the following question: ‘During the past seven days, how much did MS, on average, affect your work performance?’ Here a response of zero indicated that work performance was not affected at all by the symptoms of MS, a score of five indicated that work performance was reduced by half, while a score of ten indicated that the respondent was completely unable to perform their work duties. The cost of presenteeism associated with MS was calculated by annualising the work performance affected, equating same to worktime missed and presenting the lost productivity in terms of mean gender-stratified annual earnings.

3.8 Health Related Quality of Life

The EQ-5D-5L is a self-reported generic HRQoL instrument that was developed by the EuroQoL Group (Herdman et al, 2011) (EuroQoL Group, 1990). Respondents report their level of problems experienced in five domains of health: mobility, self-care, usual activities, pain or discomfort, and anxiety or depression, indicating whether they are having no problems or slight, moderate, severe or extreme problems in each assessed domain. Based on the combination of responses, respondents are classified into one of 3,125 unique EQ-5D-5L health-state profiles.

To rank value, each health state can be converted to a single utility value representing general population preferences (Oppe et al, 2007). Utility is measured on a cardinal scale anchored at 1 (perfect health) and 0 (absence of life/dead). Valuations less than zero (as low as -0.594), reflecting health states 'worse than death' (WTD) can exist.

In order to map the EQ-5D-5L to the EQ-5D-3L value set for the UK, the mean utility for the sample was derived by using the "EQ-5D-5L Crosswalk Index Value Calculator". This methodology also allowed estimation of index values for the EQ-5D-5L dimension scores (van Hout et al, 2012) and is the most commonly accepted while local preference elicitation studies based on the EQ-5D-5L are ongoing in Ireland (Fogarty et al, 2014).

In the EQ-5D instrument, respondents are also asked to report their self-rated health via the EQ-VAS; a tool, which using a 20-centimeter vertical visual analogue scale, with endpoints ranging from 0 to 100, asks the individual to label their health between zero "the worst health you can imagine" to one "the best health you can imagine" (Oppe et al, 2007).

Fatigue is the most common symptom or co-morbidity associated with MS. Given its particular significance and its absence, in specific terms, from the EQ-5D, the survey also included a question on: "Do you suffer from fatigue due to your MS?".

3.9 Depression & Anxiety

Levels of depression and anxiety in the MS population is expected to be considerably higher than in the general population, as is clearly demonstrated in the Irish and in the international literature (Arnett & Randolph, 2006) (Beiske et al, 2008) (Kronfol, 1985) (Brown et al, 2009) (McGuigan & Hutchinson, 2006). As a case in point, O'Connell et al, found that 34% of their sample of Irish people living with MS (n=292) reported mild to severe depressive symptoms with no prior history of depression (O'Connell et al, 2017). A rate which is 4 times higher than has been reported for the general population (Ayuso-Mateos et al, 2001). COVID-19 has compounded the co-morbidities of MS with elevations in both depression (54%) and anxiety (33%) reported (Strober et al, 2022).

In Tedstone et al. (2008) a total of 10% of the sample reported speaking at least once to their GP about being anxious or depressed, or about mental, nervous or emotional problems in the previous year, with an average of approximately 4 visits per person. The direct cost of depression and anxiety attributable to MS was then calculated on the assumption that 65% of people that reported having a diagnosis of depression and/or anxiety since the onset of MS in our sample, were being treated for same in the previous year (Arnett & Randolph, 2006). We included the estimate of four extra GP visits per year from Tedstone et al. (2008) if the respondent had both an anxiety and depression diagnosis and if depression or anxiety were the sole diagnosis, we assume 3.3 visits and 0.7 extra visits, respectively. Where 3.3 visits is the difference between the annual mean GP visits for the depressed and non-depressed population over 50 in Ireland (O'Reagan C et al, 2011). We allocate the remaining 0.7 visits to those with anxiety only. The 2015 study attained annual medication costs of €202.25 (2015€) and €8.43 (2015€) from IMS Health data, to provide estimates for treatment costs for depression and anxiety respectively. These costs were updated to 2021 values using the Irish Consumer Price Index for Health.

3.10 Relapses

For respondents with the most common form of MS (i.e., RRMS) the frequency and severity of relapses were important to capture with some consistency. The specific costs associated with MS relapses are also of interest given the nature of MS and how it is experienced, especially by those with RRMS.

Respondents to the survey were asked to consider their last relapse and to answer questions framed under the following headings:

- i. Medical Costs of Relapses.
- ii. Care Needs During a Relapse.
- iii. Impact of Relapse on Productivity.

This approach, which is consistent with the direction taken to calculate the costs associated with MS in general, allowed estimation of the direct and indirect costs associated with a single MS relapse. Once the cost of a single relapse is calculated, the resulting estimate will be multiplied by the average number of relapses reported by those who experienced a relapse in the past year (42.5%). Thus, providing an annual estimate for the cost of relapses in Ireland.

3.11 Disease Progression

The final section of the questionnaire was designed to capture how the respondent's disease was progressing and whether there were additional medical and care needs associated with their progression. Specifically, respondents were asked about additional formal and informal care due to their progression, where in the body was the most deterioration evident.

3.12 Unit Costs

Irish specific unit costs were applied to each resource component in order to estimate the total cost of MS. The sources and unit costs are presented in Table 1. All costs were inflated to the year 2021, using the Consumer Price Index for Health (Central Statistics Office www.cso.ie).

3.12.1 Medication Costs

Average medication costs were obtained from previous Irish research associated with the cost of MS and adjusted to reflect the levels of disability severity (Fogarty et al, 2014). The average annual medication costs were calculated as being €7,267 (2021€), per person with MS.

3.12.2 Aids and Adaptations

In the absence of standardised unit costs, the cost of mobility/living aids and adaptations were based on those reported in Smith et al. (Smith et al, 2012). Home adaptations were calculated on the basis that those reporting such, had adaptations on their home to the value of the average payment received for the Housing Adaptation Grant for People with a Disability, in 2015 (€7,930), plus 5% – as the grant covers 95% of the cost, the full average cost therefore was estimated at €8,347. Following the approach in Fogarty et al. (2014), these costs were annualised assuming a life-span of 5 years (mobility/living aids) or 10 years (home modifications), using a discount rate of 4.0% per annum. This was inflated to 2021 (€8,974).

3.12.3 Valuing Productivity Losses and Informal Care

Consistent with the 2015 study, the market price for labour is assumed analogous to average earnings, both hourly €26.07 and annual €35,954, as reported by the CSO for Ireland in 2021 (Central Statistics Office, 2021). However, as the sample was 80% female and indeed as the MS population in general, is predominantly female – an adjustment was required to stratify annual earnings with respect to gender. This adjustment was made using information from the CSO for the year 2020 as this is the most up to date information concerning the gender pay gap in Ireland (Central Statistics Office, 2020). Average hourly wages for males and females were €29.33 and €22.81 respectively.

Productivity losses associated with short-term sick leave and officially reduced working hours were based on national gender-stratified average hourly earnings, while illness-related, permanent withdrawal from the workforce was valued using gender-stratified average annual earnings.

As an extension of the HC approach, informal care was valued using the opportunity cost method, as earnings foregone as a result of time spent caregiving (up to a maximum of 40 hours per week), using the national gross mean hourly wage in Ireland (€26.97) (Central Statistics Office, 2021).

3.12.4 Valuing Intangible Costs

Intangible costs were valued by calculating the difference in utilities between the sample and an age- and sex-matched sample from a general population (Kind et al, 1999). This method generates an estimate of the number of quality-adjusted life-years (QALYs) lost by the MS sample in one year.

By assigning a value to (or a willingness to pay, WTP) a QALY, intangible costs due to MS can be calculated. Although there is no market price or consensus value for a QALY, we construct our estimate assuming a WTP in the range of €20,000 to €45,000 in Ireland (HIQA, 2020). These figures were chosen as they correspond to the thresholds of cost-effectiveness acceptability which are used to determine whether new health technologies are funded in Ireland.

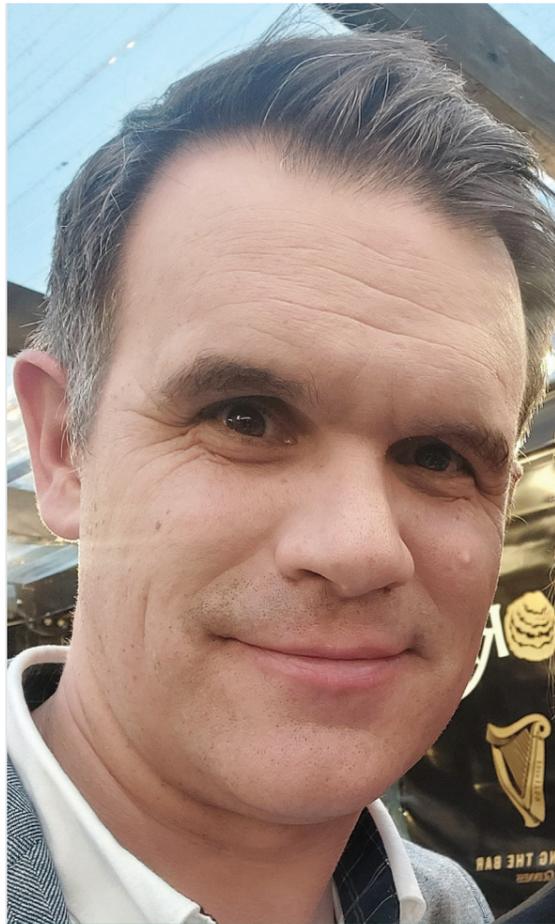
Table 1. Source and Value of Unit Costs

Resource Use Type	Measure Type	Unit Cost (2021 €)	Source
Hospital inpatient	night	€930.72	Healthcare Pricing Office, ABF 2020 Admitted Price list, Weighted average of B68a and B68b ³¹ , inflated to 2021
Nursing home	week	€1,055.82	Carney (2014), inflated to 2021
MS rehabilitation/respice	day	€168.80	
Magnetic Resonance Image (MRI)	per test	€178.11	Bourke (2014) inflated to 2021
CT/ CAT scan	per test	€86.36	
Blood test	per test	€21.48	O'Brien (2015) inflated to 2021
Lumbar Puncture (LP)/ Spinal tap	per test	€652.44	NHS reference 19/20 (SA337) cost inflated to 2021 and converted to € using PPP
Neurology clinic or infusion suite	per visit	€1,659.98	Healthcare Pricing Office, ABF 2020 Daycase Price list, Weighted average of B68a and B68b ³¹ , inflated to 2021
Other hospital outpatient visit	per visit	€186.22	Healthcare Pricing Office, personal correspondence, 2019 figure inflated to 2021
Emergency department	per visit	€160.00	Beacon Hospital
GP	visit	€47.27	PCRS annual report 2019 & Connolly (2018) inflated to 2021
Neurologist	hour	€168.52	HSE, Consolidated pay scales, October 2021 & Public Spending Code (2019) from the Department of Expenditure & Reform
Physiotherapist	hour	€38.71	
Occupational therapist	hour	€38.71	
Social worker	hour	€38.33	
Speech and Language Therapist	hour	€38.73	

Resource Use Type	Measure Type	Unit Cost (2021 €)	Source
MS Ireland caseworker	expert opinion	€23.65	Carney (2014), inflated to 2021
Medication	PwMS	€7,267.09	
Aids, e.g., wheelchair, crutch etc/ home modifications	PwMS	€746.77	Carney (2014), inflated to 2021
Formal care (home-help)	hour	€22.26	
Private paid help at home	hour	€24.02	
Productivity losses-women	hour	€22.81	CSO Average Annual Earning & CSO Quarterly Earnings
Productivity losses-men	hour	€29.33	
Informal care	hour	€26.07	Carney (2014), inflated to 2021
Intangible costs	PwMS	€9,824.31	
Cost of medication for depression	annual	€219.85	
Cost of medication for anxiety	annual	€9.16	
Housing adaptation grant	PwMS	€8,974.47	

3.13 Analysis

Descriptive statistics were used to analyse the demographic and clinical characteristics of the sample and for the resource utilisation. Percentages, means and standard deviations were reported as applicable. Differences in the demographics and resource use between groups, stratified by disability severity or disease type (i.e., RRMS, SPMS or PPMS) were compared by ANOVA and Wilcoxon–Mann–Whitney test, for parametric and non-parametric data, respectively. Statistical significance is based at the 0.05 level throughout. STATA was used for all statistical analysis.



Niall

In 2014 I was diagnosed, almost by accident, with MS. My doctor at the time wanted to check nothing sinister was going on as I was having recurring headaches...it seems something sinister was going on.

The great sports psychologist, Dr Bob Rotella, always promoted the concept of "staying in the present". I try everyday to live by this mantra. Some days are easier than others, but when I take a step back and be in the present, I take a different view. There are many people who would love to be in the present and not part of peoples past. I am very lucky, I have a fantastic family, friends and live in the most beautiful part of Ireland. I am also about to embark on a career change. MS has very much, for the most part, driven me on to not allow it to take charge of my life. Many people are in battles everyday whether it be mental, physical or health. I am lucky have the mental strength that I can deal with my challenge, so in that respect I count myself very fortunate.

Yes, having MS is hard, but I am so privileged in many other aspects of my life that the negatives pale into insignificance. I try and I emphasise try, every day, to be present so I don't miss what is in front of me and miss the great moments with my family and friends. I don't even want to go near the rabbit hole if I stop trying to live my best life. It's a constant challenge and I falter a lot. But I will keep trying everyday because I will miss so much if I don't.

My MS Story

" MS has very much, for the most part, driven me on to not allow it to take charge of my life. "

4. Results

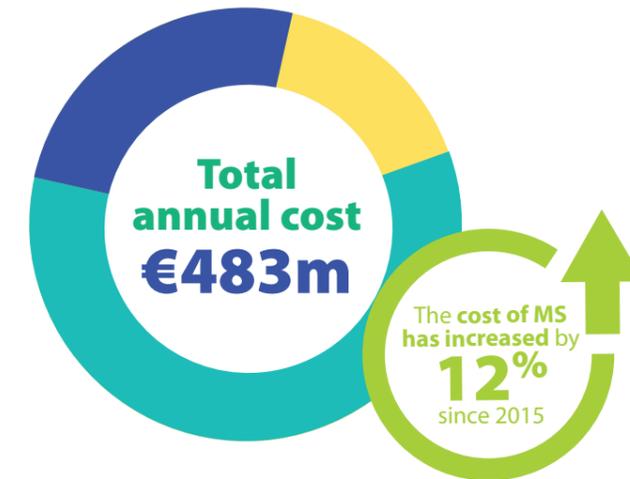
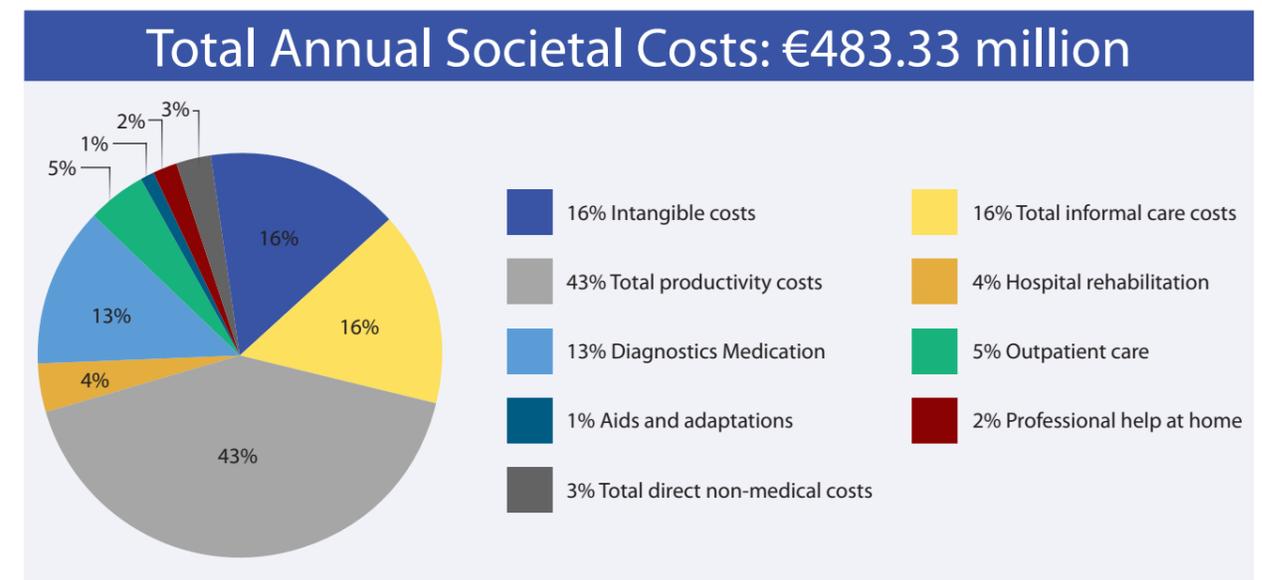


Figure 3. Total Annual Costs by Resource Use: Direct, Indirect and Intangible costs



4.1 Descriptive Statistics

Consistent with the international epidemiological literature (Pugliatti et al, 2002) (Rosati, 2001), the majority of the sample were female (80.1%). 76% of respondents were between the ages of 30-59 years. Most respondents were married or cohabiting (67%), while some (21%) reported living alone. 37% reported having no children while 29% and 35% responded that they had one child or more than one child respectively. The distribution across provinces is consistent to that of the general population of the Republic of Ireland, therefore it is assumed the sample is broadly representative of the national population of people with MS.

The profile of respondents was comparable to the 2015 study except that there was a higher proportion of female respondent in the 2021 survey (80.1% versus 71.4%). The other noticeable difference was a lower proportion of respondent with more than one 1 child in the 2021 survey compared to the 2015 survey (35% versus 46%).

Table 2. Background Information (n=328)

Age characteristics	
Mean (SE) (years)	Not reported
Proportion ≥65 years (%)	7.6
18–29 years (%)	8.23
30–39 years (%)	20.12
40–49 years (%)	28.66
50–59 years (%)	27.44
60–69 years (%)	11.89
70–79 years (%)	3.66
≥80 years (%)	0
Sex n (%) (n=327)	
Female n (%)	262 (80.1)
Male n (%)	65 (19.9)
Marital status n (%) (n=327)	
Single	85 (26)
Married/Cohabiting	218 (66.7)
Widowed	7 (2.1)
Separated/Divorced	17 (5.2)
Habitation, n (%) (n=319)	
Live alone	66 (20.7)
Live with others	252 (79)
Live in a care home	1 (0.3)
Children, n (%) (n=188)	
0	69 (36.7)
1	54 (28.7)
> 1	65 (34.6)
Breakdown of sample by province %	
Leinster	176 (53.7)
Munster	85 (25.9)
Connacht	55 (16.8)
Ulster	12 (3.7)

4.2.1 Disease information

The mean duration of disease –that is the period of time since first developing MS symptoms was 16 years.

The majority of our respondents (71.3%) reported having the relapsing remitting form of the disease, 12.2% reported having SPMS and 11.3% had primary progressive disease; 5.2% reported having benign disease or not knowing their current course of disease.

Most respondents in our study reported having mild MS (61.5%), 32.9% reported having moderate MS, while 5.5% reported having severe MS.

There were varying levels of disability severity within each disease type: 77.9% of those with RRMS reported having mild MS, while

20.3% and 1.7% reported moderate and severe disability, respectively. The majority of those with SPMS reported having moderate disability (75%) and 17.5% and 7.5% reported either severe or mild disability respectively. A similar pattern emerged with respect to those with PPMS, once more the majority reported being in the moderate category (64.9%), while 16.2% and 18.9% disclosed having mild and severe disability, respectively.

Regarding relapses, 34.5% reported having had a relapse in the past year with an average of 2.69 reported relapses per respondent. Furthermore, 59% of people with MS reported that the relapse they had experienced last year had been confirmed by a neurologist and there was an average number of 2.06 confirmed relapses per respondent.

Unexpectedly, relapses were reported across all levels of disability and disease types: 34% of those with mild MS reported having on average 1.7 relapses in the past year, while 51% and 57% of those with moderate and severe MS reported 4.9 and 2.0 relapses, respectively.

In relation to disease type: 38% of those with RRMS reported 1.8 relapses in the past year, while 55% and 38% of those with SPMS and PPMS reported 1.8 and 14.5 relapses, respectively.

Compared to the 2015 study, the average number of relapses have increased from 1.8 to 2.69 per year. This increase is driven by three respondents with PPMS who reported having 15,10 and 80 relapses; none of these relapses were confirmed by a neurologist.

The respondents in our sample also reported having been diagnosed or treated for psychological comorbidities since the onset of MS, 29% with depression and 29% with anxiety. More than 91% of our sample reported fatigue as a consequence of their condition. These figures are consistent with the 2015 study.

Table 3. Disease Information

Disease information	N (%)
Age at MS onset, mean (years)	N/R
Duration of disease, mean (years) (SE) (n=316)	16.3 (28.6)
Symptoms prior to diagnosis, mean (months) (SE) (n=307)	286 (3.3)
Course of disease, n (%)	
Relapsing remitting	234 (71.3)
Secondary progressive	40 (12.2)
Primary progressive	37 (11.3)
Benign	4 (1.2)
I do not know	13 (4)
Disability severity, n (%) (self-reported) (n=325)	
Mild	200 (61.5)
Moderate	107 (32.9)
Severe	18 (5.5)
Relapses	
Relapse in previous 12 months, n (%)	113 (34.5)
Average number of relapses (n) (SE) (n=110)	2.69 (0.7)
Confirmed by a Neurologist (n=113)	59 (52)
Average number of relapses confirmed by a neurologist (n) (SE) (n=59)	2.06 (0.18)
Disease impact	
Depression diagnosis since onset of MS, n (%) (n=306)	88 (28.8)
Anxiety diagnosis since onset of MS, n (%) (n=306)	90 (29.4)
Experience fatigue due to MS, n (%) (n=307)	280 (1.2)

4.2.2 Employment Characteristics

Over half of our sample reported that they were in paid employment (57%) and, of those working, 69% were doing so in a full-time capacity. The average working week for a full-time employee was just over 32.9 hours, while those in part-time employment, worked 19 hours per week, on average.

Over 47% of those current not employed reported having to permanently withdraw from the workforce due to their condition. In relation to work disruption, of those working 36% had officially reduced their working hours, while 45% and 78%, had felt it necessary to change career path and felt that MS had limited their career potential, respectively. In total 35% of our sample were in receipt of some form of state benefit.

The employment characteristics of people with MS in 2021 and 2015 are similar except for the fact that a higher proportion of respondents in this survey had to change their career due to MS (45% versus 26%).

Table 4. Employment Characteristics

Employment status, n (%) ^a	2021 N (%)
Employed	177 (56.6)
Full time (> 30 hrs per week)	122 (69.3)
Part time (< 30hrs per week)	54 (30.7)
Not employed	136 (43.4)
Average Hours per week	176 (32.9hrs)
<i>Situation of those who are not employed, n (%)</i>	
Housewife/husband	29 (21.3)
Student	5 (3.7)
Retired due to age	16 (11.8)
Retired early due to MS	65 (47.8)
Unemployed but seeking work	14 (10.3)
Leave of absence	10 (7.4)
Unable to work but intend to return	11 (8.1)
<i>Employment experiences of those working (n=312)</i>	
Reduced their working hours	65 (36.3)
Had to change career	139 (44.6)
Felt that MS limited their career potential	245 (78.5)
<i>In receipt of state benefit</i>	
Disability Allowance	46 (14.0)
Illness benefit	16 (4.9)
Invalidity Pension	53 (16.2)
I do not receive any of the above	213 (64.9)

^a = totals may exceed 100% due to rounding
[†] = more than one option is possible which means that the total is greater than 100%

4.2.3 Quality of life

EQ-5D and QALYs lost

The EQ-5D-5L was completed by 304 people. The mean utility for the sample derived by using this approach was 0.591. When compared to the UK population norm of 0.86, this represents almost a 32% decrease in self-reported QoL (Kind et al, 1999).

There is an insignificant difference between the men and women in our sample with scores of 0.597 and 0.590 respectively (p=0.87). There was a graded relationship between self-reported severity of disability and utility value, those with mild, moderate and severe disability reporting mean utility values of 0.722, 0.451 and 0.044 respectively.

Differences were also apparent with respect to disease course, those with the RR form of the disease reporting significantly higher mean index values (0.664) than SPMS (0.362) and PPMS (0.362) (p<0.001).

There was also a difference in the mean utility score between those who did and those who did not have a relapse in the previous year, although this difference did not reach statistical significance (p=0.001). However, when we restrict our sample to just those with RRMS, a significant difference existed, with those experiencing a relapse reporting lower utility values (0.590), than those in the no relapse cohort (0.705) (p=0.0003). The mean Visual Analogue Scale (VAS) score for our sample was 73.9.

Table 5. EQ-5D Mean Utilities

EQ-5D-5L	N (%)	Mean (SE)
Mean EQ-5D-5L index value	305 (93%)	0.591 (0.015)
<i>Sex</i>		
Female	242 (79%)	0.590 (0.018)
Male	62 (21%)	0.597 (0.030)
<i>By MS severity</i>		
Mild	187 (62%)	0.722 (0.010)
Moderate	97 (32%)	0.451 (0.023)
Severe	18 (6%)	0.044 (0.270)
<i>Disease course</i>		
RRMS	218 (71%)	0.664 (0.014)
SPMS	35 (12%)	0.362 (0.049)
PPMS	36 (12%)	0.362 (0.056)
<i>Relapse in the past year</i>		
No	192 (64%)	0.639 (0.017)
Yes	110 (36%)	0.515 (0.027)
<i>Visual analogue scale (entire sample)</i>		
VAS	304 (92%)	73.9 (12.82)

For those in our sample, issues relating to usual activities e.g., work leisure were deemed most problematic, with 42.2% reporting having at least moderate problems. This was followed by pain or discomfort (44.5%), then mobility, e.g., walking about (40.5%), followed by anxiety or depression (30.4%) and finally self-care, e.g., washing, dressing (16.7%). Compared to the 2015, a higher proportion of respondents reported at least moderate problems across all the domains.

Table 6. EQ-5D Domains

Level of problems	Mobility (n=308%)	Self-care (n=307%)	Usual activities (n=308%)	Pain/ discomfort (n=308%)	Anxiety/ depression (n=306%)
No problems	88 (28.6)	198 (64.5)	65 (21.1)	61 (19.9)	110 (40.0)
Slight problems	95 (30.8)	58 (18.9)	113 (36.7)	110 (35.7)	103 (33.6)
Moderate problems	74 (24.0)	35 (11.4)	82 (26.6)	98 (31.8)	71 (23.2)
Severe problems	37 (12.0)	10 (3.3)	32 (10.4)	28 (9.1)	15 (4.9)
Extreme problems	14 (4.5)	6 (2.0)	16 (5.2)	11 (3.6)	7 (2.3)

4.2.4 Total Costs: Direct, Indirect and Intangible Costs

Total societal costs of MS amount to €483.33 million in 2021, equating to €53,704 per person with MS. This is an increase of 12% on the costs estimated in the 2015 study (€429.15 million). Direct costs constitute 25% of total costs and amounted to €13,407 per person and year. Indirect costs represent 59% of total costs and are estimated as being €31,992 per person and year. Intangible costs calculated from QALY losses represented 16% of the total societal costs and are estimated to be €8,304 per person with MS. Corresponding percentages from the 2015 study were 31% for direct, 50% for indirect and 19% for intangible costs. This indicates that less was spent on direct medical costs in 2021 and more on indirect costs by people with MS, likely due to the Covid pandemic, discussed in more detail below.

Figure 4. Total Annual Societal Costs

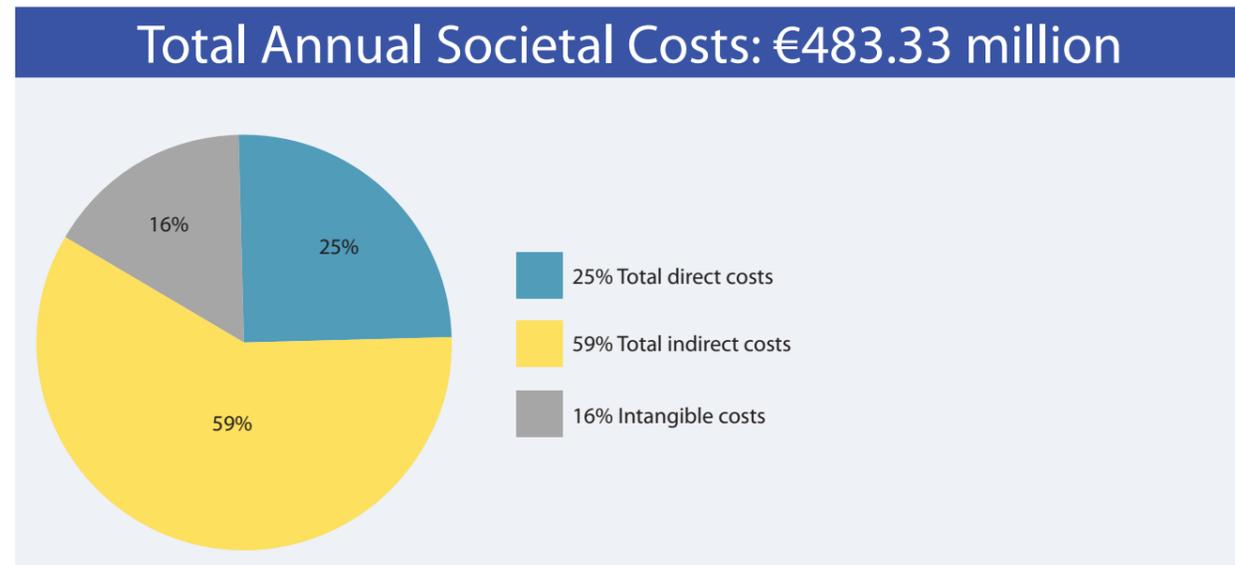


Table 7. Total Costs: Direct, Indirect, and Intangible costs

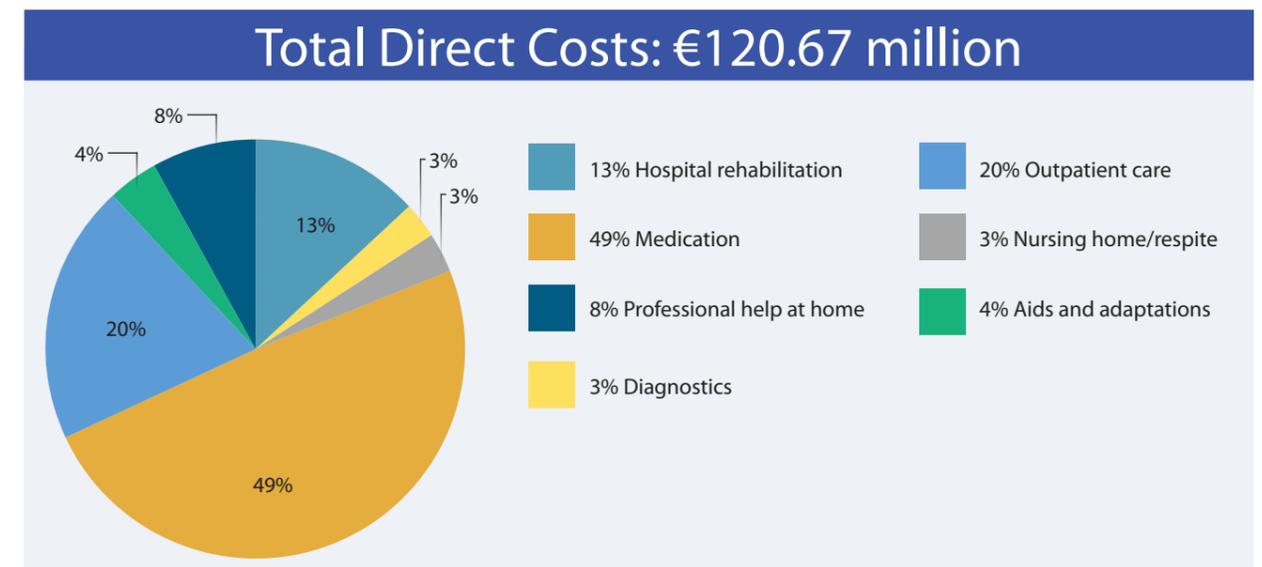
Total annual costs	Societal costs per person €2021	Extrapolated costs (n=9,000) €2021
Direct costs		
Total direct costs	13,407	120,667,401
Indirect costs		
Total productivity costs	23,362	210,261,978
Total informal care costs	8,564	77,079,521
Cost of depression	66	590,304
Total indirect costs	31,992	287,931,803
Total direct and indirect	45,400	408,599,204
Intangible costs	8,304	74,734,550
Total costs	53,704	483,333,754

4.3 Direct Costs

The total direct costs per person living with MS are estimated as being €13,407. Extrapolating from the study sample to the Irish population, assuming an overall MS prevalence of 9,000 people in Ireland – provides a total annual direct cost estimate of €120.67 million. Medication costs and costs attributable to outpatient care contribute the largest share of direct costs, 49% and 20% respectively, while hospital/rehabilitation costs constitute a further 13%. The remaining 18% is made up of costs attributable to formal care, diagnostics, aids and adaptations and nursing home/respite care (see Figure 5).

Total direct costs are lower in this study compared to the 2015 study (€134.1 million). This finding is driven by a decrease in outpatient care and visit to healthcare professionals e.g., GPs, Neurologist, Physiotherapists, Occupational Therapists etc during the Covid pandemic.

Figure 5. Total Direct Costs



Societal Cost of Multiple Sclerosis

Table 8. Total Direct Costs by Person and Extrapolated Costs

Cost Type	Average Cost Per Person €2021	Extrapolated Costs (n= 9000) €2021
Hospital/rehabilitation	1,768	15,910,196
Nursing Home/respite care	433	3,893,462
Diagnostics	418	3,763,935
Medication	6,597	59,369,145
Outpatient care	2,679	24,111,523
Total direct medical costs	11,894	107,048,260
Aids and adaptations	496	4,466,954
Professional help at home	1,017	9,152,187
Total direct non-medical costs	1,513	13,619,141
Total direct costs	13,407	120,667,401

Table 9. Direct Resource Use

Type of resource	% Using resources	Annual mean per user	SD	Total units (n=328)	Total units (n=9000)
Nights in hospital	30.8	8.4	1.5	623	17,095
Nursing home	1.8	1.5	0.2	774	21,238
Rehab centre	1.8	1.2	0.1	107	2,936
Respite centre	2.4	2.2	0.1	42	1,152
MRI	86.9	2.9	0.1	438	12,018
CAT scan	14.9	1.4	0.1	42	1,152
Blood tests	84.5	10.9	0.3	277	7,601
Lumber puncture or spinal tap...	23.2	0.2	-	76	2,085
Neurology clinic or infusion site	62.2	4.4	0.3	380	10,418
Other outpatient	35.7	2.7	0.2	307	8,424
ED not overnight	11.6	1.4	0.1	42	1,152
GP	80.2	5.7	0.2	659	18,082
Neurologist	72.3	2.4	0.1	350	9,604
Other doctor e.g., Cardiologist	12.2	2.9	0.2	246	6,750
Physiotherapist	42.7	8.8	0.5	1,456	39,951
Occupational therapist	17.1	0.8	-	56	1,537

† Standard deviation could not be calculated
* These figures have been annualised from weekly hrs

Societal Cost of Multiple Sclerosis

Social worker	4.3	1	-	14	384
Speech therapist	5.2	0.9	-	17	466
MS Ireland case worker	16.5	2.1	0.1	86	2,360
HSE home help (annual hours) *	6.7	277	61.3	6,565	180,137
HSE PA (annual hours) *	4.9	843.8	384.9	5,728	157,171
Private paid carers (annual hours) *	1.5	1061	964	2,496	68,488
<i>Aids and adaptations</i>					
Wheelchair	12.5			41	1,125
Crutches/Walking frame/ walking aids	31.4			78	2,140
Home modifications	26.8			80	2,195
Medicalised bed	5.8			19	521

4.4 Indirect costs

4.4.1 Total Indirect costs: Productivity Losses, Informal Care and Depression Costs

Total annual indirect costs are estimated as being €31,992 per person with MS, extrapolated out to the national population with MS (n=9,000), provides for a total indirect cost estimate of €287.93 million. This is an 35% increase compared to the 2015 report (€213.6 million). This increase is driven by an increase in the cost of productivity losses associated with early retirement due to MS, presenteeism and reduced working week.

The factors contributing the largest proportion of indirect costs, were early retirement due to MS (34.8%), informal care (26.8%), presenteeism (15.6%), reduced working week (13.6%) and extra hours missed due to sick days (9.0%), depression (0.2%).

Figure 6. Total Indirect Costs by Constituent Parts

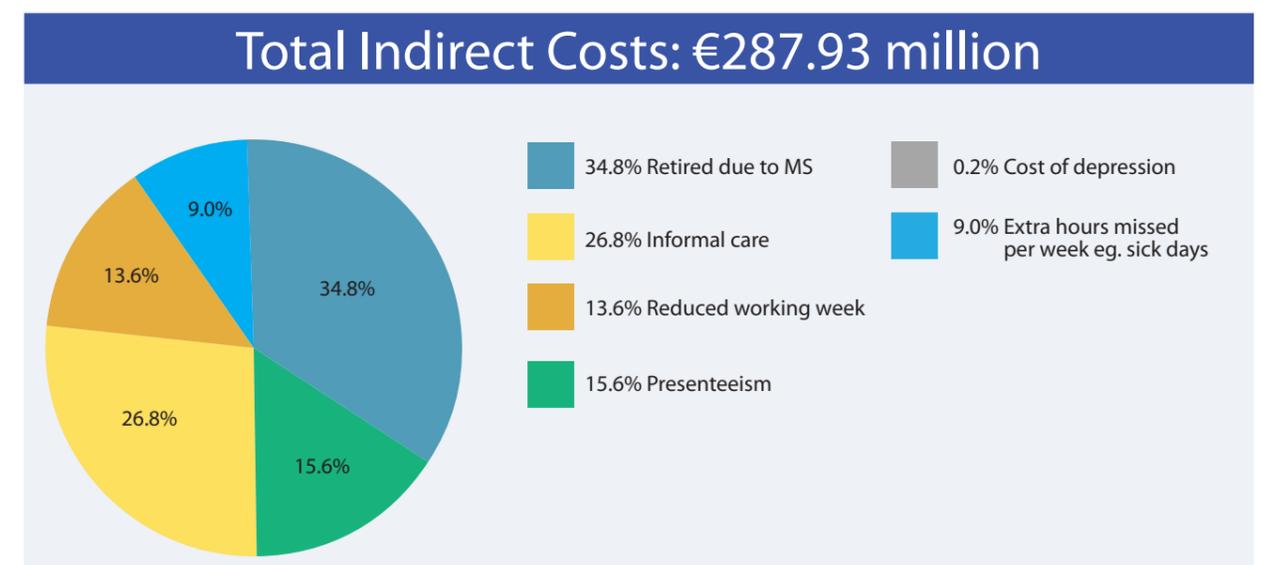


Table 10. Total Indirect Costs: Productivity Losses, Informal Care

Productivity losses & Informal care	Average costs per person with MS (2021)	Extrapolated costs (n=9,000) 2021
Officially reduced working week	€4,348	€39,132,209
Extra hours missed due to appointments, etc	€2,882	€25,938,182
Retired early due to MS	€11,149.1	€100,341,580
Presenteeism	€4,983.3	€44,850,006
Total productivity losses	€23,362.4	€210,261,978
Informal care	€8,564.4	€77,079,521
Cost of depression	€65.6	€590,304
Total indirect costs	€31,992.4	€287,931,803

4.4.2 Productivity Losses

In our sample, 55% and 48% of women and men, respectively, were in paid employment. 13% of all women and 13.8% of all men had officially reduced their working week (women: 9.2 hrs, men: 10.6 hours). A higher proportion of respondents in this survey reported missing extra hours due to appointments, sick leave in the last week: 45.0% of women missed 3.9 hours, while 46.2% of men reported missing 4.0 hours. Corresponding figures from the 2015 survey were 8.8% of women missed 14.3 hours, while 25.4% of men reported missing 14.4 hours.

Presenteeism was an issue in the workplace in the previous week for 35.8% of all women and 37.2% of all men. Corresponding figures from the 2015 survey were 27.5% and 17.8% (ref) 1 respectively. The average number of hours missed was 11 hours per week. This represents 21% of total productivity losses and 15.6% of total indirect costs. A considerable number of people in our sample reported having to permanently withdraw from the workforce due to their condition, in total 47 women and 17 men, which represents 20% of our entire sample and 47.8% of those not in employment. This represents 48% of our total productivity losses and 35% of our total indirect costs and is an increase since 2015 due people with MS retiring earlier possibly due to Covid.

The total number of workdays lost due to MS, with respect to the headings discussed above are presented in Table 12. The total days lost reported by our sample was 80,445 and extrapolating to the national population with MS in Ireland, assuming a total prevalence of 9,000 people, provides an estimate of some 2,207,612 workdays lost due to MS annually.

In our sample, (n=328) indirect costs attributable to productivity losses are estimated at being €23,362 per person. Extrapolating to the national population with MS in Ireland, assuming a total prevalence of 9,000 people, provides an estimate of total annual costs attributable to productivity losses of €210.26 million. This represents an increase in productivity losses since the 2015 survey of 55%, due to an increase in the cost of labour and a higher proportion of people with MS experiencing productivity losses.

1. As a % of all those in the sample

Figure 7. Total Productivity Losses

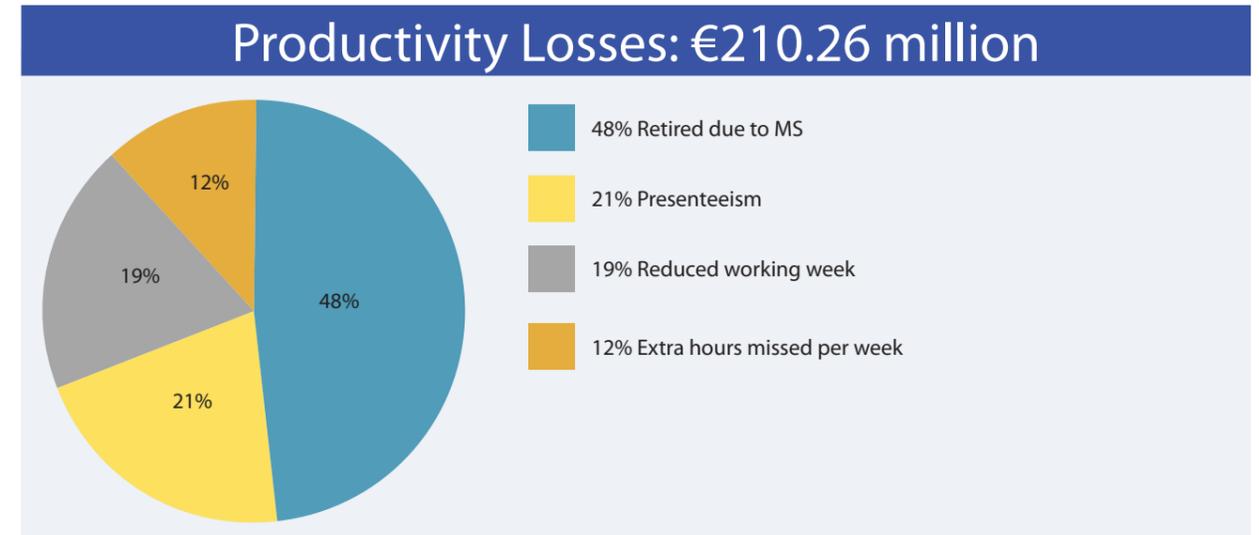


Table 11. Productivity Loss and Informal Care

Employment variables	%	Mean	SD	Total hours	Unit costs €2021	Total costs €2021
Women (n=262)						
Officially reduced working week (hrs per week)	13.0%	9.2	1.5	16,266	22.81	371,060
Extra hours missed in last week (due to appointments, sick days)	45.0%	3.9	1.4	23,930	22.81	545,914
Retired early due to MS (annual)	24.8%	n/a		n/a	41,975	2,728,382
Presenteeism (% of work performance affected, previous week)	35.8%	n/a	n/a	53,651	22.81	1,223,924
Men (n=65)						
Officially reduced working week (hrs per week)	13.8%	10.6	5.7	35,828	29.33	1,050,744
Extra hours missed in last week (due to appointments, sick days)	46.2%	4.0	1.8	13,520	29.33	396,507
Retired early due to MS (annual)	26.2%	n/a		n/a	53,962	917,362
Presenteeism (% of work performance affected, previous week)	37.2%	n/a	n/a	13831	29.33	405,627
Total productivity losses						€7,639,519
Total Productivity losses per person with MS						€23,362
Informal care						
Weekly hours of informal care provided	42.4%	14.9	2.6	107,753	26.07	€2,809,120
Informal care per person with MS						€8,564
Total productivity & informal care costs						€10,448,639
Total productivity & informal care costs per person with MS						€31,856

Table 12. Total Number of Workdays Lost Due to MS and Total Days of Informal Care Provided

Employment variables	Days lost per year (Study sample, n = 328)	Days lost per year (Extrapolated, n = 9,000)
Officially reduced working week	6,512	178,675
Extra hours missed due to appointments, etc.	4,681	128,450
Retired early due to MS	60,827	1,669,031
Presenteeism	8,435	231,456
Total number of workdays lost due to MS	80,455	2,207,612
Informal care: total annual days of care provided	107,753	2,956,637

4.4.3 Informal Care

The majority of our respondents reported having received unpaid care from family or friends in the last week; in total, 42% received on average 14.9 hours of care in the previous week. In total, we estimate that there were 107,753 days of care provided to our sample respondents, extrapolating this out to the national population of those with MS, assuming a total prevalence of 9,000 people, provides for an estimate of 2,956,637 days of care provided by the family and friends of those with MS.

4.4.4 Depression and Anxiety

A total of 123 people in our sample have since the onset of their MS been treated for depression or anxiety or both, representing 37.5% of our total sample. There was a degree of heterogeneity within our sample when it came to the diagnosis of depression or anxiety (see Figure 8 and Figure 9). The strongest predictor of a diagnosis of depression and anxiety in our sample was whether the person had experienced a relapse in the past year. Those who reported having a relapse were 9% and 16% more likely to report a depression or anxiety diagnosis respectively.

The breakdown of diagnosed depression and anxiety by disease severity and type of MS is also shown in Figure 8 and Figure 9. In contrast to the 2015 report, this sample did not show a graded relationship between disease severity and a depression and anxiety diagnosis. This is likely due to a small number of respondents with severe disease who had a relapse in the previous 12 months (n=7). Similar to the 2015 report, people with PPMS were less likely to be diagnosed with depression and anxiety compared to the other types of MS.

In the general population the annual prevalence of mental health problems including depression and anxiety is estimated as being 10% (Doherty et al, 2007). However, as our estimate was not a one year prevalence estimate, we assumed, as was reported in Koch et al, 2008, that two-thirds would report depressive symptomology in the previous year. This gave us of a figure of 15% of our sample population who would be free of depression and/or anxiety if the prevalence rates in the MS population were analogous to that of the general population. Assuming 3.3 and 0.7 extra GP visits per year and medication costs of €219.85 and €9.16 for depression and anxiety respectively (Doherty et al., 2007), we estimate the annual direct cost of depression (GP and medication use) as being €65 per person with MS. Extrapolating to the broader MS population and specifically to the excess prevalence of depression within the broader MS population; we estimate the excess cost of depression in the MS population as being in the region of €590, 304 per year.

Figure 8. Depression: Sample Breakdown

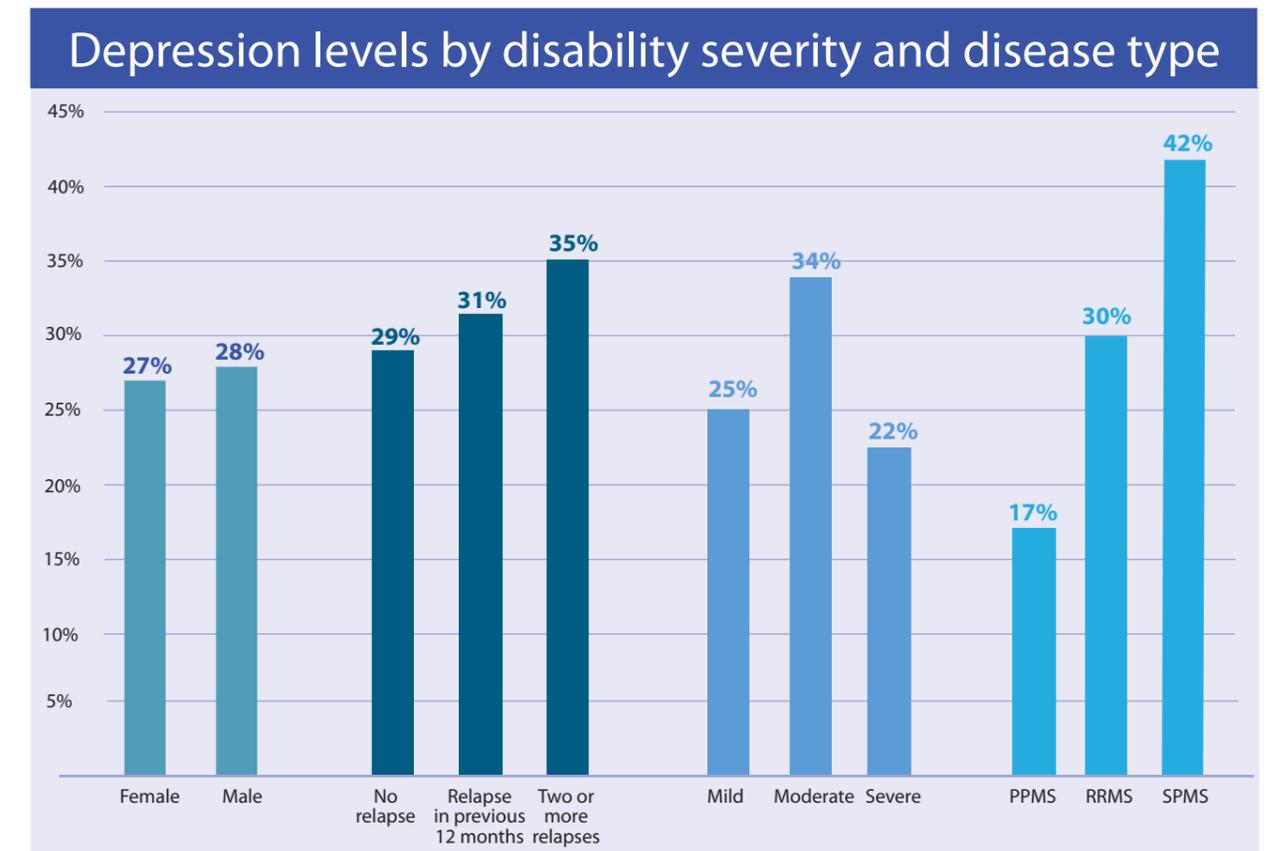
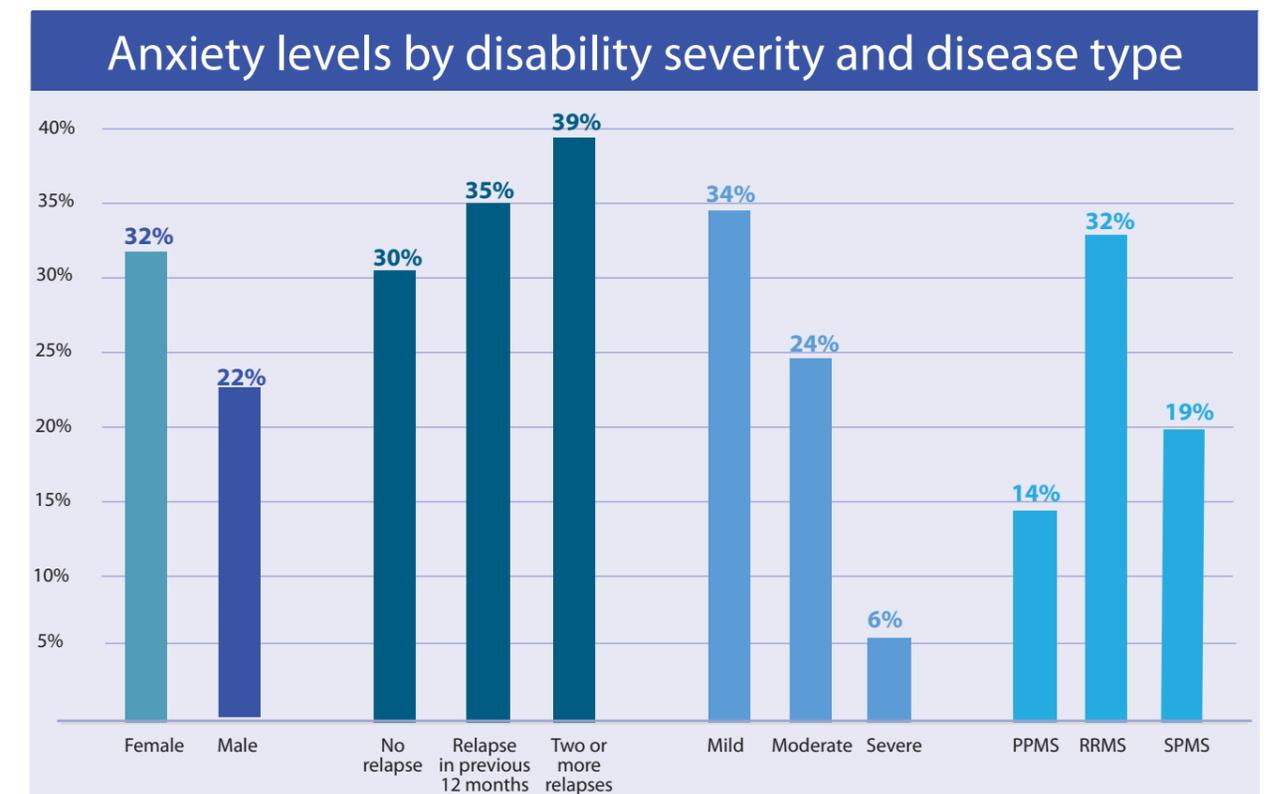


Figure 9. Anxiety: Sample Breakdown



4.4.5 Intangible costs (QALYs lost)

The cohort of 304 people experienced a total loss of 77.67 QALYs due to MS during the year, or an average of 0.26 QALYs per person and year. The current guidelines with respect to threshold or willingness-to-pay for a unit effect (life year or QALY) in Ireland, lies between €20,000 and €45,000 per QALY. Intangible costs for MS in Ireland are calculated as being in the range of €5,110 to €11,498 per person and year; the mid-point of which: €8,304 was used yielding a total intangible cost (n=9000) of €74.73 million.

Table 13. QALY Lost (Women)

Age Group	Mean Utility (UK Population)	Mean Utility (Sample)	Difference	No. of Respondents	QALY Lost
Under 25	0.94	0.651	0.29	4	1.16
25-34	0.93	0.651	0.28	45	12.56
35-44	0.91	0.690	0.22	57	12.56
45-54	0.85	0.601	0.25	70	17.41
55-64	0.81	0.573	0.24	51	12.09
65-74	0.78	0.381	0.40	13	5.19
75+	0.71	0.310	0.40	2	0.80
Total					61.77

Table 14. QALY Lost (Men)

Age Group	Mean Utility (UK Population)	Mean Utility (Sample)	Difference	No. of Respondents	QALY Lost
Under 25	0.94	0	0.94	0	0.00
25-34	0.93	0.670	0.26	4	1.04
35-44	0.91	0.701	0.21	17	3.55
45-54	0.85	0.620	0.23	20	4.60
55-64	0.8	0.522	0.28	13	3.61
65-74	0.78	0.388	0.39	7	2.74
75+	0.73	0.363	0.37	1	0.37
Total					15.91

4.5 Costs of MS Relapse

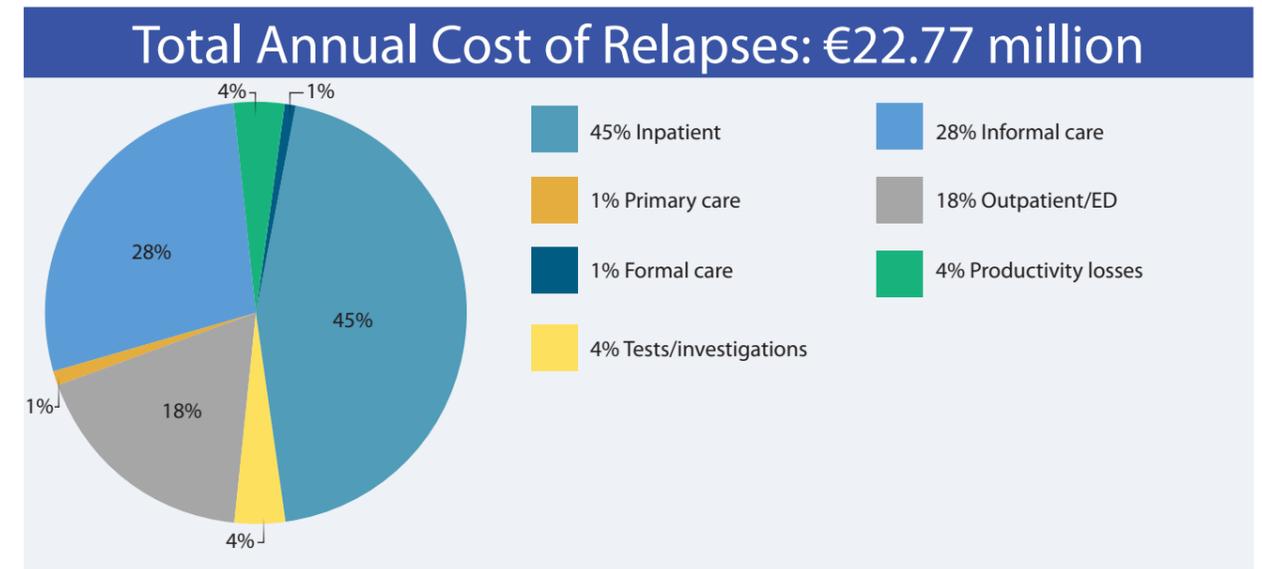
4.5.1 Total Annual Cost of MS Relapses

The direct and indirect costs associated with a single relapse in Ireland was estimated at €2,417 and €1,143, respectively. This provides for a total estimate of €3,560 for a single relapse. The corresponding figure from the 2015 survey was €2,438 per relapse.

The average number of relapses was 2.69 and 2.06 per year unconfirmed and confirmed by a neurologist respectively. The average number of relapses used in the 2015 survey was 1.85. Given that the data in the 2021 survey is highly skewed (one respondent reported having 80 relapses in the previous year, which were not confirmed by a neurologist), we use 2.06 as the average number of relapses. As such, the annual cost of relapses in Ireland was estimated at €7,333 per person (€3,560*2.06).

We extrapolate these figures to the broader population by assuming a total prevalence of 9,000 people with MS and as 34.5% of our sample had a relapse in the last year, we assume the same for the national population. Therefore, we estimate the total annual cost attributable to MS relapse of €22.77 million. The corresponding annual cost of a relapse in 2015 was €16.9 million. Higher costs associated with a relapse (both direct and indirect) and a higher average number of relapses per person can account for this increase.

Figure 10. Total Annual Cost of a Relapse



4.5.2 Direct Costs Associated with A Relapse

In total 34.5% (n=113) of our sample reported having a relapse in the previous year. The GP was the most frequently utilised medical service with 46% of our sample reporting ringing or visiting a GP as a result of their last relapse. 20% reported being admitted to hospital, this cost constitutes 66% of the total direct costs attributable to a single relapse. The total direct cost of a relapse was estimated at €2,417 per person in our sample who reported having a relapse. This is an increase since the 2015 study (€1,715) which is driven by increased usage of hospital and outpatient services for people who have experienced a relapse. This is in contrast to the overall MS population where direct costs were reduced which suggests that people with MS who really needed healthcare during the Covid pandemic received it.

Figure 11. Direct Cost Associated with a Relapse

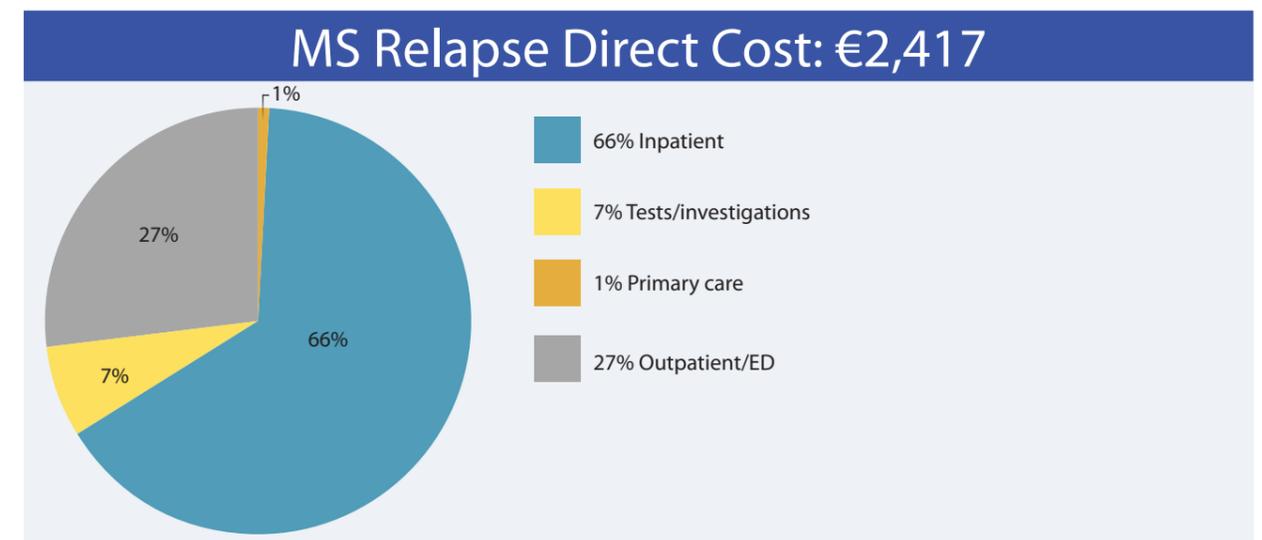


Table 15. Direct Cost of a Relapse

Resource Use Type	Measure Type	MS patients	Proportion	Mean no. units	SD	No of units	Cost per unit	Cost per relapse	Total cost, n = 113
Hospital inpatient	night	23	20%	8.4	1.0	193	€931	€1,591	€179,815
Magnetic Resonance Image (MRI)	per test	55	49%	1.0	-	55	€178	€87	€9,796
Blood test	per test	48	42%	1.0	-	48	€21	€9	€1,031
Lumbar Puncture (LP)/ Spinal tap	per test	11	10%	1.0	-	11	€652	€64	€7,177
Neurology clinic	per visit	41	36%	1.0	-	41	€1,660	€602	€68,059
Emergency department	per visit	18	16%	1.0	-	18	€160	€25	€2,880
GP	visit	52	46%	1.0	-	52	€47	€22	€2,458
Physiotherapist	hour	19	17%	1.0	-	19	€39	€7	€736
Occupational therapist	hour	30	27%	1.0	-	30	€39	€10	€1,161
Total									€ 273,113

4.5.3 Indirect Costs Associated with A Relapse

In total 73.4% of our sample reported requiring extra informal care as a consequence of their last relapse (n=113), while 1.8% received extra hours of formal care. The corresponding figures in the 2015 survey were 60% and 5% respectively. Furthermore, a higher average number of informal care per relapse was recorded in this survey.

Total indirect costs associated with a relapse are estimated as being €129,147 which equates to €1,143 per person who reported having a relapse in the past year (n=113). This is a considerable increase since 2015 (€723 per person who reported having a relapse) due to an increase in informal care hours at the expense of formal care hours.

Figure 12. MS Relapse: Indirect Costs

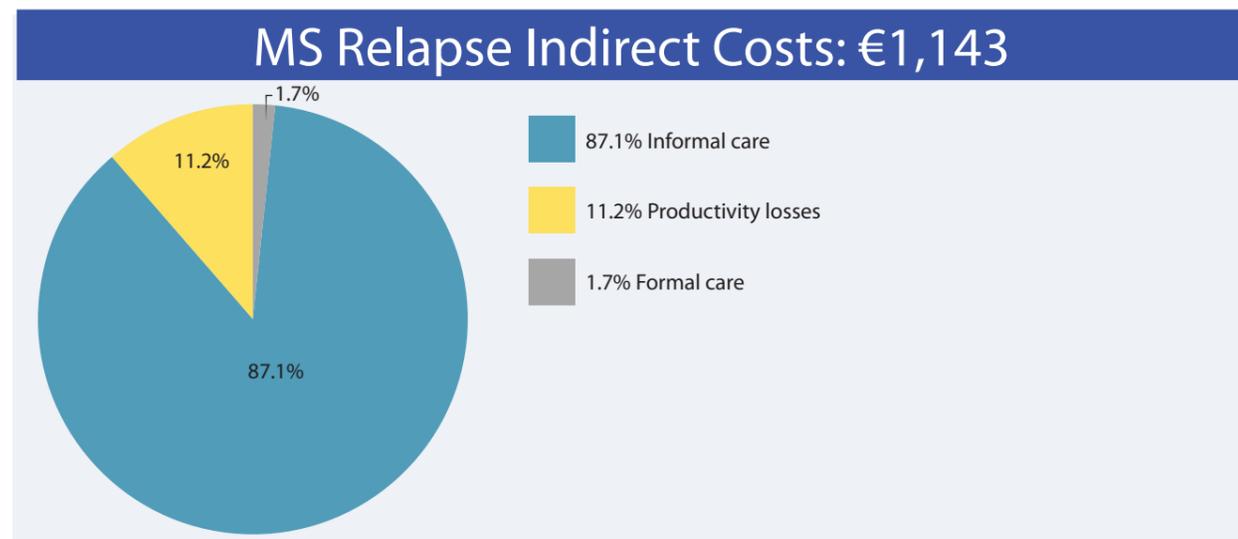


Table 16. Indirect Costs Associated with A Relapse

Resource use	Sample, n (%)	Mean per relapse (SE)	Total units	€ Cost per unit	€ Total per relapse
Formal care (hours)	6 (5.3%)	15 (9)	90	24.02	2,162
Informal care (hours)	83 (73.4%)	52 (12)	4316	26.07	112,518
Productivity losses					
Sick days (in hours)	42 (37.1%)	12 (n/a)	515	26.1	13,424
Reduced hours	1 (0.09%)	n/a	40	26.1	1,043
Total					129,147
Total per person with active MS					1,143

4.6 Costs By Disease Severity (Mild, Moderate, Severe)

4.6.1 Direct Costs by Disease Severity (Mild, Moderate, Severe)

Use of direct healthcare increased with severity of disease. Specifically, 26.5% of respondents with mild MS reported receiving inpatient care in hospitals, compared with 36.4% with moderate MS and 44.4% with severe MS. The number of days in hospitals increased with disability severity with mild, moderate and severe people with MS spending on average 8.1 and 8.4 days and 11.1 days respectively in hospital.

Six people in our sample reported requiring nursing home care, of those who did so, 5 had moderate MS. Few people reported requiring respite care in the last year: 0.5% in the mild subgroup reported receiving respite care while 4.7% and 11.1% of people with moderate and severe MS received respite care with an average of 8 and 12 nights respectively.

Investigations and tests were frequently reported by the study respondents, across all levels of disability severity, for example, 92.5% of respondents with mild MS, 78.5% of those with moderate MS and 72.2% of those with severe MS, reported having had an MRI in the last year. More than 70% of those with mild, moderate and severe MS reported seeing a GP in the last year, and the frequency of visits were similar across the disability severity categories, those with mild and moderate MS detailing 6.2 and 7 visits respectively, while those with severe MS reporting 8.4 visits.

A graded significant relationship existed between disability severity and physiotherapy visits: those with severe MS reported having 13.4 physiotherapist sessions in the previous six months compared to 11 sessions for the other disability types.

With regards to formal care, a greater proportion of those with severe disability reported requiring extra formal care such as HSE home help, HSE personal assistants and private paid carers than those with mild or moderate MS. In the case of HSE home help, those in the severe category reported receiving 24.8 hours of this service in the previous week, while those in the moderate group reported 25.9 hours; zero of the mild MS subgroup reported utilised this service.

The degree to which the respondents reported requiring specific aids and adaptations due to their condition was also associated with disability severity. In each category, significant differences were apparent across the spectrum of disability severity, for example 61% of those with severe disability reported having home adaptations, while 46% and 10% reported same in the moderate and mild groups, respectively.

Compared to the 2015 study, people with MS received less healthcare resources in 2021 across the disease spectrum with access to the GP, the Physiotherapist and formal care reduced, possibly due to Covid. For example, the average number of hospital nights, respite nights, GP visits and Physiotherapist visits for people with severe MS were 11.1 days, 2.1 nights, 8.4 visits and 13.4 visits respectively in 2021. The corresponding figures from the 2015 survey were 11.2 days 8.2 days, 7.8 visits and 20.8 visits respectively. Furthermore, formal care hours were reduced in this survey compared to the 2015 study. For example, 10.2%, 32.1% and 8.0% of respondents with severe MS received an average of 24.8 HSE Home Help, 7.6 HSE PA and 1.7 Private Care hours per week respectively. In the 2015 study 24.4%, 41.5% and 24.4% of people with severe MS received an average of 13 HSE Home Help, 10 HSE PA and 3.5 Private Care hours per week respectively.

Table 17. Direct Resource Use by Disease Severity (Mild, Moderate, Severe)

Resource Use Type	Mild = 200		Moderate = 107		Severe = 18	
	% Using	Mean (SD)	% Using	Mean (SD)	Obs %	Mean (SD)
Hospital inpatient	26.5%	8.1 (0.9)	36.4%	8.4 (1.1)	44.4%	11.1 (2.9)
Nursing home	0.5%	1.5 (0.3)	4.7%	2.1 (0.4)	0.0%	3 (1.3)
Rehab centre	0.0%	1 (0)	3.7%	2 (0.4)	11.1%	3 (1.1)
Respite centre	0.5%	1.2 (0.2)	4.7%	1.4 (0.2)	11.1%	2.1 (0.6)
Magnetic Resonance Image (MRI)	92.5%	3.8 (0.2)	78.5%	3.5(0.3)	72.2%	4.7 (1.1)
CT/ CAT scan	15.5%	1.6 (0.1)	15.0%	1.6 (0.2)	11.1%	2 (0.7)
Blood test	88.5%	15.9 (0.5)	77.6%	14 (0.7)	77.8%	17 (1.9)
Lumbar Puncture (LP)/ Spinal tap*	27.0%	-	15.9%	-	22.2%	-
Neurology clinic or infusion suite	86.0%	3.7 (0.5)	99.1%	3.4 (0.6)	72.2%	5.4 (2.6)
Other hospital outpatient visit	33.5%	3.9 (0.4)	39.3%	4.1 (0.5)	33.3%	4.1 (1.0)
Emergency department	10.5%	2.1 (0.3)	15.9%	1.8 (0.2)	0.0%	2.2 (1.2)
GP	79.0%	6.2 (0.3)	83.2%	7 (0.4)	72.2%	8.4 (1.3)
Neurologist	77.0%	3.6 (0.2)	63.6%	4.4 (0.4)	61.1%	4.3 (0.7)
Other doctor, e.g., Cardiologist	29.0%	4.2 (0.4)	27.1%	4.7 (0.6)	22.2%	8 (2.7)
Physiotherapist	38.0%	11.5 (0.9)	49.5%	11 (1.2)	50.0%	13.4 (3.4)
Occupational therapist*	8.0%	-	29.0%	-	44.4%	-
Social worker*	2.5%	-	5.6%	-	16.7%	-
Speech therapist*	2.5%	-	10.3%	-	5.6%	-
Medication*	88.0%	-	88.0%	-	88.0%	-
MS Ireland caseworker	13%	2.3 (0.3)	21%	3.1 (0.5)	39%	4.2 (1.3)
HSE home help (weekly hours)	0%	-	4.6	25.9 (3.3)	10.2	24.8 (6.1)
HSE PA (weekly hours)	0%	-	7.5	11.1 (1.3)	32.14	7.6 (1.7)
Private paid carers (weekly hours)	0%	-	2.5	3.2 (0.9)	8.0	1.7 (0.7)
Aids, e.g., wheelchair, crutch etc/ Home modifications						
Wheelchair*	2%	-	22%	-	78%	-
Crutches*	10%	-	48%	-	39%	-
Walking frame*	3%	-	38%	-	56%	-
Home modifications*	10%	-	46%	-	61%	-
Medicalised bed*	1%	-	8%	-	50%	-

* Mean and standard deviation could not be calculated

4.6.2 Indirect Costs by Disease Severity (Mild, Moderate, Severe)

A graded significant relationship existed between disability severity and employment status; those with mild MS are more than three times as likely as those with moderate disability to be in paid employment, while a similar percentage of those with moderate and severe disability are in paid employment. People with moderate MS are more likely to withdraw from the workforce due to MS compared to the mild MS subgroup (41% versus 9%). However, in contrast to the 2015 study people with severe MS are less likely to retire due to MS, which can be explained by the small number of people with severe MS in our sample compared to the 2015 study (n=18 versus N=41).

Significant differences were also apparent when it came to hours of informal care received in the previous week, with 89% of respondents with severe MS receiving informal care compared to 77% and 34% of those with moderate and mild MS respectively.

The most striking difference with this study and the 2015 study is the increase in presenteeism and informal care hours across the disease spectrum. For example, productivity at work affected 28%, 48% and 52% of people with mild, moderate and severe MS respectively in this study. Corresponding figures from the 2015 survey were 25%, 26% and 15%. Furthermore, more informal care hours were used across the disease spectrum, with an average of 3.6, 15.5 and 59.1 hours per week received by people with mild, moderate and severe MS respectively. This compares to 8.7, 13.2 and 21.8 hours for people with mild, moderate and severe MS respectively in the 2015 study.

Table 18. Indirect Costs by Disease Severity (Mild, Moderate, Severe)

Employment variables*	Mild (n=200)		Moderate (n=107)		Severe (n=18)	
	Obs %	Mean (SD)	Obs %	Mean (SD)	Obs %	Mean (SD)
In paid employment*	74%		22%		28%	
Full time (over 30 hours) *	49.5		10%		5.6	
Officially reduced working week (hrs per week)	9%	4.9 (1.5)	16%	8.3 (2.1)	50%	20.3 (4.9)
Extra hours missed in the last week	0.6	2.4 (0.6)	19%	5.1 (2.7)	28%	34.8 (29.4)
Retired due to MS*	9%		41%		17%	
Presenteeism (% of work performance affected) *	28%		48%		52%	
Informal care						
Weekly hours of informal care received	34%	3.6 (0.4)	77%	15.5 (3.0)	89%	59.1 (18.3)

* Mean and standard deviation could not be calculated

4.6.3 Costs By Disease Severity (Mild, Moderate, Severe)

As in previous studies, costs increase as disability increases, and QoL decreases as the disease progresses. Within each group, indirect costs attributable to MS, form a larger share of total costs than direct costs and increased with disease severity. For example, indirect costs represented 41%, 43% and 77% of total costs for the mild, moderate and severe subgroups respectively, which is driven by the increased use of informal care by people with severe MS. In contrast to the 2015 study, we do not find a graded relationship between disability severity and intangible costs, those with intangible costs representing 15%, 32% and 8% of total costs for those with mild, moderate and severe MS, respectively. This is due to the small number of respondents with severe MS who completed the HRQoL questionnaire (n=18).

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Table 19. Costs by Disease Severity (Costs Per Person Per Year)

Disability level	Direct costs	Total indirect costs	Productivity costs	Informal care costs	Utilities EQ-5D	Intangible costs	Total costs (€,2014)
Mild (61%)	€12,273	€11,610	€9,951	€1,659	0.722	€4,124	€28,007
Moderate (32.6%)	€16,567	€28,403	€12,300	€16,103	0.451	€21,598	€66,567
Severe (5.5%)	€19,639	€101,789	€30,573	€71,216	0.044	€10,149	€131,577

Figure 13. Total Costs by Disease Severity (Per Person and Year)



4.7 Costs By Disease Course (RRMS, SPMS, PPMS)

4.7.1 Direct Resource Use by Disease Course (RRMS, SPMS & PPMS)

The varying care needs of people with different forms of MS are explored in this section. Hospital care, MRIs, blood tests, Neurology clinics and the GP were the most frequently used medical resources. Specifically, 30.8% of respondents with RRMS reported receiving inpatient care in acute hospitals, compared with 47.5% with SPMS and 21.6% with PPMS. Investigations and tests were frequently reported by the study respondents, across the disease course spectrum, for example, 92.3% of respondents with RRMS, 77.5% of those with SPMS and 67.6% of those with PPMS, reported having had an MRI in the last year.

Table 20. Direct Resource Use by Disease Course (RRMS, SPMS & PPMS)

Resource Use Type	Measure Type	RRMS = 234		SPMS = 40		PPMS = 37	
		% Using resources	Mean (SD)	% Using resources	Mean (SD)	% Using resources	Mean (SD)
Hospital inpatient	night	30.8	8.2 (0.8)	47.5	8.9 (1.7)	21.6	8.4 (2.2)
Nursing home	day	0.9	1.2 (0.2)	7.5	3.7 (0.8)	2.7	1.9 (0.6)
Rehab centre	day	0.9	1.4 (0.2)	5.0	2.6 (0.8)	5.4	2.0 (0.6)

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Respite centre	day	1.3	1.1 (0.1)	5.0	1.9 (0.4)	8.1	1.7 (0.4)
Magnetic Resonance Image (MRI)	per test	92.3	4.0 (0.2)	77.5	3.8 (0.6)	67.6	2.8 (0.4)
CT/ CAT scan	per test	15.4	1.6 (0.1)	10.0	1.9 (0.5)	16.2	1.6 (0.3)
Blood test	per test	87.6	16.2 (0.)	77.5	16.2 (1.2)	75.7	10.8 (1.2)
Lumbar Puncture (LP)/ Spinal tap*	per test	24.4	-	20.0	-	21.6	-
Neurology clinic (infusion suite not included)	per visit	66.3	3.6 (0.4)	62.5	5.1 (1.4)	48.6	3.2 (0.9)
Other hospital outpatient visit	per visit	35.8	4.0 (0.3)	32.5	4.5 (0.9)	35.1	3.1 (0.6)
Emergency department	per visit	11.5	2.0 (0.2)	12.5	1.9 (0.5)	10.8	2.0 (0.6)
GP	visit	82.1	6.5 (0.3)	82.5	7.5 (0.9)	67.6	7.0 (0.8)
Neurologist	hour	76.9	3.8 (0.2)	67.5	4.8 (0.6)	54.1	4.0 (0.8)
Other doctor, e.g., Cardiologist		29.5	4.3 (0.4)	20.0	7.0 (1.6)	27.0	4.7 (1.1)
Physiotherapist	hour	38.0	11.3 (0.9)	62.5	14.3 (1.8)	56.8	10.4 (1.8)
Occupational therapist*	hour	11.1	-	32.5	-	40.5	-
Social worker*	hour	3.4	-	7.5	-	5.4	.
Speech therapist*	hour	3.8	-	12.5	-	5.4	-
Medication*		88	-	88	-	88	-
MS Ireland caseworker (months)	expert opinion	15.8	2.4 (0.3)	17.5	4.4 (1.2)	21.6	3.1 (0.7)
HSE home help (weekly hours)		3.8	24.3 (6.6)	6.7	24.5 (4.5)	6.0	26.5 (5.2)
HSE PA (weekly hours)		3.3	12.8 (1.7)	8.9	10.2 (1.5)	35	8.3 (1.8)
Private paid carers (weekly hours)		0.5	1.5 (0.5)	7.4	2.8 (0.8)	0.0	1 (.)
<i>Aids, e.g., wheelchair, crutch etc/ Home modifications</i>	<i>PwMS</i>						
Wheelchair*		3.8	-	40.0	-	37.8	-
Crutches*		18.8	-	37.5	-	43.2	-
Walking frame*		8.1	-	40.0	-	51.4	-
Home modifications*		14.5	-	10.7	-	54.1	-
Medicalised bed*		1.7	-	25.0	-	10.8	-

* Mean and standard deviation could not be calculated

4.7.2 Indirect Costs by Disease Course

A significant relationship existed between type of MS and employment status; 65.6% of those with RRMS were in paid employment, while for those with SPMS and PPMS fewer were working at the time of the survey; 21.6% and 34.5% respectively.

Permanent withdrawal from the workforce due to MS is also predicted by disease type; 50% of those with SPMS reported retiring as a result of their condition, this figure falls significantly when examining the PPMS (27.0%) and RRMS subgroups (12.4%). Significant differences were also apparent when it came to hours of informal care received in the previous week, those with RRMS reporting receiving 45% and 42% less hours of care, compared to those with SPMS and PPMS, respectively.

Table 21. Indirect Costs by Disease Course (RRMS, SPMS & PPMS)

	RRMS (n=234)		SPMS (n=40)		PPMS (n=37)	
	Obs %	Mean (SD)	Obs %	Mean (SD)	Obs %	Mean (SD)
Employment variables						
In paid employment*	65.6		21.6		34.5	
Full time (over 30 hours)*	82.5		87.5		81.1	
Officially reduced working week (hrs per week)	22.6	8.0 (1.9)	12.5	9.2 (3.0)	16.2	14.4 (5.5)
Extra hours missed in the last week	51.0	2.5 (0.5)	27.0	12.9 (6.2)	20.0	15.4 (15.2)
Retired due to MS*	12.4		50.0		27.0	
Presenteeism (% of work performance affected)*	67.9		90.0		89.2	
Informal care						
Weekly hours of informal care received	43.6	8.5 (2.3)	67.5	23.4 (6.9)	81.10	27.6 (9.7)

4.7.3 Costs By Disease Course

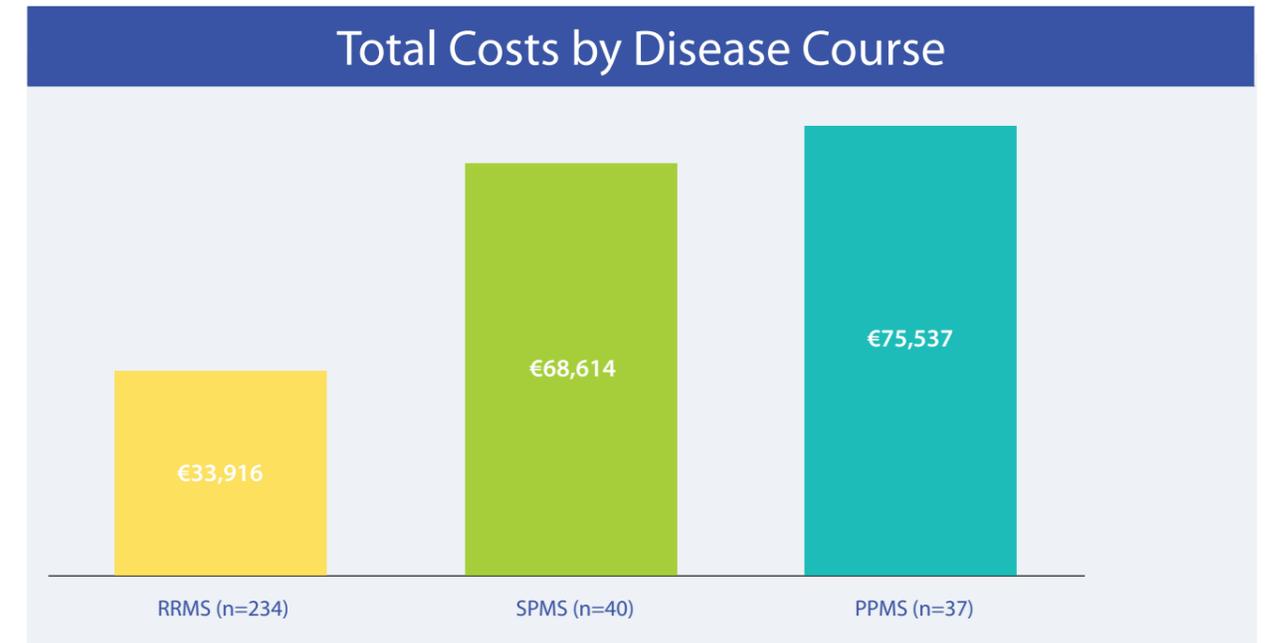
As in previous cost of MS studies, costs vary across the disease course spectrum. When looking at the component costs—within each group—indirect costs form a larger share of total costs than direct costs. The relative contributions of the cost components however, differed among the subgroups; for example, indirect costs comprised a smaller proportion of total costs in RRMS compared to both SPMS and PPMS subgroups (45% for RRMS, 56% and 62% for those with SPMS and PPMS respectively). While for those with RRMS, direct costs (36%) comprised a larger proportion than those in the SPMS (25%) or PPMS groups (21%). Informal care costs also varied across disease types, with informal care costs composing 15%, 31% and 40% for those with the relapsing-remitting, secondary-progressive and primary- progressive forms of MS, respectively.

The main difference between this study and the 2015 study in relation to cost by disease course is that PPMS is the costliest disease type in this study (SPMS was in the 2015 study). This could be due to the smaller sample size and skewness in the data for respondents with PPMS.

Table 22. Costs by Disease Course (RRMS, SPMS & PPMS)

Disability level	Direct costs	Total indirect costs	Productivity costs	Informal care costs	Utilities EQ-5D	Intangible costs	Total costs (€,2021)
RRMS (n = 234)	€12,136	€15,350	€10,310	€5,041	0.665	€6,430	€33,916
SPMS (n = 40)	€16,948	€38,762	€17,340	€21,421	0.316	€12,904	€68,614
PPMS (n =37)	€15,528	€46,578	€16,274	€30,304	0.343	€13,431	€75,537

Figure 14. Breakdown of Costs by Disease Course (RRMS, SPMS and PPMS)



5. Summary

The aim of this report was to update the 2015 study on the societal cost of MS in Ireland. In our study, we estimate that total costs attributable to MS is €53,704 per person, per year equating to total societal costs of €483.33 million per year. This represents an increase of 12% compared to the 2015 study. This increase in costs is driven by an increase in indirect costs; specifically, more people with MS retiring, more workdays lost and less productivity while at work along with a higher cost of labour compared to the 2015 study. It is important to point out that the survey supporting this analysis was administered during the Covid pandemic and this may be the reason for the increase in productivity losses.

This estimate is in line with the conclusions in the most recent cost-of-illness studies of MS in Finland (Ruutiainen et al, 2016) and in France, Germany, Italy, Spain and the United Kingdom; with total costs ranging between €39,468 to €52,232 per person with MS (Karampampa et al, 2012). Our estimate of €53,704 is higher than that reported in these studies, however, unlike in Karampampa et al., we endeavoured to estimate the intangible costs associated with having the condition, a cost which was estimated as being €8,304 per person and year. With respect to the existing Irish literature, our estimate for total costs attributable to MS is higher than that reported in Fogarty et al. (2014) (€38,226). This difference is primarily driven by the addition of intangible costs (€8,304) in our study and higher costs associated with informal care (€8,564 v €6,188).

Our results also highlight that as disability severity increases, so too does the economic burden. The total cost associated with moderate MS (€66,567) was 75% higher than our estimated cost for those with mild MS (€28,007); while the cost associated with severe MS was approximately 3.4 times the total cost for those with mild MS (€131,577). This finding echoes that of previous studies in the MS cost of illness literature, for example in Karampampa (2012) the total cost associated with moderate MS (€39,923) was almost double than their estimated total cost for people with mild MS (€21,174). In Fogarty's Irish study, a similar pattern emerged, however the costs associated with severe MS was almost five times that of mild MS (€95,968 v €19,696), while the cost estimated representing moderate MS was over double that of mild MS. (€44,851 v €19,696). The ubiquity with which MS severity is a predictor of total costs in this study and in the international literature, highlights the importance of delaying disability progression from an economic perspective as well as it being a clinical priority.

6. References

- Arnett, P. A. & Randolph, J. J. (2006) Longitudinal course of depression symptoms in multiple sclerosis. *Journal of Neurology, Neurosurgery and Psychiatry*, 77(5), 606-10.
- Ayuso-Mateos, J. L., Vázquez-Barquero, J. L., Dowrick, C., Lehtinen, V., Dalgard, O. S., Casey, P., Wilkinson, C., Lasa, L., Page, H., Dunn, G. & Wilkinson, G. (2001) Depressive disorders in Europe: prevalence figures from the ODIN study. *The British Journal of Psychiatry*, 179, 308-16.
- Balk, L. J., Tewarie, P., Killestein, J., Polman, C. H., Uitdehaag, B. & Petzold, A. (2014) Disease course heterogeneity and OCT in multiple sclerosis. *Multiple Sclerosis Journal*, 20(9), 1198-206.
- Beiske, A. G., Svensson, E., Sandanger, I., Czujko, B., Pedersen, E. D., Aarseth, J. H. & Myhr, K. M. (2008) Depression and anxiety amongst multiple sclerosis patients. *European Journal of Neurology*, 15(3), 239-45.
- Bourke, S., Burns, R. M. & Gaynor, C. (2014) Challenges in generating costs and utilisation rates associated with castration-resistant prostate cancer. *Journal of Market Access & Health Policy*, 2, 10.3402/jmahp.v2.24072.
- Brouwer, W. B., van Exel, N. J., van den Berg, B., van den Bos, G. A. & Koopmanschap, M. A. (2005) Process utility from providing informal care: the benefit of caring. *Health Policy*, 74(1), 85-99.
- Brown, R. F., Valpiani, E. M., Tennant, C. C., Dunn, S. M., Sharrock, M., Hodgkinson, S. & Pollard, J. D. (2009) Longitudinal assessment of anxiety, depression, and fatigue in people with multiple sclerosis. *Psychology and Psychotherapy: Theory, Research and Practice*, 82(Pt 1), 41-56.
- Carney, P., O'Boyle, D., Larkin, A., McGuigan, C. & O'Rourke, K. (2018) Societal costs of multiple sclerosis in Ireland. *Journal of Medical Economics*, 21(5), 425-437.
- Central Statistics Office (2020) Mean and Median Annual Earnings.
- Central Statistics Office (2021) Earnings and Labour Costs Quarterly Q2 2021 (Final) Q3 2021 (Preliminary Estimates).
- Connolly, S., Nolan, A., Walsh, B. & Wren, MA. ESRI Research Bulletin. (2018) Universal GP care in Ireland: potential cost implications.
- Cottrell, D. A., Kremenchutzky, M., Rice, G. P. A., Koopman, W. J., Hader, W., Baskerville, J. & Ebers, G. C. (1999) The natural history of multiple sclerosis: a geographically based study: 5. The clinical features and natural history of primary progressive multiple sclerosis. *Brain*, 122(4), 625-639.
- Department of Public Expenditure and Reform (2019) Public Spending Code.
- Doherty, D. T., Moran, R., Kartalova O' Doherty, Y. & Walsh, D. (2007) HRB National psychological wellbeing and distress survey: baseline results. Health Research Board (HRB).
- EuroQoL Group (1990) EuroQoL—a new facility for the measurement of health-related quality of life. *Health Policy*, 16(3), 199-208.
- Fogarty, E., Walsh, C., McGuigan, C., Tubridy, N. & Barry, M. (2014) Direct and indirect economic consequences of multiple sclerosis in Ireland. *Applied Health Economics and Health Policy*, 12(6), 635-45.
- Healthcare Pricing Office (2020) ABF 2020, Admitted Patient Price List, 2020.
- Herdman, M., Gudex, C., Lloyd, A., Janssen, M., Kind, P., Parkin, D., Bonsel, G. & Badia, X. (2011) Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). *Quality of Life Research*, 20(10), 1727-36.
- HIQA (2020) Guidelines for the Economic Evaluation of Health Technologies in Ireland. Health information and Quality Authority.
- Horwath, E., Johnson, J., Klerman, G. L. & Weissman, M. M. (1992) Depressive symptoms as relative and attributable risk factors for first-onset major depression. *Archives of General Psychiatry*, 49(10), 817-23.
- HSE (2021) Consultant I salary from HSE salary scales, 2021. Health Service Executive,
- Karampampa, K., Gustavsson, A., Miltenburger, C. & Eckert, B. (2012) Treatment experience, burden and unmet needs (TRIBUNE) in MS study: results from five European countries. *Multiple Sclerosis Journal*, 18(2_suppl), 7-15.
- Kind, P., Hardman, G. & Macran, S. (1999) UK population norms for EQ-5D, Centre for Health Economics, University of York.
- Kobelt, G., Berg, J., Atherly, D. & Hadjimichael, O. (2006a) Costs and quality of life in multiple sclerosis: a cross-sectional study in the United States. *Neurology*, 66(11), 1696-702.
- Kobelt, G., Berg, J., Lindgren, P., Fredrikson, S. & Jönsson, B. (2006b) Costs and quality of life of patients with multiple sclerosis in Europe. *Journal of Neurology, Neurosurgery and Psychiatry*, 77(8), 918-26.
- Kobelt, G., Berg, J., Lindgren, P. & Jönsson, B. (2006c) Costs and quality of life in multiple sclerosis in Europe: method of assessment and analysis. *European Journal of Health Economics*, 7 Suppl 2, S5-13.
- Koch, M., Uyttenboogaart, M., van Harten, A., Heerings, M. & De Keyser, J. (2008) Fatigue, depression, and progression in multiple sclerosis. *Multiple Sclerosis*, 14(6), 815-22.

Krol, M. & Brouwer, W. (2014) How to estimate productivity costs in economic evaluations. *Pharmacoeconomics*, 32(4), 335-44.

Kronfol, Z. (1985) Multiple sclerosis and depression. *Archives of Neurology*, 42(4), 310-310.

L. Ford, E. G., MH Johnson, A. Tennant, H. (2001) Health status and quality of life of people with multiple sclerosis. *Disability and Rehabilitation*, 23(12), 516-521.

McCrone, P., Heslin, M., Knapp, M., Bull, P. & Thompson, A. (2008) Multiple sclerosis in the UK: service use, costs, quality of life and disability. *Pharmacoeconomics*, 26(10), 847-60.

McDonald, I, Compston, A. (2006) The symptoms and signs of multiple sclerosis. *McAlpine's multiple sclerosis*, 4th Edition, 321-322.

McGuigan, C. & Hutchinson, M. (2006) Unrecognised symptoms of depression in a community-based population with multiple sclerosis. *Journal of Neurology*, 253(2), 219-23.

Multiple Sclerosis Ireland (2015) Societal Cost of MS.

NHS (2019/20) Reference Costs 2019/2020.

O'Brien, C., Fogarty, E., Walsh, C., Dempsey, O., Barry, M., Kennedy, M. J. & McCullagh, L. (2015) The cost of the inpatient management of febrile neutropenia in cancer patients—a micro-costing study in the Irish healthcare setting. *European Journal of Cancer Care (England)*, 24(1), 125-32.

O'Connell, K., Tubridy, N., Hutchinson, M. & McGuigan, C. (2017) Incidence of multiple sclerosis in the Republic of Ireland: A prospective population-based study. *Multiple Sclerosis Related Disorder*, 13, 75-80.

O'Reagan C, Cronin H & Kenny R A. (2011) The Irish Longitudinal Study on Ageing. Chapter 6: Mental Health and Cognitive Function.

Oppe, M., Devlin, N. J. & Szende, A. (2007) EQ-5D value sets: inventory, comparative review and user guide; Springer.

Patwardhan, M. B., Matchar, D. B., Samsa, G. P., McCrory, D. C., Williams, R. G. & Li, T. T. (2005) Cost of multiple sclerosis by level of disability: a review of literature. *Multiple Sclerosis Journal*, 11(2), 232-239.

PCERS 2019. Primary Care Reimbursement and Eligibility Service Annual report (2019).

Pugliatti, M., Sotgiu, S. & Rosati, G. (2002) The worldwide prevalence of multiple sclerosis. *Clinical Neurology and Neurosurgery*, 104(3), 182-91.

Reilly, M. C., Zbrozek, A. S. & Dukes, E. M. (1993) The validity and reproducibility of a work productivity and activity impairment instrument. *Pharmacoeconomics*, 4(5), 353-65.

Rosati, G. (2001) The prevalence of multiple sclerosis in the world: an update. *Neurological Sciences*, 22(2), 117-39.

Ruutiainen, J., Viita, A. M., Hahl, J., Sundell, J. & Nissinen, H. (2016) Burden of illness in multiple sclerosis (DEFENSE) study: the costs and quality-of-life of Finnish patients with multiple sclerosis. *Journal of Medical Economics*, 19(1), 21-33.

Smith, S., Horgan, F., Sexton, E., Cowman, S., Hickey, A., Kelly, P., McGee, H., Murphy, S., O'Neill, D., Royston, M., Shelley, E. & Wiley, M. (2012) The cost of stroke and transient ischaemic attack in Ireland: a prevalence-based estimate. *Age Ageing*, 41(3), 332-8.

Strober, L., Weber, E., Lequerica, A. & Chiaravalloti, N. (2022) Surviving a global pandemic: The experience of depression, anxiety, and loneliness among individuals with multiple sclerosis. *Multiple Sclerosis and Related Disorders*, 58, 103497.

Taylor, B., McDonald, E., Fantino, B., Sedal, L., MacDonnell, R., Pittas, F., Groom, T. & Beresniak, A. (2007) The cost of multiple sclerosis in Australia. *Journal of Clinical Neuroscience*, 14(6), 532-9.

Tedstone, D., Moran, R., Kartalova-O'Doherty, Y., Doherty, O. & Walsh, D. (2008) HRB National Psychological Wellbeing and Distress Survey: Baseline Results.

Trisolini, M., Honeycutt, A., Wiener, J. & Lesesne, S (2010) Global economic impact of multiple sclerosis. *Multiple Sclerosis International Federation*.

van Hout, B., Janssen, M. F., Feng, Y. S., Kohlmann, T., Busschbach, J., Golicki, D., Lloyd, A., Scalone, L., Kind, P. & Pickard, A. S. (2012) Interim scoring for the EQ-5D-5L: mapping the EQ-5D-5L to EQ-5D-3L value sets. *Value Health*, 15(5), 708-15.

Wundes, A., Brown, T., Bienen, E. J. & Coleman, C. I. (2010) Contribution of intangible costs to the economic burden of multiple sclerosis. *Journal of Medical Economics*, 13(4), 626-632.

Zhang, W. & Anis, A. H. (2014) Health-Related Productivity Loss: NICE to Recognize Soon, Good to Discuss Now. *Pharmacoeconomics*, 32(5), 425-427.

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