

1 **Abstract**

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3 Background: Relapses can have a major impact on the lives of people with Multiple Sclerosis, and yet
4 relapse-related healthcare costs have received little attention. This has limited cost-effectiveness
5 analyses of treatments for MS and hampered decision-making regarding the funding of MS healthcare
6 services.

7 Objective: To describe health/social care resource use and costs according to the frequency, severity
8 and endurance of MS relapses.

9 Methods: Data from the prospective, longitudinal UK South West Impact of Multiple Sclerosis
10 (SWIMS) cohort were used. 11,800 questionnaires from 1,441 people with MS were available,
11 including data on relapses, contacts with health/social care professionals and other MS-related
12 resource use.

13 Results: The mean (sd) six-monthly MS-related health/social care cost for individuals who reported a
14 relapse was £519 (£949), compared to £229 (£366) for those who had not did report a relapse. Care
15 costs varied widely dependent on the characteristics of the relapse. The mean (sd) cost when a
16 relapse was not treated with steroids was £381 (£780), whilst the equivalent cost was £3,579 (£1,727)
17 when a relapse resulted in hospitalisation.

18 Conclusion: The impact of relapses on health and social care resources and costs differs according to
19 their frequency, length and severity. The data provided here can be used in cost-effectiveness
20 analyses and to inform decision-making regarding healthcare provision for people with this condition.

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22 Multiple sclerosis; Relapse; Resource use; Costs; Cost-effectiveness; Decision Making

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25 **1. Introduction**

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27 Multiple Sclerosis (MS) is a chronic, disabling neurological disorder which can affect any system of
28 the body. It is one of the commonest global causes of neurological disability in young and middle-
29 aged adults [1] [2], with a worldwide prevalence of approximately 33 per 100,000 population [3]. The
30 economic impact of MS is substantial. In surveys of nine European countries Kobelt et al. [4] [5] [6] [7]
31 [8] [9] [10] [11] [12] [13] estimated the societal costs of MS to be in the region of €18,000 to €62,000
32 per patient per year, and in the UK, MS has been estimated to cost £1.4 billion per annum to the NHS
33 and society [14].

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35 Over the past 15 to 20 years, health economic analyses of treatments for people with MS have
36 received much attention in health policy contexts [15] [16] [17], and it is widely accepted that data
37 available to inform the assessment of the cost-effectiveness of treatments for MS are sparse and
38 uncertain [18] [19] [20] [21] [22]. There is limited empirical evidence on the costs of health and social
39 care for people with MS [18], with a particular lack of detail regarding resource use and costs relating
40 to the relapses experienced by people with MS.

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42 Relapses can have a major impact on the lives of people with MS [23]. Approximately 85% of people
43 when first diagnosed with MS are diagnosed with relapsing-remitting MS (RRMS) [24]. Their disease
44 course is characterised by episodes when they are well and episodes, known as relapses, when they
45 experience an acute exacerbation of existing symptoms or new symptoms [25] [26]. Relapses vary
46 widely in their presentation, involving a single symptom occurring over a few hours, or a wide range of
47 neurological dysfunction developing over days or weeks [25]; relapse frequency is highly variable [27];
48 relapses ordinarily occur unexpectedly with the length of the gap between attacks being
49 unpredictable; there is a range of severity of symptoms experienced and; there are differences in
50 terms of the length of episodes.

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52 Research to date on the costs of care relating to relapses [13] [28] [10] [29] [30] [31] [32] [33] has
53 been characterised by having considered their impact over different time periods, in a number of
54 cases being based on small samples [31] [32] [33], and has provided little detail about the nature of
55 the relapses themselves [28] [10] [32] [33]. A recent systematic review of the economic burden of MS
56 [34] concluded that, based on currently available information, the resource implications associated
57 with relapses cannot be accurately estimated, and that further work is required to determine their
58 economic impact [35].

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60 The aim of the current study was to describe health and social care resource use and costs according
61 to the frequency, severity, and endurance of relapses experienced by people with MS, based on data
62 from a UK longitudinal, cohort study.

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65 **2. Methods**

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67 **2.1. The South West Impact of Multiple Sclerosis (SWIMS) project**

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69 Data from the UK South West Impact of Multiple Sclerosis (SWIMS) project [36] were used for
70 analysis. SWIMS is a longitudinal, prospective, cohort study of people with MS in Devon and Cornwall
71 (South West England), with individuals followed-up six-monthly. Full details of the project methods
72 have been reported elsewhere [36]. Data are collected on demographics and clinical characteristics,
73 and on a range of self-report health and social care resource use items pertaining to MS. SWIMS
74 commenced recruitment in August 2004, and data from all participants who had completed baseline
75 questionnaires at October 2012 were included in this analysis.

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77 The study was approved in the UK by the Cornwall and Plymouth and South Devon Research Ethics
78 Committees, and written informed consent obtained from all participants.

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80 **2.2. Measures**

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82 *2.2.1. Clinical characteristics*

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84 Participants reported the type of MS they had and the length of time since their diagnosis. Disease
85 severity was assessed by clinician-reported Expanded Disability Status Scale (EDSS) [37] scores,
86 collected during routine clinic visits. These were matched with resource use data if recorded within the
87 same three-month window.

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89 *2.2.2. Relapse characteristics and associated resource use*

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91 For the previous six months participants reported whether they had experienced a relapse, the
92 number experienced, their length, whether they had been admitted to hospital as a result, and if they
93 had been treated with oral and/or intravenous steroids. They were asked to give these details for up
94 to four relapses in the six month period. (At recruitment, this information was reported for the previous
95 12 months).

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97 *2.2.3. Health/social care resource use*

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99 Participants reported whether they had seen the following health or social care professionals in the
100 previous six months in relation to their MS, and the number of times that they had seen them:
101 chiropodist, clinical psychologist, continence advisor, district nurse, dietician, GP, MS specialist nurse,
102 neurologist, occupational therapist, ophthalmologist, physiotherapist, rehabilitation doctor, social
103 worker, speech therapist. In addition, they stated whether they had had contact with a pain
104 management service and/or a rehabilitation/respite service, including their frequency of contact.

105 Frequency of contact was categorised as: 'not seen', '1 time', '2 to 4 times', and '5 or more times'. For
106 the purposes of analysis, these frequency categories were assigned values of 0, 1, 3 and 5,
107 respectively.

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109 **2.3. Valuation**

110

111 Service use was costed at 2012 costs using UK nationally recognised unit costs of health and social
112 care resource items. The sources used were from the Personal Social Services Research Unit [38],
113 NHS Reference Costs [39], and the British National Formulary [40], and are detailed in Table 1.

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115 **2.4. Data analyses**

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117 The demographic and clinical characteristics of the SWIMS sample were described at recruitment,
118 and were compared for representativeness with other samples of people with MS in the UK.

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120 For each six month follow-up period, the number and percentage of responses which described use
121 of each of the health/social care resources in relation to MS were calculated, as was the mean (sd)
122 number of contacts. Unit costs were applied to resource use data on a per response basis, and mean
123 (sd) costs for each item were determined.

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125 Descriptive data are presented on the mean (sd) disaggregated health/social care resource use item
126 costs relating to MS for respondents by relapse status. In addition, descriptive statistics are estimated
127 for the mean (sd) six-monthly costs of MS health/social care according to the features of relapses
128 reported: number of relapses, severity and endurance. Mean (sd) costs of care of those who reported
129 at least one relapse were estimated by EDSS stages.

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131 Data management was conducted in Excel 2007 and STATA 12.1, and all data analyses were
132 conducted in STATA 12.1, with data defined as panel data using the xt commands.

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134 **3. Results**

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136 **3.1. Description of the sample and data**

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138 As of October 2012, 11,800 questionnaires were available from 1,441 people with MS. These were
139 completed between 10th September 2004 and 4th October 2012. Respondents provided a mean (sd)
140 of 8 (4) questionnaires, with a range from one to 17. The demographic and clinical features of
141 participants on recruitment to SWIMS are given in Table 2.

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143 **3.2. Representativeness of the sample**

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145 Approximately 75% of those approached have taken part in SWIMS and response rates have been
146 remarkably high (90% at 3.5 years follow-up [23]). The sample was demographically comparable to
147 other UK samples of people with MS [23]. For example, previous population surveys over the past 20
148 years have found mean ages of between 49.3 and 52.0 years (as compared to 50.7 years in the
149 SWIMS sample), and male to female gender ratios ranging from 1:2.1 to 1:2.8 (as compared to 1:2.8
150 in the SWIMS sample) [41-47]. In addition, the relapse rates in the SWIMS sample (1.1 a year) were
151 very similar to those estimated in prospective evaluations of relapses (0.5 to 1 a year) [27].

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153 **3.3. Six-monthly relapse-related health/social care resource use and costs of care**

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155 At follow-up, 1,300 people gave 10,075 responses to the question of whether they had experienced a
156 relapse in the past six months. 5,457 (54.2%) of responses indicated that participants had not
157 experienced a relapse, 1,501 (14.9%) answers indicated that respondents did not know whether they
158 had had a relapse or not, and 3,117 (30.9%) indicated that they had experienced at least one relapse.

159

160 Table 3 presents mean (sd) costs of health/social care resource used in relation to MS in the previous
161 six months for the group of responses which reported experiencing a relapse in the previous six
162 months (n=3,117 responses) and the group of responses which did not report experiencing a relapse
163 in the previous six months (n=5,457 responses). Disaggregated mean (sd) six-monthly resource use
164 and costs of care are also given in Table 3 for those who had had a relapse and those who had not.

165

166 The main differences between those who reported a relapse and those who did not related to whether
167 participants had seen a clinical psychologist, a GP, a neurologist and a MS specialist nurse, and
168 whether they had been in contact with a pain management service. The percentage of respondents
169 who had been in contact with each of these services was greater for the group who had experienced
170 a relapse. This was also reflected in the higher mean (sd) costs for these individual resource items.
171 The general profile across the resource items was one of greater resource use and costs of care for
172 those who had had a relapse, as demonstrated by the higher mean (sd) total cost in the relapse group
173 of £519 (£949) as compared to £229 (£366) for the group who had not experienced a relapse. The

174 most costly resource item used by people who reported a relapse was admission to hospital. This was
175 followed by seeing a neurologist, a GP, and stays in a rehabilitation/respite unit.

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177 3.3.1. *Frequency of relapses*

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179 Table 4 and Figure 1 present mean (sd) six-monthly health/social care costs associated with MS for
180 respondents according to the number of relapses they reported during this time period. These figures
181 indicate that the number of relapses experienced per se does not appear to be a strong driver of
182 resource use costs.

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184 3.3.2. *Relapse severity*

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186 Table 4 and Figure 1 present mean (sd) six-monthly costs of care according to the severity of the
187 relapses reported. The figures show greater costs for more severe relapses, from those that 'limited
188 everyday activities' to those that resulted in admission to hospital. By far the greatest mean (sd)
189 health/social care costs were for six month periods in which there was an admission to hospital as a
190 result of the relapse (£3,579 [£1,727]), with multiple admissions resulting in increased costs. For
191 example, the mean (sd) costs of care for a six month period were approximately £6,348 (£2,663) if the
192 respondent had been admitted to hospital for two relapses.

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194 3.3.3. *Relapse length*

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196 There was a clear relationship between the length of the relapse and the costs of six-monthly MS-
197 related health/social care resources (Table 4/Figure 1). Relapses lasting about 48 hours were
198 associated with mean (sd) costs of £329 (£901), whilst respondents experiencing a relapse which
199 lasted longer than one month had mean (sd) costs of £808 (£1,186).

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201 3.3.4. *Relapses in relation to disease severity (EDSS)*

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203 The relationship between disease severity, according to the EDSS, and the costs of care for those
204 reporting a relapse is presented in Table 4. This indicates a reduction in costs of health/social care
205 from EDSS 0 to EDSS 3, followed by increasing costs in the more severe health states (from EDSS 4
206 to EDSS 8).

207

208 4. *Discussion*

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210 This paper presents new, disaggregated data on the health/social care resources used by people with
211 Multiple Sclerosis in relation to relapses, with estimates of costs given for a detailed breakdown of the
212 particular characteristics of relapses experienced.

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The findings indicate that the mean (sd) health/social care cost for an individual with MS who has experienced a relapse in the previous six months is approximately £519 (£949). The data presented here provide important insights on the wide variability in costs associated with relapses, and that the precision of these costs can be improved if the particular characteristics of the relapses experienced are considered. For example, six-monthly costs of care were a mean (sd) of £381 (£780) if the relapse was not treated with steroids, £634 (£1,146) if four relapses were experienced, £808 (£1,186) if the relapse lasted longer than one month, and £3,579 (£1,727) if there was an admission to hospital due to the relapse.

That costs of care are highly variable dependent on the particular characteristics of the relapse experienced, may account for some of the disparity in previously reported relapse costs. For example, in the UK, Kobelt *et al.* [10] have given a mean relapse cost of £561, whilst Parkin *et al.* [32] have reported a mean estimate of £2,115. However, it must be considered that these figures are not directly comparable with the estimates from the SWIMS data, as different items of health/social care resource use were included.

In addition, the methods for estimating relapse costs have differed in the few studies that have considered them. The most common approach has been to: i) calculate resource use costs of those who do not report a relapse in a specified time period; ii) calculate resource use costs of those who do report a relapse in the same specified time period and; iii) subtract the former from the latter [31-33,48]. The resulting relapse cost estimate is therefore time-dependent (e.g. the cost of a relapse over six months, or the cost of a relapse over three months). This methodology means that relapse costs for different time periods must be considered as such, rather than simply being defined as a 'relapse cost'.

O'Brien *et al.* [30] have approached costing relapses differently. They identified people with MS who had experienced a relapse, determined their resource use that was specifically associated with the relapse (not the time period containing the relapse e.g. six months), and estimated the cost for this resource use. This raises the difficulty of defining what is, and what is not, due to a relapse, and over what period of time the consequences of a relapse in terms of resource use should be considered. The methodological hallmark of O'Brien *et al.*'s research is that the authors did not define a relapse as a single entity. They recognised the variability in the severity of relapses by categorising them as high intensity (hospitalisation and subsequent care), medium intensity (acute treatment e.g. intravenous steroids in outpatient or home setting), and low intensity (physician office visits and symptom-related medications) and costing them separately and accordingly. The SWIMS analysis, although having taken the 'time-dependent' approach described in the previous paragraph, builds on O'Brien *et al.*'s foundation by considering the costs of care of relapses in terms of their frequency, their endurance, and their severity.

253 The descriptive results described here suggest that costs of health/social care resource use do not
254 consistently increase in line with the number of relapses that an individual has experienced in the
255 previous six months. This may imply that the number of relapses per se has a limited impact on
256 resource use, with length and severity of relapses being of greater relevance. Increased
257 understanding of the nature and experience of relapses [25], and the future use of regression analysis
258 should help to disentangle this hypothesis.

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260 Costs of health/social care reduce from EDSS 0 to EDSS 3 before gradually rising from then on as
261 disability increases, until a substantial increase from EDSS 7 to EDSS 8 (although it should be noted
262 that the sample at EDSS 8 is small). This may be reflective of an initial flurry of contacts and resource
263 use around the time of diagnosis, followed by a period of stabilisation during which resource use is
264 less concentrated. Increased contact may then occur as MS deteriorates, particularly as walking
265 impairments become evident from EDSS 4 onwards and further services and support are established.

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267 **4.1. Strengths and limitations of the study**

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269 The research described here is focussed on a NHS/social care perspective (although medication
270 costs, other than relapse-related steroids are not included). It does not account for a wider societal (or
271 care-giver) perspective (e.g. informal care, productivity losses). As such, it does not identify the full
272 economic impact of MS. This was not the intention of the study, but should be considered when
273 assessing or using the costs presented.

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275 The response format of the study questionnaire (which was pre-set) meant that respondents could
276 report that they had seen each health/social care professional a maximum of '5+ times' in a six month
277 period. For the purposes of analysis, such a response was assigned a conservative frequency of five
278 occasions. This may well mean that the reported costs underestimate the true cost of health/social
279 care resource use, and should be reflected when the figures are utilised.

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281 Of the EDSS scores available, 2,152, from 664 respondents, were reported within a three month
282 window of a SWIMS questionnaire being completed. The demographic and clinical characteristics of
283 this sub-group were compared at recruitment with the remainder of the sample. There were no
284 statistically significant differences between those with and without EDSS scores in terms of gender,
285 type of MS, having experienced a relapse, or the number of relapses, in the previous 12 months.

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287 A key strength of this research is that the findings are based on a prospective, longitudinal cohort
288 study, with very high response rates [23], and a resulting sample that appears representative of
289 people with MS in the UK [41-43,46,44,45,47]. This minimises the possibility of selection and
290 response bias in the estimates of resource use and costs, and implies the generalisability of the
291 findings to other people with MS. This marks a departure, and advance, from previous research in this
292 area which has been characterised by cross-sectional surveys, sent out via patient associations with

293 some resulting low response rates (e.g. [48,10]). The detailed breakdown of resource use and costs
294 in relation to particular characteristics of relapses is a clear development from previous research,
295 which has tended to take a generalised view of relapses when costing these events. The data
296 available provide opportunities for further analyses using statistical techniques, and the ability to
297 develop hypotheses around the resource use associated with relapses. However, given the high
298 quality data available from SWIMS, and the reported generalisability of SWIMS participants,
299 descriptive statistics are given in the present analyses to provide the data in a simple format for use
300 and interpretation by others. Regression-based analyses are a recommendation for future research.

301

302 **4.2. Conclusion**

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304 This research highlights the need for data on the resource use and costs of health/social care of
305 people with MS to be presented in a clear, disaggregated manner. Only by such an approach can 'like
306 with like' comparisons be drawn over time, across countries, and based on individual clinical
307 characteristics. The over-aggregation of information may lead to important relationships or distinctions
308 being masked and missed.

309

310 Consistency in the methods used to cost relapses is needed. This should be founded on the
311 understanding that relapses can be quite different across and within individuals over time, varying in
312 frequency, length and severity. Further research is necessary to appropriately cost relapses according
313 to their particular features.

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315 The data presented here, from a representative sample of people with MS in the UK, can be used to
316 start to improve the validity of resource use and cost information relating to relapses. This, in turn, can
317 inform the decision-making process regarding the cost-effectiveness of MS treatments and health and
318 social care provision for people with MS.

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Figure 1: Mean six-monthly costs (£) of MS-related health/social care resource use by characteristics of relapses reported

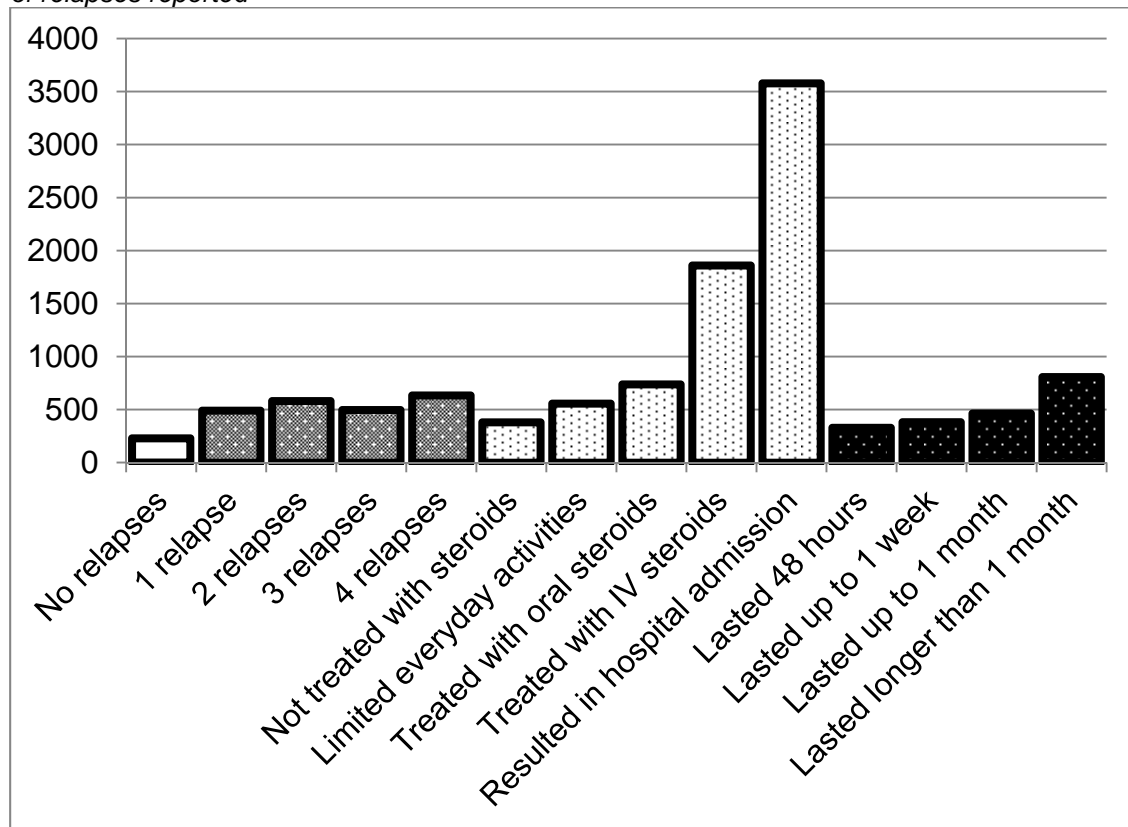


Table 1: Unit costs of health and social care resource use

Resource use item	Unit cost (£, 2012)	Source	Basis of estimate
Chiroprapist	30	Personal Social Services Research Unit (PSSRU) [38]	1 hour visit
Clinical psychologist	136	PSSRU	1 hour appointment
Continence advisor	38	PSSRU	Clinical nurse specialist 25 minute home visit
District nurse	29	PSSRU	25 minute home visit
Dietician	33	PSSRU	1 hour visit. Assumed equivalent to OT, physiotherapist and speech & language therapist.
GP	43	PSSRU	11.7 minute consultation
MS specialist nurse	38	PSSRU	25 minute home visit
Neurologist	145	NHS Reference Costs [39]	1 consultation
Occupational therapist	33	PSSRU	1 hour visit
Ophthalmologist	33	PSSRU	1 hour visit. Assumed equivalent to OT, physiotherapist and speech & language therapist.
Physiotherapist	33	PSSRU	1 hour visit
Rehabilitation doctor	33	PSSRU	1 hour visit. Assumed equivalent to OT, physiotherapist and speech & language therapist.
Social worker	214	PSSRU	1 hour visit
Speech therapist	33	PSSRU	1 hour visit
Pain management service	33	PSSRU	1 hour visit. Assumed equivalent to OT, physiotherapist and speech & language therapist.
Rehabilitation/ Respite service	667	PSSRU	1 week. Community rehabilitation unit.
Hospital admissions due to relapse	2,263	NHS Reference Costs	Non-elective inpatient admission for MS. Average stay 4.97 days
Treatment with oral steroids	145	British National Formulary[40]	Oral methylprednisolone: 500mg to 2g daily, for 3 to 5 days[49]. 20 x 100mg tablet pack, £48.32. 15 to 100 tablets requires 1 to 5 packs, £48.32 to £241.60.
Treatment with intravenous steroids	58	British National Formulary	Intravenous methylprednisolone: 500mg to 1g daily, for 3 to 5 days[49]. 500mg vial methylprednisolone powder with solvent, £9.60; 1g vial, £17.30. Requires 3 x 500mg vials to 5 x 1g vials, £28.80 to £86.50.

Table 2: Demographic and clinical characteristics of SWIMS participants at recruitment

Characteristic	
Gender (n=1,408): n (%)	
Male	368 (26.1%)
Female	1,040 (73.9%)
Not reported (n=8)	
Age (n=1,400): mean (sd)	50.7 (11.7)
[range] years	[18.2 to 83.3]
Type of MS (n=1,363): n (%)	
Relapsing-Remitting	572 (42.0%)
Primary Progressive	264 (19.4%)
Secondary Progressive	231 (17.0%)
Benign	45 (3.3%)
Combination or not known	251 (18.4%)
Not reported (n=45)	
Time since diagnosis (n=1,347): mean (sd)	9.6 (10.0)
[range]	[1 month to 53.5 years]
Not reported (n=61)	
EDSS score (n=289): mean (sd)	4.3 (2.3)
[range]	[0 to 9]
Not available (n=1,119)	
Experienced a relapse(s) in the previous 12 months (n=1,367): n (%)	
Yes	732 (53.6%)
No	455 (33.3%)
Don't know	180 (13.2%)
Not reported (n=41)	
Number of relapses in the previous 12 months (n=1,367): mean (sd)	1.1 (1.2)
n (%)	
0	638 (46.7%)
1	382 (27.9%)
2	196 (14.3%)
3	87 (6.4%)
4	64 (4.7%)
Not reported (n=41)	

Table 3: Mean (sd) six-monthly MS health/social care resource use and costs where a relapse was reported in the previous six months and where a relapse was not reported

	No relapse reported			Relapse (at least one) reported		
	n responses [n]	n (%) responses used resource	Mean (sd) cost (£, 2012)	n responses [n]	n (%) responses used resource	Mean (sd) cost (£, 2012)
Health/social care practitioner						
Chiropodist	4,210 [994]	758 (18%)	14 (33)	2,347 [772]	381 (16.2%)	12 (30)
Clinical psychologist	3,908 [974]	142 (3.6%)	11 (70)	2,191 [751]	152 (6.9%)	22 (94)
Continence advisor	4,125 [991]	787 (19.1%)	13 (32)	2,307 [773]	518 (22.5%)	16 (37)
District nurse	4,061 [984]	632 (15.6%)	15 (38)	2,245 [757]	349 (15.6%)	14 (37)
Dietician	3,879 [972]	115 (3.0%)	2 (12)	2,144 [746]	86 (4.0%)	3 (16)
GP	4,449 [1,019]	2,157 (48.5%)	45 (60)	2,778 [842]	2,102 (75.7%)	83 (68)
MS specialist nurse	4,308 [1,010]	1,567 (36.4%)	20 (34)	2,552 [813]	1,338 (52.4%)	33 (43)
Neurologist	4,280 [1,007]	1,458 (34.1%)	60 (103)	2,494 [808]	1,142 (45.8%)	91 (132)
OT	4,085 [983]	804 (19.7%)	14 (33)	2,285 [771]	533 (23.3%)	18 (40)
Ophthalmologist	3,950 [976]	507 (12.8%)	6 (19)	2,222 [756]	367 (16.5%)	9 (25)
Physiotherapist	4,299 [997]	1,443 (33.6%)	35 (59)	2,427 [790]	920 (37.9%)	39 (60)
Rehabilitation doctor	3,849 [969]	104 (2.7%)	1 (8)	2,140 [746]	67 (3.1%)	2 (14)
Social worker	3,907 [974]	295 (7.6%)	30 (126)	2,178 [750]	197 (9.1%)	39 (147)
Speech therapist	3,870 [967]	155 (4.0%)	2 (14)	2,157 [748]	132 (6.1%)	4 (19)
Service						
Pain management service	3,878 [971]	127 (3.3%)	2 (16)	2,191 [752]	160 (7.3%)	5 (21)
Rehabilitation/respite unit	3,890 [970]	199 (5.1%)	46 (235)	2,170 [749]	128 (5.9%)	63 (307)
Admission to hospital due to relapse	-	-	-	3,117 [873]	230 (7.4%)	189 (723)
Oral steroids for relapse	-	-	-	3,117 [873]	232 (7.4%)	31 (71)
Intravenous steroids for relapse	-	-	-	3,117 [873]	584 (18.7%)	5 (17)
Total mean cost	3,574 [941]		229 (366)	1,922 [710]		519 (949)

- n/a

NB: Individuals may provide data for the 'no relapse' and 'relapse' groups at different six month intervals following recruitment.

Table 4: Six-monthly MS-related costs of health/social relating to characteristics of relapses

	n responses [n]	Mean (sd) cost (£)
Number of relapses		
0 relapses	3,574 [941]	229 (366)
1 relapse	1,263 [573]	491 (863)
2 relapses	452 [263]	582 (1,104)
3 relapses	114 [84]	496 (777)
4 relapses	84 [61]	634 (1,416)
Relapse severity		
No relapse	3,574 [941]	229 (366)
Relapse, not treated with steroids	1,484 (625)	381 (780)
Relapse limited everyday activities	1,593 (634)	557 (993)
Relapse resulted in oral steroids	334 (196)	738 (887)
Relapse resulted in intravenous steroids	129 (85)	1,860 (1,869)
Relapse resulted in hospital admission	114 (90)	3,579 (1,727)
Relapse endurance		
No relapse	3,574 [941]	229 (366)
Lasted about 48 hours	188 [132]	329 (901)
Lasted up to 1 week	47 [255]	382 (919)
Lasted up to 1 month	474 [289]	464 (831)
Lasted longer than 1 month	386 [244]	808 (1,186)
EDSS score		
0	11 [9]	510 (931)
1	22 [20]	455 (789)
2	40 [33]	358 (582)
3	36 [29]	334 (485)
4	41 [29]	501 (706)
5	34 [31]	503 (699)
6	165 [109]	652 (1,210)
7	28 [20]	658 (953)
8	19 [16]	1,660 (1,723)