New insights into the burden and costs of multiple sclerosis in Europe: Results for the United Kingdom

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Short title

Burden of multiple sclerosis in the United Kingdom

Burden of illness in MS - UK

United Kingdom

Abstract

Introduction

In order to estimate the value of interventions in multiple sclerosis (MS) - where lifetime costs and outcomes cannot be observed – outcome data have to be combined with costs. This requires that cost data be regularly updated.

Objectives and Methods

This study is part of a cross-sectional retrospective study in 16 countries collecting data on resource consumption and work capacity, health related quality of life (HRQoL) and prevalent symptoms for patients with MS. Descriptive analyses are presented by level of disability, from the societal perspective, in EUR (2015).

Results

A total of 779 patients (mean age 57 years) participated; 72% were below retirement age and of these, 36% were employed. Employment was related to disease severity, and MS affected productivity at work for 84% of patients. Overall, 96% and 72% of patients experienced fatigue and cognition as a problem. Mean utility and annual costs were 0.735 and 11,400GBP at EDSS 0-3, 0.534 and 22,700GBP at EDSS 4-6.5, and 0.135 and 36,500GBP at EDSS 7-9. The mean cost of a relapse was estimated at 790GBP.

Conclusion

This study illustrates the burden of MS on UK patients and provides current data on MS that are important for development of health policies.

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Introduction

The UK has been a leading force behind the integration of economic studies into decision making in health care. The academic interest in cost of illness studies, outcome measurement and cost-effectiveness analysis dates back more than half a century and a large number of studies have been published. However, the formal integration into policy and decision-making only happened in 1999 with the creation of the National Institute for Health and Care Excellence (NICE). Since then, although its decisions are only applicable to England and Wales, NICE has been a leader in the development of methodology, and its decisions are observed with interest across Europe.

A considerable number of cost of illness studies have been performed in multiple sclerosis (MS) prior to 1999, and new studies were performed around the timing of introductions of new disease modifying treatments (DMTs).[1-5]

The availability of disease modifying treatments (DMTs) has led to changes in patient management and a focus on earlier and better diagnosis and adjustments in the diagnostic criteria themselves. One of the consequences in this regard is that the recorded prevalence of the disease is quite different from that estimated two or three decades ago,[6] leading to an increase in prevalence to 203/100,000 population in 2014.[7] With diagnosis already possible after a clinically isolated event,[8] one must also expect a different distribution of the type of MS and the severity of the disease than 10 years ago: a larger proportion of patients with relapsing remitting disease, and thus of patients in the early stages of the disease and with less disability (a low score on the Expanded Disability Status Scale, EDSS).

It is therefore important to update the information on the burden of MS, and the study presented here is part of a European-wide effort in 16 countries, endorsed by the European Platform of MS Societies (EMSP) and carried out with the support of national MS societies.[9] It uses a similar methodology as the last European survey in 2005.[10]

Materials and Methods

The detailed methodology for the European survey is published separately.[11] We therefore only provide a short summary of the general methods, and issues specific to the UK.

Data

The study aimed to estimate the costs of all health care and other resource utilisation related to MS: hospitalisation, rehabilitation, consultations, diagnostic procedures and tests, medication, community care, family support and production losses (sick leave, early retirement, invalidity). In addition, information on major

symptoms such as fatigue and cognition health related quality of life (HRQoL) as well as self-assessed disability using descriptions based on the Expanded Disability Status Scale (EDSS) was collected.

Data were collected with a standard questionnaire, at a single point in time, for a retrospective period of time. The latter was varied depending on the question in order to minimize recall bias: 1 month for use of drugs, community services and family help; 3 months for hospitalisation, consultations, tests, sick leave and relapses; 12 months for major investments. Resource utilisation is reported for these time periods, while cost calculations are annualized.

Disease information such as the type of MS, disability (EDSS), HRQoL, utility (EQ-5D[12]), symptoms (fatigue, cognition) and the effect of MS on work related to the current day or week.

The handling of missing data for the cost calculation is explained in more details in the paper describing the study methods.[11] For resource use, we present actual answers without any imputation for missing answers. Also, no imputations were made for missing information on disease status, symptoms and HRQoL.

Costs

Costs were calculated from the societal perspective, including all costs regardless of who ultimately is responsible for them. Patient co-payments and patients' out-of-pocket expenses were thus included. The cost of a relapse was calculated as the difference in quarterly costs between patients with or without a relapse and an EDSS score $\leq$6.5; patients who were unsure were excluded from the estimation. Invalidity, early retirement and DMT costs are not considered in this calculation, as they are unlikely to be affected within 3 months. In addition, investments in the UK were essentially for modifications to the house or the car, which again are unlikely to be affected directly by a relapse.

Unit costs for the individual resources were taken from public sources and are described in the paper on the study methods.[11] Results are reported in GBP (2015).

Patients

The objective was to include a sample where all levels of disease severity (defined by EDSS) were represented in sufficient numbers to permit analysis, rather than a prevalence sample. This highlights how costs and HRQoL change as the disease progresses and provides the necessary data for cost-effectiveness analysis of treatments that are expected to change the course of the disease. Mean results may thus not be representative and should neither be extrapolated directly to national costs nor be compared directly to the results in earlier studies. We

therefore report results by disease severity groups only (mild MS EDSS 0-3, moderate MS EDSS 4-6.5, severe MS EDSS 7-9).

In anonymous surveys, participation will depend heavily on the methods used for the survey: collecting data in MS centres tends to overestimate the number of patients with early but severe disease and on treatment with disease modifying treatments (DMTs); collecting data from members in patient organisations may lead to the opposite. Internet surveys may bias towards patients with better education, while postal surveys may include older patients.

The UK participants were contacted by the UK MS society and the vast majority answered the questionnaire on-line. The data were collected during the third quarter of 2015. The UK MS Society invited 5,928 individuals by e-mail, but despite two reminders the response rate reached only 13%.

Results

A total of 779 evaluable responses were received (96% on-line). Patients from all regions were well represented, with participation in Northern Ireland, Scotland and Wales proportional to the population. In England, participation from the South East, South West and London exceeded 40%, and was thus considerably higher than expected according to population density.[13]

Table 1 provides details on demographics, employment and disease.

Demographics and employment

The age of respondents in the UK ranged from 26 to 89 years (mean 56.7, median 57, SD 10.8). This makes the UK sample the oldest in our study series with a clear effect on the results - more patients with severe disease, lower DMT usage, fewer patients of working age and actually working. These differences make comparisons of mean costs in the sample with those from other countries in this study neither meaningful nor informative.

Women represented 70% of the sample; 80% of the sample lived with their family and eight patients were in a nursing home at the time of the survey. Education levels in our sample appeared to be high: 10% of patients had basic education, 52% had a secondary or a professional degree, and 38% a university degree. This compares to 36%, 37% and 27% in the general population in England and Wales in 2011,[14] and would indicate a sample with high education, as would be expected on an internet survey.

Despite the high mean age, a majority of patients in the sample were below average effective retirement age (63 years for women, 64 years for men[15]) numbering 563 patients (72%). Of these, 200 patients (36%) were employed or self-employed. Fourteen patients above retirement age also worked, bringing this

group to 214 patients (or 28% of the full sample), with a mean age of 50.8 years. The employment rate compares to an activity rate of 74.4% in the general population aged 16-64.[16] The majority of patients worked part time (92%), and of these, 82% did so because of MS. In the general population, 27% of people work part-time and of these, 3% indicated that it was due to illness or disability,[14] illustrating again how much MS affects patients' activities. Average working hours in the sample were 39 hours for full-time workers, 21.4 hours for part time employees. Sick leave during the past 3 months was reported by 22% of patients, with a mean duration of 9.2 days. This appears to be mostly due to relapses that were reported by 18% of patients.

Overall, employment decreased rapidly with increasing disease severity, as shown in Figure 1. The reasons for the difference found between patients at EDSS 2-3 and EDSS 4-5 might partly be due to the skewed disease severity distribution in this sample. The number of patients with an EDSS of 0-3 was small, with however a relatively high age (52 years) and a long mean disease duration (14-18 years) that may explain their leaving the work force for reasons other than a physical handicap (fatigue, cognition). Of non-employed patients, 57% indicated MS as the reason.

Most employed patients felt that MS affected their productivity at work (84%) and only 8% indicated that they had no problems, while 8% had not answered the question. The severity of the effect covered the entire VAS range from 0 to 10, with a mean of 4.0 (SD 2.7) (Figure 2). Fatigue was considered the most bothersome symptom (73%), followed by difficulties thinking (43%), mobility (40%), pain (31%) and low mood (21%).

Disease information

Disease information is summarized in Table 1. The mean EDSS in the sample was 5.5 (SD 2.2), with 64% of patients at EDSS 6 or higher. This makes it the most severe sample in the European study. However, the number of patients at all levels of EDSS was sufficient to yield a stable analysis, with the exception of EDSS 9 (10 patients). The mild group represented 18% of the sample, the moderate group 51% and the severe group 31%.

The proportion of patients with relapsing-remitting disease (RRMS) was 37%, with secondary progressive disease (SPMS) 38% and with primary progressive (PPMS) 24% (14 missing). Thus, while one would expect a high proportion with SPMS considering the high EDSS, the proportion stating PPMS is considerably higher than normal prevalence.[6] This suggests, as we found in previous studies, that patients might be uncertain in their answers regarding the type of disease. We therefore did not include disease type in our analyses and focused instead on EDSS levels. DMTs were used by 28% of the sample, with usage declining with higher EDSS levels, as expected (Table 1). Amongst users, 13% were on their first

DMT treatment, likely again an expression of the high age and severe disease in this sample; first-generation DMTs were used by 58% of users (Table 2).

Relapses in the preceding 3 months were reported by 141 patients (18%) of which half occurred in the past month (Table 1). However, 176 patients (23%) were unsure whether they had a relapse or not, and we assumed that the answer was no. Thus the mean relapse rate over a 3 month period was estimated at 0.3 (SD 0.7). Corticosteroids were used by 25 patients (18%) with relapses.

Symptoms and HRQoL

Fatigue and cognitive difficulties were an issue for a majority of patients, and both were related to disease severity (Figure 2). Fatigue was present in 96% of patients. The mean VAS score was 5.9 (SD 2.5) for the sample and 4.4 for patients with mild disease and 6.2 for patients in the moderate and severe groups. Cognitive difficulties were recognized by 72% of patients. The mean VAS score in this group was 4.8 (SD 2.0) overall, 4.4 in the mild, 4.8 in the moderate and 5.0 in the severe group. For the full study sample (assigning 0 to the group with no problems) the mean score was 3.5 (SD 2.9) and 2.8, 3.6 and 3.7 in the three groups, respectively.

The detailed answers to the EQ-5D indicated that both the severity and the domains affected changed with disease severity.[17] Self-care was unaffected in patients with mild disease, but declined rapidly with advancing disease. Anxiety was present in around half of the patients at all levels. For the other three domains, around half of the sample indicated problems already in early disease, with a rapid decline at higher EDSS levels (Figure 3).

Utility

Utility declined with increasing disability (EDSS) (Figure 4). Mean utility in the sample was 0.469 (SD 0.3), the lowest in this European study and explained mostly by the high EDSS.

Resource utilisation

During the preceding three months, 28 patients (4%) were admitted as inpatients, most often in a general ward (25 patients), on average 2.3 (SD 1.6) times and for a mean of 6.5 (SD 6.6) days. Fifty-five patients (7%) had day admissions, on average 2.5 (SD 1.9) times. Inpatient or day admissions to rehabilitation centres occurred for 17 patients (2%).

Two thirds of patients (524, 67%) had a consultation during the past three months, most often with a general practitioner (262, 34%), an MS nurse (209, 27%) or a neurologist (195, 25%). Investigations and tests were needed by 120 patients (15%) and medications for MS and MS related symptoms were used by 73% of

patients during the past month. Drugs other than DMTs and corticosteroids were used by 284 patients (37%), predominantly treatments for walking, spasticity and pain (199 patients, 26%), for incontinence (126 patients, 16%) and for depression (109 patients, 14%). Non-prescription drugs were purchased by 420 (54%) patients (Table 3).

Investments in equipment and devices to aid patients' mobility were made during the past 12 months for or by 380 patients (49%), most often for walking aids, wheel chairs and modifications to the car or the house.

Community and social services were used by 22% of patients, most frequently home help and transportation. Help from family was used by 69% of patients, on average 19.3 days per month and 4.9 hours per day. Both community services and informal care were related to disease severity (Figure 5).

Costs

Total mean annual costs per patient for patients with mild, moderate and severe disease and by EDSS score are presented in Figure 6 and Table 4.

The average cost of a relapse for patients with an EDSS up to 6 was estimated at 792GBP. All types of costs, but particularly informal care, increased for patients with relapses (Figure 7).

Discussion

This study provides an update to current understanding of the burden of MS on patients, the healthcare system, and society in general, based on a cross-sectional survey conducted in 2015.

The resource utilisation patterns reported here reflect the clinical needs and disease experience of patients in the UK. As was observed in previous studies of this type, we report relatively high levels of utilisation of MS nursing services and reliance on over the counter medication and informal care among study respondents. DMT use is lowest amongst the countries participating in this study, but is partly explained by the underrepresentation of people with RRMS and a short disease duration. These findings should be evaluated with reference to local clinical guidelines, such as those published by the ABN in 2015,[18] or by benchmarking versus the findings from other countries in this research programme.

It is also important to note that, in addition to clinical needs, these patterns reflect the structure of healthcare provision and delivery of various services through the UK NHS. That is, patients utilise the particular set of services and treatments that are commissioned by the NHS, which is not necessarily the same as that provided

to equivalent patients in other countries. Similarly, cultural norms also impact on how often a person will seek to visit their GP, and their willingness to present with symptoms of early disease prior to a confirmed diagnosis. Thus, comparisons of these findings with those from other countries should be interpreted with caution.

It is nevertheless possible to comment on some notable aspects of the data presented here. This is a relatively old sample of MS patients, and the distribution of EDSS scores does not represent current prevalence. Patients with severe disease and long disease duration are overrepresented and thus introduce a bias in the mean analysis for the total sample. We partly overcome this bias by presenting all results by disease severity rather than for the sample, but acknowledge that the survey underrepresents people with shorter disease duration, of whom there will be many with relapsing remitting MS and mild disability.

The mean time to diagnosis in this UK sample was 8 years. This is likely a reflection of the high age of the sample where patients received their diagnosis some 15 years ago, at which time diagnostic criteria were used that did not allow as early a diagnosis as is nowadays possible, and when a “wait-and-see” approach to clinical care of patients with MS was more likely. More recent and emerging evidence suggests longer term benefits of disease modifying treatments,[19] potentially more so with early treatment.[20] Although disease modifying treatments are a major cost item in mild MS, the observation of the large increase in costs, alongside the severe drop in utility in patients with severe disease as demonstrated in this work, suggests the potential for such treatments to ultimately result in fewer costs and better health outcomes for the NHS.

In addition to characterising various aspects of the burden of MS on patients, and capturing patterns of resource utilisation that could inform future policy recommendations, this work can provide valuable inputs into cost-effectiveness analyses for appraisals by NICE and similar bodies. The data generated by this study provides a comprehensive and contemporary source to describe the HRQoL and resource utilisation patterns of patients in the UK with MS. The level of detail in which the cost items are captured and described is a strength of this study; the methodology underlying the calculations is clearly laid out. The cross-sectional approach to data collection is mandated by the fact that the disease process of MS and related resource consumption cannot be observed over its entire duration, and covering the entire disease spectrum is key. This is seldom, if ever, possible even in randomized controlled trials. Also, the extent to which pivotal studies capture healthcare resource utilisation is patchy; furthermore, RCT populations may not reflect the true complexity of real world patients with MS, in terms of their clinical profiles or their experience of the health and social care system outside the context of a clinical study.

The UK has seen a number of cost of illness assessment studies in MS, and a number of data sets have been used in NICE appraisals. However, the most recent of these studies suffers from a much smaller data set,[5] while the larger research efforts were conducted in 2005 against the background of a different NHS.[4, 21, 22] Simply inflating the values extracted from that earlier study to suit today's needs is no longer satisfactory and this update is timely.

In summary, these data provide the latest and most comprehensive source of information on the burden of MS among UK patients. The data provided can help direct future design of healthcare provision and policy changes, but decision makers should interpret the findings carefully and be aware of the limitations of this approach. Moreover, a range of factors make inter-country comparisons of data from this research initiative difficult. In particular, the patient group represented is the oldest of all included countries, suggesting that younger patients with mild MS and short disease duration are underrepresented in this survey.

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Table 1 – Sample demographics

	Sample	Mild MS EDSS 0-3	Moderate MS EDSS 4-6.5	Severe MS EDSS 7-9	Missing EDSS
N	**779**	**144** (18.5%)	**394** (50.6%)	**240** (30.8%)	1
Proportion women	70.1%	-	-	-	
Proportion living alone	18.6%	29 (20.1)	85 (21.6)	31 (12.9)	
Mean age (SD)	56.7 (10.8)	52 (10.9)	56 (10.5)	61 (9.6)	
Education					
- Primary school	9.6%	-	-	-	
- High school degree	27.0%	-	-	-	
- Professional diploma	24.8%	-	-	-	
- University education	38.4%	-	-	-	
Employment					

- Patients of working age	563 (72.3%[1])	125 (86.8%)	300 (76.1%)	137 (57.1%)	1
- Total currently employed or self-employed	214 (27.5%[1])	84 (58.3%)	112 (28.4%)	17 (7.1%)	1
- Working age, employed or self-employed	200 (35.5%[2])	78 (62.4%)	107 (35.7%)	14 (10.2%)	1
- Working full time	17 (7.9%[3])	9 (10.7%)	6 (5.4%)	1 (5.9%)	1
- On long-term leave (>3≤12 months)	10 (4.7%[3])	-	-	-	
- Sick leave (past 3 months)	47 (22.0%[3])	-	-	-	
- Not working due to MS	311 (55.2%[2])	-	-	-	
- Invalidity pension	109 (19.4%[2])	4 (3.2%)	69 (23.0%)	36 (26.3%)	
- Early retired	155 (27.5%[2])	18 (14.4%)	77 (25.7%)	60 (43.8%)	
Disease information					
- Mean age at diagnosis (SD)	40.17 (10.88)	38 (10.1)	40 (10.8)	42 (11.3)	
- Mean age at first symptoms (SD)	32.23 (11.16)	32 (10.6)	32 (10.9)	33 (12.0)	
- Mean EDSS (SD)	5.5 (2.2)	1.6 (1.0)	5.7 (0.8)	7.5 (0.6)	
- Proportion with RRMS	286 (36.7%)	-	-	-	
- Proportion with relapses	141 (18.1%)	30 (20.8)	75 (19.0)	35 (14.6)	1
- Proportion using DMTs	218 (28.0%)	46.5%	32.0%	10.4%	

SD=Standard deviation, EDSS=Expanded disability status scale

[1]of total sample (n=779); [2]of patients of working age (N=563); [3]of patients working (N=214); [4]Missing (N=1)

Table 2 - Type of DMTs used (N=218[1])

First-generation treatments	% of total users	Second generation treatments	% of total users
interferon-beta 1b (Betaferon®/Extavia®)	3.7%	natalizumab (Tysabri®)	15.6%
interferon-beta 1a (Avonex®)	10.6%	fingolimod (Gylenia®)	11.5%
interferon-beta 1a (Rebif®)	18.3%	teriflunomide (Aubagio®)	1.8%
glatiramer acetate (Copaxone®)	22.5%	dimethyl fumarate (Tecfidera®)	14.7%
peginterferon-beta 1a (Plegridy®)	0.9%		
mitoxantron (Novantrone®)	1.4%		
azathioprine (Imurel®)	0.5%		

DMT=Disease modifying treatment

[1] *Missing information on DMT for 3 patients*

Table 3 – Resource utilisation, health care and community services

	Users	% of sample	Mean number of times (SD)	Mean number of days(SD)
Hospitalisation (3 months)				
Inpatient admission	28	3.6%		
- neurology ward	8	1.0%	2.25 (1.58)	6.5 (6.6)
- other wards	25	3.2%	2.28 (1.90)	4.5 (6.1)
Day admission	55	7.1%		
- neurology ward	33	4.2%	-	2.3 (1.9)
- other wards	33	4.2%	-	2.2 (2.0)
Rehabilitation centre	17	2.2%		
- inpatient admission	7	0.9%	-	4.0 (7.8)
- day admission	15	1.9%		4.3 (3.6)
Nursing home	17	2.2%		26.9 (31.9)
Consultations (3 months)				
Any type of consultation	524	67.3%		
Neurologist	195	25.0%	1.4 (1.2)	-
Internist	3	0.4%	1.0 (0.0)	-
Urologist	65	8.3%	1.6 (0.8)	-
Ophthalmologist	26	3.3%	1.5 (0.8)	-
Psychiatrist	11	1.4%	2.5 (2.2)	-
General practitioner	262	33.6%	2.3 (2.2)	-
MS nurse	209	26.8%	2.0 (4.6)	-
Continence advisor	68	8.7%	2.1 (1.8)	-
Physical therapist	150	19.3%	5.2 (5.0)	-
Occupational therapist	47	6.0%	2.5 (1.6)	-
Speech therapist	10	1.3%	1.9 (1.6)	-
Acupuncturist	15	1.9%	4.9 (3.6)	-
Chiropractor	13	1.7%	3.8 (3.1)	-
Counsellor	24	3.1%	4.0 (2.7)	-
Homeopath	10	1.3%	2.4 (1.3)	-
Massage therapist	53	6.8%	5.9 (9.1)	-
Telephone consultation MS nurse	141	18.1%	2.1 (2.6)	-
Telephone consultation neurologist	11	1.4%	1.5 (0.8)	-
Tests (3 months)				
Any kind of test	120	15.4%		
MRI (brain)	40	5.1%	-	-
MRI (spine)	25	3.2%	-	-
Ultrasound	21	2.7%	-	-
Blood tests	82	10.5%		-

Medication (1 month)				
Any kind of medication	572	73.4%	-	-
DMTs	218	28.0%	-	-
Corticosteroids	25	3.2%	-	-
Symptomatic prescription drugs	284	36.5%		
- Walking, spasticity, pain treatment	199	25.5%	-	-
- Urological treatments	126	16.2%	-	-
- Fatigue treatments	35	4.5%	-	-
- Depression treatments	109	14.0%	-	-
OTC drugs	420	53.9%	-	-
Equipments, aids, modifications (12 months)				
Any type	380	48.8%		
Lifts, elevators, ramps, rails	120	15.4%		-
Walking aids	171	22.0%		-
Wheelchair use (manual, electric)	181	23.2%		-
House and car modifications	202	25.9%		-
Community services (1 month)				
Any kind of service	168	21.6%		
Home help (days)	106	13.6%	-	16.92 (11.7)
Transportation (trips)	74	9.5%	-	8.74 (9.0)

SD=Standard deviation; MRI=Magnetic resonance imaging; DMT=Disease modifying treatment; OTC=Over the counter drug

Table 4 – Total mean annual cost per patient by disease severity (mild, moderate, severe), N=779 (GBP 2015)

	Mild	**Moderate**	**Severe**
	EDSS 0-3	**EDSS 4-6.5**	**EDSS 7-9**
	mean (SD), GBP	mean (SD), GBP	mean (SD), GBP
Total costs	**11,400 (14,900)**	**22,700 (20,000)**	**36,500 (26,200)**
Health care	*5,903 (8,599)*	*5,511 (7,547)*	*5,039 (9,941)*
Inpatient care	421 (4,673)	195 (1,384)	1,830 (8,644)
Day admission	321 (2,021)	399 (1,967)	311 (1,266)
Consultations	705 (1,504)	1,188 (1,770)	1,322 (1,996)
Tests	77 (259)	81 (276)	80 (295)
Medication	172 (383)	250 (597)	337 (890)
DMTS	4,206 (5,292)	3,397 (5,618)	1,160 (3,585)
Services and informal care cost	*1,050 (4,601)*	*6,924 (10,132)*	*19,624 (19,257)*
Community services	100 (525)	865 (3,837)	5,786 (13,477)
Investments	366 (4,167)	1,618 (5,785)	2,500 (6,144)
Informal care	585 (1,719)	4,441 (6,507)	11,337 (10,469)
Total medical and non-medical direct cost	**6,953 (10,715)**	**12,435 (13,531)**	**24,662 (21,895)**
Short term absence	191 (1,117)	118 (834)	0 (0)

Long term absence, invalidity, early retirement	4,289 (10,009)	10,166 (12,937)	11,875 (13,831)
Total production losses	**4,480 (9,989)**	**10,284 (12,871)**	**11,875 (13,831)**

GBP=British Pound; EDSS=Expanded Disability Status Scale; SD=Standard deviation; DMT=Disease modifying treatment

Figure legends UK

Figure 1 – Proportion of patients below retirement aged employed or self-employed. 563 patients (72%) were below retirement age and of these, 36% were employed or self-employed.

Figure 2 – Mean score on the visual analogue scales (0=no problem; 10=severe problems) for fatigue, cognitive difficulties and impact of MS at work (only for patients working). Patients with missing EDSS (1) or missing answers are excluded.

Figure 3 – Proportions of patients at different levels of disease severity experiencing difficulties in the five domains of the EQ-5D. Difficulties are increasing with increasing disease severity, with the exception of anxiety/depression that appears similar at all stages of the disease.

Figure 4 – Utility by EDSS level using the EQ-5D. Utility is calculated by relating the scores (1=no problem; 2=some problems; 3=severe problems) of the five domains to a health state valuation system established with the general population using decision analytic methods.[15] Values decrease from levels comparable to the population to negative values in severe disease.

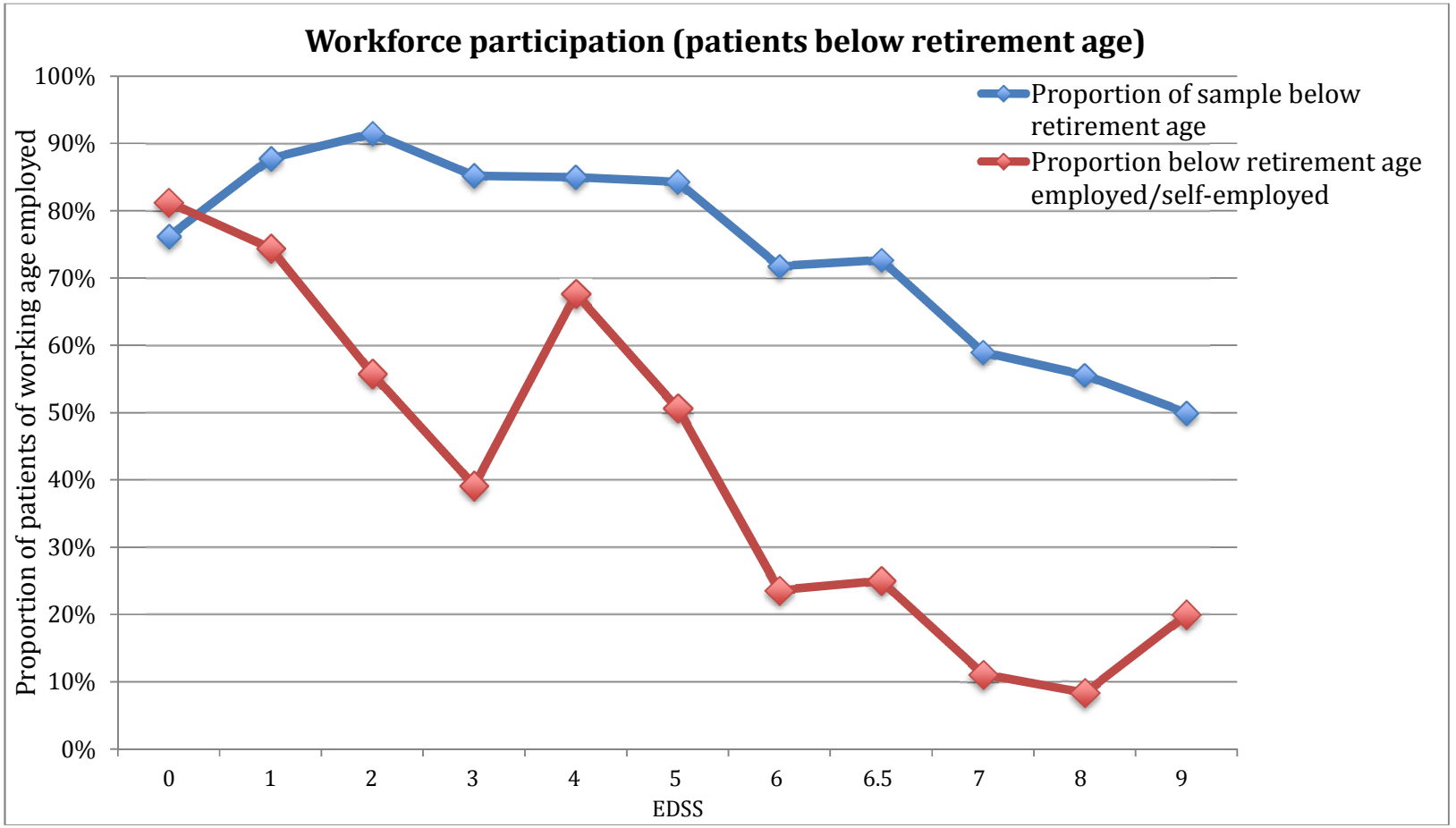
Figure 5 – Intensity of use of informal care (number of days and hours per day during the past month). 69% of the sample use help from the family, but use is clearly concentrated in the severe group: 26% of patients in the mild, 74% in the moderate and 86% in the severe group are relying on family support.

Figure 6 – Mean total annual costs per patient by level of EDSS. Total costs increase with disease severity, but the type of resources change. Overall, health care costs dominate in mild disease; production losses, informal care, investments and community services dominate in more severe disease. However, due to the underrepresentation of younger patients with a short disease duration, production losses are already high at low EDSS levels, while the cost of DMTs is lower than expected.

Figure 7 – Mean 3-month cost of a relapse, estimated as the difference of costs of patients below EDSS 6.5 with and without a relapse (N=83 and N=367, respectively). Patients who were unsure (N=176, 23%) were excluded from the estimation. Invalidity, early retirement and DMT costs are not considered in this calculation, as they are unlikely to be affected within 3 months. In addition, we excluded investment costs as they related for their vast majority to transformations of the car or house unlikely to be affected by a relapse. The cost of a relapse is thus estimated at 792GBP. The use of all types of resources increases during a relapse, with the biggest increase seen for inpatient care (22%) and informal care (24%).

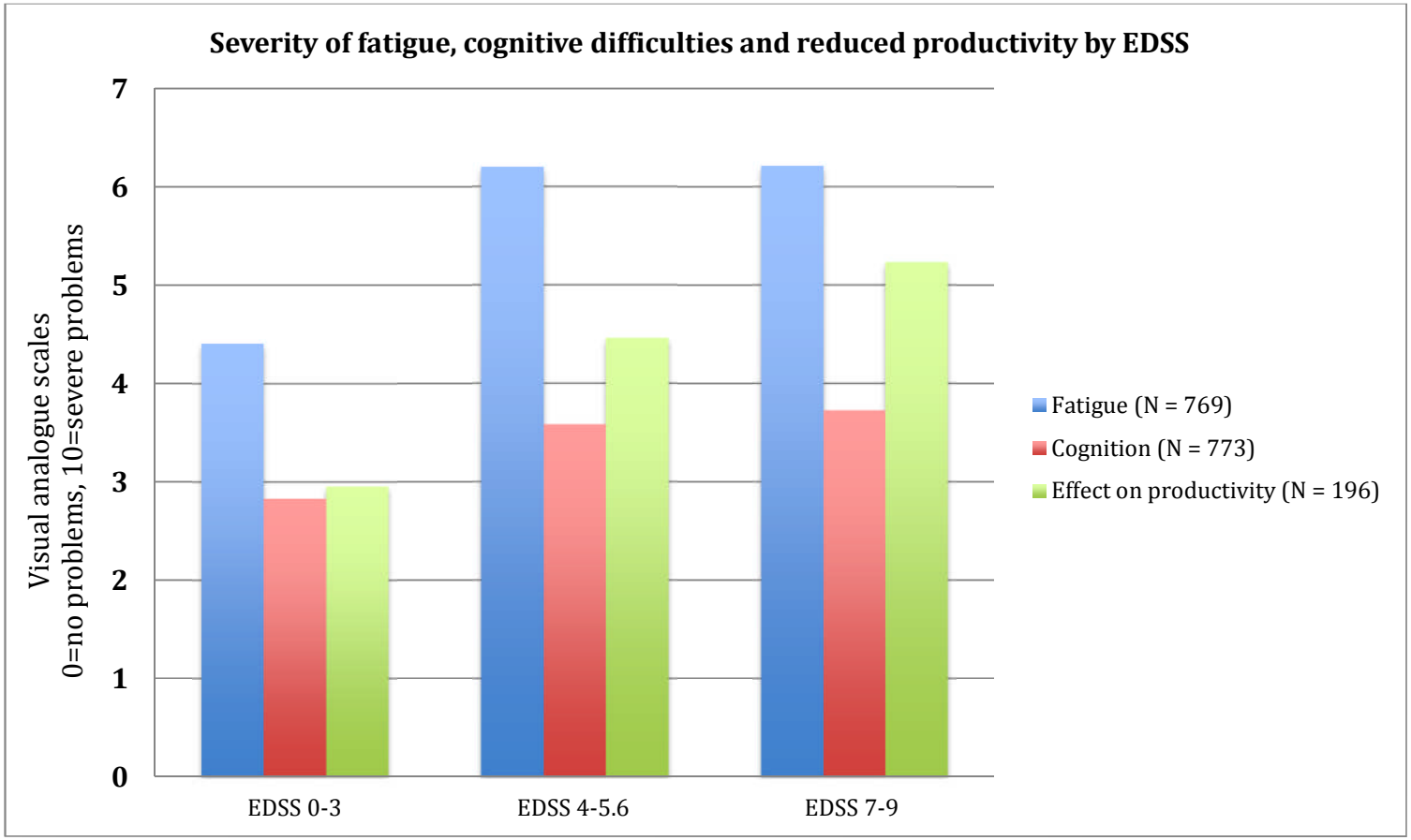
Burden of illness in MS, 2015 – United Kingdom

Figure 1 – Employment by disease severity.



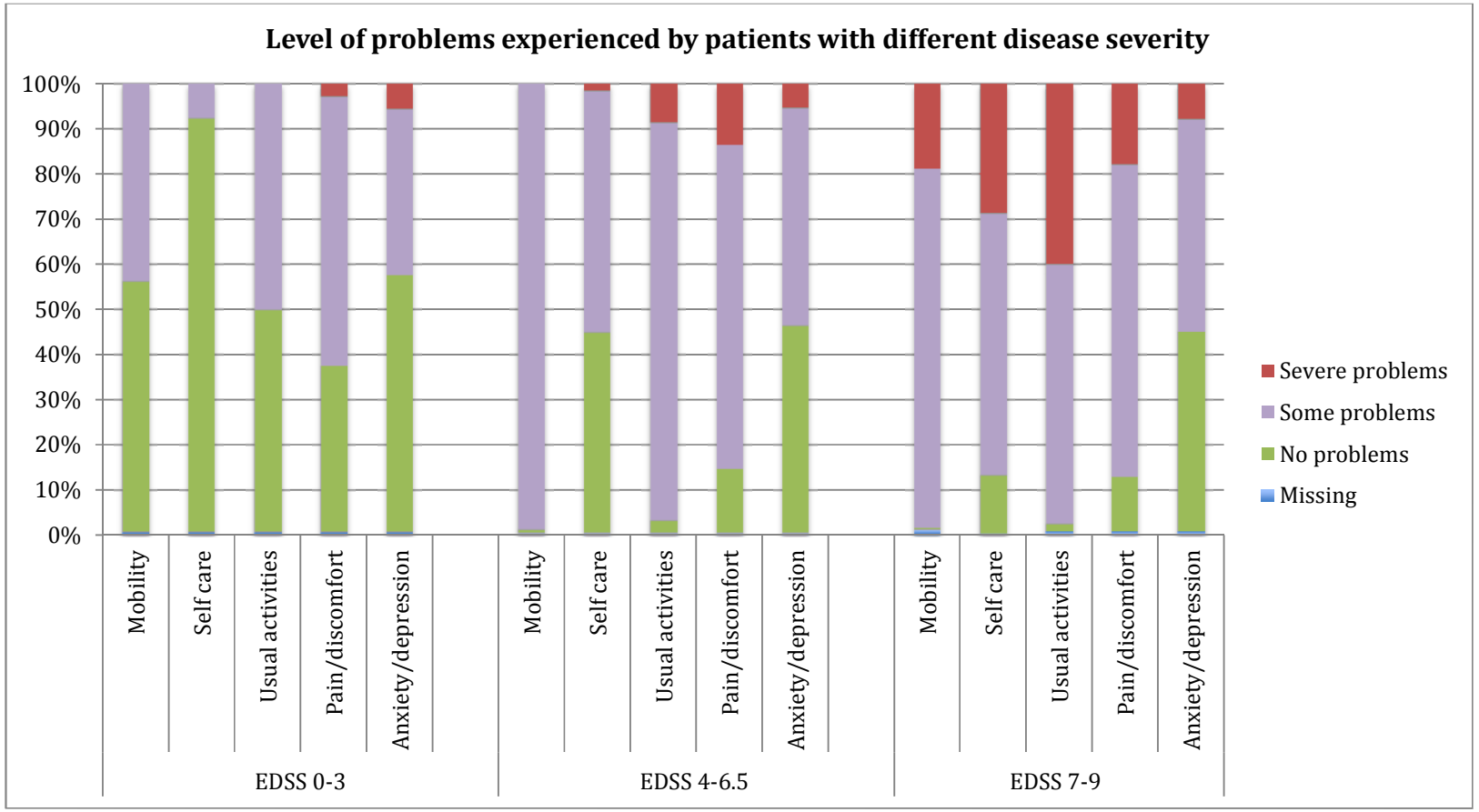
EDSS=Expanded Disability Status Scale

Figure 2 – Fatigue, cognitive difficulties, effect of MS on productivity at work.



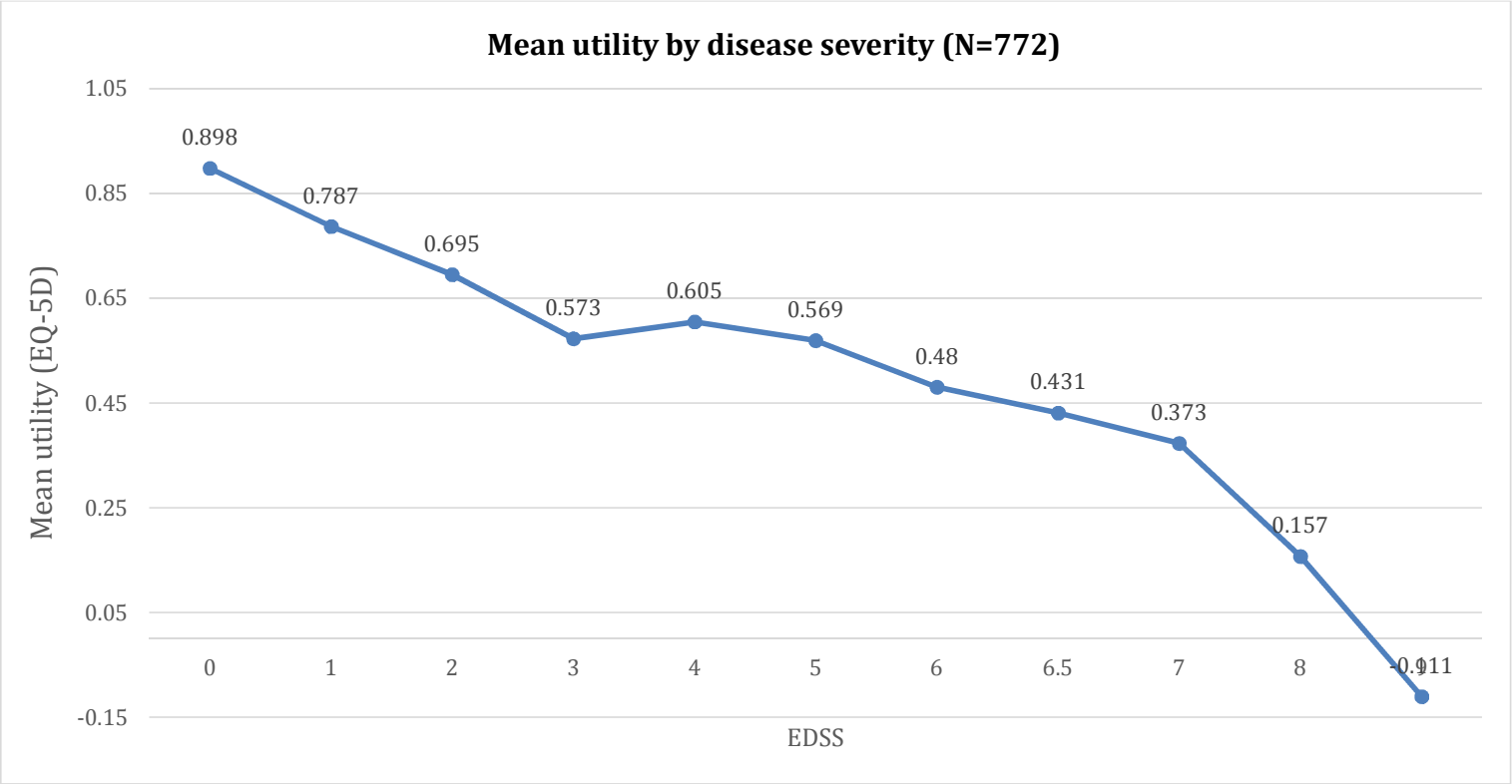
EDSS=Expanded Disability Status Scale

Figure 3 – Problems in different domains of HRQoL (EQ-5D), N=772



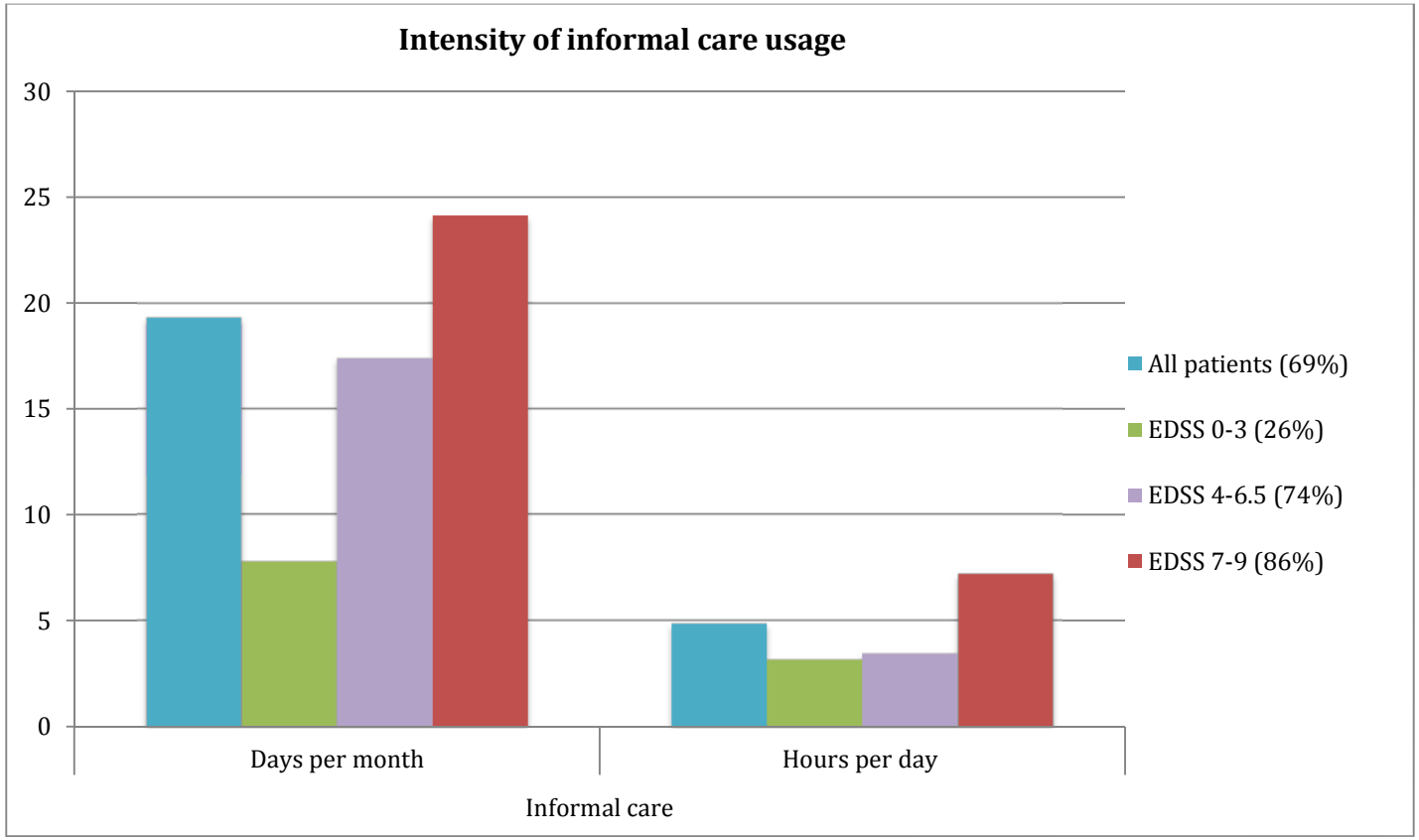
EDSS=Expanded Disability Status Scale; QoL=Quality of life; EQ-5D=EuroQoL-5 dimensions

Figure 4 – Utility by EDSS (N=772)



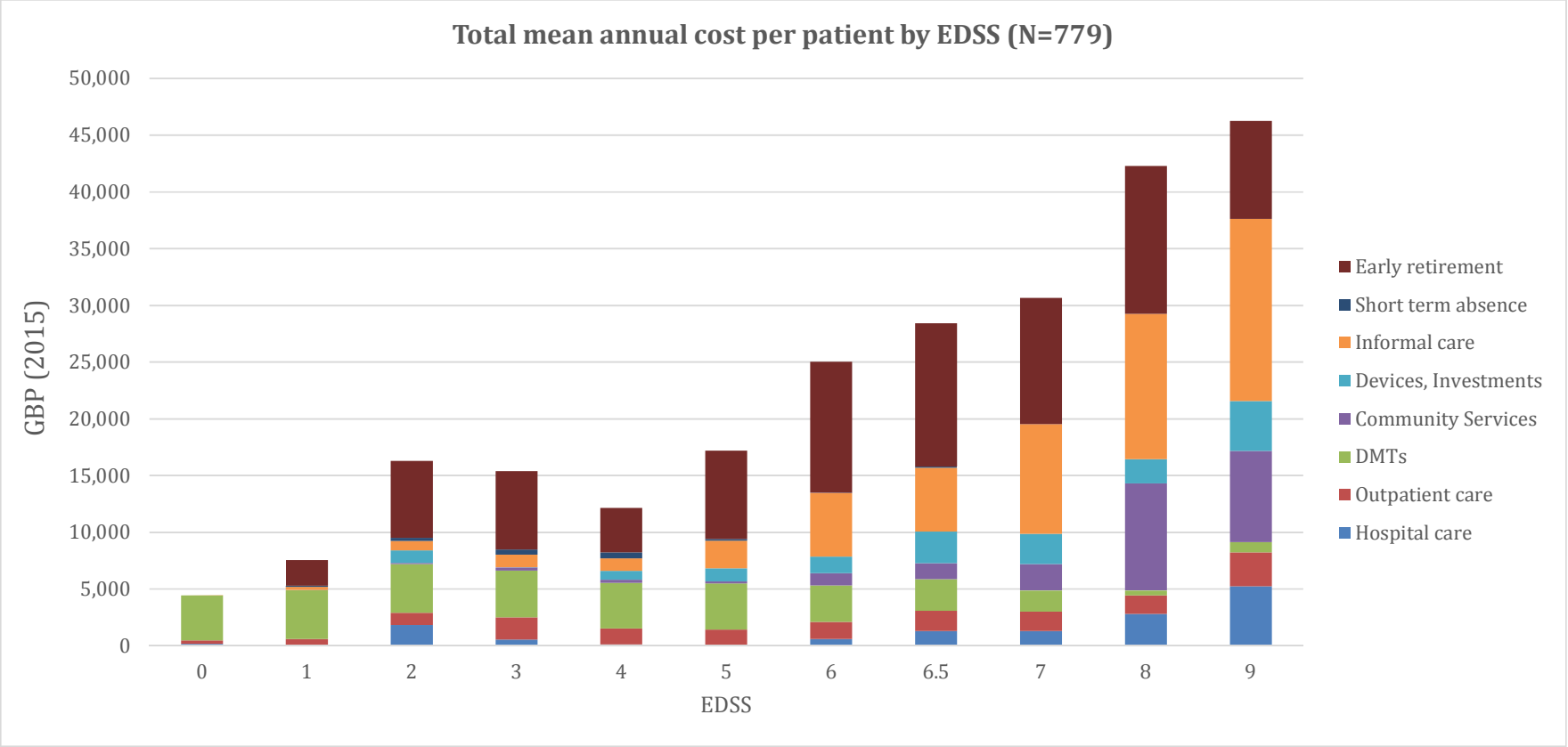
ED-5D=EuroQoL-5 dimensions; EDSS=Expanded Disability Status Scale

Figure 5 – Use of informal care (days per month and hours per day, per user)



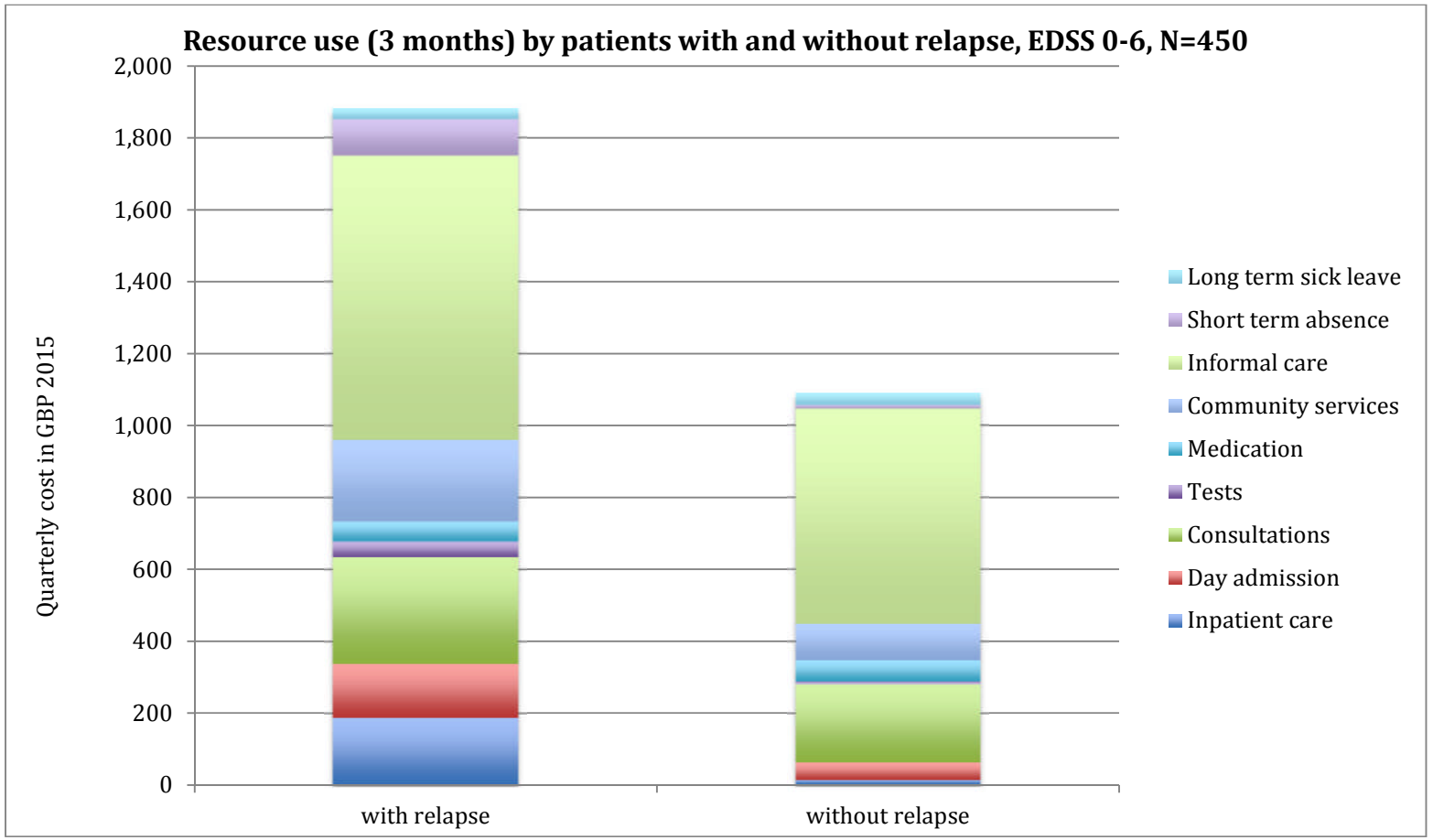
EDSS=Expanded Disability Status Scale

Figure 6 – Total mean annual cost per patient by disease severity (N=779)



GBP=British Pound; EDSS=Expanded Disability Status Scale

Figure 7 – Relapse costs (3 months) GBP 2015



GBP=British Pound; EDSS=Expanded Disability Status Scale