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Personal and societal costs of multiple sclerosis in the UK: A population-based MS Registry study

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Abstract

Objectives: To investigate through survey and data linkage, healthcare resource use and costs (except drugs), including who bears the cost, of multiple sclerosis in the United Kingdom by disease severity and type.

Methods: The United Kingdom Multiple Sclerosis Register deployed a cost of illness survey, completed by people with multiple sclerosis and linked this with data within the United Kingdom Multiple Sclerosis Register and from their hospital records. Resource consumption was categorised as being medical or non-medical and costed by National Health Service and social services estimates for 2018.

Results: We calculated £509,003 in non-medical costs over a year and £435,488 in medical costs generated over 3 months. People with multiple sclerosis reported self-funding 75% of non-medical costs with non-medical interventions having long-term potential benefits. Costs increased with disability as measured by patient-reported Expanded Disability Status Score and Multiple Sclerosis Impact Scale, with Multiple Sclerosis Impact Scale physical being a more powerful predictor of costs than the patient-reported Expanded Disability Status Score. Two distinct groups were identified: medical and non-medical interventions ($n = 138$); and medical interventions only ($n = 399$). The medical and non-medical group reported increased disease severity and reduced employment but incurred 80% more medical costs per person than the medical-only group.

Conclusions: The importance of disability in driving costs is illustrated with balance between medical and non-medical costs consistent with the United Kingdom health environment. People with multiple sclerosis and their families fund a considerable proportion of non-medical costs but non-medical interventions with longer term impact could affect future medical costs.

Keywords: Resource use, medical and non-medical costing, multiple sclerosis, disability, UKMS register

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Introduction

Over the past 20 years, health economic analyses of treatments for people with multiple sclerosis (PwMS) have received increasing attention in health policy. This has arisen from the need to balance the increasing cost of MS therapy against its benefits. In the United Kingdom (UK) this has been principally driven by the National Institute for Health and Care Excellence (NICE), which makes guidance recommendations for treatment use in England. In NICE single technology, appraisals of MS treatments[1,2] utilise data to estimate the personal and social service costs by disease severity category[3,4] that is balanced against the costs of therapy. The appropriateness of the data used has been questioned and it is widely accepted that data available to inform the assessment of the cost-effectiveness of treatments for MS are sparse and uncertain.[5]

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The economic impact of MS is substantial and in the UK MS has been estimated to cost £1.4 billion per annum.[6] In surveys of nine European countries, the estimated societal costs of MS were in the region of €18,000–€62,000 per patient per annum (pppa) at current estimates around 126,000 people with MS in the UK.[7] The categories of costs used have traditionally been aggregated, making it difficult to separate costs paid for by individuals out of their own pockets from those that relate to NICE reference items or from other agencies – charitable or otherwise. There is limited empirical evidence on the UK costs of health and social care for people with MS,[5] with a particular lack of detail regarding resource use, costs by disease type and by disability typically measured by the Expanded Disability Status Score (EDSS).[8]

The UKMS Register (UKMSR) is one of the largest repositories of Patient Reported Outcome Measures (PRO) in Europe, with more than 300,000 individual responses collected over 9 years. These PRO data are linked to patients' healthcare records provided by National Health Service (NHS) hospitals allowing for diagnostic validation and deep record linkage on a proportion of the cohort.[9]

Utilising the access to MS patients afforded through the UKMSR[10] we set out to establish a comprehensive range of 1) medical resource use, excluding disease-modifying therapy (DMT) costs, and how they are funded and 2) non-medical resource use for pwMS. We also aimed to understand in detail who bears the cost of the non-medical resource use. Resource use was then quantified by disease severity as measured by PROs and the patient-reported (pr) EDSS score.[11]

Methods

Recruitment

Participants of the UKMSR (ethical approval: South West Central Bristol National Research Ethics Service 16/SW/0194) who were both on the web portal and linked through their NHS centre and fitted the eligibility criteria (18 years of age and had a validated diagnosis of MS from a neurologist) were emailed about the survey. On accessing the UKMSR website they were automatically presented with a participant information screen and a consent form for the questionnaire. Populations analysed included the responders, the email contacted population and the total UKMSR population.

Questionnaire

The online health resources usage questionnaire (HRUQ) (Appendix, Figure 1) consisted of eight high-level topic questions that defaulted to a 'No' entry if no answer was given. Participants actively selected 'Yes' to see the resulting sub-questions. Topics included: unplanned/emergency admission; planned inpatient hospital admissions (arranged in advance and including an overnight stay); planned day case hospital admissions (1 day, without staying overnight); investigations/tests; rehabilitation; nursing home/sheltered living/day care centre; and investments in adaptations/modifications.

Questionnaires could be completed by the participant themselves and/or their representative.

Participants were asked to provide details of their medical interventions for the past 3 months. For adaptations (including wheelchairs) and modifications to the home, a recall period of 12 months was used. Unit costs were applied to derive the cost per MS item for the recall period.

For a number of items, additional questions were asked to allow a distinction to be made between NHS and Personal Social Services funded costs and costs paid for by the participant. The HRUQ is not a validated instrument in MS, although it contains elements that have been asked in other costs of illness studies in MS research. However, all the questionnaires that these responses were linked to have been validated in MS.

Completed questionnaires are marked as 'complete' by the questionnaire engine within the UKMSR. This means all required fields have been finished and the participant has clicked the 'submit survey' button when they finish answering. The Register engine also periodically saves questionnaires as participants go through their responses. Normally these results are discarded once the submit survey button is pressed and the form sent. However, if more than 60% of a survey is completed and the form is never submitted (authentication time out, browser closed, network failures) those responses are kept as 'partials'.

Questionnaire responses were linked with PRO data collected as part of the UKMSR web portal: prEDSS,[11] normalised MS Impact Score 29v2: physical (MSIS-physical) and psychological (MSIS-psychological) sub-scores,[12,13] and demographic data including MS disease type at the time of completing the questionnaire; gender; current age; age of disease

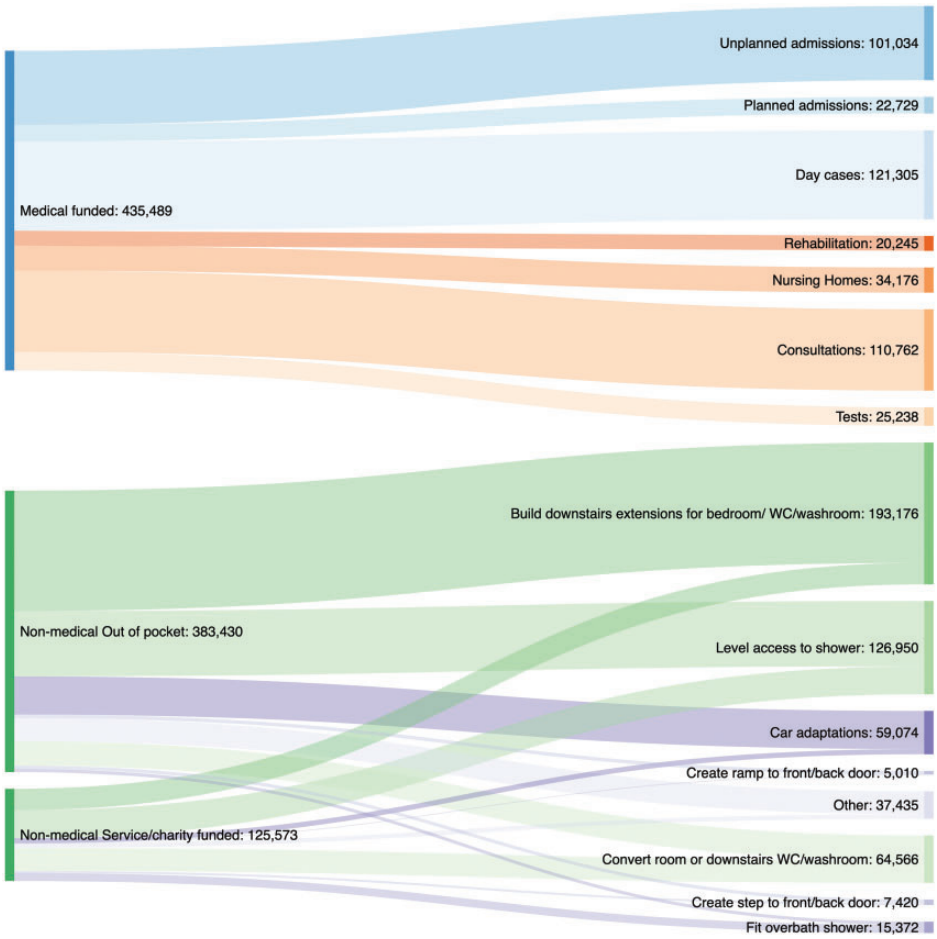

Figure 1. Sankey diagram illustrating the funding flow for 3 months medical and 12 months non-medical costs (Other: combined costs from stair-lifts, raising electrical sockets/lower light switches, wheelchairs, purchase of items to help with daily activities, laying new paths, widening doorways for wheelchair access, installing lighting to outside steps/path, fitting handrails and moving beds downstairs).

onset; employment status;[14] educational achievement;[15] household composition[16] and whether they were currently on an MS DMT. To avoid small cell counts, where required participants were grouped together into suitable categories. Data on current DMT use were only collected in the responder group as they have visited the portal to update it as part of completing the questionnaire.

Costs calculation and data analysis

Unit costs, expressed in current year British pounds sterling (GBP, £), were derived from NHS Reference Costs[17] and Personal Social Services[18] costs. Maximum and minimum potential costs were calculated using the limits of these estimates and a midpoint between these limits utilised in average cost estimates. Medical and non-medical costs were derived according to Giovannoni et al.[19] Medical costs calculated from the responses for 3 months were multiplied by four to allow presentation of results as annual cost estimates as set out by Tyas et al.[3] Costs pp were derived by dividing the total costs by the number of people generating that cost. Study data were collected using REDCap electronic data capture tools hosted at Swansea University Medical School.[20] Data were staged in a Microsoft SQL Server 2014 database and analyses were performed using SPSS[21] and R.[22] The chi-square test was used to establish the association between categorical variables. The Student *t*-test was used to compare average costs between groups.

Results

Study population

From the UKMSR population of 13,244 patients, on 1 November 2018, 3035 subjects were contacted by

email, 621 consented (20.4% response rate) and of these 537 completed sufficient data to be included in the analysis (481 were complete and 56 partially complete). The average age at diagnosis and age completing the survey is 41 and 51 years respectively, with most respondents having relapsing-remitting MS (60%) (Table 1).

The responder population was compared to all those contacted by email and the UKMSR population (Table 1). Compared to the contacted population responders were older, had an older age of diagnosis and higher levels of progressive MS vs relapsing MS (Primary Progressive [PP] or Secondary Progressive [SP] vs Relapsing Remitting [RR] MS, $\chi^2=32$, $p<0.0001$ excluding missing/benign values), but disability was not different (prEDSS ≤ 6 vs >6, $\chi^2=32$, $p=0.1$, excluding missing values). In contrast, compared to the total UKMSR population the responder population was younger with a later age of diagnosis and lower levels of progressive MS (PP or SP vs RR, $\chi 2=4.7$, $p=0.031$ excluding missing/benign values) and disability was lower than the UKMSR population (prEDSS ≤ 6 vs >6, $\chi^2=11.6$, $p=0.0007$, excluding missing values).

Medical and non-medical costs in the UKMSR population

A complete list of the medical and non-medical costs included in the study is given in Table 2 below. In total 6935 interventions were recorded in 537 people with an estimated mid-range total cost of £435,488 (£3244 pppa) for medical costs (Appendix, Table 1) over 3 months. Non-medical (Appendix, Table 2) interventions equating to £504,012 (£939 pppa) costs were incurred over 1 year. Thus, when extrapolating the medical costs from 3 months to 1 year, over 1 year non-medical costs made up 22.4% of all costs. In Figure 1 it is clear there were no 'out of pocket' expenses for medical costs whereas non-medical costs are predominantly covered by out of pocket expenses. Day-case appointments formed the largest medical cost group, closely followed by consultations. The bulk of consultation costs were generated through interaction with MS specialist nurses, physiotherapy and neurology services. People with a relapsing-remitting MS disease type reported the greatest use of consultations, generating 73% of all the neurology costs and 68% of MS nurse costs. Of the 138 participants with non-medical costs, the recollected costs range from the purchase of a simple aid to major home extensions with the major costs coming from home adaptations (Figure 1). It emerged that in contrast to the medical costs, the non-medical costs were not recurrent. Overall 75% of these costs were reported as out of pocket expenses; the other 25% were mainly funded by a combination of NHS and social services/local authority funds, with 5% provided by charity organisations.

DMT is associated with lower medical and non-medical costs

Of the responder group, 16% were on a DMT when they took part in the survey. However, 205/537 (38%) had been on a DMT at some point. The 16% of responders known to be taking MS DMTs have a different disease severity profile to those not known to be taking DMTs. We found 62% of them had a prEDSS score of less than six, as opposed to 42% in the DMT naïve group. The DMT group is also demonstrably more active, as defined as being still in employment, ($\chi^2=5.6$, $p<0.02$). Not including the costs of DMTs themselves, the medical and non-medical costs for those on a DMT were lower pp. Overall the costs generated by the DMT group was £781 pp as opposed to £1,935 pp in those not known to be taking DMTs.

Impact of population demographics, employment status and education on costs

The demographic profile of pwMS had an impact on costs. Medical costs were highest in the youngest age group (18–34 years) and those with primary progressive MS generated the highest medical and non-medical costs pppa.

Those classified as being inactive (unemployed) generated medical costs approaching double that of those who were economically active pwMS. However, the active group had 37% of non-medical costs paid by service providers, compared to 11% in the inactive group.

Almost 70% of the study population have higher than secondary school education: 34% have an occupational diploma or certificate, 22% a bachelor's level degree and 13% a postgraduate qualification. Of those with known educational status, the highest medical costs were generated by those with a bachelor's degree school education, at £4711 pppa. Those with a university degree were able to secure non-medical cost funding of 47% through service providers, compared to just 10% from people with secondary school education. The proportion of funding for non-medical interventions varied by household composition, with retired couples receiving just 2% and 'other adult households' securing 67% from service providers.

Table 1. Demographics and disease characteristics of the cost of the MS responder population (n=537), the contacted population (n=3035) and the total UKMSR population (n=13244). P values calculated using t-test or χ-square goodness of fit. Current DMT use was only available in the responder population as they were the only group who had reviewed the DMT use question as part of completing the cost of MS questionnaire.

Variable	Cost of MS population *n = 537*	Contacted population *n = 3035*	Total UKMSR population *n = 13,244*
Age at diagnosis: (mean±SD)	40.2±10.5	37.7±9.6*	39.1±10.4**
Age at questionnaire: (mean±SD)	51.1±10.5	48.4±9.8*	53.5±12.0**
MS type: *n* (%)			
PPMS / RRMS / SPMS / Benign or unknown	52 (10) / 322 (60) / 127 (24) / 36 (7)	225 (7) / 1859 (71) / 422 (14) / 529 (17)**	1401 (11) / 5731 (43) / 2742 (21) / 3370 (25)**
Gender: *n* (%) *female*	392 (73)	2213 (73) NS	9688 (73) NS
Employment: *n* (%)			
Active / Inactive / Unknown	287 (53) / 222 (41) / 28 (5)	1625 (54) / 962 (32) / 448 (14)**	5546 (42)/ 6164 (42) / 1534 (12)**
Education: *n* (%)			
University / occupational certificate / secondary school / other or unknown	189 (35) / 182 (34) / 105 (20) / 61 (11)	989 (33) / 775 (26) / 616 (20) / 655 (21)**	4212 (32)/ 3821 (29) / 2860 (22)/ 2351 (18)**
Household: *n* (%)			
Married couple / married couple with pension / other adult household / single or single parent / unknown	237 (44) / 101 (19) / 78 (15) 92(17) / 29 (5)	1366 (45) / 285 (9) / 384 (13) / 517 (17) / 473 (16)**	5007 (38) / 2547 (19) / 1454 (11) / 2530 (19) / 1706 (13)**
DMT: *n* (%) *yes*	86 (16)	-	-
prEDSS: , *n* (%)			
0-2 / 3 / 4 / 5 / 6 / 6.5 / 7 / 8-9 / Unknown	78 (15) / 64 (12) / 66 (12) / 33 (6) / 55 (10) / 104 (19) / 43 (8) / 12 (2) / 82 (15)	353 (12) / 259 (9) / 257 (8) / 118 (4) / 135 (4) / 333 (11) / 165 (5) 27 (1) / 1388 (46)**	935 (7) / 656 (5) / 705 (5) / 363 (3) / 542 (4) / 1306 (10) / 868 (7) / 192 (1) / 7677 (58)**
Normalised MSIS: *n* (%)	Phys: / Psych:	Phys:** / Psych:**	Phys:** / Psych:**
0-19 / 20-39 / 40-59 / 60–79 / Unknown	164 (31) / 178 (33) / 154 (29) / 186 (35) / 150 (28) / 122 (23) / 53 (10) / 35 (7) / 16 (3) / 16 (3)	714 (24) / 588 (19) / 586 (19) / 678 (22) / 590 (19) / 710 (23) / 444 (15) / 404 (15) / 701 (23) / 655 (22)	2218 (17) / 2259 (17) / 2281 (17) / 3021 (23) / 2622 (20) / 3238 (24) / 2667 (20) / 1871 (14) / 3456 (26) / 2885 (22)

DMT: disease-modifying therapy; MS: multiple sclerosis; MSIS: MS Impact Score; NS: not significant; PPMS: Primary Progressive Multiple Sclerosis; prEDSS: patient-reported Expanded Disability Status Score; RRMS : Relapsing Remitting Multiple Sclerosis; SPMS: Secondary Progressive Multiple Sclerosis; UKMSR: United Kingdom MS Register.
*p<0.002,**p<0.0001.

Table 2. Medical and non-medical costs included in the study.

Medical		Non-medical
Hospitalisation	*Consultations*	
Unplanned admissions	MSN / MSN telephone	Build downstairs extension for WC/washroom
Planned admissions	Physiotherapy	Build downstairs extension for bedroom
Outpatients	Neurology	Build downstairs extension for bedroom and en-suite facilities
Rehabilitation	Community district nurse	Stairlift (straight)
Nursing homes etc	Occupational therapy	Stairlift (more complex)
	General practitioner	Raise electrical sockets
	Urology	Wheelchair (non-powered)
Tests	Chiropody	Purchase of items to help with daily activities
Blood tests	Ophthalmology	Level access to shower
MRI scan	Clinical psychology	Convert room or downstairs WC/washroom
Ultrasound	Psychiatry	Lay new path
Lumbar puncture	Gastroenterologist	Widen doorway for wheelchair access
ECG	Social services	Install lighting to outside steps/path
CT scan	Rheumatology	Move bed to downstairs room
X-rays	Nephrology	Fit handrail – external
	Gynaecology	Fit handrail – internal
	Speech therapy	Fit handrail to bath
	Medical oncology	Fit over bath shower
	Dietician	Create step to front/back door
	Continence	Create ramp to front/back door
	Endocrinology	Wheelchair (powered)
	Dermatology	Car adaptations
	Emergency department	

CT: computed tomography; ECG: electrocardiogram; MRI: magnetic resonance imaging; MSN: multiple sclerosis nurse.

Increasing disability increases medical and non-medical costs in the UKMSR population

In total, 45% of the study sample have a prEDSS score between 0 and 5.5. A further 40% have a prEDSS of 6 or more. We confirmed that the cost profile with increasing disability score was similar for the prEDSS compared to an earlier measure of disability based on the EDSS (Appendix, Figure 2). Using the prEDSS we demonstrated a fluctuating range of medical costs across the range of EDSS, increasing rapidly from EDSS 7 and higher. Non-medical costs pp occur predominantly among those with an EDSS of 6 or more and are greatest for those with an EDSS score of 7.0 (Figure 2(a)). For both the MSIS-physical and psychological scores, the medical costs pp increase gradually with severity. Non-medical costs increase more dramatically by physical score than by psychological score with increasing severity (Figure 2(b)). Stepwise multivariate analysis of a complete dataset (n=445) was performed using medical and non-medical costs as separate outcomes, with the variables: age, age at diagnosis, gender, MS type, employment, education, household, DMT use, prEDSS and MSIS physical and psychological scores. For non-medical costs (adjusted R^2 0.048, p=0.017) two variables were included employment (estimate 95% confidence intervals (upper, lower): 370.1043 (-92.5, 832.7), p=0.117) and an increasing MSIS physical score (57.43 (34.6, 80.3), 0.0028) and for medical costs two variables were included: (adjusted R^2 0.042, p=0.019) being of a younger age (-21.5 (-37.8, -5.3), p=0.0096) and an increasing MSIS physical score (17.0 (8.5, 25.4), p=0.0004).

Non-medical costs are associated with higher medical costs and more advanced MS

Given the nature of the non-medical costs we identified earlier, we investigated this group in more detail. The average medical cost in the 138 pwMS with non-medical costs was £1211, significantly increased compared to £673 in the 399 pwMS with

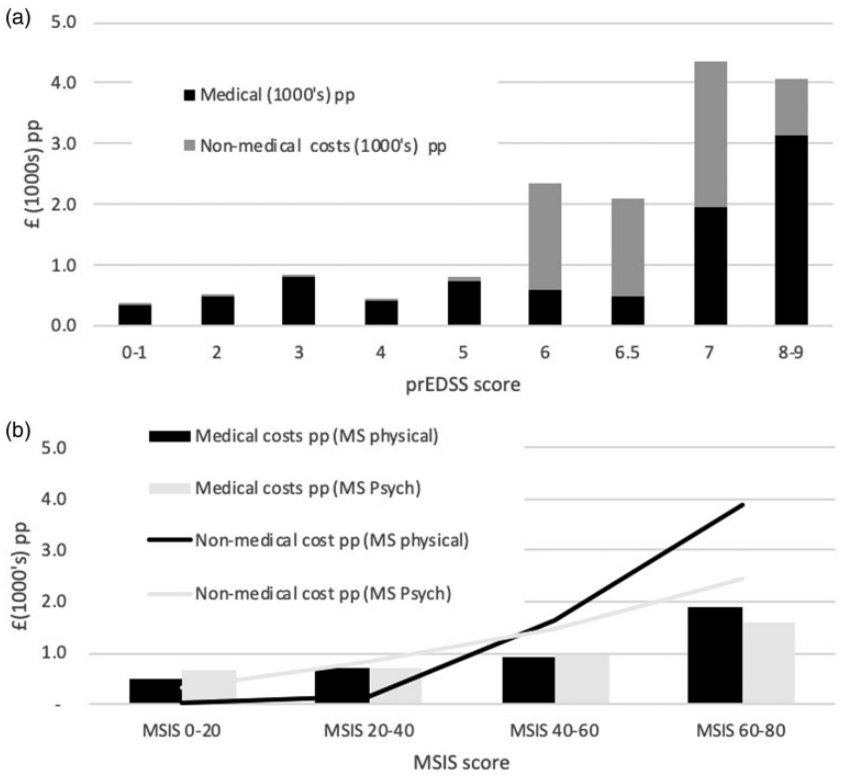

Figure 2. (a) The total medical and non-medical costs pp reported by people with multiple sclerosis (pwMS) (n=455) with a patient reported Expanded Disability Status Score (prEDSS) score. (b) Total medical and non-medical costs by Multiple Sclerosis Impact Scale (MSIS) physical (n=521) and psychological component (n=521).

no non-medical costs ($p < 0.004$). In addition, the non-medical population, despite having a similar gender ratio, age of onset and age at completing the questionnaire, had more progressive disease and higher disability in terms of prEDSS (Figure 3) and MSIS physical and psychological scores (Table 3).

Discussion

The UKMSR is a UK-wide population that focuses on using PROs via a web interface together with clinical input via a network of 46 NHS centres. PROs have the potential to give a deeper understanding of the impact MS has on the person and offer a wider view of the disease but are often not anchored to clear outcomes. Together with the UK-wide span of the MS Register, this led us to generate a nationwide snapshot of costs but for the first time to generate costing based on PROs and to integrate detailed medical and non-medical costs for pwMS aiming to understand where the burden of non-medical costs impacts most.

Previous studies have targeted different populations that are either MS centre[4] or community based.[3,6] The UK-wide and community-based structure of the UKMSR backed up by NHS centre involvement is a strength but there are limitations to this study. This study targeted subjects by email who had signed up to the UKMSR both via the web portal and through an NHS centre independently confirming their diagnosis. However, the population attending NHS centres is more likely to have RRMS and this was reflected in the contacted population. The responder group were more severely affected than those contacted by email but in turn they were less severely affected than the UKMSR registry population as a whole, with lower levels of progressive MS and lower disability. DMT use in the responder population is lower (16%) than in prior UK and European populations making the applicability of our results unclear.[6] However, it is difficult to make a direct comparison with other studies as the question was whether they were on DMTs when they completed the questionnaire and we relied on pwMS to update this field; we could confirm that 38% had being on DMTs at some point in their disease

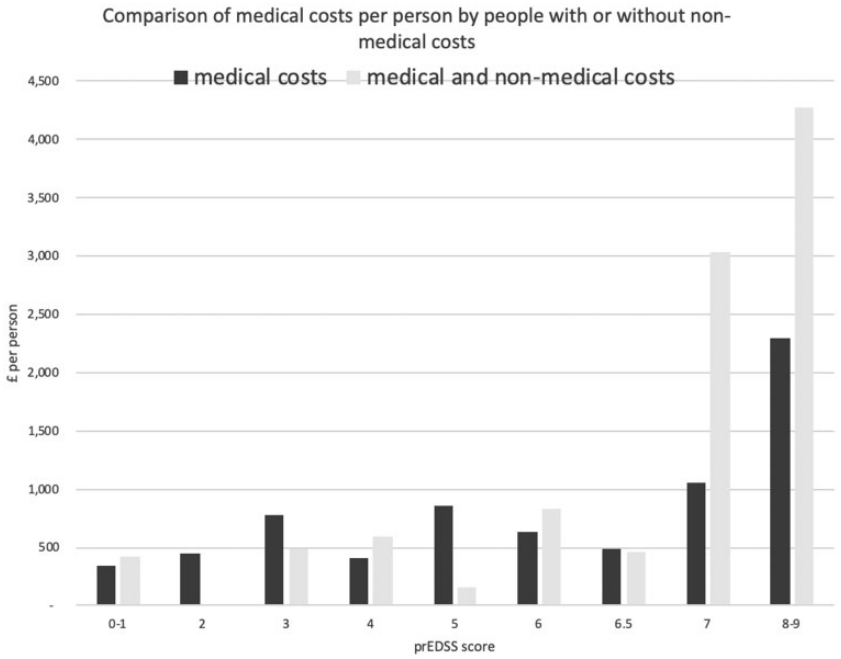

Figure 3. Comparison of medical cost per patient per annum (pppa) for those with non-medical and medical costs. Excludes people who only reported a single non-medical cost for the purchase of items to help with daily activities. This has been done to eliminate small number effects.

pathway, which is more consistent with prior UK DMT use. We relied on pwMS to remember interventions and this led us to capture medical and non-medical costs over different timeframes as longer timeframes rely on memory, which can be an issue for pwMS; this is an issue affecting all such surveys. Although the questionnaire was not validated for completion by pwMS and their representatives, it was built from other questionnaires that had been. In addition, the answers defaulted to no, thus we could have underestimated costs if a participant did not want to answer.

Using a questionnaire based on the MS HRUQ, adapted for the UK based on previous cost of illness studies,[3,4,6] we have demonstrated a similar pattern of medical costs based on disability using the prEDSS that have previously been seen with the clinical EDSS.[3] We have extended these observations using an established UK-wide community-based population where a wide range of prior PROs were available including the PRO, the MSIS-29, an outcome that is associated with an increasing risk of mortality.[23] In line with the prEDSS and EDSS we find that costs in general increase with increasing MSIS-29 scores both physical and psychological. Thus, despite the MSIS-29 psychological score being developed to capture aspects of MS that did not incorporate mobility issues, the score rises as mobility is affected. However, non-medical costs increase more steeply with increasing MSIS-29 physical scores than MSIS-29 psychological scores. In contrast, for non-medical costs the MSIS-29 psychological score rises above MSIS-29 physical at lower scores. In this population an unbiased analysis favoured the MSIS physical over the prEDSS as a predictor of increased costs. PROs capturing quality of life, fatigue and cognitive impairment have previously been found to be independently predictive of costs from the prEDSS[6]but the span of the MSIS-29 physical capturing the wider impact MS may make it more useful alone in predicting costs.

We show that all costs are highest in those with primary progressive MS where there is currently no available therapy and that medical costs are increased in those who are not in employment, but this is further affected by the fact that their non-medical costs are derived from their own resources. We also show that DMTs are associated with lower costs, but this appears to be predominantly through their use in pwMS who have less disability.

Here using a detailed breakdown of cost flows we demonstrate that no out of pocket medical expenses were incurred, this is likely unique to the UK as a result of the NHS provider system. It also shows that

Table 3. Demographics and disease characteristics of the medical and non-medical population at baseline.

Variable	Medical (n=399)	Non-medical (n=138)	χ^2 (p)
MS type: *n* (%)			
PP	30 (8)	22 (16)	64.6 (<.00001)
RR	275 (69)	47 (34)	
SP	65 (16)	62 (45)	
Benign or unknown	29 (7)	7 (5)	
Employment: active / inactive / unknown, *n* (%)	236 (59) / 143 (36) / 20 (8)	51 (37) / 79 (57) / 5 (5)	21.4 (<.00002)
DMT: yes, *n* (%)	75 (19)	11 (8)	8.9 (<.003)
prEDSS: *n* (%)			
0–5	219 (55)	22 (16)	85.1 (<.0001)
6	35 (9)	20 (14)	
6.5	54 (14)	50 (36)	
7	19 (5)	24 (17)	
8–9	7 (2)	5 (4)	
unknown	65 (16)	17 (12)	
Normalised MSIS Phys/psych, *n* (%)			
0–20	157 (39) / 147 (37)	7 (5) / 31 (22)	122.0 (<.00001) / X^2=36.8 (<.00001)
21–40	129 (32) / 149 (37)	25 (18) / 37 (27)	
41–60	79 (20) / 70 (18)	71 (51) / 52 (38)	
61–80	20 (5) / 19 (5)	33 (24) / 16 (12)	
unknown	14 (4) / 14 (4)	2 (1)/ 2 (1)	

DMT: disease-modifying therapy; MS: multiple sclerosis; MSIS: MS Impact Score; prEDSS: patient-reported Expanded Disability Status Score.

the non-medical costs are principally house adaptations and shows the limited impact of charities in covering non-medical expenses. Non-medical costs made up on average 22% of total costs pppa in this study and three-quarters of these non-medical costs were paid by the PwMS or their family. This is remarkably consistent with estimates of non-medical costs overall.[24] However, this study gives us an insight into details of these costs and at an individual level they appear to require a capital investment that may benefit the individual for many years in terms of quality of life. Thus, planning for such costs requires a different approach both at an individual and society level. By looking at those who had or did not have non-medical costs separately, we identify that those reporting non-medical costs within the last year incurred consistently higher medical costs. These medical costs were predominantly unplanned admission, rehabilitation and nurse home care. Their disease profile differed in that those with non-medical costs were less likely to be on DMTs, have progressive disease as well as being more disabled and unemployed. Thus, non-medical costs potentially arise at a time when they are more likely to lose income and when they require additional medical support. However, due to the long-term benefit of non-medical cost investment, they may offer potential impact on medical costs in the future and here we see that non-medical costs peak at prEDSS 7 then fall off. Indeed, it is likely there will be people in this study whose non-medical interventions were either in place prior to the study reporting timeframe or were provided in a way not captured by the study. The nature of the non-medical interventions we have seen will reduce medical costs through providing appropriate home environments, facilitating early discharge and less need for rehabilitation and nursing home services. Furthermore, the physical and psychological impact of MS is likely to be reduced on a daily basis when living in an appropriately adapted environment.

This study has elucidated in detail some of the wider cost impacts for pwMS and their families as well as society. We confirm that worsening mobility as measured by an increasing EDSS is a major driver of costs but we have also addressed the wider physical

and psychological effects using PROs prior to mobility loss. We have also incorporated the non-medical costs to pwMS and their families, enabling us to gain a deeper understanding of the impact has on both the person and society as whole. In particular we find, unlike medical costs, non-medical costs have the potential to have a positive impact on the pwMS and could modify future medical costs.

Conflict of Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: Richard Nicholas reports non-financial support from Roche, personal fees and non-financial support from Novartis, personal fees and non-financial support from Biogen, grants from UK MS Society, outside the submitted work. R Pulikottil-Jacob is an employee of Sanofi Genzyme and M Chevli is a former employee of Sanofi Genzyme. The other authors have no conflicts of interest to declare.

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Supplemental material

Supplemental material for this article is available online.

References

1. NICE. Alemtuzumab for treating relapsing-remitting multiple sclerosis [Internet]. National Institute for Health and Care Excellence, https://www.nice.org.uk/Guidance/TA312 (2014, accessed 2 November 2019)
2. NICE. Teriflunomide for treating relapsing–remitting multiple sclerosis [Internet]. https://www.nice.org.uk/guidance/ta303. (2014, accessed 2 November 2019)
3. Tyas D, Kerrigan J, Russell N, et al. The distribution of the cost of multiple sclerosis in the UK: How do costs vary by illness severity? *Value Health* 2007; 10(5): 386–389.
4. Karampampa K, Gustavsson A, Miltenburger C, et al. Treatment experience, burden and unmet needs (TRIBUNE) in MS study: Results from five European countries. *Mult Scler J* 2012; 18(2_suppl): 7–15.
5. Hawton A and Green C. Health utilities for multiple sclerosis. *Value Health* 2016; 19(4): 460–468.
6. Kobelt G, Thompson A, Berg J, et al. New insights into the burden and costs of multiple sclerosis in Europe. *Mult Scler J* 2017; 23(8): 1123–1136.
7. Mackenzie IS, Morant SV, Bloomfield GA, et al. Incidence and prevalence of multiple sclerosis in the UK 1990–2010: A descriptive study in the General Practice Research Database. *J Neurol Neurosurg Psychiatry* 2014; 85(1): 76–84.
8. Kurtzke JF. Rating neurologic impairment in multiple sclerosis: An expanded disability status scale (EDSS). *Neurol* 1983; 33(11): 1444–1152.
9. Middleton R, Rodgers W, Chataway J, et al. Validating the portal population of the United Kingdom Multiple Sclerosis Register. *Mult Scler Relat Disord* [Internet], http://linkinghub.elsevier.com/retrieve/pii/S2211034818301767 (2018, accessed 25 May 2018)
10. Ford DV, Jones KH, Middleton RM, et al. The feasibility of collecting information from people with Multiple Sclerosis for the UK MS Register via a web portal: Characterising a cohort of people with MS. *BMC Med Inform Decis Mak* 2012; 12(1): 73.
11. Leddy S, Hadavi S, McCarren A, et al. Validating a novel web-based method to capture disease progression outcomes in multiple sclerosis. *J Neurol* 2013; 260(10): 2505–2510.
12. Hobart J. The Multiple Sclerosis Impact Scale (MSIS-29): A new patient-based outcome measure. *Brain* 2001; 124(5): 962–973.
13. Jones KH, Ford DV, Jones PA, et al. The physical and psychological impact of multiple sclerosis using the MSIS-29 via the web portal of the UK MS Register. *PLoS ONE* 2013; 8(1): e55422.
14. Office for National Statistics. Standard Occupational Classifications 2010 [Internet]. The current standard occupational classification for the UK, published in three volumes. https://www.ons.gov.uk/methodology/classificationsandstandards/standardoccupationalclassificationsoc/soc2010 (2016, accessed 25 February 2019)
15. UNESCO Institute for Statistics. International Standard Classification of Education [Internet]. International Standard Classification of Education (ISCED). http://uis.unesco.org/en/topic/international-standard-classification-education-isced (2011, accessed 25 February 2019)
16. Office for National Statistics. Families and Households [Internet]. Families and children in the UK by family type including married couples, cohabiting couples and lone parents. Also shows household size and people living alone. https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/families/datasets/familiesandhouseholdsfamiliesandhouseholds/current (2017, accessed 25 February 2019)
17. NHS Improvement. Reference Costs [Internet]. Better healthcare, transformed care delivery and sustainable finances. https://improvement.nhs.uk/resources/reference-costs/ (accessed 2 December 2019)

18. Curtis L and Burns A. Unit Costs of Health and Social Care [Internet]. Personal Social Services Research Unit. https://www.pssru.ac.uk/project-pages/unit-costs/unit-costs-2018/ (accessed 2 December 2019)
19. Giovannoni G, Butzkueven H, Dhib-Jalbut S, et al. Brain health: Time matters in multiple sclerosis. *Mult Scler Relat Disord* 2016; 9: S5–48.
20. Harris PA, Taylor R, Thielke R, et al. Research electronic data capture (REDCap): A metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform* 2009; 42(2): 377–381.
21. IBM SPSS Statistics for Windows. Armonk, NY: IBM Corp; 2017.
22. R Core Team. *R: A language and environment for statistical computing [online]*. Vienna, Austria. (2018, accessed 16 October 2017)
23. Raffel J, Wallace A, Gveric D, et al. Patient-reported outcomes and survival in multiple sclerosis: A 10-year retrospective cohort study using the Multiple Sclerosis Impact Scale–29. *PLOS Med* 2017; 14(7): e1002346.
24. Appleby J. What does the UK spend on health and social care? *BMJ* 2019; l1619.