Evaluation of the Economic Burden of Psoriatic Arthritis and the Relationship Between Functional Status and Healthcare Costs

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Key Indexing Terms:

PSORIATIC ARTHRITIS, ECONOMIC BURDEN OF DISEASE, HEALTHCARE COSTS, REGRESSION ANALYSIS

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Supported by Celgene Ltd.

Conflicts of interest: N. McHugh has received speaker/consultancy fees and/or grants from AbbVie, Celgene Ltd, Eli Lilly, Pfizer and UCB. Á. Maguire has received grant/research support from Cogentia Healthcare Consulting Ltd. I. Handel has received personal fees for statistical analyses from Visible Analytics Limited. W. Tillett has received speaker/consultancy fees and/or grants from AbbVie, Celgene Ltd, Eli Lilly, Janssen, Novartis, Pfizer and UCB. J. Morris has received consultancy

fees from Celgene Ltd. N. Hawkins has received grant/research support from Celgene Ltd. C. Cavill has received grant/research support from Celgene Ltd. E. Korendowych has received grant/research support from AbbVie, Celgene Ltd and Pfizer, and consultancy/speaker fees from AbbVie, Celgene Ltd, Janssen, Novartis and Pfizer. F. Mughal was an employee of Celgene Ltd at the time of study conduct.

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Short running head: Economic burden of PsA

Word count: ~~2204~~2455

ABSTRACT.

Objective. This analysis aimed to evaluate the economic burden of patients with psoriatic arthritis (PsA) on the UK healthcare system and estimate the relationship between functional status and direct healthcare costs.

Methods. Functional status (measured using the Health Assessment Questionnaire–Disability Index [HAQ-DI]), demographics, disease history and healthcare resource use data were extracted from a cohort of patients at the Royal National Hospital for Rheumatic Diseases, Bath, UK. Each resource use item per patient was then allocated a unit cost. Linear regression models were used to predict costs as a function of HAQ-DI. Medication costs were not included in the primary analysis, which was carried out from the UK National Health Service perspective.

Results. Data were available for 101 patients. Mean HAQ-DI score was 0.84 (SD 0.75) and mean age at HAQ-DI measurement was 57.8 (SD 10.7). Total annual healthcare costs per patient, excluding medication costs, ranged between £174 and £8,854, with a mean of £1,586 (SD £1,639). A 1-point increase in HAQ-DI score was associated with an increase in total costs of £547.49 (SE £224), with secondary care consultations appearing to be the primary factor. Subgroup analyses suggested higher cost increases in patients with HAQ-DI scores 2–3 and with a disease duration >10 years.

Conclusion. Patients with PsA have a significant economic burden on the healthcare system. Functional status is highly correlated with costs and appears to be driven mainly by the cost of secondary care consultations. Results were similar to previous studies in rheumatoid arthritis populations.

Psoriatic arthritis (PsA) is a chronic, systemic inflammatory joint disease that is often associated with the inflammatory skin condition, psoriasis. PsA affects the peripheral joints, axial skeleton, periarticular structures, skin and nails, with patients experiencing pain, swelling and joint tenderness. Joint damage is progressive, leading to reduced mobility and function, as well as impaired quality of life (1). Joint damage in PsA is significantly less marked than in rheumatoid arthritis (RA) after equivalent disease duration (2,3), and PsA was originally thought to be a milder condition than RA. However, the impact on patients' quality of life is similar in the 2 conditions (2,3), and PsA is now widely recognised to be as severe as RA (2).

Current treatment options for PsA include non-steroidal anti-inflammatory drugs, disease-modifying antirheumatic drugs (such as methotrexate and sulfasalazine), biologic therapies (e.g. tumour necrosis factor, IL-17 and IL-12/23 inhibitors), and apremilast (4-6). However, development of policies, recommendations and guidelines for management of patients requires an evaluation of both the different treatments available and the impact of these on the use of healthcare resources. Those involved in making clinical decisions need information about costs as well as evidence of efficacy.

In RA, the relationship between cost and functional status is well documented (7,8). However, similar work in PsA is limited. In a recent economic evaluation, the relationship between functional status and costs was derived from an RA dataset rather than from patients with PsA (9). A further evaluation of biologics was inconclusive on the relationship between cost and functional status due to several uncertainties surrounding model parameters, including limited evidence for rebound following withdrawal of biologic therapy. Poole et al (10) demonstrated a relationship

between functional status and costs in PsA; however, their approach was limited by the use of separate patient cohorts for derivation of functional status and cost data.

Here, we present the findings of an analysis designed to estimate the relationship between functional status and healthcare costs in PsA using data from patients in a single, longitudinal cohort.

MATERIALS AND METHODS

Data sources. Since 1989, patients with PsA at the Royal National Hospital for Rheumatic Diseases (RNHRD; Bath, UK) have been recruited into an observational cohort as part of their routine care. Patients who fulfil the CASPAR criteria for PsA (11,12) and attend the clinic every 3 to 6 months, depending on their clinical need, were included in this analysis. At each appointment, patients undergo a full clinical assessment, including 66 swollen and 68 tender joint counts, body surface area skin assessment, dactylitis and enthesitis count, and nail assessment. Patient-reported outcomes are also collected, including the Health Assessment Questionnaire–Disability Index (HAQ-DI). For the purposes of this study, a convenience sample of 101 patients was selected from a total eligible cohort of 660 patients.

Data from the HAQ-DI, which was originally developed for the assessment of physical function in RA (12), support its use in PsA (13,14). The index assesses 8 categories of function; within each category, patients report how much difficulty they have in performing specific activities. The highest score within each category is taken as the overall score for that category; these are then added together and divided by the number of categories answered to give a summary score. ~~Scores of 0 to 1 g~~Generally, ~~represent~~ mild to moderate functional difficulty is represented by scores of 0 to 1, ~~scores of 1 to 2 represent~~ moderate to severe functional difficulty is

represented by ~~and~~ scores of 1 to 2 ~~to 3 indicate~~, and severe to very severe functional difficulty is represented by scores of 2 to 3 (15).

Patients who had 6 months of health outcomes and resource use data before and after a HAQ-DI measurement were selected the RNHRD PsA cohort. Resource use data included tests and investigations, primary and secondary consultations, accident and emergency department (A&E) attendances, and hospital admissions (admitted care). Demographic, health outcomes and resource use data for eligible patients were extracted and entered into a database. In addition, a detailed questionnaire was sent to all eligible patients requesting permission to contact their general practitioner (GP) to obtain access to their prescription records. The questionnaire was used to corroborate electronic records relating to secondary care activities for each patient. Data covering the period 2011 to 2014 were extracted in January 2015.

Following full data extraction, unit costs were allocated to all healthcare resource utilisation items for each patient in the study. Costs for hospital episodes were sourced from the published National Health Service reference costs datasets for 2012/2013 and 2014/2015 (16)~~(15)~~. Where the reason for hospital admission was unclear, costs for elective procedures were assigned. With regards to outpatient activity, it was unclear for most appointment entries whether they were a first attendance, follow-up attendance, consultant-led attendance, or attendance by other clinical team members. In the absence of more detailed information, we assumed a follow-up appointment cost for all outpatient activity. Primary care costs were assigned according to whether the appointment was in person with a GP or nurse, or whether patients received a telephone call from their GP or nurse (17)~~(16)~~. Costs for prescription medications were taken from the British National Formulary (18)~~(17)~~ and

the NHS drug tariff (19)~~(18)~~ where relevant. Detailed prescription information (e.g. dose, pack size) was missing for a large proportion of the medication data. These data were missing completely at random and therefore mean imputation methods were used to derive a complete dataset.

The study was approved by the South West-Central Bristol NRES Committee (institutional review board approval number BA74/00-01) and was conducted in accordance with the Declaration of Helsinki. All patients signed informed consent.

Statistical analyses. Statistical analyses were carried out using R software (R Foundation for Statistical Computing, Vienna, Austria) (20)~~(19)~~. Linear regression modelling was used to predict cost data as a function of HAQ-DI and other predictors (age at the HAQ-DI measurement and gender). In addition to simple linear regression models, alternatives were considered with logarithmic transformation of cost outcomes, ~~and~~ quadratic transformation of the HAQ-DI predictor and generalised linear models with a gamma error distribution (using identity and inverse link functions). During model selection, ~~*T*~~*t*-tests were used to assess the significance of individual predictors with a null hypothesis that the predictor's coefficient was zero. Models were simplified by removal of non-significant predictors. Model fit and predictive accuracy were compared by estimation of root mean squared error (RMSE), Akaike's information criterion (a parameter-penalised measure of model fit) and examination of the distribution of residuals. As cost data were not normally distributed, standard errors (SEs), 95% confidence intervals and P values were estimated by bootstrap resampling (100,000 samples).

Models including total healthcare costs (with medication costs) were non-significant. Subsequently, models were explored for a subset of healthcare costs, excluding medication costs. Final model selection was therefore based on the

outcome ‘total cost without medication’ and the selected model was used to estimate the association between the HAQ-DI score and individual cost components (i.e. primary and secondary care consultations, tests and investigations, admitted care and A&E attendances).

The following subgroups were analysed to determine if identified associations between the HAQ-DI score and cost remained approximately consistent: HAQ-DI cut-off (0 to <1, 1 to <2, ≥2), disease duration (<5 years, 5 to <10 years, ≥10 years) and gender.

The analysis was carried out from the UK healthcare perspective.

RESULTS

The HAQ-DI, age at onset, age at HAQ-DI assessment, gender and cost data were collated for the study sample of 101 patients. Fifty-eight patients were female. **Table 1** shows patients’ characteristics, including the mean HAQ-DI score, age and disease duration. Total mean annual healthcare costs were £3,870 (SE £394) per patient. Medication costs were the largest component (£2,284 [SE £350]). For the subset of costs (excluding medication costs), the mean cost per patient was £1,586 (SE £161) (**Table 2**).

Models with total healthcare costs, including medication costs, were non-significant. For analyses using the subset of costs without medications, age at HAQ-DI assessment, disease duration and gender were not significant predictors of cost, so they were removed from the models.

Table 3 shows the details of the simple regression model. The simple linear regression modelling residuals were moderately skewed to the right. Logarithmic transformation of cost normalised the distribution of residuals but increased RMSE;

the quadratic transformation of the HAQ-DI gave a similar RMSE to the linear model, but increased the Akaike's information criterion. The generalised linear models with gamma distributed errors had a marginally higher RMSE than the linear model. The simple linear model was therefore selected as its coefficient (cost increase per unit increase in the HAQ-DI) allowed a simple interpretation with no significant loss in model fit compared with more complex strategies, and bootstrap resampling allowed robust estimation of confidence intervals as the model residuals were not normally distributed.

The modelling showed that, in general, patients with a worse functional disease status (i.e. higher HAQ-DI scores) had higher total healthcare costs (excluding medication costs; **Figure 1**). However, some patients with low HAQ-DI scores had high healthcare costs and *vice versa*. Similar overall findings were observed when this analysis was repeated excluding the 6 patients whose total costs exceeded £5,000 (**Supplementary Table 1**). The estimated association of total costs without medication with the HAQ-DI score changed from £547/unit to £386/unit, as the excluded patients had high admitted care costs which correlated with the HAQ-DI score. A 1-point increase in the HAQ-DI score was associated with an estimated increase in total healthcare costs of £547.49 (**Table 4**). Costs associated with secondary care appeared to be the primary factor in the relationship between the HAQ-DI score and healthcare costs (**Figure 2**). Results from the model on log-transformed costs are provided in **Supplementary Table 2**.

Results of the subgroup analyses (excluding medication costs) are shown in **Table 4**. There appeared to be a trend for greater cost increases per 1-point increase in the HAQ-DI score among males, patients with HAQ-DI scores ≥2, and

those who have had PsA for >10 years. Interestingly, patients with a HAQ-DI score of 0 to <1 had a greater cost increase than those with scores between 1 and 2.

DISCUSSION

This study demonstrates a relationship between disease severity in PsA and healthcare costs, with the estimated HAQ-DI score being a significant predictor of total healthcare costs. Total annual healthcare costs in PsA represent a significant burden for healthcare systems and increase markedly with increasing disease severity. When the cost of medications is excluded, secondary care consultations appear to be the main driver of the association between disease severity and cost.

A previous study by Poole *et al* (10) also demonstrated an increase in costs with increasing HAQ-DI score in PsA. However, mean annual healthcare costs estimated in our study (£1,586, excluding medication costs) were higher than those estimated by Poole *et al* (10) (£1,446, including medication costs), suggesting that the economic burden of PsA may be greater than previously thought. One possible reason for this is that patients in our study were older (mean age, 57.8 vs. 46.7 years in the study by Poole *et al* (10)), which could mean more comorbidities, and had PsA for longer (almost 20 vs. 11 years in the study by Poole *et al* (10)). It is important to note that the study by Poole *et al* (10) was limited by the use of separate cohorts for the derivation of the HAQ-DI and resource use data; use of a single patient cohort in our study allowed more accurate mapping of the relationship between the HAQ-DI score and cost.

Overall, our findings were similar to previous research in RA populations, showing a similar increase in costs with increasing disability, as measured by the HAQ-DI (9). In an analysis of 1,487 French patients with RA (mean disease duration,

18 years), the HAQ-DI score was a very strong predictor of costs and was significantly correlated with direct medical costs (8). Similarly, an analysis of 201 Spanish patients with RA (mean disease duration, 7.7 years) showed a significant increase in costs with increasing HAQ-DI score (7).

When the burden of articular disease and spinal/enthesitis/dactylitis/skin disease and extra-articular manifestations are considered, the total burden of disease in PsA is felt to be similar to RA. This is supported by studies demonstrating similar levels of HAQ (2,21,22)~~(2,20,21)~~.

In our sensitivity analyses using linear regression modelling to predict total cost as a function of disease duration, duration of 0 to <5 years or 5 to <10 years was not statistically significantly associated with total cost; however, the association between total cost and disease duration of >10 years was statistically significant. The point estimates for the 3 categories suggest a possible monotonic increase in total cost with increasing disease duration, but the number of patients in the lowest 2 categories was small and the parameter estimates unstable.

Our final model excluded medication costs, for which there was a substantial amount of missing information in the original dataset. Our use of mean imputation of medication costs may under-represent uncertainty in the relevant estimates; however, as we found no significant association between medication costs and HAQ-DI, more complex strategies such as multiple imputation would not change this conclusion. The exclusion of medication costs in our statistical model is a limitation of the study, as medication costs are likely to make a substantial contribution to the overall costs associated with PsA. In addition, PsA has an important impact on societal costs (23-26)~~(22-25)~~. For example, a survey of 50 patients in Poland found those who were employed were absent from work for an average of 2.88 days/month

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and had an on-the-job productivity loss of 24.1% (26)~~(25)~~. A systematic review by Tillett *et al* (27)~~(26)~~ showed that levels of work disability comprising absenteeism (i.e. absence from work) and presenteeism (i.e. reduced effectiveness at work) range from 16% to 39% in patients with PsA. A study of UK patients with PsA found absenteeism, presenteeism and productivity loss rates of 14%, 39% and 46%, respectively (28)~~(27)~~. The findings from our study are therefore likely to underestimate the true burden of costs associated with PsA.

Given the relatively small sample size, potential selection bias is another limitation of our study. The small number of patients sampled may not adequately reflect the diversity of PsA disease manifestations or severity. In addition, only those patients whose GP responded to a request for access to prescription data were included. This could have been avoided by making the decision not to include prescription data at an earlier stage.

In conclusion, our study demonstrates that PsA can cause a significant burden on the resources of healthcare systems such as the National Health Service. Finally, it has also been demonstrated that there exists a significant relationship between functional status and healthcare costs in patients with PsA, although further research is needed to gain a deeper understanding of this relationship and aid decision makers in the development of policies and treatment guidelines.

ACKNOWLEDGMENT

This study was sponsored by Celgene Ltd, which co-designed the study with expert input from N. McHugh, W. Tillett, and C. Cavill, and was involved in the collection, analysis and interpretation of the data. All authors drafted the article or revised it critically, and all authors read and approved the final version. Medical writing and

editorial support was provided by Dr. Joanna Todd (Stellar Medical Communications Limited, Ely, UK) and was funded by Celgene Ltd.

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Table 1. Patient characteristics.

Characteristics	Study Population
Patients, N	101
Age, mean (SD), years	57.83 (10.66)
Sex, female / male, n (%)	58 (57) / 43 (43)
HAQ-DI score, mean (SD)	0.84 (0.75)
Disease duration, mean (SD), years	18.23 (11.26)

HAQ-DI: Health Assessment Questionnaire–Disability Index; SD: standard deviation.

Table 2. Healthcare costs per patient* by resource use category (£/unit, 2016 prices).

Resource use category	Mean (SD)	Median (IQR)	Range
Tests	£146 (£117)	£126 (£137)	£0 to £690
A&E visit	£14 (£35)	£0 (£0)	£0 to £154
Primary care consultation	£247 (£198)	£195 (£256)	£0 to £1,101
Secondary care consultation	£678 (£445)	£594 (£445)	£0 to £2,635
Admitted care	£502 (£1,415)	£0 (£0)	£0 to £6,660
Medication costs	£2,284 (£3,493)	£390 (£3,560)	£0 to £16,326
Total costs	£3,870 (£3,986)	£2123 (£4,952)	£175 to £17,771
Total costs (excluding medication costs)	£1,586 (£1,639)	£1,111 (£1,213)	£174 to £8,854

* Based on study population of 101 patients, the n values used to calculate values shown may vary slightly across cost categories due to missing data. A&E: accident and emergency department; SD: standard deviation.

Table 3. Output results of the linear regression modelling.

Covariate	β (SE)	*P* value	95% CI for β
HAQ-DI total cost (excluding medications)	£547 (£224)	0.006	197 to 1,120
Intercept total cost (excluding medications)	£1,128 (£200)	<0.001	792 to 1,596
Number of observations	101		
Log likelihood	−887.1		
~~Akaike's information criterion~~	~~1,780~~		
Adjusted R^2	0.053		

CI: confidence interval; HAQ-DI: Health Assessment Questionnaire–Disability Index; SE: standard error.

Table 4. Results of the regression modelling: estimated HAQ-DI coefficient.

	Estimated HAQ-DI coefficient from regression of costs in HAQ-DI (£/unit)		
	Estimate (SE)*	95% CI	*P* value
Primary analysis			
Tests	£21.45 (£14)	−7 to 48	0.121
A&E visit	£15.67 (£6)	7 to 29	0.001
Primary care consultation	£69.98 (£25)	21 to 117	0.007
Secondary care consultation	£278.14 (£50)	185 to 381	<0.001
Medications	£58.07 (£447)	−788 to 966	0.903
Admitted care	£162.25 (£200)	−131 to 716	0.437
Total costs (w/o meds)	£547.49 (£224)	197 to 1,120	0.006
Sensitivity analyses for total costs (excluding medication cost)			
Disease duration			
0 to <5 years (n=6)	£−76.97 (£499)	−1,335 to 779	0.852
5 to <10 years (n=12)	£390.47 (£834)	−275 to 4,118	0.656
≥10 years (n=63)	£626.50 (£264)	212 to 1,298	0.008
HAQ-DI			
0 to <1 (n=58)	£981.68 (£572)	−15 to 2,263	0.066
1 to <2 (n=33)	£116.88 (£904)	−2,066 to 1,615	0.849
≥2 (n=10)	£3,340.13 (£3,693)	883 to 15,303	0.051
Gender			
Female (n=58)	£480.3 (£377)	−123 to 1,407	0.208
Male (n=43)	£520.92 (£264)	148 to 1,273	0.014

* Bootstrapped SE. A&E: accident and emergency department; CI: confidence interval; HAQ-DI: Health Assessment Questionnaire–Disability Index; SE: standard error.

Figure 1. Relationship between HAQ-DI and total healthcare costs: a regression model scatter plot. HAQ-DI: Health Assessment Questionnaire–Disability Index.

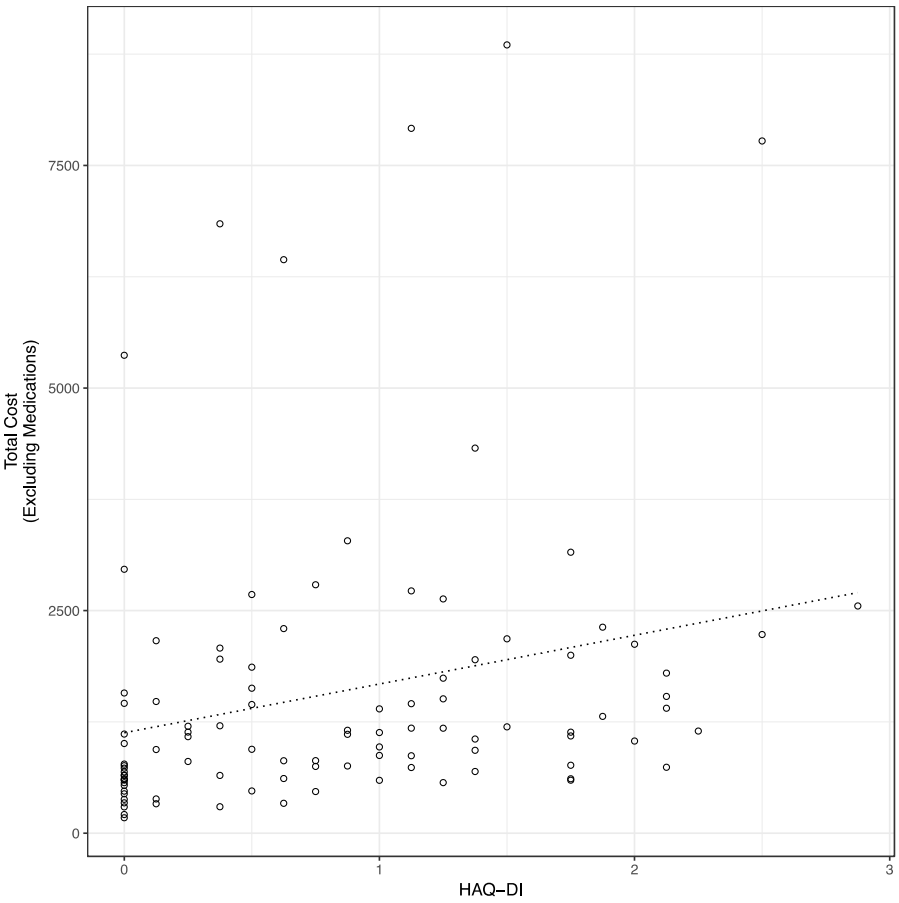
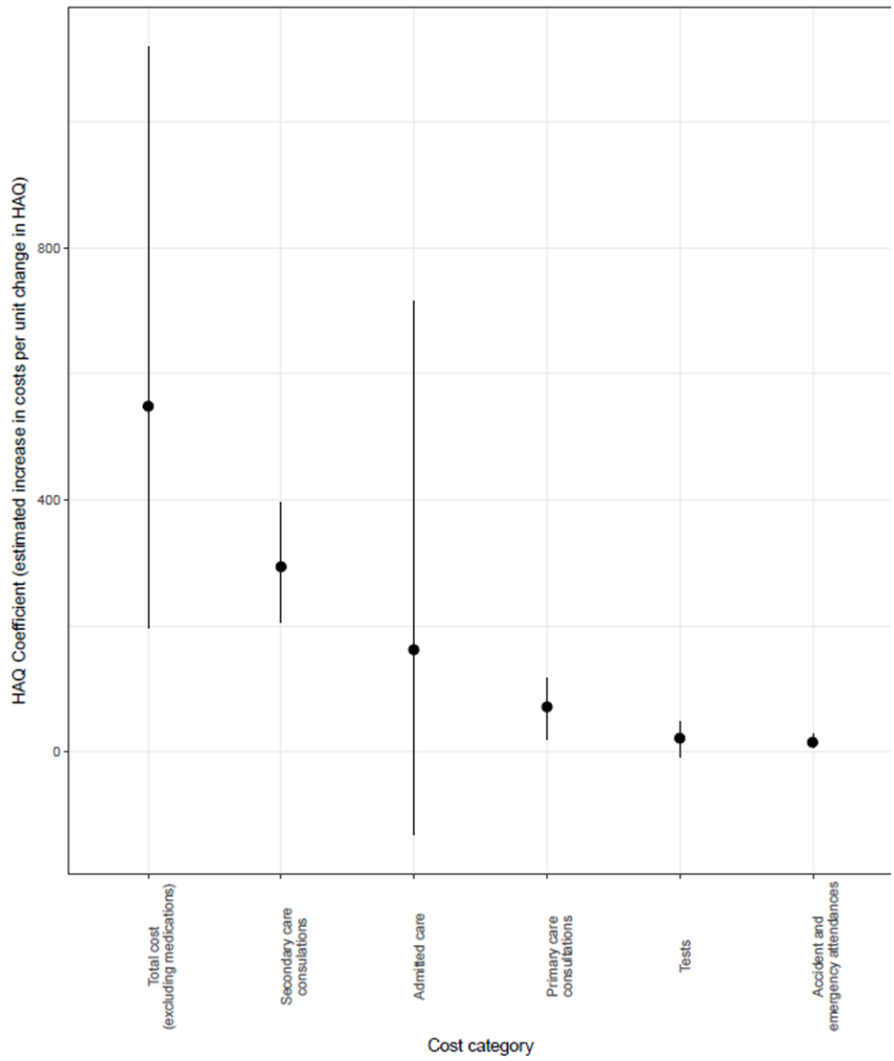


Figure 2. HAQ-DI coefficient for resource use categories. Coefficient for medications (£58.07) and confidence interval (−788 to 966) not shown. A&E: accident and emergency department; HAQ-DI: Health Assessment Questionnaire-Disability Index.



Supplementary Table 1. Results of the regression model excluding 6 patients whose total costs without medications exceeded £5,000: estimated HAQ-DI coefficient.

	Estimated HAQ-DI coefficient from regression of costs in HAQ-DI (£/unit)		
Primary analysis	Estimate (SE)*	95% CI	*P* value
Tests	£18.19 (£15)	−12 to 46	0.209
A&E visit	£17.27 (£6)	7 to 31	0.001
Primary care consultation	£67.26 (£27)	14 to 119	0.015
Secondary care consultation	£264.55 (£51)	170 to 369	<0.001
Medications	£−57.78 (£439)	−873 to 857	0.884
Admitted care	£18.86 (£48.389)	−101 to 97	0.654
Total costs (without medication)	£386.13 (£93)	202 to 566	<0.001

A&E: accident and emergency department; CI: confidence interval; HAQ-DI: Health Assessment Questionnaire–Disability Index; SE: standard error.

Supplementary Table 2. Results of the regression modelling: estimated HAQ-DI coefficient from regression of log^{10} (costs +1).

	Estimated HAQ-DI coefficient from regression of log_{10} (costs + 1) in HAQ-DI (£/unit)		
	Estimate (SE)*	Estimate ^10 (CI)	*P* value
Tests	0.129 (0.066)	1.344 (0.966 to 1.814)	0.053
A&E visit	0.300 (0.089)	1.997 (1.331 to 2.995)	0.001
Primary care consultation	0.130 (0.070)	1.350 (0.981 to 1.856)	0.065
Secondary care consultation	0.147 (0.050)	1.403 (1.116 to 1.764)	0.004
Medications	0.073 (0.128)	1.182 (0.660 to 2.118)	0.571
Admitted care	0.275 (0.173)	1.882 (0.854 to 4.149)	0.116
Total costs (without medication)	0.172 (0.042)	1.485 (1.223 to 1.803)	<0.001