Healthcare costs and productivity losses directly attributable to ankylosing spondylitis

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Abstract

Objective

To describe the healthcare resource use and productivity losses associated with patients with ankylosing spondylitis (AS) and explore the relationship between disease severity and total costs.

Methods

A cross-sectional postal survey was conducted on a sample of 1,000 patients with AS randomly selected from registries at 10 secondary care rheumatology centres in the UK. Information on demographic characteristics, disease and functional activity, healthcare use and work status (presenteeism and absenteeism) during the previous three months was collected. The relationship between disease severity and total costs was explored using a two-part regression model, controlling for age, gender and disease duration and validated on respondents (n=470) of the second round of the survey.

Results

Respondents at baseline (n=612) covered the full spectrum of AS, had a mean BASDAI of 4.6 and 55.3% of individuals scored at least 4 on the BASDAI scale. The mean (median) three month total cost was £2,802 (£1,160). Both physical function and disease activity were significant predictors of total costs. Mean (median) three month total costs for patients with BASDAI <4, 4–6 and >6 were £1,331 (£502), £2,790 (£1,281) and £4,840 (£5,017) respectively. Direct National Health Service funded healthcare costs contributed to just 15% of total costs while unemployment, absenteeism from work and reduced productivity at work accounted for 63.2%, 1.4% and 19.0% of total costs, respectively.

Conclusion

This study shows that direct healthcare costs alone do not describe the total costs associated with AS and that productivity losses associated with AS are considerable.

Key words

ankylosing spondylitis, cost, work, presenteeism, indirect cost

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Introduction

Ankylosing spondylitis (AS) is characterised by pain and stiffness of the back and involves peripheral joints and extra-articular sites. It is a chronic, progressive disease typically presenting in young men and prognosis is often poor. AS has a considerable impact on quality of life and the capacity to work (1, 2). Management focuses on controlling pain and improving physical function. Recent advances in treatment include anti-TNF agents which are shown to reduce both axial and peripheral inflammation and to provide a benefit in terms of health related quality of life, disease activity and functional ability (3). Treatment with anti-TNF agents also appears to improve capacity for work (3, 4).

In addition to the direct costs associated with healthcare resources, individuals with AS incur substantial indirect costs associated with self-funded healthcare (5), absenteeism from work and early retirement (6, 7). Precise evaluation across this spectrum is required to ascertain an estimate of the true costs of AS. This evaluation clearly needs to include early retirement and time off sick (6-8) but should also reflect how productive an individual with AS is whilst at their workplace (presenteeism).

The objective of the current study was to investigate the total costs directly attributable to AS using data collected from patients attending rheumatology centres in the UK. A secondary objective was to explore the relationship between disease severity and costs.

Patients and methods

Patients

A sample of 1,000 patients with confirmed diagnosis (modified New York criteria) (9) of AS were randomly selected from registries of ten secondary care rheumatology centres in the UK. Full details of the survey are described elsewhere (2). In summary, respondents were invited to self-complete a postal questionnaire at baseline (first round of the survey) and at six months (second round of the survey) with reminders sent at two and four weeks after the postal questionnaire.

Questionnaire

Respondents were asked to provide details of healthcare resource consumption, work status and disease severity during the previous three months. Disease severity was measured using the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and the Bath Ankylosing Functional Index (BASFI) (10, 11). The BASDAI consists of six visual analogue scales dealing with fatigue, spinal pain, joint pain, localised tenderness and quality and quantity of morning stiffness over the past week. Using the average of the latter two items, the resulting five scores are summed and transformed to a 0–10 scale where higher scores indicate higher disease activity. The BASFI consists of eight visual analogue scales dealing with physical function and two scales reflecting the patient's ability to cope with daily activities. Scores are summed and transformed to a 0–10 scale where higher scores indicate higher functional disability.

Resource consumption directly attributable to AS included: medications (disease-modifying anti-rheumatic drugs [DMARDs] and anti-tumour necrosis factor [anti-TNF] agents), hospital inpatient duration, hospital outpatient appointments (physiotherapy, hydrotherapy) and GP appointments. Physiotherapy and hydrotherapy sessions were identified as either National Health Service (NHS) funded or self-funded by the patient. The impact of AS on work status was described in terms of unemployment or early retirement due to AS, unemployment or early retirement unrelated to AS, absenteeism (number of days off work due to AS) and presenteeism (the percentage decrease in work productivity due to AS relative to a healthy worker norm). Presenteeism was measured using the Work Limitations Questionnaire (WLQ-16) (12) which covers four domains: mental demands (6 items), output demands (4 items), time management demands (2 items) and physical demands (4 items). The individual scales range from 0 (limited none of the time) to 100 (limited all the time) and the overall WLQ is calculated by averaging the four limitation scales. The percentage of productivity

is then calculated by multiplying the WLQ score by 25% (12).

Healthcare costs

Direct healthcare costs included costs attributable to the NHS, while total healthcare costs also included costs incurred by the patients (self-funded). The cost of medications were obtained from the British National Formulary (13) and the costs associated with inpatient hospital admissions, GP appointments, outpatient clinic attendances and physiotherapy sessions funded by the NHS were obtained from national reference costs (14, 15). The unit cost associated with self-funded physiotherapy sessions was obtained from a private health company and the National Ankylosing Spondylitis Society (NASS) (16, 17). Costs were inflated to 2008 using the hospital and community health services (HCHS) pay and price inflation (15). Unit cost multipliers were applied to the quantity of each healthcare resource used at the individual level. Results were summed to obtain the total three-month healthcare costs.

Non-medical indirect costs

Productivity losses were calculated for a three-month period using the human capital approach and comprised of unemployment/early retirement, absenteeism and presenteeism due to AS. Absenteeism cost was ascertained using the number of days of absence from work during the three months and the assumption that individuals work on average five days per week. Respondents who reported they did not work due to AS were assigned 100% productivity losses over the full three-month period. Presenteeism was quantified by the relative reduction of productivity while at work (relative to a healthy worker norm) using the calculated WLQ index score. Productivity losses were calculated among patients within the working age (using a maximum limit of 65 years). Productivity losses were valued using the reported income where available, or the average weekly/hourly gross pay in England sub-grouped by age and sex categories (18).

Statistical analyses

Data analysis was performed with the statistical packages SPSS (version 14) (19) and STATA (version 10) (20). Summary statistics were calculated for demographic variables (age, gender), disease characteristics (BASDAI, BASFI), health resource use and associated costs. Descriptive statistics for healthcare use and costs were compared using the following sub-groups: employment status (employed *vs*. unemployed), disease severity (BASDAI <4 *vs*. BASDAI ≥4), function (BASFI <4 *vs*. BASFI ≥4), and gender. Independent *t*-tests (assuming unequal variances) were used for continuous variables, χ^2 for categorical variables and one-way ANOVA were used where appropriate to compare more than two groups of patients (21) with significance set at the $p<0.05$ level.

Despite the relatively good completion of the survey, there were some inconsistencies in the data and some incomplete information such as missing data. The following rules were used to overcome these issues. Where there was evidence of hospital resource consumption, the mean number of hospitalisation days/visits were imputed. Furthermore, missing data relating to absenteeism or work productivity were treated as no absenteeism and no loss in productivity respectively.

A statistical regression model was constructed to evaluate the impact of disease activity and demographics on the total costs using data (n=612) collected during the first round of the survey. The independent variables included BASFI, BASDAI, the interaction between BASFI and BASDAI, age, gender and disease duration. A two-part model was used to account for the substantial proportion of patients who incurred no healthcare resources and the skewed distribution of costs for those who did incur healthcare resources. The first part consisted of a logistic regression to model the probability of incurring a cost within the three-month period. The second part consisted of a generalised linear model (GLM) to estimate the total costs incurred, conditional on incurring any costs. The modified Park test was used to select the appropriate distribution (Poisson) assuming a log link (22).

The performance of the model was evaluated by applying the estimated two-part model to the data (n=470) collected during the second round of the survey. The goodness of fit was assessed using standard statistics (mean, SD, range) while the predictive ability was assessed using the mean error (ME), mean absolute error (MAE) and root mean squared error (RMSE). The predictive ability was assessed using both individual level data and mean values for cohorts sub-grouped by disease severity.

Results

Patient demographics

Of the 1,000 patients invited to take part in the survey 61.2% (n=612) completed the questionnaire. Of those patients, 76.8% (n=470/612) completed the questionnaire at both points in time and 23.2% (n=142/612) at baseline only. The majority of respondents at baseline were male (441/612) and the mean age was 51 years. The average BASDAI (BASFI) at baseline was 4.57 (4.60) and 55.3% (54.8%) had a BASDAI score greater than or equal to 4. When sub-grouping by employment status and comparing individuals who reported being in employment (n=336), with those who reported being either unemployed due to AS (n=151), or unemployed due to other reasons (n=125), there were statistically significant differences in mean BASDAI scores (3.6 *vs*. 6.6; 3.6 *vs*. 4.8, ANOVA F=97.22, $p<0.0001$), mean BASFI scores (3.2 *vs*. 7.2; 3.2 *vs*. 5.3, ANOVA F=171.92, $p<0.0001$) and disease duration (13.9 *vs*. 19.6 years; 13.9 *vs*. 23.6 years, ANOVA F=36.07, $p<0.0001$). Furthermore, comparing respondents at baseline and six months (Table I), no significant differences were found for age, gender, disease duration, BASDAI or BASFI ($p>0.05$).

Healthcare utilisation over three months during the first round of the survey

Of the 612 respondents who completed the first questionnaire, a large proportion (41%) reported using no healthcare

Table I. Characteristics of patients completing the questionnaires.

	All respondents		Base *vs*. 6-month
	Baseline	6-month	*p*-value
n	612	470	
Male, (%)	72.0	72.3	0.905
Age in years, mean (range)	50.8 (20–81)	51.9 (20–81)	0.128
% aged ≤64 years old	87.3	85.2	0.319
Disease duration in years, mean (range)	17.3 (1–60)	17.9 (1–60)	0.387
BASFI, mean (SD)	4.60 (2.86)	4.69 (2.91)	0.601
BASDAI, mean (SD)	4.57 (2.57)	4.35 (2.67)	0.175

resources due to AS and 45% consumed no NHS funded healthcare resources. There were 10 hospitalisations due to AS (mean duration of stay =11.1 days) with one individual hospitalised for 43 days. Thirty-five percent (n=217) reported at least one consultation with a GP (mean number of consultations =2.4). Individuals were more likely to consult their GP if they had greater disease activity (BASDAI <4, BASDAI ≥4; 20.5% *vs*. 47.8%; $p<0.001$), greater loss of function (BASFI <4, BASFI ≥4; 21.2% *vs*. 46.7%; $p<0.001$) or were not working (41.7% *vs*. 30.4%; $p=0.004$). Similarly, the mean number of consultations was higher for respondents with a greater disease activity (2.6 *vs*. 1.7; $p<0.001$), higher loss of function (2.6 *vs*. 1.8; $p<0.005$) and non workers (2.8 *vs*. 1.9; $p<0.01$).

Only 26.6% (n=163) reported they received at least one of the following medications; sulphasalazine, methotrexate, infliximab, etanercept or adalimumab and approximately half of these (44%; n=71/163) were on anti-TNF therapy. While individuals were more likely to receive medications if they had greater disease activity (21.6% *vs*. 30.9%; $p<0.05$) or greater loss of function (17.5% *vs*. 33.7%; $p<0.001$), there was no statistically significant difference between workers and non-workers ($p=0.054$) or gender ($p=0.735$).

Over 19% (n=118) and 11% (n=65) of respondents attended at least one physiotherapy or hydrotherapy session respectively. Physiotherapy was more likely for females than males (26.9% *vs*. 16.1%; $p<0.005$) but there was no difference when sub-grouped by either disease activity (BASDAI <4 *vs*. BASDAI ≥4; $p=0.1$), loss of function (BASFI <4 *vs*. BASFI ≥4; $p=0.054$) or work status (employed *vs*. not employed; $p=0.109$). Hydrotherapy was more likely for those with greater disease activity (7.3% *vs*. 13.4%; $p<0.05$), greater loss of function (5.8% *vs*. 14.8%; $p<0.001$) and the non-workers (13.4% *vs*. 8.3%; $p<0.05$), but there was no significant difference for males ($p=0.363$). Among those attending physiotherapy or hydrotherapy sessions, approximately 33% (n=39) and 46% (n=30) had at least one self-funded physiotherapy or hydrotherapy session respectively. Of particular note, the mean number of physiotherapy (hy-

Table II. Resource consumption and 3-month costs associated with AS sub-grouped by disease severity.

	BASDAI <4 (n=273)			4≤ BASDAI <6 (n=137)			BASDAI ≥6 (n=198)					
	n (%)	mean number	mean cost	n (%)	mean number	mean cost	n (%)	mean number	mean cost	n (%)	mean number	mean cost
Hospital (days)	1 (0.4)	2	£1.69	1 (0.7)	1	£1.68	8 (4.0)	13.5	£124.44	10 (1.6)	11.1	£41.80
Doctor visit (visits)	56 (20.5)	1.7	£18.28	49 (35.8)	1.7	£30.80	112 (56.0)	3.1	£89.06	217 (35.5)	2.4	£44.16
NHS physiotherapy (session)	30 (11.0)	1.9	£4.32	18 (13.1)	2.3	£6.32	37 (18.5)	2.4	£9.43	85 (13.9)	2.2	£6.42
NHS hydrotherapy (session)	12 (4.4)	5.1	£13.70	10 (7.3)	8.7	£38.97	16 (8.0)	7.5	£36.85	38 (6.2)	7.1	£26.88
NHS consultation and inpatient costs			£38.00			£77.78			£259.79			£119.26
Sulphasalazine	26 (9.5)		£2.61	13 (9.5)		£2.60	34 (17.0)		£4.66	73 (11.9)		£3.27
Methotrexate	17 (6.2)		£0.57	9 (6.6)		£0.60	25 (12.5)		£1.14	51 (8.3)		£0.76
Infliximab	9 (3.3)		£102.73	4 (2.9)		£90.99	7 (3.5)		£109.07	20 (3.3)		£101.84
Etanercept	13 (4.8)		£110.65	10 (7.3)		£169.62	15 (7.5)		£174.28	38 (6.2)		£144.29
Adalimumab	6 (2.2)		£51.07	3 (2.2)		£50.89	4 (2.0)		£46.48	13 (2.1)		£49.36
Drug cost costs			£267.64			£314.69			£335.62			£299.51
Direct healthcare costs (NHS)			£305.63			£392.46			£595.41			£418.77
Private Physiotherapy	17 (6.2)	7.2	£7.87	9 (6.6)	6.3	£5.08	13 (6.5)	7.8	£9.52	39 (6.4)	7.2	£7.76
Private Hydrotherapy	9 (3.3)	7	£2.37	6 (4.4)	7.3	£16.68	15 (7.5)	14.3	£86.66	30 (4.9)	10.7	£33.11
NASS Subscription cost	15 (5.5)		£0.12	8 (5.8)		£0.13	11 (5.5)		£0.06	34 (5.6)		£0.10
Healthcare cost (private only)			£10.37			£21.88			£96.24			£40.98
% employed	204 (74.7)			81 (59.1)			50 (25.0)			336 (54.9)		
% unemployed due to AS	19 (7.0)			27 (19.7)			105 (52.5)			151 (24.7)		
% other	50 (18.3)			29 (21.2)			45 (22.5)			125 (20.4)		
Absenteeism (days)	16 (5.9)	6.9	£23.97	14 (10.2)	4.8	£36.97	20 (10.0)	13.1	£60.10	50 (8.17)	8.78	£38.61
Presenteeism (%)	173 (63.4)	13.3	£509.07	80 (58.4)	25.1	£811.58	48 (24.0)	36.5	£370.28	302 (49.35)	20.1	£531.83
Unemployment, early retirement			£481.53			£1,526.67			£3,717.68			£1,771.48
Cost of productivity losses			£1,014.56			£2,375.22			£4,148.05			£2,341.92
Total Cost			£1,3330.56			£2,789.56			£4,839.70			£2,801.67

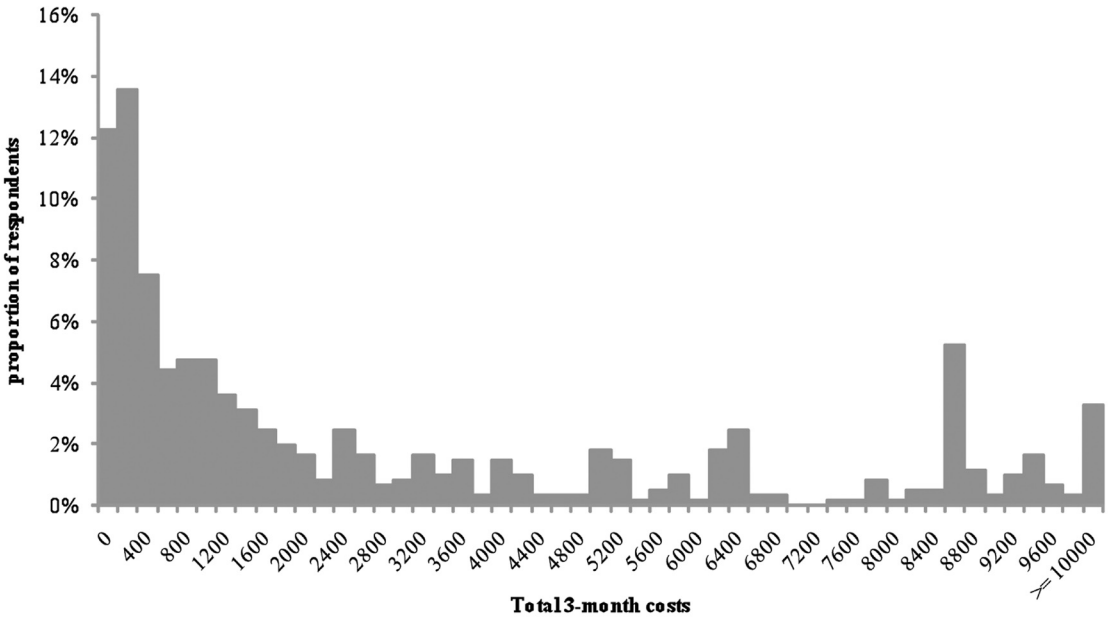

Fig. 1. Distribution of 3-month total costs.

drotherapy) sessions for those who had at least one self-funded session was 7.6 (11.3) compared to 2.2 (7.1) for those who received only the NHS sessions ($p<0.05$). Among respondents with self-funded physiotherapy sessions, no significance difference was observed for the number of self-funded physiotherapy sessions when sub-grouped by disease activity ($p=0.966$), loss of function ($p=0.571$), work status ($p=0.903$) or gender ($p=0.772$). On the other hand, respondents with greater disease activity had more self-funded hydrotherapy sessions than those less severely affected (12.3 *vs*. 7.0; $p<0.05$). Similarly, respondents who were not working had more self-funded hydrotherapy sessions than those who were working (13.1 *vs*. 7.1; $p<0.05$). No difference was observed by gender ($p=0.071$) or loss of function ($p=0.089$).

Employment status and productivity losses

Approximately 25% (n=151) of respondents reported either not working or retiring early due to AS (Table II) while 20% (n=125) reported not working due to other causes. Of the respondents who were in employment (n=336); 14.9% (n=50) and 89.9% (n=302) reported being absent from work due to AS or a reduction in productivity while at work due to AS respectively. The mean number of days absent from work due to AS over the three-month period was 8.78 (range = 1 to 62 days) and the mean reduction in productivity while at work was 20% (range = 1 to 90%) among employed patients. When sub-grouping by disease activity; a significant difference was found for the reduction in productivity (13.3% *vs*. 29.4%, $p<0.001$) but not for the number of days absent from work ($p=0.548$). Similarly, a significant difference was found for the reduction in productivity when sub-grouping by loss of function (15.1% *vs*. 28.3%; $p<0.001$) but not for the number of days absent from work ($p=0.826$).

Total costs

A substantial proportion (41%) of patients did not incur any healthcare costs. Of those who did, the distribution of costs was heavily skewed with a small number incurring relatively high costs (Fig. 1). The average three-month direct healthcare cost from a NHS perspective was £419±£985 (median=£27). Seventy-one percent of direct costs were due to anti-TNF agents, less than one percent was due to DMARDs, and 20.5% were due to GP consultations and hospitalisations.

When including self-funded healthcare costs, and productivity losses due to absenteeism and presenteeism, the average three-month total cost increased to £2,802±£3,376 (median=£1,160). The majority of these costs (63%) were attributable to unemployment or early retirement due to AS while presenteeism and absenteeism represented 19.0% and 1.4% of the total cost respectively. When sub-grouping, there was a significant difference in the mean total costs for those with greater disease activity (£1,331 *vs*. £4,006; $p<0.001$), those with greater loss of function (£1,208 *vs*. £4,131; $p<0.001$), those not working (£1,376 *vs*. £4,537; $p<0.001$) and males (£1,916 *vs*. £3,137, $p<0.001$).

Exploring the relationship between disease severity and total costs

The three-month total cost correlated with both disease activity (BASDAI, r=0.46, $p<0.001$) and functional impairment (BASFI, r=0.53, $p<0.001$). When sub-grouped by disease severity (Fig. 2), using bands informed by the Assessments in Ankylosing Spondylitis Working Group (ASAS) and the British Society of Rheumatology (BSR) guidance (4, 10), respondents in the moderate group (BASDAI <4.0, n=273) had a mean total cost of £1,331 (median £502), respondents in the severe group (4.0 ≤ BASDAI <6.0, n=137) had a mean total cost of £2,790 (median £1,281) and respondents in the very severe group (BASDAI ≥6, n=200) had a mean total cost of £4,840 (median £5,017).

Table III provides the coefficients and standard errors that can be used to predict the three-month total costs. The

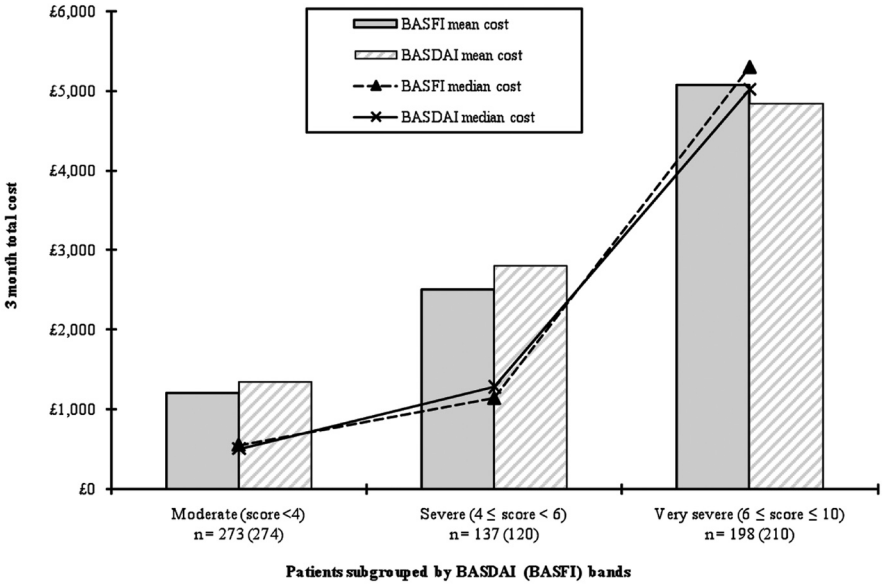

Fig. 2. Mean 3-month total costs sub-grouped by disease severity.

Table III. Regression equations to derive the probability of incurring total costs, conditional on incurring a cost.

	Including anti-TNF costs	
	Coefficient	Standard error
First part: equation to obtain the probability of incurring costs		
BASFI	0.16716	0.12083
BASDAI	0.37053	0.14822*
BASFI*BASDAI	-0.02468	0.02178
Male	0.33778	0.29682
Age	-0.04389	0.01335*
Disease duration	-0.01373	0.01229
Constant	2.71795	0.74958
Second part: equation to obtain the 3-month total costs conditional on costs being incurred		
BASFI	0.27548	0.00075*
BASDAI	0.13265	0.00099*
BASFI*BASDAI	-0.01602	0.00013*
Male	0.46458	0.00202*
Age	-0.01656	0.00009*
Disease duration	0.00381	0.00008*
Constant	6.79876	0.00578*

First part is derived using a logistic regression model, second part is derived using a generalised linear model. *p<0.05.

first part is a logistic regression to model the probability of incurring any costs, and the second part is a GLM model to predict the three-month cost, conditional on incurring any cost. Only age and disease activity were significantly associated with the probability of incurring costs while disease activity, function, disease duration, age and gender were all significant predictors of total costs conditional on incurring costs.

Model validation

The predictive ability of the model was assessed on the data collected during the second round of the survey. Comparing the summary statistics for the individual level predictions (n=470), the predicted mean total cost (£2,814±£2,110, range: £228–£10,604) was comparable with the observed value (£2,927±£3,455, range: £0–£13,313) and the RMSE was £2,754.

When sub-grouping by BASDAI score (Fig. 3), the mean observed costs during the second round of the survey ranged from £636 for the least severely affected (BASDAI <1) to £5,539 for the most severely affected (BASDAI >9). These are comparable with the corresponding predicted mean values of £605 and £5,839.

Discussion

In this study we report the healthcare use and the work related costs associated with patients with AS using a large sample randomly selected from registries of 10 secondary care rheumatology centres in the UK. Healthcare use, employment status and productivity losses were all influenced by disease severity and activity. While the mean three-month cost from a NHS perspective was £419 (median £27), when including self-funded healthcare costs and indirect costs associated with unemployment, early retirement and productivity losses, the mean total three-month cost associated with AS increased to £2,802 (median £1,160) with productivity losses accounting for about 84% of total costs.

A substantial proportion (45%) of respondents did not consume any direct healthcare resources. Individuals with higher levels of disease activity reported using more healthcare resources, including outpatient appointments and therapy sessions. From a societal perspective, the costs associated with pharmacological interventions (DMARDs and anti-TNF agents) were small. Other studies have reported drug costs ranging from less than one percent of total costs (including indirect costs) in the Netherlands to 18% in Belgium (23). However, when looking at the cost from a NHS perspective, due to the high cost of anti-TNF treatments, the costs associated with pharmacological treatment represented about 72% of direct costs in our study. Costs associated with NHS funded physiotherapy and hydrotherapy sessions contributed to 26% of our NHS consultation and inpatient costs, but as was shown in another UK cohort, AS patients personally fund a substantial number of sessions (24). In the current study, approximately 9.5% of patients funded private sessions and the mean number of sessions was larger for those with greater disease activity (BASDAI ≥4) and those not working, particularly for hydrotherapy sessions.

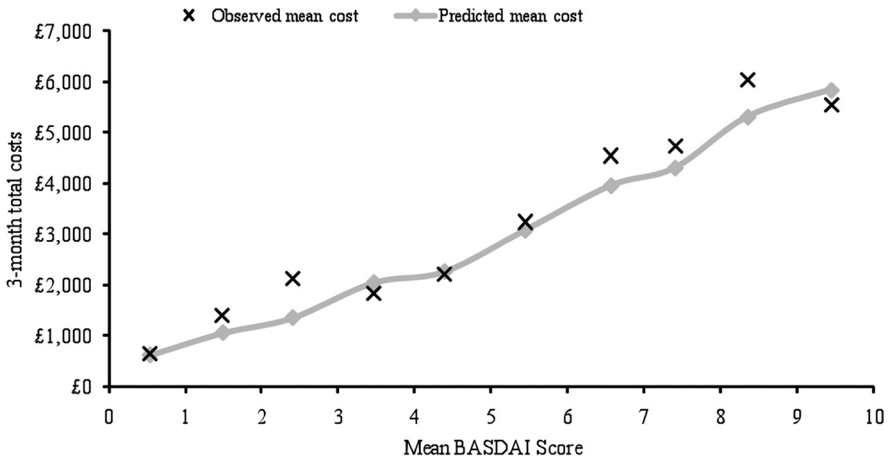

Fig. 3. Observed and predicted mean three-month total costs sub-grouped by disease severity.

As shown in previous studies, direct healthcare costs represent a small (approximately 16%) proportion of the total cost associated with AS (8). Approximately 25% of respondents in the current study were not working due to AS. This is comparable to proportions reported in previous studies: 23.1% in the UK (8), 17% in China (7) and 24.5% in Spain (23). About 62% of respondents of working age were employed/self-employed compared to 70% of females and 79% of males in the general population in the UK (25). Our data are similar to employment rates (54%) reported for a Dutch cohort with AS (23). In the current study, 15% of working respondents had days off sick (mean 8 days) and 90% of working respondents had a reduction in productivity (mean 20%) due to AS. In the literature, reported levels of sick leave due to AS range from 86% (mean annual duration of 8 days) in China (7) to 27% (mean duration of 55 hours per annum) in Europe (23). Productivity losses accounted for about 84% of costs in our study compared to 60% in Spain (26).

The mean total annualised cost per patient (£11,207) is approximately 1.7 times higher than the mean total cost (£6,765) reported in a previous UK study (8). The difference is due to a larger proportion of respondents in the current study reporting a reduction in productivity while at work (49% *vs*. 7%) and unemployment or early retirement due to AS (25% *vs*. 23%). There was also a large difference in the mean cost associated with early retirement/unemployment due to AS when annualised (£3,183 *vs*. £7,086). In addition, respondents in our study were younger (51 *vs*. 57 years) and had a shorter disease duration (17 *vs*. 30 years). However, a larger proportion of respondents of working age in our study were in employment (62% *vs*. 51%). For comparison, a recent review of cost-of illness studies in AS estimated the overall mean costs of AS to be €9,374 per year, but did not included presenteeism (27, 28).

As in other studies (7, 8), both BASDAI and BASFI were shown to be independent predictors of total costs. When used to predict total costs using the data collected during the second round of the survey, the estimated model was found to have reasonable predictive performance both on an individual basis and when sub-grouping by disease severity.

Many patient cohorts used in AS research are derived from large tertiary referral centres or from patients who are members of AS related societies. There is a concern that these patients are more likely to either have more severe AS or originate from higher social groups, as they are self-selected. AS patients recruited from secondary care centres are more likely to be representative of the patients seen in most treatment centres and the sites used in the survey were selected to provide a diverse socio-economic and geographic population (29), hence the results are generalisable to AS patients across the UK. When comparing the data used in this study with those in a previous UK study (8), the respondents in the current study were more severely affected by AS with a higher proportion of respondents reporting a BASDAI (BASFI) greater than or equal to 7 (21% *vs*. 13%; 25% *vs*. 22%).

While this study provides valuable information about direct healthcare use and total costs associated with AS, there are several limitations. Firstly, the inherent nature of the survey may have introduced a bias as respondents were asked to provide information on healthcare use during the previous three months. Consequently responses were based on the memory of patients. Secondly, patients were asked to provide details about medical healthcare resources directly associated with AS. This may have underestimated the total direct healthcare resources associated with AS as data for prevalent co-morbidities such as cardiovascular disease and uveitis were excluded (5). Conversely, as respondents were asked to make a judgement on whether healthcare utilisation was caused by AS or other disease they may have incorrectly assumed they were for AS. Thirdly, healthcare resources were limited to hospitalisations, GP visits, physiotherapy/hydrotherapy session and a selected set of medications. The cost associated with NSAIDs was not included in our study, and while not high, a substantial proportion of patients are expected to receive such treatment. Information on diagnostic tests, which have been reported to contribute to 32% of AS direct healthcare costs were not collected (7). Likewise, information on the amount of informal care received was not collected and this too has been shown to be associated with a large cost for patients with AS (7, 8, 26). Finally, hospitalisation costs were valued using the length of stay and an average unit cost in the absence of information about the reason for hospitalisation. This may represent a limitation given hospital costs can vary considerably. A micro-costing study informed with detailed resource and cost data would provide more accurate information.

A recent study has concluded that anti-TNF agents appear to improve capacity for work (4, 30) and given that the

majority of costs in the current study are attributable to work related components, the findings are encouraging. Our survey was conducted in 2008, a few months after NICE recommendations on the usage of these treatments in AS patients which explains the relatively small proportion of patients treated with anti-TNF therapies (approximately 10%). It is therefore likely that the anti-TNF medication costs for a similar cohort will rise as anti-TNFs become more widely prescribed. Due to the nature of the survey, it was not possible to determine the effect of anti-TNF agents on the capacity to work as data collected from patients before and after initiation of these agents were not available. It is likely that prior to treatment, the individuals receiving anti-TNF agents were in a group of patients with more severe disease. Additional research examining interventions and measures that improve both presenteeism and absenteeism while in work will have the largest effect on the cost to society.

Conclusion

This study shows that direct healthcare costs alone do not describe the total societal costs associated with AS and that productivity losses associated with AS are considerable. Additional research examining interventions and measures that maintain employment, encourage return to work, and improve both presenteeism and absenteeism in work are likely to have the largest effect on the cost to society.

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