# Costs and work limitation of patients with ankylosing spondylitis in China

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# Abstract Objective

To access the annual direct, indirect costs and work limitation of AS patients in the Chinese population and explore the determinants of cost.

#### Methods

A retrospective, cross-sectional study was performed in 257 patients with AS in China. The participants completed questionnaires about disease characteristics, quality of life and direct and indirect costs. Only the patients with paid-work completed the Work Limitation Questionnaire (WLQ), a 25-item questionnaire that accesses the impact of chronic health conditions on job performance and productivity. Functional impairment and disease activity were assessed using the Bath Ankylosing Spondylitis Functional Index (BASFI) and the Bath Akylosing Spondylitis Disease Activity Index (BASDAI).

Quality of life was measured by the Short Form-36.

#### Results

Of the 257 patients who completed the questionnaires, the mean age was 28.5 (SD=0.5) with mean disease duration of 6.52 years (SD=0.44). The mean BASDAI and BASFI score was 3.28 and 1.3, respectively. Among the 257 patients, 21.8% are students, 64.2% have a paid job and 10.5% without a job because of AS. 165 participants finished the WLQ with a mean WLQ index of 0.19 which corresponds to a 17% decrease in productivity. The annual estimated costs of each patient was \$2714.18 while the indirect cost accounted for 64.7%. The annual direct cost significantly correlated with disease activity.

#### Conclusion

Our research is the first to provide information about the burden of AS and the work status of AS patients in mainland China, which may help to establish the treatment strategy and a policy of support.

#### **Key words**

ankylosing spondylitis, cost of illness, quality of life

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#### Introduction

Ankylosing spondylitis (AS) is a chronic inflammatory disease with characteristics of pain and stiffness of the back. It can also involve peripheral joints and extra-articular sites. As it affects young men typically and has a considerable impact on the work capacity and quality of life, the substantial burden of patients and society is huge. In China, the prevalence of AS is 0.24% (1) (ranged from 0.06-0.54%) (2) compared with which is 0.075-0.85% in Western Europe (3). According to a study compared the difference of clinical features of AS patients between southern and northern in China, the male to female ratio is 4:1 and the mean age at onset of AS is mostly in the early 20s (4). Due to the large population of China, there are a good deal of patients who are suffering from AS not only for the painfulness in everyday life but also the grave burden on economics. Besides, with the progression of AS, part of patients will develop into serious deformity which will have a great influence on people' daily life. Treatments which can relieve pain and slow down the progress of this disease will ameliorate the quality of life and help patients work better.

The amount of annual total costs of AS varies from country to country, and the direct costs have generally increased due to the use of biological therapy. Biological therapy is very expensive and is not covered by the social insurance in China. In addition to the direct costs correlated to healthcare resource, indirect costs are also considerable which include absenteeism from work, loss of productivity and early retirement. Individuals with ankylosing spondylitis have a high prevalence of workrelated disabilities, ranging from 4% at 5 years after disease diagnosis to 50% at 45 years (5) after diagnosis. For this reason, costs due to productivity loss were estimated to be the major part of the total costs in the previous studies (6-10). Treatments in order to relieve pain and improve work capacity may help to reduce the indirect costs and can compensate for the high cost of expensive drugs. The cost effectiveness of biological agents in AS is controversial. McLeod et al. concluded that

the short-form economic assessment indicated that none of the three anti-TNF agents is likely to be considered cost-effective at current acceptability thresholds, with infliximab consistently the least cost-effective option. However, some studies have found that anti-TNF therapy would be cost-effective from the societal perspective. Without a standard acceptable threshold, it is hard to access the cost-effectiveness of anti-TNF agents. Long-term study would be needed in order to estimate the longterm effect of anti-TNF treatment on disease activity and work capacity and have a better understanding of the costeffectiveness of these new drugs.

The objective of this study was to access the annual direct, indirect costs and work limitations of AS patients in a Chinese population and explore the possible predictors of costs.

#### Materials and methods

A sample of 257 patients was admitted from the Rheumatology centre of the 3<sup>rd</sup> affiliated hospital of Sun-Yat University between March 2012 and May 2013. These patients were diagnosed as AS according to the modified New York criteria and agreed to complete the questionnaire we designed for this study.

The respondents were invited to provide information about healthcare resource consumption, work status and quality of life during the previous few months. Disease severity was measured by the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and the Bath Ankylosing Spondylitis Functional Index (BASFI) was used to measure physical function, both ranging from 0 to 10 and higher score indicate higher disease activity or worse physical function. Additionally, the Health Assessment Questionnaire disability index was used to detect 8 functional areas including dressing, rising, eating, walking, hygiene, reaching, gripping and usual activities. The score of each area can be ranged from 0 (no difficulty) to 3 (unable to do) and the scores of 8 functional area are averaged to get the HAQ disability index.

Resource consumption includes direct costs and indirect costs caused by AS. Direct costs were estimated including

medications, hospital outpatient appointments and hospital inpatient durations. Physical therapy and traditional Chinese therapy were also accounted. The non-healthcare related direct cost comprised transportation fees and paid helper for household. Indirect costs were described in term of unemployment, sick leave, reduced work productivity and early retirement due to AS. People who have paid-work were asked to finish the Work Limitation Questionnaire (WLQ) (11) which covers 4 domains: mental demands, output demands, time management demands and physical demands. Four individual scale scores were created to provide a summary of the amount of time in the prior two weeks that the employee was limited in each job task dimension. Then, the scale was weighted to form a productivity loss score indicating an estimated percentage of at-work productivity loss due to disease. Presenteeism was assessed with the reduction of productivity while at work using the WLO index score. Absenteeism cost was estimated using the number of days of absence from work during the previous month. Individuals who reported they did not have work due to AS were considered as 100% productivity loss over the past 2 weeks. Productivity loss was valued using the reported income where available, or the average weekly pay in China. The human capital approach was used to calculate indirect costs and three months resource consumption was multiplied by four to obtain one-year costs (12). Quality of life was accessed with a validated Chinese translation of the SF-36 which contains 36 items. Eight multiitem scales were created to measure the physical and mental function. These scales include the dimensions physical functioning, physical role functioning, social functioning, emotional role functioning, mental health, vitality, bodily pain, and general health. Both the scales and summary scores may vary from 0 to 100, and lower scores indicate a worse health status. The reliability and validity of Chinese version short form SF-36 had been confirmed to be valid in Chinese population (13). The data was analysed with the statis-

**Table I.** Demographics of 257 AS patients in China.

Item	Mean, %	SD	Range
Male	83.3% (214)	_	_
Age (year)	28.53	0.54	(13–57)
Patients with paid-work	64.20% (165)	NA	NA
Disease duration (year)	6.52	0.44	(0.02-38)
BASDAI	3.28	0.12	(0-8.94)
BASFI	1.30	0.12	(0-9.57)
HAQ (range 0–3)	0.22	0.26	(0-2)
SF-36 general health (range 0–100)	46.61	1.45	(0-100)
SF-36 mental health (range 0–100)	62.83	1.62	(15–100)

BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; HAQ: Health Assessment Questionnaire; SD: standard deviation; NA: not applicable.

tical packages SPSS (version 13.0). Summary statistics were calculated for demographic variables such as age, gender, disease duration and etc. Descriptive statistics for direct and indirect cost were compared using the BASDAI sub-groups. Stepwise multiple linear regression analysis was used to determine the drivers of the costs and productivity loss score.

#### Results

Of the 257 participants, the mean age was 28.5 years old with a mean disease duration of 6.5 years and 214 were male. The mean BASDAI and BASFI score were 3.28 and 1.3, respectively. The mean SF-36 general health score was 46.6 and the mental health score was 62.8, indicating the physical and mental function of AS patients were impaired compared with normal people. The mean HAQ disability index score was 0.22 suggesting mild functional impairment. (The demographics of this sample are presented in Table I).

#### Resource consumption

Hospitalisation was very limited in this sample and only 14 patients with a total of 149 inpatient days, establishing a mean of ten days per patient per year. Only 1 patient underwent spinal orthopaedics in the past three months. A total of 362 outpatient visits were calculated in the past 3 months (Table II). According to that, 5.6 outpatient visits was estimated per patient per year and most of them came to rheumatology department for help. Most of these examinations are for diagnosis and observation of effectiveness of treatment such as erythrocyte sedimentation rate

**Table II.** Health resource consumption of AS patients in the past three months.

Item	Frequency	
Hospitalisation	14	
Outpatient visits	362	
Rheumatology visits	240	
Surgical visits	62	
Medicine visits	26	
Massage	20	
Traditional Chinese medicine visit	s 7	
Ophthalmology visits	7	
Examinations	618	
X-ray	83	
MRI scans	46	
CT scans	27	
Blood tests	462	

and C-reactive protein. About 10% patients had not come for medical help in the past three months until they visited the clinic of our department.

The mean annual cost per patient was \$2714.18 with indirect costs representing 64.7%. Drug costs represented about 33% of the direct cost and 11.7% of the total costs while examination cost accounted 21% of the direct costs and 7.4% of the total costs (The annual total costs per patient are shown in Table III). Additionally, 27 participants went for traditional Chinese medication help and the average cost per patient was \$133.88 per year. Hospitalisation was occasionally seen in 14 patients of our group, where the cost per patient per year was \$1736.8. Costs were not normally distributed because a s,all part of the patients had higher costs. Only sixteen participants reported that they did not have any cost because of AS during the past 3 months. When we divided all the patients into 5 groups according to the BASDAI score, the patients with a higher BASDAI score

Table III. Annual costs per patient per year in China (2012 US dollar).

	Mean cost (\$)	SD	% of total cost
Direct cost	958.48	100.74	35.3%
Inpatient cost	233.43	18.41	8.6%
Outpatient attendence	35.90	8.18	1.3%
Medications	318.45	41.83	11.7%
Tests	200.56	17.65	7.4%
Emergency cost	22.87	1.85	0.84%
Non-medical costs	147.27	23.8	5.46%
Indirect cost	1755.69	140.41	64.7%
Productivity loss	1608.90	136.68	59.3%
Sick leave	146.79	30.62	5.4%
Total cost (n=257)	2714.18	173.43	-

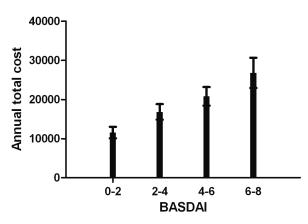
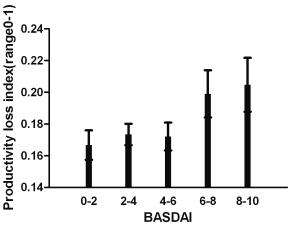


Fig. 1. The annual total costs per patient by disease activity. Only 2 patients' BASDAI score was between 8 to 10, so that the data was not covered in this figure. The severer the disease activity was, the higher costs would be.

Fig. 2. Productivity loss index

by BASDAI.



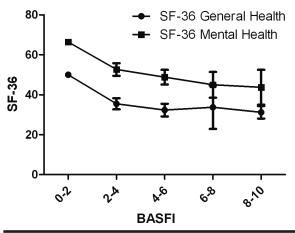


Fig. 3. Utility (SF-36 General Health and SF-36 Mental Health) by BASFI. Scores in the most severe group must be considered carefully since they are based on fewer than 10 patients.

had a higher annual cost (Fig. 1). Costs ranged from \$1839.1 with BASDAI≤2 to \$4265.2 for BASDAI≥6. In our group, BASDAI and SF-36 physical health were the meaningful cost drivers while age, disease duration, BASFI, SF-36 general health and SF-36 mental health were not. When one BASDAI was increased, it cost \$287.6 per patient per year on average and the 95% confidence interval was 202.1–490.9. Patients with worse disease activity accrued more health resources consumption and costs.

#### Work status

In our research, 64.2% AS patients had paid-work, 21.8% of the studied patients were students, 10.5% of them thought they could not work due to AS, and 3.5% patients did not have a job because of other reasons. Most participants (98%) had impaired work productivity with a mean WLQ index of 0.19 which corresponds to a 17% decrease in productivity. A quarter of paid-work patients reported that they needed sick leave for the past month with a mean duration of one day per month and the estimated sick leave per year was 12.5 days. The productivity loss score (PLS) was negatively correlated with disease duration and had a positive relationship with BASDAI. The longer the disease duration, the more severe the productivity loss. The mean PLS was 0.16 with the patients whose BASDAI scores were less than 2, while it would increase to 0.20 when the BASDAI score came to 8–10 (Fig. 2). The worse disease activity a patient had, the more critical the productivity loss.

## Quality of life

Multiple linear regressions were performed to explore the possible relationship between SF-36 general health, mental health and BASDAI, BASFI, disease duration, HAQ index. The result was that SF-36 general health was related to both BASFI score and disease duration. And BASFI was the only meaningful predictor of SF-36 mental health. As a result of AS, QOL was mildly impaired and had a close relationship with functional impairment (Fig. 3).

#### Discussion

Only one article has described costs and quality of life of AS patients in Hong Kong, China (10). Due to the difference of medical policy and health care insurance system between Chinese mainland and Hong Kong, it is valuable for us to investigate the costs, work status and quality of life of AS patients in Chinese mainland.

In our study, 83% of patients were male, with a mean age of 28.5 years, which are much younger than in other studies (6-7, 14-15). Meanwhile, the mean disease duration of our research was much shorter compared to Brazil (7), England (6) and Spain (15) (6.5 vs. 16, 17, 19 years). This may be explained by the improvement of early diagnosis of AS in recent years. Both doctors and patients know more about this disease and come to help earlier. Besides, the way the data was collected was different: for the patients who were admitted to our study it was the first time they had come to our hospital. As a result of younger age and shorter disease duration, the functional capacity was less impaired in our group. The mean BASFI score of our research was 1.3 while it was 5 in the Brazilian group, 4.6 in the UK group and 3.8 in the Spanish group. About 80% of BASFI scores were less than 2. The mean BAS-DAI score was 3.3, which was similar to the other studies.

The employment rate of AS patients in this research was similar to the previous studies which was ranged from 34%-96% (5). According to WLQ, the estimated productivity loss was about 17% which was similar to the study in England (20%) (6). The work disability rate was assumed to increase to 2.1% per year (16) and the mean age of this study was much younger than other researches. This may be a possible reason why the productivity loss of our sample was not as high as the previous studies. The sick leave days were similar to the previous research (12.3 days/year vs. 12-46 days/year), resulting in 5.4% of the annul total costs. The costs due to productivity loss took up 92% of the indirect costs and it may explain why AS would bring our society a considerable burden. We revealed an average of 6 outpatient visits per patient per year which was the

same as the research in Brazil, when studies from the European detected 4.9 visits to physicians per patient per year. And most of the patients came to rheumatology department. Only one patient underwent surgery due to AS in our group. According to the previous study, hip arthroplasty was the most common orthopaedic surgery performed in AS patients with an operating rate of 5%–10% (17). This may be explained by the limited sample, the short disease duration and short follow-up time of our study.

The mean annual total cost was \$2714.18 and indirect costs accounted for the largest part of the total costs. Compared to other countries, mean costs per patient was much lower in our study than in European countries (3) where the average cost per patient was \$15,000. In Hong Kong (10), the total average costs were \$9120 and indirect costs accounted for 61.8%. This may be explained by two points, one may be that there was hardly any patient that had never used biological drugs during our research so that the direct cost was much lower, and the second one is that about a quarter of our participants were students so that it is impossible to estimate the indirect cost which was proved to be the predominant component of the total costs. The biological drug was too expensive for Chinese AS patients to afford because it was not included in the basic social insurance, and the disease severity of our group was so slight that the use of biological drugs was limited. In addition, because of the differences in data collection, treatment practices and cost preference, it is difficult to make a comparison between different countries. The composition of total costs we estimated was similar to other countries (3, 7, 9-10, 18), in which the indirect costs made up the greatest part of the total costs, indicating that AS had a greater impact on the work capacity than it used to. This may be explained by the development of methods to estimate work productivity and remind us to take the cost due to work capacity impairment into account when estimating the cost effectiveness of treatments like anti-TNF therapy.

Several studies have found that disease

activity and functional impairment are the major drivers of costs. According to a recent review of the economic impacts of AS (19), the authors observed that the factors affecting direct medical cost was the worsening of quality of life with increasing disease duration. Indirect costs associated with days of absence from work and the relative productivity losses are the most important determinant of total costs and are related with the high patient' functional limitations due to AS. But the results of our study are different, we found that the BASDAI score was the most important predictor of total costs while BASFI was not. This may be due to the fact that the BASFI score of our study was much smaller than other studies. The progress of AS was slow, and with a short disease duration of this sample, the functional impairment was limited. Given that these two indexes are significantly correlated with each other in our study, we suggest that both of them are important to predict the cost of AS.

There are some limitations of our study such as the cross-sectional, uncontrolled nature, the short follow-up time the recall bias. However, as a result of the young population and short disease duration of the study, the direct and indirect costs may be underestimated. At the same time, the use of anti-TNF therapy was limited because it was not covered by health insurance. Therefore, the drug cost was much lower than in other countries. From the societal viewpoint, our data provide important information about the burden of AS patients in China, and set up the base of cost effectiveness of anti-TNF treatments. Treatments that control disease activity may result in a reduction in loss of work productivity, and are likely to compensate for the high drug cost. Further research with a larger sample and strict design should be done to get more information about the burden and cost effectiveness of different treatments and help to set up policy to help AS patients.

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