The costs associated with ankylosing spondylitis/ axial spondyloarthritis in Aotearoa/New Zealand

Douglas White, Chunhuan Lao, Megan Williams, Ross Lawrenson, Nicola Dalbeth

ABSTRACT

AIMS: To evaluate costs associated with a diagnosis of spondyloarthritis (SpA) in an Aotearoa/New Zealand cohort.

METHODS: Patients with SpA attending specialist SpA clinics in Auckland and Hamilton completed a series of questionnaires on costs associated with ankylosing spondylitis, disease parameters (BASDAI), work productivity (WPAI, WLQ) and quality of life measures (EQ-5D, ASAS-HI).

RESULTS: Eighty-one patients (median age 43 years) completed the study. All fulfilled the ASAS criteria for axial spondyloarthritis and 44 (58%) fulfilled the Modified New York Criteria for ankylosing spondylitis. The mean (SD) score on the EQ-VAS was 69mm (24.1). More than half reported difficulties with usual activities and more than 80% had moderate pain or discomfort despite current treatment. Sixty-six (82%) were in the workforce, and the mean work productivity loss was 4.8%. The mean (SD) annual cost was NZ$15,677 (NZ$11,269) with NZ$12,189 direct cost and NZ$3,488 productivity loss. The largest cost driver was use of biologic medications, which were used by 48% patients.

CONCLUSIONS: This study has quantified the direct and indirect costs of spondyloarthritis (SpA) in Aotearoa/New Zealand, and demonstrates meaningful reduction in quality of life and work productivity in patients with SpA. The major driver of direct costs in SpA are biologic medications.

Axial spondyloarthritis (axSpA) and ankylosing spondylitis (AS) are part of a spectrum of spondyloarthritis (SpA); chronic inflammatory conditions characterised by spinal involvement, with pain, stiffness and reduced range of movement. The condition typically starts in the second or third decades of life and affects men 2–4 times more commonly than women. Physical functioning and quality of life are affected, and previous studies have identified a significant burden in terms of work impairment, early retirement, lifetime health and social care resource utilisation.[1–18]

In 2018, Arthritis New Zealand released a report on the economic burden of arthritis in Aotearoa/New Zealand.[19] This report used data from the New Zealand Health Information Service (NZHIS) to gather data on inpatient episodes, the Royal New Zealand College of General Practitioners (RNZCGP) database for data on GP visits, and data from Pharmac on medication costs to generate the reported data. A number of limitations are acknowledged within this report, in particular the lack of comprehensive 'bottom-up' or 'top-down' data in Aotearoa/New Zealand. This project aims to address the lack of 'bottom-up' data on the effect of SpA on quality of life and the economic impact in New Zealand.

ISSN 1175-8716

Methods

Data collection

Participants who fulfilled the Assessment of Spondyloarthritis International Society (ASAS) Criteria for SpA, and a subset who also fulfilled the modified New York criteria for AS, attending specialist clinics at Auckland District Health Board and Waikato District Health Board were invited to participate. Patients were offered the option of completing a paper version of the questionnaires or completing them online using a custom built website. We linked the questionnaires to clinical data on disease duration, activity and severity contributed by the treating physician. The combined dataset included: 1) patient information: age, gender, ethnicity, education level, occupation, marriage status, AS diagnostic date and HLA-B27; 2) disease severity and patient's health: using the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath AS metrology Index (BASMI) and ASAS Health Index; 3) work and activity limitation: using the Work Limitations Questionnaire (WLQ) and Work Productivity and Activity Impairment Questionnaire (WPAIQ); 4) quality of life: using the EQ-5D-3L and EQ visual analogue scale (EQ-VAS); 5) AS related costs/resources: transport, accommodation, subsidised and unsubsidised medications, investigations, general practitioner consultations, outpatient specialist consultations, inpatient, and self-funded visits to other health professionals. The list of medications used for SpA was obtained from the treating clinician, sourced from hospital records.

The BASDAI consists of six questions rated on a 0 (no problem) through 10 (worst problem) scale assessing the five major symptoms of AS: fatigue, spinal pain, joint pain/swelling, areas of localised tenderness, morning stiffness duration and morning stiffness severity.[20] BASMI includes clinical measurements of cervical rotation, tragus to wall distance, lumbar flexion, lumbar side flexion and intermalleolar distance, with 0 for mild, 1 for moderate and 2 for severe on each measurement giving a total score of 0–10.[21] Clinicians were asked to provide the most recent scores prior to the study visit. The ASAS Health Index (HI) questionnaire contains 17 items measuring 'functioning, disability and health' with a sum score range from 0 (good functioning) to 17 (poor functioning).[22]

The WLQ is a self-administered questionnaire measuring the degree to which health problems interfere with the ability to perform job roles.[23] We used the 25-item version measuring four WLQ scales: time management scale, physical tasks scale, mental-interpersonal tasks scale and output tasks scale. The responses on these scales were then converted to a percentage of at-work productivity loss. WPAIQ measures absenteeism, presenteeism as well as the impairments in unpaid activity during the past seven days.[24]

The EQ-5D-3L consists of five dimensions (mobility, self-care, usual activities, pain/discomfort and anxiety/depression) with three levels for each dimension (no problems, some problems, severe problems). Based on the answers to the EQ-5D, the quality of life was estimated using the New Zealand EQ-5D tariff.[25] The EQ-VAS records self-rated health on a vertical, visual analogue scale where the endpoints are labelled 'Best imaginable health state (score 100)' and 'Worst imaginable health state (score 0)'.

Cost analyses

A cost estimation was derived from the societal perspective. All costs were valued in 2017/2018 New Zealand dollars (NZ$). Direct costs were calculated by adding up out-of-pocket costs and costs of public healthcare services. Costs of public healthcare services were computed using the bottom-up approach, by multiplying the amount of medical resources with the unit costs of each medical resource type. The unit costs of pharmaceuticals were from the PHARMAC online Pharmaceutical Schedule.[26] The unit costs of inpatient and outpatient services were provided by the Waikato District Health Board. Indirect productivity loss costs were calculated using the human capital approach. Costs of productivity loss included the loss of salary because of absenteeism and presenteeism due to AS.

Statistical analyses

Quality of life and total costs were compared by gender, ethnicity, age group (18–24, 25–44, 45–64, 65+ years), disease

duration (0–5, 6+ years), ASAS HI score (<6, 6+), BASDAI score (<4,4+) and biologic drugs user (Yes, No). Biologic drugs include adalimumab, etanercept, and infliximab. Mann-Whitney U test and Kruskal-Wallis 1 way ANOVA were used to examine the differences between subgroups. All data cleaning and analyses were performed in IBM SPSS statistics 25 (New York, US). For all tests, $p<0.05$ was taken as the level of significance.

Ethics

Ethical approval for the study was granted through the Central Health and Disability Ethics Committee, reference: 16/CEN/172. Institutional approval was obtained from Auckland District Health Board and Waikato District Health Board.

Results

Our study cohort included 81 patients. Table 1 shows the patient characteristics and disease information. Nine patients chose to use the website for data collection, and the remainder used the paper version of the questionnaires. There were 17 (21%) women and 64 (79%) men; eight (10%) identified as Māori and 71 (90%) as non-Māori. The majority of patients (83%) were aged 25–64 years old, and most (66, 82%) were in paid employment. Half of patients (40, 53%) were diagnosed within five years of participation in the study. Twenty-five (31%) patients had private medical insurance. Forty-four (58%) patients fulfilled the Modified New York Criteria for AS. Sixty-five (86%) patients

Table 1: Patient characteristics and disease information.

	Number	**Percentage**
Gender		
Female	17	21%
Male	64	79%
Ethnicity		
Māori	8	10%
NZ European	64	81%
Asian	5	6%
Middle Eastern	2	3%
Not reported	2	
Age at survey (years)		
18–24	4	5%
25–44	39	48%
45–64	29	36%
65+	9	12%
Marital status		
Married/living with partner	59	73%
Single/widow(er)	22	27%
Highest education		
Bachelor degree or above	29	36%
Others	52	64%
Employment (working for pay)		
Yes	66	82%
No	15	19%

Table 1: Patient characteristics and disease information (continued).

Private medical insurance		
Yes	25	31%
No	56	69%
Disease duration (n=76/81)		
0–5 years	40	53%
6–10 years	12	16%
11–20 years	9	12%
21+ years	15	20%
Modified New York Criteria fulfilled		
Yes	44	54%
No	37	46%
HLA-B27 (n=76/81)		
Negative	11	14%
Positive	65	86%
BASMI (n=73/81)		
0–1	42	58%
2–3	11	15%
4–5	7	10%
6–7	11	15%
8–9	2	3%
BASDAI Score (n=80/81)		
0–<2	30	38%
2–<4	21	26%
4–<6	19	24%
6+	10	13%
Biologic medication user		
Yes	39	48%
No	42	52%

were HLA-B27 positive. More than half of patients had a BASMI score of 6–9 (13, 18%), and 10 (13%) patients had a BASDAI score of 6+. Biologic medications were used by 39 (48%) patients.

Seventy-two patients answered the WLQ, and the estimated average at-work productivity loss was 4.8% (Table 2). From the WPAIQ, on average one hour in the prior seven days was missed from work and two hours of productivity were affected due to SpA.

All patients provided the EQ-5D-3L data, with a mean (SD) score of 0.66 (0.18) (Table 2). The mean (SD) score on the EQ VAS was 69.0 (SD 24.1). The ASAS Health Index questionnaire (ASAS-HI) found a mean (SD) score of 5.7 (3.9). Thirty-four (42%) patients had some problems in mobility, 16 (20%) patients had some problems with self-care, more than half of patients had some problem with usual activities (43, 53%), 65 (80%) patients had moderate pain or discomfort, and 28 (35%) patients had moderate anxiety or depression (Table 3).

Table 2: WLQ and EQ-5D results.

Measurement tools	Number of answers	Average score (SD)	Non-biologic user	Biologic user
WLQ At-Work Productivity Loss	72	4.8% (4.5%)	4.9% (4.1%)	4.8% (5.0%)
WPAIQ (in the past 7 days)				
Hours missed from work due to SpA	67	1.0 (2.9)	1.1 (3.4)	1.0 (2.2)
Hours with affected productivity due to SpA	67	2.0 (2.0)	2.3 (2.0)	1.8 (2.0)
Hours actually worked	67	36.4 (15.9)	40.6 (12.4)	31.8 (18.2)
EQ-5D	81	0.66 (0.18)	0.65 (0.17)	0.68 (0.18)
EQ VAS	81	69.0 (24.1)	63.9 (25.1)	73.7 (22.4)
ASAS Health Index	81	5.7 (3.9)	5.5 (3.5)	5.8 (4.2)

Table 3: EQ-5D results by dimension.

Dimensions	Number	Percentage
Mobility		
I have no problems in walking about	47	58%
I have some problems in walking about	34	42%
I am confined to bed	0	0%
Self-care		
I have no problems with self-care	65	80%
I have some problems washing or dressing myself	16	20%
I am unable to wash or dress myself	0	0%
Activity		
I have no problems with performing my usual activities	37	46%
I have some problems with performing my usual activities	43	53%
I am unable to perform my usual activities	1	1%
Pain/discomfort		
I have no pain or discomfort	14	17%
I have moderate pain or discomfort	65	80%
I have extreme pain or discomfort	2	3%
Anxiety/depression		
I am not anxious or depressed	53	65%
I am moderately anxious or depressed	28	35%
I am extremely anxious or depressed	0	0%

Mean (SD) annual salary was $62,167 ($35,332). The average (SD) annual costs were $15,677 ($11,269) with $12,189 (78%) direct cost and $3,488 (22%) productivity loss (Table 4). The majority of the direct cost was medication cost ($10,701, 88%). Other direct costs included GP cost ($189), outpatient cost ($688) and other out-of-pocket costs ($611). Among the productivity loss, $1,078 (31%) were due to absenteeism and $2,410 (69%) were due to presenteeism.

There was no significant difference in quality of life or costs by gender, ethnicity, age or disease duration (Table 5).

Patients who had an ASAS-HI score of less than 6 had better quality of life than patients with an ASAS-HI score of 6+ (0.75 vs 0.56, p<0.001), and had lower costs ($13,408 vs $18,245, p=0.03). Patients who had an BASDAI score of less than 4 had better quality of life than patients with an BASDAI score of 4+ (0.73 vs 0.54, p<0.001), but similar costs ($16,327 vs $14,512, p=0.75). The costs for biologic medication users were 4.5 times the costs for those not on biologic medications ($25,073 vs $5,559, p<0.001).

Discussion

This is the first study in Aotearoa/New Zealand that has gathered bottom-up health economic data on people with spondyloarthritis (SpA). The cohort studied is representative of those attending hospital-based secondary care clinics and thus may be skewed towards patients with more severe disease, as those with milder SpA may be managed—if not diagnosed—in primary care. However, the characteristics of the current cohort are similar to other published cohorts of patients with spondyloarthritis.[27,28]

Identifying where additional costs are being incurred both by patients and the public health system, may help to identify areas where improvements in health provision and efficiency, could save health dollars and improve patients' quality of life. The majority of the costs were related to the use of biologic medications (~77%) with a smaller but significant contribution from lost productivity (~22%). The costs of biologic medications may fall a little over time with the introduction of biosimilar medications. Additionally, newer agents being developed to treat spondyloarthritis are available as tablets, which may reduce the medication costs further. Productivity loss is likely therefore to become a greater proportion of the total costs over time. Although this study has not looked at the effect of diagnosis or treatment on productivity loss, others have found that earlier diagnosis and treatment can reduce the detrimental impact of this condition on work productivity.[30]

Table 4: Components of annual costs.

List of items	**Costs**	
	Mean	**SD**
All direct costs	$12,189	$10,623
GP costs (government contribution)	$98	$106
GP costs (patient contribution)	$91	$123
Outpatient cost	$688	$588
Inpatient cost	$0	-
Medication cost	$10,701	$10,327
Other out-of-pocket cost	$611	$1,230
Productivity loss	$3,488	$5,045
Absenteeism	$1,078	$3,021
Presenteeism	$2,410	$3,116
Total costs	$15,677	$11,269

Table 5: Quality of life and annual costs by subgroup.

Subgroups	Quality of life		Costs	
	mean	p-value	mean	p-value
Gender				
Female	0.70	0.69	$13,987	0.52
Male	0.65		$16,126	
Ethnicity				
Māori	0.61	0.27	$21,326	0.12
Others	0.67		$15,289	
Age (years)				
18–24	0.58	0.33	$13,200	0.16
25–44	0.66		$16,581	
45–64	0.67		$16,759	
65+	0.75		$15,686	
Disease duration (years)				
0–5	0.64	0.88	$15,825	0.65
6+	0.68		$15,795	
ASAS-HI				
<6	0.75	<0.001	$13,408	0.03
6+	0.56		$18,245	
BASDAI				
<4	0.73	<0.001	$16,327	0.75
4+	0.54		$14,512	
Biologic medication user				
No	0.65	0.86	$5,559	<0.001
Yes	0.68		$25,073	

It is evident from the data presented in Table 2 that those on biologic medications have similar levels of work productivity loss but appear to work fewer hours than those not on biologic. Since biologic medications are given to those with more severe disease. This is a cross-sectional study and it is not possible to make any conclusion about the use of these medications on change in quality of life or work productivity. This would require a detailed analysis of our prospective data and will be the subject of future work. Data from the British Society of Rheumatology Biologics Registry showed that biologic medication use does improve work productivity for those with spondyloarthritis; in a study of 161 patients commencing biologic therapy, at 12-month follow-up, there were significantly greater improvements (relative to those on non-biologic therapy) in presenteeism, overall work impairment and overall activity impairment.[28] The proportion of patients receiving biologic therapy in our study (48%) is equivalent to overseas cohorts.[27] In Aotearoa/New Zealand, the precise cost of biologic medications is confidential and for this study, the 'list price', which is likely to be higher than the actual cost, was used.

In 2015, Cooksey et al[29] found an annual cost of £19,016 per patient per year in the UK, including direct medical costs, direct non-medical costs and productivity loss costs. Even for those on biologic therapy, our cost data published here compare favourably.

It is perhaps surprising that the mean time taken off work was just over one hour in the past week. This may be subject to recall bias but is very similar to the UK data published by Cooksey et al[29] who found a mean of 1.15 hours absence in the past seven days using the same questionnaire. Shim et al[28] also reported that absenteeism did not change when commencing biologic therapy, suggesting that this may be independent of disease activity.

There were some limitations to our study. Recruitment proved harder than we expected. We did not gather data on early retirement in this study, which may have increased the amount of productivity loss related to spondyloarthritis.

Despite the above limitations, we have found evidence to suggest that spondyloarthritis is associated with a meaningful reduction in quality of life and reduced work productivity in Aotearoa/New Zealand. Understanding the health economic implications can assist with service provision and funding of treatment options. Data from Aotearoa/New Zealand are needed across a range of musculoskeletal conditions to help us understand the impact these conditions are having.

Competing interests:
Douglas White reports speaker fees for Abbvie outside the submitted work and has been an investigator on several clinical trials sponsored by Abbvie. Nicola Dalbeth reports speaker fees from Abbvie and Janssen, outside the submitted work.

Acknowledgements:
We acknowledge A/Prof Simon Stebbings who discussed the study and reviewed the manuscript.

Author information:
Douglas White, Rheumatology Department, Waikato Hospital, Hamilton; Waikato Clinical School, University of Auckland, Auckland; Chunhuan Lao, Waikato Medical Research Centre, University of Waikato, Hamilton; Megan Williams, Auckland District Health Board, Auckland; Ross Lawrenson, Waikato Medical Research Centre, University of Waikato, Hamilton; Waikato District Health Board, Hamilton; Nicola Dalbeth, Auckland District Health Board, Auckland; University of Auckland, Auckland.

Corresponding author:
Douglas White, Rheumatology Department, Waikato Hospital, Private Bag 3200, Hamilton.
douglas.white@waikatodhb.health.nz

URL:
http://www.nzma.org.nz/journal/read-the-journal/all-issues/2010-2019/2019/vol-132-no-1505-8-november-2019/8039

REFERENCES:

1. Boonen A, van der Heijde D, Landewe R, et al. Work status and productivity costs due to ankylosing spondylitis: comparison of three European countries. Annals of the rheumatic diseases. 2002; 61:429–37.
2. Boonen A, van der Heijde D, Landewe R, et al. Direct costs of ankylosing spondylitis and its determinants: an analysis among three European countries. Annals of the rheumatic diseases. 2003; 62:732–40.
3. Boonen A, van der Heijde D, Landewe R, et al. Costs of ankylosing spondylitis in three European countries: the patient's perspective. Annals of the rheumatic diseases. 2003; 62:741–7.
4. Hulsemann JL, Mittendorf T, Merkesdal S, et al. Direct costs related to rheumatoid arthritis: the patient perspective. Annals of the rheumatic diseases. 2005; 64:1456–61.
5. Merkesdal S, Ruof J, Huelsemann JL, et al. Indirect cost assessment in patients with rheumatoid arthritis (RA): comparison of data from

the health economic patient questionnaire HEQ-RA and insurance claims data. Arthritis and rheumatism. 2005; 53:234–40.

6. Verstappen SM, Boonen A, Verkleij H, Bijlsma JW, Buskens E, Jacobs JW. Productivity costs among patients with rheumatoid arthritis: the influence of methods and sources to value loss of productivity. Annals of the rheumatic diseases. 2005; 64:1754–60.
7. Huscher D, Merkesdal S, Thiele K, Zeidler H, Schneider M, Zink A. Cost of illness in rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis and systemic lupus erythematosus in Germany. Annals of the rheumatic diseases. 2006; 65:1175–83.
8. Kobelt G, Andlin-Sobocki P, Maksymowych WP. Costs and quality of life of patients with ankylosing spondylitis in Canada. The Journal of rheumatology. 2006; 33:289–95.
9. Verstappen SM, Jacobs JW, van der Heijde DM, et al. Utility and direct costs: ankylosing spondylitis compared with rheumatoid arthritis. Annals of the rheumatic diseases. 2007; 66:727–31.
10. Ara RM, Packham JC, Haywood KL. The direct healthcare costs associated with ankylosing spondylitis patients attending a UK secondary care rheumatology unit. Rheumatology (Oxford, England). 2008; 47:68–71.
11. Kobelt G, Sobocki P, Mulero J, Gratacos J, Pocovi A, Collantes-Estevez E. The burden of ankylosing spondylitis in Spain. Value in health : the journal of the International Society for Pharmacoeconomics and Outcomes Research. 2008; 11:408–15.
12. Zhu TY, Tam LS, Lee VW, et al. Costs and quality of life of patients with ankylosing spondylitis in Hong Kong. Rheumatology (Oxford, England). 2008; 47:1422–5.
13. Singh JA, Strand V. Health care utilization in patients with spondyloarthropathies. Rheumatology (Oxford, England). 2009; 48:272–6.
14. Boonen A, Brinkhuizen T, Landewe R, van der Heijde D, Severens JL. Impact of ankylosing spondylitis on sick leave, presenteeism and unpaid productivity, and estimation of the societal cost. Annals of the rheumatic diseases. 2010; 69:1123–8.
15. Poole CD, Lebmeier M, Ara R, Rafia R, Currie CJ. Estimation of health care costs as a function of disease severity in people with psoriatic arthritis in the UK. Rheumatology (Oxford, England). 2010; 49:1949–56.
16. Strombeck B, Englund M, Bremander A, et al. Cost of illness from the public payers' perspective in patients with ankylosing spondylitis in rheumatological care. The Journal of rheumatology. 2010; 37:2348–55.
17. Bakland G, Gran JT, Becker-Merok A, Nordvag BY, Nossent JC. Work disability in patients with ankylosing spondylitis in Norway. The Journal of rheumatology. 2011; 38:479–84.
18. Rafia R, Ara R, Packham J, Haywood KL, Healey E. Healthcare costs and productivity losses directly attributable to ankylosing spondylitis. Clinical and experimental rheumatology. 2012; 30:246–53.
19. Deloitte Access Economics. The economic cost of arthritis in New Zealand in 2018. Wellington, New Zealand, 2018.
20. Bobek D, Zagar I, Kovac-Durmis K, Peric P, Curkovic B, Babic-Naglic E. [Scoring of disease activity using BASDAI and ASDAS method in ankylosing spondylitis]. Reumatizam. 2012; 59:5–10.
21. Chilton-Mitchell L, Martindale J, Hart A, Goodacre L. Normative values for the Bath Ankylosing Spondylitis Metrology Index in a UK population. Rheumatology (Oxford). 2013; 52:2086–90.
22. Kiltz U, van der Heijde D, Boonen A, Braun J. The ASAS Health Index (ASAS HI) - a new tool to assess the health status of patients with spondyloarthritis. Clinical and experimental rheumatology. 2014; 32:S-105-8.
23. Lerner D, Amick BC, 3rd, Rogers WH, Malspeis S, Bungay K, Cynn D. The Work Limitations Questionnaire. Medical care. 2001; 39:72–85.
24. Zhang W, Bansback N, Boonen A, Young A, Singh A, Anis AH. Validity of the work productivity and activity impairment questionnaire--general health version in patients with rheumatoid arthritis. Arthritis Res Ther. 2010; 12:R177-R.
25. Devlin NJ, Hansen P, Kind P, Williams A. Logical inconsistencies in survey respondents' health state valuations -- a methodological challenge for estimating social tariffs. Health economics. 2003; 12:529–44.
26. PHARMAC. Pharmaceutical Schedule. Edition. Wellington, New Zealand, cited.Available from: http://www.pharmac.govt.nz/tools-resources/pharmaceutical-schedule/
27. Reveille JD, Ximenes A, Ward MM, Deodhar A, Clegg D. Economic Considerations of the

Treatment of Ankylosing Spondylitis. The American Journal of the Medical Sciences. 2012; 343:371–4.

28. Shim J, Jones GT, Pathan EMI, Macfarlane GJ. Impact of biological therapy on work outcomes in patients with axial spondyloarthritis: results from the British Society for Rheumatology Biologics Register (BSRBR-AS) and meta-analysis. Annals of the rheumatic diseases. 2018; 77:1578–84.

29. Cooksey R, Husain MJ, Brophy S, et al. The Cost of Ankylosing Spondylitis in the UK Using Linked Routine and Patient-Reported Survey Data. PloS one. 2015; 10:e0126105.

30. Claudepierre P, Van den Bosch F, Sarzi-Puttini P, Vastesaeger N, Govoni M, Kachroo S. Treatment with golimumab or infliximab reduces health resource utilization and increases work productivity in patients with ankylosing spondylitis in the QUO-VADIS study, a large, prospective real-life cohort. International journal of rheumatic diseases. 2019; 22(6):995–1001.

ISSN 1175-8716