

Disease Severity in Ankylosing Spondylitis: Variation by Region and Local Area Deprivation

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ABSTRACT. *Objective.* To investigate whether patient disease severity in ankylosing spondylitis (AS) varies among regions or by local area social deprivation.

Methods. Eight hundred patients with AS from 8 specialist rheumatology centers across England were invited to participate in a cross-sectional survey. Sociodemographic and disease-related variables were collected [pain (numerical rating scale), disease activity (Bath AS Disease Activity Index), and physical function (Bath AS Functional Index)]. Deprivation was measured using the Index of Multiple Deprivation 2004.

Results. Of the 800 patients invited, 468 responded (adjusted response rate 62.8%). Most were male (72.9%), with a mean age of 50.2 years (SD 12.1), and a mean diagnosed disease duration of 17 years (SD 11.4). Across all centers, those living in more deprived areas demonstrated significantly greater disease severity and poorer psychological health. After controlling for age, gender, disease duration, and region, greater deprivation was significantly associated with greater disease activity (OR 3.39; 95% CI 1.65, 6.98) and poorer function (OR 4.46; 95% CI 2.11, 9.44). There was a non-significant trend toward more pain (OR 1.98; 95% CI 0.97, 4.07). There was also a significant independent association between region and disease severity.

Conclusion. The need for healthcare is greatest for patients with AS who are living in more socially deprived areas. With the growing use of interventional therapies, these findings have important implications if health service resources are to be allocated equitably; particularly as deprived patients are known to access healthcare less frequently. (J Rheumatol First Release Feb 1 2010; doi:10.3899/jrheum.090899)

Key Indexing Terms:

ANKYLOSING SPONDYLITIS

DEPRIVATION

DISEASE IMPACT

The strong correlation between social deprivation and health is well known¹. There is growing evidence of the widening health gap related to socioeconomic inequality, even in Western societies^{2,3}. Previous research has highlighted that living in a less affluent area is associated with higher levels of disabling pain⁴. Explanations for this have included the

presence of socially determined exposure to risk (injury in manual jobs), social variations in risk exposure (smoking, obesity), impact of social stressors (poor housing, unemployment), and perceived inequalities and barriers to obtaining healthcare (poor education)⁴.

Patients with rheumatoid arthritis (RA) who have lower socioeconomic status are known to have more severe disease, more comorbidity, and higher mortality⁵. Significant relationships have also been found between higher deprivation (measured by the Townsend Deprivation Index) and higher disease activity, greater pain, poorer function, poorer mental health, and lower quality of life⁶. Similarly, the patients with RA who are from more deprived areas had more severe disease as judged by the Health Assessment Questionnaire (HAQ score) and joint counts⁷. Disease status may be worse in socially deprived patients because of delays in reaching clinical attention, differences in clinical management, variation in compliance to treatment, and greater vulnerability to disease progression due to comorbidity and behavioral and lifestyle factors such as smoking, diet, stress, and occupation⁷.

In contrast, a study conducted in Norway⁸ found that patients with RA from 2 different areas of Oslo were equal with regard to objective disease process and joint damage

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measures. However, according to self-reported physical and psychosocial health status, there were higher levels of disease severity in the less affluent area⁸. Blank and Diderichsen⁹ concluded that patients with low socioeconomic status are exposed to double suffering, having both a higher prevalence of disease and more severe disease.

Because of the early onset of ankylosing spondylitis (AS), extraspinal involvement, and longterm functional loss, AS has a substantial socioeconomic burden¹⁰. Studies looking at the socioeconomic effects of AS have generally concentrated on the effects on work capacity¹¹⁻¹³. A study of men with AS found those who were unemployed had higher levels of pain and disease impact and poorer psychological well-being¹⁴. While this helps determine the effect of social deprivation on patients with AS, little is known about the effect of area-level social deprivation on the health of patients with AS. We investigated whether patient disease severity is related to local area deprivation, and whether there is a wider regional variation in disease severity across England. The secondary aim was to determine whether the psychological effect of severe disease activity is increased in areas of greater deprivation.

MATERIALS AND METHODS

Subjects. Eight hundred patients with a confirmed diagnosis of AS (modified New York criteria, 1984)¹⁵ under the clinical care of 8 specialist rheumatology centers across England (Bristol, Cambridge, Cannock, Kent, Lancaster, Newcastle-upon-Tyne, Stoke-on-Trent, Torbay) were invited by their consultants to participate in a postal survey (April to July 2007). The centers were specifically chosen in regions that provided a diverse socioeconomic and geographic population by covering both urban and rural areas across England. Tertiary rheumatology centers were specifically avoided to allow the results to be generalizable to secondary-care patients. Exclusion criteria included learning difficulties and an inability to comprehend written English. The number of patients was based on the main study objective of evaluating a new AS measure of quality of life.

The multicenter cross-sectional survey was approved by the North Staffordshire Local Research Ethics Committee and the 8 center-specific National Health Service Trusts. Written consent was obtained from all patients according to the Declaration of Helsinki.

Patients were invited to self-complete a mailed questionnaire. Those who did not wish to participate were asked to return uncompleted, precoded questionnaires in a prepaid envelope. Nonresponders were sent reminders at 2 and 4 weeks.

Data collection. The Index of Multiple Deprivation (IMD) 2004 for England¹⁶ examines specific features of local neighborhoods (e.g., employment and education), and can be used to determine their specific influence on an individual's health. The index is based geographically at the lower-level Super Output Area (SOA), of which there are 32,482 in England with a mean population of 1500. Patients are allocated to an SOA based on their postcode. The IMD has an overall score, based on a weighted combination of 7 domains. The domains are based on characteristics of the local area and cover (1) extent of income deprivation; (2) involuntary exclusion of working-age population from work (employment); (3) rates of premature death, poor quality of life, and disability (health); (4) education deprivation for children and lack of skills and qualifications in working-age adults (education, skills, and training); (5) barriers to housing, and access to primary care physicians' premises, supermarket/convenience store, schools, and post office; (6) crime (burglary, theft, criminal damage, violence); and (7) poor-quality housing, poor air quality, and road traffic accidents of pedestrians and cyclists (living

environment). Each domain is ranked from 1 (most deprived) to 32,482 (least deprived) across the SOA. The SOA from which the patients in this study were drawn were categorized for each domain into 3 groups: the least deprived 20%, the most deprived 20%, and the middle 60%^{4,16,17}.

Participating patients returned a self-assessment questionnaire including both disease-specific and generic measures. Completion of the Bath AS Functional Index (BASFI)¹⁸ and the Bath AS Disease Activity Index (BASDAI)¹⁹ assessed physical functional and disease activity, respectively. Both the BASFI and BASDAI indices are scored between 0 and 10, with higher values indicating worse function or disease activity, respectively. Patients also completed a 100 mm numerical rating scale for pain (0 = no pain, 100 = most severe pain). Self-efficacy was assessed by an AS-specific modification of the Arthritis Self Efficacy Scale (ASES)²⁰. The modified ASES has not been evaluated in AS, but there is good evidence for its measurement properties in similar population groups²¹. This 8-item scale asks patients to score from 1 (very uncertain) to 10 (very certain) how certain they are about their ability to undertake specific tasks. Emotional well-being was assessed by the Hospital Anxiety and Depression scale (HAD)²², a 14-point scale that contains 7 questions about anxiety and 7 about depression; a score ≥ 8 defines probable anxiety or depression.

Disease-specific information including disease duration and demographic information including age, gender, and marital status were also collected.

Data analysis. Mean scores of measures reflecting disease severity (pain, disease activity, and physical function) were compared between regions using ANOVA. Each disease-specific measure of disease severity (pain, disease activity, physical function) was then dichotomized ($< / \geq 4$) to reflect national NICE guideline cutoffs for 2008²³ and to aid interpretation of the results. The 2 sections of the HAD scale were also dichotomized, with any score ≥ 8 reflecting probable anxiety and/or depression²². Prevalence of severe disease, anxiety, and depression, and self-efficacy score were compared by deprivation status of the local area over all IMD deprivation domains. Logistic regression analysis was then conducted to examine the independent effects of local area deprivation measured by the overall weighted IMD classification and region after controlling for each other and for age, gender, and disease duration. Results are presented as odds ratios with 95% CI. As there were only 8 centers, and most (94%) of the study SOA included only 1 patient with AS, single-level rather than multilevel analysis was performed.

A severe group (patients who reported either pain, disease activity, or physical function ≥ 4) was then selected from the cohort and levels of anxiety and depression and self-efficacy within this subgroup were compared by overall deprivation status. All analyses were performed using SPSS version 15.0 for Windows (SPSS Inc., Chicago, IL, USA).

RESULTS

A total of 468 patients (Table 1) gave written consent to participate in the study. After taking into account deaths and changes of address ($n = 35$), the adjusted response rate was 62.8%. Information on the nonresponders was not obtained.

The 468 responders resided in 422 different SOA. The median IMD rank for the group was 19,854, slightly higher than the median for England as a whole (16,241). Patients were divided based on deprivation domain quintile scores, with 93 patients in the least and most deprived categories, and the middle 3 quintiles combined into a middle group ($n = 282$). There was a good spread of deprivation levels among the 8 regions, with Cambridge and Bristol being least deprived and Stoke-on-Trent and Newcastle being most deprived (Table 2). Patients from the most deprived areas were also more likely to be older, single men.

Table 1. Patient characteristics. Values are the mean \pm SD unless otherwise indicated.

Characteristic	n = 468
Gender, % male	72.9
Age, yrs	50.2 \pm 12.1
Disease duration, yrs	17 \pm 11.4
Disease activity (BASDAI; 0–10)	4.5 \pm 2.5
Function (BASFI; 0–10)	4.9 \pm 2.8
Pain (NRS; 0–100)	48 \pm 26
Probable anxiety, %*	43.2
Probable depression, %*	31.6

* Hospital Anxiety and Depression score \geq 8 suggests probable anxiety or depression. BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath AS Functional Index; NRS: numerical rating scale.

There were significant differences in disease activity ($p = 0.001$) and physical function ($p = 0.001$) among the regions (Figure 1). Newcastle, Torbay, Stoke-on-Trent, and Cannock had mean scores above the recommended cutoff of 4 to indicate severe disease on all 3 measures.

Those living in the most deprived local areas had higher rates of disease severity (pain, disease activity, and physical function) and worse psychological health (depression, anxiety, and self-efficacy). This trend was evident for each of the IMD domains except for the housing domain (Table 3). In

Table 2. Number (%) of patients from each center within each deprivation category.

Center	Deprivation Category		
	Least, n (%)	Middle, n (%)	Most, n (%)
Cambridge (n = 75)	37 (49.3)	37 (49.3)	1 (1.4)
Stoke-on-Trent (n = 69)	8 (11.6)	38 (55.1)	23 (33.3)
Torbay (n = 47)	1 (2.1)	36 (76.6)	10 (21.3)
Bristol (n = 51)	19 (37.3)	26 (51)	6 (11.7)
Lancaster (n = 58)	8 (13.8)	37 (63.8)	13 (22.4)
Cannock (n = 58)	10 (17.2)	37 (63.8)	11 (19)
Kent (n = 64)	9 (14.1)	44 (68.8)	11 (17.1)
Newcastle (n = 46)	1 (2.2)	27 (58.7)	18 (39.1)

this cohort, 12.4% (n = 58) reported taking anti-tumor necrosis factor (TNF) treatment. When looking at these patients on anti-TNF treatment, 15.5%, 55.2%, and 29.3% were in the least, middle, and most deprived groups, respectively. While there was no significant difference among the percentage of patients on anti-TNF across the 3 deprivation categories ($p = 0.13$), there was a significant difference among sites with regard to anti-TNF use ($p = 0.001$).

After controlling for age, gender, disease duration, and region, greater overall local area deprivation was significantly associated with greater disease activity (OR 3.39,

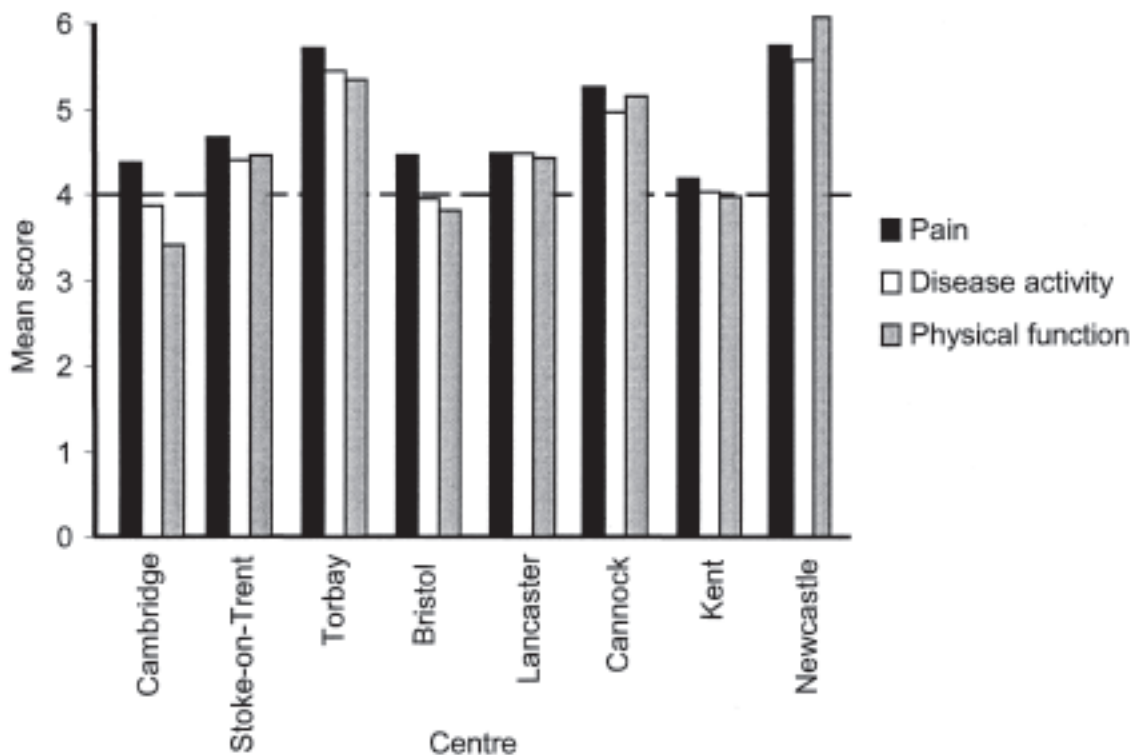


Figure 1. Levels of disease severity compared across 8 specialist rheumatology centers in England. Pain is measured by a numerical rating scale, disease activity by the Bath AS Disease Activity Index (BASDAI), and physical function by the Bath AS Functional Index. Horizontal line indicates the > 4 BASDAI cutoff score used for anti-TNF treatment. Difference between sites: pain $p = 0.06$, disease activity $p = 0.001$, physical function $p = 0.001$.

95% CI 1.65, 6.98) and poorer function (OR 4.46, 95% CI 2.11, 9.44). The association with greater pain was of borderline significance (OR 1.98, 95% CI 0.97, 4.07; Table 4). Higher levels of disease severity, independent of local area deprivation, were apparent in Newcastle and to a lesser extent, Torbay. For example, independent of the extent of deprivation in their local area, patients with AS who were based in Newcastle were more likely to report high levels of

disease activity (OR 4.77, 95% CI 1.69, 13.51) compared to Cambridge.

The severe disease group (patients reporting pain, disease activity, or physical function ≥ 4) demonstrated worse psychological health. Self-reported depression, anxiety, and self-efficacy were worse in the more deprived areas. Depression was significantly worse with increasing deprivation (Table 5).

Table 3. Disease severity and psychological health of patients in the least, mid, and most deprived categories for overall deprivation and each of the 7 Index of Multiple Deprivation (IMD) domains.

IMD Domain	Deprivation Status	Pain ≥ 4 , n (%)	Disease Activity ≥ 4 , n (%)	Function ≥ 4 , n (%)	Anxiety ≥ 8 , n (%)	Depression ≥ 8 , n (%)	Self-efficacy, mean (SD)
Overall	Least (n = 93)	49 (52.7)	34 (36.6)	34 (36.6)	34 (36.6)	24 (25.8)	6.1 (2.2)
	Mid (n = 282)	178 (63.1)	159 (56.4)	149 (52.8)	121 (42.9)	82 (29.1)	5.5 (2.2)
	Most (n = 93)	67 (72.0)	63 (67.7)	66 (71.0)	50 (53.8)	36 (38.7)	4.9 (2.3)
Employment	Least (n = 93)	53 (57.0)	39 (41.9)	37 (40.0)	39 (41.9)	32 (34.4)	5.9 (2.3)
	Mid (n = 282)	174 (61.7)	154 (54.6)	121 (42.9)	113 (40.1)	73 (25.9)	5.4 (2.2)
	Most (n = 93)	67 (72.0)	63 (67.7)	62 (66.7)	50 (53.8)	43 (46.2)	5.0 (2.3)
Income	Least (n = 93)	52 (55.9)	36 (36.6)	40 (43.0)	34 (36.6)	23 (24.7)	6.0 (2.3)
	Mid (n = 282)	172 (61.0)	155 (55.0)	143 (50.7)	123 (43.6)	83 (29.4)	5.6 (2.5)
	Most (n = 93)	69 (74.2)	65 (70.0)	66 (71.0)	46 (49.5)	42 (45.2)	4.9 (2.1)
Housing	Least (n = 93)	57 (61.3)	51 (54.8)	49 (52.7)	36 (36.6)	28 (30.1)	5.7 (2.3)
	Mid (n = 282)	182 (64.5)	155 (55.0)	154 (54.6)	122 (43.3)	91 (32.3)	5.5 (2.3)
	Most (n = 93)	55 (59.1)	50 (53.7)	46 (49.4)	44 (47.3)	29 (31.2)	5.6 (2.3)
Education	Least (n = 93)	53 (57.0)	45 (48.4)	45 (48.4)	36 (36.6)	29 (31.2)	6.0 (2.3)
	Mid (n = 282)	175 (62.1)	147 (52.1)	138 (48.9)	119 (42.2)	75 (26.6)	5.6 (2.2)
	Most (n = 93)	66 (71.0)	64 (68.8)	66 (71.0)	48 (51.6)	44 (47.3)	4.8 (2.3)
Health	Least (n = 93)	48 (51.6)	33 (35.5)	35 (37.6)	34 (36.6)	29 (31.2)	5.9 (2.3)
	Mid (n = 282)	178 (63.1)	157 (55.7)	152 (53.9)	116 (41.1)	76 (26.9)	5.6 (2.2)
	Most (n = 93)	68 (73.1)	66 (71.0)	63 (67.7)	53 (56.9)	43 (46.2)	5.0 (2.2)
Crime	Least (n = 93)	50 (53.8)	39 (41.9)	42 (45.2)	44 (47.3)	28 (30.1)	5.8 (2.3)
	Mid (n = 282)	179 (63.5)	160 (56.7)	143 (50.7)	112 (39.7)	82 (29.1)	5.5 (2.3)
	Most (n = 93)	65 (69.9)	57 (61.3)	64 (68.8)	46 (49.5)	38 (40.8)	5.3 (2.0)
Environment	Least (n = 93)	57 (61.3)	48 (51.6)	49 (52.7)	40 (43.0)	30 (32.2)	5.5 (2.3)
	Mid (n = 282)	171 (60.6)	148 (52.5)	142 (50.4)	121 (42.9)	86 (30.5)	5.6 (2.2)
	Most (n = 93)	66 (71.0)	60 (64.5)	58 (62.4)	41 (44.1)	32 (34.4)	5.3 (2.3)

Table 4. Disease severity (pain, disease activity, physical function) and its association with overall deprivation and region.

	Pain ≥ 40 OR (95% CI)		Disease Activity ≥ 4 OR (95% CI)		Physical Function ≥ 4 OR (95% CI)	
	Unadjusted Analysis	Adjusted Analysis [†]	Unadjusted Analysis	Adjusted Analysis [†]	Unadjusted Analysis	Adjusted Analysis [†]
Overall IMD						
Least (ref)	1.00*	1.00	1.00*	1.00*	1.00*	1.00*
Mid	1.58 (0.98 to 2.54)	1.37 (0.81 to 2.33)	2.24 (1.38 to 3.64)*	1.99 (1.16 to 3.40)*	1.97 (1.22 to 3.20)*	1.76 (1.02 to 3.05)*
Most	2.31 (1.26 to 4.25)*	1.98 (0.97 to 4.07)	3.64 (1.99 to 6.68)*	3.39 (1.65 to 6.98)*	4.24 (2.29 to 7.85)*	4.46 (2.11 to 9.44)*
Region						
1 (ref)	1.00*	1.00	1.00*	1.00*	1.00*	1.00*
2	1.33 (0.68 to 2.63)	1.01 (0.47 to 2.14)	1.17 (0.61 to 2.25)	0.73 (0.34 to 1.56)	1.43 (0.74 to 2.76)	0.70 (0.32 to 1.53)
3	3.14 (1.33 to 7.42)*	2.71 (1.07 to 6.18)*	2.47 (1.16 to 5.25)*	1.51 (0.66 to 3.48)	3.17 (1.46 to 6.87)*	1.96 (0.82 to 4.69)
4	0.91 (0.44 to 1.86)	0.88 (0.41 to 1.89)	1.13 (0.55 to 2.31)	0.98 (0.46 to 2.12)	1.29 (0.63 to 2.64)	1.04 (0.47 to 2.28)
5	0.92 (0.46 to 1.83)	0.78 (0.36 to 1.68)	1.57 (0.79 to 3.12)	1.07 (0.49 to 2.31)	1.34 (0.68 to 2.68)	0.91 (0.41 to 1.99)
6	1.61 (0.78 to 3.32)	1.48 (0.68 to 3.21)	2.08 (1.04 to 4.19)*	1.53 (0.71 to 3.30)	2.30 (1.14 to 4.67)*	1.52 (0.69 to 3.35)
7	0.84 (0.43 to 1.65)	0.91 (0.43 to 1.90)	1.06 (0.54 to 2.06)	0.90 (0.43 to 1.90)	0.86 (0.44 to 1.70)	0.65 (0.30 to 1.40)
8	3.06 (1.29 to 7.23)*	2.59 (0.99 to 6.80)	6.05 (2.49 to 14.70)*	4.77 (1.69 to 13.51)*	3.81 (1.71 to 8.49)*	2.34 (0.92 to 5.97)

* $p \leq 0.05$. [†] Adjusted for age, gender, and disease duration. IMD: Index of Multiple Deprivation.

Table 5. Psychological health in patients with severe disease (pain, disease activity, or physical function ≥ 4) across deprivation categories.

	Deprivation Status, n = 337	Self-efficacy Score 0–10 (SD)	Probable Anxiety ≥ 8 , n (%)	Probable Depression* ≥ 8 , n (%)
IMD Overall	Least (n = 57)	4.97 (1.79)	27 (47.4)	20 (35.1)
	Mid (n = 202)	4.81 (1.93)	102 (50.7)	72 (35.6)
	Most (n = 75)	4.51 (2.09)	45 (60.0)	41 (54.7)

* Significant differences among deprivation groups ($p = 0.01$). IMD: Index of Multiple Deprivation.

DISCUSSION

The biopsychosocial model highlights the importance of factors such as socioeconomic deprivation and social stressors in the generation of pain and disability⁴. It has been demonstrated that those from more deprived areas report greater levels of widespread pain and disability²⁴.

Research examining specific patient groups, including those with RA, has shown that physical and psychological health status is worse in those from more deprived local areas^{7,25}. Our study found that patients with AS who are from more deprived neighborhoods also reported greater disease severity and worse psychological health than those from the more affluent areas. This was true for overall deprivation and 6 of the 7 IMD domains. The housing domain was the only domain that did not show this pattern, which is in accord with previous research in musculoskeletal conditions⁴. As individual lifestyle issues appear to contribute to disease severity, this has obvious implications for clinical management⁷. Those with greater disease severity are more likely to be eligible for, and in need of, clinical interventions. However, evidence suggests that patients from more deprived areas are less likely to visit a healthcare professional²⁵. This has important implications for appropriate healthcare resource allocation and healthcare delivery in terms of targeting care toward those most in need.

After controlling for age, gender, disease duration, and region, higher levels of deprivation were still associated with disease severity (higher levels of pain, greater disease activity, and poorer function). This suggests that living in a deprived area is associated with a higher level of disease severity, regardless of the particular region. A regional effect was also apparent, which suggested that regardless of deprivation in the immediate local vicinity, there is some variation in disease activity across England. Further analysis, examining only those with high disease severity (i.e., those with pain, physical function, or disease activity ≥ 4), found greater levels of anxiety and depression in those living in the more deprived local areas. This suggests that living in a neighborhood of high deprivation may make the effects of severe disease even worse. For example, of all the regions, Newcastle had the lowest (0%) and highest (55%) percentages of patients in the least and most deprived categories of the health IMD domain, respectively. Therefore, looking at

the effect of other comorbidities, and whether these are more prevalent in some regions over others, may be of importance.

Our study shows how socioeconomic status may be reflected in how patients perceive and self-report their health status. Patients from less deprived areas readily reported better health status and showed more confidence in their ability to influence their disease through reporting greater self-efficacy, compared to the patients in more deprived areas. The greater disease severity reported by those from more deprived areas may reflect potential issues with access to care, and could be linked to their low self-efficacy status²⁵. It has been suggested that those with higher education and self-efficacy may be better equipped to negotiate for medical care although they are not necessarily in more need²⁵. With regard to future health, self-efficacy has been shown to be an important predictor of outcome²⁰. Therefore, examining the levels of self-efficacy of patients from more deprived areas may be a good way of targeting those in greater need.

Our study demonstrates that disease severity and hence the need for healthcare interventions in patients with AS is greatest among those living in more deprived areas. This has important implications for health services resource allocation, as earlier research suggests that this group is the least likely to access healthcare and receive health interventions. With the advent of new therapies for patients with AS, this has important implications if health service resources are to be allocated equitably.

These findings have important implications for all members of the rheumatology multidisciplinary team. They suggest that patients with AS who are from more deprived areas may require more support in terms of better patient education, low mood identification, and treatment and self-efficacy enhancement.

Limitations of our study. The patient sample was taken from a secondary care setting and therefore may have more severe disease than a community-based cohort. However, normal practice in the UK dictates that if a primary care physician suspects AS, the physician usually refers the patient to a rheumatologist within secondary care for diagnosis and ongoing treatment.

We did not collect any clinical measures of physical

restriction due to AS. As the study is cross-sectional, causal interpretations cannot be made; therefore we can only describe the associations between socioeconomic measures and health status variables.

The overall response rate (62.8%) is acceptable and the response rates from the individual regions varied from 51% to 70.6%. The spread of patients over a number of diverse sociodemographic categories and geographic areas suggests that the results can be generalized to patients with AS across England. We do not have access to any data relating to the nonresponders and hence response bias was not assessed. However, the response rate does not seem to be related to site affluence. For example, Cambridge and Bristol were the 2 least deprived sites and they had the best and worst response rates, respectively. Patients with low literacy levels (more frequent in socially deprived and ethnic minority groups) are less likely to have responded to this postal questionnaire study. Although the inability to comprehend written English may have slightly lowered the overall response rate, we were not specifically excluding patients on the basis of ethnic background.

It is possible that having AS reduces educational and employment opportunities, a situation that may lead to the patient gravitating to a more deprived area because of lower income and more affordable accommodation. Unfortunately, we did not have access to information about the SOA when the patient was first diagnosed, and hence this cannot be assessed.

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