

## EXTENDED REPORT

## Health status of patients with ankylosing spondylitis: a comparison with the general population

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**Objective:** To examine the subjective health in patients with ankylosing spondylitis (AS) compared with the general population, and to explore the associations between health status and age, sex of the patients, and educational level in AS.

**Methods:** Health status was assessed with a generic instrument (SF-36) in 314 patients with AS and in 2323 people from the general population. Subgroup analyses were performed according to age, sex, and educational level. Standard difference scores (s-scores) were calculated to ensure the clinical meaningfulness of the norm based comparisons.

**Results:** Both men and women with AS reported significantly impaired health on all scales of the SF-36. Women reported significantly worse health on physical health domains. However, when calculating differences from the general population, numerically larger s-scores were found for men (except for physical role and vitality). The relative impact of AS seems to diminish with increasing age. In AS, better health was significantly associated with higher education across all scales. Deviations from the general population on the non-physical health aspects were especially pronounced in patients with low education.

**Conclusions:** All key dimensions of health are affected by AS. The physical aspects seem to be most severely affected, but in the less educated group of patients, the disease impact on the mental health aspects was also considerable. Evaluation and management planning should take the complexity of AS into consideration. The focus on physical function should be maintained, and additional attention should be paid to the mental and social consequences of AS.

Ankylosing spondylitis (AS) is a chronic, inflammatory progressive disease. Its prevalence is most commonly reported to be 0.1–0.2%, with a 3:1 to 2:1 male:female ratio.<sup>1–5</sup> The affected people typically contract the disease between the ages of 20 and 40 years and have pain, joint stiffness, and a gradual loss of spinal mobility, resulting in various degrees of functional limitation. The characteristic radiographic changes evolve over years, primarily in the axial skeleton and especially in the sacroiliac joints.<sup>6–7</sup> Some inequalities in the skeletal manifestations are apparent between men and women,<sup>4–10</sup> indicating a milder disease course in the female patients. Most important treatments are physiotherapy aiming at preventing loss of mobility, and anti-inflammatory drugs and biological agents to modify the inflammatory process.<sup>1–11–14</sup>

The medical findings of AS are well known,<sup>5–15–17</sup> but empirical knowledge on the subjective health of the affected person is relatively scarce. Health is usually considered to reflect the person's evaluation of physical, social, and mental functioning as well as wellbeing, thus capturing the person's experience of illness and how it influences his/her life.<sup>18–19</sup> For example, limitations in physical functioning may influence the ability to remain in employment and participate in leisure and domestic activities. The ability to fulfil social roles in family and society may thereby be restricted, thus influencing the person's emotional state. Consequently, there is a need to explore the burden of the disease in AS, focusing on a wide range of health dimensions.

To understand the burden of a specific disease in a particular group of patients, a comparison with the general population is the best method.<sup>20</sup> However, this presupposes measurements acceptable in both diseased and healthy populations. The Short Form-36 (SF-36) is such an instrument, which covers the most central dimensions of health

and allows for comparisons across diseased populations and between diseased populations and healthy people.

The main objective of this study was to examine the self reported health status in patients with AS compared with the general population. Furthermore, we wanted to explore the associations between health status and age, sex of the patients, and educational level in AS and to estimate the burden of the disease by controlling for the normal variations in health status in the general population.

Our hypothesis before the study was that patients with AS would report impaired health in comparison with the general population, especially for the physical health aspects. Secondly, we expected that the male patients with AS would report a more severe disease course than women, and that the disease burden would increase with increasing age.

## PATIENTS AND METHODS

### Patients

The patients participating in this study were recruited from a register of patients with AS at the Department of Rheumatology, Diakonhjemmet Hospital, Oslo. The register includes patients examined by a rheumatologist and fulfilling the New York classification criteria.<sup>21</sup> The register comprises a total of 465 patients with AS.

### Controls

Data from a previous study of the general population were used for comparison.<sup>22</sup> The Norwegian Government Computer Centre performed a random draw from the

**Abbreviations:** ANOVA, analysis of variance; AS, ankylosing spondylitis; BASDAI, Bath Ankylosing Disease Activity Index; BASFI, Bath Ankylosing Functional Index; RA, rheumatoid arthritis; SF-36, Short Form-36

**Table 1** Characteristics of patients with AS and the general population

| Characteristic                      | AS<br>(n=314) | GP<br>(n=2323) | p Value                  |
|-------------------------------------|---------------|----------------|--------------------------|
| Age (years), mean (SD)              | 43.7 (12.3)   | 50.9 (16.5)    | p<0.0001                 |
| Men (%)                             | 63            | 49             | $\chi^2=21.8$ , p<0.0001 |
| Disease duration (years), mean (SD) | 13.3 (11.3)   |                |                          |
| Employed (%)                        | 67            | 64.5           | $\chi^2=0.55$ , p=0.46   |
| >12 Years education (%)             | 57            | 29             | $\chi^2=106$ , p<0.0001  |
| BASDAI                              | 49.7 (22.4)   |                |                          |
| BASFI                               | 31.2 (24.6)   |                |                          |

Results are shown as mean (SD) for continuous variables, percentage for counts.

AS, ankylosing spondylitis; GP, general population; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index (VAS scales, 0=best, 100=worst); BASFI, Bath Ankylosing Spondylitis Functional Index (VAS scales, 0=best, 100=worst).

National Register of Norway including all Norwegian inhabitants aged 19–80 years with the same last digit in their social security number. The sample is considered to reflect the general sex and age distribution of the Norwegian population. In total, 3500 subjects were drawn out and contacted in 1996. The data collected from 2323 (66%) respondents were used in this study.<sup>23</sup>

### Data collection

All patients in the AS register received a mailed questionnaire in 2002. Non-respondents received a reminder after 6 weeks. Health status was assessed by the SF-36 health survey in patients with AS and controls. The questionnaire to the patients with AS also examined demographic variables and some disease-specific instruments. The study was approved by the ethical committee for medical research.

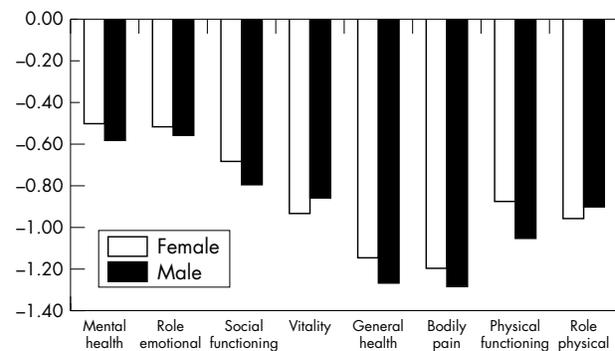
### Generic instrument

The MOS SF-36 is a generic instrument providing information about eight different aspects of subjective health. It is widely used in health surveys in the general population as well as in various diseased populations.<sup>20–24</sup> Cross sectional studies have shown that the SF-36 correlates well with corresponding dimensions of disease-specific instruments.<sup>25–26</sup> The items of the SF-36 are grouped into eight subscales: physical functioning (10 items), role limitation due to physical problems (4 items), role limitation due to emotional problems (3 items), bodily pain (2 items), social functioning (2 items), mental health (5 items), vitality (4 items), and general health perception (5 items). The response choices in the role-functioning scales (physical and emotional) are dichotomous (yes/no). The other items have three to six response choices. The raw scores were coded and recalibrated following the standard guidelines, and the items were then summed and transformed to the eight 0–100 scales (0 = worst health, 100 = best health).<sup>24</sup> The SF-36 has been

translated into Norwegian according to a strictly defined protocol. The instrument is validated and performs well in patients with rheumatoid arthritis (RA).<sup>27</sup>

### Disease-specific instruments

The Association of Assessment in Ankylosing Spondylitis (ASAS) has agreed upon a core set of domains and measures to be used in AS for clinical and research purposes.<sup>28–30</sup> Included in the core set are the Bath Ankylosing Functional Index (BASFI) and the Bath Ankylosing Disease Activity Index (BASDAI). 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. The BASDAI consists of six visual analogue scales dealing with fatigue, spinal pain, joint pain, localised tenderness, and quality and quantity of morning stiffness (BASDAI and BASFI: 0 = best, 100 = worst score).<sup>31–33</sup>



**Figure 1** Standard difference scores (s-scores) for female and male patients with AS (calculation of s-scores was based on the separate male and female general population values).

**Table 2** Mean (SD) SF-36 scores and s-scores in patients and the general population (GP) (total samples and for men and women separately)

|                      | All           |                |          | Women         |                |          | Men           |                |          |
|----------------------|---------------|----------------|----------|---------------|----------------|----------|---------------|----------------|----------|
|                      | AS<br>(n=314) | GP<br>(n=2323) | s-Scores | AS<br>(n=117) | GP<br>(n=1192) | s-Scores | AS<br>(n=197) | GP<br>(n=1131) | s-Scores |
| Mental health        | 70 (19)       | 79 (17)        | -0.52    | 69 (19)       | 78 (17)        | -0.49    | 71 (20)       | 80 (16)        | -0.58    |
| Role emotional       | 66 (42)       | 82 (32)        | -0.50    | 62 (43)       | 79 (35)        | -0.51    | 68 (41)       | 85 (30)        | -0.55    |
| Social functioning   | 70 (27)       | 86 (22)        | -0.71    | 68 (28)       | 84 (23)        | -0.68    | 71 (26)       | 88 (21)        | -0.80    |
| Vitality             | 43 (23)       | 60 (21)        | -0.83    | 37 (22)       | 57 (21)        | -0.93    | 46 (23)       | 63 (20)        | -0.86    |
| General health       | 51 (24)       | 77 (22)        | -1.20    | 50 (24)       | 76 (23)        | -1.15    | 51 (24)       | 77 (21)        | -1.26    |
| Bodily pain          | 44 (22)       | 75 (26)        | -1.21    | 41 (21)       | 73 (27)        | -1.19    | 45 (23)       | 77 (25)        | -1.28    |
| Physical functioning | 71 (23)       | 87 (19)        | -0.88    | 67 (23)       | 85 (21)        | -0.87    | 74 (24)       | 90 (16)        | -1.05    |
| Role physical        | 44 (41)       | 77 (36)        | -0.97    | 36 (38)       | 75 (38)        | -0.75    | 49 (41)       | 79 (34)        | -1.16    |

Value of p<0.001 for all comparisons (one sample t test with mean value for each scale of the general population as test value).

**Table 3** Mean (SD) SF-36 scores in male and female patients with AS

|                      | Female (n = 117) | Male (n = 197) | p Value* |
|----------------------|------------------|----------------|----------|
| Mental health        | 69 (19)          | 71 (20)        | 0.45     |
| Role emotional       | 61 (43)          | 68 (41)        | 0.19     |
| Social functioning   | 68 (27)          | 71 (26)        | 0.33     |
| Vitality             | 37 (22)          | 46 (22)        | 0.001    |
| General health       | 50 (24)          | 51 (24)        | 0.10     |
| Bodily pain          | 41 (21)          | 45 (23)        | 0.12     |
| Physical functioning | 67 (23)          | 73 (24)        | 0.01     |
| Role physical        | 36 (38)          | 49 (41)        | 0.01     |

\*Independent sample *t* test.

**Statistics and data analyses**

The data were analysed using the SPSS for Windows, version 11 (SPSS Inc, Chicago, IL). Descriptive statistics are given as means (SD). Differences between patients and the general population were examined by  $\chi^2$  tests of categorical variables. Owing to the different number of participants in the two samples, a one sample *t* test was used to compare the mean scores of the SF-36 scales in the patient group and the general population. Standard difference scores (s-scores) were calculated by subtracting the mean scores of the patients from the mean scores of the general population, followed by dividing these deviations by each scale's standard deviation in the general population.<sup>23</sup> The values of the s-scores were interpreted according to Cohen's effect size index, in which 0.2 refers to a small difference, 0.5 to a moderate difference, and 0.8 or more to a large difference.<sup>34</sup>

Possible interactions between the independent variables (age, sex, educational level) and the presence or absence of AS, were explored using analysis of variance (ANOVA) with the different SF-36 scales as dependent variables.

Within the patient group, two sample independent *t* tests were used for comparisons. For comparisons between educational groups, the sample was divided into a low educational group (12 years or less) and a high educational group (more than 12 years). ANOVA was performed to examine the effect of age on the different SF-36 scales when adjusting for sex and disease severity (BASDAI and BASFI).

A Pearson correlation analysis was performed between the disease-specific instruments (BASDAI, BASFI) and the corresponding items in the generic instrument (data not shown).

Owing to multiple comparisons with increasing risk of type 1 errors, the level of statistical significance was set at 0.01.

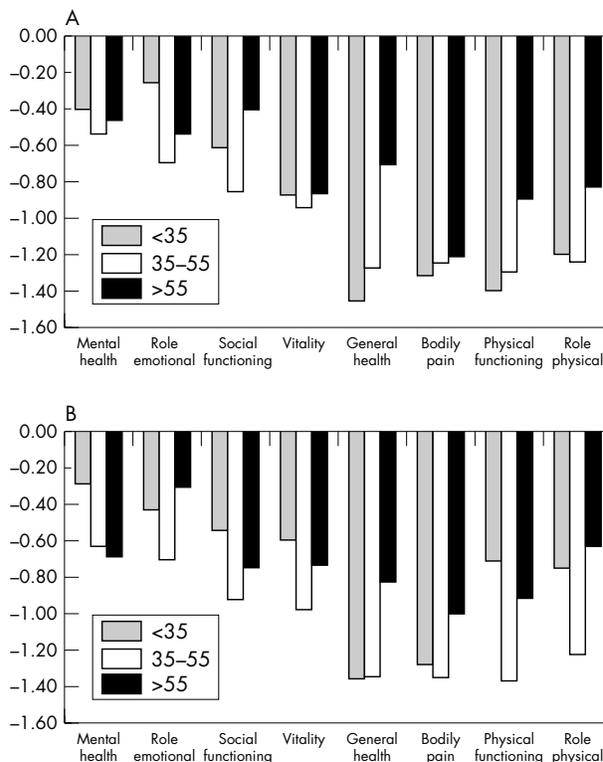
**RESULTS**

**Study samples**

Of the 465 patients with AS receiving the questionnaire, 314 (68%) responded. The non-respondents were numerically younger than the respondents and 63% of the non-

**Table 4** Effect of age on the SF-36 scales when adjusted for sex and disease severity (BASDAI and BASFI)

|                      | Unstandardised $\beta$ (CI) | p Value |
|----------------------|-----------------------------|---------|
| Mental health        | 0.14 (-0.02 to 0.3)         | 0.09    |
| Role emotional       | 0.27 (-0.1 to 0.7)          | 0.17    |
| Social functioning   | 0.16 (-0.05 to 0.4)         | 0.13    |
| Vitality             | 0.21 (0.02 to 0.4)          | 0.03    |
| General health       | 0.32 (0.1 to 0.5)           | 0.001   |
| Bodily pain          | 0.11 (-0.02 to 0.2)         | 0.12    |
| Physical functioning | -0.12 (-0.2 to -0.01)       | 0.05    |
| Role physical        | 0.09 (-0.2 to 0.4)          | 0.57    |



**Figure 2** Standard difference scores (s-scores) for age groups of female (A) and male (B) patients with AS (calculation of s-scores was based on the values of separate general population age and gender groups).

respondents were men. Table 1 shows the characteristics of the respondents. Age ranged from 23 to 81 years and the disease duration ranged from 1 to 53 years. The mean age of the general population sample was higher than that of the AS sample, and as expected the proportion of men was different (table 1).

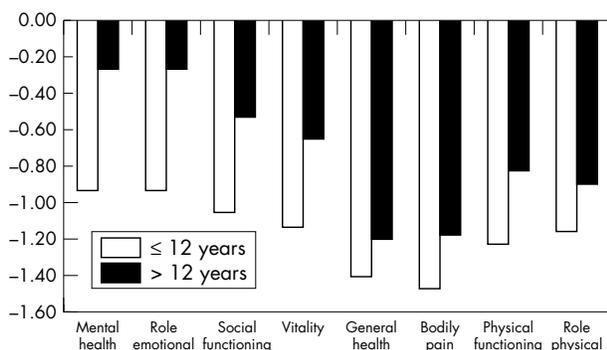
Both men and women with AS reported significantly worse health on all scales of the SF-36 than the general population (table 2).

An ANOVA analysis was performed to explore the possible interactions between age, sex of the patients, education, and the presence or absence of AS. The high education groups reported significant better health across all domains in both the general population and in the AS group, but the effect of education was even stronger in the AS group than in the general population across all the SF-36 scales ( $p < 0.001$ ). The general population reported poorer scores with increasing age on the general health scale, while the AS group tended to report better general health with increasing age. There were

**Table 5** Mean (SD) SF-36 scores in patients with AS with low ( $\leq 12$  years) and high ( $> 12$  years) education

|                      | Low (n = 136) | High (n = 178) | p Value* |
|----------------------|---------------|----------------|----------|
| Mental health        | 63 (22)       | 76 (15)        | <0.0001  |
| Role emotional       | 50 (45)       | 77 (36)        | <0.0001  |
| Social functioning   | 62 (29)       | 76 (23)        | <0.0001  |
| Vitality             | 36 (22)       | 48 (22)        | <0.0001  |
| General health       | 44 (24)       | 55 (23)        | <0.0001  |
| Bodily pain          | 35 (22)       | 51(20)         | <0.0001  |
| Physical functioning | 62 (24)       | 78 (21)        | <0.0001  |
| Role physical        | 31 (37)       | 53 (41)        | <0.0001  |

\*Independent sample *t* test.



**Figure 3** Standard difference scores (s-scores) for high and low education groups of patients with AS (calculation of s-scores was based on the values of separate high and low education groups of the general population).

no differences in the effect of the sex of patients in the two groups ( $p > 0.01$ ). Women reported poorer health in both groups across all scales except for the general health scale, which was similar for men and women in both groups.

Significant differences were found between men and women in the AS group for physical functioning ( $p = 0.01$ ), role physical ( $p = 0.01$ ), and vitality scales ( $p < 0.001$ ), with women reporting worse health than men (table 3). No differences were found for the remaining scales ( $p > 0.10$ ). However, when calculating s-scores between the AS group and the general population, numerically larger scores (larger difference from the general population) were found for men than for women on all scales except for vitality and role physical (fig 1). The differences in Cohen's index were large ( $\geq 0.8$ ) for men and women in vitality, general health, bodily pain, and physical function. Additionally, large differences were found in social functioning and role physical for men (table 2).

When adjusting for sex and disease severity (BASDAI and BASFI) in a multiple model, only physical functioning was shown to be worse with increasing age ( $\beta$  (confidence interval (CI)) =  $-0.12$  ( $-0.2$  to  $-0.01$ ),  $p = 0.05$ ) (table 4).

Figures 2A and B show the s-scores for men and women presented in age groups. For both men and women the largest differences from the general population were seen in the physical health aspects. The deviation from the general population in these scores diminished with increasing age across most of the scales (figs 2A and B).

Table 5 shows data from the two educational levels within the AS group. Patients with more than 12 years' education reported better health on all subscales than the less educated group ( $p < 0.0001$ ).

Figure 3 illustrates the differences from the general population in subgroups of different educational level. Patients with low education showed a considerably larger deviation from the general population in mental health, role emotional, social functioning, and vitality, indicating that these dimensions are relatively more affected in the low education group.

## DISCUSSION

In this health survey, patients with AS reported significantly impaired health on all scales of the SF-36, compared with the general population. This result was consistent in men and women. Thus, this study highlights the fact that AS affects people across all major dimensions of health, including mental and social functioning.

AS is a chronic condition with a variable disease course, but some studies indicate that the disease course to some extent can be predicted early. Carrette *et al* found that more than 80% of the patients who had severe spinal restrictions

were severely restricted within the first 10 years of disease,<sup>35</sup> and a French study concluded that predictive factors of poor or benign long term outcome could be defined very early after the onset of spondyloarthritis.<sup>36</sup> The results of our study indicate that when controlling for the sex of the patients and disease severity, increasing age in the AS group was associated with poorer health only for physical functioning. However, physical functioning is affected by age also in the general population. Our findings indicate that increasing age reduces the deviation from the general population, indicating that the relative impact of AS diminishes with increasing age. On the other hand, the middle aged group was the most affected, supporting the need to provide relevant treatment to prevent physical disabilities.

Some early reports suggested differences between men and women in the course of the disease.<sup>4 8 9 37 38</sup> Women are supposed to have a later age of onset, milder disease course, longer asymptomatic periods, but more extraspinal involvement.<sup>38</sup> Eustace *et al* reviewed the radiographic features of 83 patients, and found more peripheral arthritis and more asymptomatic sacroiliitis in women, but the prevalence of spinal involvement was similar in men and women.<sup>10</sup> When subjective health was measured in this study, women with AS reported worse physical functioning, more physical limitations, and a greater reduction in vitality than men. However, when the differences from the general population were calculated, larger differences were found for men than for women on all scales except vitality and role physical. Thus, when eliminating the normal differences in men and women's self assessment of their health, and the underlying reasons for these inequalities, the crude effect of the disease is greater in men.

It is well recognised that AS may result in physical impairment. However, the results of this study indicate that the impact of AS is broad, and includes mental as well as physical aspects of health. Even if the physical aspects were mostly affected, and this finding is supported by other studies,<sup>39 40</sup> subgroup analyses showed that the difference in disease impact between low and high educated patients is considerably greater in the non-physical health dimensions (fig 3), indicating that special attention should be paid to these aspects of health in patients with low education.

The patients included in this study were recruited from a department of rheumatology. It might be assumed that patients who have been in contact with a rheumatological department are more severely affected by the disease than those who have not. However, in Norway, patients with AS are referred from the general practitioner to a rheumatological department to confirm the diagnosis, and thus they will be included in the register regardless of disease severity. Access to a rheumatologist in Oslo is good, as indicated by the completeness of the register of patients with RA in Oslo.<sup>41</sup> The patients included in this study were of a wide range of age and disease duration and the distribution of disease severity among the patients was broad. The sample is thus likely to be representative for patients with AS, as has been demonstrated in the Oslo RA register.<sup>41</sup>

Disease-specific instruments have been constructed to measure physical limitations,<sup>32 42</sup> disease activity,<sup>31</sup> global wellbeing,<sup>33</sup> and the quality of life<sup>43</sup> in patients with AS. However, when comparing health status in a patient group with a general population, a generic instrument has to be applied. Generic instruments are designed to capture various aspects of health status in any population irrespective of disease or condition, and may thus provide information on disease consequences that disease-specific instruments cannot detect.<sup>44 45</sup> A concern is, however, that the broad scope of the generic instruments might not adequately reflect health status in populations with specific disorders. In a study of

patients with low back pain, the patients showed more impaired physical function on the disease-specific instrument Oswestry Disability Questionnaire than on the SF-36 physical functioning scale.<sup>46</sup> A possible explanation is that the SF-36 physical functioning scale evaluates activities which perhaps are not as strongly affected by low back pain as the activities included in the disease-specific disability instrument. In the present study, however, the disease-specific and the generic instruments correlated well (BASDAI and SF-36 bodily pain:  $r = 0.7$ ; BASFI and SF-36 physical functioning:  $r = 0.8$ , additional data not shown). This finding is supported by a study of the Norwegian version of the SF-36, in which the instrument was found to perform similarly to disease-specific health status measures in patients with RA.<sup>47</sup>

Interpretation of health status scores may be problematic. The meaning and clinical relevance of high and low scores cannot be defined unambiguously. In studies including large number of participants, the results frequently will reach statistical significance, but a statistically significant difference is not necessarily clinically meaningful. Comparing the results with norm based data is one method of deciding whether an observed score implies a significant difference from the scores typical for the general population. However, health status measures may have substantial variance.<sup>44</sup> In a health survey of the general Norwegian population, Loge *et al* found that self reported physical health was strongly affected by age, women reported poorer health than men on nearly all health aspects, and educational status affected both physical and mental health, but the effect was smallest in the mental aspects.<sup>22</sup> Therefore, when using norm based comparisons, this variance must be taken into consideration. Our approach to overcoming this methodological concern was to compute s-scores—that is, to divide the difference scores with the variability in the general population (the standard deviation). This allows interpretation of the clinical meaningfulness of observed scores and comparison of scores across the different scales.<sup>48–49</sup>

Traditional clinical evaluation of patients with AS includes examination of the musculoskeletal system and measures of impairment like pain and spinal range of motion. However, the results of this study indicate that the traditional evaluation may fail to understand and describe the multi-dimensional issues and complexity of AS. Our study confirms that the physical aspects of health seem to be most severely affected. However, all dimensions of health were significantly affected, and in the less educated group of patients, the disease impact on mental health was considerable. A management programme for patients with AS and the planning of the healthcare services should take these findings into account by maintaining the focus on impairment and physical function, but also focusing on the mental and social consequences of the disease.

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