Raising the bar for classification and outcome assessment for clinical studies in axial spondyloarthritis

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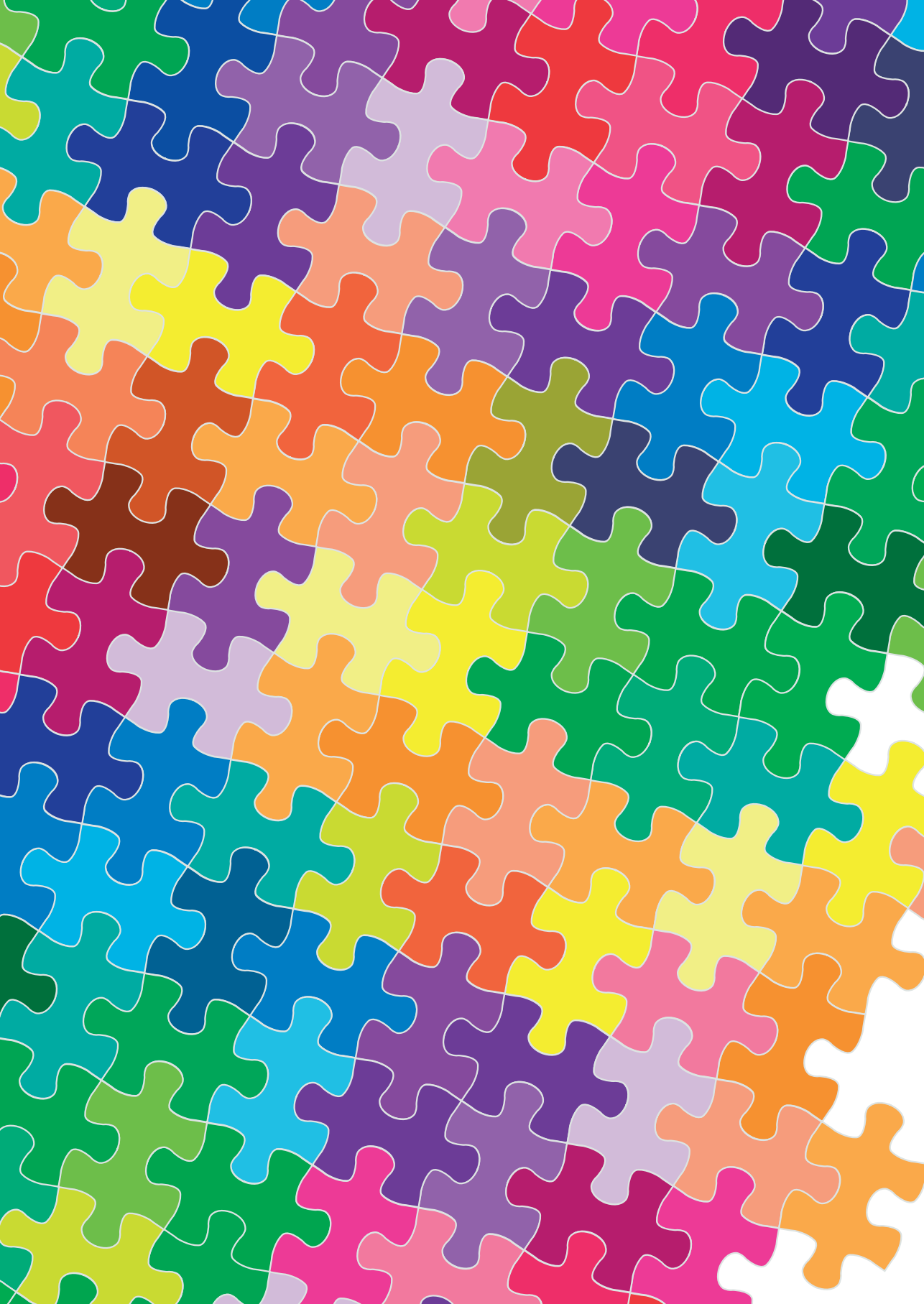

PART III

PATIENT REPORTED OUTCOMES IN EARLY AXIAL SPONDYLOARTHRITIS

CHAPTER 9

PATIENTS WITH EARLY AXIAL SPONDYLOARTHRITIS HAVE BETTER WORK AND ACTIVITY OUTCOMES AND HEALTH-RELATED QUALITY OF LIFE COMPARED TO CHRONIC BACK PAIN PATIENTS WITHOUT SPONDYLOARTHRITIS AT TWO YEARS: RESULTS FROM THE SPONDYLOARTHRITIS CAUGHT EARLY COHORT.

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ABSTRACT

Background

As with other causes of chronic back pain (CBP), axial spondyloarthritis (axSpA) negatively affects health-related quality of life (HRQoL) and work outcomes. The aim of this study was to compare HRQoL and work and activity outcomes between patients with and without an axSpA diagnosis over two years in routine care.

Methods

Two-year follow-up data from the Spondyloarthritis Caught Early cohort was used. CBP patients were allocated to the axSpA or no-axSpA group, based on the rheumatologist's diagnosis at two-year follow-up. HRQoL was assessed by the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36); work and activity outcomes by the Work Productivity and Activity Impairment (WPAI). Outcome measures at two-year follow-up were compared between groups using linear regression models, corrected for baseline values, NSAID-use over time, gender and age. Wilcoxon signed-rank tests were used to investigate change within groups.

Results

In total, results from 337 CBP patients (209 axSpA and 128 no-axSpA) were analysed. Physical Component Summary scores were significantly higher (better) in the axSpA group (40(±SD12) vs 35(15), $p<0.001$), and levels of all WPAI outcomes were significantly lower (better) in the axSpA group at two years (presenteeism: 20(25) vs 30(28), $p=0.029$, absenteeism: 3(1) vs 8(2), $p=0.041$, WPL: 21(26) vs 34(32), $p=0.012$, activity impairment: 23(25) vs 31(27), $p=0.030$), after correction for gender, age, NSAID-use over time and baseline values. There was no difference between groups regarding the mental component summary score ($p=0.272$).

Conclusion

After two years axSpA patients in routine care had significantly better outcomes compared to patients without axSpA.

INTRODUCTION

Axial spondyloarthritis (axSpA) is an inflammatory arthritis of the spine. The disease can be subdivided into two subtypes: non-radiographic axSpA (nr-axSpA) and radiographic axSpA (r-axSpA) (also known as ankylosing spondylitis(AS)). In the latter radiographic abnormalities consistent with sacroiliitis on plain radiographs are present, in the former the abnormalities are not (yet) present.

Chronic back pain (CBP) is the hallmark of axSpA, but also a symptom of many other diseases. This contributes to the substantial diagnostic delay in axSpA. Given that effective treatment is available for axSpA including nr-axSpA, experts have designated improving identification of early SpA and early referral to rheumatologists as important unmet needs in the clinical care of spondyloarthritis[1].

As with other causes of CBP, axSpA negatively affects health-related quality of life (HRQoL) and work outcomes, with an increasing impact with increasing severity of CBP[2-4]. Work productivity loss (WPL)-mainly caused by a decrease in work productivity while being at work (so called presenteeism)- contributes to the substantial societal costs of axSpA[5].

Early axSpA cohorts have reported improvement in HRQL and WPL following diagnosis, suggesting a beneficial effect of early diagnosis and subsequent treatment[5-7]. However, lack of a comparator group makes these results difficult to interpret and it is particularly difficult to attribute the observed improvement to axSpA treatment. Ideally, a study should be performed where immediately after diagnosis patients are randomized to receive either routine treatment or no treatment. Apart from ethical issues of withholding recommended treatment[8], such a study would be challenging to execute given that nonsteroidal anti-rheumatic drugs (NSAIDs)-which is the first-line pharmacological treatment of axSpA- are available as *over the counter* medications in most countries.

The Spondyloarthritis Caught Early (SPACE) cohort commenced in 2009 with the aim of identifying early axSpA in patients presenting with back pain of short duration. For this purpose, the SPACE cohort started off with a single inclusion criterion: chronic back pain present for at least three months, not exceeding two years with an onset before the age of 45. All included patients were followed for at least two years, at which point the baseline diagnosis had to be confirmed or rejected. By design, this resulted in a group of patients with an axSpA diagnosis with high certainty at 2-year follow-up, and a group of patients with a diagnosis of 'no axSpA' at 2-year follow-up. This set-up provides a unique opportunity to compare patient reported outcomes including HRQoL and work and activity outcomes between CBP patients with and without a diagnosis of axSpA in a daily practice setting during the first two years after diagnosis.

METHODS

The SPACE cohort has been described in detail previously; in brief, patients over 16 years of age referred to the rheumatology outpatient clinic-in the Netherlands, Italy, Norway and Sweden- with CBP (duration of back pain ≥ 3 months and <2 years) starting before the age of 45 were included in the SPACE cohort. Follow-up was performed only in patients with at least two SpA features or one feature with a positive likelihood ratio for axSpA ≥6.4[9]. Using information on all SpA features and imaging, the treating rheumatologists provided a preliminary baseline diagnosis (axSpA or no axSpA) and a definite 2-year diagnosis, as well as the level of confidence (LoC) regarding this diagnosis on a 0-10 scale (0, not confident; 10, very confident).

Patients

Patients were allocated to one of two groups based on the 2-year diagnosis from the rheumatologist and the LoC regarding that diagnosis. The first group consisted of all patients with a diagnosis of axSpA with a LoC of at least 7: the axSpA group; the second group consisted of all patients without a diagnosis of axSpA, as well as those with a diagnosis of axSpA with a LoC of 6 or smaller: the no axSpA group. For this study, patients were included if they completed 2 years of protocolised follow-up, meaning a diagnosis and accompanying LoC and MRI had to be available at two-year follow-up. Additionally, there had to be complete clinical data and data for and at least one questionnaire (i.e. HRQoL or work outcomes) at both timepoints.

Outcomes

Health-related quality of life was assessed using the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36) version 1[10]. Age-, sex- and country-weighted scale scores were created for each of the 8 subscales of the SF-36[11-13]. Numeric scores ranged from 0 (worst health) to 100 (best health), after recoding and recalibration. In absence of Italian age- and sex-matched scores, Dutch age-and sex-matched scores were used for the Italian patients (n=46). The physical (PCS) and mental component summary (MCS) scores were calculated from the adjusted scores on each of the respective subscales and transformed to enable comparison to the general population mean of 50. Higher scores indicated better HRQoL[14]. A few cases (n=17) had a negative PCS, these were set to 0[6]. Additionally, the proportion of patients with an improvement or worsening of the PCS and MCS above the minimal clinically important difference (MCID) was assessed. We applied the MCID commonly used in clinical trials with biological disease modifying anti-rheumatic drugs (bDMARD) in axSpA of 5 points for the PCS and MCS[15-17].

Work productivity and activity impairment were assessed using the Work Productivity and Activity Impairment (WPAI) questionnaire[18,19]. Consisting of 6 items, the WPAI assesses the

impact of chronic back pain complaints on presenteeism, absenteeism and work productivity loss (WPL). Presenteeism reflects the reduction in performance while at work due to disease; presenteeism was calculated from the influence of disease on work productivity as reported by the patient (on a 0-10 scale). Absenteeism indicated the hours missed from work due to disease; absenteeism was calculated by taking the reported number of hours missed at work due to disease and dividing this number by ten. WPL was derived from presenteeism and absenteeism (WPL=absenteeism+((1-absenteism)×(presenteeism))) and provided an indication of the total loss of work productivity due to disease. Finally, activity impairment was defined as impairment due to disease in all non-work-related activities; activity impairment was calculated from the reported influence of disease on regular daily activities. All WPAI outcomes were presented as percentages between 0-100; higher scores implied greater impairment. Additionally, the proportion of patients with any (>0%) absenteeism, presenteeism, WPL and activity impairment were assessed.

Assessment of presenteeism, absenteeism and WPL was restricted to the working population, which was defined as those with paid work at baseline and 2-year follow up. Activity impairment was assessed for the entire study population. In addition, the proportion of employed patients was assessed for baseline and two-year follow-up; and expressed as the percentage of the employable population (defined as everyone of working age (>16), who was not a fulltime student). Patients were considered employed if they reported to have worked for at least one hour in the previous week or had a permanent job during the previous week[20].

Analyses

The database was locked on January 1st 2020, at that time a total of 807 patients were included in the SPACE cohort, of whom 468 completed at least 2 years of follow-up. 396 of these patients had a MRI and a diagnosis with corresponding LoC available at 2-year follow-up. Of these 396 patients, 337 patients with complete clinical data and data at both timepoints for at least one questionnaire (i.e. SF-36 or WPAI) were available for analysis (Supplementary figure S.1).Categorical variables were reported as frequencies (proportions) and continuous variables as means and standard deviation (SD). Wilcoxon signed-rank tests were used to compare data within groups over time. Linear regression models were built for the SF-36 (PCS and MCS) and WPAI outcomes (presenteeism, absenteeism, WPL and activity impairment) with diagnosis at 2 years as the independent variable, the respective outcomes as dependent variable and the baseline value of the respective outcome as covariate to compare 2-year outcomes between groups.

Age at baseline, gender and NSAID-use over time were added to the models as potential confounders. Age was considered as axSpA might have a different impact on the QoL and work-related outcomes in those just starting their working life than in those who

have been working for a while[21,22]. Gender was considered as it is known that women experience a larger impact of axSpA on their QoL and work productivity[6,21]. NSAID-use over time was considered since efficacious treatment is known to improve QoL and work-related outcomes[23].

As treatment with bDMARDs was only available to those patients who got a diagnosis of axSpA, it was decided it would be worthwhile to perform sensitivity analyses. In these sensitivity analyses the patient population was restricted to patients not using bDMARDs at any point during the 2-year period of follow-up to ensure potential differences between groups could not be explained by the availability of treatment.

Data was analysed using STATA SE V.16 (Statacorp). P-values < 0.05 were considered statistically significant.

RESULTS

In total 209 patients with a diagnosis of axSpA and 128 patients without a diagnosis (no axSpA) were analysed in this study. Patients with an axSpA diagnosis were more often male and HLA-B27 positive, had a slightly lower age at baseline, and a higher number of SpA features than the no axSpA patients, whereas no axSpA patients more often had a positive family history (Table 1). Furthermore, sacroiliitis on MRI and radiographs according to the local radiologist was frequent in the axSpA group, but uncommon in the no axSpA group. Contrary to use of NSAIDs -which was high in both groups-, use of biological DMARDs (bDMARD) was very limited at baseline: 1 patient in the no axSpA group used a bDMARD for concomitant inflammatory bowel disease (IBD); 8 patients in the axSpA group used a bDMARD at baseline, of whom 5 had psoriasis and 1 uveitis. At two-year follow-up 56 patients in the axSpA group were using a bDMARD; in the no axSpA group there were 4 bDMARD-users, 3 as treatment for IBD and 1 for psoriasis.

Mean total back pain was significantly lower at two-year follow-up compared to baseline in both groups (axSpA 3.1 (±SD 2.5) vs. 4.5 (2.5), p<0.01; no axSpA (4.2 (3.0) vs. 5.3 (2.5),p<0.01).

Table 1 Baseline characteristics of CBP patients included in the SPACE cohort stratified by two-year clinical diagnosis.

Characteristic	Diagnosis axSpA (n=209)	CBP (n=128)
Male, n(%)	117 (56)	38 (30)
Age (years), mean (SD)	29 (7)	31 (8)
Symptom duration (months), mean (SD)	13 (7)	13 (7)
HLA-B27 positive, n(%)	157 (75)	50 (39)
IBP, n(%)	174 (83)	92 (72)
Good response to NSAIDs[†], n(%)	100 (48)	48 (38)
Positive family history of SpA, n(%)	94 (45)	80 (63)
Past history or current symptoms*		
Peripheral arthritis, n(%)	55 (26)	14 (11)
Enthesitis, n(%)	68 (33)	21 (16)
Dactylitis, n(%)	25 (12)	2 (2)
Psoriasis, n(%)	35 (17)	12 (9)
IBD, n(%)	11 (5)	9 (7)
Acute anterior uveitis, n(%)	25 (12)	8 (6)
Elevated CRP/ESR, n(%)	96 (46)	24 (19)
Sacroiliitis radiographs[‡], n(%)	54 (26)	3 (2)
Sacroiliitis MRI[‡], n(%)	149 (71)	9 (7)
Number of SpA features[§], mean (SD)	3 (2)	2 (1)
Use of bDMARDs, n(%)	8 (4)	1 (1)
Use of NSAIDs, n(%)	158 (75)	88 (69)

*Past or present condition, either diagnosed or confirmed by a physician

[†] Back pain no longer present or much better 24–48 hours after a full dose of NSAID

[‡] Based on reading of local radiologists

[§] Excluding HLA-B27 status and sacroiliitis on imaging

axSpA, axial Spondyloarthritis; **bDMARD**, biological Disease Modifying Anti-Rheumatic Drug; **CBP**, Chronic Back Pain; **CRP**, C-reactive protein; **ESR**, Erythrocyte Sedimentation Rate; **HLA-B27**, Human Leucocyte Antigen B27; **IBD**, Inflammatory Bowel Disease; **IBP**, Inflammatory Back Pain; **MRI**, Magnetic Resonance Imaging; **NSAIDs**, Non-Steroidal Anti Inflammatory Drugs; **SpA**, Spondyloarthritis.

SF-36

At baseline the mean PCS score was comparable between the axSpA and no axSpA groups (28(14) vs 27(13)). In both groups the mean PCS score significantly improved over two years. However, the PCS was higher in the group with an axSpA diagnosis compared to the no axSpA group at two-year follow-up (40(12) vs 35(15)). In the linear regression analysis, a diagnosis of axSpA was an independent predictor of better PCS scores at two-year follow-up after correction for baseline PCS scores, NSAID-use over time, gender and age ($p<0.001$)(Table 2). Despite the improvements over time, PCS scores were still well below the general population mean of 50 in both groups at two-year follow-up.

The MCS scores were also comparable between the axSpA and no axSpA groups at baseline (47(14) vs 47(12)). Mean MCS scores did not significantly change over time within the groups, nor were MCS scores significantly different between groups at follow-up ($p=0.272$). Moreover, MCS scores in both groups were close to the general population mean of 50, especially at two-year follow-up.

Table 2 Health-related quality of life measured by the SF-36 in CBP patients stratified by two year clinical diagnosis

	axSpA (n=205)		**No axSpA** (n=125)		**p-value** between groups at 2 years
	Baseline	**2 years**	**Baseline**	**2 years**	
PCS, mean (SD)	28 (14)	40 (12)†	27 (13)	35 (15)†	p<0.001*
% Improvement >MCID		67		58	
% Worsening >MCID		11		14	
MCS, mean (SD)	47 (14)	48 (12)‡	47 (12)	49 (11)‡	p=0.272
% Improvement >MCID		34		36	
% Worsening >MCID		30		22	

* Significant difference between groups at two years; after correction for baseline values, gender, age and NSAID use over time (p<0.05)
†Signed-rank test: significant improvement within group over time (p<0.05)
‡Signed-rank test: not significant
axSpA, Axial Spondyloarthritis; **CBP**, Chronic Back Pain; **MCID**, Minimal Clinically Important Difference; **MCS**, Mental Component Summary; **PCS**, Physical Component Summary; **SF-36**, Short-Form Health Survey

Although the proportion of patients with an improvement above the MCID of 5 points was higher in the axSpA group, over half of the patients in both groups (axSpA 67%, no axSpA 58%) had such an improvement of their PCS score. The proportion of patients whose PCS score worsened more than 5 points was low in both groups (axSpA 11%, no axSpA 14%). For the MCS scores the proportion of patients with an improvement and worsening of more than 5 points was less distinct. Approximately one-third had an improvement above the MCID in both groups (axSpA 34%, no axSpA 36%), in the axSpA group the proportion of patients with a worsening of more than 5 points was 30%, this was slightly lower in the no axSpA group (20%).

WPAI

The working population (paid work both at baseline and 2-year follow-up) consisted of 141 patients (69%) in the axSpA group and 87 patients (71%) in the no axSpA group, for these patients presenteeism, absenteeism and WPL were assessed. At baseline, presenteeism was lower in the axSpA group (32(28)% vs 41(27)%), absenteeism was lower in the axSpA group too (7(2)% vs 9(2)%), thus WPL was also lower in the axSpA group (34(29)% vs 44(28)%). In both groups mean percentage of WPL was significantly lower at two-year follow-up, the same applied to presenteeism, yet mean percentages of presenteeism (20(25) vs 30(28)) and WPL (21(26) vs 34(32)) were better at two-year follow-up in the axSpA group (Table 3). For absenteeism, only the axSpA group showed a significant reduction over two years and mean percentages of absenteeism were significantly lower (3(1) vs 8(2)) at two-year follow-up in the axSpA group (Table 3).

Activity impairment could be assessed for all patients, and the mean percentage of activity impairment was lower in the axSpA group (38(27)% vs 48(25)%). At two-year follow-up activity impairment improved significantly in both groups, nevertheless, mean percentages of activity impairment (23(25) vs 31(27)) were better at two-year follow-up in the axSpA group (Table 3).

In linear regression analysis, a diagnosis of axSpA was an independent predictor of better presenteeism (p=0.029), absenteeism (p=0.041), WPL (p=0.012) and activity impairment(p=0.030) at two-year follow-up after correction for baseline scores, NSAID-use over time, gender and age (table 3).

Although the proportion of patients with any WPL and any activity impairment decreased over time, over half of the patients in both groups still experience productivity loss at work (55% in axSpA and 68% in no axSpA) and impairment in non-work related activities (66% in axSpA and 72% in no axSpA).

We found an increase in the employable population over time in both groups (from 89% to 95% in the axSpA group and from 91% to 98% in the no axSpA group). This could be explained by the fact that there were quite a few students (15 in the axSpA group and 10 in the no axSpA group) in the SPACE cohort who completed their studies and found a job in the first two years of study follow-up. Even though the employable population increases, the proportion of patients with paid work remains similar in the axSpA group (from 86 to 89%), which indicated an increase in the number of patients with paid work over time in this group. In the no axSpA group the proportion of patients with paid work slightly decreases (from 84% to 82%) as the employable population increased.

Table 3 Results from the work productivity and activity impairment questionnaire in CBP patients stratified by two-year clinical diagnosis

	axSpA		**no axSpA**		**p-value** between
	Baseline	**2 years**	**Baseline**	**2 years**	groups at 2 years
Working population	*n=141*		*n=87*		
Presenteeism, mean % (SD)	32 (28)	20 (25)†	41 (27)	30 (28)†	p=0.029*
% Presenteeism present	74	56	91	69	
Absenteeism, mean % (SD)	7 (2)	3 (10)†	9 (20)	8 (20)‡	p=0.041*
% Absenteeism present	21	8	25	16	
Work productivity loss, mean % (SD)	34 (29)	21 (26)†	44 (28)	34 (32)†	p=0.012*
% Work productivity loss present	73	55	91	68	
Total population	*n=204*		*n=123*		
Activity impairment, mean % (SD)	38 (27)	23 (25)†	48 (25)	31 (27)†	p=0.030*
% Activity impairment	86	66	96	72	

* Significant difference between groups at two years; after correction for baseline values, gender, age and NSAID use over time (p<0.05)
†Signed-rank test: significant improvement within group over time (p<0.05)
‡Signed-rank test: not significant

Sensitivity analyses

To ensure the differences found between groups were not only due to a difference in the availability of biological treatment, we performed sensitivity analyses in which we included only patients who did not use a bDMARD during the 2 years of follow-up.

For the PCS there was still a highly significant difference (42 (12) vs 36 (14),p<0.001) between those with and without a diagnosis of axSpA at two-year follow-up (supplementary table S.1), when the analysis was restricted to patients not using biologicals. The MCS remained comparable between groups (50 (11) vs 49(11), p=0.655), the subgroup of patients with an axSpA diagnosis not using bDMARDs actually reached an MCS equal to the population mean.

For the WPAI variables, the differences between those with and without a diagnosis became even more apparent for presenteeism (16 (22) vs 30 (28), p=0.002), WPL (17 (23) vs 34(32), p=0.008) and activity impairment (19 (22) vs 31 (27), p<0.001) when analyses were restricted to patients not on bDMARD therapy (supplementary table S.2). However, for absenteeism, the difference between groups was no longer present (2 (12) vs 7 (20), p=0.174).

DISCUSSION

The SPACE cohort-an inception cohort of back pain patients suspected of axSpA- provided a unique opportunity to compare HRQoL and work and activity outcomes between CBP patients with and without a diagnosis of axSpA in a daily practice setting during the first two years after diagnosis. The performed analyses showed an improvement over time in physical HRQoL, WPL, presenteeism, absenteeism and activity impairment over two years of protocolised follow-up in all patients with chronic back pain complaints, regardless of diagnosis. Improvement in both groups suggests that some improvements are due to regression to the mean, with complaints being most severe at the first visit to the rheumatology outpatient clinic regardless of diagnosis. Nonetheless, we showed that a diagnosis of axSpA was an independent predictor of better PCS and WPAI scores at two-year follow-up, emphasizing the value of the comparator group available in this study.

One of the differences between those who get a diagnosis of axSpA versus those who do not get diagnosed is the availability of treatment. At two years NSAID-use was higher in axSpA patients (11% on full-dose) compared to the no axSpA group (5% on full-dose). Moreover, treatment with biologicals is solely available to those diagnosed with axSpA. At two years the number of axSpA patients treated with biological was about a quarter. Therefore, sensitivity analyses were performed to investigate the role of biological therapy in the improvement of the outcomes. These showed that the differences in outcomes between those with and without a diagnosis of axSpA remained when analyses were restricted to patients not on biological therapy, indicating that treatment with biologicals did not explain the differences between the groups.

Another possible explanation for the difference between patients with and without a diagnosis could be their illness perceptions and subsequent influence on coping. Compared to non-specific back pain axSpA has a much clearer pathophysiological framework, and there is a better understanding of what causes the complaints of these patients. For example, in the current ASAS-EULAR management recommendation for axSpA, the primary goal of treating patients with axSpA is to maximise long-term HRQoL through control of-among others- inflammation[8]. Through patient education such a relatively clear conceptual framework could increase patients' understanding of disease and influence illness perceptions, which will be investigated in the future. Finally, there are numerous active patient societies for axSpA patients to turn to for information and support. These factors combined may enhance acceptance of a chronic disease. In future research we will investigate the role of illness perceptions and coping strategies and whether these might help explain the differences between groups found in this study.

A potential limitation of the study is the use of patient reported outcomes for all primary outcomes. An alternative in assessing work productivity loss would have been to use absenteeism numbers reported by employers to get a more objective measure of the hours lost due to disease instead of relying on patient reported information. However, the major cause of work productivity loss was presenteeism and not absenteeism, and this would have been missed by relying solely on employer reported absenteeism.
By design, the patients who did not get diagnosed with axSpA were excluded from the SPACE cohort after two-year follow-up, which meant the maximum follow-up time for which a control group was available was two years. In the cohort, axSpA patients are followed beyond those two years and this will allow us to continue monitoring if the observed improvements in health-related quality of life and work productivity are maintained by using the national population mean of the SF-36 and the European Working Conditions surveys by Eurofound[24] as comparators.

CONCLUSION

In chronic back pain patients suspected of axSpA, we found significant improvements in physical functioning and work-related outcomes over two years of protocolised follow-up. Nonetheless, axSpA patients had significantly better outcomes in physical functioning and work-related outcomes compared to patients with chronic back pain without axSpA.

SUPPLEMENTARY DATA

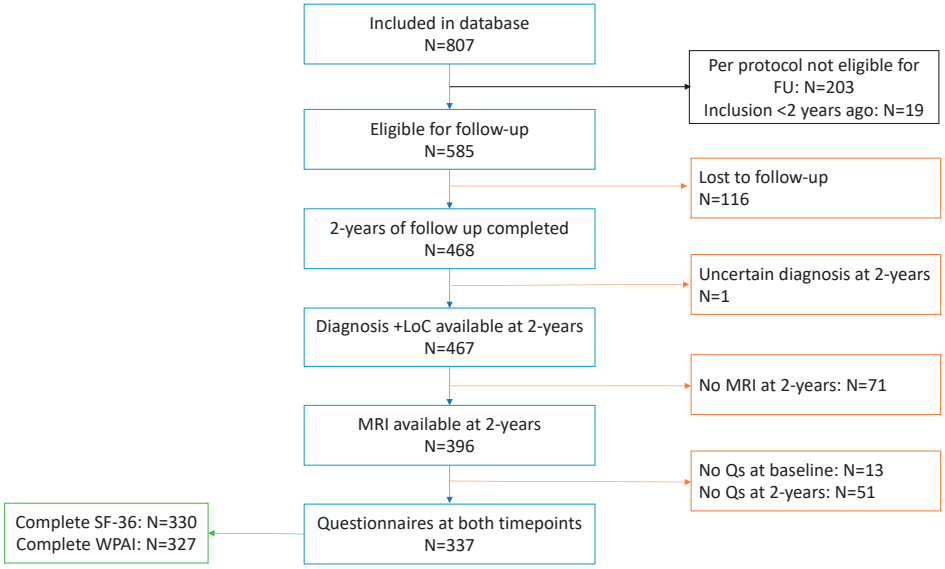

Figure S.1 Flowchart of inclusion

Table S.1 Health-related quality of life measured by the SF-36 in CBP patients stratified by two year clinical diagnosis, restricted to those patients not using bDMARDs.

	axSpA (n=147)		**No axSpA** (n=121)		**p-value** between groups at 2 years
	Baseline	**2 years**	**Baseline**	**2 years**	
PCS, mean (SD)	29 (15)	42 (12)†	27 (13)	36 (14)†	p<0.001*
MCS, mean (SD)	48 (14)	50 (11)‡	47 (12)	49 (11)‡	p=0.655

* Significant difference between groups at two years; after correction for baseline values, gender, age and NSAID use over time (p<0.05); †Signed-rank test: significant improvement within group over time (p<0.05); ‡Signed-rank test: not significant

axSpA, Axial Spondyloarthritis; **CBP**, Chronic Back Pain; **MCID**, Minimal Clinically Important Difference; **MCS**, Mental Component Summary; **PCS**, Physical Component Summary; **SF-36**, Short-Form Health Survey

Table S.2 Results from the work productivity and activity impairment questionnaire in CBP patients stratified by two-year clinical diagnosis, restricted to those patients not using bDMARDs.

	axSpA		**no axSpA**		**p-value** between groups at 2 years
	Baseline	**2 years**	**Baseline**	**2 years**	
Working population	*n=92*		*n=83*		
Presenteeism, mean % (SD)	27 (25)	16 (22)†	41 (27)	30 (28)†	p=0.002*
Absenteeism, mean % (SD)	3 (9)	2 (12)‡	9 (20)	7 (20)‡	p=0.174
Work productivity loss, mean % (SD)	27 (25)	17 (23)†	44 (28)	34 (32)†	p=0.008*
Total population	*n=148*		*n=117*		
Activity impairment, mean % (SD)	37 (28)	19 (22)†	48 (25)	31 (27)†	p<0.001*

REFERENCES

1. Winthrop KL, Weinblatt ME, Crow MK, et al. Unmet need in rheumatology: reports from the Targeted Therapies meeting 2018. *Ann Rheum Dis* 2019;78(7):872-78.
2. Husky MM, Ferdous Farin F, Compagnone P, et al. Chronic back pain and its association with quality of life in a large French population survey. *Health Qual Life Outcomes* 2018;16(1):195.
3. Sadosky AB, Taylor-Stokes G, Lobosco S, et al. Relationship between self-reported low-back pain severity and other patient-reported outcomes: results from an observational study. *J Spinal Dis Tech* 2013;26(1):8-14.
4. Hoy D, March L, Brooks P, et al. The global burden of low back pain: estimates from the Global Burden of Disease 2010 study. *Ann Rheum Dis* 2014;73(6):968-74.
5. van Lunteren M, Ez-Zaitouni Z, Fongen C, et al. Disease activity decrease is associated with improvement in work productivity over 1 year in early axial spondyloarthritis (SPondyloArthritis Caught Early cohort). *Rheumatology* 2017;56(12):2222-28.
6. van Lunteren M, Ez-Zaitouni Z, de Koning A, et al. In Early Axial Spondyloarthritis, Increasing Disease Activity Is Associated with Worsening of Health-related Quality of Life over Time. *J Rheumatol* 2018;45(6):779-84.
7. López-Medina C, Dougados M, Collantes-Estévez E, et al. Adherence to recommendations for the use of anti-tumour necrosis factor and its impact over 5 years of follow-up in axial spondyloarthritis. *Rheumatology* 2018;57(5):880-90.
8. van der Heijde D, Ramiro S, Landewé R, et al. 2016 update of the ASAS-EULAR management recommendations for axial spondyloarthritis. *Ann Rheum Dis* 2017;76(6):978-91.
9. Rudwaleit M, van der Heijde D, Khan MA, et al. How to diagnose axial spondyloarthritis early. *Ann Rheum Dis* 2004;63(5):535-43.
10. Ware JE, Jr., Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Medical care* 1992;30(6):473-83.
11. Aaronson NK, Muller M, Cohen PD, et al. Translation, validation, and norming of the Dutch language version of the SF-36 Health Survey in community and chronic disease populations. *J Clin Epidemiol* 1998;51(11):1055-68.
12. Loge JH, Kaasa S. Short form 36 (SF-36) health survey: normative data from the general Norwegian population. *Scand. J. Soc. Med* 1998;26(4):250-8.
13. Sullivan M, Karlsson JJJoce. The Swedish SF-36 Health Survey III. Evaluation of criterion-based validity: results from normative population. 1998;51(11):1105-13.
14. Ware JE, Kosinski M. Interpreting SF-36 summary health measures: a response. *Qual Life Res* 2001;10(5):405-13; discussion 15-20.
15. Davis JC, Jr., Revicki D, van der Heijde DM, et al. Health-related quality of life outcomes in patients with active ankylosing spondylitis treated with adalimumab: results from a randomized controlled study. *Arthritis Rheum* 2007;57(6):1050-7.
16. Chen MH, Lee MH, Liao HT, et al. Health-related quality of life outcomes in patients with rheumatoid arthritis and ankylosing spondylitis after tapering biologic treatment. *Clinical Rheum* 2018;37(2):429-38.
17. van der Heijde D, Deodhar A, Braun J, et al. The effect of golimumab therapy on disease activity and health-related quality of life in patients with ankylosing spondylitis: 2-year results of the GO-RAISE trial. *J Rheumatol* 2014;41(6):1095-103.
18. Reilly MC, Gooch KL, Wong RL, et al. Validity, reliability and responsiveness of the Work Productivity and Activity Impairment Questionnaire in ankylosing spondylitis. *Rheumatology* 2010;49(4):812-19.
19. Reilly MC, Zbrozek AS, Dukes EM. The validity and reproducibility of a work productivity and activity impairment instrument. *PharmacoEconomics* 1993;4(5):353-65.
20. OECD. OECD Employment Outlook 2019. 2019.
21. Boonen A, Chorus A, Miedema H, et al. Withdrawal from labour force due to work disability in patients with ankylosing spondylitis. *Ann Rheum Dis* 2001;60(11):1033-9.
22. van Lunteren M, Landewé R, Fongen C, et al. Do Illness Perceptions and Coping Strategies Change Over Time in Patients Recently Diagnosed With Axial Spondyloarthritis? *J Rheumatol* 2020
23. Kroon FP, van der Burg LR, Ramiro S, et al. Nonsteroidal Antiinflammatory Drugs for Axial Spondyloarthritis: A Cochrane Review. *J Rheumatol* 2016;43(3):607-17.
24. Eurofound. [Available from: https://www.eurofound.europa.eu/surveys/european-working-conditions-surveys-ewcs accessed 09-11 2020.