The burden of early axial spondyloarthritis

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Chapter 5

Disease activity decrease is associated with improvement in work productivity over 1 year in early axial spondyloarthritis (SPondyloArthritis Caught Early cohort)

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ABSTRACT

Objective

To assess if a change in disease activity is associated with a change in work productivity loss (WPL) over 1 year in early axial SpA (axSpA) patients.

Methods

Baseline and 1 year data of axSpA patients in the SPondyloArthritis Caught Early cohort were analysed. Linear regression models were built explaining the change in the Ankylosing Spondylitis Disease Activity Score (ASDAS) over time by the change in absenteeism, presenteeism, WPL, and activity impairment over time. Effect modification and confounding were tested for age, gender, arm of Assessment of SpondyloArthritis international Society classification criteria, HLA-B27, duration of chronic back pain, profession, and medication.

Results

At baseline, in 105 axSpA patients (48% female, mean age 30.8 years, mean symptom duration 13.6 months, 92% HLA-B27 positive, 24% radiographic sacroiliitis), the mean ± SD ASDAS was 2.4 ± 1.0, absenteeism 9% ± 23, presenteeism 33% ± 28, WPL 36% ± 30, and activity impairment 37% ± 25. After 1 year, the mean ASDAS decreased to 2.0 ± 0.8 and absenteeism, presenteeism, WPL, and activity impairment improved to 6% ± 22, 26% ± 26, 27% ± 29, and 27% ± 26, respectively. Models showed that if ASDAS decreased 1 unit, absenteeism, presenteeism, WPL, and activity impairment improved by 5%, 17%, 16%, and 18%, respectively. The impact of disease activity on work productivity was higher in patients with shorter symptom duration and the impact on absenteeism was higher in patients starting pharmacological treatment.

Conclusion

In early axSpA patients, work productivity and daily activities are seriously impacted at baseline and 1 year. However, decreasing disease activity is associated with marked improvements in work productivity and daily activities.

INTRODUCTION

Axial spondyloarthritis (axSpA) has an early disease onset, usually in the second or third decade of life.[1, 2] As a consequence, patients are affected by axSpA at an early stage in their professional career. Patients with longstanding AS are three times more likely to withdraw from work due to disability than individuals in the general population.[3] A persistently high disease activity is associated with more sick leave and disability in patients with axSpA.[4] AxSpA patients lose productivity because of sick leave absenteeism), but also because of inefficiency at work (presenteeism). In addition, presenteeism is an important indicator for future sick leave in patients with AS.[5] Taken together, work productivity loss (WPL) in AS leads to substantial costs to patients and society.[3, 6]

There is little data suggesting that gender, age, and disease duration co-determine the impact of a diagnosis of axSpA on work productivity. One study showed that AS had more impact on days being absent from work in women than in men.[5] In line with this finding, Haglund et al.[7] reported that women with SpA experience more loss of work productivity than men. A Dutch study reported that younger AS patients more often withdrew from work than older patients when compared with age and gender-matched population controls. This study also showed that the likelihood of work withdrawal increased with longer disease duration.[3] Finally, a recent cohort study showed that gender, age, and disease duration are important determinants of absenteeism.[8]

Most studies on work productivity have focused on patients with AS with long disease duration. It is less well known if and how axSpA impacts work productivity in patients with short symptom duration and if prognostically relevant subgroups are similarly affected.

Thus the aims of this study are to describe WPL in patients with an early onset of axSpA at baseline and 1 year after diagnosis, to assess if a change in disease activity is associated with a change in work productivity and to assess if the impact of the Ankylosing Spondylitis Disease Activity Score (ASDAS) on work productivity is similar according to prognostically relevant subgroups.

METHODS

Design and subjects

The present study was conducted in the SPondyloArthritis Caught Early (SPACE) cohort. The design of this cohort has been described in detail previously.[9] The SPACE cohort is an ongoing inception cohort established in 2009 that includes patients ≥ 16 years of age with chronic back pain (CBP) persisting ≥ 3 months but ≤ 2 years with the onset of back

pain at < 45 years of age. Patients were excluded if they had another painful condition not related to axSpA that could interfere with evaluation of the disease. For this analysis we used baseline and 1 year data of patients who were diagnosed with axSpA, fulfilled the Assessment of SpondyloArthritis international Society (ASAS) criteria for axSpA at baseline, had paid work and had their baseline and 1 year visit between January 2009 and January 2017.

Data from four medical centres in Europe participating in the SPACE study were included in the current analysis: Leiden University Medical Center, Leiden, The Netherlands; Diakonhjemmet Hospital, Oslo, Norway; Academic Medical Center, Amsterdam, The Netherlands, and the University of Padua, Padua, Italy. The SPACE study protocol was approved by the Ethical Committee ''Azienda Ospedaliera di Padova'' (reference number 2438P), Regional Committee for Medical and Health Research Ethics in South East Norway (reference number 2010/426), the Medical Ethical Committee of the Leiden University Medical Center (reference number P08.105), and all participants provided informed consent, in accordance with the Declaration of Helsinki, before the start of the first visit. Data from 14 Italian patients included in this analysis have been published previously elsewhere.[10]

Methods of measurement

At baseline and 12 months, a medical history was taken followed by a physical examination, questionnaires, and laboratory assessments, including CRP, ESR, and HLA-B27. Radiographic images and MRIs (1.5 T, 4mm slice thickness) of the sacroiliac joints and spine were obtained at baseline. The diagnosis was made by the treating rheumatologist using local reading of the imaging. Treating rheumatologists were asked to provide a level of confidence regarding the diagnosis on a numerical scale ranging from 0 (not confident at all) to 10 (very confident). Patients diagnosed with axSpA were classified according to the ASAS axSpA criteria to the imaging arm or clinical arm[11] based on central reading, in which images were evaluated by three central readers per modality and were considered to be positive for sacroiliitis when two or more readers agreed. Patients were classified in the imaging arm if patients either fulfilled the imaging arm alone or fulfilled both the imaging and clinical arms. Patients were classified in the clinical arm if they fulfilled the clinical arm exclusively.

The Work Productivity and Activity Impairment questionnaire (WPAI, general health, version 1.0) was used to assess the impact of the disease on work productivity in the past 7 days. It consists of six questions, in which patients are asked to report about current employment status (Question (Q)1), amount of missed working hours due to axSpA (Q2), amount of missed working hours due to other reasons such as holidays (Q3), amount

of actually worked hours according to the patient (Q4), the impact of axSpA on work productivity on a visual analogue scale (VAS) scale (Q5), and the impact of axSpA on regular daily activities outside work on a VAS scale (Q6). Four summary measures could be calculated ranging from 0 to 100%; presenteeism is decreased functionality at work due to disease (calculated as Q5/10), absenteeism is absence at work due to disease (Q2/(Q2 + Q4)), WPL is the total work impairment due to disease (presenteeism + ((1 – presenteeism) * absenteeism)), and activity impairment is the impairment in daily activities (Q6/10). Percentages were calculated by multiplying all scores by 100. Higher scores indicate greater impairment.[12]

The CRP-based ASDAS was used to assess disease activity.[13, 14] For reference, a change of ASDAS ≥ 1.1 is considered to reflect a clinically important improvement and a change of ≥ 2.0 reflects a major improvement.[15]

Patients were asked to report the use of NSAIDs, conventional synthetic DMARDs (csDMARDs) and biologic DMARDs (bDMARDs) at baseline and 1 year. Medication was categorized as no change in treatment (i.e. either no medication or the same treatment group) between baseline and 1 year, start of any treatment (NSAID, csDMARD, or bDMARD) between baseline and 1 year, and stopping all treatment between baseline and 1 year. Eight patients were already treated with csDMARDs at baseline because of psoriasis, peripheral arthritis, IBD, uveitis, dactylitis or a combination thereof.

The question about a patient's profession was a multiple-choice question with the following options: (i) management position (e.g. director, manager, member of the board of directors); (ii) professional specialist (engineer, teacher, nurse practitioner, systems analyst); (iii) commercial profession (representative, agent, clerk, sales person); (iv) technical support (lab technician, legal officer, information technology); (v) administrative support (secretary, invoice administration); (vi) service profession (security officer, janitor), and (vii) operator or labourer (assembler, mechanic, carpenter, builder). Answer options 1, 2, 4, and 5 were labelled as *white collar work*. Answer options 3, 6 and 7, were labelled as *blue collar work*.

Analysis

Continuous variables were described as mean ± SD; categorical variables were described as number (percentage). Linear regression models were built to explain the change in each WPAI measure (i.e. ΔWPL, Δpresenteeism, Δabsenteeism and Δactivity impairment) between baseline and 1 year (dependent variable) by the change in ASDAS (ΔASDAS; continuous) between baseline and 1 year (independent variable). Age at baseline, gender, ASAS axSpA subclassification (imaging versus clinical arm), HLA-B27 carrier status

(positive versus negative), duration of CBP, medication as well as profession were tested for their potential to modify the association between ASDAS and a WPAI measure one by one in these linear regression models. Effect modification was considered relevant if the P-value of the interaction term was <0.10. Models were stratified in subgroups if an effect modification was found. To prevent spurious effects due to small sample sizes, stratification for dichotomous variables was only performed if each subgroup consisted of at least 15 patients and stratification for continuous variables was only performed for the subgroups of at least 15 patients. These factors were also tested for relevant confounding (defined as a change >10% of the crude regression coefficient of the univariable model). Models were adjusted for each confounder. Data were analysed using STATA SE version 14 (StataCorp, College Station, TX, USA). P-values <0.05 were considered to be statically significant.

RESULTS

In total, 361 patients in the SPACE cohort provided data at baseline as well as 1 year. Rheumatologists diagnosed 247 patients with axSpA. Of the 247 axSpA patients, 174 patients fulfilled the ASAS classification criteria. Patients who did not have a job (n=46) could not complete the WPAI questionnaire. Of the remaining 128 patients, 16 patients missed the WPAI either at baseline or at 1 year and information to calculate the ASDAS at one or both time points was insufficient in 7 patients. The WPAI and ASDAS were available at both time points in 105/128 (82%) patients diagnosed with axSpA meeting the ASAS criteria. Excluded patients (n=23) did not differ from included patients, except for a good response to NSAIDs (P=0.034; included patients 69%, excluded patients 46%).

Of the 105 patients included in the analysis, 48% were female, the mean ± SD age was 30.8 years ± 7.2, and the mean symptom duration was 13.6 months ± 7.1 (**Table 1**). On average, patients had 3.3 ± 1.6 SpA features in addition to imaging and HLA-B27 status and the level of confidence regarding the diagnosis of SpA by the rheumatologist was 8 ± 2. In these patients, 46% fulfilled the clinical arm, 12% the imaging arm, and 42% both arms.

At baseline, the mean ± SD ASDAS was 2.4 ± 1.0. Twelve per cent of patients had inactive disease and 29% had moderate disease activity. The mean WPL was 36% ± 30, presenteeism 33% ± 28, absenteeism 9% ± 23, and activity impairment 37% ± 25 (**Table 2**). Thirty-four per cent of the patients had a '*blue collar*' job at baseline. Over 1 year, the mean ASDAS decreased to 2.0 ± 0.8, which was statistically significant; 22% had inactive disease and 37% had moderate disease activity. The mean WPL, presenteeism, absenteeism, and activity impairment improved statistically significantly (27% ± 29, 26% ± 26, 6% ± 22, and 27% ± 26, respectively). The mean number of missed working hours per

week due to CBP decreased from 4.3 at baseline to 1.9 at 1 year.

Figures 1 and 2 show the relationship between the 1 year change in ASDAS and the 1 year change in WPAI. Linear trend lines show that a 1 unit decrease in ASDAS is associated with a 16% decrease in WPL (**Figure 1A**), a 17% decrease in presenteeism (**Figure 1B**), a 5% decrease in absenteeism (**Figure 2A**), and 18% less activity impairment (**Figure 2B**). All associations between the ΔASDAS and ΔWPAI measures were statistically significant (P<0.001 for ΔWPL, ΔPresenteeism, and ΔActivity Impairment and P=0.016 for ΔAbsenteeism).

The duration of CBP was an effect modifier for ΔWPL (P=0.06) and Δpresenteeism (P=0.03) and the start of treatment between baseline and 1 year was an effect modifier for Δabsenteeism (P=0.08; **Supplementary Table S1**). Based on these results, patients were stratified for the duration of CBP and the start of medication in each model (**Table 3**).

Regardless of the duration of CBP or the start of medication use, an improvement in ASDAS remained positively associated with an improvement in WPL, presenteeism, and activity impairment. However, an improvement in ASDAS was only associated with an improvement in absenteeism in patients with a short duration of CBP and in patients who started any treatment between baseline and 1 year. The impact on work productivity and activity impairment was higher per unit ASDAS in patients with a shorter symptom duration. HLA-B27 positivity was a statistically significant effect modifier, however, the HLA-B27-negative group had < 15 patients, so patients were not stratified for this factor (**Supplementary Table S1**). No confounding for age, gender, arm of the ASAS classification criteria for axSpA, HLAB27 positivity and profession was found (**Supplementary Table S2**).

Table 1. Baseline characteristics of patients with axSpA in the SPACE cohort included in the analysis

Characteristics	n=105
Age (years) at inclusion, mean ± SD	30.8 ± 7.2
Female	50 (48%)
Symptom duration (months), mean ± SD	13.6 ± 7.1
Inflammatory back pain	87 (83%)
Good response to NSAIDs[a]	72 (69%)
Uveitis[b]	19 (18%)
Psoriasis[b]	17 (16%)
Inflammatory bowel disease[b]	4 (4%)
Positive family history	54 (51%)
Enthesitis[b]	26 (25%)
Dactylitis[b]	7 (7%)
Peripheral arthritis[b]	19 (18%)
HLA-B27 positive	97 (92%)
Elevated ESR/CRP level	45 (43%)
X-SI positive	25 (24%)
MRI-SI positive	46 (44%)
Number of SpA features[c], mean ± SD	3.3 ± 1.6
Confidence of diagnosis by rheumatologist, mean ± SD	8 ± 2
ASAS classification	
Clinical arm only	48 (46%)
Imaging arm only	13 (12%)
Both arms	44 (42%)
Use of NSAIDs	83 (79%)
Use of csDMARDs	8 (8%)
Use of bDMARDs	0 (0%)

Results are presented as n (%) unless otherwise indicated. [a] Back pain not present anymore or is much better 24-48 h after a full dose of an NSAID. [b] Past or present condition, either diagnosed or confirmed by a physician. [c] Excluding HLA-B27 testing and imaging. ASAS, Assessment of SpondyloArthritis international Society; bDMARD, biological disease-modifying antirheumatic drugs (DMARD); CRP, C-reactive protein; csDMARD, conventional synthetic DMARD; ESR, erythrocyte sedimentation rate; MRI-SI, MRI of the sacroiliac (SI) joint; NSAID, nonsteroidal anti-inflammatory drugs; X-SI, radiography of the SI-joint.

Table 2. Disease activity, work impairment, and activity impairment at baseline and 1 year of axSpA patients

Characteristics	Baseline	1 year
ASDAS, mean ± SD	2.4 ± 1.0	2.0 ± 0.8
Inactive disease (< 1.3)	13 ± 12	23 ± 22
Moderate disease activity (< 2.1)	30 ± 29	39 ± 37
High disease activity (< 2.1)	48 ± 46	38 ± 36
Very high disease activity (> 3.5)	14 ± 13	5 ± 5
BASDAI, mean ± SD	3.8 ± 2.1	3.1 ± 2.0
Blue collar job[a,b]	25 (34%)	26 (36%)
Working hours, mean ± SD	29.5 ± 15.6	30.2 ± 15.5
Missed working hours due to chronic back pain, mean ± SD	4.3 ± 12.4	1.9 ± 6.6
Work productivity loss (%), mean ± SD	36 ± 30	27 ± 29
Presenteeism (%), mean ± SD	33 ± 28	26 ± 26
Absenteeism (%), mean ± SD	9 ± 23	6 ± 22
Activity Impairment (%), mean ± SD	37 ± 25	27 ± 26

Results are presented as n (%) unless otherwise indicated. [a] Blue collar job is defined as a physically demanding job. [b] Available for 73 patients. ASDAS, Ankylosing Spondylitis Disease Activity Score; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index.

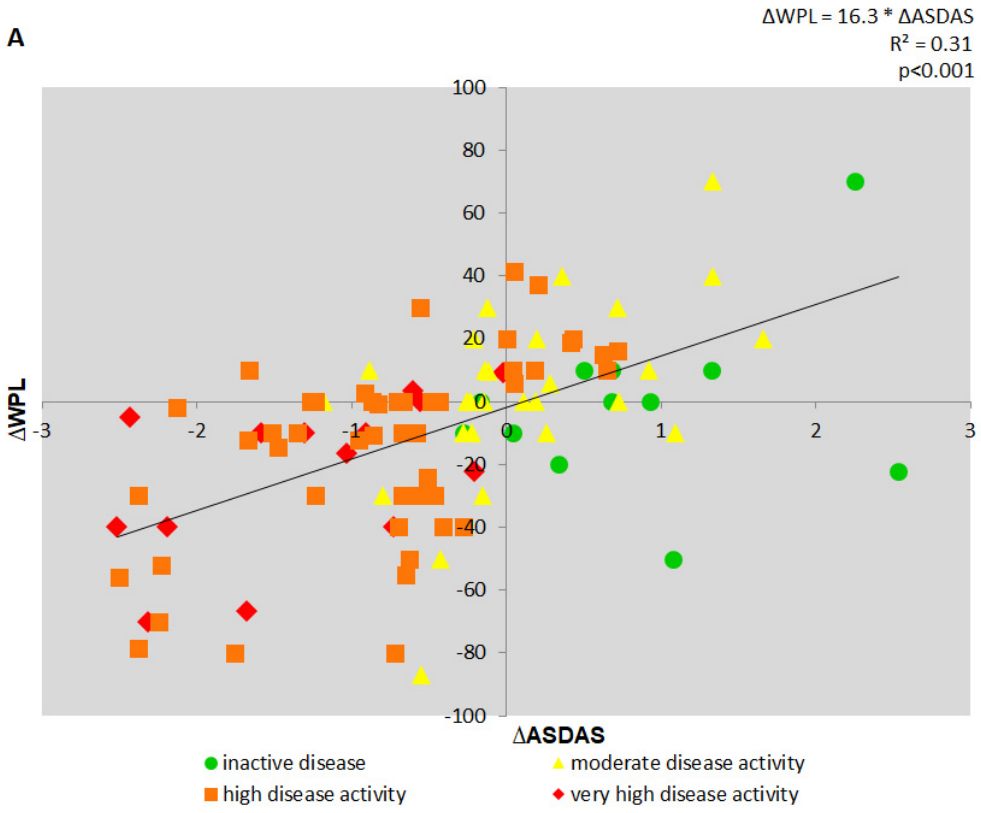

Figure 1. Scatter plot of the results between 0 and 1 year with baseline disease status indicated by symbols. (A) Results between change in ASDAS and change in WPL.

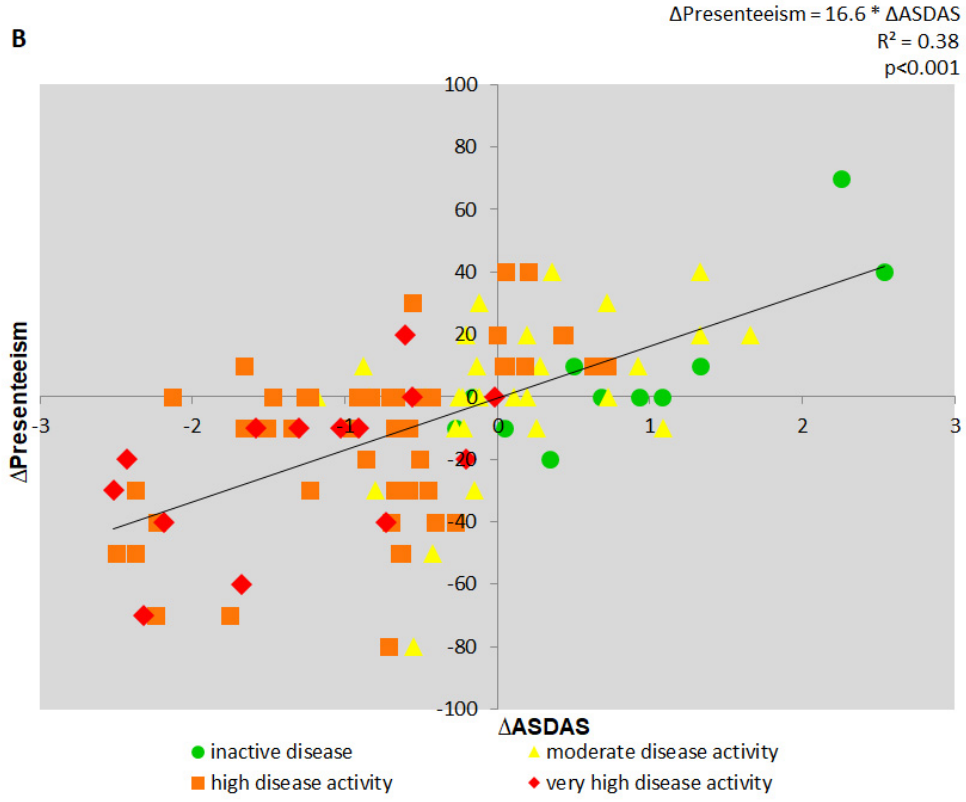

Figure 1. Scatter plot of the results between 0 and 1 year with baseline disease status indicated by symbols. (B) Results between change in ASDAS and change in presenteeism.

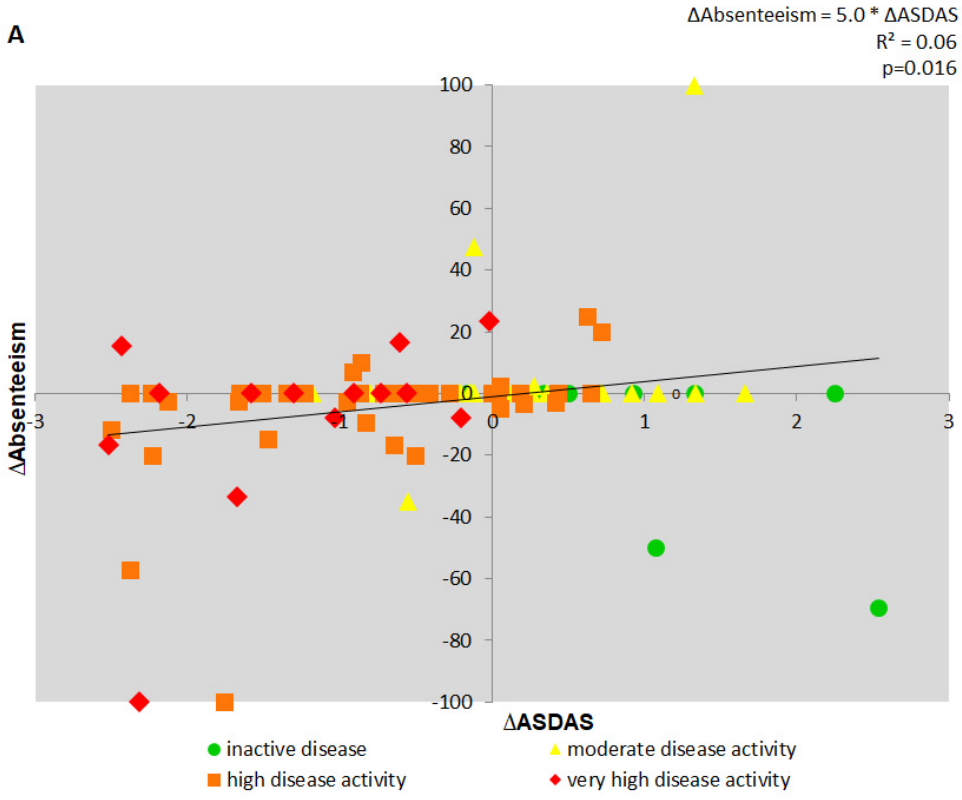

Figure 2. Scatter plot of the results between 0 and 1 year with baseline disease status indicated by symbols. (A) Results between change in ASDAS and change in absenteeism.

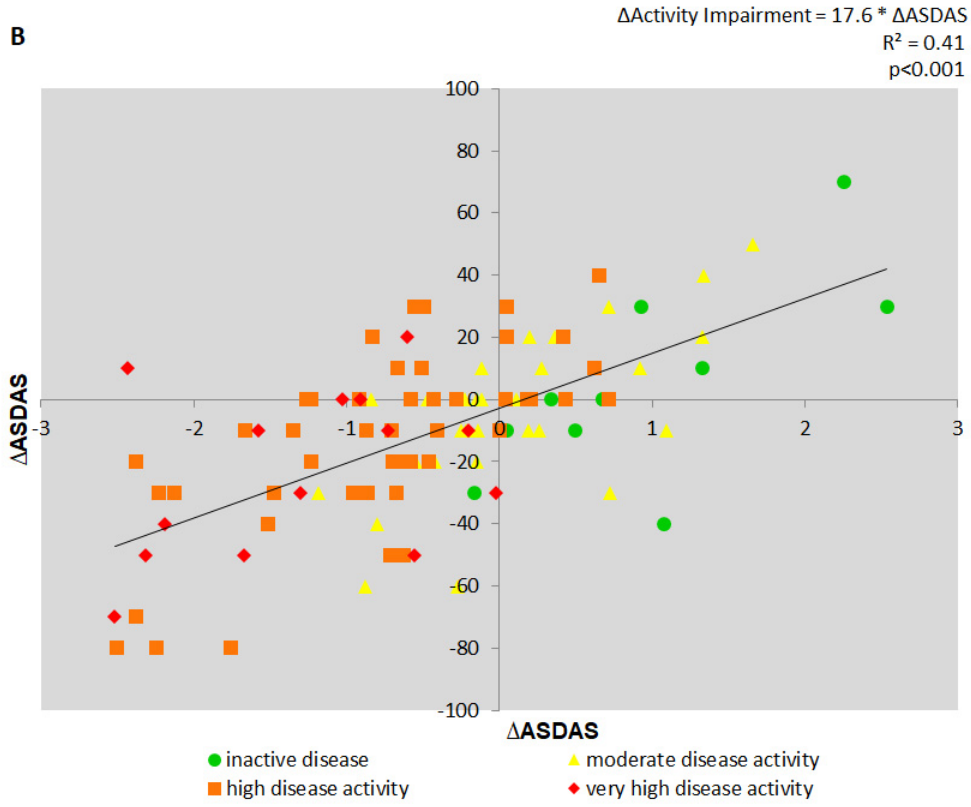

Figure 2. Scatter plot of the results between 0 and 1 year with baseline disease status indicated by symbols. (B) Results between change in ASDAS and change in activity impairment.

Table 3. Association between change in disease activity and change in work productivity and daily activities

		ΔWPL		ΔPresenteeism		ΔAbsenteeism		ΔActivity Impairment	
	n	β (SE)	P-value	β (SE)	P-value	β (SE)	P-value	β (SE)	P-value
Model stratified for mean duration of chronic back pain[a]									
<13.6 months ΔASDAS	56	19.5 (3.0)	<0.001	19.8 (2.5)	<0.001	6.6 (3.2)	0.046	20.0 (2.5)	<0.001
≥13.6 months ΔASDAS	47	9.0 (3.9)	0.027	8.9 (3.9)	0.026	0.6 (1.2)	0.640	12.4 (3.7)	0.002
Model stratified for medication use[b]									
No change[c] ΔASDAS	55	17.4 (3.6)	<0.001	18.0 (3.2)	<0.001	1.7 (1.7)	0.310	16.8 (3.6)	<0.001
Started[d] ΔASDAS	42	16.7 (3.8)	<0.001	16.0 (3.3)	<0.001	9.4 (4.2)	0.031	18.2 (2.5)	<0.001

Results are corrected for age and gender and stratified in case of effect modification P<0.10. [a] No exact duration of chronic back pain was available for 2 patients. [b] Patients who stopped all treatment were excluded from the table as stated in the methods (this subgroup consisted of 8 patients). [c] No medication or same treatment group (NSAID, csDMARD, bDMARD). [d] Started with any treatment (NSAID, csDMARD, bDMARD). ASDAS, Ankylosing Spondylitis Disease Activity Score; WPL, Work productivity Loss.

DISCUSSION

In early axSpA patients, in which the majority has non-radiographic axSpA, work productivity and daily activities were already seriously impacted at baseline and 1 year. Over a 1 year period, a reduction in disease activity was associated with improvement in both work productivity and daily activities, while an increase in disease activity leads to more work and activity impairment.

In our cohort, presenteeism, absenteeism, WPL, and activity impairment were comparable to recent results from a European cross-sectional study of non-radiographic axSpA patients with disease duration ranging from 3 to 7 years. In this study, presenteeism ranged from 16% to 28%, absenteeism 9% to 10%, WPL 19% to 37%, and activity impairment 23% to 31% among patients treated with bDMARDs and patients not treated with bDMARDs, respectively.[16] Due to differences in methodology, it is challenging to compare our results with the general population. In the European Working Conditions Survey of 44 000 workers in 35 European countries, 41% of men and 44% of women reported any form of presenteeism in the past year.[17] In our cohort, presenteeism (defined as presenteeism > 0) was present in 76% of men and 82% of women. In addition, in The Netherlands, sick leave percentages in the general population are available for various age categories for 2015. The majority of the patients who were included in our analyses were Dutch (51%). Compared with the Dutch population, absenteeism was slightly lower in our Dutch patients in the 15–25 years age category but considerably higher in the last two age categories (0% vs 2% for 15–25 years, 10% vs 3% for 25–35 years, and 26% vs 4% for 35–45 years in the SPACE cohort vs the general population).[18] Taken together, presenteeism and absenteeism are higher in early axSpA compared with the general population.

Previously it has been shown that in patients with AS, increased disease activity is associated with increased WPL and presenteeism in particular.[19-21] Several randomized controlled trials (RCTs) have shown that an improvement in disease activity invoked by active drug treatment led to an improvement in work productivity in AS patients.[22, 23] This was also confirmed for patients with non-radiographic axSpA in a recent RCT.[24] Our data show that even in the earliest phase of the disease, work productivity is greatly reduced and daily activities are impaired and fluctuations in disease activity are associated with fluctuations in WPL and activity impairment.

In our cohort, the impact of disease activity on work productivity and daily activities was higher in patients with a shorter duration of CBP as compared with patients with a longer duration of CBP. A possible explanation for this difference is that patients cope differently with limitations, depending on the symptom duration. This is currently being evaluated

in our cohort. Change of work or work adaptations may also play a role. Of note, the proportion of patients with blue collar jobs remained rather stable over 1 year. Medication may also play a role, but in our study, patient groups became too small to detect meaningful differences if stratified for both disease duration and medication. The impact of disease activity on absenteeism was higher in patients who started any treatment than in patients who did not change their treatment. This might be explained by a response to the new treatment.

An important finding in our cohort was that, on average, disease activity remained high 1 year after diagnosis. Recently an international task force recommended remission or low disease activity as the preferred treatment target in SpA, although it was acknowledged that the evidence was not strong and needed to be expanded by future research.[25] Consequently, clinical trials are under way aimed at improving disease outcomes in axSpA using more intensive treatment (treat to target) approaches in order to obtain remission or low disease activity (e.g. NCT02897115 and NCT03043846 at ClinicalTrials.gov). Our results suggest that in early axSpA, lowering disease activity is associated with less WPL and activity loss, which may imply that remission or low disease activity in early axSpA is a valuable target.

The strength of this study is the thorough diagnostic workup according to protocol, including imaging (MRI and radiographs) in all patients, leading to a high diagnostic certainty. Self-reported questionnaires were used to determine work productivity and activity loss. The response rate was 82%, which is in line with previous cohort studies.[26] Due to the limited sample size, no additional effect modification could be studied except for the duration of CBP and medication. Unfortunately, no separate effect per treatment group (NSAIDs, csDMARDs, and bDMARDs) could be evaluated because of small numbers in several subgroups. In particular, the subgroup of patients who are starting a bDMARD is small. However, this is a result of the short duration of CBP as an inclusion criteria (42 years). Multiple NSAIDs are prescribed before patients are treated with bDMARDs. Another limitation is that the exact starting and/or stopping date of csDMARDs and bDMARDs are unknown. We therefore recommend addressing these issues in future studies. Finally, absenteeism has many zeroes, which causes skewness of the data, and this might explain the different effect of disease activity on absenteeism per subgroup.

In conclusion, in patients with early axSpA, absenteeism, presenteeism, WPL, and activity impairment were considerably increased at baseline, showing that WPL and impairment of daily activities already affects patients with axSpA in the earliest phase of the disease. More importantly, although WPL and activity impairment improved somewhat over a 1 year period, they remained rather substantial. Finally, our data show that in early axSpA,

decreasing disease activity is associated with improvement in work productivity and daily activities.

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SUPPLEMENTARY MATERIAL

Supplementary Table S1. Effect modifiers in model ΔASDAS and Δwork productivity and Δactivity measures between baseline–one year

	ΔWPL	ΔPresenteeism	ΔAbsenteeism	ΔActivity Impairment
Variable	**p-value**	**p-value**	**p-value**	**p-value**
Gender	0.52	0.76	0.68	0.68
Age (mean)	0.76	0.63	0.24	0.87
Arm of ASAS classification	0.71	0.92	0.74	0.86
HLA-B27 positivity	0.11	0.97	*0.01*	**0.35**
Duration of chronic back pain (mean)	*0.06*	*0.03*	0.22	0.14
Profession[a]	0.94	0.97	0.79	0.52
Medication between 0-1 year				
No change (n=55)[b]	(ref.)	(ref.)	(ref.)	(ref.)
Started (n=42)[c]	0.903	0.706	*0.080*	0.758
Stopped (n=8)[d]	0.758	0.591	0.661	0.458

Statistically significantly p-values (p<0.10) are printed in italics. ASAS, Assessment of Spondyloarthritis International Society; HLA-B27, Human Leucocyte Antigen B27; ref., reference; WPL, Work productivity Loss. [a] Data available of only 73 patients. [b] No medication or same treatment group (NSAID, csDMARD, bDMARD). [c] Started with any treatment (NSAID, csDMARD, bDMARD). [d] Stopped with all treatment (NSAID, csDMARD, bDMARD).

Supplementary Table S2. Confounders in the model of ΔASDAS–Δwork productivity and activity measures between baseline–one year

	ΔWPL		ΔPresenteeism		ΔAbsenteeism		ΔActivity Impairment	
	β (SE)	p-value	β (SE)	p-value	β (SE)	p-value	β (SE)	p-value
Univariable model (n=105)								
ΔASDAS	16.3 (2.4)	<0.001	16.6 (2.1)	<0.001	5.0 (2.0)	0.016	17.6 (2.1)	<0.001
Model corrected for age (n=105)								
ΔASDAS	16.3 (2.4)	<0.001	16.6 (2.1)	<0.001	5.0 (2.0)	0.017	17.6 (2.1)	<0.001
Model corrected for gender (n=105)								
ΔASDAS	16.4 (2.4)	<0.001	16.7 (2.1)	<0.001	5.0 (2.0)	0.017	17.6 (2.1)	<0.001
Model corrected for the arm of ASAS classification for axSpA (n=105)								
ΔASDAS	16.3 (2.4)	<0.001	16.6 (2.1)	<0.001	4.9 (2.0)	0.019	17.4 (2.0)	<0.001
Model corrected for HLA-B27 positivity (n=105)								
ΔASDAS	16.4 (2.4)	<0.001	16.7 (2.1)	<0.001	5.0 (2.0)	0.014	17.6 (2.1)	<0.001
Univariable model with the axSpA patients with data about profession (n=73)								
ΔASDAS	18.9 (2.5)	<0.001	16.4 (2.4)	<0.001	9.5 (2.4)	<0.001	18.8 (2.5)	<0.001
Model corrected for profession (n=73)								
ΔASDAS	18.9 (2.6)	<0.001	16.4 (2.4)	<0.001	9.6 (2.4)	<0.001	18.8 (2.6)	<0.001

Variables were considered to be confounder is the regression coefficient (β) changed with >10%. ASAS, Assessment of Spondyloarthritis International Society; ASDAS, Ankylosing Spondylitis Disease Activity Score; axSpA, axial spondyloarthritis; HLA-B27, Human Leucocyte Antigen B27; WPL, Work productivity Loss.