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ORIGINAL RESEARCH

Work productivity in patients with axial spondyloarthritis initiating biological or targeted synthetic disease-modifying antirheumatic drugs: a systematic literature review and meta-analysis

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ABSTRACT

Background Axial spondyloarthritis (axSpA) can limit work participation. Our objective was to characterise productivity in patients with axSpA, including changes after 12–16 weeks of treatment with biological and targeted synthetic disease-modifying antirheumatic drugs (b/tsDMARDs).

Methods A systematic literature review identified studies published from 1 January 2010 to 21 October 2021 reporting work productivity using the Work Productivity and Activity Impairment (WPAI) questionnaire in patients with axSpA initiating b/tsDMARDs. Baseline and Week 12–16 overall work productivity, absenteeism, presenteeism and activity impairment scores were used in a random-effects meta-analysis to calculate absolute mean change from baseline for each WPAI-domain.

Results Eleven studies in patients with axSpA who received either placebo (n=727) or treatment with adalimumab, bimekizumab, etanercept, ixekizumab, secukinumab or tofacitinib (n=994) were included. In working patients initiating a b/tsDMARD, mean baseline overall work productivity impairment, absenteeism and presenteeism scores were 52.1% (N=7 studies), 11.0% and 48.8% (N=6 studies), respectively. At Week 12–16, the pooled mean change from baseline in overall work impairment for b/tsDMARDs or placebo was −21.6% and −12.3%. When results were extrapolated to 1 year, the potential annual reductions in cost of paid and unpaid productivity loss per patient ranged from €11 962.88 to €14 293.54.

Conclusions Over 50% of employed patients with active axSpA experienced work impairment, primarily due to presenteeism. Overall work productivity improved at Weeks 12–16 to a greater extent for patients who received b/tsDMARDs than placebo. Work productivity loss was associated with a substantial cost burden, which was reduced with improvements in impairment.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ The symptom burden of axial spondyloarthritis (axSpA) impairs a patient's ability to work and perform activities, in particular when the disease is active. Treatments such as biological and targeted synthetic disease-modifying antirheumatic drugs (b/tsDMARDs) may improve productivity for patients.

WHAT THIS STUDY ADDS

⇒ This systematic literature review and meta-analysis demonstrated that patients with axSpA have restricted overall work productivity, with more presenteeism (decreased performance at work) than absenteeism (missed work). After b/tsDMARD treatment for 12–16 weeks, work productivity, presenteeism and absenteeism improved to a greater extent than with placebo, potentially leading to cost savings.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ These findings support the socioeconomic benefit of b/tsDMARD treatment for patients with axSpA in terms of reduced overall work productivity impairment, presenteeism and absenteeism, and indirect cost savings, which may help inform clinical and access decision-making.

INTRODUCTION

Axial spondyloarthritis (axSpA) is a chronic, inflammatory disease that predominantly affects the axial skeleton (ie, sacroiliac joints and spine);[1 2] axSpA is an umbrella term that includes radiographic axSpA (r-axSpA), also referred to ankylosing spondylitis (AS), and non-radiographic axSpA (nr-axSpA).[3–5]

AxSpA is diagnosed based on a combination of clinical features and laboratory features, including human lymphocytic antigen-B27 and C-reactive protein, and imaging evidence of axial inflammation. In r-axSpA, evidence of sacroiliitis can be detected on X-rays, whereas in nr-axSpA sacroiliitis is not

seen on X-rays but often presents on MRI.[4–6] The main goal of treatment of axSpA is control of disease-related inflammation in order to reduce symptoms, maintaining function and health-related quality of life (HRQoL) and ultimately preventing disease progression inflammation and comorbidities.[7] Biological or targeted-synthetic disease-modifying antirheumatic drugs (b/tsDMARD) are recommended for patients when first-line non-steroidal anti-inflammatory drugs (NSAID) fail or are contraindicated/not tolerated and axial symptoms due to active inflammation persist.[7]

Patients with axSpA are predominantly in their prime working years at the time of disease onset, with symptom presentation typically occurring prior to age 45.[8] Regardless of the clinical subtype of axSpA, the chronicity of symptoms and resulting comorbidities may impact physical functioning and lead to missed work (absenteeism) and decreased performance at work (presenteeism).[9 10] Further, physically intense and challenging jobs may exacerbate bone inflammation and disease progression in patients with axSpA.[11] axSpA also impairs patients ability to perform unpaid work or activities such as housework, shopping, voluntary work and education.[10] Decreased work participation and productivity have detrimental effects on the HRQoL of these patients and confer a substantial economic burden,[10 12] underscoring the need to assess the effect of axSpA in work participation and productivity.

The Work Productivity and Activity Impairment (WPAI) questionnaire is a commonly employed tool to assess work impairment in paid and unpaid work.[13–15] The WPAI quantifies the impact of disease on hours of paid work, productivity while at work and activities of daily living as percentages over the previous week, where higher percentages indicate greater impact on work participation and productivity. Presenteeism and absenteeism are combined into an overall work impairment score. The use of the WPAI questionnaire to measure productivity impairment in patients with axSpA has been validated in clinical trials of DMARDs.[9 16]

Treatment with b/tsDMARDs has been shown to control inflammation, improve clinical outcomes and delay the progression of radiographic damage in patients with axSpA.[17] Despite clear clinical benefits, the effect of b/tsDMARDs on workplace productivity and outcomes in patients with axSpA has not yet been extensively described. Hence, we performed a systematic literature review (SLR) and meta-analysis to quantify workplace productivity using the WPAI questionnaire at Weeks 12–16 in patients with nr-axSpA and r-axSpA treated with b/tsDMARDs.

METHODS
Systematic literature review
The SLR was designed to evaluate the overall HRQoL in patients with axSpA. It was conducted in accordance with the Centre for Reviews and Dissemination methodological

guideline and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) reporting guideline.[18–20] Here, we report the results of a subset of studies from the SLR that present workplace productivity in patients with axSpA, as measured by the WPAI questionnaire at Weeks 12–16 following treatment.

Database and searches
MEDLINE, Embase, EconLit and Cochrane databases were searched for full-text articles published in English between 1 January 2010 and 21 October 2021 (online supplemental table S1). Relevant conferences including the American College of Rheumatology, EULAR, British Society for Rheumatology (BSR), Academy of Managed Care Pharmacy and The Professional Society for Health Economics and Outcomes Research were hand-searched between 1 January 2018 and 21 October 2021 for eligible studies. The full search strategy is provided in online supplemental table S2. Database searches were supplemented by cross-referencing data in the bibliographies of relevant SLRs and grey literature searches of clinical trial registries to identify eligible studies for inclusion. In August of 2022, data on file for the WPAI results from BE MOBILE 1 and BE MOBILE 2 studies were added to the evidence base. The studies included in the current review and meta-analysis were selected from the entire set of included studies from the SLR on the basis of their reporting results of the WPAI and represent a focused subset of publications focused on work productivity.

Study selection
The eligibility criteria for study selection in the SLR per population, intervention, comparators, outcomes and study design criteria is presented in online supplemental table S3. The population of interest was adults with nr-axSpA or r-axSpA; interventions included b/tsDMARDs indicated for the treatment of axSpA at approved dosages only; comparators included standard-of-care treatments for axSpA, including NSAIDs and non-biologics. The included studies for the current review and analysis were further selected based on the outcome of interest in this was, which was overall health-related productivity and activity impairment as measured by any version of the WPAI questionnaire at Weeks 12–16; and randomised controlled trials (RCT) were eligible for inclusion. Several versions of the WPAI are available, including WPAI:General Health (GH), WPAI:Specific Health Problem (SHP) and WPAI:Ankylosing Spondylitis (WPAI:SpA); however, since the structure and scoring is the same across all versions of the WPAI questionnaire, study inclusion was not restricted based on questionnaire type.[14] In the WPAI:SpA, 'spondyloarthritis' is used to refer to the health condition of patients.[14]

Screening and extraction
Screening was done by two independent reviewers at both the title/abstract and full-text levels. Any disagreements

between the reviewers were resolved via discussion or moderation by a third reviewer.

A single reviewer performed data extraction of study characteristics and outcomes of the included studies. In cases where multiple publications reported results on the same cohort of patients or study, only the most recent and updated results were included. Data pertaining to study design, patient demographics (number, age, sex and employment status at study baseline), disease (type of axSpA, patient-reported activity limitations as measured by the Bath Ankylosing Spondylitis Functional Index and disease activity as measured by the Bath Ankylosing Spondylitis Disease Activity Index) and treatment characteristics and baseline WPAI domain scores from the included studies were extracted into tabulated Microsoft Excel worksheets. The data extraction was validated by a senior researcher.

Meta-analysis

A random-effects meta-analysis was performed for baseline and mean change from baseline in WPAI domain scores following treatment with b/tsDMARDs or placebo. A random-effects (DerSimonian-Laird method) model was chosen to account for the expected heterogeneity across included studies.[21 22] Meta-analysis was run in the statistical program RStudio (R V.4.0.2, Boston, Massachusetts, USA).

The analysis included RCTs reporting WPAI outcomes at Weeks 12–16, as mean change or least-squares mean (LSM) change from baseline. Studies that did not report sample size, mean and SD for WPAI domain scores were included in the narrative synthesis but not included in the final model. Due to the homogeneity of various WPAI versions in structure and scoring, pooling and meta-analysis was deemed feasible. Most placebo-controlled clinical trials in axSpA have their primary clinical outcomes, including other assessments, after 12–16 weeks. Therefore, WPAI outcomes at Weeks 12–16 from all included studies were pooled for this meta-analysis. Further, a subgroup analysis was performed for the WPAI domain scores of patients with nr-axSpA or r-axSpA.

Pooled effects were presented as mean baseline and mean change from baseline with corresponding 95% CIs and displayed graphically as forest plots. Levels of heterogeneity (T^2, H^2, I^2 parameters) were identified and measured per outcome. Heterogeneity levels (ie, I^2 parameter) were assessed based on the thresholds per the Cochrane Handbook.[22]

Standardised mean difference (SMD) was calculated to express an estimation of the size of the treatment effect in each study relative to the variability observed in the study, per treatment class. Only studies reporting a change from baseline with SD at Weeks 12–16 were included as part of this analysis.

The pooled baseline and mean change from baseline overall work impairment scores for paid work were converted to hours lost due to overall work impairment per patient per week. It was assumed that patients in the included studies worked a 40-hour week and that none of the productivity loss due to presenteeism or short-term absenteeism would be compensated:

$$Hours\ lost\ per\ week\ =\ Total\ work\ impairment\ score\ \times\ 40\ hours$$

Hours of productivity loss due to presenteeism were calculated as follows:

$$Hours\ lost\ per\ week\ =\ \frac{Degree\ problem\ affected\ productivity\ while\ working\ +\ Degree\ other\ health\ problems\ affected\ productivity\ while\ working}{10}\ \times\ Hours\ at\ work$$

Indirect costs associated with axSpA-related overall work impairment per patient per year (PPPY) were calculated for the European Union and the USA using the 2021 reported average hourly labour costs (€29.10/hour and US$40.35/hour, respectively)[23 24]:

$$Indirect\ costs\ associated\ with\ overall\ work\ impairment\ PPPY\ =\ Hours\ of\ overall\ work\ impairment\ per\ patient\ per\ week\ \times\ 52.143\ weeks/year\ x\ Average\ hourly\ labour\ cost$$

RESULTS

Study characteristics

The SLR identified 5580 records, of which 412 records were selected for full-text review. An additional 14 publications were identified by hand-searching conference proceedings and cross-referencing relevant SLRs. In total, 180 publications from 61 unique studies were included in the HRQoL SLR. After screening for studies reporting WPAI outcomes at Weeks 12–16, 11 unique records were included for the analyses. Figure 1 presents the PRISMA diagram.

Of the 11 included studies, 7 studies used either WPAI:SHP or WPAI:SpA, 1 used WPAI:GH[25] and 3 studies did not report the version of the WPAI questionnaire used. The sample sizes in the included studies ranged from 103[26] to 334[27] (table 1). Seven studies evaluated patients with r-axSpA, and four studies included patients with nr-axSpA. Approximately 57.6%[16] to 91.4% of patients with r-axSpA and 60.0%[28] to 74.0% with nr-axSpA were employed on a full-time or a part-time basis.

The majority of the identified studies reported WPAI outcomes for study patients employed at baseline following treatment with adalimumab and ixekizumab (n=3, each), followed by bimekizumab and tofacitinib (n=2, each) and etanercept and secukinumab (n=1, each). Further, the WPAI outcomes for patients treated with adalimumab in the ABILITY-1 trial were stratified by Assessment of Spondyloarthritis International Society 40% (ASAS40) response, as ASAS40 responders and
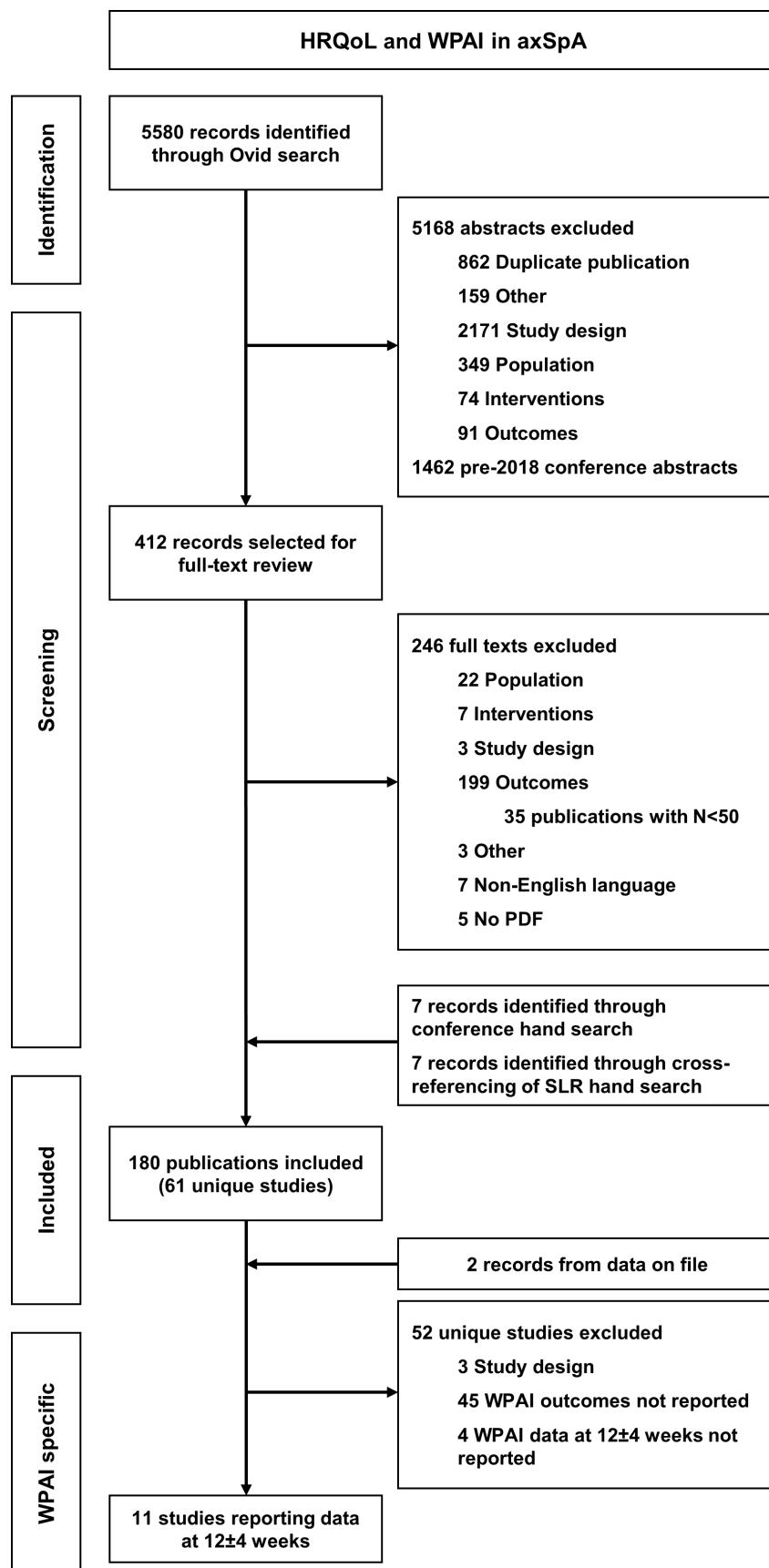
HRQoL and WPAI in axSpA

Identification

5580 records identified
through Ovid search

5168 abstracts excluded
862 Duplicate publication
159 Other
2171 Study design
349 Population
74 Interventions
91 Outcomes
1462 pre-2018 conference abstracts

Screening

412 records selected for
full-text review

246 full texts excluded
22 Population
7 Interventions
3 Study design
199 Outcomes
35 publications with N<50
3 Other
7 Non-English language
5 No PDF

7 records identified through
conference hand search
7 records identified through cross-
referencing of SLR hand search

Included

180 publications included
(61 unique studies)

2 records from data on file

WPAI specific

52 unique studies excluded
3 Study design
45 WPAI outcomes not reported
4 WPAI data at 12±4 weeks not
reported

11 studies reporting data
at 12±4 weeks

Figure 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses diagram for identifying studies reporting Work Productivity and Activity Impairment outcomes in axSpA at week 12 (±4 weeks). axSpA, axial spondyloarthritis; HRQoL, health-related quality of life; PDF, Portable Document Format; SLR, systematic literature review; WPAI, Work Productivity and Activity Impairment.

Table 1 Study characteristics of included studies reporting Work Productivity and Activity Impairment baseline outcomes

Intervention class	Study, year (ClinicalTrials.gov ID number)	Population	Intervention, dose	N	Age in years, mean (SD)	Males (%)	Disease duration in years, mean (SD)	Employed at baseline (%)	Baseline WPAI domain scores* (%), mean (SD)			
									Absenteeism	Presenteeism	Overall work impairment	Activity impairment
TNFi	ABILITY-1 2016 (NCT00939003)[38]	nr-axSpA	Adalimumab 40 mg Q2W	91	38 (11.3)	48.4	2.7 (4.2)	66	NR	NR	NR	NR
			Placebo	94	38 (10.4)	42.6	3.0 (3.8)		NR	NR	NR	NR
TNFi, IL-17Ai	COAST-V 2018 (NCT02696785)[16]	r-axSpA	Adalimumab 40 mg, Q2W/Q4W	90	42 (11.4)	81.0	7.5 (7.5)	74.1	13.6 (27.2)	53.2 (21.9)	55.0 (23.3)	58.2 (20.5)
			Ixekizumab 80mg, Q4W	81	41 (12.1)	84.0	8.3 (9.6)		8.0 (20.4)	57.1 (21.3)	58.7 (21.8)	58.8 (18.1)
			Placebo	87	43 (12.0)	83.0	6.8 (7.6)		7.2 (14.8)	61.4 (19.5)	63.2 (20.3)	62.4 (20.5)
TNFi	Huang 2014 (NCT01114880)[27]	r-axSpA	Adalimumab 40 mg Q2W	229	30 (8.7)	80.8	3.0 (3.8)	NR	NR	NR	60.0 (25.3)	58.8 (21.7)
			Placebo	115	30 (4.5)	82.6	3.0 (3.2)		NR	NR	67.5 (24.6)	61.0 (21.0)
TNFi	EMBARK 2020 (NCT01258738)[28]	nr-axSpA	Etanercept 50mg, QW	106	32 (7.8)	64.1	2.4 (1.9)	60	9.1 (25.0)	44.9 (26.7)	45.0 (26.2)	53.2 (25.9)
			Placebo	109	32 (7.8)	56.9	2.5 (1.8)		11.8 (27.7)	42.2 (26.3)	43.9 (27.8)	52.1 (24.3)
IL-17Ai	COAST-W 2019 (NCT02696798)[16]	r-axSpA	Ixekizumab 80mg, Q4W	114	47 (13.4)	79.8	10.1 (7.8)	57.6	22.9 (33.2)	60.0 (19.7)	64.0 (20.8)	72.5 (19.6)
			Placebo	104	47 (12.7)	83.7	13.0 (10.5)		14.6 (22.0)	58.8 (24.5)	62.3 (25.7)	67.5 (20.1)
IL-17Ai	COAST-X 2021 (NCT02757352)[39]	nr-axSpA	Ixekizumab 80mg, Q4W	96	41 (14.5)	52.1	4.2 (5.5)	64.7†	12.1 (27.0)	50.2 (22.3)	51.9 (22.8)	63.3 (21.5)
			Placebo	105	40 (12.4)	41.9	3.1 (4.5)		15.6 (26.8)	62.1 (18.7)	65.6 (20.2)	66.4 (20.4)
IL-17Ai	MEASURE 1 2016 (NCT01358175)[25]	r-axSpA	Secukinumab 150 mg	125	40 (11.6)	67.0	6.5 (6.9)	NR	11.6 (21.6)	45.3 (24.1)	49.7 (26.2)	56.7 (23.9)
			Placebo	122	43 (12.4)	70.0	8.3 (8.9)		15.3 (25.7)	51.7 (18.7)	56.7 (19.8)	58.9 (21.3)
IL-17Ai/17Fi	BE MOBILE 1 (NCT03928704) 2022	nr-axSpA	Bimekizumab 160mg	128	40 (11.1)	57.0	3.7 (6.2)	74.0	12.78 (25.0)	49.19 (25.1)	52.18 (26.6)	57.27 (22.9)
			Placebo	126	40 (11.8)	51.6	3.6 (5.4)		11.6 (26.7)	47.14 (20.9)	49.06 (21.5)	53.41 (21.7)
IL-17Ai/17Fi	BE MOBILE 2 (NCT03928743)2022	r-axSpA	Bimekizumab 160mg	221	41 (12.1)	72.4	6.7 (8.3)	91.4	11.52 (23.6)	46.11 (24.9)	49.24 (25.6)	53.26 (23.6)
			Placebo	111	39 (12.6)	72.1	5.7 (6.9)		10.86 (26.9)	42.30 (23.4)	43.91 (24.5)	54.05 (24.2)
JAKi	A3921119 2020 (NCT01786668)[26]	r-axSpA	Tofacitinib 5 mg, BID	52	41 (10.3)	75.0	3.5	NR	9.0 (23.7)	42.6 (26.0)	44.0 (28.0)	52.5 (25.7)
			Placebo	51	42 (12.9)	62.7	3.0		6.8 (19.0)	48.0 (23.3)	50.4 (25.5)	53.3 (26.5)

Table 1 Continued

Intervention class	Study, year (ClinicalTrials.gov ID number)	Population	Intervention, dose	N	Age in years, mean (SD)	Males (%)	Disease duration in years, mean (SD)	Employed at baseline (%)	Baseline WPAI domain scores* (%), mean (SD)			
									Absenteeism	Presenteeism	Overall work impairment	Activity impairment
JAKi	A3921120 2021 (NCT03502616)[40]	r-axSpA	Tofacitinib 5 mg, BID	133	42 (11.9)	87.2	8.9 (9.1)	NR	9.9 (22.4)	48.4 (26.3)	50.8 (27.4)	56.5 (23.4)
			Placebo	136	40 (11.1)	79.4	6.8 (6.9)		11.5 (24.6)	49.6 (22.2)	53.5 (23.1)	56.0 (21.4)

All trials were phase 3 except for A3921119 2020 (phase 2).
*Baseline WPAI domain score for study patients employed at baseline.
†For publications that did not report the number of patients employed, but specified that productivity was assessed only in those who were employed, we have calculated the employed percentage based on the number of patients included in the productivity study (responders to the WPAI) versus the study population.
axSpA, axial spondyloarthritis; BID, two times per day; IL-17Ai, interleukin 17A inhibitor; IL-17Ai/17Fi, interleukin-17A/17F inhibitor; JAKi, Janus kinase inhibitor; NR, not reported; nr-axSpA, non-radiographic axSpA; QW, one time per week; Q2W, every 2 weeks; Q4W, every 4 weeks; r-axSpA, radiographic axSpA; TNFi, tumour necrosis factor inhibitor; WPAI, Work Productivity and Activity Impairment.

ASAS40 non-responders. Patients not employed at baseline were excluded as it was assumed they would not gain employment within 12–16 weeks. There was substantial heterogeneity ($I^2 > 40\%$) among the populations of the included studies. The characteristics of included studies reporting WPAI baseline outcomes and change-from-baseline outcomes at Weeks 12–16 are reported for all studies in table 1 and table 2, respectively.

Change in WPAI domain scores from baseline
Overall work impairment
In seven studies, the mean overall work impairment score at baseline among employed patients who received b/tsDMARDs (n=994) was 52.1% (95% CI: 48.8% to 55.5%) (online supplemental figure S1), which equates to approximately 21 hours lost per patient per week over a 40-hour work week due to either absenteeism or presenteeism. In the placebo group (n=727), the mean overall score at baseline was 54.9% (95% CI: 50.1% to 59.6%), corresponding to approximately 22 hours of work lost per patient per week.

The absolute mean change from baseline in overall work impairment at Weeks 12–16 in patients who received b/tsDMARDs (n=634) was estimated at −21.6% (95% CI: −23.6% to −19.7%) (figure 2) with a mean relative improvement of 41.5% from baseline. This was greater than the improvement reported by patients who received placebo (n=426; overall absolute mean change at Weeks 12–16 from baseline: −12.3% (95% CI: −16.5% to −8.2%], for a relative improvement of 22.4%) (figure 2).

The pooled SMD was −0.9 (95% CI: −1.1 to −0.8) for patients treated with an interleukin (IL)-17 inhibitor (IL-17i; including IL-17Ai and IL-17Ai/17Fi) and −0.8 (95% CI: −1.0 to −0.6) for those treated with a tumour necrosis factor inhibitor (TNFi).

Absenteeism
In six studies, the overall mean absenteeism score at baseline among employed patients who received b/tsDMARDs (n=828) was 11.0% (95% CI: 8.9% to 13.1%) (online supplemental figure S2), equating to approximately 4.4 hours of missed work per patient over a 7-day period. In patients who received placebo (n=691), the overall mean absenteeism score at baseline was 11.5% (95% CI: 9.5% to 13.6), amounting to approximately 4.6 hours of work lost per patient per week.

At Weeks 12–16 from baseline, the overall mean change from baseline in absenteeism scores was higher in patients who received b/tsDMARDs (n=523; −3.0% (95% CI: −5.7% to −0.2%)) than in patients who received placebo (n=392; 0.01% (95% CI: −2.0% to 2.1%)) (figure 3). The corresponding estimated absolute number of hours at work gained was 1.2 hours per week with b/tsDMARDs and 0 hours with placebo. Patients treated with b/tsDMARDs experienced a mean relative improvement of 27.0% at Weeks 12–16 from the baseline absenteeism scores. The pooled SMD was −0.1 (95% CI: −0.2 to 0.02)

Table 2 Study characteristics of included studies reporting Work Productivity and Activity Impairment change-from-baseline outcomes at Weeks 12–16

Intervention class	Study, year (ClinicalTrials.gov ID number)	Population	Intervention, dose	N	Age in years, mean (SD)	Males (%)	Disease duration in years, mean (SD)	Employed at baseline (%)	CFB WPAI domain scores* (%), mean (SD)			
									Absenteeism	Presenteeism	Overall work impairment	Activity impairment
TNFi	ABILITY-1 2016 (NCT00939003)[38]	nr-axSpA	Adalimumab 40 mg Q2W	91	38 (11.3)	48.4	2.7 (4.2)	66	Responders: −9.1 (NR) Non-responders: −5.7 (NR)	Responders: −25.4 (NR) Non-responders: −1.4 (NR)	Responders: −26.8 (NR) Non-responders: −1.1 (NR)	Responders: −33.8 (NR) Non-responders: −4.2 (NR)
			Placebo	94	38 (10.4)	42.6	3.0 (3.8)		Responders: 4.9 (NR) Non-responders: 1.7 (NR)	Responders: −20.5 (NR) Non-responders: −3.1 (NR)	Responders: −16.4 (NR) Non-responders: −3.5 (NR)	Responders: −31.8 (NR) Non-responders: 1.2 (NR)
TNFi, IL-17Ai	COAST-V 2018 (NCT02696785)[16]	r-axSpA	Adalimumab 40 mg, Q2W/Q4W	90	42 (11.4)	81.0	7.5 (7.5)	74.1	−4.1 (23.9)	−20.0 (23.2)	−20.7 (24.2)	−20.9 (23.0)
			Ixekizumab 80 mg, Q4W	81	41 (12.1)	84.0	8.3 (9.6)		1.7 (17.6)	−24.6 (24.9)	−23.6 (25.3)	−23.7 (24.6)
			Placebo	87	43 (12.0)	83.0	6.8 (7.6)		−1.0 (13.8)	−21.4 (23.2)	−21.7 (24.5)	−16.4 (20.6)
TNFi	Huang 2014 (NCT01114880)[27]	r-axSpA	Adalimumab 40 mg Q2W	229	30 (8.7)	80.8	3.0 (3.8)	NR	NR	NR	−18.8 (23.7)	−21.1 (24.1)
			Placebo	115	30 (4.5)	82.6	3.0 (3.2)		NR	NR	−12.3 (32.0)	−10.1 (20.3)
TNFi	EMBARK 2020 (NCT01258738)[28]	nr-axSpA	Etanercept 50 mg, QW	106	32 (7.8)	64.1	2.4 (1.9)	60	−0.2 (NR)	−21.2 (NR)	−20.8 (NR)	−18.9 (NR)
			Placebo	109	32 (7.8)	56.9	2.5 (1.8)		−4.9 (NR)	−12.1 (NR)	−12.1 (NR)	−12.1 (NR)
IL-17Ai	COAST-W 2019 (NCT02696798)[16]	r-axSpA	Ixekizumab 80 mg, Q4W	114	47 (13.4)	79.8	10.1 (7.8)	57.6	−7.5 (20.2)	−21.3 (23.6)	−23.0 (24.2)	−20.2 (23.9)
			Placebo	104	47 (12.7)	83.7	13.0 (10.5)		−2.6 (28.6)	−8.8 (32.7)	−9.8 (32.8)	−8.3 (29.4)
IL-17Ai	COAST-X 2021 (NCT02757352)[39]	nr-axSpA	Ixekizumab 80 mg, Q4W	96	41 (14.5)	52.1	4.2 (5.5)	64.7†	−9.2 (NR)	−23.8 (NR)	−24.4 (NR)	−23.0 (NR)
			Placebo	105	40 (12.4)	41.9	3.1 (4.5)		−3.7 (NR)	−11.1 (NR)	−12.1 (NR)	−12.6 (NR)
IL-17Ai	MEASURE 1 2016 (NCT01358175)[25]	r-axSpA	Secukinumab 150 mg	125	40 (11.6)	67.0	6.5 (6.9)	NR	−1.0 (21.5)	−20.1 (24.8)	−20.8 (26.1)	−18.7 (25.9)
			Placebo	122	43 (12.4)	70.0	8.3 (8.9)		1.9 (22.4)	−12.8 (26.0)	−10.2 (27.0)	−7.0 (27.2)
IL-17Ai/17Fi	BE MOBILE 1 (NCT03928704) 2022[35]	nr-axSpA	Bimekizumab 160 mg	128	40 (11.1)	57.0	3.7 (6.2)	74.0	−1.4 (32.2)	−24.5 (24.4)	−26.5 (26.2)	−24.3 (26.9)
			Placebo	126	40 (11.8)	51.6	3.6 (5.4)		2.8 (28.9)	−14.1 (25.1)	−14.1 (25.6)	−9.7 (25.4)
IL-17Ai/17Fi	BE MOBILE 2 (NCT03928743)2022[35]	r-axSpA	Bimekizumab 160 mg	221	41 (12.1)	72.4	6.7 (8.3)	91.4	−5.5 (17.7)	−20.8 (23.5)	−22.2 (23.9)	−23.3 (22.9)
			Placebo	111	39 (12.6)	72.1	5.7 (6.9)		−1.2 (18.3)	−6.1 (23.0)	−6.7 (23.3)	−14.4 (21.6)

Continued

Table 2 Continued

Intervention class	Study, year (ClinicalTrials.gov ID number)	Population	Intervention, dose	N	Age in years, mean (SD)	Males (%)	Disease duration in years, mean (SD)	Employed at baseline (%)	CFB WPAI domain scores* (%), mean (SD)			
									Absenteeism	Presenteeism	Overall work impairment	Activity impairment
JAKi	A3921119 2020 (NCT01786668)[26]	r-axSpA	Tofacitinib 5 mg, BID	52	41 (10.3)	75.0	3.5	NR	−5.2 (NR)	−20.9 (NR)	−21.7 (NR)	−19.5 (NR)
			Placebo	51	42 (12.9)	62.7	3.0		−1.4 (NR)	−6.1 (NR)	−5.4 (NR)	−11.2 (NR)
JAKi	A3921120 2021 (NCT03502616)[40]	r-axSpA	Tofacitinib 5 mg, BID	133	42 (11.9)	87.2	8.9 (9.1)	NR	−3.7 (NR)	−19.8 (NR)	−21.5 (NR)	−19.0 (NR)
			Placebo	136	40 (11.1)	79.4	6.8 (6.9)		0.9 (NR)	−6.9 (NR)	−7.6 (NR)	−5.6 (NR)

All trials were phase 3 except for A3921119 2020 (phase 2).
*Baseline WPAI domain score for study patients employed at baseline.
†For publications that did not report the number of patients employed, but specified that productivity was assessed only in those who were employed, we have calculated the employed percentage based on the number of patients included in the productivity study (responders to the WPAI) versus the study population.
axSpA, axial spondyloarthritis; BID, two times per day; CFB, change from baseline; IL-17Ai, interleukin 17A inhibitor; IL-17Ai/17Fi, interleukin-17A/17F inhibitor; JAKi, Janus kinase inhibitor; NR, not reported; nr-axSpA, non-radiographic axSpA; Q2W, every 2 weeks; Q4W, every 4 weeks; QW, one time per week; r-axSpA, radiographic axSpA; TNFi, tumour necrosis factor inhibitor; WPAI, Work Productivity and Activity Impairment.

for patients who received an IL-17i and −0.2 (95% CI: −0.5 to −0.2) for those treated with a TNFi.

Presenteeism

In six studies, the overall mean presenteeism score at baseline among employed patients who received b/tsDMARDs (n=855) was 48.8% (95% CI: 45.6% to 52.0%) (online supplemental figure S3), amounting to approximately 17.3 hours of work lost per patient due to presenteeism over a 7-day period assuming a 40-hour work week and accounting for hours absent from work. In patients who had received placebo (n=667), the overall mean presenteeism score at baseline was 50.5% (95% CI: 46.0% to 55.0%), the equivalent of approximately 20.2 hours of work with diminished productivity per person week.

At Weeks 12–16 from baseline, the overall mean change in presenteeism scores was higher in patients who received b/tsDMARDs (n=486; −21.5 (95% CI: −23.6% to −19.4%)) than in patients who received placebo (n=366; −12.7 (95% CI: −17.7 to −7.7%]) (figure 4). This translated into an estimated absolute number of hours of productive work gained of 8.6 hours per week with b/tsDMARD treatment and 5.1 hours per week with placebo. Patients treated with b/tsDMARDs experienced a mean relative improvement of 44.4% from the baseline presenteeism scores at Weeks 12–16. The pooled SMD was −0.9 (95% CI: −1.1 to −0.8) with IL-17i treatment and −0.9 (95% CI: −1.3 to −0.6) with a TNFi.

Activity impairment

In seven studies, the overall mean activity impairment score at baseline among patients who received b/tsDMARDs (n=1463) was 58.0% (95% CI: 54.7% to 61.2%) (online supplemental figure S4), which amounts to 23.2 hours of axSpA-related impairment in typical daily activities. In patients who received placebo (n=1097), the overall mean score at baseline was 58.2% (95% CI: 55.0% to 61.5) or 23.3 hours.

At Weeks 12–16 from baseline, the overall mean change from baseline in activity impairment scores was higher in patients who received b/tsDMARDs (n=970; −21.8% (95% CI: −23.3% to −20.3%)) than in patients who received placebo (n=648: −11.2% (95% CI: −14.0% to −8.3%)) (figure 5). This translated into an estimated gain of 8.7 hours per week for patients treated with b/tsDMARDs and 4.5 hours per week for those who received placebo. Patients treated with b/tsDMARDs experienced a mean relative improvement of 37.7% in activity impairment at Weeks 12–16 from baseline. The pooled SMD was −1.0 (95% CI: −1.2 to −0.8) with IL-17i treatment and −1.0 (95% CI: −1.2 to −0.8) with a TNFi.

Indirect costs associated with axSpA-related overall work impairment

Based on the previously stated assumptions, the estimated annual per-person cost of lost productivity in paid work (range) associated with axSpA-related overall work impairment at baseline amounted to €31 646.09 (€29 606.75 to
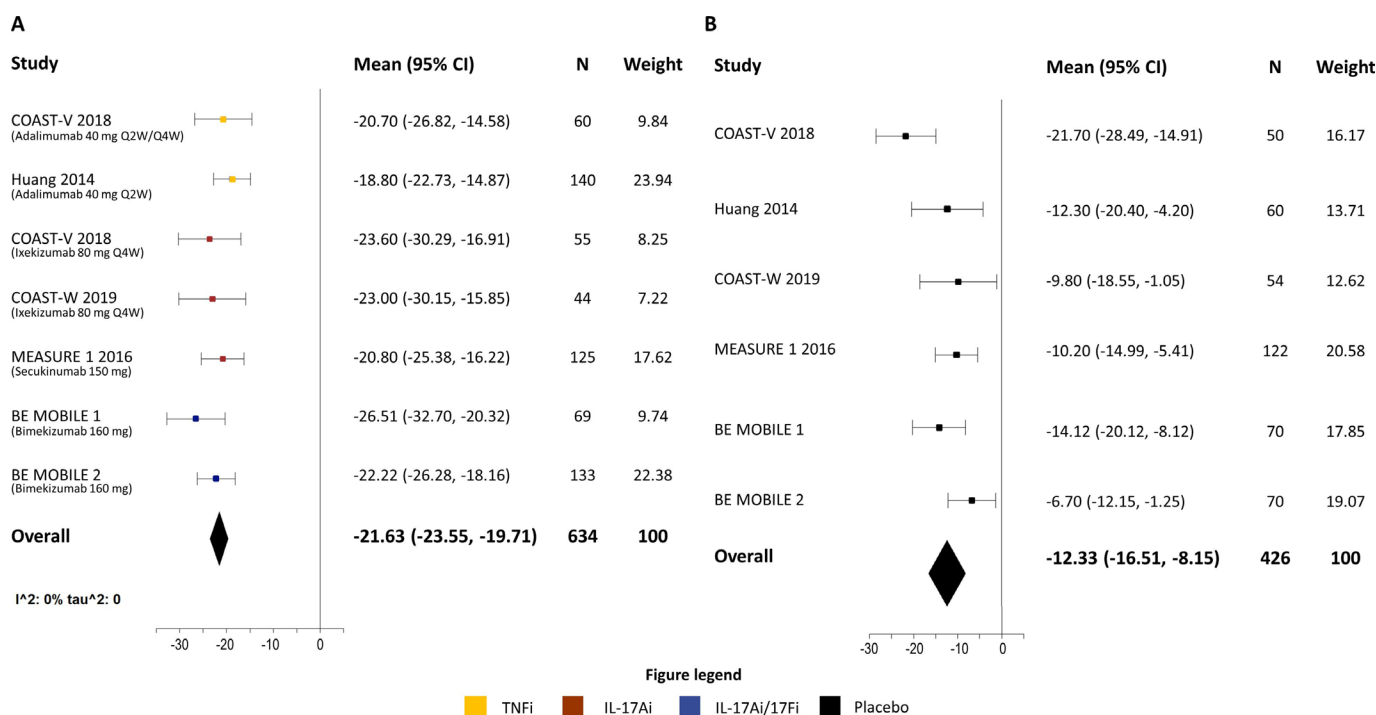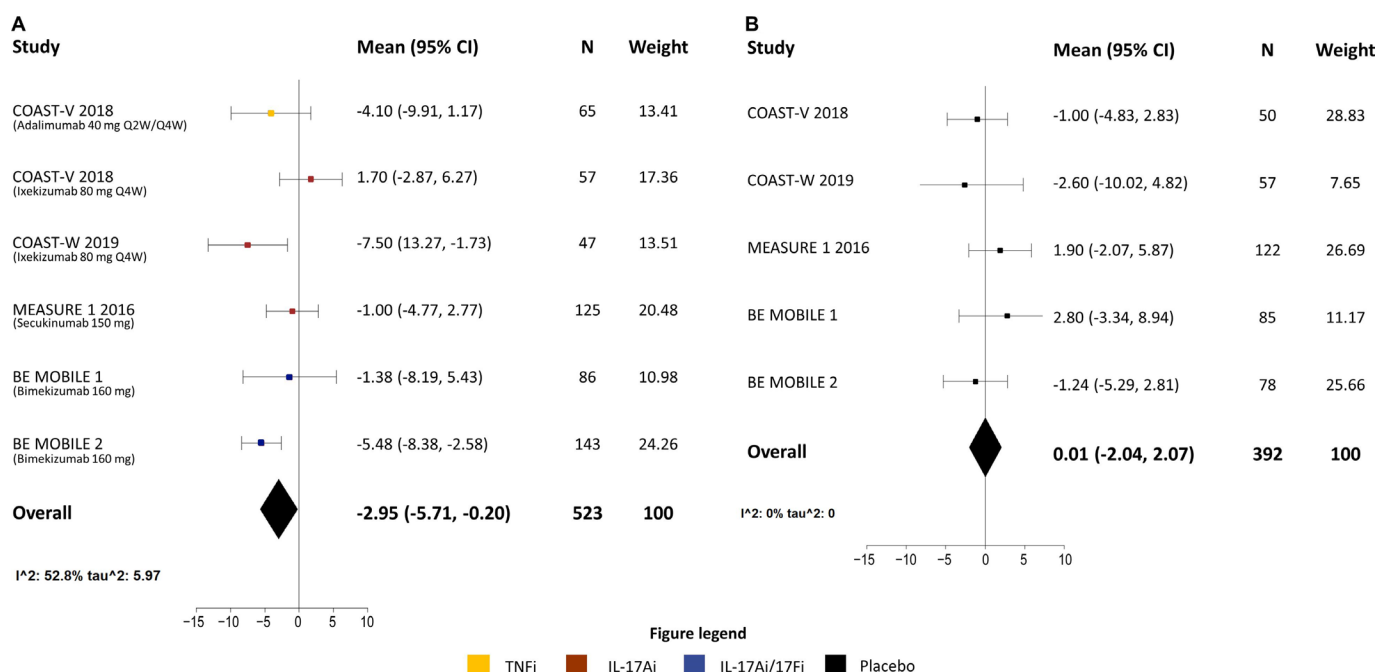
Figure 2 Meta-analysis of mean change in overall work impairment scores at Weeks 12–16 from baseline. (A) Treated with b/tsDMARDs and (B) placebo. b/tsDMARD, biological or targeted-synthetic disease-modifying antirheumatic drug; IL-17Ai, interleukin-17A inhibitor; IL-17Ai/17Fi, interleukin-17A/17F inhibitor; Q2W, every 2 weeks; Q4W, every 4 weeks; TNFi, tumour necrosis factor inhibitor.

€33 691.49) or US$43 880.40 (US$41 052.66 to US$46 716.55), of which €6658.00 or US$9232.22 was due to absenteeism (table 3). Following 12–16 weeks of treatment with b/tsDMARDs, overall productivity costs decreased from baseline by €13 128.21 (€11 962.88 to

€14 293.54) or US$18 203.55 (US$16 587.70 to US$19 819.40), €1790.00 or US$2482.68 of which was due to the decrease in absenteeism. In the placebo group, the estimated annual per-person cost of overall work impairment was €33 296.98 (€30 426.13 to €36 167.82) or

Figure 3 Meta-analysis of mean change in absenteeism scores at Weeks 12–16 from baseline. (A) Treated with b/tsDMARDs and (B) placebo. b/tsDMARD, biological or targeted-synthetic disease-modifying antirheumatic drug; IL-17Ai, interleukin-17A inhibitor; IL-17Ai/17Fi, interleukin-17A/17F inhibitor; Q2W, every 2 weeks; Q4W, every 4 weeks; TNFi, tumour necrosis factor inhibitor.
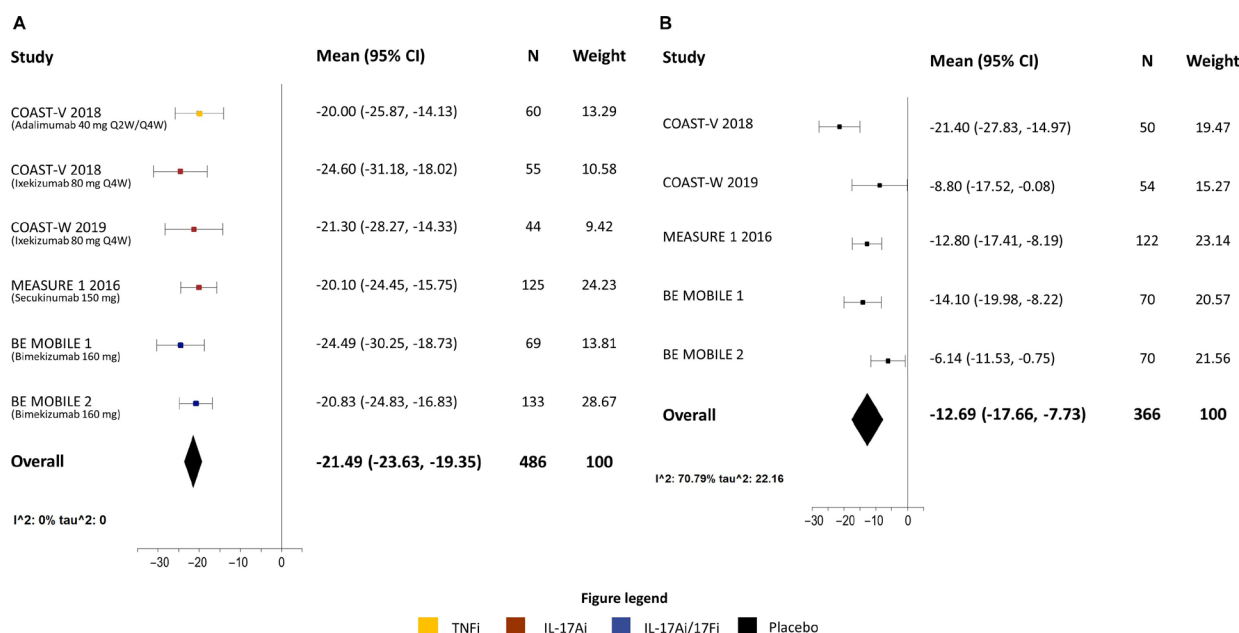
Figure 4 Meta-analysis of mean change in presenteeism scores at Weeks 12–16 from baseline. (A) Treated with b/tsDMARDs and (B) Placebo. b/tsDMARD, biological or targeted-synthetic disease-modifying antirheumatic drug; IL-17Ai, interleukin-17A inhibitor; IL-17Ai/17Fi, interleukin-17A/17F inhibitor; Q2W, every 2 weeks; Q4W, every 4 weeks; TNFi, tumour necrosis factor inhibitor.

US$46 198.52 (US$42 188.81 to US$50 150.22), of which or €6979.86 or US$9678.26 was due to absenteeism. The corresponding decrease from baseline in estimated indirect costs at Weeks 12–16 with placebo was €7483.63 (€10 020.65 to €4946.60) or US$10 376.79 (US$6858.95 to US$13 894.61), of which €606.94 or US$841.58 was due to reduced absenteeism.

Meta-analysis by subgroups: nr-axSpA versus r-axSpA

At baseline, overall work impairment scores were reported for 289 employed patients with nr-axSpA and 705 employed patients with r-axSpA, with overall absolute mean scores of 48.7% (95% CI: 44.6% to 52.8%) and 54.2% (95% CI: 49.9% to 58.5%), respectively. Due to limitations in reporting of SDs, only data from the BE
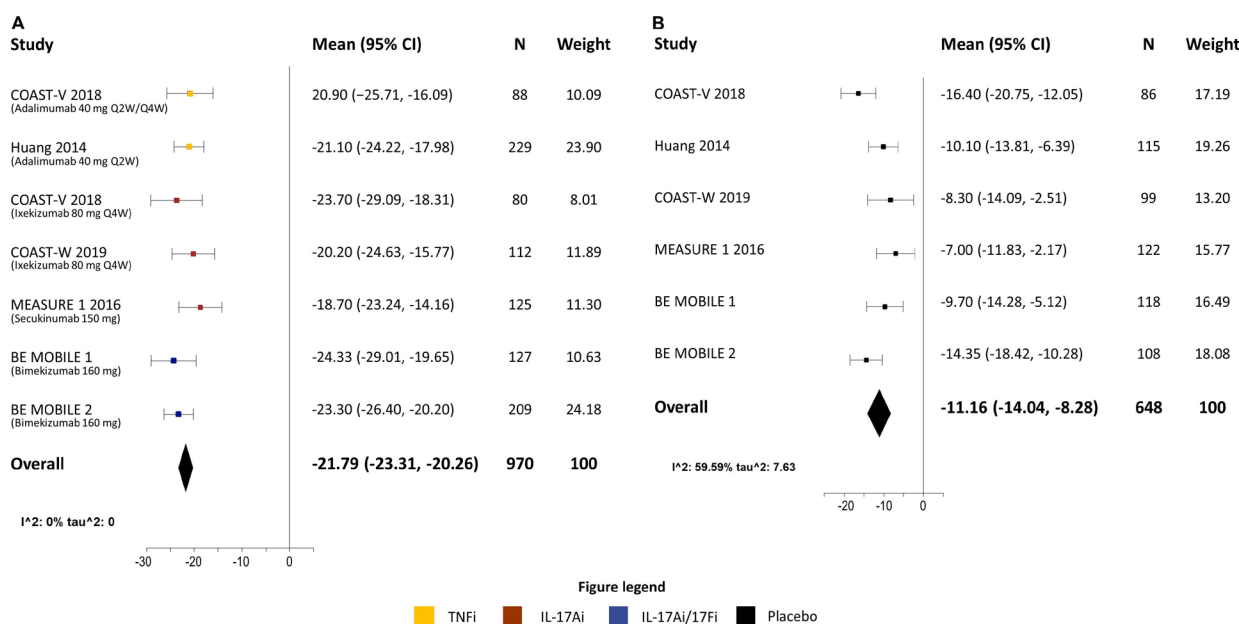
Figure 5 Meta-analysis of mean change in activity impairment scores at Weeks 12–16 from baseline. (A) Treated with b/tsDMARDs and (B) placebo. b/tsDMARD, biological or targeted-synthetic disease-modifying antirheumatic drug; IL-17Ai, interleukin-17A inhibitor; IL-17Ai/17Fi, interleukin-17A/17F inhibitor; Q2W, every 2 weeks; Q4W, every 4 weeks; TNFi, tumour necrosis factor inhibitor.

MOBILE 1 study were included in the analysis of patients with nr-axSpA at Weeks 12–16. After treatment with b/tsDMARDs, the absolute mean change from baseline in overall work productivity impairment at Weeks 12–16 was −26.5% (95% CI: −32.4% to −20.7%) in patients with nr-axSpA (online supplemental figure S5) and −21.1% (95% CI: −23.1% to −19.0%) in patients with r-axSpA (online supplemental figure S6).

The overall absolute mean baseline scores for absenteeism, presenteeism and activity impairment in patients with nr-axSpA were 10.0% (95% CI: 6.1% to 13.8%), 46.4% (95% CI: 42.9% to 50.0%) and 56.9% (95% CI: 52.4% to 61.5%), respectively. The corresponding scores in patients with r-axSpA were 11.6% (95% CI: 9.0% to 14.1%), 50.5% (95% CI: 45.9% to 55.1%) and 58.6% (95% CI: 54.2% to 63.0%), respectively. Baseline scores were lower in all domains for patients with nr-axSpA when compared with r-axSpA.

At Weeks 12–16, overall mean change from baseline scores for patients with nr-axSpA and r-axSpA, respectively, were −1.4% (95% CI: −8.2% to −5.4%) and −3.2% (95% CI: −6.3% to −0.02%) for absenteeism (online supplemental figures S7 and S8), −24.5% (95% CI: −30.3% to −18.7%) and −21.0% (95% CI: −23.3% to −18.7%) for presenteeism (online supplemental figures S9 and S10) and −24.3% (95% CI: −29.0% to −19.7%) and −21.5% (95% CI: −23.1% to −19.9%) for activity impairment (online supplemental figures S11 and S12).

Indirect costs associated with nr-axSpA- or r-axSpA-related overall work impairment

The estimated annual per-patient indirect costs related to overall work productivity impairment at baseline were €29 533.92 (€27 051.52 to €32 016.32) or US$40 951.67 (US$37 509.58 to US$44 393.77) for nr-axSpA and €32 908.53 (€30 304.74 to €35 512.32) or US$45 630.90 (US$42 020.49 to US$49 241.32) for r-axSpA (table 3). In patients with nr-axSpA and r-axSpA who received b/tsDMARDs, the estimated indirect cost savings following 12–16 weeks of treatment were €16 090.10 (€12 333.11 to €19 847.09) or US$22 310.50 (US$17 101.07 to US$27 519.93) and €12 776.18 (€11 538.02 to €14 008.28) or US$17 715.43 (US$15 998.59 to US$19 423.85), respectively. Absenteeism costs amounted to €6051.24 or US$8390.63 for nr-axSpA and €7016.28 or US$9728.76 for r-axSpA. Corresponding savings related to reduced absenteeism at Weeks 12–16 of b/tsDMARD treatment were €837.58 or US$1161.39 for nr-axSpA and €1911.88 or US$2651.00 for r-axSpA.

DISCUSSION

An SLR and meta-analysis were performed to evaluate the mean change in WPAI outcome scores in patients with nr-axSpA and r-axSpA, following treatment with b/tsDMARDs at Weeks 12–16. Among patients with active axSpA who were employed at baseline, the mean overall work impairment at baseline ranged from 52.1% to 54.9%. When assuming a 40-hour work week, this equates to approximately 20.8 to 22.0 hours per week of overall work impairment per patient, due to either absenteeism or presenteeism. Presenteeism was the major contributor to overall work impairment.

In the meta-analysis, the mean overall work impairment scores at Weeks 12–16 decreased by 21.6% (8.6 hours per week) from baseline with b/tsDMARDs compared with 12.3% (4.9 hours per week) with placebo. Such improvements were associated with estimated annual

Table 3 AxSpA-related costs of overall work impairment and absenteeism

| | Overall work impairment | | Absenteeism only | |
	Baseline cost PPPY (range)	Week 12–16 savings PPPY (range)	Baseline cost PPPY (range)	Week 12–16 savings PPPY (range)
All axSpA	€31 646.09 (€29 606.75 to €33 691.49) US$43 880.40 (US$41 052.66 to US$46 716.55)	€13 128.21 (€11 962.88 to €14 293.54) US$18 203.55 (US$16 587.70 to US$19 819.40)	€6658.18 (€5383.60 to €7932.76) US$9232.22 (US$7464.89 to US$10 999.56)	€1790.49 (€3465.65 to €121.39) US$2482.68 (US$168.32 to US$4805.47)
nr-axSpA	€29 533.92 (€27 051.52 to €32 016.32) US$40 951.67 (US$37 509.58 to US$44 393.77)	€16 090.10 (€12 333.11 to €19 847.09) US$22 310.50 (US$17 101.07 to US$27 519.93)	€6051.24 (€3708.43 to €8394.04) US$8390.63 (US$5142.10 to US$11 639.16)	€837.58 (€4970.88 to €−3295.71) US$1161.39 (−US$4569.82 to US$6892.61)
r-axSpA	€32 908.53 (€30 304.74 to €35 512.32) US$45 630.90 (US$42 020.49 to US$49 241.32)	€12 776.18 (€11 538.02 to €14 008.28) US$17 715.43 (US$15 998.59 to US$19 423.85)	€7016.28 (€5486.78 to €8539.71) US$9728.76 (US$7607.96 to US$11 841.14)	€1911.88 (€12.14 to €3811.61) US$2651.00 (US$16.83 to US$5285.17)

Negative value indicates increased cost.
axSpA, axial spondyloarthritis; nr-axSpA, non-radiographic axSpA; PPPY, per person per year; r-axSpA, radiographic axSpA.

cost savings per person of €13 128.21 with b/tsDMARDs and €7483.63 with placebo. Presenteeism was the major contributor to the mean change from baseline in overall work impairment scores at Weeks 12–16, consistent with baseline observations.

These findings confirmed the substantial impact of axSpA on workplace productivity and outcomes as aligned with results from previous studies.[29–31] A meta-analysis of RCTs and controlled cohorts in chronic, inflammatory arthritis, including axSpA, demonstrated improvements in absenteeism and presenteeism in patients treated with bDMARDs compared with conventional treatments.[30] The assessment of workplace productivity and outcomes among patients with axSpA in the BSR Biologics register in Axial Spondyloarthritis by Shim *et al* showed that patients initiating biological therapy reported high work impairments at baseline. Productivity loss due to presenteeism was higher than that due to absenteeism (41.0% vs 10.9%, respectively).[31] This was consistent with the baseline presenteeism and absenteeism in the present study. Further, the meta-analysis of WPAI outcomes by Shim *et al* also revealed substantial improvements in presenteeism and minimal improvements in absenteeism in patients with axSpA treated with bDMARDs at 12 months from baseline.[31] This aligned with the present meta-analysis, where the improvement in presenteeism (−21.5%) was numerically higher than improvements in absenteeism (−3.0%). Taken together, the results of the current analysis and existing evidence suggest that presenteeism is a greater contributor to overall work impairment than absenteeism among the employed patients with axSpA.

Findings from the subgroup analysis of patients with nr-axSpA and r-axSpA in the present study contrast with results reported by López-Medina *et al*.[29] In our analysis, presenteeism and activity impairment scores, respectively, were higher among the r-axSpA population (50.5% and 58.6%) than the nr-axSpA population (46.4% and 56.9%), whereas López-Medina *et al* reported lower presenteeism and activity impairment in patients with r-axSpA (24.2% and 28.6%) than nr-axSpA (31.6% and 36.6%).[29] Overall, presenteeism and activity impairment scores were higher in the current study as well. Generally, patient characteristics between López-Medina *et al* and this study were similar (eg, mean age, proportion of females and duration of disease) for both r-axSpA and nr-axSpA. One slight difference was that the mean duration of disease was slightly longer for nr-axSpA in López-Medina *et al* than the range of 2–4 years reported in this analysis (table 1). However, the reason for these differences may be attributed to the lack of RCTs informing the analysis by López-Medina *et al*, in which 50 of the 60 included studies were cohort, cross-sectional and case–control studies which were not designed to compare r-axSpA and nr-axSpA subgroups, while the current study only included RCTs.[29]

Strengths and limitations

This study has several strengths. Our analyses were based on evidence retrieved through a systematic search of the literature with updates to account for the rapidly changing treatment landscape in axSpA. Standard electronic database search techniques were supplemented with cross-referencing SLRs and grey literature searches to identify all relevant data. Further, only WPAI domain scores reported in RCTs were included in the analyses.

This study should be considered with the following limitations. This analysis focused only on studies that measured productivity using the WPAI questionnaire, a widely used and validated measure in axSpA.[13 14] Studies that evaluated the productivity outcomes using other tools (eg, Work Instability Scale for AS, Work Productivity Survey)[32 33] were excluded. Considering that the WPAI is one of the six instruments identified by the Outcome Measures in Rheumatology Worker Productivity Group as a candidate for assessing at-work limitations of productivity loss,[34] and is consistent regardless of WPAI version, this measurement instrument enabled the comparison of findings across the included studies and the potential to compare results across all interventions. While a formal quality assessment was not performed, our analysis included only RCTs, which generally have a low risk of bias and high internal validity. We also acknowledge that the results from BE MOBILE 1 and 2 were not published at the time of this review and analysis and were therefore sourced from data on file, which may be considered as a potential source of bias. After the completion of this review and analysis, some of these results were presented as an abstract at ACR Convergence 2023.[35]

Certain assumptions were made in the meta-analysis to accommodate for the variations in the reporting of WPAI outcomes among the included studies. For example, following a scenario analysis, the data reported as means and LSM were pooled. In addition, the reporting of patient characteristics and outcomes in the included studies limited the number of studies that were eligible for inclusion in our meta-analysis (6–7 out of 11 studies), as well as our ability to interpret the results of this meta-analysis. Since WPAI is often considered as a secondary outcome measure, the included studies varied widely in reporting patient characteristics such as prior TNFi experience, physical function, spinal mobility, employment type (blue collar or white-collar jobs, etc), educational and socioeconomic status and other factors. It would be of interest for future research to further define how these characteristics contribute to work and/or activity impairment in patients with axSpA. Moreover, because these results consider only employed people, there may be some bias toward reporting productivity outcomes for a patient population with potentially less severe disease who are able to maintain employment. Additionally, the studies were conducted in various countries where different labour markets and arrangements could influence employment and productivity. For instance, some countries may support maintained employment for

individuals with reduced productivity, whereas others may not, leading to early retirement or unemployed status for impacted people.

Additional analyses of interest, such as TNFi-experienced versus b/tsDMARD-naïve patients or patients with early versus established disease, were not feasible due to the lack of sufficient information in the included studies. Additionally, not all studies included SD for change from baseline analyses, which prevented their inclusion in the models. It is possible that some studies included in the analyses, which were conducted during the COVID-19 pandemic, could also have affected results due to limited reporting. However, these effects were not explored in this meta-analysis. Missingness of data also limited our ability to explore the difference between ASAS40 responders and non-responders in the ABILITY 1 trial, which would have been a valuable exploration. Notably, patients who respond well to treatment will stay on treatment longer, leading to additional improvements in work impairment, but our results were limited to data from Weeks 12–16.

The assumption that all patients worked a 40-hour week for estimating the hours lost due to axSpA-related work impairment could be an overestimation. We are aware of one survey of employed patients with spondyloarthritis in Italy reporting the average number of hours worked per week was 32.2.[36] Lastly, the indirect costs were associated with overall work impairment in axSpA and cannot be generalised, as these costs were calculated for work participation over the previous 7 days and assumed a 40-hour work week per year, with the same hourly cost used for absenteeism and presenteeism. In addition, it has been shown that short-term sickness absences and presenteeism might be compensated by workers on return to work or when they feel healthier. On the other hand, estimation of productivity-related indirect costs did not consider other contributing factors including short-term and long-term disability absence, unemployment, early retirement due to disease and premature death. The estimated indirect cost of absenteeism amounted to €6658.16 or US$9232.22 PPPY, which decreased by €1790.49 or US$2482.68 PPPY following 12–16 weeks of treatment with b/tsDMARDs. Moreover, some unemployed/underemployed patients who experience improvements due to treatment may also return to work, which we were not able to capture in terms of cost savings due to the requirement of employment for several key domains of the WPAI. This is important to consider in the context of the costs of b/tsDMARD treatment over time, which can be substantial, but may be offset at least in part by improved productivity.

The generalisability of this study is limited by the fact that work productivity was explored only in patients with axSpA treated with b/tsDMARDs. These patients are considered to have a severe form of axSpA, as their condition does not respond to NSAIDs and other conventional DMARDs.[37] Future studies should explore the impact of patient and disease characteristics and previous treatment on the productivity of patients with axSpA.

CONCLUSION

This SLR and meta-analysis demonstrated that patients with active axSpA experience substantial work impairment, with presenteeism being a more substantial contributor than absenteeism. Improvement from baseline in overall work impairment at Weeks 12–16 with b/tsDMARD treatment was equivalent to an estimated savings of €13 128.21 or US$18 203.55 PPPY. Results also suggested that costs related to overall work impairment were slightly higher in r-axSpA than nr-axSpA. Ability to work is a vital determinant of psychological, social and economic well-being. Evaluating the impact of axSpA on work participation and productivity should be considered an essential aspect of the assessment of the overall burden of axSpA on patients and society.

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level data and redacted trial documents which may include analysis-ready data sets, study protocol, annotated case report forms, statistical analysis plans, data set specifications and clinical study reports. Prior to the use of data, proposals need to be approved by an independent review panel at www.Vivli.org and a signed data-sharing agreement needs to be executed. All documents are available in English only, for a prespecified time, typically 12 months, on a password-protected portal. This may change if the risk of re-identifying trial participants is determined to be too high after the trial is completed; in this case, individual patient-level data would not be made available.

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