A Systematic Literature Review and Meta-Analysis of Work Productivity According to the Work Productivity and Activity Impairment Questionnaire in Patients With Axial Spondyloarthritis Treated With Biologic or Targeted Synthetic Disease-Modifying Antirheumatic Drugs

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Objectives

To quantify short-term changes in health-related productivity impairment as measured by the Work Productivity and Activity Impairment (WPAI) questionnaire in patients with axial spondyloarthritis (axSpA) treated with biologic or targeted synthetic disease-modifying antirheumatic drugs (b/tsDMARDs).

Background

- axSpA is a chronic inflammatory disease primarily affecting the axial skeleton, namely the sacroiliac joints and spine.[1] Patients with axSpA are predominantly of active working age at disease onset, and the disease-related symptoms and manifestations severely impact daily activities and work participation leading to unemployment, missed work (absenteeism), and reduced productivity at work (presenteeism).[2-4]
- Treatment with b/tsDMARDs is aimed at decreasing disease activity, relieving symptoms, improving function, and preventing disability, which may support patients' ability to work.[1]
- The WPAI questionnaire is a patient-reported outcome measure commonly used to assess the short-term impact of axSpA on daily activities and workplace productivity in clinical trials of DMARDs.[4-6]

Methods

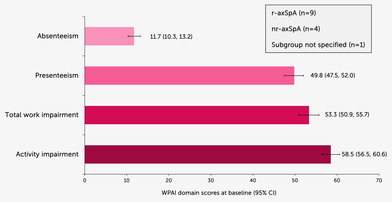
- A systematic literature review (SLR) was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines to identify randomized and non-randomized studies published between January 2010 and October 21, 2021, that reported health-related quality of life and productivity outcomes as measured by any version of the WPAI questionnaire in patients with axSpA starting a b/tsDMARD.[6,7]
- A random-effects meta-analysis of all doses of the identified b/tsDMARDs and placebo (including non-steroidal anti-inflammatory drugs [NSAIDs] and conventional DMARDs) was performed for each WPAI domain (absenteeism, presenteeism, work impairment, and activity impairment) scores at baseline and the mean change in scores from the baseline. WPAI outcomes reported at Weeks 12 (± 4 weeks) from baseline were pooled for this analysis.
- Percentage of total work impairment was converted into hours of productivity loss per week, assuming a 40-hour work European week, and the associated indirect costs per year were calculated for the Union (EU) and the United States (US) as the product of hours lost and the average hourly labor costs reported in the respective regions (assuming presenteeism contributes to indirect costs associated with loss of productivity).[8,9]

Results

- The SLR identified 5580 publications, of which 14 unique studies, including unpublished data from BE MOBILE 1 and BE MOBILE 2, reporting WPAI outcomes at Weeks 12 (± 4 weeks) from baseline were included **(Table 1)**.
- At baseline, the overall mean total work impairment score in patients (n=3,889) with axSpA was 53.3% (95% confidence interval [CI] 50.9, 55.7), equating to 21.3 hours per week of productivity loss **(Figure 1 and Figure 2a)**, compared with an estimated 2 hours per employee per week in lost productive time due to any health condition among individuals of working age group (18 to 65 years) in the US.[10]
- Pooled results from the meta-analyses showed substantial heterogeneity (I^2=67%) among the population of the included studies **(Figure 4a and Figure 4b)**. At Weeks 12 to 16, patients treated with b/tsDMARDs had a greater reduction in total work impairment, with a mean change from baseline WPAI total work impairment domain score of -21.1% (95% CI -23.7, -18.6) in randomized controlled trials (RCTs) to -19.7% (95% CI -24.5, -15.0) **(Figure 2b)** in observational studies, compared with placebo (-11.1% [95% CI -13.9, -8.4]) **(Figure 3 and Figure 4)**.

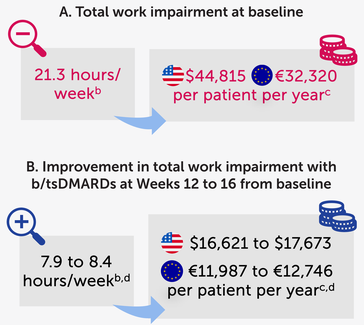
Results

Figure 1 Baseline WPAI domain scores in patients with active axSpA: Results from the meta-analysis



'n' denotes the number of studies.

Figure 2 Total work impairment and associated indirect costs in patients with axSpA (assuming a 40-hour standard work week)[a]



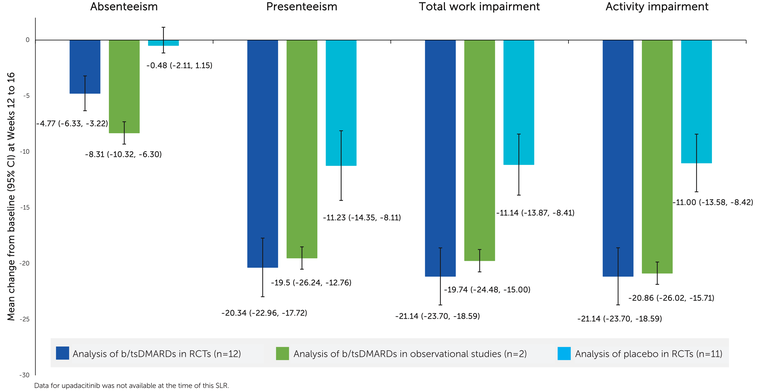
[a] Assuming presenteeism contributes to indirect costs associated with loss of productivity.

[b] Domain scores (mean) were multiplied by 40 hours (assuming a standard work week).
Total work impairment per week = Mean WPAI total work impairment score X 40 hours per week.

[c] Total work impairment per week was multiplied by 2021 average hourly labor costs in the EU (€29.10/hour)[9] and 2021 employer cost for employee compensation in the US ($40.35/hour).[9] The results were rounded-off to the nearest whole number.
Indirect costs per year = Total work impairment per week X Average hourly labor cost (EU or US) X 52.143 weeks.

[d] The range refers to values calculated based on the pooled mean total work impairment scores at Weeks 12 to 16 from baseline for observational studies and RCTs, respectively.

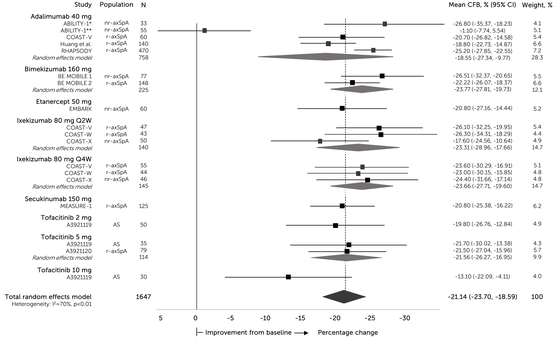
Figure 3 Mean (95% CI) change in WPAI domain scores in patients with axSpA at Weeks 12–16: Results from the meta-analysis



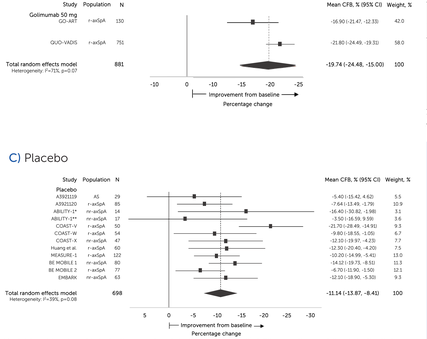
Data for upadacitinib was not available at the time of this SLR.

Figure 4 Meta-analysis of mean change from baseline in total work impairment scores in patients with axSpA: Outcomes pooled at Weeks 12–16

A) Randomized controlled trials



B) Observational studies



C) Placebo

Data for upadacitinib was not available at the time of this SLR. Data for BE MOBILE 1 and BE MOBILE 2 were retrieved from data on file. The overall pooled random effect model for total work impairment indicates there may be substantial heterogeneity (I^2=67%) among the population, indicating that further exploration into patient characteristics and subgroup data may be worthwhile.
* ASAS40 responders; ** ASAS40 non-responders.

Table 1 Characteristics of the studies included in the meta-analysis[a]

Study (year)	Study design	Population	Employed (%)[b]	Intervention	Drug and dose	N
BE MOBILE 1 (2022)[c]	RCT, phase 3	nr-axSpA	74.0%	**IL-17Ai/17Fi**	Bimekizumab 160 mg	128
					Placebo	126
COAST-X (2021)	RCT, phase 3	nr-axSpA	64.7%	**IL-17Ai**	Ixekizumab 80 mg Q2W[d]	102
					Ixekizumab 80 mg Q4W	96
					Placebo	105
ABILITY-1 (2016)	RCT, phase 3	nr-axSpA	66.0%	**TNFi**	Adalimumab 40 mg	91
					Placebo	94
EMBARK (2020)	RCT, phase 3	nr-axSpA	60.0%	**TNFi**	Etanercept 50 mg	106
					Placebo	109
BE MOBILE 2 (2022)[c]	RCT, phase 3	r-axSpA	91.4%	**IL-17Ai/17Fi**	Bimekizumab 160 mg	221
					Placebo	111
COAST-W (2019)	RCT, phase 3	r-axSpA	57.6%	**IL-17Ai**	Ixekizumab 80 mg Q2W[d]	102
					Ixekizumab 80 mg Q4W	96
					Placebo	105
MEASURE 1 (2016)	RCT, phase 3	r-axSpA	NR	**IL-17Ai**	Secukinumab 150 mg	125
					Placebo	122
COAST-V (2018)	RCT, phase 3	r-axSpA	74.1%	**TNFi**	Adalimumab 40 mg	90
				IL-17Ai	Ixekizumab 80 mg Q2W[d]	83
					Ixekizumab 80 mg Q4W	81
					Placebo	87
Huang et al. (2014)	RCT, phase 3	r-axSpA	NR	**TNFi**	Adalimumab 40 mg	229
					Placebo	115
RHAPSODY (2011)	Single-arm trial	r-axSpA	NR	**TNFi**	Adalimumab 40 mg	1250
GO-ART (2020)	Observational	r-axSpA	78.1%	**TNFi IV**	Golimumab 50 mg	249
QUO VADIS (2019)	Observational	r-axSpA	NR	**TNFi IV**	Golimumab 50 mg	751
A3921120 (2021)	RCT, phase 3	r-axSpA	NR	**JAKi**	Tofacitinib 5 mg	133
					Placebo	136
A3921119 (2020)	RCT, phase 2	AS	NR	**JAKi**	Tofacitinib 2 mg[e]	52
					Tofacitinib 5 mg	52
					Tofacitinib 10 mg[e]	52
					Placebo	51

'N' indicates the total number of patients in each arm of the study. [a] Data for upadacitinib was not available at the time of this SLR. [b] At baseline. [c] Data for BE MOBILE 1 and BE MOBILE 2 were retrieved from data on file. [d] Ixekizumab 80 mg Q2W is not the approved dose for AS and nr-axSpA.[11,12] [e] Tofacitinib 2 mg and 10 mg are not the approved doses for AS.[13,14]

Conclusions

- Patients with axSpA experience substantial productivity impairment with a total work impairment of 53.3% at baseline, costing $44,815 or €32,320 per patient per year (assuming a 40-hour work week for each patient) in productivity loss associated with absenteeism and presenteeism.
- Consistent with the literature, presenteeism is the major contributor to total work impairment in patients with axSpA.
- Compared with baseline, patients treated with b/tsDMARDs reported a mean change of -19.7% (observational studies) to -21.1% (RCTs) in total work impairment at Weeks 12 to 16 from baseline, equivalent to $16,621 to $17,673 or €11,987 to €12,746 per patient per year (assuming a 40-hour work week for each patient) compared with -11.1% reported by patients who received placebo.
- In this analysis, improvement in mean total work impairment was greater with b/tsDMARD treatment than with placebo.

%: percentage; **AS:** ankylosing spondylitis; **ASAS:** Assessment in SpondyloArthritis International Society; **axSpA:** axial spondyloarthritis; **b/tsDMARD:** biologic and targeted synthetic disease-modifying antirheumatic drugs; **CFB:** change from baseline; **CI:** confidence interval; **EU:** European Union; **IL-17Ai:** interleukin 17A inhibitor; **IL-17Ai/17Fi:** interleukin 17A and 17F inhibitor; **IV:** intravenous; **JAKi:** Janus kinase inhibitor; **mg:** milligram; **NR:** not reported; **nr-axSpA:** non-radiographic axial spondyloarthritis; **NSAID:** non-steroidal anti-inflammatory drug; **PDF:** Portable Document Format; **Q2W:** once every 2 weeks; **Q4W:** once every 4 weeks; **r-axSpA:** radiographic axial spondyloarthritis; **RCT:** randomized controlled trial; **SD:** standard deviation; **SLR:** systematic literature review; **WPAI:** Work Productivity and Activity Impairment; **TNFi:** tumor necrosis factor inhibitor; **US:** United States

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