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Requires Data Access? No

Are external grants or funds being used to support this research?: External grants or funds are being used to support this research.
Project Funding Source: Assessment of SpondyloArthritis International Society (ASAS)
How did you learn about the YODA Project?: Colleague

Conflict of Interest

https://yoda.yale.edu/wp-content/uploads/2024/07/COI-DC-1.pdf
https://yoda.yale.edu/wp-content/uploads/2024/11/Molto_Coi_disclosure-1.docx
https://yoda.yale.edu/wp-content/uploads/2024/11/Lopez-medina_Coi_disclosure-1.docx
https://yoda.yale.edu/wp-content/uploads/2024/11/Coi_disclosure-_Sofia-Ramiro.docx

Certification

Certification: All information is complete; I (PI) am responsible for the research; data will not be used to support litigious/commercial aims.

Data Use Agreement Training: As the Principal Investigator of this study, I certify that I have completed the YODA Project Data Use Agreement Training

1. NCT00207701 - C0168T51 - A Randomized, Double-blind Trial of the Efficacy of REMICADE (Infliximab) Compared With Placebo in Subjects With Ankylosing Spondylitis Receiving Standard Anti-inflammatory Drug Therapy
2. NCT00265083 - C0524T09 - A Multicenter, Randomized, Double-blind, Placebo-controlled Trial of Golimumab, a Fully Human Anti-TNFa Monoclonal Antibody, Administered Subcutaneously, in Subjects with Active Ankylosing Spondylitis
3. NCT02186873 - CNTO148AKS3001 - A Study of Golimumab in Participants With Active Ankylosing Spondylitis
4. NCT01453725 - P07642 - A Multicenter, Randomized, Double-blind, Placebo-controlled Study of the Effect of Golimumab Administered Subcutaneously in Subjects With Active Axial Spondyloarthritis (Also Known as MK-8259-006-02)

What type of data are you looking for?: Individual Participant-Level Data, which includes Full CSR and all supporting documentation

Research Proposal

Project Title

Assessment of peripheral arthritis and related disease activity measurement instruments in spondyloarthritis

Narrative Summary:

Currently the recommended instruments for the assessment of disease activity due to peripheral arthritis in axial spondyloarthritis (axSpA) is the number of swollen joint from the 44-joint count (SJC44).
Nevertheless, no composite score was formally assessed in axSpA or peripheral SpA (pSpA)
The aim of the project is to compare the psychometric properties (construct validity and discrimination) of different measurement instruments to assess disease activity due to peripheral arthritis in patients with SpA (either axSpA or pSpA), with the aim of selecting the most adequate and best performing measurement instrument to be recommended.

Scientific Abstract:

Background. Spondyloarthritis (SpA) is a chronic disease that can present in different physical and clinical forms such as axial SpA (axSpA) which mainly presents as back pain, or peripheral SpA (pSpA) which is characterized by inflammation and pain in joints located outside the spine. Currently the recommended instrument for the peripheral arthritis assessment is the 44-count of swollen joints (SJC44).
Objective. To compare the psychometric properties (construct validity and discrimination) of different measurement instruments to assess disease activity due to peripheral arthritis in patients with spondyloarthritis (either axSpA or pSpA), with the aim of selecting the most adequate and best performing measurement instrument to be endorsed by Assessment of SpondyloArthritis International Society (ASAS).
Study design. Measurement properties to be assessed for disease activity measurement instruments: Construct validity - hypotheses for strength of correlation between the assessed instrument and other instruments assessing disease domains and discriminatory capacity between known groups; Discrimination -- Test-retest reliability, longitudinal construct validity and discrimination in clinical trials.

Participants. axSpA and pSpA
Primary and secondary Outcomes: SJC and Tender joint count (TJC)44, SJC66, TJC68, PGA, CRP, DAS28, DAS44, BASDAI, ASDAS, DAPSA, SDAI, CDAI.
Statistical analyses: Spearman correlation, standardised mean difference (SMD), Guyatt's effect size (ES), standardized responsiveness mean (SRM).

Brief Project Background and Statement of Project Significance:

Spondyloarthritis (SpA) is a chronic disease in which the spine and other areas of the body become inflamed. SpA can present in different physical and clinical forms such as axial SpA (axSpA) which mainly presents as back pain, or peripheral SpA (pSpA) which is characterized by inflammation and pain in joints located outside the spine.
A clinician's instrument called the ASAS-OMERACT core outcome set (The Assessment of Spondylarthritis international Society-Outcomes Measures in Rheumatology core outcome set (COS)) has recently been updated to allow it to be used to assess axSpA, however for pSpA the 44-swollen joint count (SJC44), which looks at 44 joints in the body to assess swelling, was chosen as the preferred instrument recommended for use in clinical trials, but no combination of scoring systems were assessed in that project.
Although scarce, there is some evidence of the good performance of composite scores when assessing disease activity in the pSpA population. For example, in a study addressing the sensitivity to change and discriminatory aspects of different measurement instruments, the combination of Axial Spondyloarthritis Disease Activity (ASDAS), Bath Ankylosing Spondylitis Disease Index (BASDAI), patient global assessment (PGA), and physician global assessment (PhGA) had the highest performance, whereas the SJC, tender joint count (TJC) and C-reactive protein (CRP) performance was not good enough. In another attempt at assessing the validity of measurement instruments in pSpA, good performance was found for the Disease Activity Index for Psoriatic Arthritis (DAPSA), Psoriatic Arthritis (PsA) Disease Activity Score (PASDAS) and Ankylosing spondylitis disease activity score (ASDAS), although the agreement among the three instruments when classifying disease activity states was not sufficient. This finding emphasized the need of further analysis of the existing thresholds of those instruments in pSpA.
Recently, a study was conducted, called ASAS-perSpA, which included patients with axSpA, pSpA and PsA, and the validity of several measurement instruments was assessed, including the SJC, but also different composite scores validated for SpA and even in other inflammatory diseases such as the Disease Activity Score (DAS) 28 and 44. Results from this analysis showed that composite scores including joint counts have superior construct by discriminating better between active/inactive patients. Simultaneously, the psychometric properties of 9 measurement instruments were assessed in the CRESPA trial. In this study, conducted in patients with pSpA, both the ASDAS and DAPSA showed good validity and clinical trial discrimination.
The aim of this study is to compare the construct validity (the degree to which an outcome measure measures the construct it purports to measure) and discrimination (capacity to discriminate between different groups and scenarios) of different measurement instruments to assess disease activity due to peripheral arthritis in patients with spondyloarthritis (either axSpA or pSpA), with the aim of selecting the most adequate and best performing measurement instrument to be endorsed by ASAS.

Specific Aims of the Project:

To compare the psychometric properties of different measurement instruments to assess disease activity due to peripheral arthritis in patients with spondyloarthritis (either axSpA or pSpA), with the aim of selecting the most adequate and best performing measurement instrument to recommended.

Study Design:

Individual trial analysis

What is the purpose of the analysis being proposed? Please select all that apply.

Other: To compare the psychometric properties -construct validity and discrimination- of different measurement instruments to assess disease activity due to peripheral arthritis in patients with

spondyloarthritis (either axSpA or pSpA), with the aim of selecting the most adequate and best performing measurement instrument to be endorsed by ASAS.

Research Methods

Data Source and Inclusion/Exclusion Criteria to be used to define the patient sample for your study:

All axSpA and pSpA patients from RCTs without missing data will be included in the analysis. There will be none exclusion criteria.
Besides the Janssen trials requested in this platform the following RCTs were requested in Vivli: NCT01064856, NCT03178487, NCT02696785, NCT02696798, NCT02757352, NCT01258738, NCT00247962, NCT03502616, NCT02552212, NCT01087762, NCT00195819, NCT00085644, NCT00939003.
We would like to perform the analyses of all the studies together in the Vivli platform.

Primary and Secondary Outcome Measure(s) and how they will be categorized/defined for your study:

The candidate disease activity measurement instruments to be assessed in the domain peripheral (articular) manifestations will be: Swollen joint count (SJC) with 66 and with 44 joints (SJC66 and SJC44), Disease Activity Score-28 for Rheumatoid Arthritis (DAS28), Disease Activity Score-44 for Rheumatoid Arthritis (DAS44), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Ankylosing Spondylitis Disease Activity Score (ASDAS), Disease Activity in PSoriatic Arthritis (DAPSA), Simplify Disease Activity Index (SDAI), Clinical Disease Activity Index (CDAI), C-reactive protein (CRP).

Main Predictor/Independent Variable and how it will be categorized/defined for your study:

Construct validity:
-Construct validity will be considered as "good" if >=75% of the hypotheses are confirmed; "adequate" if 50-75% of the hypotheses are confirmed; or poor, if <50% of the hypotheses are confirmed, as recommended by the Outcome Measures in Rheumatology (OMERACT) Handbook and the core outcome set (COS) exercise. The correlation cut-offs used will be: weak <0.30, moderate 0.30 to 0.69 and strong >=0.70. For discrimination between known-groups, a SMD above 0.8 will be considered as 'good'.(3)
Discrimination:
-For longitudinal construct validity, a Guyatt's effect size (ES), standardized responsiveness mean (SRM) and ES >=0.8 will be considered as good performance; >=0.5 and <0.75 adequate performance and <0.5 poor performance. The same cut-off points will be used for the Clinical trial discrimination.

Other Variables of Interest that will be used in your analysis and how they will be categorized/defined for your study:

For the calculation of some of the composite scores (mainly DAPSA, DAS28/44, SDAI, CDAI) we will need the following variables:

Physician global assessment
Peripheral pain (and/or BASDAI Question 3)

Statistical Analysis Plan:

Construct validity - To assess construct validity, hypotheses for strength of correlation between the assessed instrument and other instruments assessing disease domains (other than disease activity, i.e. BASFI, ASAS HI, ASQoL and EuroQoL) will be used. The hypotheses will be derived from the ASAS-

perSpA ancillary analysis (Capelusnik, 2024) where they were previously defined by the working group. The Spearman correlation coefficients will be estimated.
Additionally, as part of the "hypothesis testing" from the construct validity, the mean (SD) and discriminatory capacity between known groups (i.e. active/inactive disease defined based on existing constructs, e.g. PGA, SJC, combination of both) will be also calculated through the standardised mean difference (SMD). The SMD represents the difference between the group means divided by the pooled standard deviation (SD). It is unitless, representing the higher value, the higher discriminatory capacity.

Discrimination -- For the Test-retest reliability analysis, to assess how much day-to-day variability there is in the score in a situation when the patients should not be changing, screening and baseline data from randomized controlled trials (RCTs) will be used to calculate the Intraclass correlation coefficient (ICC) (two-way random effect model with absolute agreement, which is designed to deal with paired data-same people, two measures over time-). Bland and Altman plots will be created for each instrument to assess mean difference and 95% limits of agreement and to evaluate homoscedasticity. Measurement error as a measure of the scale will be assessed by analysing the smallest detectable change (SDC) based on the 95% limits of agreement.
For the Responsiveness analysis (Longitudinal construct validity), to assess to what extent the instruments can detect changes in the domain of interest over time (can measure change accurately) the Guyatt's effect size (ES) and the standardized response mean (SRM) will be calculated using data from RCTs (from baseline to the timing of the primary endpoint).
For the Discrimination in Clinical Trials, to assess the degree to which the instruments are sensitive to the related change between the arms of a trial (i.e., a comparative effectiveness study or a placebo-controlled trial, or active comparison arm), the standardised mean difference (SMD) will be calculated using data from RCTs.

We are not aiming at pooling the different studies, but simply at analysing them separately.
Missing data will be excluded.

Software Used:

STATA

Project Timeline:

Target Analysis Start Date 2/1/25
Estimated Analysis Completion Date 10/30/25
Presentation in the ASAS community: 01/15/2026
Date manuscript drafted: 03/01/2026
First submitted for publication: 06/01/2026
Date results reported back to the YODA Project: 06/01/2026

Dissemination Plan:

Submission to the American Congress of Rheumatology, the EULAR (European Congress of Rheumatology), and Publication on a high-impact Rheumatology Journal.

Bibliography:

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