A systematic scoping literature review to identify the humanistic burden attributed to living with Primary Sjogren's Disease

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Background

- Sjogren's Disease (SjD) is a systemic, chronic autoimmune disorder caused by lymphocytic infiltration of the lacrimal and salivary glands, often causing significant eye and mouth dryness, pain, and fatigue. Additionally, up to 50% of patients experience extra-glandular involvement presenting articular, neurological, respiratory, and renal symptoms [1,2].
- The prevalence of Primary Sjogren's Disease (pSjD) varies between 0.4% and 1% of the population, depending on the classification criteria used and the chosen study population [3]. The disease typically begins in middle age, with a female-to-male ratio of roughly 9:1 [3].
- The most serious complication of pSjD is the development of non-Hodgkin lymphoma (NHL), for which patients with pSJD have a significantly higher risk compared to the general population [4].
- Given the complexity of pSjD, its substantial impact on patients' HRQoL, and the current unmet medical need for effective systemic treatments, it is essential to review and summarize all available data on the HRQoL of adult patients with moderate-to-severe disease activity as measured by EULAR Sjogren's syndrome disease activity index (ESSDAI) ≥5.

Objective

- To define the humanistic outcomes of adult pSjD patients with moderate-to-severe disease activity (ESSDAI ≥5) using a scoping systematic literature review (SLR).

Methods

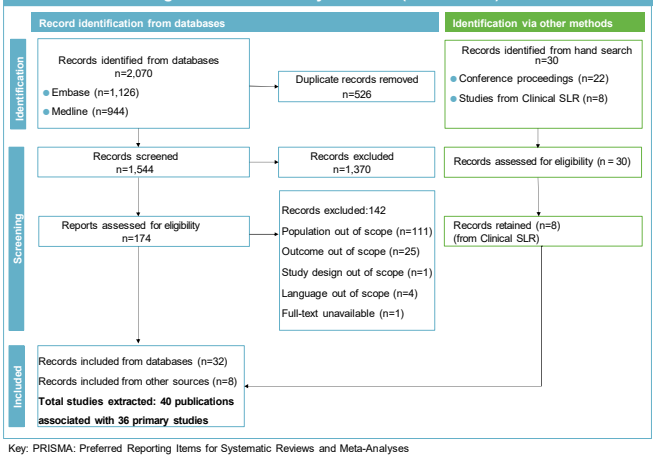
- A systematic search conducted in Medline and EMBASE targeted English-language studies reporting disease-specific or generic HRQoL measures or any patient-reported outcomes (PRO) published from 2013 onwards, with conference abstracts included from January 2022 to June 2024.
- Study eligibility was assessed using population, intervention, comparison, outcome, and study design (PICOS) criteria:
  - Population: adults with pSjD with moderate-to-severe disease activity (mean ESSDAI score ≥5 in at least one arm in multi-arm studies)
  - Intervention: no restrictions
  - Comparator: no restrictions
  - Outcomes: utilities and disutilities (including complications) using general QoL measures with any utility measure, and quality or disability adjusted life years
  - Study design: economic evaluations, clinical trials, Health Technology Assessments (HTA), utility elicitation/validation studies and mapping/cross-walking studies.
- Additionally, a search of HTA agencies covering the UK and conference abstracts from the Canadian Rheumatology Association (CRA) & Arthritis Health Professions Association (AHPA), the European Alliance of Associations for Rheumatology (EULAR), the American College of Rheumatology (ACR), and the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) meetings, which are not indexed in EMBASE, was also conducted.
- All records identified during the search were independently reviewed by two reviewers based on abstracts and titles using pre-determined eligibility criteria using the PICOS framework, with disagreements resolved through discussion or arbitration by a third reviewer. Potentially relevant records were further assessed through full-text review, with exclusions noted in an excluded studies table and the process summarized in the PRISMA flow diagram.

Results

Search results

- Overall, 40 publications associated with 36 primary studies were included (Figure1). Out of the 36 included studies, 18 were RCTs, 1 was a cost-effectiveness analysis, 12 were cross-sectional, 2 were open-label, and 4 were prospective studies.

Figure 1: PRISMA Study Selection (HRQoL SLR)

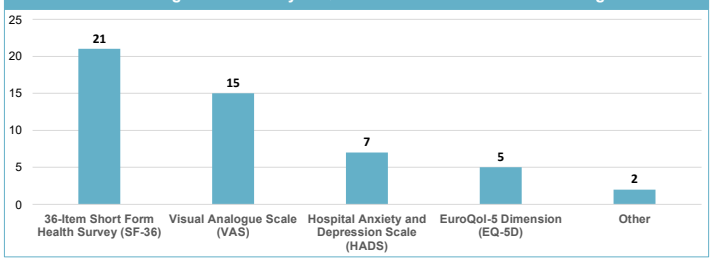


Key: PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses

Summary of relevant studies

- The study durations varied from 12 to 104 weeks, with the majority of studies being published in 2020 or later.
- Figure 2 summarizes the most widely used QoL assessment tools across various studies, highlighting the number of studies that employed each tool for evaluating patient-reported outcomes.

Figure 2: Summary of QoL Assessment Tools and Their Usage



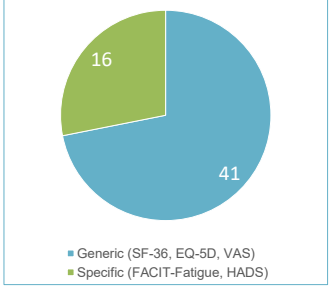
Demographic and baseline characteristics

- Participants' average age ranged from 40 to 62 years, with most studies having a majority female population (72% to 100%) and predominantly white patients (66% to 100%), with some studies reporting geographical distribution from the US, Europe, China, and Brazil.
- The SLR focused on pSjD patients with moderate-to-severe disease activity, as determined by a baseline ESSDAI score of at least five points for at least one arm. The mean baseline ESSDAI scores ranged from 3.8 (in one arm of study) to 20.3, and twelve studies reported mean baseline ESSDAI score of ≥10. All studies included primarily patients with moderate disease activity.
- The EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI) measures symptom severity in pain, fatigue, and dryness; in this study, total mean ESSPRI scores ranged from 3.9 to 22, reflecting varying symptom burden.

Generic HRQoL questionnaire outcomes

- The mean baseline SF-36 physical component scores ranged from 33 to 46, and mental component scores from 36 to 46 (subscale range: 0 to 100, with higher scores indicating better HRQoL).
- Better SF-36 scores were generally associated with lower disease activity (ESSDAI <5) and lower symptom burden (ESSPRI <5) as well as the absence of peripheral nervous system (PNS) involvement.
- The mean baseline EQ-5D VAS scores in a randomized controlled trial in pSjD patients ranged between 59 and 65, signalling impaired overall well-being.
- Most studies used the Visual Analogue Scale (VAS) to evaluate key symptoms like dryness, pain, and fatigue, primarily on a 1-10 scale. Baseline median pain scores ranged from 0 to 2.3 in observational studies and from 4 to 5 in trials.
- Figure 3 compares the usage of generic and specific HRQoL outcomes in studies.

Figure 3: Comparison Of Usage Of Main Generic And Specific HRQoL Outcomes in Studies



Key: FACIT, Functional Assessment of Chronic Illness Therapy; HADS, Hospital Anxiety and Depression Scale

Specific HRQoL questionnaire outcomes

- HADS scores were reported in nine studies, with the mean anxiety (HADS-A) scores ranging from 6.1 to 8.5 and the mean depression (HADS-D) scores from 6 to 7.4.
- Patients with ESSPRI scores ≥5 had statistically significant increases in both anxiety and depression, highlighting an association between symptom burden and psychological distress.
- FACIT-Fatigue mean baseline scores ranged from 21.2 to 33.2, indicating moderate-to-severe fatigue in patients with pSjD.
- Patients with moderate disease activity experienced similar fatigue levels to those with conditions like psoriatic arthritis and rheumatoid arthritis, demonstrating the significant impact of fatigue in pSjD.
- Table 1 provides overview of generic and specific questionnaire outcomes based on the study design.

Table 1: HRQoL Questionnaire Outcomes Summary

Measure	Mean Baseline Score (Controlled setting studies)	Mean Baseline Score (Observational studies)
SF-36	Physical component: 33-46 Mental component: 36-46	Physical component: 35-76 Mental component: 33-73
VAS	Pain: 4-5 (Median) Dryness:56-77.3 Fatigue: 5.8-85.1 PGA: 4.3-53.7	Pain: 0-2.3 (Median) Dryness: 2.8-7.8 Fatigue: 6.9* PGA: NR
EQ-5D	59-65	61-63
HADS	HADS-A: 8.6-9.4* HADS-D: 7.7-8.1*	HADS-A: 6.1 to 8.5 HADS-D: 6.3 to 7.4

Key: HRQoL, Health Related Quality of Life; SF-36, Short Form-36 Questionnaire; VAS, Visual Analogue Scale; EQ-5D, EuroQol 5-Dimension; HADS, Hospital Anxiety and Depression Scale; HADS-A, Hospital Anxiety and Depression Scale-Anxiety; HADS-D, Hospital Anxiety and Depression Scale-Depression; PGA, Physical Global Assessment; NR, not reported
*Based on a single study

Conclusion

- Patients with pSjD experience significant impairments in both physical and mental health, as evidenced by lower SF-36 scores and EQ-5D scores, particularly in those with higher ESSDAI and ESSPRI scores.
- Fatigue and psychological distress (anxiety and depression) are a major burdens for pSjD patients, as highlighted by FACIT-Fatigue and HADS scores, and associated with more severe symptom burden.
- VAS measures indicate wide variability in symptom severity, ranging from moderate-to-severe, particularly in dryness, pain, and fatigue.
- Higher disease activity is consistently associated with poorer humanistic outcomes across both generic and specific measures, emphasizing the need for targeted interventions in patients with moderate-to-severe pSjD.
- This SLR clarified the significant impact of moderate-to-severe pSjD on HRQoL, demonstrating the substantial physical and mental challenges patients face, and underscoring the importance of comprehensive treatment strategies.
- These findings highlight the substantial humanistic burden faced by patients with pSjD, and highlight the need for additional studies, particularly those focusing on patients with high disease activity (ESSDAI score >13), who may experience an even greater burden.

References

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