

Understanding the Humanistic Burden of Sjögren's Disease (SjD): A Systematic Literature Review (SLR)

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KEY FINDINGS AND CONCLUSIONS

- This SLR underscores the substantial multidimensional and complex burden SjD imposes across physical, emotional, cognitive, and social domains
- The humanistic burden of SjD remains under-recognized despite significant HRQoL impairment
- Reliance on diverse and predominantly generic PROs highlights fragmented measurement and incomplete capture of disease burden
- These insights highlight an urgent need for therapeutic strategies that move beyond symptomatic relief and effectively modify disease activity, with the downstream effect of improved HRQoL in patients with SjD

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BACKGROUND

- Sjögren's disease (SjD) is a chronic, systemic, autoimmune disease affecting multiple organs and associated with debilitating fatigue, pain, and social impairment, all of which negatively impact health-related quality of life (HRQoL).^{1,2}
- SjD can present alone (primary SjD) or with other autoimmune diseases (associated SjD)³
- Currently there are no approved treatments for SjD;⁴ consequently, substantial unmet needs persist in improving patient-reported outcomes (PRO)
- Studies evaluating humanistic burden of SjD have used a wide variety of PRO instruments focusing on varied outcomes

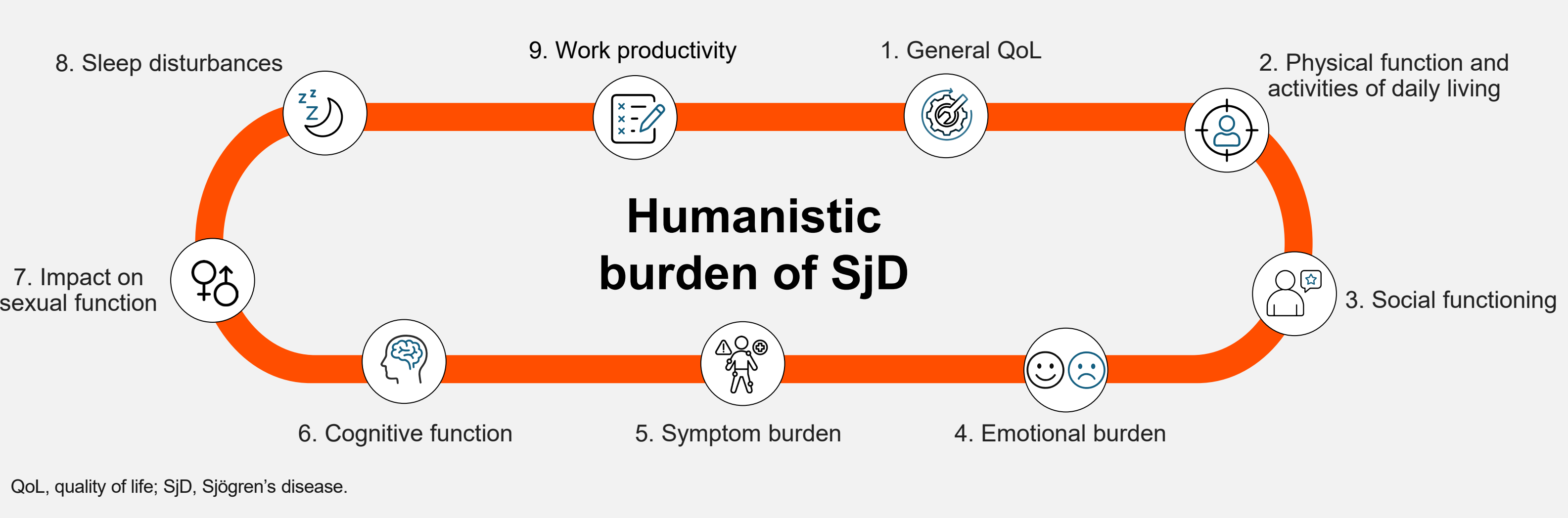
OBJECTIVE

- To identify and summarize the published evidence on the humanistic burden of SjD

METHODS

- This SLR was conducted according to established guidelines including National Institute for Health and Care Excellence (NICE) and Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)
- The National Institutes of Health (NIH) study quality assessment tools checklist was used to assess the quality of included studies and results categorized by key humanistic burden domains (Figure 1)
- Key biomedical databases (Embase® and MEDLINE®) were searched between January 2012 and January 2025, while conference proceedings were manually screened from 2022 to 2024 (Figure 2) using predefined PICOS inclusion and exclusion criteria (Supplemental Table 1, available with QR code)

Figure 1. Domains of Humanistic Burden of SjD

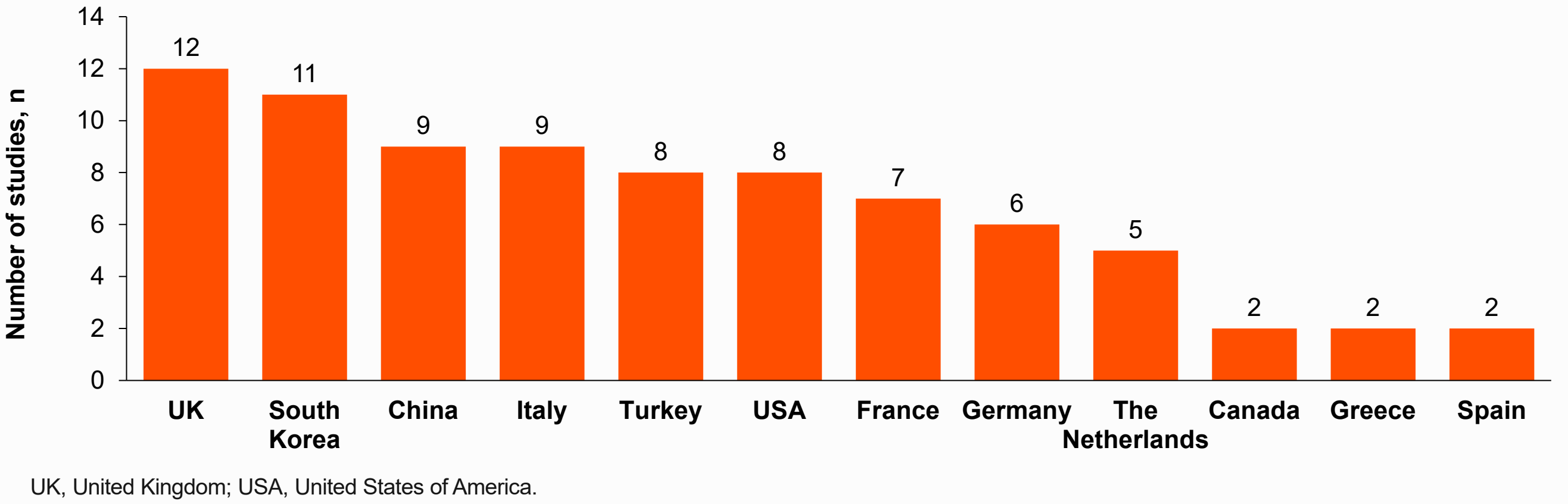


RESULTS

Study and patient characteristics

- 101 studies of various design (cross-sectional [n = 54], prospective [n = 21], and retrospective [n = 13]) across a wide geographic distribution (Figure 3) were included
- Mean age at diagnosis ranged from 44 to 66 years,^{5,6} women comprised 75% to 100% of patients across studies,^{7,8} and most patients were White (46%-99.4%)^{9,10}
- The most frequently reported SjD symptoms included ocular dryness (90.9%-94.2%)^{5,11} and oral dryness (51.8%-96%)^{9,12}

Figure 3. Number of Included Studies by Geographic Distribution



Outcome measures

- The most frequently used disease-specific outcome measure were ESSPRI, EULAR Sicca Score (EULAR-SS) and Sjogren's-specific questionnaires (Figure 4A)
- A wide range of generic HRQoL scales were used e.g., visual analog scale (VAS) measuring dryness, pain and fatigue, Hospital Anxiety and Depression Scale (HADS), and the 36-Item Short Form Health Survey (SF-36) (Figure 4B)

Humanistic burden: SjD vs healthy controls

- Patients with SjD experienced worse fatigue and dryness (ESSPRI), higher anxiety and depression (HADS), lower functionality (EQ-5D), poorer physical and social functioning, reduced ability to perform activities of daily living, higher mental fatigue, and a high prevalence of poor sleep vs healthy controls (Figure 5; Table 1)

Table 1. Humanistic Burden For Patients with SjD vs Healthy Controls

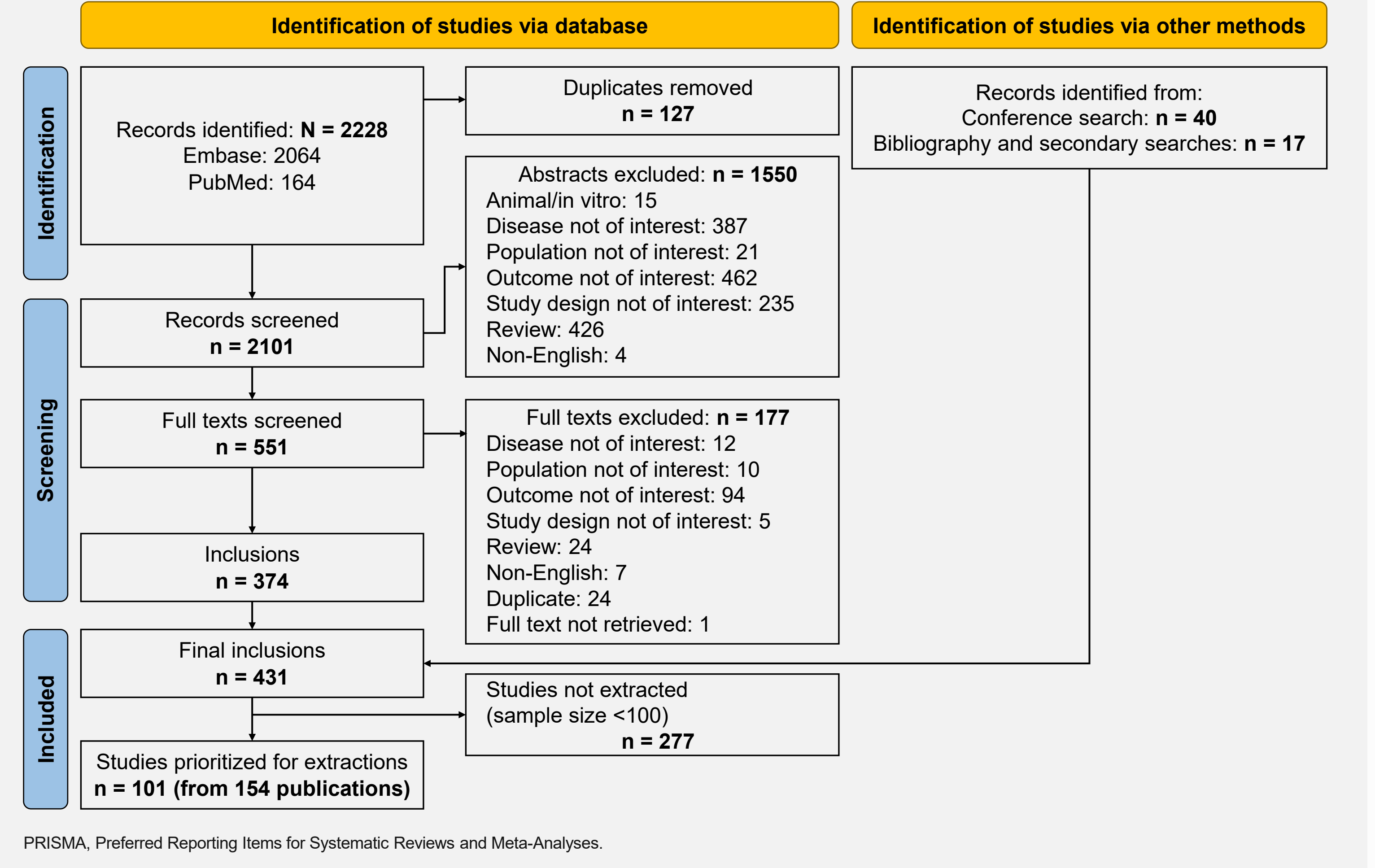
Domains	Scales	Scores (SjD vs healthy controls)
Symptom	Pain	SF-36: 37.3-74.5 vs 73.7-88.3
	Dryness	ESSPRI: 5.1 vs 2.3
	Fatigue	VAS: 6.3-6.6 vs 0.4-0.6
	Anxiety	PROFAD: 3.4-3.8 vs 0.6-0.8
Emotional	Depression	HADS-A: 6-7.6 vs 3.3-6
		SAS: 37.5 vs 30.5
		HADS-D: 4-6.7 vs 4-5.1
Cognition		PHQ-9: 8.2 vs 3.3
		SDS: 56.7 vs 55.5
		MFI: 11.0 vs 8.4
Physical function	Physical function	PROFAD: 3.4 vs 0.8
	Role-physical	SF-36: 55.3-78.7 vs 80.9-93.0
	Vitality	SF-36: 21.8-68.6 vs 77.5-92.6
	PCS	SF-36: 29.6-55.2 vs 60.9-74.1
Activities of daily living	EQ-5D	42.6-55.7 vs 44.6-86.0
Social function		Problems with self care: 3.9% vs 2.7% Usual activities: 37.6% vs 9.8%
		SF-36: 45.4-71.3 vs 77.4-87.3
Sleep	PSQI	6.6-10.9 vs 4.9-6
General quality of life		SF-36: 27.2-45.8 vs 62.5-71.9
		EQ-5D: 64.8 vs 77.9
		EQ-5D: 0.8 vs 0.9
Utility	SF-6D	0.7 vs 0.8

ESSPRI, EULAR Sjögren's Syndrome Patient-Reported Index; EQ-5D, EuroQol-5 Dimension; HADS, Hospital Anxiety and Depression Scale; MFI, Multidimensional Fatigue Inventory; PCS, Physical Component Summary; PHQ-9, Patient Health Questionnaire-9; PROFAD, Profile of Fatigue and Discomfort; PSQI, Pittsburgh Sleep Quality Index; SAS, Self-Rating Anxiety Scale; SF-36, 36-Item Short Form Health Survey; SF-6D, Short Form 6-Dimension; SJD, Sjögren's disease; VAS, visual analog scale.

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Figure 2. PRISMA Flow Diagram of Included Studies



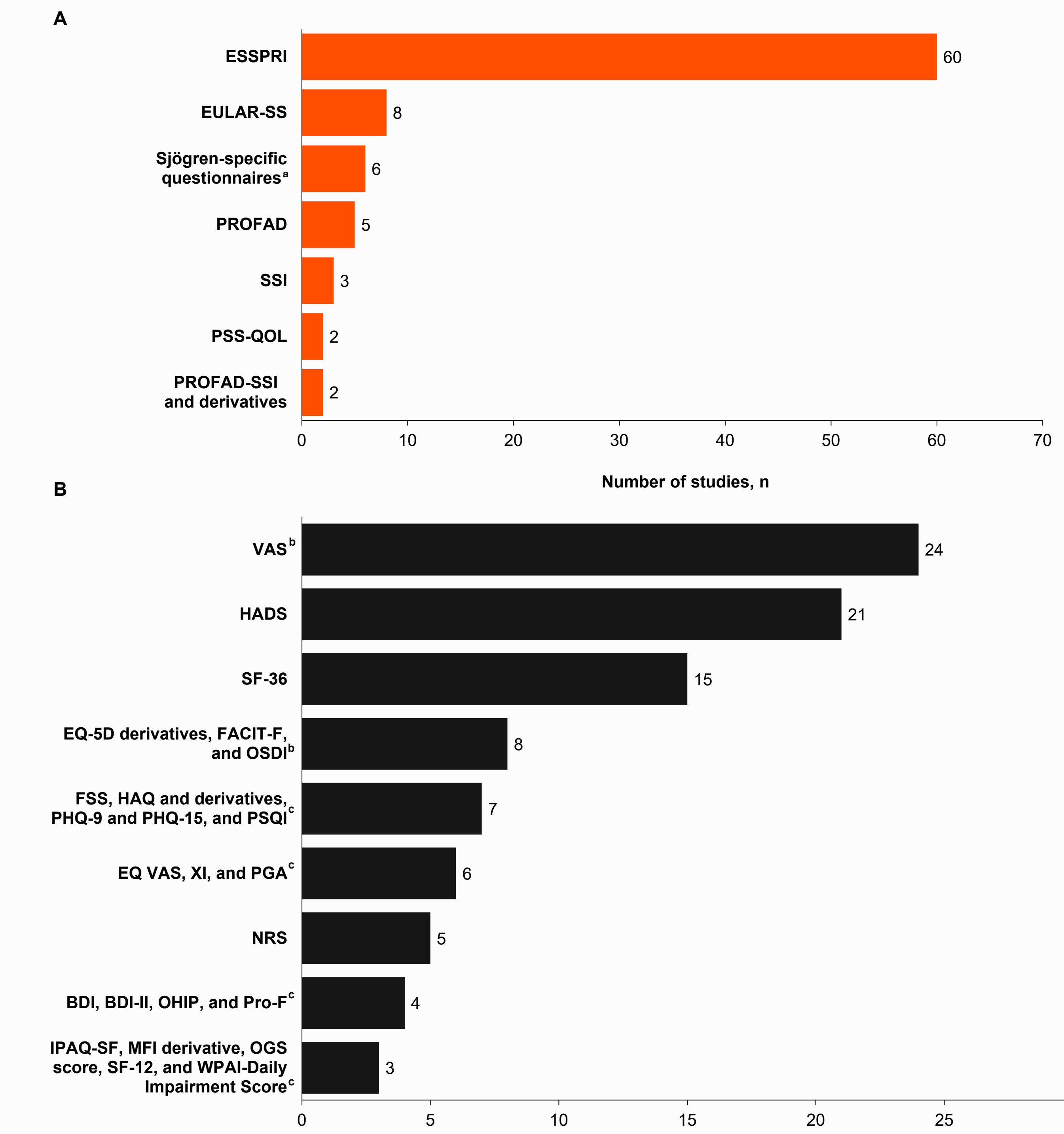
1. General quality of life

- EQ-5D VAS (range: 0-100) consistently demonstrated lower QoL among patients with SjD (60-72). Increasing disease severity was strongly associated with lower QoL with scores declining between mild (78.1), moderate (67.0), and severe (57.4) disease
- Disease activity, high ESSDAI (≥ 14), and high symptom burden (ESSPRI scores ≥ 5) were significantly associated with low SF-36 scores ($P < .001$ for each)
- PGA (range:0-100 VAS) was between 42 and 63, reflecting moderate disease burden

2. Physical functioning and activities of daily living

- Patients with SjD had significantly lower physical functioning scores (Figure 5)
- Differences were even greater among those with higher ESSDAI (low ESSDAI < 5 : 48.4; moderate 5-13, 44.1; high ≥ 14 , 42.0; $P < .001$ for high vs low) and ESSPRI scores (ESSPRI < 5 , 48.9 vs ≥ 5 : 41.0, $P < .001$)

Figure 4. Number of Studies Using (A) Disease-Specific PRO Scales and (B) Generic PRO Scales in Patients with SjD



BDI, Beck Depression Inventory; EQ-5D, EuroQol-5 Dimension; EQ VAS, EuroQol visual analog scale; ESSPRI, EULAR Sjögren's Syndrome Patient-Reported Index; EULAR-SS, EULAR Sicca Score; FACIT-F, Functional Assessment of Chronic Illness Therapy - Fatigue; FSS, Fatigue Severity Scale; HADS, Hospital Anxiety and Depression scale; HAQ, Health Assessment Questionnaire; IPAQ-SF, International Physical Activity Questionnaire - Short Form; MFI, Multidimensional Fatigue Inventory; NRS, numerical rating scale; OGS, Oxford Grading Scale; OHIP, Oral Health Impact Profile; OSDI, Ocular Surface Disease Index; PGA, Patient's Global Assessment; PHQ-9, Patient Health Questionnaire-9; PHQ-15, Patient Health Questionnaire-15; Pro-F, Profile of Fatigue, PROFAD, Profile of Fatigue and Discomfort; PROFAD-SSI, PROFAD - Sicca Symptoms Inventory; PSQI, Pittsburgh Sleep Quality Index; PSS-QOL, Primary Sjögren's Syndrome Quality of Life Questionnaire; SF-12, 12-Item Short Form Health Survey; SF-36, 36-Item Short Form Health Survey; SSI, Sicca Symptoms Inventory; VAS, visual analog scale; WPAI, Work Productivity and Activity Impairment; XI, Xerostomia Inventory. *Includes Sjögren's Foundation patient survey and Sjögren's International Collaborative Clinical Alliance (SICCA) questionnaire. †Measures pain, dryness, and fatigue. ‡Number of studies for each category.

3. Social functioning

- Mean SF-36 social functioning scores were lower in patients with SjD compared with general population (Figure 5). Higher disease severity and symptom burden were associated with greater impairment of social functioning among patients with SjD

4. Emotional burden (anxiety and depression)

- Studies using HADS [range: 0-21] reported higher anxiety and depression in patients with SjD vs healthy controls (HADS-A, 6.0-7.6 vs 3.3-6.0; HADS-D, 4.0-6.7 vs 4.0-5.1)

5. Symptom burden (pain, fatigue and dryness)

- ESSPRI pain scores ranged from 2.5 to 6.31, and VAS-Fatigue scores ranged from 46 to 70, indicating moderate to high burden
- Patients with SjD also reported significantly greater ocular dryness (median VAS: 6.3 vs 0.4) and dryness of the mouth (6.6 vs 0.6) vs healthy controls (both $P < .001$)

6. Cognitive function

- Cognitive impairment, including mental fatigue or brain fog, was a common psychological symptom. Problems with thinking clearly were more frequent in patients with SjD vs healthy controls (Profile of Fatigue and Discomfort [PROFAD], 3.4 vs 0.8)
- Fatigue-related cognitive difficulties were also greater, with higher Multidimensional Fatigue Inventory (MFI) scores (11-12 vs 8.4)

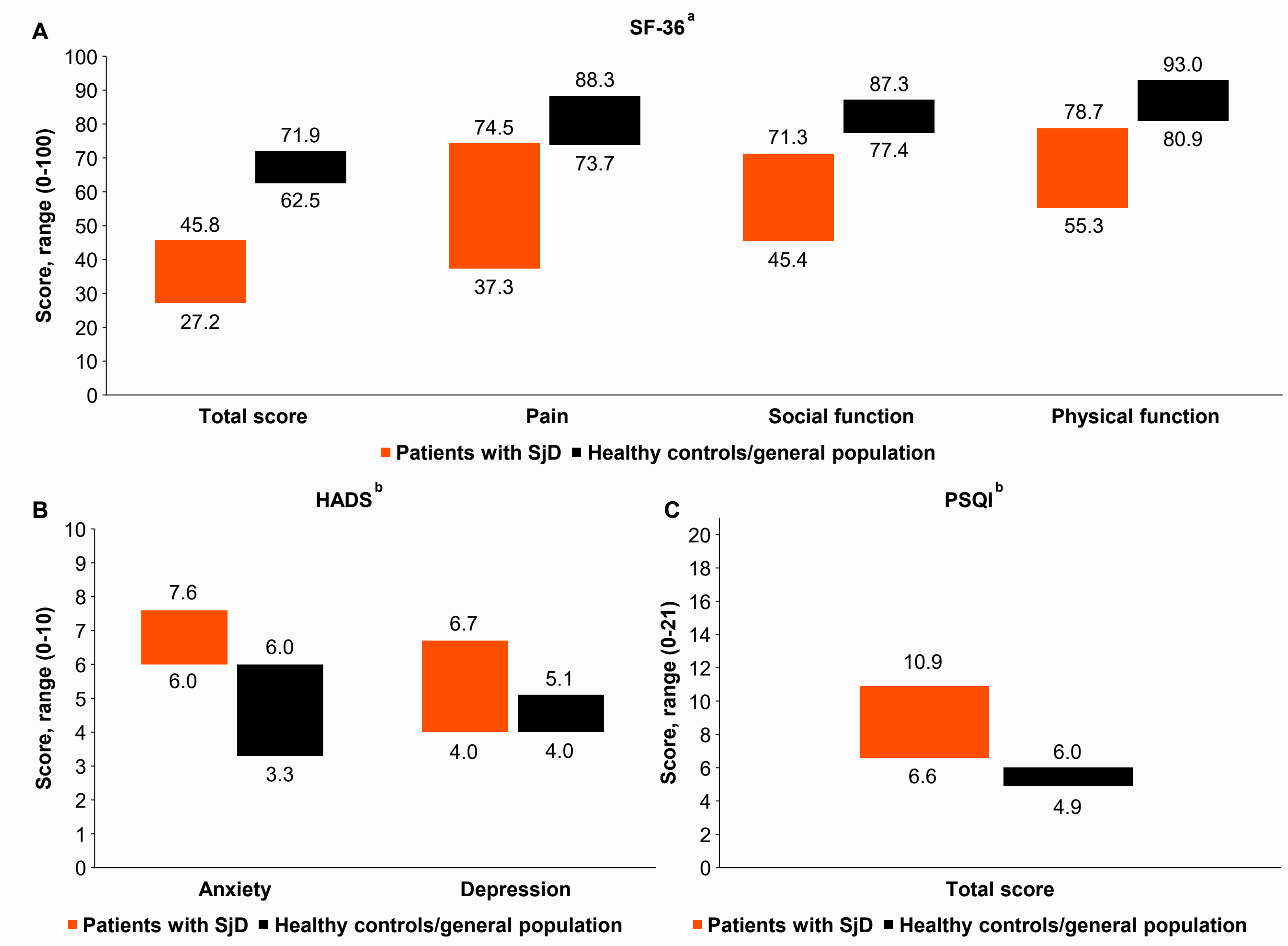
7. Sexual dysfunction

- Sexual dysfunction was reported in only 4 studies, despite being an important yet underrecognized component of the humanistic burden in patients with SjD
- The Comprehensive Pain Evaluation Questionnaire (CPEQ) demonstrated impairment across sexual health dimensions, with mean scores ranging from 2 to 3

8. Sleep disturbance

- Poor sleep was highly prevalent (73%-88%) and associated with worse HRQoL

Figure 5. Comparison of Generic and Domain-Specific QoL Scores for (A) SF-36, (B) HADS, and (C) PSQI in Patients with SjD vs Healthy Controls/General Population



HADS, Hospital Anxiety and Depression Scale; PSQI, Pittsburgh Sleep Quality Index; SF-36, 36-Item Short Form Health Survey; SJD, Sjögren's disease. † Lower scores indicate greater impact. ‡ Higher scores indicate greater impact.

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