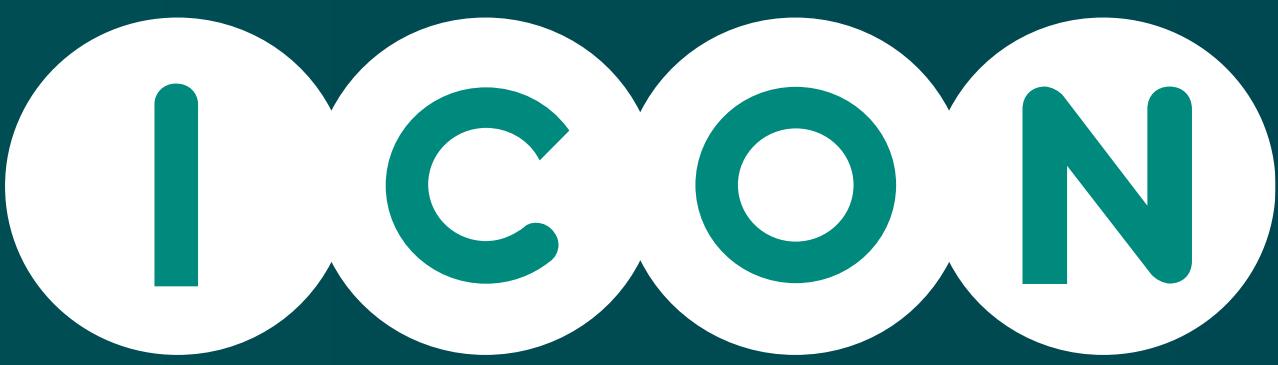


Healthcare Cost and Resource Use in Patients with Sjogren’s Syndrome: A Systematic Literature Review of Real-World Evidence Studies

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Introduction

Sjögren's syndrome (SS), an underrecognized autoimmune disease affecting a small percentage of the population, imposes substantial economic and healthcare resource burdens that remain inadequately quantified. Despite its significant impact on patients' quality of life and healthcare systems, comprehensive data on the economic consequences and resource utilization patterns associated with SS remain limited.^{1,2}

Objective

- To conduct a systematic literature review (SLR) analyzing the direct costs, indirect costs, and resource utilization associated with patients diagnosed with SS.

Methods

- The SLR methodology followed the recommendations published in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement, the Centre for Reviews and Dissemination, and the Cochrane Collaboration.^{3,4}

Eligibility Criteria

- The eligibility criteria for the SLR are outlined below in **Table 1**, according to the PICOS (Patients, Interventions, Comparators, Outcomes, Study Design) statement.

Table 1. Included Studies

PICOS Element	Inclusion Criteria	Exclusion Criteria
Population	Adults with SS	Non-SS populations
Intervention/Comparator	NA	NA
Outcomes	Healthcare costs and resource utilization	Studies not reporting relevant outcomes
Study Design	Observational studies and economic models reporting costs	Other non-included designs
Other	English only, US, Canada, and EU-5, published in the last 10 years	Non-peer reviewed, geographic locations not of interest

Abbreviations: EU-5, European Union; NA, not applicable; SS, Sjögren's syndrome; US, United States

Information sources

- Searches for published studies were run in Embase, Medline, EconLit through the OVID platform, combining free-text and Controlled vocabulary terms.

Study Selection

- Abstracts were screened by two independent reviewers, with a third reviewer resolving any disagreements. Relevant abstracts were then advanced to full-text screening using the same process.

Data Extraction and Critical Appraisal

- Data from included studies were extracted into pre-made sheets capturing healthcare costs and resource utilization. Extractions were validated by an independent reviewer.

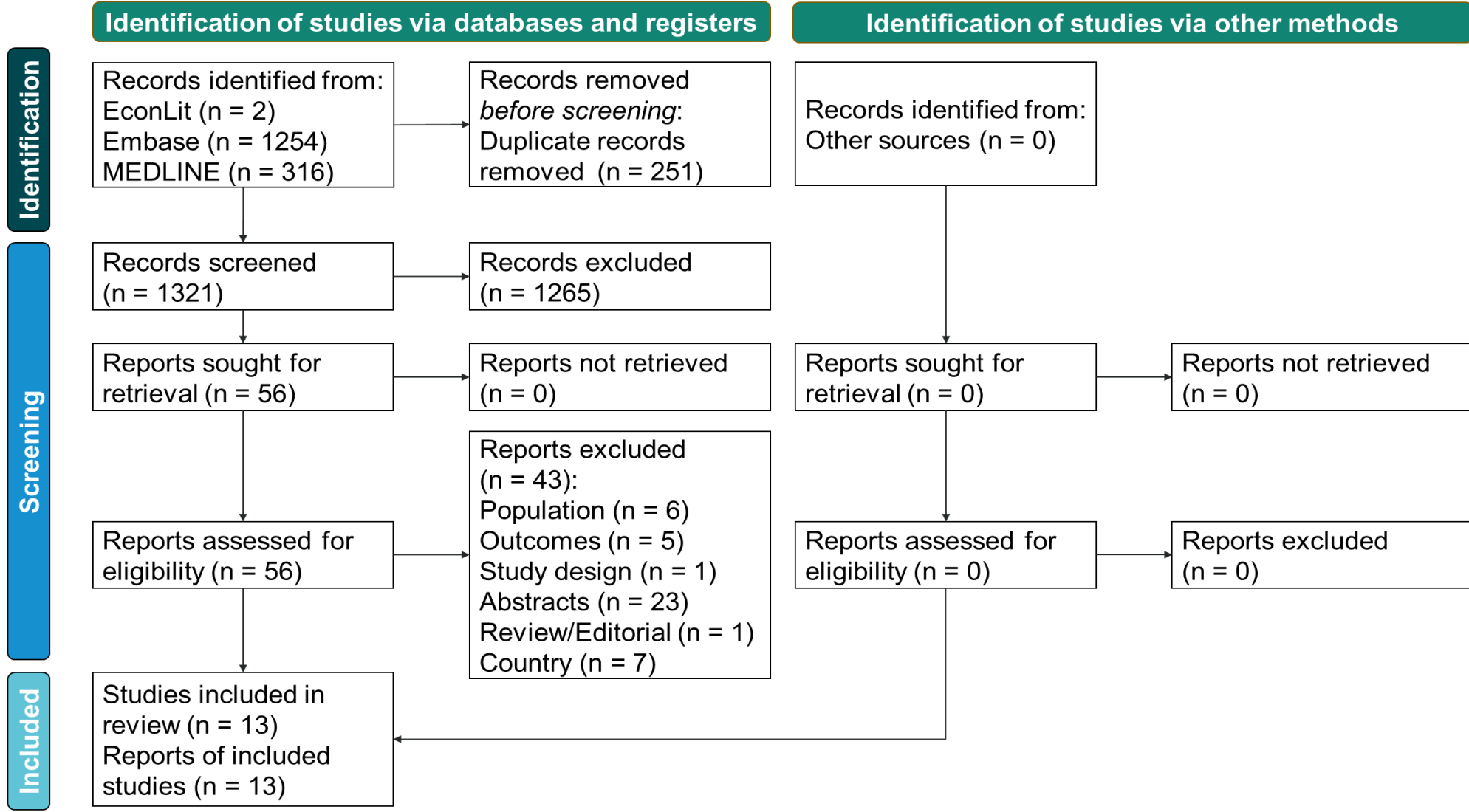
- Critical appraisal was conducted using the Newcastle-Ottawa Scale⁵

Results

Literature Search Finding

- From 1,572 initial abstracts identified, 1,321 were screened after removing 251 duplicates, with 1,265 excluded during abstract screening.
- After full-text screening of the remaining 56 records, 13 studies (13 records) were included in the final systematic literature review. (**Figure 1**).⁶⁻¹⁸

Figure 1. PRISMA Flow Diagram



Included Studies

- The 13 studies came from various countries, with study designs comprising cohorts (n = 5), case-control (n =4), and cross-sectional (n = 4) methodologies.
- The studies utilized different data sources claims databases, health surveys, and clinical databases, and currency reporting in USD, EUR, and CAD.

Table 2. Included Studies

Study & Country	Study Design	Data	Ref Year (Currency)	NOS Score
Albrecht 2021 (DE)	Case-control	Claims	-	8
Birt 2017 (US)	Cohort	Claims	2014 (USD)	8
Cafaro 2024 (IT)	Case-control	Database	2018 (EUR)	8
Callhoff 2019 (DE)	Cohort	Database	-	8
Chan 2021 (CA)	Cross-sec	Survey	2018 (CAD)	8
Goulabchand 2022 (FR)	Case-control	Claims	-	8
Lee 2022 (US)	Case-control	Claims	2020 (USD)	8
Maciel 2018 (US)	Cohort	Database	-	8
McCormick 2019 (CA)	Cross-sec	Survey	2015 (USD)	8
McCoy 2019 (US)	Cross-sec	Survey	2016 (USD)	8
Seghieri 2021 (EU)	Cross-sec	Survey	-	8
Seror 2024 (FR)	Cohort	Claims	2017 (-)	8
Singh 2021 (US)	Cohort	Database	- (USD)	8

Abbreviations: CA, Canada; CAD, Canadian Dollar; DE, Germany; EU, Europe; EUR, Euro; FR, France; IT, Italy; NOS, Newcastle-Ottawa Scale, US, United States; USD, US dollar

Patient Characteristics

- Studies predominantly include female patients (87%¹² - 97%¹⁴), with sample sizes of 12¹⁰ – 69,239¹⁸ and mean ages of 53^{9,12} - 66¹⁸ years.
- 8/13 studies included primary SS (pSS) patients^{6,8,9,10,11,13,16,17}, two included secondary SS^{6,18}, and the remaining studies didn't report the type of SS.

Healthcare Costs

- In the USA, total costs increased 40% one-year post-diagnosis (\$14,612 to \$20,416), with outpatient visits comprising 51% of costs.⁷
- SS patients with interstitial lung disease (ILD) had double the costs of SS-only patients (adjusted cost ratio = 1.95; 95% CI = 1.76-2.15).¹²
- In Canada, SS patients incurred 22% higher direct costs (CAD \$2,689) and 132% higher indirect costs (CAD \$41,094) versus non-SS patients.¹⁰
- In France, despite the decline of pSS incidence from 2011 to 2018, the mean annual costs have increased (€5780 vs €9710).¹⁷

Table 3. Healthcare Costs

Study	Total Cost - Mean (SD)	Direct Cost - Mean (SD)
Birt 2017	Annual cost per person <ul style="list-style-type: none">• Pre-diagnosis: \$14,612 (\$29,914)• Post-diagnosis: \$20,416	Annual cost per person <ul style="list-style-type: none">• Outpatient visits: \$1,260 (\$7278)• ED visits: \$24 (\$226)• Hospitalizations: \$459 (\$3,745)• Total medical visits: \$1,742 (\$8,275)
Lee 2022	180-day total costs <ul style="list-style-type: none">• Cases: \$8,648 (\$17,478)• Controls: \$23,192 (\$48,189)	Cases - 180-day costs <ul style="list-style-type: none">• Inpatient: \$1,952 (\$11,769)• ED visit: \$140 (\$645)• Pharmacy: \$1,977 (\$4,472)• Physician office visit: \$799 (\$921)• Other outpatient: \$3,781 (\$8,723) Controls - 180-day costs <ul style="list-style-type: none">• Inpatient: \$8,997 (\$36,824)• ED visit: \$232 (\$964)• Pharmacy: \$3,785 (\$8,212)• Physician office visit: \$1,036 (\$1,076)• Other outpatient: \$9,142 (\$21,304)
McCoy 2022	Annual Cost: \$5,748	Annual costs <ul style="list-style-type: none">• Dental care: \$2,026• Prescription medications: \$1,319• Healthcare appointments/co-pay: \$896• Over the counter medications: \$686• Alternative therapies: \$604• Medical equipment: \$217
Singh 2021	-	Mean total hospital charges: \$37,857
Chan 2021	Annual cost <ul style="list-style-type: none">• pSS: \$43,783• No known SS: \$19,898	Annual cost <ul style="list-style-type: none">• pSS: \$2,689• No known SS: \$2,203
Cafaro 2024	Annual costs per capita <ul style="list-style-type: none">• Cases: €1,171• Control: €372	Cases - Annual costs per capita <ul style="list-style-type: none">• Drug cost: €501• Hospitalization: €416• Outpatient specialized visit: €200 Control - Annual costs per capita <ul style="list-style-type: none">• Drug cost: €161• Hospitalization: €129• Outpatient specialized visit: €75
Seror 2024	Annual cost per person <ul style="list-style-type: none">• 2011: €5780• 2018: €9710	-

Abbreviations: ED, emergency department; pSS, primary Sjögren's Syndrome; SD, standard deviation

Healthcare provider utilization

- In the US, significant (20%) increase in all cause visits 1- year post-diagnosis, 99% of patients had outpatient visits, with an average of 26.9 visits per person, mean ED visit per person was 0.6 (SD 1.5), and total all cause mean medical visits per person was 28.8 (SD 23.4).⁷
- In Europe, the mean special visits ranged from 3.56 in Sweden to 11.15 in Spain.¹⁶
- In Germany, the mean hospitalizations due to pSS from year 1966 to 2016 (p=0.08) and work participation increased, with fewer pSS patients taking sick leaves (p=0.09) and less patients taking early retirement (p=0.01).⁹

Table 4. Inpatient and Outpatient utilization

Study	Inpatient visit	Outpatient visit
Birt 2017	All cause mean event per person: 1.3 (SD 5.3)	All cause mean event per person: 26.9 (SD 20.3)
Maciel 2018	Hospitalization rate: 24.2 per 100 person-years	-
Seghieri 2021	-	Mean visits with a specialist <ul style="list-style-type: none">• France:9.15 (SD 1.02)• Germany: 8.91 (SD 1.12)• Italy: 8.12 (SD 0.49)• Norway: 3.84 (SD 0.67)• Spain: 11.15 (SD 0.87)• Sweden: 3.56 (SD 0.45)• UK: 5.78 (SD 0.5)• Overall: 7.45 (SD 0.29)
Goulabchand 2022	Mean number of hospitalizations before index date <ul style="list-style-type: none">• Cases: 3.7 (SD 9)• Controls: 0.21 (SD 1.1)	-
Albrecht 2021	Primary SS <ul style="list-style-type: none">• 2007: 34%• 2018: 32% Secondary SS <ul style="list-style-type: none">• 2007: 34%• 2018: 39%	-
Callhoff 2019	Hospitalized due to pSS <ul style="list-style-type: none">• 1996: 13%• 2016: 7%	-
Cafaro 2024	At least one hospitalization <ul style="list-style-type: none">• pSS: 7.8%• Controls: 3.9%	At least one outpatient specialized service <ul style="list-style-type: none">• pSS: 49.8%• Controls: 30.6%

Abbreviations: pSS, primary Sjögren's syndrome; SD, standard deviation

Hospital Length of Stay (LOS)

- An Italian study found longer LOS in pSS patients than controls (14.3 vs 8.4 days) with more frequent hospitalizations (1.5 vs 1.3 times)⁸
- Conversely, a US study reported shorter LOS in pSS patients (3.9 vs 4.7 days) with similar readmission rates (18% vs 19%).¹³

Loss of Productivity

- McCormick 2019¹⁴ estimated annual productively losses \$4,357 per person, with the majority (64%) attributed to presenteeism rather than absenteeism.

Limitations

- The included studies were retrospective in nature, which may introduce biases related to data completeness and accuracy.
- Several studies cited limitations such as insufficient clinical detail and potential inaccuracies in diagnosis coding.
- There is a limited body of evidence on healthcare cost and resource use specifically for patients with SS.
- A key limitation of this SLR is the lack of comparable data; only 13 studies met the inclusion criteria, and they reported heterogenous healthcare costs and utilizations outcomes.
- Most studies did not stratify data by disease severity, limiting the ability to access cost and resource use differences across patient subgroups.

Conclusions

- This SLR highlights the significant socioeconomic challenges faced by SS patients.
- Although work participation has improved over the past two decades, SS patients continue to experience higher hospitalization rates and incur greater healthcare costs compared to the general population.
- Productivity losses remain considerable, largely driven by presenteeism and impairments in unpaid work.
- Despite a decline in hospitalization rates, overall healthcare costs for SS patients remain high and are rising across Europe, underscoring the urgent need for optimized management strategies and further research into cost-effective interventions.
- Additionally, limited availability of stratified data hinders a comprehensive understanding of how disease severity impacts economic burden.

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