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Economic burden and healthcare resource utilization in Sjögren’s disease: a systematic literature review

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Disclosures

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Background

- Epidemiology
  - Sjögren's disease (SjD) is a chronic autoimmune disease characterized by lymphocytic infiltration of exocrine glands[1]
  - Most patients experience disease onset between the ages of 40 and 60 years old, with women developing the disease significantly more frequently than men[2]
  - SjD is one of the most common autoimmune rheumatic diseases; a 2008 epidemiologic study estimated the prevalence of SjD between 0.4 and 3.1 million individuals in the United States[3]
- Cost burden
  - Patients with SjD incur higher healthcare service costs compared with healthy individuals
  - A study in the United States reported the average annual cost per SjD patient was 1.6 times higher for all causes, and 1.5 times higher for disease-related causes than healthy individuals[4]
  - In England, annual healthcare costs for SjD patients (£2,188) were found to be more than twice that of healthy controls (£949), and comparable to patients with rheumatoid arthritis (£2,693)[5]

1. Patel R, et al. Clin Epi. 2014;6:247-255. 2. Peri Y, et al. Best Pract Res Clin Rheumatol. 2012;6(1):105-117. 3. Helmick CG, et al. Arthritis Rheum. 2008;58(1):15-25. 4. Perea S, et al. J Health Econ Outcomes Res. 2017;5(2):150-161. 5. Vivino FB, et al. Rheum Dis Clin North Am. 2016;42(3):531-551.

Objective

- To describe and characterize the landscape of evidence with respect to economic burden and healthcare resource utilization (HCRU) in patients with SjD including:
  - Direct costs and the value of expenditures on diagnosis, treatment, in-hospital and out-patient care, visits to physicians, and prescription medications
  - Indirect costs and the value of labor and productivity losses, such as lost income and economic output due to illness-related absences from work, reduced productivity at work due to illness, or premature death
  - Impact of the illness on the healthcare resources utilized such as hospital length of stay, intensive care length of stay, emergency department visits, and prescriptions

Methods: systematic literature review

- Systematic literature review of English-language studies reporting direct costs, indirect costs or HCRU in adults with SjD
- Searches were conducted in 2022 covering several major electronic databases
  - Searches of key conferences (2020-2022), United States and European clinical trial registries, and previous reviews were also conducted
- Review was conducted and reported as per Cochrane Handbook for Systematic Reviews of Interventions[6] and Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines[7]
  - Artificial intelligence tools were not used

Databases searched via Ovid SP

(database inception to September 2022)

- Embase
- MEDLINE®

Databases searched via EBSCO

(database inception to September 2022)

- EconLit

6. Higgins JP, et al. Cochrane handbook for systematic reviews of interventions. John Wiley & Sons; 2019. 7. Page MJ, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021; 372:n71.

Methods: study eligibility criteria

- Study selection and data extraction of included studies were performed by two independent investigators
- Key study and patient characteristics, as well as economic outcomes were extracted from each study

PICO element	Inclusion criteria
Population	Adults (aged ≥18 years) with SjD, including: • SjD without another systemic autoimmune rheumatic disease • SjD associated with another autoimmune disease such as systemic lupus erythematosus, rheumatoid arthritis, or systemic sclerosis
Intervention/ comparator	Any or none
Outcomes	**Economic outcomes:** • Direct costs • Indirect costs • Total direct and indirect costs • Healthcare resource utilization
Study design	• Economic and cost studies • Observational studies • Clinical trials **Included for referencing only:** • Systematic literature reviews
Language	English language

PICO – population, intervention, comparator, and outcome; SjD – Sjögren's disease

Methods: cost conversion

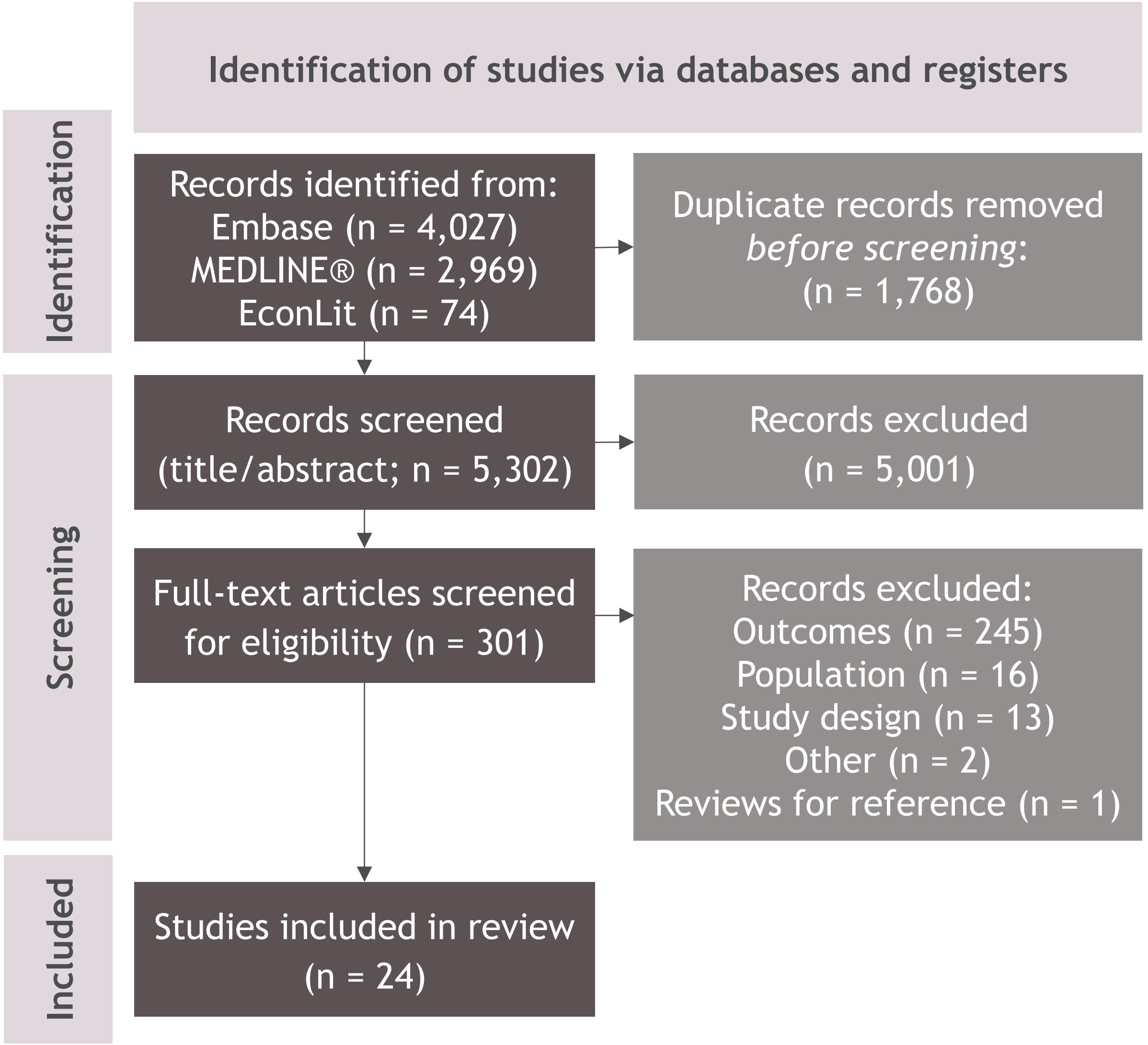
- Both direct and indirect costs were converted to 2024 United States dollars (USD)
  - Costs for health care items were inflated to 2024 values using the healthcare component of the Consumer Price Index data obtained from Federal Reserve Bank of St. Louis,[8] where necessary
  - Costs for non-health care items were inflated to 2024 values using the general Consumer Price Index data obtained from Federal Reserve Bank of St. Louis[9]
- Costs derived from outside of the United States were converted to USD using the historical Purchasing Power Parity indexes available from the OECD10, and inflated to 2024 values accordingly

8. Organisation for Economic Co-operation and Development. Consumer Price Index for All Urban Consumers: Medical Care in U.S. City Average [CPIMEDSL]. Retrieved March 28, 2024, from FRED, Federal Reserve Bank of St. Louis [https://fred.stlouisfed.org/series/CPIMEDSL]. 9. Organisation for Economic Co-operation and Development. Consumer Price Index for All Urban Consumers: All Items in U.S. City Average [CPIAUCSL]. Retrieved March 28, 2024, from FRED, Federal Reserve Bank of St. Louis [https://fred.stlouisfed.org/series/CPIAUCSL]. 10. Organisation for Economic Co-operation and Development. Purchasing Power Parities. Retrieved March 28, 2024, from [https://data.oecd.org/conversion/purchasing-power-parities-ppp.htm]

OECD - Organisation for Economic Co-operation and Development

Results: evidence base

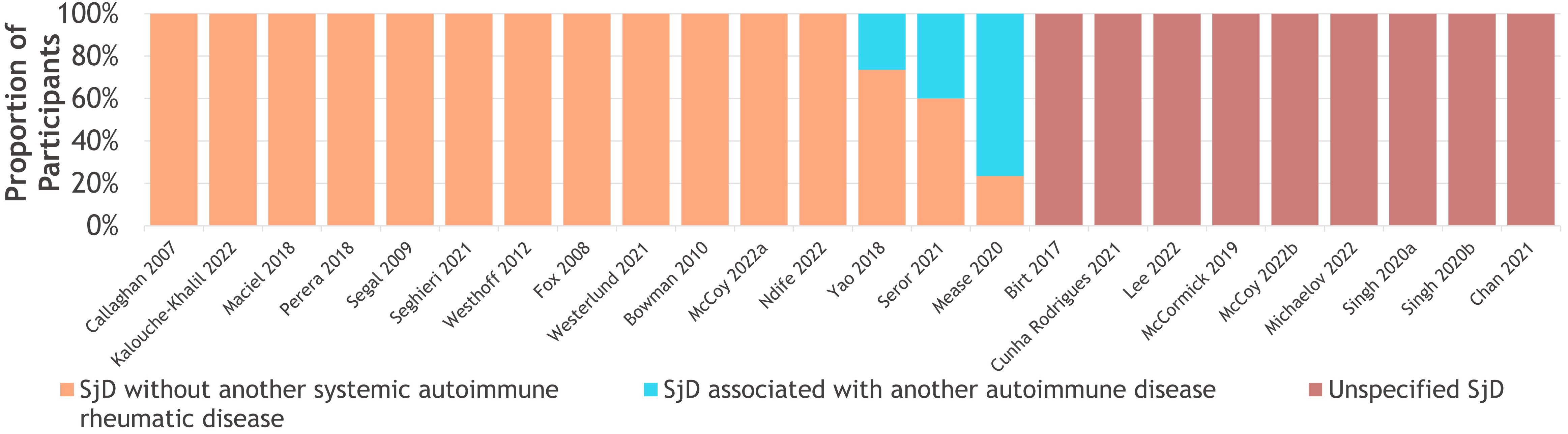
- 7,070 abstracts identified via databases:
  - No additional relevant records were identified from other sources
- 24 unique studies were included in the review:
  - 18 studies reported on direct costs
  - 4 studies reported on indirect costs
  - 12 studies reported on HCRU
- Sample size ranged from 55 to 69,239 participants (median: 924)
- Data were collected from hospital or claims databases, surveys, or electronic health records
- Studies were conducted in the North America (US: 13 studies; Canada: 3), Europe (7), and China (1)



n - number of records

Results: patient characteristics

- Mean patient age at enrollment ranged from 51 to 65.4 years old (overall median: 60 years)
  - At disease diagnosis, range was 46 to 58 years old (overall median: 53 years)
- Proportion of female patients ranged from 73 to 97% (median: 90%)
- Twelve studies reported solely on SjD without another systemic autoimmune rheumatic disease (historically known as “primary” SjD)



SjD – Sjögren’s disease

Results: direct costs in the United States

- Total mean direct costs of SjD within the United States ranged from **6,401** to **39,482 USD** per patient per year (4 studies)

Reference; currency country (currency year)	Group	Subgroup	N	Time point	Mean direct costs per patient per year (2024 USD)
Kalouche-Khalil 2022; **US** (2000-2020)[a]	SjD without another systemic autoimmune rheumatic disease	Patients with at least 5 years of follow-up	6,000	-	Range: $31,031 - $39,482[a]
Lee 2022; **US** (2020)	Unspecified SjD	Interstitial lung disease	815	6 months	$24,788 (SD: 51,505)/patient
		Matched controls	4,075	6 months	$9,243 (SD: 18,680)/patient
McCoy 2022; **US** (2016)	Unspecified SjD	-	-	-	$6,926
Perera 2018; **US** (2013)	Unspecified SjD	Glandular disease only	4,827	10 years	$6,401
		Extra-glandular disease	7,720	10 years	$18,880

[a] Since no exact currency year was reported, an assumption was made that the currency year was 2010 (average of 2000 and 2020); SD - standard deviation; SjD - Sjögren's disease; US - United States. Purple font indicates lower and upper bounds of ranges

Results: direct costs in Europe

- Within Europe, total mean or median direct costs per patient per year were **2,725** (Switzerland; out-of-pocket), **5,715** (United Kingdom [UK]), **9,241 - 21,014** (France), and **3,344 – 5,464 USD** (Sweden; 1 study each)

Reference; currency country (currency year)	Group	Subgroup	N	Time point	Mean direct costs per patient per year (2024 USD)
Cunha Rodrigues 2021; **Switzerland** (2019)	Unspecified SjD	-	55	-	Median: $2,725 (IQR: 2,971)[b]
Callaghan 2007; **UK** (2004)	SjD without another systemic autoimmune rheumatic disease	-	129	-	Mean: $5,715 (95% CI: 4,783 – 6,651)
Seror 2021; **France** (2011-2018)[a]	SjD	-	-	-	Mean range: $9,241 - 15,230[a]
	SjD with another autoimmune disease	-	-	-	Mean range: $14,101 - 21,014[a]
Westerlund 2021; **Sweden** (2015)	SjD without another systemic autoimmune rheumatic disease	Prevalent cohort	7,396	1 year	Median: $3,344 (IQR: 1,395-8,197)
		Incident cohort	692	1 year	Median: $5,464 (IQR: 2,436-11,294)

[a] Since no exact currency year was reported, an assumption was made that the currency year was 2014 (average of 2011 and 2018); [b] Out-of-pocket costs; CI – confidence interval; IQR – interquartile range; SjD – Sjögren’s disease; UK – United Kingdom

Results: indirect costs

- Indirect costs were scarcely reported (4 studies); no studies in the US
  - Mean total indirect costs per patient per year were **15,573 - 27,390** in the UK, **42,004** in Canada, and **268 USD** in China

Reference; currency country (currency year)	Group	N	Cost type	Mean indirect costs per patient per year (2024 USD)
Bowman 2010; **UK** (2008)	SjD without another systemic autoimmune rheumatic disease	84	Low estimate, paid work + housework loss (replacement) + helper's missed paid work High estimate, paid work + housework loss (replacement) + helper's missed paid work	$15,573 (95% CI: 11,279 – 19,868) $27,390 (95% CI: 19,356 – 35,425)
Chan 2021; **Canada** (2018)	Unspecified SjD	12	Total indirect costs	$42,003.5
McCormick 2019; **Canada** (2015)	Unspecified SjD	90	Absenteeism Presenteeism Presenteeism and absenteeism Unpaid work Paid and unpaid work	$199.1 (SD: 419.7)/patient/week $334.3 (SD: 392.4)/patient/week $403.7 (SD: 315.0)/patient/week $169.3 (SD: 345.6)/patient/week $393.5 (SD: 483.1)/patient/week
Yao 2018; **China** (2016)	Unspecified SjD with dry eyes	34	Total indirect costs	$267.6 (SD: 603.1)

CI – confidence interval; SD – standard deviation; SjD – Sjögren's disease; UK – United Kingdom

Results: emergency department visits or urgent care visits

- Mean emergency department visits or urgent care visits ranged from **0.19** to **1.7** visits per patient per year within the United States (4 studies)

Reference; country	Group	Subgroup	N	Time point	HCRU type	Mean visits per patient per year
Birt 2017; **US**	Unspecified SjD	12 months pre-diagnosis	10,414	5 years	Emergency department visits	0.6 (SD: 1.8)
		12 months post-diagnosis	10,414	5 years	Emergency department visits	0.6 (SD: 1.5)
McCoy 2022; **US**	Unspecified SjD	-	2,961	-	Emergency department visits	0.2 (SD: 0.9)
					Urgent care visits	0.2 (SD: 0.8)
Ndife 2022; **US**	Unspecified SjD	-	213	-	Emergency department visits	0.19
Perera 2018; **US**	Unspecified SjD	Glandular disease only	4,997	10 years	Emergency department visits	1.3
					Urgent care visits	1.4
		Extra-glandular disease	7,720	10 years	Emergency department visits	1.7
					Urgent care visits	1.7

HCRU - healthcare resource utilization; SD - standard deviation; SjD - Sjögren's disease; US - United States. Purple font indicates lower and upper bounds of ranges

Results: hospitalizations or inpatient visits

- Hospitalizations or inpatient visits ranged from **0.1** to **1.4** visits per patient (7 studies) in the United States and **0.5** in Sweden (1 study)

Reference; country	Group	Subgroup	N	Time point	HCRU type	Mean events per patient
Birt 2017; **US**	Unspecified SjD	12 months pre-diagnosis 12 months post-diagnosis	10,414 10,414	5 years 5 years	Hospitalizations Hospitalizations	0.7 (SD: 4.3) 1.3 (SD: 5.3)
Maciel 2018; **US**	SjD without another systemic autoimmune rheumatic disease	-	160	1,592 person-years	Hospitalizations	0.2; 24.2 events per 100 person-years
McCoy 2022; **US**	Unspecified SjD	-	2,961	-	Hospitalizations	0.1 (SD: 0.5)
Mease 2020; **US**	Unspecified SjD	-	9,108	-	Inpatient visits	0.6 per year
Ndife 2022; **US**	Unspecified SjD	-	213	-	Inpatient visits	0.17
Perera 2018; **US**	Unspecified SjD	Glandular disease only Extra-glandular disease	4,997 7,720	10 years 10 years	Inpatient visits Inpatient visits	1.1 1.4
Singh 2020; **US**	Unspecified SjD	-	49,966,570	-	Hospitalizations[a]	69,239 total events
Westerlund 2021; **Sweden**	SjD without another systemic autoimmune rheumatic disease	Prevalent cohort	7,396	-	Hospitalizations	0.5 (SD: 1.2)

[a] Hospitalization due to serious infection; HCRU - healthcare resource utilization; SD - standard deviation; SjD - Sjögren’s disease; US - United States. Purple font is lower and upper bounds of ranges

Results: dentist or dental specialist visits

- Mean dentist visits per patient ranged from **3.8** to **4.0** in the United States (2 studies) and **2.3** in Sweden (1 study). Up to 97% of patients visited a dentist

Reference; country	Group	Subgroup	N	Time point	HCRU type	Dentist visits
Birt 2017; **US**	Unspecified SjD	12 months post-diagnosis	10,414	1 year	Dental specialist Dentist	n: 132 (1.3% of patients) n: 55 (0.5% of patients)
Fox 2008; **US**	SjD without another systemic autoimmune rheumatic disease	Physician-referred patient	227	Lifetime 1 year	Dentist Oral medicine specialist/surgeon Dentist	96% of patients 49% of patients 4.0 (SD: 3.7) mean visits/patient
	SjD without another systemic autoimmune rheumatic disease	Sjögren’s Syndrome Foundation	1,225	Lifetime 1 year	Dentist Oral medicine specialist/oral surgeon Dentist	97% of patients 43% of patients 3.8 (SD: 3.3) mean visits/patient
Westhoff 2012; **Germany**	SjD without another systemic autoimmune rheumatic disease	Females	176	6 months	Dentist	n: 144 (81.7% of patients)
Westerlund 2021; **Sweden**	SjD without another systemic autoimmune rheumatic disease	Prevalent cohort	7,396	-	Dentist Dental procedures	2.3 (SD: 2.3) mean visits/patient 3.8 (SD: 4.0) mean procedures/patient

HCRU - healthcare resource utilization; SD - standard deviation; SjD - Sjögren’s disease; US - United States. Purple font indicates lower and upper bounds of ranges

Results: healthcare specialist visits

- Visits to various healthcare specialists were reported 6-12 months post-diagnosis:
  - Rheumatologists
    - US: 52.2% of patients visited; GER: 97.2%
  - Family practitioners
    - US: 48.7%; GER: 85.1%
  - Obstetricians or gynecologists
    - US: 30.9%; GER: 55.6%
  - Ophthalmologists
    - US: 19.2%; GER: 81.7%
- One study conducted in Germany showed significant differences in visits to various healthcare specialists between SjD and non-SjD patients within the past 6 months

HCRU type, n (%) patients visiting	Birt 2017; US	Westhoff 2012; Germany	
	10,414 unspecified SjD patients; 12 months post-diagnosis	176 females with SjD without another systemic autoimmune rheumatic disease; past 6 months	155 non-SjD controls
Rheumatologist	5,441 (52.2)	171 (97.2)	4 (2.6)
Family healthcare provider	5,068 (48.7)	150 (85.1)	104 (67.0)
Internal medicine provider	4,875 (46.8)	81 (46.3)	32 (20.9)
Obstetrician/gynecologist	3,213 (30.9)	98 (55.6)	84 (53.9)
Dermatologist	2,365 (22.7)	66 (37.7)	36 (23.5)
Ophthalmologist	2,000 (19.2)	144 (81.7)	63 (40.9)
Neurologist/psychiatrist	1,421 (13.6)	55 (31.4)	7 (4.3)
Urologist	734 (7.0)	-	-
Allergist/immunologist	493 (4.7)	-	-
Oncologist	434 (4.2)	-	-
Otolaryngologist	1,958 (18.8)	-	-
Gastroenterologist	1,565 (15.0)	-	-
Cardiologist	1,442 (13.8)	-	-
Orthopaedic surgeon	-	71 (40.6)	53 (33.9)
Ear/nose/throat specialist	-	76 (42.9)	24 (15.7)
Surgeon	-	14 (8.0)	5 (3.5)
Other specialists	1,235 (11.9)	56 (31.6)	11 (7.0)

GER – Germany; HCRU – healthcare resource utilization; SjD – Sjögren's disease; US – United States. Purple font indicates a significant difference between study groups ($p < 0.05$)

Conclusions

- SjD patients experience significant economic burden including substantial costs related to diagnosis, treatment, and specialist visits
- Data on indirect costs is lacking, yielding a gap in understanding the full impact of SjD on patients’ lives
- There is a need for improved therapies for managing SjD to reduce treatment costs, absenteeism, and healthcare resource utilization
- Limitations
  - Restriction of publications to those published in English may have introduced a language bias
  - Heterogeneity in the data made it not feasible to conduct a meta-analysis

Thank you!

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References of included studies

1. Chan C, et al. BMJ Open Ophthalmol. 2021;6(1):e000709.
2. McCormick N, et al. Arthritis Care Res. 2019;71(1):142-154.
3. Michaelov E, et al. J Clin Med. 2022;11(10):2809.
4. Bowman SJ, et al. J Rheumatol. 2010;37(5):1010-1015.
5. Callaghan R, et al. Rheumatol. 2007;46(1):105-111.
6. Seror R, et al. Ann Rheum Dis. 2021;80(SUPPL 1):214-215.
7. Westerlund A, et al. Rheumatol Ther. 2021;8(2):955-971.
8. Cunha Rodrigues K, et al. Swiss Med Wkly. 2021;151(SUPPL 252):16S.
9. Kalouche-Khalil L, et al. Ann Rheum Dis. 2022;81(SUPPL 1):410-411.
10. Lee TY, et al. J Manag Care Spec Pharm. 2022;28(7):786-794.
11. McCoy SS, et al. Clin Rheumatol. 2022;41(7):2071-2078.
12. Perera S, et al. J Health Econ Outcomes Res. 2018;5(2):150-161.
13. Birt JA, et al. Clin Exp Rheumatol. 2017;35(1):98-107.
14. McCoy SS, et al. Arthritis Rheumatol. 2022;74(9):1569-1579.
15. Ndife B, et al. J Manag Care Spec Pharm. 2022;28(3-A SUPPL):S67-S68.
16. Singh JA, et al. BMC Musculoskelet Disord. 2020;21(1):492.
17. Singh JA, et al. Clin Exp Rheumatol. 2020;38(4 SUPPL 126):47-52.
18. Fox PC, et al. J Am Dent Assoc(1939). 2008;139(12):1592-1601.
19. Segal B, et al. Health Qual Life Outcomes. 2009;7:46.
20. Yao W, et al. BMJ Ophthalmol. 2018;18(1):23.
21. Maciel G, et al. RMD Open. 2018;4(1):e000575.
22. Mease PJ, et al. Ann Rheum Dis. 2020;79(SUPPL 1):1052-1053.
23. Westhoff G, et al. Rheumatol. 2012;51(2):262-269.
24. Seghieri C, et al. Clin Exp Rheumatol. 2021;39(6):S123-S130.