

Economic Burden and Healthcare Resource Utilization in Patients with Systemic Lupus Erythematosus: A Systematic Literature Review

Jiyoon Choi¹, Samantha Pomponi¹, Antonia Andonova², Divya Pushkarna², Mir Sohail Fazeli², Ann E. Clarke³

¹Bristol Myers Squibb, Princeton, New Jersey; ²Evidinno Outcomes Research Inc., Vancouver, BC, Canada; ³University of Calgary, Calgary, AB, Canada

Background

- Systemic lupus erythematosus (SLE) is a heterogeneous multi-organ systemic autoimmune disease of significant complexity, morbidity, and mortality^{1,2}
- There are approximately 3.7 million prevalent cases of SLE worldwide, and is estimated to affect nearly 1.5 million persons in the United States (US)³
- Young women are disproportionately affected by SLE, with a greater prevalence and incidence of disease in certain ethnic populations such as Black, Asian, and Hispanic populations⁴
- A previous systematic literature review (SLR) conducted in 2020 focused on the economic burden and healthcare resource utilization (HCRU) of SLE in the US. The current SLR captured the economic burden and HCRU globally.⁵

Objective

To systematically review all available globally published literature on the economic burden and HCRU in patients with SLE

Methods

- An SLR was conducted according to Cochrane guidelines; MEDLINE®, Embase®, and NHSEED via OvidSP, and EconLit via EBSCO host were searched from database inception to September 29, 2022
- Conference proceedings were searched via Embase between 2020-2022
- Study eligibility was based on the following criteria:
 - Patients were adults (>18 years of age) with SLE
 - Observational studies with any interventions of interest
 - Any or no comparator studies were included
 - Outcomes were assessed during full-text screening, and included direct costs, indirect costs, and HCRU
- Study quality was assessed via a modified version of NICE single technology appraisal (STA) template developed for economic evaluations⁶
- Among studies reporting cost year, cost estimates were adjusted for inflation to January 2024 US\$ using the medical care component of the Consumer Price Index

Results

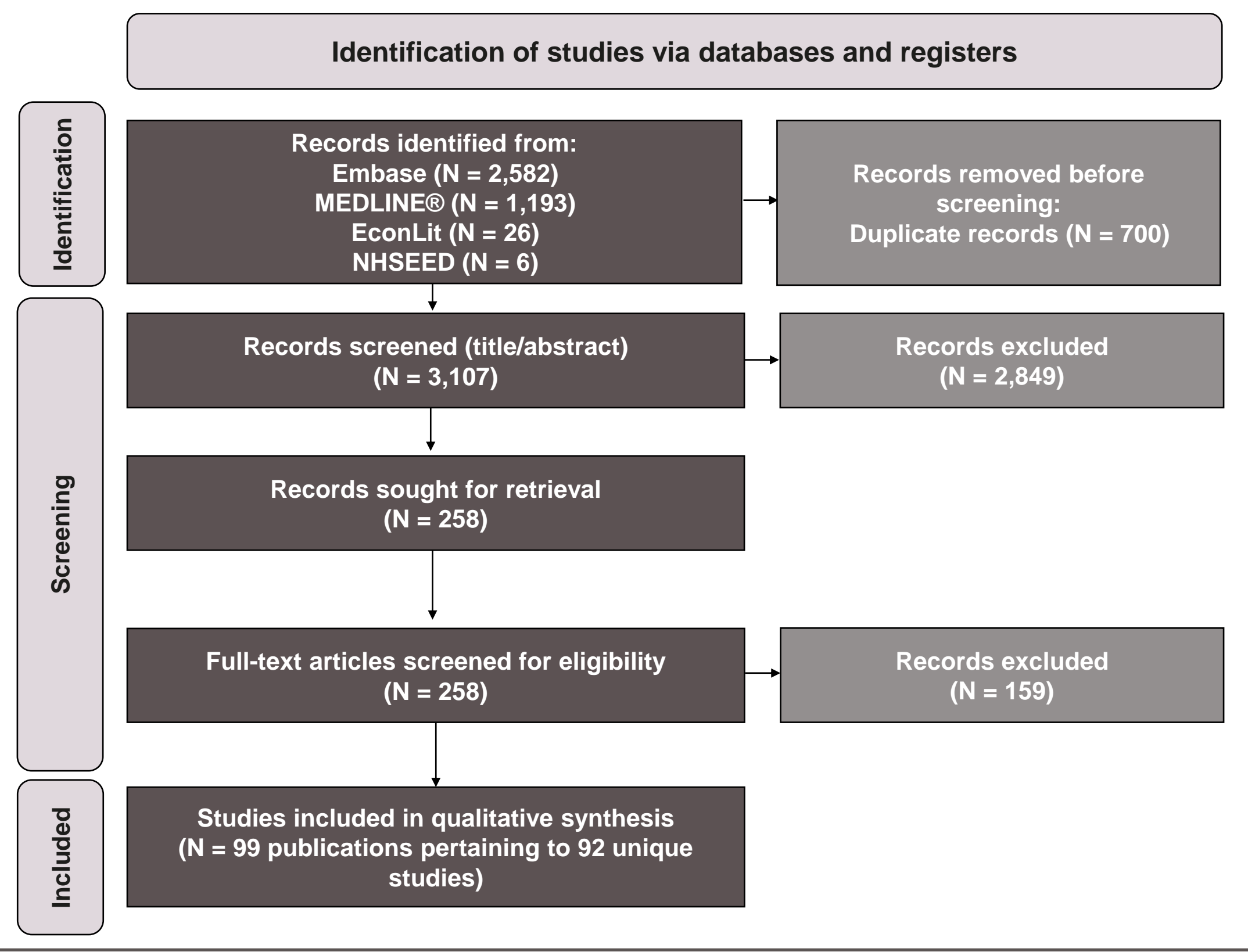
Study selection

- Of 3,807 records identified, 92 unique studies were included (Figure 1)

Study characteristics

- 67 retrospective cohort studies, 16 cross-sectional studies, and 9 prospective cohort studies were included
- Most studies were conducted in the US (number of studies, N = 71 studies), followed by multinational studies (N = 8), Germany (N = 5), United Kingdom (N = 4), and one each in Spain, France, Hong Kong, and Japan
- Study populations (sample size, n) ranged from 105 to 299,595 patients
- Studies were generally considered high to moderate quality

Figure 1: PRIMA flow diagram



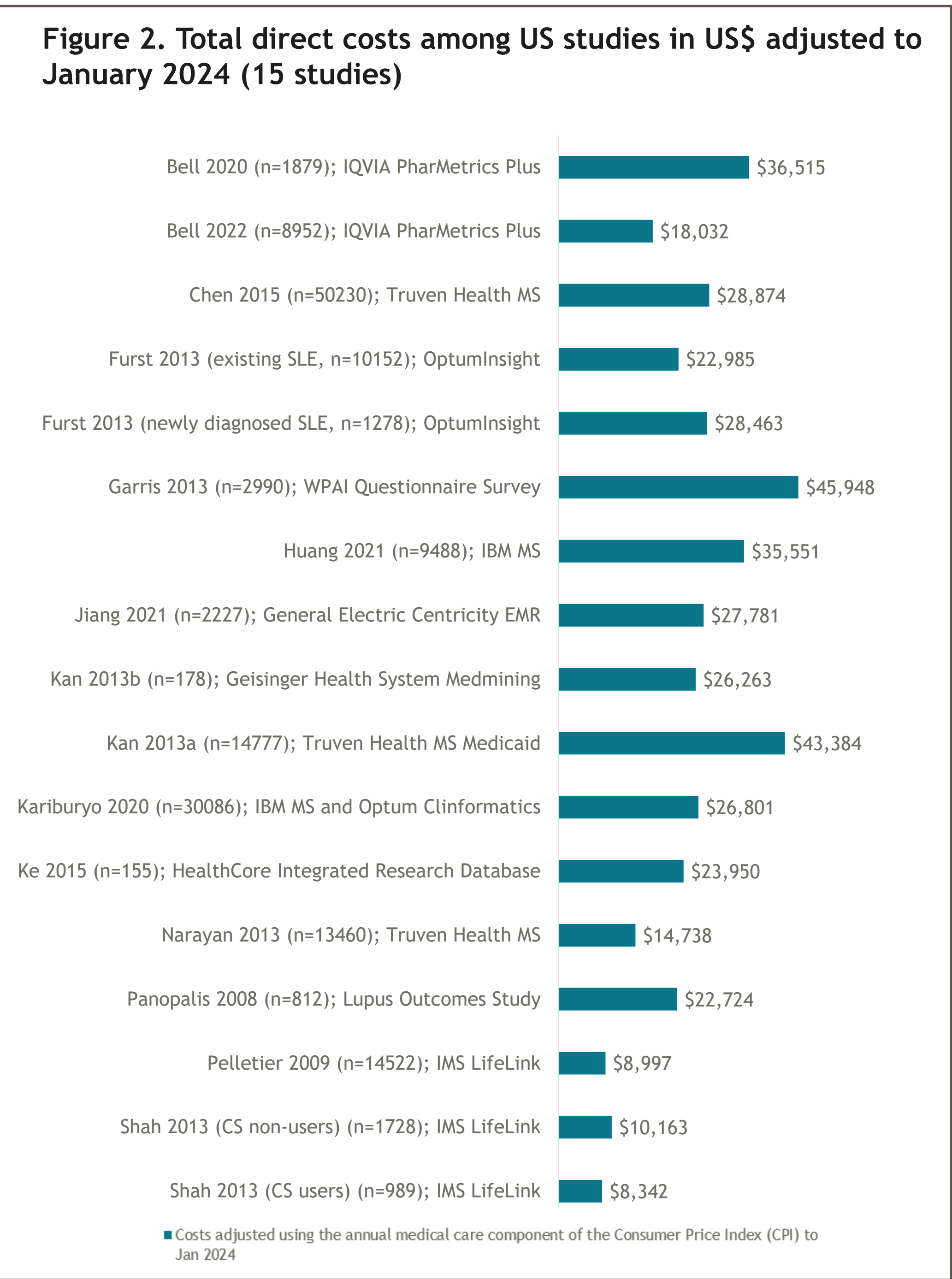
Results (continued)

Table 1. Patient characteristics

Patient Characteristic (number of reporting studies, N)		Median	Range
Mean age (N = 68)		46.5 years	39.4 - 71.4 years
Percentage of female patients (N = 76)		89.0%	3.5% - 100%
Ethnicity (N = 43)	White	57.4%	5.2% - 95.5%
	Black	27.4%	1.6% - 63.0%
	Latino/Hispanic	11.3%	0.5% - 51.3%
	Asian	4.0%	0.8% - 59.7%
Mean Charlson Comorbidity Index (N = 14)		1.16	0.3 - 4.5

Total direct costs (N = 30)

- Among US-based studies reporting cost year (N = 15), direct costs (adjusted to January 2024) ranged from \$8,342⁷ to \$45,948⁸ (Figure 2); 5 additional US-based studies did not report cost year
- Two additional US studies reported mean total healthcare costs by severity and noted that costs were 2.3-fold and 5.7-fold higher for patients with moderate and severe SLE, respectively, compared with mild SLE^{9,10}
- Country-specific unadjusted mean total direct cost were:
 - 3 UK studies: £2,613,¹¹ £7,532,¹² and CAD 4,763¹³ per patient (pp)
 - 2 German studies: 3,191¹⁴ and €5,929¹⁵ pp
 - 1 Spanish study: €6,065¹⁶ per patient per year (pppy)
 - 1 study reported cost across France (€4,003), Germany (€3,067), Spain (€4,156), and UK (€3,651)¹⁷
 - 1 Japanese study reported ¥1,017,012¹⁸



CS = corticosteroid; EMR = electronic medical record; MS = MarketScan; SLE = systemic lupus erythematosus; WPAI = Work Productivity and Activity Impairment. Note: Newly diagnosed patients had no claims with a diagnosis of systemic lupus erythematosus in the 24 months prior to the date of the medical service used.

Indirect costs (N = 23)

- Of the 23 studies, 8 studies reported costs quantifiable in monetary terms, whereas the remaining 15 studies did not report quantifiable costs
- Eight studies reported monetary costs due to absenteeism, short term disability (STD), or lost productivity (Table 2)

Table 2. Mean indirect costs per patient per year (pppy)

Author/Year/ Country	Source	Sample Size	Mean Cost in Respective Currency	
Anandarajah 2017 - US	Strong Memorial Hospital patient chart review	All SLE patients 2014 n=104	Total cost from lost productivity: US\$330,22*	
		All SLE patients 2015 n=98	Total cost from lost productivity: US\$284,619*	
		Fiscal year 2014/2015 n=NR	US\$3,066 pppy	
Carls 2009 - US	Thomson Reuters MarketScan Commercial Claims and Encounters database	SLE without LN n=130	Absence cost: US\$3,368 pppy	
		SLE without LN n=240	STD cost: US\$2,346 pppy	
Garris 2013 - US	Survey data (WPAI Questionnaire)	Employed SLE n=281	Lost income due to SLE: US\$346 weekly	
			Cost paid by SLE employers for lost work (paid leave): US\$174 weekly	
Huscher 2006 - Germany	National Database of the German Collaborative Arthritis Centres	Overall SLE n=844	Sick leave cost	EUR1,835 pppy
		Hannover Functional Status Questionnaire or Health Assessment Questionnaire >70; FFbH/HAQ (<1.2) n=643		EUR1,486 pppy
		FFbH/HAQ 50-70; FFbH/HAQ (1.2-1.7) n=114		EUR5,947 pppy
		FFbH/HAQ <50; FFbH/HAQ (>1.7) n=63		EUR6,941 pppy
Narayanan 2013 - US	Truven Health MarketScan Commercial Claims and Encounters Database	Commercially insured employees n=227	Absence cost: US\$1,606 pppy	
		Patients with absenteeism claims n=196	Absence cost: US\$6,195 pppy	
		Commercially insured employees n=619	STD cost: US\$2,008 pppy	
		Patients with absenteeism claims n=244	STD cost: US\$6,220 pppy	
Panopolis 2008 - US	Interview data	All employed SLE n=651	Income loss: US\$8,659	
		SLE patients with the lowest level of disease n=NR	Increase in productivity: US\$ 1,476 pppy	
		SLE patients with the highest level of disease n=NR	Productivity loss: US\$16,163	
Panopolis 2007 - US, Canada, UK#	Questionnaires on HCRU	US n=269	Cost due to diminished market activity	CAD56,745#
		Canada n=231		CAD38,642#
		UK n=215		CAD42,213#
Roman Ivorra 2019 - Spain	Valencian Community Records	Employed SLE n=190	Labour cost related to sick leave and productivity loss: EUR4,788	

*total annual cost reported; #cumulative costs over a 4-year period evaluated and annualized 2002 CAD costs are being reported; LN= lupus nephritis; NR = not reported; pppy = per patient per year; STD = short term disability; WPAI = Work Productivity and Activity Impairment

Healthcare resource utilization (N = 77)

- Of the 77 studies, 27 studies reported mean emergency department (ED) visits, ranging from 0.3¹⁰-3.5^{8,18,20,22,23} per year; and 14 studies reported mean hospitalizations, ranging from 0.1^{8,17,24,25} to 2.4^{26,27} pppy (Table 3)
- In eight studies, 92.1% to 100% of patients had ≥1 annual visit to their primary physician,^{8,22,24,29,30,31} 54.7% to 71% of patients had ≥1 annual visit to a rheumatologist,^{21,22,31,32} and 6% to 53% had at least one annual visit to a nephrologist^{22,31}
- Patients with SLE had 10 to 26 physician visits annually (N = 22)
 - Patients visited primary care physicians 5 to 6, rheumatologists 3 to 5, and nephrologists 0.2 to 5.9 times per year^{22,31,32}
- Other outcomes reported across studies included medication use, length of hospitalization stay, and ambulatory health care services

Table 3. Mean number of hospitalizations per patient (pp)

Author/ Year/ Country	Population Defined and Sample Size		Mean inpatient admissions unless otherwise stated (annualized)
Anandrajah 2022 - US	Strong Memorial Hospital patient chart review n=202		Admission visits: 2.3 pp 30-days re-admission visits: 0.6 pp
Bell 2020 - US	IBM MarketScan CCAE 6 mo pre-t/t n=1879 IBM MarketScan CCAE 6 mo post t/t: n=1879		0.14 pp 0.3 pp
Clarke 2020 - US	IBM-MarketScan CCAE; Mild n=2680		0.3 pp
	IBM-MarketScan CCAE; Moderate/severe n=5551		0.5 pp
	Medicaid; Mild n=202		1.8 pp
	Medicaid; Moderate/severe n=600		1.8 pp
Feldman 2020 - US	SLE pts with Medicaid Analytic eXtract data n=40381		Hospitalizations: 0.7 pp
Jiang 2021 - US	IBM MarketScan and GE EMR data 1-year post SLE-diagnosis n=2227		Hospitalizations: 0.44 pp
Kan 2013 - US	SLE pts from Truven Health MarketScan Multi-State Medicaid Database n=14262		0.7 pp
Katz 2020 - US	SLE pts with known flare frequency n=1288		SLE-related hospital admissions: 0.38 pp
Lokhandwala 2021 - US	IBM MarketScan CCAE and Medicare database Pre-index n=908		0.3 pp
	IBM MarketScan CCAE and Medicare database Post-index n=908		0.3 pp
Murimi 2021 - US	Humedica electronic health record (EHR) data	2011 n=4551	0.2 pp
		2012 n=7208	0.2 pp
		2013 n=9469	0.2 pp
		2014 n=11275	0.2 pp
		2015 n=9063	0.2 pp
Panopalis 2008 - US	SLE pts with Interview data (University of California, San Francisco (UCSF)) n=812		Overall acute care hospitalizations: 0.3 pp Overall long-term care hospitalizations: 0.01 pp
Pelletier 2009 - US	SLE pts with claims data IMS LifeLink: Health Plan Claims database n=14522		Inpatient hospitalizations (admitted patients): 1.55 pp Inpatient days in hospital: 9.69 days pp
Prete 2001 - US	Males (Department of Veterans Affairs) n=2188		Admissions over 10-year: 2.2 pp
	Females(Department of Veterans Affairs) n=426		Admissions over 10-year: 2.4 pp
Tkacz 2021* - US	IBM MarketScan CCAE; Mild n=5219		0.1
	IBM MarketScan CCAE; Moderate n=9756		0.1
	IBM MarketScan CCAE; Severe n=7410		0.4
	Medicare; Mild n=408		0.1
	Medicare; Moderate n=784		0.2
	Medicare; Severe n=843		0.5
	Medicaid; Mild n=1190		0.1
	Medicaid; Moderate n=2788		0.3
	Medicaid; Severe n=4213		0.9
Miyazaki 2020 - Japan	Claims data from the Japan Medical Data Center database n=4733		Admissions: 0.07 pp

CCAIE = Commercial Claims & Encounters; Pp = per patient; mo = months; □ = monthly value reported; *Unit for hospitalization was not reported

Conclusions

- Despite advances in treatment and management of SLE, patients experience significant HCRU and direct and indirect costs
- Patients with moderate to severe disease experience higher economic burden compared to mild disease
- Findings of this review suggest the need for therapies that can improve outcomes by reducing disease activity and economic burden

Acknowledgments

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- JC and SP report employment with Bristol Myers Squibb. AA, DP and MSF report employment with Evidinno Outcomes Research Inc.

The references have been integrated into a supplementary document and is accessible online.