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ORIGINAL RESEARCH

Clinical and Economic Burden of Systemic Lupus Erythematosus in the Years Preceding End-Stage Kidney Disease Diagnosis: A Retrospective Observational Study

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ABSTRACT

Introduction: This study aimed to describe the clinical burden, healthcare resource utilisation (HCRU) and healthcare costs for patients with systemic lupus erythematosus (SLE) in the 12–-60 months preceding an end-stage kidney disease (ESKD) diagnosis in the USA.

Methods: This retrospective observational study identified adult patients with SLE with newly diagnosed ESKD between 1 March 2012 and 31 December 2018 using administrative claims data. Clinical characteristics, mean all-cause HCRU (i.e. any HCRU visit and pharmacy fill) and total all-cause healthcare costs (comprising medical and pharmacy costs in 2019 US dollars) were assessed during the 12 months pre-ESKD diagnosis and yearly during the 5 years pre-ESKD diagnosis among patients with ≥ 5 years of continuous health plan enrolment.

Results: Of the 1356 patients included, 51.2% had severe SLE, 71.2% had lupus nephritis (LN) and 20.6% underwent kidney biopsy during the 12 months pre-ESKD. The mean (standard deviation [SD]) number of HCRU visits during the 12 months pre-ESKD was 78.0 (64.1) per patient. The mean (SD) total healthcare costs per patient in the 12 months pre-ESKD diagnosis was $64,887 (106,822), driven by medical costs $51,764 (96,458). The proportions of patients with severe SLE, LN and those undergoing biopsy increased from year 5 to year 1 pre-ESKD diagnosis. The mean (SD) number of HCRU visits increased from year 5 (61.6 [54.0]) to year 1 (83.2 [62.1]) pre-ESKD. Mean (SD) total healthcare costs rose year on year from year 5 ($34,890 [74,346]) to year 1 ($73,236 [114,584]) pre-ESKD.

Conclusion: There were substantial clinical burden and healthcare costs among patients with SLE in the 12 months pre-ESKD diagnosis. The clinical burden and healthcare costs generally increased with each year approaching ESKD diagnosis. Early interventions for patients with SLE could prevent the development of ESKD, mitigating the burden of the disease.

Keywords: Cost of illness; Health services research; Lupus erythematosus, systemic; Lupus nephritis; Therapeutics

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Key Summary Points

Why carry out this study?

Up to 40% of patients with systemic lupus erythematosus (SLE) develop lupus nephritis (LN), approximately 20% of whom may progress to end-stage kidney disease (ESKD).

Patients with SLE and ESKD incur a greater clinical and economic burden compared with patients without ESKD; however, there are few published data showing the burden of SLE preceding a patient's ESKD diagnosis.

The aim of this study was to describe the clinical burden, healthcare resource utilisation and healthcare costs among patients with SLE in the 12 months preceding an ESKD diagnosis; longitudinal trends of these outcomes were also evaluated in the 5-year period pre-ESKD diagnosis.

What was learned from this study?

The clinical and economic burden of patients with SLE is substantial in the year preceding their ESKD diagnosis and generally increases as patients approach their diagnosis, with increases observed as early as 5 years pre-ESKD.

Further studies are needed to determine the association between early diagnosis and interventions with subsequent substantial clinical and economic burden associated with ESKD.

INTRODUCTION

Systemic lupus erythematosus (SLE) can affect any organ, but inflammation of the kidneys is one of the most severe manifestations, with up to 60% of patients showing signs of renal involvement [1, 2]. Lupus nephritis (LN), a type of glomerulonephritis, is one of the most severe organ manifestations of SLE and affects approximately 40% of patients with SLE [3, 4].

Despite therapeutic advances, the treatment of LN remains challenging; without effective prevention of renal damage, up to 10–30% of patients with LN progress to end-stage kidney disease (ESKD) within 10–15 years of LN diagnosis, and subsequently need dialysis or kidney transplantation [2, 3, 5, 6].

Patients with SLE or LN may experience periods of increased disease activity (flares) that can affect multiple organ systems [7, 8]. Renal flares represent a particular concern among patients with LN as they are associated with nephron loss [4]. This shortens the kidney's lifespan, causes a decline in renal function and increases the risk of renal failure and death [4, 9]. Several studies have demonstrated that LN is associated with an increased risk of mortality [3, 10]; in a study by Yap et al. (2012), the risk of death among patients with LN increased approximately sixfold compared with the general population [11].

Managing the clinical course of LN incurs substantial healthcare costs. Annual medical costs in the USA are higher for patients with SLE with LN than those with SLE without LN, with costs ranging from approximately $29,000 to $62,000 and $12,000 to $17,000 (US dollars, USD), respectively [12, 13]. Similarly, in Canada, annual healthcare costs are higher among patients with SLE with LN than those with SLE without LN at approximately $13,000 and $11,000 (Canadian dollars), respectively [14]. Additionally, patients with LN who have ESKD were shown to incur greater healthcare costs (up to $106,982 [USD] per year) compared with patients with LN without ESKD ($38,434 per year) [15].

Moreover, the mean annual healthcare resource utilisation (HCRU; inpatient, outpatient and emergency room visits) was higher for patients with SLE with LN than patients with SLE without LN [13, 15, 16].

Despite this substantial clinical burden, data reporting HCRU and associated healthcare costs in the time preceding an ESKD diagnosis among patients with SLE are limited. The aim of this study was to characterise patients with SLE in

the USA as they progress to ESKD by assessing their clinical burden, HCRU and healthcare costs (in 2019 USD) in the 12 months preceding an ESKD diagnosis. The longitudinal trends of HCRU and healthcare costs were also evaluated in the 5-year period pre-ESKD diagnosis.

METHODS

Study Design

This retrospective, observational study used administrative claims data from the IBM MarketScan Commercial Database (MarketScan) to assess the HCRU and healthcare costs of patients with SLE pre-ESKD diagnosis in the USA. MarketScan contains data on the healthcare coverage eligibility as well as inpatient, outpatient and pharmacy service use of employees and their dependents; over 132 million lives were covered in the database between 1995 and 2015.

The study period spanned from 1 March 2011 through 31 December 2019. The study population comprised patients with SLE who were newly diagnosed with ESKD between 1 March 2012 and 31 December 2018 (identification period); this allowed for the evaluation of HCRU and associated costs in the 12 months (baseline period) and 5 years pre-ESKD diagnosis (Fig. 1). The index date was the date of the first observed medical encounter with an ESKD International Classification of Diseases (ICD)-9-clinical modification (CM) or ICD-10-CM diagnosis code within the identification period.

Study Population

Patients were eligible for the study if they were at least 18 years of age at index, with at least 12 months of continuous health plan enrolment preceding the index date, were newly diagnosed with ESKD (based on at least one medical claim with an ICD-9-CM or ICD-10-CM diagnosis code in any position, with no evidence of ESKD in the 12 months pre-index) and had a diagnosis of SLE (based on at least two outpatient medical claims at least 30 days apart, or at least one inpatient or emergency room claim with an ICD-9/ICD-10-CM diagnosis code) prior to the index date. Diagnosis codes for ESKD and SLE are shown in the Supplementary Materials.

Variables and Data Collection

Patient baseline demographics were collected on the index date and included age, gender and geographic region. Baseline clinical characteristics were collected in the 12 months pre-ESKD diagnosis and included Charlson Comorbidity Index (CCI) scores, comorbidities (defined by either primary or secondary diagnosis of selected conditions), SLE clinical manifestations of interest, the number of physician visits (nephrologists, primary care, rheumatologists, internal medicine and radiologists; identified using specialty codes), SLE organ involvement, numbers of patients with kidney biopsies, SLE disease severity, the number and severity of SLE flares (identified using the previously published Garris claims-based algorithm) [17], and numbers of patients with LN (identified on the basis

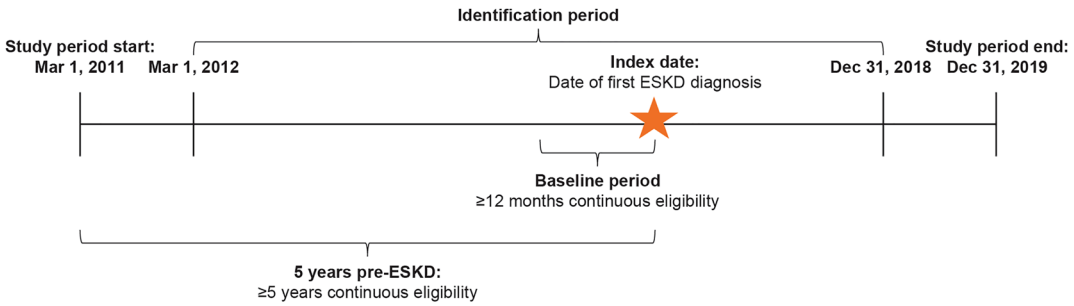

Fig. 1 Study design. *ESKD* end-stage kidney disease

of the presence of at least two renal diagnosis codes separated by at least 30 days and less than 6 months apart). Unless otherwise stated, clinical characteristics were identified using diagnosis codes on medical claims.

The number of patients using SLE-related medications (antimalarials, oral corticosteroids, immunosuppressants and biologics) was captured. HCRU was captured as the mean number of any HCRU visits (ambulatory [physician office and hospital outpatient], emergency room, inpatient and other encounters) and pharmacy fills.

Total healthcare costs (in 2019 USD) comprised medical (inpatient, emergency room, ambulatory and ancillary encounters) and pharmacy costs, and were calculated using the combined costs of the health plan and patient paid amounts.

Clinical characteristics, SLE-related medication use, all-cause HCRU and healthcare costs were captured in the 12 months pre-ESKD diagnosis, and each year during the 5 years pre-ESKD diagnosis.

Statistical Analysis

Based on previous estimates that the mean (standard deviation, SD) annual cost of ESKD among patients with SLE was $43,614 (44,044) [15], we estimated that a sample size of 2000 would be sufficient to describe the healthcare costs for this population.

All study data were analysed descriptively. Numbers and proportions were reported for categorical variables; means, medians and SD were reported for continuous variables. All analyses were conducted using the Panalgo (formerly Boston Health Economics) Instant Health Data tool. No imputation analyses were performed for missing data.

When describing the HCRU and costs during the 5 years pre-ESKD diagnosis, data from a subpopulation of patients with at least 5 years of continuous health plan enrolment were used.

Patients and Public Involvement

Patients or the public were not involved in the design or implementation of the study, or the dissemination of its results.

Study Conduct and Ethics

All database records are de-identified and fully compliant with US patient confidentiality requirements, and no direct patient contact or primary collection of individual patient data occurred. Therefore, informed consent and ethics committee or institutional review board approval was not required as study results are presented as aggregate analyses of anonymised data.

RESULTS

Patient Disposition

A total of 234,172 patients with ESKD were identified during the study period, of whom 1356 met the eligibility criteria and were included in this study (Supplementary Table 1). Of the 1356 patients, 616 had 5 years of continuous enrolment pre-ESKD diagnosis.

12-Months Pre-ESKD Diagnosis

At index, patients had a mean (SD) age of 46.7 (12.3) years. Most patients were female (81.8%), and the majority were from southern geographic regions (50.2%; Table 1).

Approximately half of patients had severe SLE (51.2%). A total of 80.8% of patients had renal involvement, 71.2% had LN pre-ESKD diagnosis and 20.6% of patients underwent kidney biopsy (Table 2). The most common comorbidities were hypertension (82.6%), renal disease (81.3%), cardiovascular disease (55.8%) and nephritis (50.8%; Table 2). The most frequently occurring SLE clinical manifestations included haematological disorders (41.2%). The most commonly visited physician specialties included radiology (75.7%), internal medicine (65.6%) and nephrology (63.2%; Table 2). A

Table 1 Patient baseline demographics at index*

	12 months pre-ESKD diagnosis (*N* = 1356)
Age, mean (SD)	46.7 (12.3)
Female, *n* (%)	1109 (81.8)
Geographical region†, *n* (%)	
North east	223 (16.8)
South	664 (50.2)
Midwest	228 (17.2)
West	209 (15.8)
Index year, *n* (%)	
2012	243 (17.9)
2013	255 (18.8)
2014	237 (17.5)
2015	175 (12.9)
2016	176 (13.0)
2017	149 (11.0)
2018	121 (8.9)

ESKD end-stage kidney disease, *ICD-CM* International classification of diseases-clinical modification, *SD* standard deviation

*Index was the date of the first observed medical encounter with an ESKD ICD-9-CM or ICD-10-CM diagnosis code

†Among patients with available data for region (*N* = 1324)

total of 94.0% of patients had at least one flare of any severity, whilst the mean (SD) number of flares of any severity was 5.8 (3.3) per patient (Table 2).

In the 12 months pre-ESKD diagnosis, the most commonly prescribed medications were oral corticosteroids (58.0%), followed by immunosuppressants (47.0%) and antimalarials (35.3%; Supplementary Table 2).

The mean (SD) number of any HCRU visits per patient (not including pharmacy fills) during the 12 months pre-ESKD diagnosis was 78.0 (64.1), which was mainly driven by ambulatory visits (24.1 [18.1]). The mean (SD) number of pharmacy fills was 41.7 (39.2; Fig. 2).

The mean (SD) total healthcare cost per patient with SLE in the 12 months pre-ESKD diagnosis was $64,887 (106,822), with total medical and pharmacy costs of $51,764 (96,458) and $13,122 (39,075), respectively (Fig. 3a). Total medical costs were driven mostly by inpatient and outpatient costs at $35,845 (87,835) and $11,586 (18,707), respectively (Fig. 3b).

5-Years Pre-ESKD Diagnosis

The proportions of patients with severe SLE, a diagnosis of LN and those with renal involvement increased from year 5 to year 1 pre-ESKD (Table 2). The proportions of patients diagnosed with comorbidities also increased from year 5 to year 1 pre-ESKD diagnosis: from 59.9% to 84.7% of patients with hypertension; from 45.6% to 80.7% of patients with renal disease; and from 35.6% to 59.4% of patients with cardiovascular disease (Table 2). The proportions of patients with at least one visit to a radiologist or a nephrologist increased from year 5 (59.1% to 32.0%, respectively) to year 1 pre-ESKD diagnosis (76.1% and 59.9%, respectively; Table 2). The number of kidney biopsies also increased from year 5 to year 1 pre-ESKD, with 18.0% of patients undergoing kidney biopsy in the year preceding ESKD diagnosis (Table 2).

The use of SLE-related medications generally increased from year 5 to year 1 pre-ESKD diagnosis (Supplementary Table 2).

Increases in HCRU were observed with each year preceding ESKD diagnosis; the mean (SD) number of any HCRU visits (excluding pharmacy fills) per patient was 61.6 (54.0) in year 5 pre-ESKD, rising to 83.2 (62.1) in the year pre-ESKD diagnosis. Pharmacy fills also increased from year 5 to year 1 pre-ESKD diagnosis in this population (Fig. 2).

Mean (SD) total healthcare costs per patient increased from year 5 pre-ESKD diagnosis ($34,890 [74,346]) to year 1 pre-ESKD diagnosis ($73,236 [114,584]; Fig. 3a). Medical costs represented the greater share of the total healthcare costs relative to pharmacy costs. Inpatient admissions accounted for the majority of medical costs (Fig. 3b).

Table 2 Patient clinical characteristics during the 12 months and 5 years pre-ESKD diagnosis

	12 months pre-ESKD diagnosis (*N* = 1356)	Patients with at least 5 years continuous health plan enrolment (*N* = 616)				
		Year 1 pre-ESKD diagnosis	Year 2 pre-ESKD diagnosis	Year 3 pre-ESKD diagnosis	Year 4 pre-ESKD diagnosis	Year 5 pre-ESKD diagnosis
CCI score, mean (SD)	3.0 (1.9)	3.1 (2.0)	2.4 (1.8)	2.1 (1.6)	1.9 (1.5)	1.8 (1.5)
Comorbidity, *n* (%)						
Hypertension	1120 (82.6)	522 (84.7)	444 (72.1)	421 (68.3)	412 (66.9)	369 (59.9)
Renal disease	1102 (81.3)	497 (80.7)	377 (61.2)	339 (55.0)	303 (49.2)	281 (45.6)
Cardiovascular disease	756 (55.8)	366 (59.4)	277 (45.0)	265 (43.0)	239 (38.8)	219 (35.6)
Nephritis*	689 (50.8)	299 (48.5)	216 (35.1)	173 (28.1)	156 (25.3)	139 (22.6)
Pulmonary disease	279 (20.6)	149 (24.2)	112 (18.2)	103 (16.7)	90 (14.6)	75 (12.2)
SLE clinical manifestations, *n* (%)						
Haematological disorders	558 (41.2)	266 (43.2)	179 (29.1)	166 (27.0)	147 (23.9)	137 (22.2)
Anaemia	355 (26.2)	167 (27.1)	114 (18.5)	109 (17.7)	96 (15.6)	83 (13.5)
Arthralgia	479 (35.3)	223 (36.2)	216 (35.1)	194 (31.5)	182 (29.6)	183 (29.7)
Rash	281 (20.7)	109 (17.7)	102 (16.6)	97 (15.8)	105 (17.1)	79 (12.8)
Fever	229 (16.9)	103 (16.7)	79 (12.8)	56 (9.1)	63 (10.2)	61 (9.9)
Physician specialty visits, at least 1 visit, *n* (%)						
Radiology	1027 (75.7)	469 (76.1)	387 (62.8)	392 (63.6)	358 (58.1)	364 (59.1)
Internal medicine	890 (65.6)	396 (64.3)	328 (53.2)	309 (50.2)	307 (49.8)	309 (50.2)
Nephrology	857 (63.2)	369 (59.9)	262 (42.5)	238 (38.6)	221 (35.9)	197 (32.0)
Primary care	697 (51.4)	322 (52.3)	279 (45.3)	267 (43.3)	271 (44.0)	269 (43.7)
Rheumatology	667 (49.2)	287 (46.6)	266 (43.2)	235 (38.1)	229 (37.2)	225 (36.5)
SLE disease severity,† *n* (%)						
Mild	64 (4.7)	26 (4.2)	91 (14.8)	117 (19.0)	130 (21.1)	139 (22.6)
Moderate	598 (44.1)	275 (44.6)	276 (44.8)	292 (47.4)	277 (45.0)	284 (46.1)
Severe	694 (51.2)	315 (51.1)	249 (40.4)	207 (33.6)	209 (33.9)	193 (31.3)
SLE flare severity,† at least 1 flare, *n* (%)						
Any	1275 (94.0)	584 (94.8)	540 (87.7)	526 (85.4)	526 (85.4)	496 (80.5)
Mild	515 (38.0)	240 (39.0)	253 (41.1)	259 (42.0)	257 (41.7)	239 (38.8)
Moderate	1207 (89.0)	547 (88.8)	520 (84.4)	499 (81.0)	480 (77.9)	457 (74.2)
Severe	433 (31.9)	204 (33.1)	102 (16.6)	66 (10.7)	86 (14.0)	73 (11.9)

Table 2 continued

	12 months pre-ESKD diagnosis (N = 1356)	Patients with at least 5 years continuous health plan enrolment (N = 616)				
		Year 1 pre-ESKD diagnosis	Year 2 pre-ESKD diagnosis	Year 3 pre-ESKD diagnosis	Year 4 pre-ESKD diagnosis	Year 5 pre-ESKD diagnosis
Number of flares per patient, mean (SD)						
Any	5.8 (3.3)	5.8 (3.4)	5.6 (3.3)	5.3 (3.2)	4.8 (3.1)	4.7 (2.9)
Mild	0.9 (1.4)	0.9 (1.4)	1.0 (1.5)	1.1 (1.5)	1.1 (1.5)	1.1 (1.4)
Moderate	4.3 (3.0)	4.3 (3.1)	4.2 (2.9)	4.0 (2.9)	3.4 (2.6)	3.4 (2.5)
Severe	0.6 (1.1)	0.6 (1.0)	0.3 (0.9)	0.2 (0.6)	0.3 (0.7)	0.3 (0.8)
SLE organ involvement, n (%)						
Musculoskeletal system and connective tissue	1302 (96.0)	597 (96.9)	545 (88.5)	537 (87.2)	517 (83.9)	507 (82.3)
Unknown/other	1240 (91.5)	565 (91.7)	515 (83.6)	491 (79.7)	476 (77.3)	476 (77.3)
Circulatory	1238 (91.3)	568 (92.2)	497 (80.7)	472 (76.6)	462 (75.0)	432 (70.1)
Genitourinary	1225 (90.3)	553 (89.8)	476 (77.3)	466 (75.6)	446 (72.4)	413 (67.0)
Renal	1096 (80.8)	489 (79.4)	381 (61.9)	348 (56.5)	319 (51.8)	290 (47.1)
Skin and subcutaneous tissue	1139 (84.0)	518 (84.1)	499 (81.0)	530 (86.0)	517 (83.9)	507 (82.3)
Respiratory system	833 (61.4)	381 (61.9)	320 (51.9)	307 (49.8)	297 (48.2)	291 (47.2)
Nervous system and sense organs	764 (56.3)	368 (59.7)	327 (53.1)	321 (52.1)	307 (49.8)	302 (49.0)
Digestive	678 (50.0)	326 (52.9)	237 (38.5)	233 (37.8)	219 (35.6)	217 (35.2)
Kidney biopsy, n (%)	280 (20.6)	111 (18.0)	58 (9.4)	42 (6.8)	50 (8.1)	30 (4.9)
LN*, n (%)	966 (71.2)	432 (70.1)	292 (47.4)	275 (44.6)	243 (39.4)	212 (34.4)

CCI Charlson comorbidity index, *ESKD* end-stage kidney disease, *LN* lupus nephritis, *SD* standard deviation, *SLE* systemic lupus erythematosus

*Incidence of nephritis is based on a specific diagnosis code, whilst incidence of LN was identified on the basis of the presence of at least two renal codes at least 30 days apart and no less than 6 months apart

†SLE disease and flare severity were identified using the previously published Garris claims-based algorithm [17]

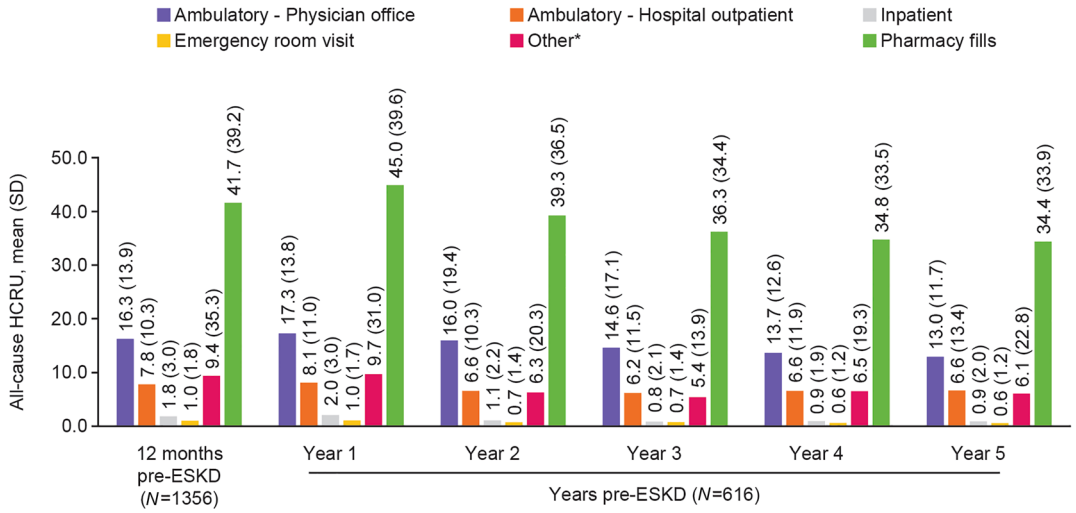

Fig. 2 Annual mean all-cause HCRU in the 12 months and 5 years pre-ESKD diagnosis *Other encounters included ambulance, assisted living facilities, comprehensive rehabilitation facilities, custodial care facilities, hospice/home care services, intermediate care facilities, psychiatric facilities and skilled nursing facilities. *ESKD* end-stage kidney disease, *HCRU* healthcare resource utilisation, *SD* standard deviation

DISCUSSION

This retrospective, observational study showed that patients with SLE incurred substantial clinical burden, HCRU and healthcare costs in the 12 months pre-ESKD diagnosis, with HCRU and healthcare costs increasing from 5 years to 1 year pre-ESKD. This highlights the need for early intervention for patients with SLE with the aim of preventing disease progression and worsening of renal function.

Renal outcomes became more common and severe as patients approached their ESKD diagnosis, with the proportion of patients with renal involvement and LN increasing from year 5 to year 1 pre-ESKD diagnosis. Additionally, the proportion of patients with comorbidities increased in the years preceding ESKD; specifically, the majority of patients had a diagnosis of hypertension in the year pre-ESKD diagnosis. A similar increase in the proportion of patients requiring radiologist and nephrologist visits was also observed. Most patients had severe SLE and the mean number and severity of SLE flares increased as patients approached their ESKD diagnosis. This may have contributed to the deterioration in kidney function, as each subsequent flare reduces the lifespan of the kidney [4, 9].

According to the European Alliance of Associations for Rheumatology and European Renal Association–European Dialysis and Transplant Association (EULAR/ERA-EDTA) recommendations for LN, patients with SLE with any signs of kidney involvement (such as proteinuria $\geq$ 0.5 g/24 h and/or an unexplained decrease in glomerular filtration rate) should be considered for a kidney biopsy to confirm suspected LN diagnosis [18]. A significant fraction of biopsies is performed by radiologists [19]; however, in this study, we observed a low rate of kidney biopsies compared with radiologist visits in the 12 months pre-ESKD (20.6% vs 75.7% of patients, respectively). As patients approach their ESKD diagnosis, they are at an advanced stage in their disease course and their eGFR is likely to be less than 25 ml/min/1.73 m^2 [20]; biopsies may be precluded in these instances as information critical to the management of their disease is unlikely to be obtained. Another explanation for the low rate of kidney biopsies may be that biopsies were performed prior to the observation period. This suggests that all

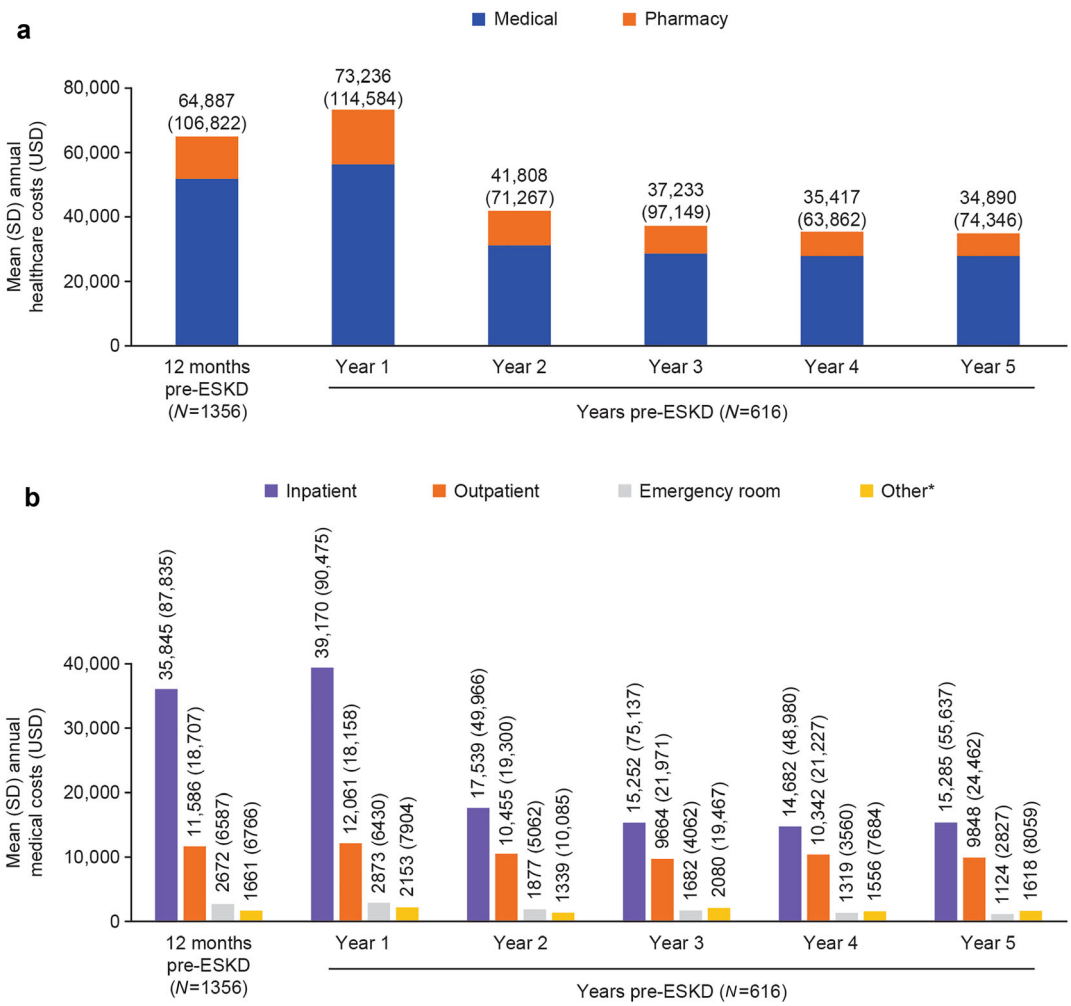

Fig. 3 **a** Mean (SD) total annual healthcare costs and **b** breakdown of mean (SD) annual medical costs*Other encounters included ambulance, assisted living facilities, comprehensive rehabilitation facilities, custodial care facilities, hospice/home care services, intermediate care facilities, psychiatric facilities, and skilled nursing facilities. *ESKD* End-stage kidney disease, *HCRU* Healthcare resource utilisation, *SD* standard deviation

biopsies that were conducted may not have been captured in this study.

Mean total healthcare cost per patient was $64,887 in the 12 months pre-ESKD diagnosis. This is consistent with findings reported in a previous study that showed annual healthcare cost was up to $52,951 per patient with severe SLE [21]. Furthermore, most of the costs were attributed to inpatient admissions and outpatient care, consistent with the results reported in a previously published retrospective study of economic outcomes in patients with SLE in the USA [16].

Additionally, we have demonstrated that the healthcare costs progressively increased from year 5 to year 1 pre-ESKD diagnosis. In particular, inpatient costs were markedly increased in the year before diagnosis, likely as a direct result of declining kidney function and increasing comorbidities.

Pharmacy fills, followed by ambulatory visits (physician office and hospital outpatient), constituted the greatest HCRU in the 12 months pre-ESKD diagnosis, consistent with reports of a previous study that showed pharmacy fills and outpatient visits were the most significant source of HCRU among patients with SLE [22].

Additionally, the increased use of oral corticosteroids and immunosuppressants may have caused more infections and infestations due to their immunosuppressive properties [23, 24] and, in turn, contributed to an increased rate of hospitalisations pre-ESKD diagnosis, as reflected by the results of this study.

These findings highlight the substantial downstream healthcare burden of patients with SLE who develop LN and progress to ESKD, emphasising the need for early intervention among patients with LN, which may mitigate disease progression. One study has previously identified that early diagnosis among patients with SLE is associated with lower inpatient and corresponding SLE-related hospitalisation costs compared with those with a late diagnosis [25]. In addition, data from the Hopkins Lupus Cohort showed that patients who achieved a renal response (defined as an eGFR $\leq$ 20% below baseline value or $\geq$ 60 ml/min/1.73 m^2 or urine protein/creatinine ratio $\leq$ 0.7 g/day) had a lower risk of ESKD or death and chronic renal insufficiency over a median follow-up of 6 years compared with patients without a renal response [26]. These results further suggest that early diagnosis and treatment to improve renal responses may prevent disease progression, the long-term sequelae and burden associated with LN.

This study had several limitations that are common to retrospective observational claims-based studies. Firstly, evidence of an SLE or ESKD diagnosis was available only from ICD-9-CM or ICD-10-CM codes associated with medical claims; these codes are subject to possible misspecification if diagnostic codes are inaccurate or misclassified. Additionally, the use of an algorithm to classify SLE disease severity does not necessarily provide an accurate indication of disease activity or organ damage. Similarly, the algorithm used to identify the incidence and severity of flares relies on the patient's use of healthcare services and prescriptions of SLE medications; despite this, the algorithm is a validated way of capturing flare data [17, 27]. Some patients are only diagnosed with SLE once they have developed manifestations, such as LN. The cost of care of these patients may be greater compared with those with pre-existing SLE; however, the cost of these patients specifically has not been captured. The definition of patients with LN was also based on the presence of renal diagnosis codes on medical claims, rather than biopsy-confirmed LN or renal laboratory results. Additionally, renal involvement was identified on the basis of the presence of specific diagnosis codes on medical claims. As a result of the limitations of claims-based data noted above, it is not possible to determine whether ESKD was caused by LN or other renal involvement in this population. Furthermore, race and ethnicity data were not available in this data set; therefore, analysis to determine the effect of race or ethnicity on these outcomes could not be conducted, despite being known predictors of increased SLE disease incidence among patients of Black African ancestry [28]. This study lacked comparators, such as patients with ESKD but with no SLE; thus, statistical comparisons with other patient populations could not be conducted. Nonetheless, this study demonstrates the economic burden (measured in terms of HCRU and associated costs) in patients with SLE who are approaching ESKD diagnosis, providing a better understanding of the ESKD burden at a population level in a routine clinical practice setting. Finally, only patients with insurance coverage were included in the study, which may limit the generalisability of these outcomes to the uninsured population. However, despite its limitations, this study retrospectively followed a sizable cohort of patients with SLE over 5 years, providing a comprehensive and real-world depiction of their clinical burden, treatment patterns, HCRU and healthcare costs over time.

CONCLUSIONS

In the 12 months before a diagnosis of ESKD, patients with SLE incur a considerable clinical and economic burden, primarily driven by inpatient costs, which generally increase as patients approach their ESKD diagnosis. Early diagnosis of SLE, improved strategies for monitoring kidney function, and early interventions may be important in limiting the development of damaging chronic conditions like ESKD,

ultimately reducing the economic and clinical burden of the disease. Further studies are required to evaluate the relationship between early interventions and economic outcomes.

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Disclosures. Christopher F. Bell and Bernie Rubin are employees of GSK and hold stocks and shares in the company. Shirley P. Huang is a former postdoctoral fellow at GSK and held stocks and shares in the company; and is a current employee of Horizon Therapeutics. Amy Guisinger was an hourly contracted GSK employee at the time of the study; and is a current employee of AESARA. Carlyne Averell was an employee of GSK and held stocks and shares at the time of the study and is now retired.

Compliance with Ethics Guidelines. All results presented here utilised de-identified patient data and, therefore, informed consent and ethics committee or institutional review board approval was not required.

Data Availability. The data sets generated and/or analysed during the current study are not publicly available as they were used under license from MarketScan for the current study.

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