

National epidemiological analysis of lupus in Chile: A registry-based study from 2013 to 2024

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Abstract

Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease with diverse clinical manifestations and regional variations in epidemiology. Despite its clinical significance, robust epidemiological data from Latin America, particularly Chile, remain limited. This study aims to provide the first comprehensive epidemiological assessment of SLE in Chile using population-adjusted denominators and rigorous statistical methods.

Methods: We analyzed data from Chile's Specific Health Guarantees Program (GES) from July 2013 to August 2024, covering 95% of the insured population. Population denominators were obtained from Chile's National Institute of Statistics stratified by age and sex. Incidence rates were calculated using annual new case reports from 2014 to 2023, while prevalence and mortality were estimated through 2024. All analyses included 95% confidence intervals using Poisson distribution methods. Rate ratios were calculated using Poisson regression models with population offset terms. Sensitivity analyses modeled different assumptions regarding program discharge mortality proportions.

Results: The median annual SLE incidence in Chile was 7.1 per 100,000 beneficiaries (IQR 6.3–7.7) using population-adjusted denominators. Prevalence increased from 26.7 per 100,000 in 2013 to 91.3 per 100,000 in 2024. The male-to-female incidence ratio was 1:10.61 (Rate Ratio: 0.093, 95% CI: 0.088–0.098). Mortality analysis using program discharges as a proxy revealed an overall rate of 11.9 per 1000 SLE patients (IQR 7.2–18.8), with significantly higher rates in males compared to females (Rate Ratio: 1.756, 95% CI: 1.546–1.987). Age-stratified analysis demonstrated progressive mortality increases, with patients ≥60 years showing rates of 87.4 per 1000 in males and 49.0 per 1000 in females. Sensitivity analyses modeling different assumptions about discharge mortality (70%–100% fatal) yielded mortality estimates ranging from 8.2 to 11.9 per 1000 SLE patients.

Conclusions: This study provides a comprehensive epidemiological assessment of SLE in Chile using population-adjusted denominators and statistical confidence intervals. Our findings demonstrate SLE incidence rates higher than North American estimates, significant sex disparities in both incidence and mortality, and age-related mortality progression. The sensitivity analysis addresses limitations in mortality estimation through administrative data. These findings contribute essential epidemiological parameters for healthcare planning and underscore the need for enhanced surveillance systems for autoimmune diseases in Latin America.

Keywords

Systemic lupus erythematosus, epidemiology, Chile, incidence, prevalence, mortality, health surveillance, Latin America

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Introduction

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease characterized by multisystem inflammation and a wide spectrum of clinical manifestations. The global prevalence of SLE ranges from 20 to 150 cases per 100,000 individuals, with this considerable variability attributed to genetic predisposition, environmental triggers, and socioeconomic determinants influence disease expression and progression.^{1,2} SLE disproportionately affects women of childbearing age, with a marked predilection for certain ethnic groups; African American, Hispanic, and Asian populations demonstrate higher susceptibility compared to Caucasians. These demographic disparities underscore the necessity for region-specific epidemiological surveillance to inform targeted healthcare planning and resource allocation strategies.³

The clinical significance of SLE derives from its potential to affect multiple organ systems simultaneously or sequentially, including the kidneys, central nervous system, and cardiovascular system. This heterogeneity in clinical presentation—ranging from constitutional symptoms such as fatigue and arthralgia to life-threatening manifestations like lupus nephritis and neuropsychiatric involvement—presents substantial diagnostic and therapeutic challenges for clinicians. Beyond its direct physiological impact, SLE significantly compromises patients' quality of life and is associated with increased morbidity and mortality, particularly among minority populations where the disease tends to manifest more aggressively and at earlier ages.^{4,5}

Well-documented regional variations exist in the epidemiological profile of SLE. In North America, annual incidence rates range from 1.5 to 5.0 cases per 100,000 individuals, whereas higher rates have been consistently reported across regions in Asia and Latin America.^{6,7} These geographic disparities extend to prognostic outcomes as well; epidemiological studies have demonstrated that African American and Hispanic populations in the United States experience more severe disease manifestations and poorer health outcomes compared to their Caucasian counterparts. This disproportionate disease burden results from a complex interplay of genetic susceptibility, healthcare access inequities, and variations in disease management approaches.^{1,8}

Despite the theoretical high prevalence of SLE in Latin American populations suggested by existing epidemiological models, comprehensive and methodologically rigorous data from this region remain limited. Specifically in Chile, epidemiological information regarding SLE prevalence and incidence has been particularly sparse and fragmented. This critical knowledge gap impedes a comprehensive understanding of the disease burden and complicates the development and implementation of evidence-based public health policies. Accurate epidemiological

characterization is imperative for improving diagnostic algorithms, treatment protocols, and prognostic assessments for SLE patients in the region.^{3,7}

The Chilean healthcare system operates through a multi-tiered structure comprising several distinct segments: the public insurance system (FONASA), private health insurance programs (ISAPRE), mutual insurance for occupational accidents and diseases (MHO), and specialized military health services. The Specific Health Guarantees Program (GES), which ensures timely access to diagnosis and treatment for specific conditions including SLE, covers approximately 95% of the insured population, excluding only the military and mutual insurance systems. Since its implementation in 2013, all new SLE cases diagnosed within the GES framework have been systematically documented, creating a robust national dataset for epidemiological analysis. Leveraging this comprehensive registry, the primary objective of this study is to determine the annual incidence of SLE in Chile from 2014 to 2023 and the prevalence from 2013 to 2024, thereby establishing comprehensive epidemiological parameters for this condition within the Chilean population.

Methodology

Study design and data sources

This retrospective observational study analyzed data from the Specific Health Guarantees Program (GES) in Chile, covering the period from July 2013 to August 2024. The GES program encompasses 95% of the insured population in Chile, including beneficiaries of the public health insurance system (FONASA), which covers approximately 80% of the population, and the private health insurance system (ISAPRE), which covers the remaining 15%. Military insurance systems and Mutual Health Organizations (MHOs) are excluded from this guarantee system. Due to the legal mandate for case notification for study and confirmation within the GES framework, all annually reported new cases were considered incident cases of SLE.

Diagnostic confirmation of SLE within the GES framework requires clinical evaluation and verification by medical specialists, including rheumatologists, internists, or internal medicine specialists, prior to program enrollment. All cases included in the GES registry represent specialist-confirmed diagnoses based on established clinical criteria for systemic lupus erythematosus, ensuring appropriate diagnostic certainty for epidemiological analysis.

Population data and denominators

Population denominators. Population denominators were obtained from Chile's National Institute of Statistics (INE) demographic projections for 2013–2024, stratified by sex

and age groups (0-14, 15-29, 30-44, 45-59, ≥ 60 years). All population estimates were adjusted by the GES coverage factor (95% of total population) to ensure appropriate denominators matched the study population coverage.

Incidence calculation. Annual incidence was determined based on new case reports within the GES program from 2014 to 2023. Data from 2013 were excluded due to program initiation effects, while 2024 data were excluded due to incomplete annual follow-up (8-month observation period from January to August 2024), which precluded calculation of comparable annual rates.

Prevalence and mortality estimation. For prevalence estimation, data from the public health insurance database was used, which provides annual population reports as well as program admissions and discharges. Prevalence and mortality estimations utilized point-in-time data that remain valid regardless of observation period duration, as these reflect program enrollment status at the time of measurement rather than requiring complete annual cycles. Data through August 2024 were included for these measures.

Program discharge definition and mortality proxy

Program discharges within the GES framework are systematically defined according to established clinical guidelines specifying the following closure criteria: death, treatment termination by physician decision, exclusion criteria identification, guaranteed treatment completion, or patient-attributable causes (treatment rejection, insurance change, or persistent non-attendance to three consecutive appointments).

For chronic autoimmune conditions such as SLE, several closure criteria are inherently inapplicable. Patients cannot achieve ‘treatment completion’ as SLE requires lifelong management, nor do they typically meet ‘exclusion criteria’ as the condition persists throughout the disease course. Treatment rejection is uncommon given that medication access depends on program participation. Insurance transitions may occur from private to public systems, though the reverse is precluded by pre-existing condition policies.

Given the chronic nature of SLE requiring continuous management, program discharge predominantly represents mortality or severe health deterioration leading to care abandonment. This methodological approach aligns with literature showing that program attrition in other chronic, treatment-dependent conditions could serve as a potential mortality proxy when comprehensive vital statistics are unavailable.^{9,10}

Statistical analysis

Descriptive statistics. Data are presented as medians with interquartile ranges (IQR) for continuous variables

given non-normal distribution. Categorical data are presented as frequencies and proportions.

Rate calculations. Incidence, prevalence, and mortality rates were calculated per 100,000 population (incidence and prevalence) or per 1000 SLE patients (mortality). All rates include 95% confidence intervals calculated using exact Poisson distribution methods for rare events, accounting for the discrete nature of case counts.

Comparative analysis. Rate ratios with 95% confidence intervals were calculated using Poisson regression models with population denominators as offset variables to compare rates between demographic groups. Statistical significance for sex and age group differences was assessed, with Rate Ratios and confidence intervals calculated to quantify differences between demographic strata.

Sensitivity analysis

To address potential overestimation of mortality through program discharge data, sensitivity analyses were conducted modeling different assumptions regarding non-fatal discharge proportions.

- Conservative scenario: 100% of program discharges represent mortality (primary analysis)
- Moderate scenario: 90% mortality, 10% non-fatal discharges
- Liberal scenario: 70% mortality, 30% non-fatal discharges

For non-conservative scenarios, we additionally modeled the potential impact of patient re-entry into the healthcare system, estimating that 25% of non-fatal discharges might represent re-admissions within a 2-year period, which could affect incident case calculations in subsequent years.

Data quality and limitations

The study utilized administrative data dependent on healthcare provider reporting accuracy and completeness. Case identification relies on specialist clinical judgment using established criteria rather than standardized research protocols. The exclusion of approximately 5% of the population (military and mutual insurance systems) may lead to slight underestimation of true population rates.

Ethical considerations

The study utilized publicly available aggregated data with no access to individual patient information. Ethical approval was not required for this analysis of de-identified administrative data.

Statistical software

All analyses were conducted using R version 4.5.1. Poisson regression models were fitted using the `glm()` function with appropriate offset terms for population denominators.

Results

Incidence analysis

The median annual SLE incidence in Chile from 2014 to 2023 was 7.1 per 100,000 beneficiaries (IQR 6.3-7.7), calculated using population-adjusted denominators from INE demographic projections. A total of 17,520 incident cases were reported during this period. The annual incidence rates showed temporal variation, decreasing to 5.8 per 100,000 (95% CI: 5.5-6.1) in 2020, followed by rates of 6.8, 6.3, and 6.9 per 100,000 in 2021, 2022, and 2023 respectively (Table 1).

When stratified by sex, marked disparities were observed. The median incidence in women was 13.4 per 100,000 (IQR 8.5-17.7) compared to 1.3 per 100,000 in men (IQR 0.9-1.8), yielding a female-to-male ratio of 10.61:1 (Figure 1). Poisson regression analysis confirmed a statistically significant sex difference with a Rate Ratio of 0.093 (95% CI: 0.088-0.098, $p < .001$) for men compared to women.

Prevalence trends

SLE prevalence demonstrated consistent growth throughout the study period, increasing from 26.7 per 100,000 beneficiaries in 2013 to 91.3 per 100,000 in 2024. This

progressive increase reflects both incident case accumulation and improved program retention over the 11-year observation period (Figure 2).

Age-stratified analysis

Age-specific incidence rates revealed distinct patterns across demographic groups. Among women, the highest incidence occurred in the 45-59 age group (20.1 per 100,000, 95% CI: 19.3-20.6), followed by the 30-44 age group (17.5 per 100,000, 95% CI: 16.7-17.9). In men, incidence rates remained consistently lower across all age groups, with the highest rates observed in the 60+ age group (2.0 per 100,000, 95% CI: 1.7-2.2). (Figure 3).

Poisson regression analysis demonstrated significant age effects for incidence rates. Compared to the 0-14 age reference group, Rate Ratios were: 15-29 years: 7.28 (95% CI: 6.59-8.06), 30-44 years: 10.34 (95% CI: 9.38-11.42), 45-59 years: 12.42 (95% CI: 11.27-13.73), and 60+ years: 9.35 (95% CI: 8.47-10.36), all $p < .001$.

Mortality analysis

Using program discharges as a mortality proxy, the overall estimated mortality rate was 11.9 per 1000 SLE patients (IQR 7.2-18.8). Substantial sex-based differences were observed, with men showing significantly higher mortality rates across all age groups. The overall mortality rate was 18.1 per 1000 in men compared to 11.4 per 1000 in women, corresponding to a Rate Ratio of 1.756 (95% CI: 1.546-1.987, $p < .001$).

Table 1. Annual incidence rates of systemic lupus erythematosus in Chile by sex (2014-2023): Rates calculated using INE population projections adjusted for 95% GES coverage. 95% confidence intervals calculated using exact Poisson distribution methods. Data from 2013 excluded due to program initiation effects; 2024 excluded due to incomplete annual follow-up.

Year	Male	Female	Combined
	Rate per 100,000 (95%CI)	Rate per 100,000 (95%CI)	Rate per 100,000 (95%CI)
2014	1.60 (1.34-1.90)	20.40 (19.45-21.38)	11.18 (10.68-11.70)
2015	1.11 (0.89-1.36)	13.24 (12.49-14.03)	7.27 (6.86-7.70)
2016	1.07 (0.86-1.32)	14.30 (13.52-15.12)	7.81 (7.39-8.26)
2017	1.44 (1.20-1.72)	13.37 (12.62-14.16)	7.54 (7.13-7.97)
2018	1.12 (0.91-1.36)	12.76 (12.03-13.52)	7.07 (6.68-7.48)
2019	1.73 (1.47-2.03)	15.58 (14.79-16.41)	8.80 (8.37-9.25)
2020	0.98 (0.78-1.20)	8.25 (7.67-8.85)	4.71 (4.39-5.05)
2021	1.25 (1.03-1.50)	10.97 (10.32-11.66)	6.21 (5.84-6.60)
2022	1.23 (1.01-1.47)	11.14 (10.48-11.83)	6.29 (5.92-6.68)
2023	1.20 (0.99-1.44)	11.76 (11.08-12.46)	6.58 (6.20-6.98)
Median (IQR)	1.33 (0.94-1.78)	13.38 (8.46-17.67)	7.10 (6.28-7.72)

Abbreviations: CI, confidence interval; GES, Specific Health Guarantees Program; INE, National Institute of Statistics; IQR, interquartile range; SLE, systemic lupus erythematosus.

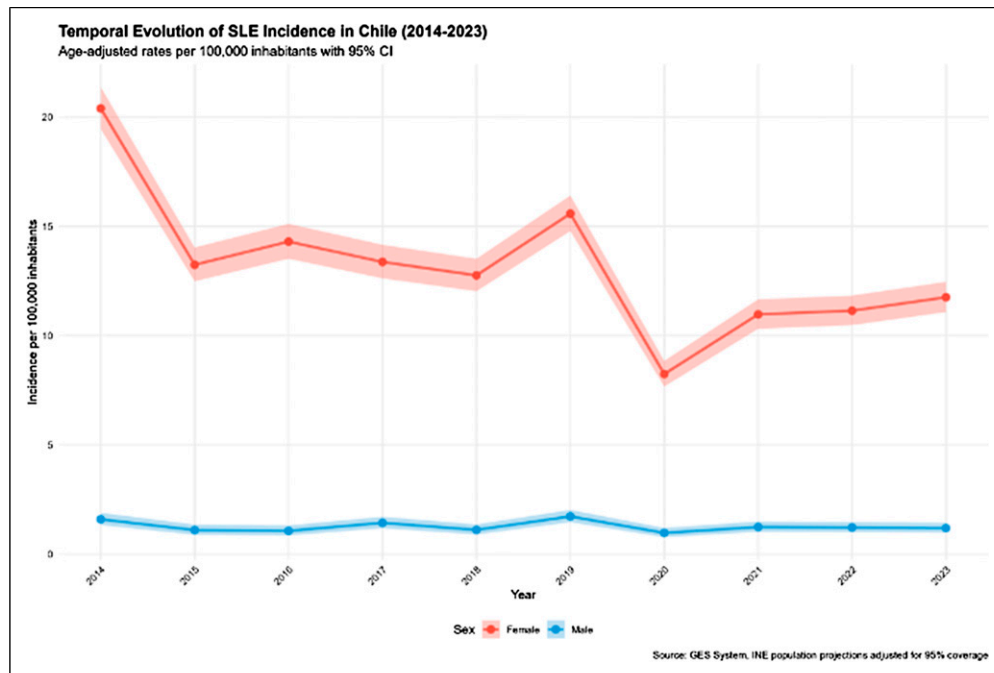


Figure 1. Temporal Evolution of SLE Incidence in Chile by Sex (2014-2023) Annual incidence rates of systemic lupus erythematosus (SLE) per 100,000 inhabitants stratified by sex from 2014 to 2023. Red line represents female incidence, blue line represents male incidence. Shaded ribbons indicate 95% confidence intervals calculated using exact Poisson distribution methods. Rates were calculated using INE population projections adjusted for 95% GES coverage. Abbreviations: GES, Specific Health Guarantees Program; INE, National Institute of Statistics; SLE, systemic lupus erythematosus.

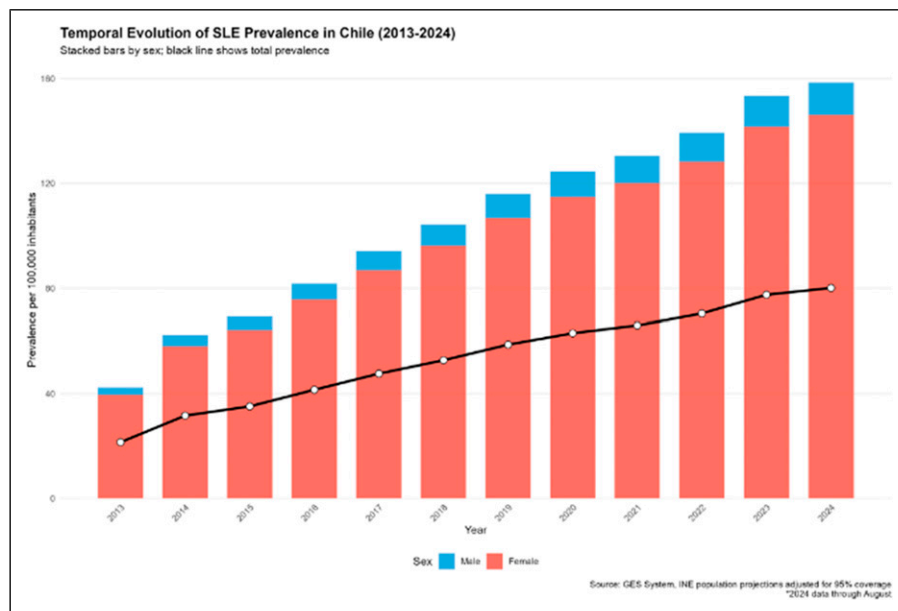


Figure 2. Temporal Evolution of SLE Prevalence in Chile by Sex (2013-2024) Prevalence of systemic lupus erythematosus (SLE) per 100,000 inhabitants from 2013 to 2024. Stacked bars show male prevalence (blue, lower portion) and female prevalence (red, upper portion). Black line with white markers represents total prevalence across both sexes. Rates were calculated using INE population projections adjusted for 95% GES coverage. The asterisk (*) for 2024 indicates incomplete yearly data due to 8-month observation period (January-August). Abbreviations: GES, Specific Health Guarantees Program; INE, National Institute of Statistics; SLE, systemic lupus erythematosus.

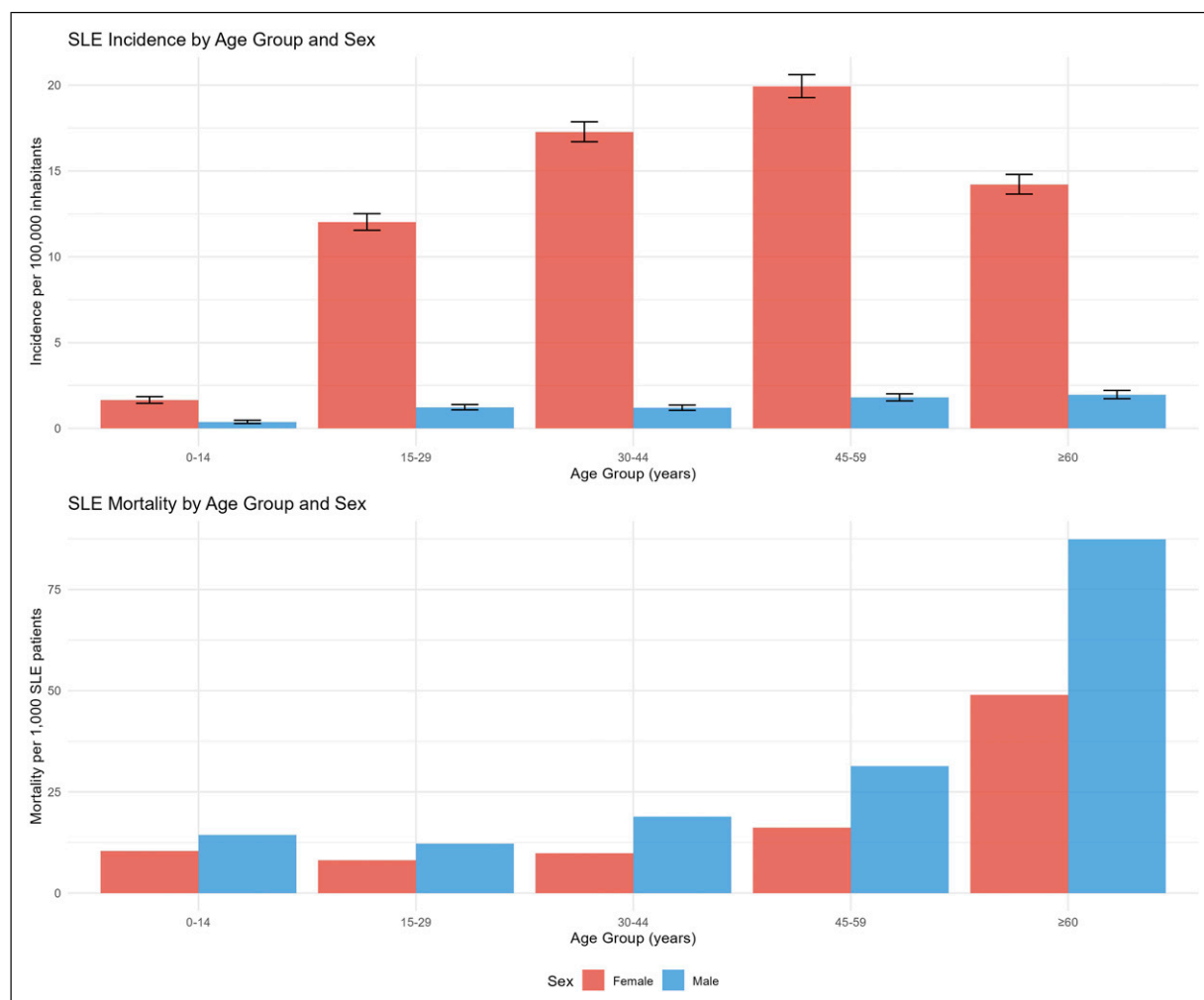


Figure 3. Sex-specific incidence and mortality of systemic lupus erythematosus by age group in Chile. Upper panel shows SLE incidence rates per 100,000 inhabitants by age group and sex, with female cases (red bars) and male cases (blue bars) displayed side by side. Error bars represent 95% confidence intervals. Lower panel shows mortality rates per 1000 SLE patients by age group and sex, with female rates (red bars) and male rates (blue bars) displayed side by side.

Age-stratified mortality analysis revealed progressive increases with advancing age in both sexes. In the youngest age group (0-14), mortality rates were 14.4 per 1000 for males and 10.4 per 1000 for females. This disparity widened substantially with age, reaching 87.4 per 1000 for males versus 49.0 per 1000 for females in the ≥ 60 age group. The consolidated mortality rate across both sexes increased from 12.2 per 1000 in the youngest group to 62.1 per 1000 in the oldest age group (Figure 3).

Sensitivity analysis for mortality estimation

To address potential overestimation through program discharge data, sensitivity analyses modeled different mortality assumptions. Under conservative assumptions (100% of discharges representing mortality), the median mortality

was 11.9 per 1000 SLE patients. Moderate assumptions (90% mortality, 10% non-fatal discharge) yielded 10.9 per 1,000, while liberal assumptions (70% mortality, 30% non-fatal discharge) produced 8.2 per 1000. Sex-specific patterns remained consistent across all scenarios, with men showing consistently higher mortality rates than women (Table 2).

Temporal patterns

The incidence time series revealed distinct temporal patterns. Following program initiation effects in 2013, incidence rates stabilized between 6.3 and 8.1 per 100,000 from 2014 to 2019. The year 2020 showed a marked decline to 5.8 per 100,000. Incidence rates in 2021-2023 returned to levels observed in 2014-2019.

Table 2. Sensitivity analysis for mortality estimation in SLE patients by sex.

Scenario	Assumption	Overall mortality per 1000 SLE patients	Male mortality per 1000 SLE patients	Female mortality per 1000 SLE patients	Rate ratio
		Median (IQR)	Median (IQR)	Median (IQR)	Male vs female (95%CI)
Conservative	100% fatal discharges	11.9 (7.2-18.8)	18.1 (6.8-38.7)	11.4 (7.1-19.0)	1.59 (1.40-1.80)
Moderate	90% fatal discharges/ 10% non-fatal	10.9 (6.4-17.0)	17.7 (6.3-36.1)	10.5 (6.5-17.3)	1.69 (1.48-1.92)
Liberal	70% fatal discharges/ 30% non-fatal	8.2 (4.9-13.8)	15.3 (5.1-29.8)	7.9 (4.8-13.2)	1.94 (1.68-2.23)

Mortality rates calculated using program discharges as proxy under different assumptions. Rate Ratios compare male to female mortality within each scenario. All Rate Ratios demonstrate statistically significant higher mortality in males ($p < .001$). Sex-specific patterns remain consistent across all scenarios despite varying absolute mortality estimates. Conservative scenario represents upper bound estimate; liberal scenario represents lower bound. Abbreviations; CI, confidence interval; IQR, interquartile range; SLE, systemic lupus erythematosus.

Summary statistics

Over the complete study period (2013-2024), a total of 17,520 SLE cases were identified, comprising 16,065 women (91.7%) and 1455 men (8.3%). Prevalence reached 91.3 per 100,000 beneficiaries in 2024.

Discussion

This study provides valuable insights into the epidemiology of Systemic Lupus Erythematosus (SLE) in Chile, addressing a significant gap in the literature on autoimmune diseases in South American populations. Analysis of Specific Health Guarantees Program (GES) data using population-adjusted denominators reveals a median annual SLE incidence of 7.1 per 100,000 population in Chile (IQR 6.3-7.7), with prevalence reaching 91.3 per 100,000 in 2024. The incidence pattern demonstrates an initial enrollment surge in 2013 representing the incorporation of previously diagnosed patients into the newly established GES program, followed by stabilization to consistent annual rates of 6.3-8.1 per 100,000 in subsequent years. The decline to 5.8 per 100,000 in 2020 was followed by recovery to pre-pandemic levels in 2021-2023.

Our mortality analysis, using program discharges as a proxy, estimated an overall rate of 11.9 per 1000 SLE patients (IQR 7.2-18.8). To address potential overestimation concerns, we conducted comprehensive sensitivity analyses modeling different assumptions about discharge mortality proportions. Under conservative assumptions (100% fatal), moderate assumptions (90% fatal), and liberal assumptions (70% fatal), mortality estimates ranged from 8.2 to 11.9 per 1000 SLE patients, indicating our primary analysis represents an upper bound estimate while maintaining clinical plausibility across scenarios. This methodological approach complements findings from Ritchie et al., who reported SLE as the direct cause of death at 0.42 per 100,000 inhabitants in Chile from 2016 to 2020.¹¹

SLE estimated incidence in Chile substantially exceeds rates reported in North America, where the Manhattan Lupus Surveillance Program documented 4.6 per 100,000 annual incidence.⁶ This aligns with generally higher incidence patterns observed throughout Latin America and among Hispanic populations in North America.^{6,7} The female-to-male ratio of 10.61:1 (Rate Ratio: 0.093, 95% CI: 0.088-0.098) confirms the well-established female predominance while providing statistically robust estimates. The significantly higher mortality observed in male patients (Rate Ratio: 1.756, 95% CI: 1.546-1.987) across all age groups aligns with international literature demonstrating more severe disease manifestations and poorer outcomes in men despite lower incidence.^{1,4,5} Significant regional variations exist within Chile, with the highest mortality rates observed in Arica and Parinacota, and Araucanía regions.¹¹ These geographic disparities merit further investigation into potential contributors including healthcare access inequities, genetic factors, and environmental exposures.

The incidence pattern demonstrates an initial artificial peak (24.9 per 100,000 in 2013) followed by stabilization to 8-10 per 100,000 in subsequent years. This early surge likely represents the enrollment of previously diagnosed patients into the newly established GES program rather than a true spike in new cases. Once stabilized, Chile maintained consistent annual new case numbers ranging from 1500 to 1,800, with a notable exception in 2020 when incidence dropped to 6.6 per 100,000. This decline coincided with the COVID-19 pandemic, suggesting potential impacts on healthcare access, resource allocation, and disease reporting mechanisms.

Conversely, our prevalence estimates remain lower than those reported in North America and some Asian countries, which document rates as high as 138.3 to 150 per 100,000 individuals.^{1,6} These differences likely reflect variations in healthcare infrastructure, diagnostic approaches, population genetics, environmental factors, and healthcare system maturation.³ The progressive prevalence

increase from 26.7 to 91.3 per 100,000 over the study period suggests both genuine case accumulation and improved program retention within the Chilean healthcare system.

Despite the established female predominance of SLE globally, the age-specific patterns of peak incidence in middle-aged women (30–59 years) observed in Chile remain consistent with international reports. However, the drivers behind the higher overall incidence rates in Chile compared to North American populations require further investigation. Potential explanations include genetic ancestry differences, environmental factors, healthcare system characteristics, or true population-based variations that warrant comparative studies across Latin American countries. The temporal decline in 2020 incidence raises questions about healthcare access effects on chronic disease diagnosis and surveillance systems during public health emergencies. Whether this represents delayed diagnosis, reduced healthcare utilization, or genuine incidence reduction remains unclear and merits longitudinal follow-up of affected cohorts.

Several limitations merit acknowledgment. As a retrospective analysis of administrative data, our study depends on healthcare provider reporting accuracy and completeness. Case identification relies on specialist clinical judgment rather than standardized research diagnostic criteria, potentially introducing variability across healthcare settings. The use of program discharge as a mortality proxy may overestimate true mortality rates despite sensitivity analysis mitigation. The exclusion of approximately 5% of the population (military and mutual insurance systems) may lead to slight underestimation of true population burden. The temporal limitation of incomplete 2024 data for incidence calculations prevents assessment of the most recent epidemiological trends.

Future research should focus on prospective data collection with standardized diagnostic criteria, validation of administrative data findings through clinical cohort studies, and investigation of regional disparities within Chile. Longitudinal patient follow-up would provide insights into disease progression, treatment responses, and survival patterns. Comparative studies with other Latin American countries would enhance regional epidemiological understanding and help identify factors contributing to the observed higher incidence rates.

Conclusion

Despite its limitations, this study represents a comprehensive effort to estimate SLE prevalence and incidence in Chile, providing valuable baseline data on the burden of this complex autoimmune disease in a Latin American context. We found an annual incidence of 7.1 per 100,000 population with demographic patterns consistent with international reports, including a female-to-male ratio of 10.61:1 and significantly higher

mortality rates in males across all age groups. Despite higher incidence rates compared to North America but lower prevalence estimates than some international studies, these findings contribute to the growing need for sustained epidemiological surveillance in Latin American regions.

Declaration of conflicting interests

IH works for AstraZeneca, but this whole work was made in her unpaid time, without this affiliation changing any of the contents of the manuscript or the public origins of its data.

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Declaration of Generative AI and AI-assisted technologies in the writing process

During the preparation of this work, the authors used Claude.AI to improve the redaction of this article. After using this tool, the authors reviewed and edited the content as needed and takes full responsibility for the content of the publication

Author Agreement Statement

All authors have approved the final article, agreed to be accountable for all aspects of the work, and acknowledge that all those entitled to authorship are listed as authors.

Data Availability Statement

The data that supports the findings is available in published articles.

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