Epidemiology of systemic sclerosis in Quebec, Canada: a population-based study

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Summary

Background Systemic sclerosis (SSc) is a systemic life-threatening autoimmune rheumatic disease. We aimed to assess the incidence, prevalence, mortality and spatiotemporal trends of SSc in Quebec, Canada with stratification by sex and age.

Methods SSc cases were identified from Quebec populational databases from 1989 to 2019. Negative Binomial (NB) Generalized Linear Models were used for age-standardized incidence rates (ASIR) analyses and NB random walk for prevalence and mortality. A Poisson Besag-York-Mollié regression model was used for spatial analysis.

Findings 8180 incident SSc cases were identified between 1996 and 2019 with an average age of 57.3 ± 16.3 years. The overall ASIR was 4.14/100,000 person-years (95%, Confidence Interval (CI) 4.05–4.24) with a 4:1 female predominance. ASIR increased steadily over time with an Average Annual Percent Change (AAPC) of 3.94% (95% CI 3.49–4.38). While the highest incidence rates were in those aged 60–79 years old among females and >80 years old among males, the highest AAPC (~10%) was seen in children. Standarized incidence ratios varied geographically between 0.52 to 1.64. The average prevalence was 28.96/100,000 persons (95% CI 28.72–29.20). The Standardized Mortality Ratio (SMR) decreased from 4.18 (95% CI 3.64–4.76) in 1996 to 2.69 (95% CI 2.42–2.98) in 2019. Females had a greater SMR until 2007 and males thereafter. The highest SMR was in children and young adults [31.2 (95% CI 8.39–79.82) in the 0–19-year age group].

Interpretation We showed an increasing trend in SSc incidence and prevalence and a decline in SMR over a 25-year period in Quebec. An uneven geographic distribution of SSc incidence was demonstrated.

Keywords: Systemic sclerosis; Incidence; Prevalence; Mortality; Epidemiology; Populational

Introduction

Systemic sclerosis (SSc) is a life-threatening fibrosing Systemic Autoimmune Rheumatic Disease (SARD).[1] SSc is usually diagnosed clinically in patients with skin thickening proximal to the metacarpophalangeal joints and the presence of SSc-related abnormalities (*e.g.,* Raynaud's phenomenon, SSc-specific antibodies, abnormal nailfold capillaroscopy).[1] Several advancements made in the last decade, such as the use of nailfold capillaroscopy and SSc-specific autoantibodies,

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Research in context

Evidence before this study

Systemic sclerosis (SSc) is a chronic, autoimmune disease characterised by fibrosis of the skin and internal organs. The diagnosis is usually established based on characteristic clinical manifestations and SSc-specific antibodies. The introduction of the American College of Rheumatology (ACR) and European League Against Rheumatism (EULAR) classification criteria in 2013 and the preliminary criteria for the very early diagnosis of SSc (VEDOSS) in 2011 further refined the diagnostic process enabling earlier identification and treatment initiation.

We searched PubMed for epidemiological studies assessing incidence, prevalence, or mortality of SSc patients for articles published before March 2023 without language restriction. We used the following search terms: (("systemic sclerosis" OR "scleroderma") AND ("incidence" OR "prevalence" OR "mortality" OR "epidemiology"). Additional articles from internet searches (Google) and reference searches of identified papers were included along with the authors' own clinical knowledge.

Recent systematic reviews demonstrated higher SSc incidence estimates in North America. Few assessed trends in incidence over time, especially after 2013, when classification criteria were developed. In terms of geographic distribution, several studies in Europe and only two cohort studies in North America outlined an uneven distribution. Hence, further assessment based on populational data in North America is warranted. Furthermore, limited studies suggested an improved survival in SSc patients in the last decades however, conflicting evidence exists regarding differences between males and females.

Added value of this study

Using populational data from Quebec, Canada, spanning over two decades (1996–2019), our study provides an in-depth analysis of the incidence, prevalence, and mortality rates of SSc, stratified by age and sex. Notably, we observed increasing trends in both incidence and prevalence, with the greatest increase in incidence over time noted among children. Mortality, while still higher in SSc patients compared to the general population (especially in younger age groups), has shown a decline during the study period, suggesting possible benefits from early detection and improved treatment strategies. Additionally, our spatial analysis demonstrated a non-uniform geographic distribution of SSc incidence in Quebec, suggesting the potential role of environmental or regional factors influencing disease risk.

Implications of all the available evidence

The increasing trends in SSc incidence and prevalence emphasize the need for heightened awareness and ongoing surveillance. The higher incidence rates in certain age groups, notably children, call for specialized care and research to understand the underlying causes. Further studies on environmental risk factors are warranted to identify possible contributing factors to the rising incidence and geographic disparities. Our findings on declining mortality provide a hopeful outlook, underscoring the potential benefits of early diagnosis and intervention. This comprehensive epidemiological analysis serves as a foundation for future research, disease awareness, and healthcare planning related to SSc.

have enabled an earlier diagnosis of SSc.[1] This led to the development of the new SSc classification criteria by the American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR) in 2013 as well as the preliminary criteria for the very early diagnosis of SSc (VEDOSS) in 2011.[1,2] VEDOSS criteria aim to diagnose SSc before fibrosis onset, enabling early intervention to reduce disease damage and enhance patient outcomes.[3]

Recent systematic reviews on SSc epidemiology highlighted growing incidence and prevalence trends worldwide, especially in North/South Americas and Oceania.[4,5] However, data post-2013 (EULAR classification criteria) and spatial analyses are scarce and hence, more recent and demographically diverse data are necessary. Furthermore, limited studies suggested an improved survival in SSc patients in the last decades, however additional, as well as age- and sex-specific data are needed.[6]

This study used data from 1989 to 2020 in Quebec, Canada, to delve into the incidence, prevalence, and mortality rates of SSc, breaking it down by sex and age. Spatial analyses were conducted to study geographic variability in incidence rates on a jurisdictional level.

Methods

Study design and data reporting were performed in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist.[7]

Data sources

Quebec, Canada, with a population of approximately 8.5 million, provides its citizens with universal health services. The health data is captured in provincial databases which are linked by a unique patient's identifier. Specifically, the *Fichier d'inscription des personnes assurées* (FIPA) includes age and sex (assigned at birth) of the registered individual, physician billing codes (based on the International Classification of Diseases 9th and 10th revision, ICD-9 and ICD-10 codes) are

recorded in the *Régie de l'Assurance Maladie du Québec* (RAMQ), hospitalization data in the *Maintenance et Exploitation des Données pour l'Étude de la Clientèle Hospitalière* (MED-ÉCHO) and mortality statistics in the Provincial Vital Statistics (PVS) database. Data on the provincial population distribution of Quebec by age and sex for all available years was sourced from RAMQ database (Supplementary Table S1).

Identification of patients with systemic sclerosis
The following, validated, case identification algorithm was used: ≥2 ICD-9 (710.1) and/or ICD-10 (M34) diagnostic codes for SSc at least 2 months apart and within 2 years; or ≥1 billing code (ICD-9 or ICD-10) for SSc in the RAMQ database by a specialist (rheumatologist); or ≥1 hospitalization with a primary or secondary diagnosis for SSc in MED-ECHO (ICD-9 or ICD-10).[8] Morphea (*i.e.,* localized scleroderma) codes were excluded to avoid misclassification.

Statistical analysis
Incidence
A 7-year washout was applied to remove prevalent cases. Crude incidence rate trends over time and stratified by age (0–19, 20–39, 40–59, 60–79, ≥80) and sex were estimated using NBGLM as it accommodates for data overdispersion.[9] These age groups were selected for consistency as there would be too few cases of pediatric SSc if smaller age intervals were used. Annual sex-specific age-standardized incidence rates (ASIR) from 1996 to 2019 were calculated using the provincial population distribution in the corresponding years as the standard population. Trends in sex specific ASIR and Average Annual Percent Change (AAPC) were assessed using NBGLM.[9]

Prevalence
To identify prevalent cases, a 7-year lookback window was used. Similarly, trends in crude prevalence rates from 1996 to 2019 were estimated using flexible negative binomial random walk (NBRW) models for the entire population and by sex. This model had a better fit compared to the NBGLM.

Mortality
Trends in sex-stratified annual age-specific Standardized Mortality Ratios (SMR) from 1996 to 2019 were estimated using the flexible NBRW model with the general Quebec population as the standard population (denominator, for the complete list refer to Supplementary Table S1). The models only controlled for age and sex.

Geographic distribution
Age and sex Standardized Incidence Ratios (SIR) were computed for each Forward Sortation Area (FSA, a 3-digit of a postal code) from 1996 to 2019. SIR represents the observed ASIR divided by the expected ASIR if the incidence rate of SSc in the FSA was not different from that of the general population during the study period (1996–2019). To protect patients' confidentiality, as per RAMQ/MED-ECHO rules, FSAs with fewer than a total of 5 residents of a certain age group and certain year were excluded from the analysis. The SIR per FSA was modeled using a Poisson Besag-York-Mollié (BYM) regression model with a spatially correlated random effect and smoothing.[10] Maps showing the geographic distribution of the SIR over the study period were created using ArcMap 10.1.

Software and statistical models
Negative Binomial Generalized Linear Models (NBGLM), random walk models and the BYM spatial model were fitted using the Integrated Nested Laplace Approximation (INLA) implemented in the R-INLA package. INLA is a method for approximate Bayesian inference that represents an efficient alternative to other Markov chain Monte Carlo methods. For all model parameters and hyperparameters, we used the default non-informative prior distributions in R-INLA. SMRs over the full study period were estimated using the epi.smr function in the epiR R package and confidence intervals (CI) for SMR were computed using the default Byar's approximation method. Additional details regarding the statistical models used can be found in the Supplementary Material.

Role of the funding source
The study sponsors were not involved in the design of the study; the collection, analysis, and interpretation of data; the writing of the report; or the decision to submit the paper for publication.

Results
Incidence
In total, 8180 individuals received a new diagnosis of SSc from 1996 to 2019. Most (80.3%; 6565/8180 were females. The median age (interquartile range, IQR) at diagnosis was similar for females [58.0 (22.0)] and males [59.0 (22.0)]. Of the study individuals, 2.3% were <20 years, 11.6% (20–39 years), 39.1% (40–59 years), 40.1% (60–79 years) and 7.0% (≥80 years).

The ASIR over the study period was 4.14/100,000 person-years (PYs) (95% CI 4.05–4.24) and was higher among females 6.61/100,000 PYs (95% CI 6.45–6.78) compared to males 1.63/100,000 PYs (95% CI 1.55–1.72). Among females, ASIR increased by more than 2.4-fold from 3.62/100,000 PYs (95% CI 3.37–3.88) in 1996 to 8.90/100,000 PYs (95% CI 8.40–9.45) in 2019 (Fig. 1). The AAPC for ASIR was 3.99% (95% CI 3.50–4.49) over the study period. Among males, a similar increasing trend was observed in ASIR from 0.87/100,000 PYs (95% CI 0.76–1.00) in 1996 to
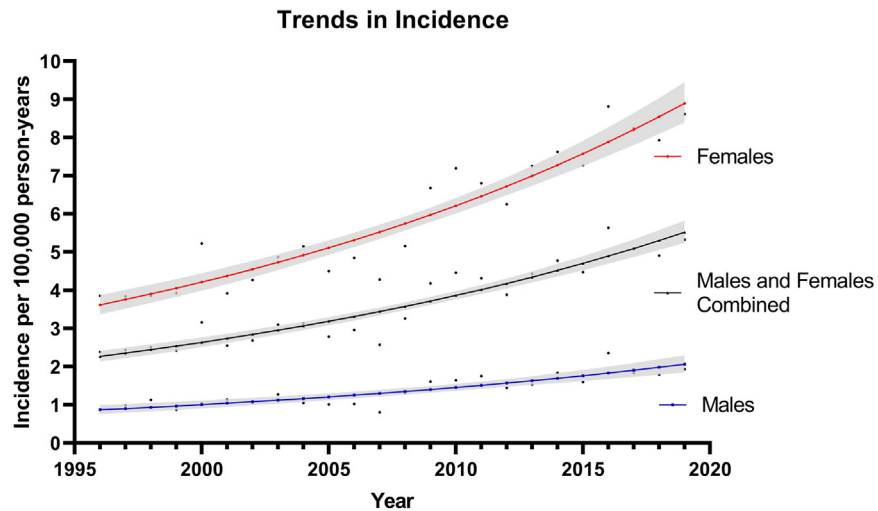
Trends in Incidence

Fig. 1: Age-standardized incidence rates (ASIR) over time (1996–2019) for females, males, and both. The grey shading depicts the 95% confidence intervals for the annual point estimates from the model. The points around the curve illustrate the true observed values for each year.

2.06/100,000 PYs (95% CI 1.85–2.30) in 2019 and a similar AAPC of 3.78% (95% CI 2.87–4.71). Additionally, ASIR F:M ratio increased over time (Supplementary Fig. S1).

A steady increase in the incidence rate of SSc over time was also observed for each age group for both sexes (Fig. 2). The highest incidence was consistently observed in females ages 60–79 years old with the highest rate of 19.85/100,000 PYs (95% CI 17.87–22.01) in 2019 (Fig. 2). The AAPC in this group was 3.3% (95% CI 2.41–4.17). However, the largest AAPC of 9.43% (95% CI 6.29–12.74) was observed
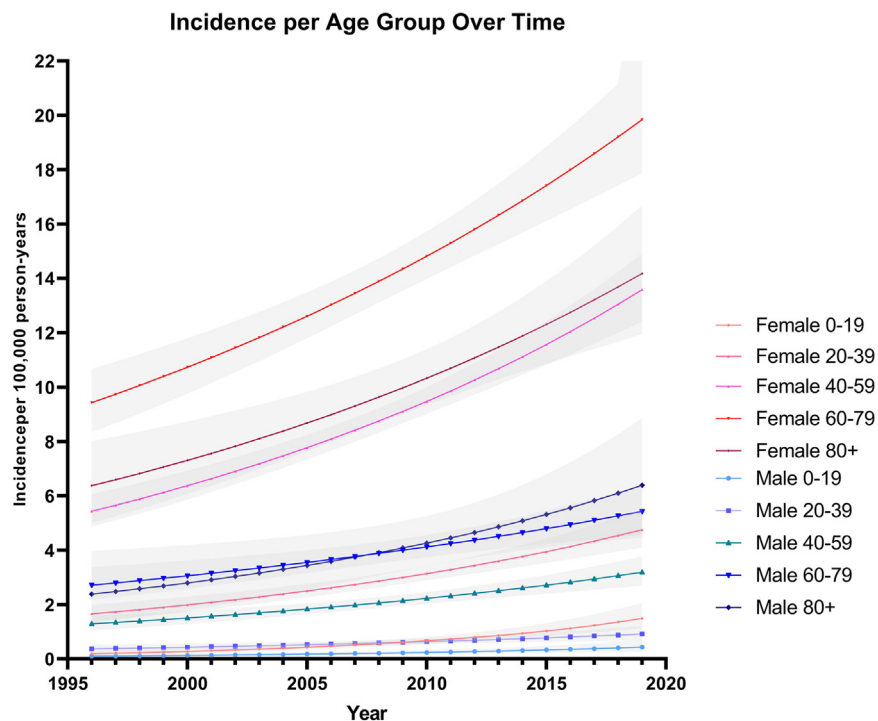
Incidence per Age Group Over Time

Fig. 2: Crude incidence rate for females over time (1996–2019) per age group (0–19, 20–39, 40–59, 60–79, 80+) for males and females. Grey shading depicts the 95% confidence intervals for the annual point estimates from the model.

among children (0–19 years old). For males, the greatest incidence rate was observed among the ≥80 years old group reaching the highest rate in 2019 with an incidence rate of 6.39/100,000 PYs (95% CI 4.46–8.86) and an average AAPC in this group of 4.49% (95% CI 1.02–8.04). The largest AAPC in males was also seen in children (0–19 years old) with an AAPC of 6.62% (95% CI 1.91–11.57).

Prevalence

The average prevalence over the study period was 28.96/100,000 persons (95% CI 28.72–29.20). Higher average prevalence was noted in females with 47.79 (95% CI 47.36–48.23) *vs.* 9.83 (95% CI 9.63–10.03)/100,000 persons in males. A steady increase in prevalence of SSc was noted for both sexes with rates varying from 23.26/100,000 (95% CI 22.20–24.39) in 1996 to 81.59/100,000 persons (95% CI 79.15–84.09) in 2019 in females (Fig. 3) and 4.96/100,000 (95% CI 4.53–5.42) in 1996 to 16.93/100,000 persons (95% CI 15.99–17.90) in 2019 in males. The AAPC from 1997 to 2019 was 5.6% for females (95% CI 5.36–5.88) and 5.5% for males (95% CI 5.04–5.97).

The prevalence in females increased at a faster rate compared to males until 2008 (Supplementary Fig. S1), at a similar rate from 2009 to 2016, and at a lower rate thereafter.

The highest prevalence for both sexes combined was observed in the 60 to 79 year old group (61.91/100,000 persons; 95% CI 61.07–62.75) (Fig. 4). The same age group also had the highest prevalence for females (98.68/100,000 persons; 95% CI 97.22–100.14) and males (21.01/100,000 persons; 95% CI 20.31–21.73).

Mortality

There were 2190 deaths reported in the cohort (26.8%). The median age at death (IQR) was 72.0 (17.0) [70.0 (18.0) for males and 73.0 (17.0) for females]. The overall SMR over the time period was 3.31 (95% CI 3.18–3.45) with a decrease from 4.18 (95% CI 3.64–4.76) in 1996 to 2.69 (95% CI 2.42–2.98) in 2019. The SMR for females over the study period was 3.29 (95% CI 3.14–3.45) with a peak SMR of 4.21 (95% CI 3.61–4.87) in 1996 and a decreasing trend over time to an SMR of 2.63 (95% CI 2.34–2.95) in 2019. The SMR for males was 3.40 (95% CI 3.10–3.71) with a peak at 4.14 (95% CI 3.20–5.25) in 1996 with reducing trends over time reaching an SMR of 2.94 (95% CI 2.41–3.55) in 2019 (Fig. 5). While initially females had higher SMR than males, this trend reversed in 2007 and until the end of the study, males had higher SMR compared to females. SMR was higher for younger age groups with the highest SMR of 31.2 (95% CI 8.39–79.82) in the 0–19-year age group. Distribution by age for males, females, and combined is shown in Fig. 6.

Geographic distribution

There were 401 FSAs in Quebec included in the study. Spatial analysis revealed an uneven geographic distribution of SIRs over Quebec (Fig. 7a and b). Higher SIR areas are observed both within the Greater Montreal Area (urban) as well as in more rural areas including G0K, G0J, G0E (Fig. 7b). Several high SIR FSAs were also found clustered in the southern part of Quebec. The overall SIRs with spatial modelling spanned generally between 0.52 and 1.64. The top 10 and lowest 10 FSAs are shown in Supplementary Table S2.
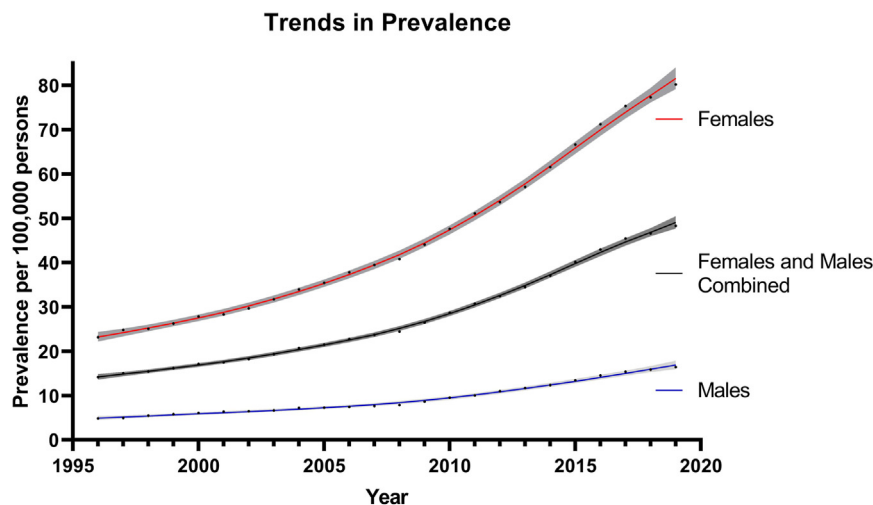

Fig. 3: Prevalence rates over time (1996–2019) for females and males. The peak prevalence for females was 81.59/100,000 persons with a 5.6% (95% Confidence Interval, CI 5.36–5.88) average annual percent increase compared to 16.93/100,000 persons for males with a 5.5% (95% CI 5.04–5.97). Average annual percent increase. Grey shading depicts the 95% CI for the annual point estimates from the model. The points around the curve illustrate the true observed values for each year.
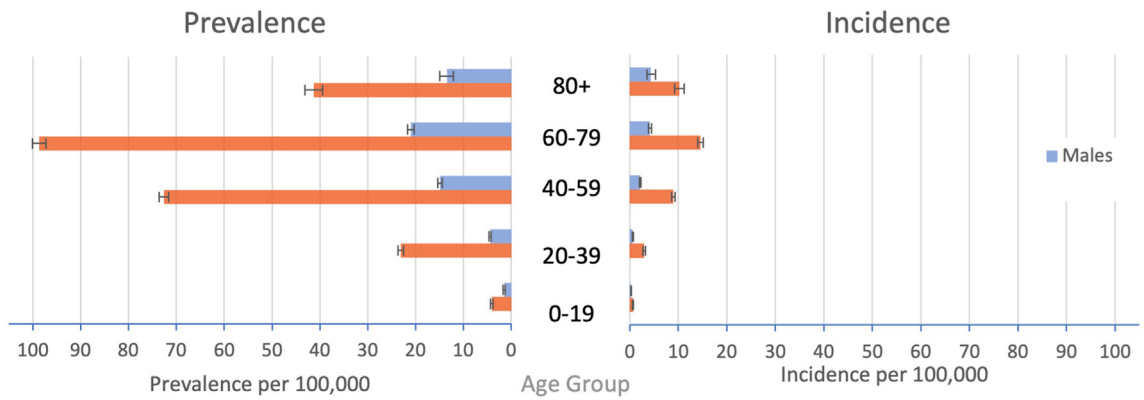
Prevalence / Incidence

Fig. 4: Average prevalence and incidence of systemic sclerosis per 100,000 persons and person-years, respectively, between 1996 and 2019 stratified by sex and age. The lines for each bar represent the 95% confidence intervals.

Discussion

Using populational data for the largest province in Canada by land area, Quebec, we demonstrated increasing incidence and prevalence rates, overall and by age and sex, of SSc from 1996 to 2019. However, SMR decreased steadily over time indicating improved survival likely due to earlier detection and better treatments. There was an uneven geographic distribution observed for the SIR in the province, the factors for which are not yet known and warrant further investigation.

We used a validated case definition with an estimated sensitivity of 80.5% and specificity of 94.9%.[8] Similarly,

other studies assessing concordance of incidence estimates based on 2013 ACR criteria *vs.* ICD codes revealed similar results and a study from Denmark revealed a positive predictive value of 94% compared to ACR/EULAR 2013 criteria as reference.[5,11]

Over the study period (1996–2019), the observed ASIR was 4.14/100,000 PYs (95% CI 4.05–4.24) with 4-fold greater incidence in females consistent with the annual incidence observed in North America (1.4–5.6/100,000 PYs),[12] but higher than pooled global estimates of 1.4/100,000 PYs.[5] ASIR of SSc gradually increased in our study between 1996 and 2019 with the peak ASIR reaching 8.90/100,000 PYs for females and 2.06/100,000
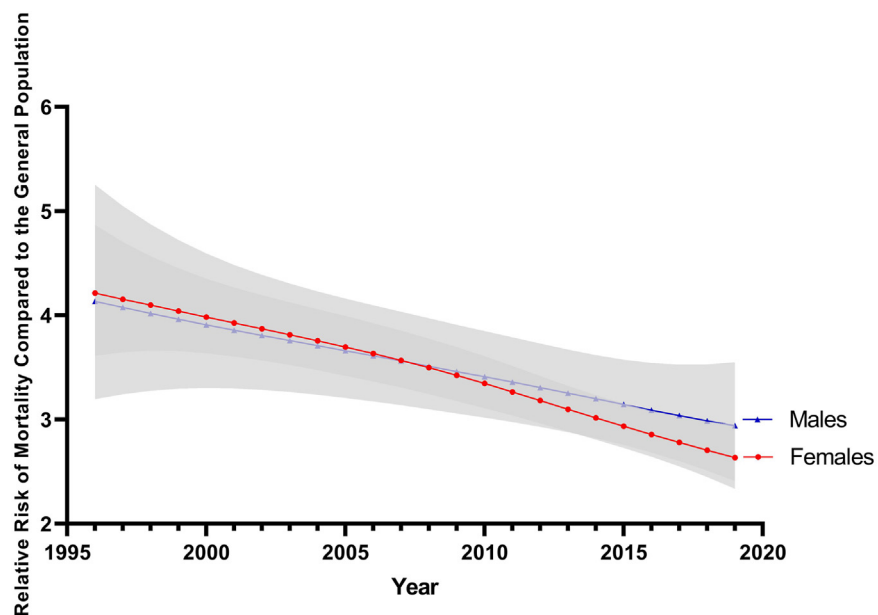

Fig. 5: Trends in standardized mortality ratios (SMR), standardized by age and sex, over time (1996–2019) for females and males. Grey shading depicts the 95% confidence intervals.
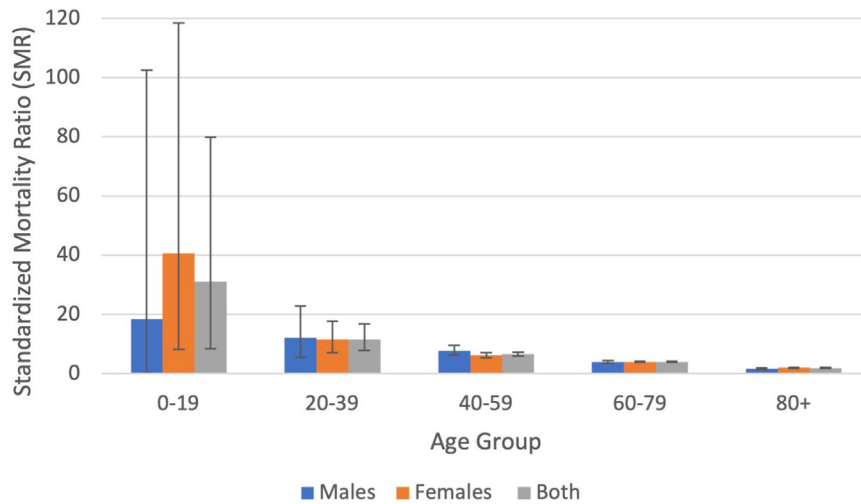
Fig. 6: Standardized Mortality Ratios (SMR) over the study period per age group and sex. The lines for each bar represent the 95% confidence interval.

PYs for males in 2019 with ~4% annual increase. The increasing incidence over time has also been reported in other studies focusing on SSc or autoimmunity in general.[5] A US study demonstrated that the prevalence of antinuclear antibody positivity (a hallmark of autoimmunity) increased from 11.0% (years 1988–1991) to 11.5% (1999–2004) to 15.9% (2011–2012) despite adjusting for multiple confounders and accounting for improved detection rates.[13] A study of over 22 million individuals with the 19 most common autoimmune
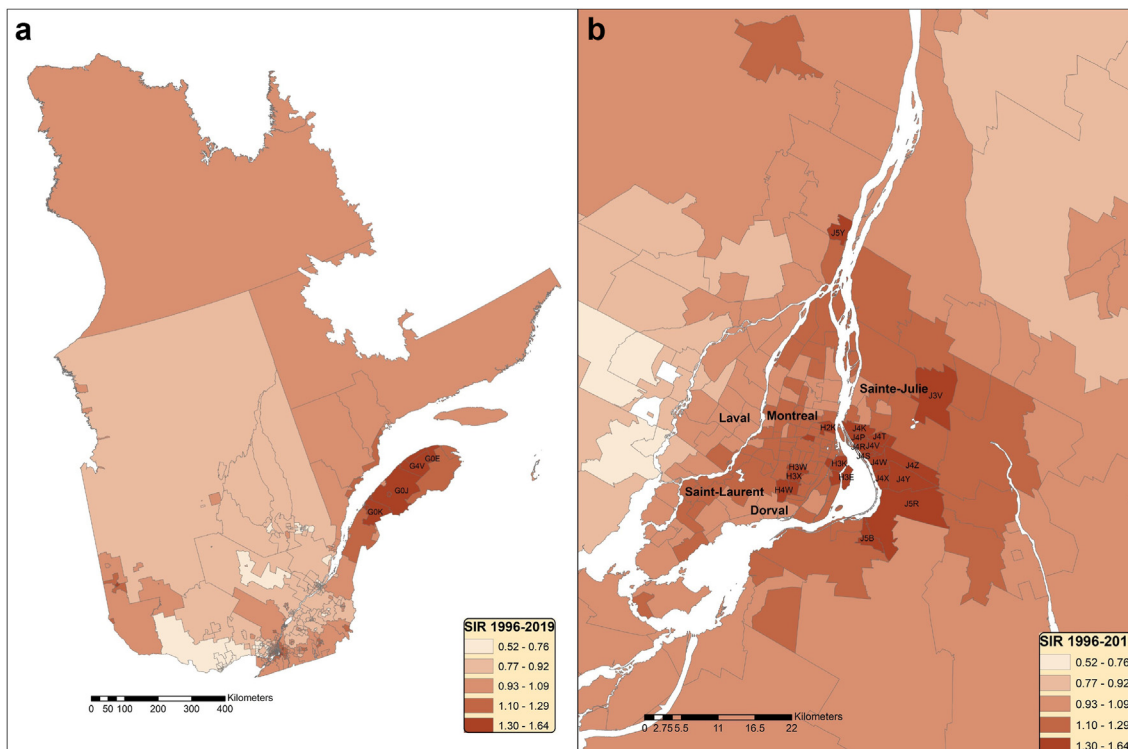

Fig. 7: (a) Geographic distribution of SIR in Quebec 1996–2019. (b) Geographic distribution of SIR in the greater Montreal area over the study period (1996–2019).

diseases showed that ASIR of any autoimmune diseases increased over time (incidence rate ratio in 2017/19 *vs.* 2000/02 of 1.04; 95% CI 1.00–1.09) and that 10.2% of the population had an autoimmune disease.[14] The hypothesized causes for this included alterations in our foods, xenobiotics, air pollution, infections, personal lifestyles, stress, and climate change.[15] Although the increase in incidence identified in our study could also in part be attributed to better diagnostic criteria and awareness of the disease, and hence more frequent diagnosis, in the context of rising autoimmune disease rates worldwide, it is likely that there is a true increase in SSc incidence.

In our study, the average age of SSc diagnosis was 57 years for both males and females. Among age groups, the highest incidence occurred in 60–79 years-old females and >80 years-old males. While there is very limited age-specific incidence data, in 2003, Mayes et al. similarly reported a peak SSc incidence in 65–74-year-old White females and 75-84-year-old White males.[16] A study in the UK found that 55-69 years-old had the highest crude incidence rate 1994–2013.[17] Previous studies have shown a higher incidence of SSc in African American individuals compared to Caucasians and higher association with diffuse cutaneous SSc and more severe disease manifestations/increased mortality.[18,19] The populational data used in our study, does not contain information on race or ethnicity as there is no standard reporting required and hence, we were not able to control for this factor in the analysis.

Children represented only 2.3% of all incident SSc cases in our study with an overall incidence of 0.43 /100,000 PYs. While this is slightly higher than the previously reported incidence rates for pediatric SSc ranging from 0.03 to 0.29/100,000 children-year, all of the previous studies in children were conducted prior to 2016.[20,21] We showed that the incidence of pediatric SSc had the highest AAPC of almost 10% which could account for this difference. To our knowledge, this increase in incidence hasn't been previously reported in children and needs to be investigated further in future studies and other populations.

The average prevalence in our study was 28.96/ 100,000 persons consistent with the reported rates in North America (13.5–44.3/100,000).[5,12] In fact, in North America, high prevalence estimates were seen in the majority of studies, despite considerable methodological variations among them, which indicates the occurrence of SSc is amongst the highest in the world.[5] Globally the data is heterogeneous with broad ranges of prevalence between 3.1 and 144.5/100,000 individuals with a pooled prevalence of 17.6/100,000 (95% CI 15.1–20.5).[5] An increasing prevalence over the study period is likely attributed to increasing incidence (as above) as well as improved survival over time.[22,23]

In our study, separation by sex revealed a prevalence rate of 58.7/100,000 in females and 12.2/100,000 persons in males (4.8-fold difference) consistent with previous research.[5] The highest prevalence was observed in the 60–79 year old group for both males and females. This is similar to other studies that found the highest prevalence in the 70–84 year old group.[17] Another study, however, found the highest prevalence in the 51-60 year old group with 61–70 closely following.[24]

The SMR reports the relative risk of death in patients with SSc compared to the general population accounting for age and sex. We observed a declining trend in SMR for both males and females over the study period and a decreasing risk towards older age groups. Mortality in females also appeared to decrease at a faster rate and hence by the end of the study period (2019) was lower compared to males. This corresponds with findings from a population-based study in the US over a 48-year period where initially, there was an increase in mortality between 1968 and 2000, followed by a decline between 2001 and 2015.[25] This trend was hypothesized to be attributed to multiple factors, including improved SSc recognition, with formalized classification criteria and autoantibody profiles being proposed in the 1980s.[16,26] The introduction of VEDOSS and a better understanding of the connection between autoantibody profiles and prognosis, has allowed for earlier diagnosis and treatment, leading to a decline in mortality.[3] Additionally, the recognition of adverse effects associated with the use of systemic steroids is SSc (*i.e.,* precipitation of renal crisis), discovery of new therapeutic agents and management strategies and consequent practice changes, have likely contributed to the improved survival seen in more recent decades.[6] Despite this improvement, mortality in patients with SSc remains higher than in the general population.[25]

Notably, in our study, since 2009, the SMR was greater in males. This is supported by the literature, which suggests that males are diagnosed later (as in our study), have more severe disease phenotype, and hence, worse outcomes with increased mortality. However, conflicting results have been published regarding mortality, where some of the rates/SMR in males and females are nearly identical, while in others, males have increased mortality (as seen in our findings).[27] A study in Italy reported a combined SMR of 2.8 (95% CI 1.9–3.8), with an SMR of 3.8 (95% CI 2.9–5.1) in males and 2.6 (95% CI 1.8–3.6) in females.[21] A New Zealand study showed an overall SMR of 2.59 (95% CI 1.67–4.01) which was higher in males (4.17, 95% CI 1.74–10.02 *vs.* 2.30, 95% CI 1.39–3.81).[28] Additionally, a study compared SMR between the inception cohort (recruited within 4 years of SSc disease onset) *vs.* prevalence cohort (all patients irrespective of disease duration) conducted in 3 registries including Canadian, Australian, and Spanish.[27] In Canada, the SMR for the inception cohort was found to be 5.1, compared to 3.8 in the prevalent cohort. Separation by sex showed that males had higher SMR in both inception and prevalent cohort (8.6 and 5.9, respectively) compared to females (4.4 *vs.* 3.4

respectively).[27] Prior to 2009, females had a higher SMR than males. Several factors could have contributed to this higher mortality in females in the 90s and early 2000s including lower disease awareness leading to a later diagnosis and limited treatment options.

Interestingly, we observed the highest SMR in the 0-19-year age group. Given the relatively lower prevalence of SSc in children, mortality data in this specific age group are limited in the literature. However, a Danish cohort study found the highest SMR in their 5–34 year age group, with an SMR of 13 (95% CI 2.7–37).[29] Determinants of mortality in pediatric SSc need to be further studied.

We observed an uneven geographic distribution of the SIR, indicating certain FSAs have an increased ASIR compared to the national average. Our previous study using the Canadian Scleroderma Research Group identified uneven geographic distribution of prevalence across Canada with higher than expected prevalence FSAs correlating with higher industrial density and increased levels of air pollution.[30] Another study from Massachusetts, USA, similarly identified non-uniform distribution of prevalent cases, correlated with proximity to hazardous waste facilities and oil release or disposal sites.[31] Otherwise, no other studies examined the spatial epidemiology of SSc in North America to our knowledge. In Europe, higher prevalence was found in Italy, Spain and Sweden compared to France, Netherlands, and Norway.[5] In our study, a visually higher incidence was seen in Northern and Eastern Quebec. While previous studies hypothesized the reasons for observed gradients or uneven distribution, there is a lack of objective evidence for the exact contributing factors. When occupational factors have been studied, only about 30% of patients reported occupational exposures as contributory, hence assessing risk factors at a populational level is of high interest and should be addressed in the future.[32]

This study provided an update on epidemiology of SSc in Quebec, Canada based on a populational database over a 23-year period. Our results should be interpreted within the study characteristics as we conducted a populational study using administrative databases. As SSc case ascertainment was based on ICD 9/10 codes, this may result in misidentification or missed cases. However, previous studies have validated this approach, including Quebec data, and the sensitivity and specificity are high.[8] Trends over time may be influenced by billing/coding practices among physicians which would not be accounted for. Based on the nature of the data, it is not possible to analyze clinical features such as subtypes of SSc, internal organ involvement, autoantibody profiles, and specific disease manifestations. Unfortunately, we did not have data on race/ethnicity for our population and we acknowledge this limitation. As this was a populational study, it was not possible to assess individual risk factors.

In conclusion, in this observational study, we identified increasing trends in incidence and prevalence of SSc in Quebec for both sexes and age groups with the highest incidence noted for females aged 60–79 years and >80-year-old males with the steepest incidence increase seen in children. While there was a progressive decrease in SMR over time, mortality remains higher than in the general population, in particular for the younger age groups. We also report an uneven geographic distribution of the incidence which could prompt future studies on risk factors.

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