Prevalence of systemic sclerosis in a French multi-ethnic county

V. Le Guern, A. Mahr, L. Mouthon, D. Jeanneret¹, M. Carzon¹ and L. Guillevin

Objective. To assess the prevalence of systemic sclerosis (SSc) in a French multi-ethnic population and to examine ethnic differences.

Methods. This survey was conducted in Seine–Saint-Denis County, a suburb of Paris, home to 1,094,412 adults (≥15 yr), among whom 26% are of non-European background with mainly northern and sub-Saharan African, Asian and Caribbean ancestries. The study period comprised the entire calendar year 2001. Patients were ascertained through four sources: public and private hospitals, general practitioners and community specialists, the French SSc patient support group, and the National Public Health Insurance System database. Only cases meeting either the 1980 ACR and/or LeRoy and Medsger’s classification criteria were included and assigned to three clinical subsets: limited (normal skin) (l), limited cutaneous (lc) or diffuse cutaneous (dc) SSc. Capture-recapture (CR) analyses using log-linear modelling were performed to correct for incomplete case finding.

Results. We retained a total of 119 patients with SSc, including 15 extrapolated from inaccessible files. CR analysis estimated that 54.2 additional cases were missed by all the sources. The overall SSc prevalence (per million adults) was 158.3 (95% confidence interval, 129–187); those of ISSc, lcSSc and dcSSc were, respectively, 32.3 (16–48), 83.1 (66–101) and 42.9 (25–60); and respective values for Europeans and non-Europeans were 140.2 (112–170) and 210.8 (128–293).

Conclusion. Regarding the heterogeneity of previously published estimates, this population-based survey using CR analysis might contribute to obtaining a better appraisal of SSc prevalence. Despite overlapping confidence intervals, the higher prevalence observed for non-Europeans could support potential influences of ethnic origin on the pathogenesis of SSc.

Key words: Systemic sclerosis, Epidemiology, Prevalence, Ethnicity, Capture-recapture analysis.

Systemic sclerosis (SSc) is a connective tissue disorder characterized by excessive collagen production resulting in skin and visceral fibrosis, and is closely associated with selective autoantibodies. The natural history of this disease shows marked heterogeneity regarding the extent of cutaneous and internal organ involvement, serological features and outcome [1–3]. To date, the aetiology of SSc remains uncertain, with knowledge obtained from numerous case-control studies suggesting variable links to genetic and environmental factors [4, 5].

Over the last three decades, SSc epidemiology in many parts of the world has been described in a number of articles, which reported widely divergent SSc prevalences ranging from 7 to 1580 per million inhabitants [6–20]. Further support for a putative role of geographical factors came from data suggesting that the SSc phenotype might differ among subjects from different ethnic backgrounds [1, 9, 21–27] and indicating a higher incidence of SSc in black versus white individuals [9, 23, 28]. However, most of those studies were based on hospital cohorts and hence subject to referral bias, and data on such ethnicity-related differences in population-based surveys remain scarce [9].

We therefore decided to undertake the present population-based survey in a French multi-ethnic county with the aims of adding another SSc prevalence estimate to the figures published hitherto and examining potential differences as a function of ethnicity.

Patients and methods

Study population

The study population consisted of residents of the Seine–Saint-Denis County, a northeastern suburb of Paris, France (Fig. 1), that served as the basis for a previous epidemiological study on primary systemic vasculitides [29]. This 236 km² area is part of the highly urbanized Parisian agglomeration (Île-de-France Region), where 81% of the employees work in the tertiary sectors (services, commerce, transportation) and 18% in industry and construction [30]. Furthermore, two airports (Le Bourget and Roissy/Charles-de-Gaulle), the latter being the largest French airport, are partially located in Seine–Saint-Denis County.

Derived from the 1999 national census estimates [31] and additional data provided by the Institut National des Statistiques et Etudes Economiques (INSEE), Seine-Saint-Denis County is home to 1,382,928 residents including 1,094,412 adults aged ≥15 yr (male-to-female ratio 0.94). Based on data on birth nationalities and place of birth of its residents, respectively, 231,797 of those adults had non-European nationalities and 48,524 had ancestors from the French Caribbean Islands or other French overseas counties and territories. Consequently, the size of the non-European adult population can be estimated to be 280,321 individuals (26% of the general adult population) originating in the Maghreb (Morocco, Algeria, Tunisia) (11%),

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sub-Saharan Africa (5%), Asian countries (5%), the French Caribbean Islands and other overseas countries and territories (4%), and other areas (America, Oceania/South Pacific) (1%) (Fig. 2). Comparison of the demographic characteristics of the non-European and European subgroups reveals a different age distribution, with the non-Europeans having a higher percentage of subjects aged 25–39 yr (36% vs 28%) and 40–59 yr (37% vs 32%), and a lower percentage of subjects aged ≥60 yr (9% vs 22%) (Fig. 3). Slight differences also exist with respect to the male-to-female ratio with a female preponderance for the Europeans (male-to-female ratio 0.89) and male preponderance for the non-Europeans (1.11).

Study period and sources of case ascertainment

The study covered the entire calendar year 2001. Patients were retrieved through four separate sources: (1) letters (with a stamped self-addressed envelope enclosed for the reply) and telephone follow-up to 30 departments of internal medicine, rheumatology, pneumatology, dermatology, and nephrology including all the public hospitals, two of the largest private clinics of the study area and one university hospital in the area not in consideration, as well as five additional selected hospital departments of the Ile-de-France region specializing in SSC (referred to as hospitals); (2) sending follow-up questionnaires (with a stamped self-addressed envelope for the reply) to all general practitioners (n = 1100) and community specialists—rheumatologists, pneumologists, angiologists and dermatologists (n = 123)—registered in the College for Physicians of the area (referred to as community physicians); (3) members of the French SSC patient support group (Association des Sclérodérmiques de France); and (4) data from the main fund (regime general) of the Public Health Insurance System of Seine–Saint-Denis County. For individuals with costly or chronic diseases, e.g. SSC, the French Public Health Insurance system accords, upon application, full exoneration of payment for all treatments associated with their disease. Based on an individual’s professional activity, the French Public Health Insurance System distinguishes three branches: the main fund covers salaried employees and insures 93% of the Seine–Saint-Denis residents, and two other funds cover the self-employed or agricultural workers.

We asked these four sources to report any known adult (aged ≥15 yr) with SSC living in the study area during the calendar year 2001. Questionnaires sent to the community physicians requested that they report such cases with the first three initials of the patient’s last name, the first two initials of the first name, gender, birth date, residential postal code, date of patient’s last assessment and, if pertinent, the address of the hospital where they are/had been followed. Members of the patient support group were recruited after their oral consent to participate had been obtained by a telephone call from one of the group’s board members. The Public Health Insurance System provided semi-anonymous data (initials, gender, birth date, residential postal code) for patients registered by 31 December 2001, with the codes 710.0 or M34 of the 9th International Classification of Diseases (ICD-9) and the revised ICD-10. For patients recruited exclusively through this source, a follow-up letter was sent, with a subsequent telephone call to non-responders, by a Public Health Insurance System physician to obtain consent to be contacted by the clinical investigators.

Inclusion criteria

Once the treating physician’s accord had been obtained, we carefully reviewed the hospital charts or the information provided by the community physicians to verify the diagnoses of all the patients. For each case, standardized data forms were filled out collecting the following items: (1) demographic data including date of birth, gender, ethnic background and location of residence; (2) date of first diagnosis of SSC by any physician and (3) clinical and laboratory findings, and, when available, results of nailfold capillaroscopy, pulmonary function tests and pulmonary computed tomography (CT) scans. A patient’s ethnic background

FIG. 2. Distributions of the ethnic backgrounds of the study population of Seine–Saint-Denis County (A) and 104 patients with SSC (B).
was defined according to that of their first-degree relatives and required that both parents be of the same ethnic group. Raynaud's phenomenon (RP) and nailfold capillaroscopy abnormalities were considered to be present only when a hospital-based specialist corroborated the diagnosis. Serological tests were assessed with respect to the search for antinuclear antibodies (ANA), anticientromere antibodies (ACA) and/or antitopoisomerase I (anti-Scl70) antibodies. Interstitial lung disease was defined according to CT images suggestive of parenchymal involvement combined with, when available, a restrictive airway pattern on pulmonary function tests.

To ensure homogeneous classification, all the data were recorded by the same physician (VLG). A case was definitively included in the study when he/she was a resident of Seine–Saint-Denis County for at least part of 2001, was aged ≥15 yr and fulfilled the 1980 American College of Rheumatology (ACR) diagnostic criteria [32] and/or those established by LeRoy and Medsger [33] for classification purposes of early SSc. ACR criteria require one major criterion, taut skin involvement proximal to the metacarpophalangeal joints, or two or more minor criteria among the following three items: sclerodactyly, digital pitting scars or loss of substance of the distal finger pad, bibasilar pulmonary fibrosis. LeRoy and Medsger's criteria require objective RP as a major criterion combined with nailfold capillary abnormalities (dilatation and/or avascular areas) and/or presence of SSc-associated autoantibodies [33]. Patients with overlap features of systemic lupus erythematosus (e.g. facial rash, photosensitivity, serositis, glomerulonephritis) or polymyositis (e.g. elevated creatinine kinase levels combined with a myopathic pattern on electromyography or histologically proven myositis) and antiribonucleoprotein (RNP) antibodies alone were considered to have undifferentiated mixed connective tissue disease and were not accepted for this study.

The disease duration was calculated from the date at which a given patient first fulfilled one of the abovementioned classification criteria to the time of the last update of the patient's status after 1 January 2001. According to the presence and the extent of skin involvement at the last time of disease assessment, the patients were categorized into three distinct SSc subtypes: limited (l) (normal skin), limited cutaneous (lc) (sclerodactyly or skin thickening distal to the elbows) or diffuse cutaneous (dc) (skin thickening proximal to the elbows and/or of the trunk) [33]. The presence of taut facial skin did not differentiate between lcSSc and dcSSc.

Statistical analyses

Capture-recapture analysis was used to overcome potential incomplete case finding so as to correct the calculation of prevalence rates. As described elsewhere [29, 34], this technique takes advantage of duplicate information derived from multiple, disaggregated sources of case ascertainment and provides estimates of the number of cases missed by any one source, and thus of the total number of cases in a given area. For the present study, cases were considered duplicates upon concordance of the first three initials of the last name, the first two initials of the first name, date of birth, gender and the residential postal code. To obtain a conventional three-source capture-recapture design, the two numerically least important sources of case retrieval (community physicians and the patient support group) were pooled into a single source.

Log-linear modelling was used to assess—and eventually to adjust for—potential violations of the assumptions of intersource independency and equal catchability [35, 36]. Source dependency was investigated by constructing the eight models accounting for all possible two-source dependency interactions. Based on the results of maximum of likelihood statistics [deviance $G^2$, Akaike information criterion (AIC), Bayesian information criterion (BIC)] and the weighted BIC [37], we selected the model that best fitted the data and, when ambiguous, the one that contained the fewest interaction terms (principle of parsimony). Subsequently, we verified the assumption of equal catchability by assessing the representativeness of the sources. For each of the three sources used for capture-recapture analysis, we analysed the patient distribution with respect to SSc subtype (l, lc or dc), ethnic background (European or non-European origins) and disease duration (stratified into two groups according to the median
analyses were two-tailed and performed using the PROC GENMOD procedure. All statistical when appropriate, Fisher's exact tests. Log-linear modelling was performed using the PROC GENMOD procedure. All statistical analyses were two-tailed and P values <0.05 were considered to be significant. Confidence intervals were calculated at the 95% level (95% CI).

Ethical aspects
This study was approved by the Commission Nationale de l’Informatique et des Libertés (National Commission of Informatics and Freedom) (no. 792764).

Results
Response rates and number of patients ascertained
All the contacted hospital departments participated in the study and 91 patients were recorded by this source. Concerning the questionnaires sent to the community physicians, responses from 57% of the general practitioners and 57% of the specialists yielded 74 cases. All 13 patients identified through their membership of the patient support group consented to participate in the study and 102 patients were registered by the Public Health Insurance System as having SSc. After excluding intersource matches (according to the abovementioned matching criteria), a total of 218 cases had been identified by at least one source. Among those, case records were inaccessible for 34 patients, all exclusively retrieved from the Public Health Insurance System, due to refusal or non-response to our request for study participation.

Review of the 184 medical charts studied in detail led to the exclusion of 80 additional cases given other diagnoses (n = 33), not fulfilling the diagnostic criteria (n = 27), living outside the area studied (n = 12), having been diagnosed after the year 2001 (n = 4) or because of death before 2001 (n = 4). The remaining 104 cases satisfying our inclusion criteria comprised 17, 64 and 23 cases with lSSc, lcSSc and dcSSc respectively, and 32 patients of non-European background. To estimate the number of definite SSc cases among the 34 patients whose medical files could not be screened, we calculated the proportion of patients who met our diagnostic criteria among the other individuals ascertained exclusively through the Public Health Insurance System and to whose medical charts we had access. The obtained value of 0.44 was then multiplied by 34, yielding 15 additional hypothetically definite SSc cases including, according to similar algorithms, two, nine and four cases with lSSc, lcSSc and dcSSc, respectively, and five individuals of non-European background.

Ultimately, we retained a total of 119 patients, including 19 lSSc, 73 lcSSc and 27 dcSSc, and 37 individuals of non-European origin.

Table 1. Main characteristics of 104 patients with SSc

<table>
<thead>
<tr>
<th>SSc subtype</th>
<th>n</th>
<th>Age at onset (yr) (mean ± s.d.)</th>
<th>Female gender (%)</th>
<th>Non-European ancestry (%)</th>
<th>Disease duration (yr) (mean ± s.d.)</th>
<th>Abnormal nailfold capillaroscopy (%)</th>
<th>Interstitial lung disease (%)</th>
<th>Autoantibodies (%)</th>
<th>Classification criteria met (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All SSc</td>
<td>104</td>
<td>50.2 ± 14.7</td>
<td>92</td>
<td>31</td>
<td>8.4 ± 7.7</td>
<td>100</td>
<td>87 (n = 68)</td>
<td>40 (n = 101)</td>
<td>ANA 96</td>
</tr>
<tr>
<td>lSSc</td>
<td>17</td>
<td>58.9 ± 14.1</td>
<td>94</td>
<td>12</td>
<td>6.7 ± 5.7</td>
<td>100</td>
<td>85 (n = 13)</td>
<td>0 (n = 15)</td>
<td>ACA 100</td>
</tr>
<tr>
<td>lcSSc</td>
<td>64</td>
<td>51.0 ± 14.5</td>
<td>92</td>
<td>30</td>
<td>9.1 ± 8.5</td>
<td>100</td>
<td>86 (n = 44)</td>
<td>38 (n = 63)</td>
<td>Anti-Scl70 89</td>
</tr>
<tr>
<td>dcSSc</td>
<td>23</td>
<td>41.6 ± 11.4</td>
<td>91</td>
<td>48</td>
<td>7.8 ± 6.7</td>
<td>100</td>
<td>91 (n = 11)</td>
<td>70 (n = 23)</td>
<td>Anti-Scl70 100</td>
</tr>
</tbody>
</table>

ANA, antinuclear antibodies; ACA, anticientromere antibodies; RP, Raynaud’s phenomenon.

1 Number of patients for whom this information was available.

Table 1 summarizes the main demographic, clinical and laboratory data, disease duration, and the frequencies of patients fulfilling the ACR and LeRoy and Medsg’s classification criteria for the 104 patients whose medical files could be examined. SSc was diagnosed in a university hospital for 101 of those patients and in private clinics for the remaining three. Results are shown for the entire cohort and with respect to the SSc subtype. Notably, eight of the 17 lSSc patients had both abnormal nailfold capillaroscopy and positive ACA and/or anti-Scl70 serologies (one patient was positive for both ACA and Scl70 antibodies); moreover, 13 cases were found to have additional characteristic manifestations of SSc with telangiectasia (n = 7), calcinosis (n = 3), digital infarctions (n = 2), clinical symptoms consistent with oesophageal hypomotility (n = 6) and/or pulmonary hypertension as assessed by Doppler echocardiography (n = 1). The 32 individuals of non-European ancestry came from Maghreb (n = 17), sub-Saharan Africa (n = 7), Asia (n = 7) and the French Caribbean islands (n = 1), i.e. presenting a distribution similar to that of the background population (Fig. 2); none of them had been diagnosed with SSc before living in continental France. Comparison of disease expression according to the ethnic background showed that non-Europeans were significantly younger at disease onset (45.3 ± 14.3 vs 52.4 ± 14.5 yr; P = 0.02), more frequently diagnosed with dcSSc (34 vs 17%; P = 0.04) and tended more frequently to have anti-Scl70 antibodies (38 vs 20%; P = 0.05) and interstitial lung disease (53 vs 33%; P = 0.06). Conversely, the sex ratio (P = 0.25), mean disease duration (P = 0.89) and ACA positivity (41 vs 46%; P = 0.58) did not differ between individuals of non-European and European ancestry.

Patient data
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**Capture–recapture analysis**

Fig. 4 shows the relative contributions of the three individual sources used for capture–recapture analysis to identifying the 119 retained cases.

The results of the log-linear regression model including the different 2-source-dependency interactions are reported in Table 2. The model with a single interaction term between the hospitals and the community physicians/patient support group had a non-significant $P$-value for $G^2$, the lowest AIC and BIC values, and an estimated number of cases missed close to that estimated by the weighted BIC, and was thus selected as the best-fitting model. This model estimated the number of cases missed by any source to be 54.2 and, thus, a 69% completeness of case ascertainment.

Examination of the characteristics of the three sources with respect to the variables chosen to potentially generate unequal catchability showed that case capture was heterogeneous regarding the ethnic background (results not shown). In fact, for the community physician/patient support group source, the percentage of non-Europeans observed was significantly lower than expected by the log-linear model (14% vs 31%; $P = 0.02$). However, the log-linear model including the corresponding interaction term (community physician/patient support group × ethnic background) yielded an only slightly better fit to the data but did not affect the estimated number of cases missed (Table 2). Applying the principle of parsimony, inclusion of this interaction term was consequently restricted to the capture–recapture estimates stratified for the ethnic backgrounds (Table 2).

Eventually, capture–recapture analysis estimated the total number of cases to be 173.2 and, after stratification, 35.3 lSSc, 91.0 lcSSc and 46.9 dcSSc. The stratified capture–recapture analysis estimated that a total of 114.1 patients were of European ancestry with 59.1 cases of non-European origin (Table 2).

**Prevalence estimates**

Table 3 summarizes the derived prevalence estimates for all SSc, and according to the SSc subtype and ethnic origin for the adult population of the study area. Thus, the overall prevalence estimates for the non-European population (210.8; 95% CI 128–293) was found to be 1.5-fold higher than that for the Europeans (140.2, 95% CI 112–170), even though the 95% CI intervals overlapped.

**Discussion**

This population-based survey has enabled us to estimate the prevalence of SSc in the Seine–Saint-Denis County, France, to be...
TABLE 3. Capture-recapture estimates of the prevalence of SSc in Seine–Saint-Denis County

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Prevalence (per 1,000,000 adults) [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>All SSc</td>
<td>158.3 [129–187]</td>
</tr>
<tr>
<td>SSc subtype</td>
<td></td>
</tr>
<tr>
<td>ISSc</td>
<td>32.3 [16–48]</td>
</tr>
<tr>
<td>lcSSc</td>
<td>83.1 [66–101]</td>
</tr>
<tr>
<td>dcSSc</td>
<td>42.9 [25–60]</td>
</tr>
<tr>
<td>Ethnic background</td>
<td></td>
</tr>
<tr>
<td>Europeans</td>
<td>140.2* [112–170]</td>
</tr>
<tr>
<td>Non-Europeans</td>
<td>210.8* [128–293]</td>
</tr>
</tbody>
</table>

Non-European/European prevalence ratio = 1.5.

158.3 per million adults. To the best of our knowledge, this study is also the first prevalence estimate based on a European multi-ethnic population, with our results demonstrating a slightly higher prevalence among the subjects of non-European ancestry.

Using multiple sources of case retrieval is a major prerequisite for achieving complete case identification in population-based surveys. For the present study, patients were recruited through four distinct sources, including inquiries addressed to hospital departments, general practitioners and community specialists, and data provided by a patient support group and the Public Health Insurance System. The latter source, in particular, referred a number of patients who would have been overlooked by case retrieval based exclusively on direct medical care dispensers, an observation that emphasizes the importance of the selected sources implying diverse routes of patient identification. Because of issues of confidentiality, however, the diagnoses of 34 subjects recorded as having SSc in the Public Health Insurance database could not be verified. We therefore assumed that these patients comprised the same proportion of definite SSc cases as the other subjects retrieved uniquely through the same source.

Moreover, we performed capture-recapture analysis to appreciate the degree of completeness of case finding and to correct our estimates for potential under-ascertainment. In a setting with at least three separate case-retrieval sources being available, log-linear modelling can be applied to accurately handle violations of this method's major assumptions of independence and homogeneous case-capture among sources. Because of the exponential relationship between the number of sources included and the number of source interactions to assess, we pooled the two numerically least important sources (community physicians and patient support group) to obtain the logistically most effective three-source design. Finally, capture-recapture analysis estimated the crude rate of completeness of patient identification to be 69%, a value that might be a reflection of the difficulty of achieving exhaustive case ascertainment in cross-sectional studies.

Disease definitions used in this study were based on the 1980 preliminary ACR classification criteria for SSc [32] and those recently proposed by LeRoy and Medsger [33]. Although it is widely accepted that ACR criteria enable dcSSc to be classified with a high sensitivity, major criticism has been expressed concerning their inadequate incorporation of lcSSc [3, 40, 41]. Authors of earlier epidemiological surveys resolved this problem by using—in addition to the ACR criteria—other specifically designed criteria with the purpose of classifying patients with lcSSc [3, 40, 41]. For the present study, we addressed this issue by applying the LeRoy–Medsger criteria [33], which may represent the currently most valuable approach for consensual classification of lcSSc. Although they have not yet been validated, our findings based on the 104 patients whose medical charts could be reviewed indirectly indicated that these criteria assure classification of lcSSc with high sensitivity. Indeed, 69% of the patients considered to have lcSSc satisfied the ACR criteria (Table 1), a result that is in agreement with previously reported sensitivities of 75% [3] and 79% [41] for the ACR criteria for patients that had been diagnosed with lcSSc by an expert clinician.

Another issue raised at the time this study was designed was whether or not we should include patients presenting with features of SSc but no sclerodermatous skin changes. Referred to as sine scleroderma SSc [2, 42], normal skin SSc [43] or limited SSc (ISSc) [33], there has been an increasing tendency to include this form in the spectrum of SSc disease and we eventually adopted such a three-subtype system categorizing patients as having ISSc, lcSSc or dcSSc [33]. In response to the criticism of the LeRoy–Medsger criteria as lacking specificity to allow classification of ISSc as definite SSc [44], most of the ISSc cases that we identified also had other signs typical of SSc, e.g. telangiectasia, calcinosis, digital infarctions and/or internal organ involvement. According to stratification analysis, ISSc accounted for 20% of our overall prevalence estimate, a finding that would suggest the true frequency of this subtle variant of SSc to be higher than previously described based on hospital cohorts [42, 43].

It is likely that the heterogeneity of published SSc prevalence estimates might partly have resulted from differing methodologies. Studies retrieving patients through single sources of ascertainment [10, 11, 16, 19, 20] and/or using the ACR criteria alone to define cases [10, 11, 16, 19] might have underestimated the real frequency of SSc, whereas the inverse effect could be suspected by inclusion of overlap diseases [6, 14] and/or estimates based on longer study periods [8, 9, 13]. The highest reported prevalence figures of 750 [19] and 1580 per million [12] were derived from sample surveys based on the screening of SSc patients among individuals with self-reported, and then confirmed, RP, and subsequent multiplication of the observed percentage by that of RP in the general population. Notably, those studies identified only a small number of SSc cases and it could also be hypothesized that their results might have been positively biased by an increased tendency of individuals suffering from SSc to participate in those investigations. Regarding the currently available data, it has been postulated that SSc might be more frequent in the US than in Europe or Japan [5] and, although among the highest reported for a European area, our estimate would roughly fit this gradient (Table 4).

This study moreover aimed to look for ethnic disparities in the prevalence of SSc. So as to obtain sufficiently large denominators allowing meaningful statistical analysis, we approached this objective by pooling the inhabitants with a non-European background in a single population. Although these results must be interpreted with caution because of overlapping confidence intervals, the SSc prevalence for the non-Europeans was 1.5-fold higher than that for those of European origin. Further prudence is warranted because our non-European population comprised a higher percentage of middle-aged individuals at risk for SSc, although this potential confounding effect might have been counterbalanced by the higher male-to-female ratio. Notably, our results would be consistent with previously reported 1.2-fold higher prevalence in black versus white individuals [9] and 1.8-fold higher incidence in black versus white women [23]. Additionally, in accordance with previous findings in African–American [1, 9, 23, 25–27], Hispanic–American [27] or Asian [21, 24] SSc patients, as compared with white Americans [1, 9, 21, 23, 25–27] or Australians [24], the non-Europeans were significantly more likely to have dcSSc [9, 23, 24, 27], anti-Scl70 antibodies [24–26] and interstitial lung disease [21, 25] and were younger at diagnosis [1, 9, 23, 25], with this latter finding potentially also being accounted for by the younger age structure of the non-European population.

Thus, these results would support the idea of ethnicity influencing the susceptibility to develop SSc and its clinical profile. Admitting this assumption, a fundamental—and as yet unresolved—is whether this effect of ethnicity on SSc might reflect a genetic or, alternatively, an environmental input [45]. The disparate geographical origins of the non-European patients...
<table>
<thead>
<tr>
<th>References</th>
<th>Study area</th>
<th>Study period</th>
<th>Size of study population</th>
<th>Methods of case ascertainment</th>
<th>Inclusion criteria</th>
<th>Prevalence (per 1,000,000)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Michet et al. [20]</td>
<td>Rochester, MN (USA)</td>
<td>1980</td>
<td>56,447</td>
<td>Hospital-record review</td>
<td>ACR</td>
<td>138</td>
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<tr>
<td>Mayes et al. [9]</td>
<td>Detroit tricounty area, MI (USA)</td>
<td>1989–1991</td>
<td>2,917,000</td>
<td>Multiple sources, capture-recapture analysis</td>
<td>Not stated</td>
<td>242–276 c</td>
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<tr>
<td>Maricq et al. [19]</td>
<td>South Carolina (USA)</td>
<td>Not stated</td>
<td>6998</td>
<td>Multistage population survey</td>
<td>ACR</td>
<td>190–750</td>
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<tr>
<td>Englert et al. [15]</td>
<td>Sydney</td>
<td>1988</td>
<td>Not stated</td>
<td>Multiple sources</td>
<td>ACR and study-specific</td>
<td>86</td>
</tr>
<tr>
<td>Chandran et al. [14]</td>
<td>South Australia</td>
<td>1993</td>
<td>1,460,000</td>
<td>Hospital-record review</td>
<td>Not stated</td>
<td>147–208 a</td>
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<td>Roberts-Thomson et al. [6]</td>
<td>South Australia</td>
<td>1999</td>
<td>1,490,000</td>
<td>Multiple sources</td>
<td>ACR and study-specific</td>
<td>233 b</td>
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<tr>
<td>Giordano [17]</td>
<td>Region of Campania (Italy)</td>
<td>1980</td>
<td>Not stated</td>
<td>Tertiary referral hospital</td>
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<td>11</td>
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<tr>
<td>Silman et al. [7]</td>
<td>West Midlands (UK)</td>
<td>1986</td>
<td>~4,100,000</td>
<td>Multiple sources</td>
<td>Not stated</td>
<td>31 b</td>
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<td>Geirsson et al. [16]</td>
<td>Iceland (nationwide)</td>
<td>1990</td>
<td>255,708</td>
<td>Multiple sources</td>
<td>ACR</td>
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<tr>
<td>Haustein et al. [18]</td>
<td>Leipzig (Germany)</td>
<td>Not stated</td>
<td>Not stated</td>
<td>Hospital-record review</td>
<td>Study-specific</td>
<td>100</td>
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<tr>
<td>Asboe-Hansen [13]</td>
<td>Denmark (nationwide)</td>
<td>1977–1979</td>
<td>5,100,000</td>
<td>Hospital-discharge records</td>
<td>Not stated</td>
<td>126</td>
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<tr>
<td>Present study</td>
<td>Seine-Saint-Denis County (France)</td>
<td>2001</td>
<td>1,094,412</td>
<td>Multiple sources, capture-recapture analysis</td>
<td>ACR and LeRoy–Medsger</td>
<td>158 b</td>
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<td>Valter et al. [12]</td>
<td>Estonia</td>
<td>Not stated</td>
<td>14,467</td>
<td>Multistage population survey</td>
<td>ACR and study-specific</td>
<td>1580 c</td>
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aPrevalence estimates include overlap scleroderma disorders.
bEstimates for the adult population (aged ≤15 yr).
cEstimates for the adult population (aged ≥18 yr).
identified in our survey might render improbable the role of a universal ethnic-specific environmental or lifestyle trigger, but it cannot be ruled out that these individuals share socio-economic or reproduction-related risk factors. On the other hand, higher frequencies of SSc in specific ethnic groups could also have a genetic basis. To date, the most stringent evidence for genetics determining the ethnic susceptibility for SSc came from an isolated Amerindian Choctaw tribe with high SSC prevalence and in which the disease was primarily observed in full-blooded descendants [46]. Thus, although SSc has been associated with diverse human leucocyte antigen (HLA) alleles, analysis of the current data does not clearly confers a central role to HLA genes in the differing risks across ethnic backgrounds [45].

In summary, accurate description of SSc epidemiology in different geographical regions represents an important approach to unravelling the aetiological mechanisms underlying this disease. Our observations should encourage further investigation of ethnically heterogeneous populations to discern the role that ethnicity might play in the risk of developing SSc. In light of the rather moderate relative risk of developing SSC associated with ethnic background, our results support that this factor represents only one among a variety of, and possibly interacting, keys to the pathogenesis of SSc.

<table>
<thead>
<tr>
<th>Rheumatology</th>
<th>Key messages</th>
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<tbody>
<tr>
<td>• SSC prevalence in this French county is estimated to be 158.3 per million.</td>
<td></td>
</tr>
<tr>
<td>• SSC appears to be slightly more frequent and more severe in the non-European subpopulation.</td>
<td></td>
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</tbody>
</table>

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References


