

# The worldwide incidence and prevalence of systemic lupus erythematosus: a systematic review of epidemiological studies

Frances Rees<sup>1,2</sup>, Michael Doherty<sup>1</sup>, Matthew J. Grainge<sup>3</sup>, Peter Lanyon<sup>1,2</sup> and Weiya Zhang<sup>1</sup>

## Abstract

**Objectives.** The aim was to review the worldwide incidence and prevalence of SLE and variation with age, sex, ethnicity and time.

**Methods.** A systematic search of MEDLINE and EMBASE search engines was carried out using Medical Subject Headings and keyword search terms for Systemic Lupus Erythematosus combined with incidence, prevalence and epidemiology in August 2013 and updated in September 2016. Author, journal, year of publication, country, region, case-finding method, study period, number of incident or prevalent cases, incidence (per 100 000 person-years) or prevalence (per 100 000 persons) and age, sex or ethnic group-specific incidence or prevalence were collected.

**Results.** The highest estimates of incidence and prevalence of SLE were in North America [23.2/100 000 person-years (95% CI: 23.4, 24.0) and 241/100 000 people (95% CI: 130, 352), respectively]. The lowest incidences of SLE were reported in Africa and Ukraine (0.3/100 000 person-years), and the lowest prevalence was in Northern Australia (0 cases in a sample of 847 people). Women were more frequently affected than men for every age and ethnic group. Incidence peaked in middle adulthood and occurred later for men. People of Black ethnicity had the highest incidence and prevalence of SLE, whereas those with White ethnicity had the lowest incidence and prevalence. There appeared to be an increasing trend of SLE prevalence with time.

**Conclusion.** There are worldwide differences in the incidence and prevalence of SLE that vary with sex, age, ethnicity and time. Further study of genetic and environmental risk factors may explain the reasons for these differences. More epidemiological studies in Africa are warranted.

**Key words:** incidence, prevalence, epidemiology, systemic lupus erythematosus, systematic review

## Rheumatology key messages

- There is wide geographical variation in the reported incidence and prevalence of SLE.
- Males with SLE have an older peak age of incidence and prevalence compared with females.
- There appears to be a trend of increasing prevalence of SLE with time.

<sup>1</sup>Division of Rheumatology, Orthopaedics and Dermatology, University of Nottingham, <sup>2</sup>Rheumatology Department, Nottingham University Hospitals NHS Trust and <sup>3</sup>Division of Epidemiology and Public Health, University of Nottingham, Nottingham, UK

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Correspondence to: Frances Rees, Academic Rheumatology, The University of Nottingham, Room A27, Clinical Sciences Building, City Hospital, Nottingham NG5 1PB, UK.  
E-mail: frees@doctors.org.uk

## Introduction

Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease with a varying clinical phenotype. It is known to affect women more frequently than men, with a ratio of approximately six women to every one man [1]. The aetiology of SLE is not fully understood, but both genetic predisposition and environmental triggers are believed to be involved [2]. Studying the epidemiology of SLE allows us to identify and explore changes in potential

risk factors for the disease and allows planning of health services in response to overall disease burden [3]. A review of the incidence and prevalence of SLE was last published in 2006 by Danchenko *et al.* [4] and found marked disparities in incidence and prevalence worldwide. This was attributed to both true geographical variation and variation in study design. It could be a result of differences in the age and ethnic mix between populations, the definition of SLE used or, as found in some studies in the same population, a change in the incidence and prevalence of SLE with time [1, 5–7]. The aim of this study was to review the current literature published on the incidence and prevalence of SLE throughout the world.

## Methods

A systematic literature review was undertaken. The search strategy used both Medical Subject Headings (MeSH) and keyword search terms for Systemic Lupus Erythematosus combined with MeSH and keyword terms for incidence and epidemiology, followed by prevalence and epidemiology (see supplementary Table S1, available at *Rheumatology* Online, for search strategy). The databases searched were Ovid MEDLINE from 1946 to August 2013 and EMBASE from 1974 to August 2013. All articles were downloaded into Endnote software and were selected on the basis of title and then abstract for full review. Hand-searching of citations also occurred. Articles were included if they were written in English or French language and were regarding humans. Exclusion criteria were review articles, conference proceedings, abstracts or editorials, articles in press, articles involving drug-induced lupus or neonatal lupus, and those solely regarding paediatric patients or a subtype of SLE, such as LN or discoid lupus. Searches were updated in September 2016. Table 1 shows the number of articles retrieved from each database in August 2013 and the additional articles added in September 2016.

Information on author, journal, year of publication, country, region, case-finding method, study period, number of incident or prevalent cases, incidence (per 100 000 person-years) or prevalence (per 100 000 persons) was collected by F.R. In addition, any age, sex or ethnic group-specific

incidence or prevalence rates reported were collected. Age-adjusted or standardized results were presented whenever available. PRISMA guidelines were used.

## Results

### Incidence

#### Geography

Table 2 and Fig. 1A summarize the reported worldwide incidence estimates of SLE. Figure 1A uses the most recent estimates from Table 2. There was worldwide variation, with the highest incidence reported in North America (23.2/100 000 person-years, 95% CI: 22.4, 24.0) [8] and the lowest incidences reported in Africa (0.3/100 000 person-years) [9] and Ukraine (0.3/100 000 person-years, 95% CI: 0.0, 1.5) [10]. In general, European countries had a lower incidence of SLE, whereas Asia, Australasia and the Americas had a higher incidence. The most frequent methods for case-finding were local secondary care hospital-based outpatient lists or discharge registries, or National Health Insurance databases.

#### Age and sex

In all studies reviewed, females had a higher incidence of SLE compared with males. The sex ratio ranged from 2:1 [36] to 15:1 [46]. As an example, Somers *et al.* [31] estimated the UK incidence to be 7.89/100 000 person-years (95% CI: 7.46, 8.31) for females compared with 1.53/100 000 person-years (95% CI: 1.34, 1.71) for males. This higher incidence in females remained true for every age group, although the ratios were smaller at both extremes of age.

In the majority of studies, there was a peak age of incidence before declining. In females, the peak age ranged from the third to seventh decades of life. For males, the peak incidence was usually later, in the fifth to seventh decades. Three selected studies taken from three different geographical regions demonstrate this in Fig. 2A.

#### Ethnicity

In studies that reported differences between ethnic groups [1, 8, 21, 29, 33, 35, 37, 41, 42, 58, 59], incidence rates

TABLE 1 Summary of literature search

| Search term | Database | Number of articles retrieved | Number of articles after removing duplicates | Number of articles selected for review on the basis of title and abstract | Number of articles selected for inclusion after reading the full text article, including additional articles found by hand searching | Number of additional articles selected on updated search in September 2016 |
|-------------|----------|------------------------------|--|---|--|--|
| Incidence   | Medline  | 542                          | 1617   | 76  | 46   | 11   |
|             | Embase   | 1175                         |  |   |  |  |
| Prevalence  | Medline  | 929                          | 2744   | 92  | 76   | 14   |
|             | Embase   | 2290                         |  |   |  |  |

TABLE 2 Worldwide incidence of SLE

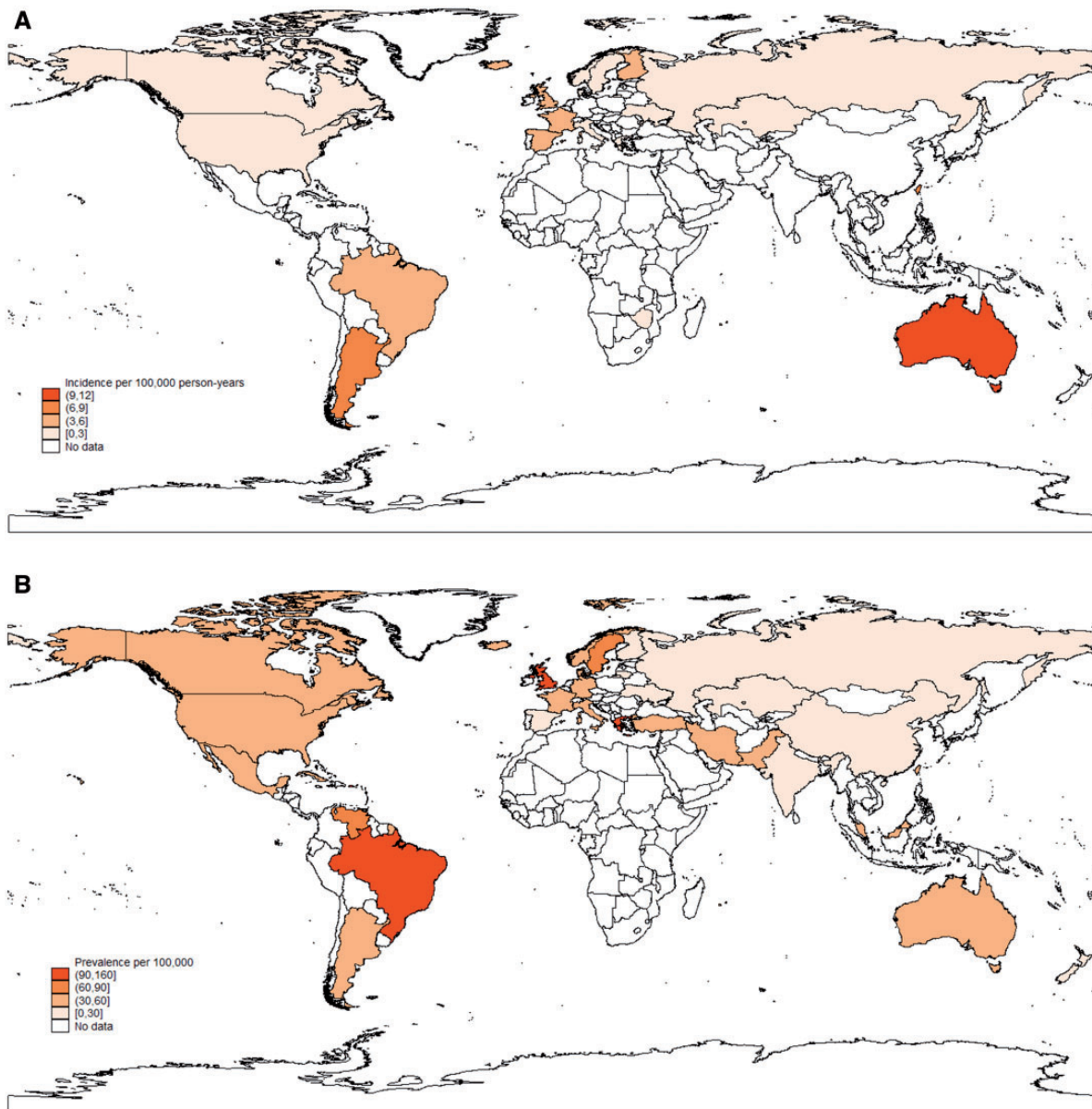
| Continent     | Country | References                         | Region               | Case-finding method                     | Number of incident cases      | Incidence per 100 000 person-years (95% CI)                              |
|---------------|---------|------------------------------------|----------------------|---|-------------------------------|--|
| Europe        | Denmark | Voss <i>et al.</i> [5]             | Funen                | Hospital and community records          | 127                           | 1.0 (0.3, 2.9) <sup>a</sup> [1980]<br>3.6 (2.0, 6.1) <sup>a</sup> [1994] |
|               |         | Lastrup <i>et al.</i> [11]         | Funen                | Hospital and community records          | 35                            | 1.0 (0.3, 2.7)   |
|               | France  | Hermansen <i>et al.</i> [12]       | National             | National patient registry               | 1644                          | 2.35 (2.24, 2.49)  |
|               | Finland | Arnaud <i>et al.</i> [13]          | National             | National health insurance database      | 1931                          | 3.32   |
|               | Greece  | Elfvig <i>et al.</i> [14]          | Northern Savo        | Hospital and community records          | 7                             | 3.6 (3.0, 4.2) <sup>a</sup>  |
|               | Iceland | Alamanos <i>et al.</i> [15]        | North-west           | Hospital records                        | 178                           | 1.9 (1.5, 2.3) <sup>a</sup>  |
|               | Italy   | Gudmundsson <i>et al.</i> [16]     | National             | Hospital registers                      | 76                            | 3.3  |
|               |         | Govoni <i>et al.</i> [17]          | Ferrara              | Hospital records                        | 2000: 7<br>2001: 4<br>2002: 9 | 2.0<br>1.2<br>2.6  |
|               | Norway  | Tsioni <i>et al.</i> [18]          | Valtrompia           | Hospital and community records          | 9                             | 2.0 (0.9, 3.8)   |
|               |         | Nossent [19]                       | North                | Hospital records                        | 83                            | 2.9 (2.4, 3.3) <sup>a</sup>  |
|               | Spain   | Eilertsen <i>et al.</i> [20]       | North                | Hospital records                        | 58                            | 3.0 (2.0, 4.0)   |
|               |         | Lerang <i>et al.</i> [21]          | Oslo                 | Hospital records                        | 116                           | 3.0 (2.4, 3.5)   |
|               |         | López <i>et al.</i> [22]           | Asturias             | Hospital records                        | 116                           | 2.2 (1.8, 2.5)   |
|               |         | Gómez <i>et al.</i> [23]           | Asturias             | Hospital records                        | –                             | 1.9 (1.1, 2.7)   |
|               | Sweden  | Alonso <i>et al.</i> [24]          | Lugo                 | Hospital records                        | 150                           | 3.6 (3.0, 4.2) <sup>a</sup>  |
|               |         | Leonhardt [7]                      | Malmö                | Hospital records                        | 16                            | 1.0 <sup>a</sup>   |
|               |         | Eyrich <i>et al.</i> [25]          | Halmstad             | Hospital records                        | 41                            | 1.8 [1957, 1964]<br>3.0 [1964, 1971]                                     |
| North America | UK      | Jonsson <i>et al.</i> [26]         | Lund and Orup        | Hospital and community records          | 39                            | 4.0 (1.6, 6.4) <sup>a</sup>  |
|               |         | Ståhl-Hallengren <i>et al.</i> [6] | Lund and Orup        | Hospital and community records          | 41                            | 4.8  |
|               |         | Ingvarsson <i>et al.</i> [27]      | Lund and Orup        | Hospital and community records          | 55                            | 2.8 (1.4, 4.2)   |
|               |         | Hopkinson <i>et al.</i> [28]       | Nottingham           | Hospital records                        | 23                            | 4.0 (2.3, 5.6) <sup>a</sup>  |
|               |         | Johnson <i>et al.</i> [29]         | Birmingham           | Hospital records                        | 33                            | 3.8 (2.5, 5.1)   |
|               |         | Nightingale <i>et al.</i> [30]     | Whole UK             | CPRD                                    | 390                           | 3.0 (2.7, 3.3)   |
|               |         | Somers <i>et al.</i> [31]          | Whole UK             | CPRD                                    | 1638                          | 4.7 (4.5, 4.9) <sup>a</sup>  |
|               |         | Rees <i>et al.</i> [1]             | Whole UK             | CPRD                                    | 2740                          | 4.9 (4.7, 5.1)   |
|               |         | Bernatsky <i>et al.</i> [32]       | Quebec               | Physician billing database              | 219                           | 3.0 (2.6, 3.4)   |
|               |         | Siegel <i>et al.</i> [33]          | New York and Alabama | Hospitalization database                | 203                           | 2.8 (2.6, 3.0)   |
|               | Canada  |                                    |                      | Hospital records                        | New York: 98<br>Alabama: 63   | 1.9<br>1.0   |
|               | USA     | Fessel [34]                        | San Francisco        | Hospital records                        | 74                            | 7.6  |
|               |         | Hochberg [35]                      | Baltimore            | Hospital records                        | 302                           | 4.6 <sup>a</sup>   |
|               |         | Michet <i>et al.</i> [36]          | Minnesota            | Hospital records and death certificates | 25                            | 1.8 (1.1, 2.5) <sup>a</sup>  |
|               |         | McCarty <i>et al.</i> [37]         | Pennsylvania         | Community and hospital records          | 191                           | 2.4 (2.1, 2.8) <sup>a</sup>  |

(continued)

TABLE 2 Continued

| Continent       | Country   | References                       | Region              | Case-finding method                     | Number of incident cases | Incidence per 100 000 person-years (95% CI) [study year] |
|-----------------|-----------|----------------------------------|---------------------|---|--------------------------|--|
| Central America | Caribbean | Uramoto <i>et al.</i> [38]       | Minnesota           | Hospital records                        | 48                       | 5.6 (3.9, 7.2) <sup>a</sup>                              |
|                 |           | Naleway <i>et al.</i> [39]       | Wisconsin           | Medical records                         | 44                       | 5.1 (3.6, 6.6) <sup>a</sup>                              |
|                 |           | Feldman <i>et al.</i> [8]        | Whole US            | Medicaid database                       | 3490                     | 23.2 (22.4, 24.0)  |
|                 |           | Furst <i>et al.</i> [40]         | Whole US            | Medical claims database                 | 1557                     | 7.2 (6.8, 7.7) <sup>a</sup>                              |
|                 |           | Lim <i>et al.</i> [41]           | Georgia             | Georgia Lupus registry                  | 267                      | 5.6 (5.0, 6.3) <sup>a</sup>                              |
| South America   | Argentina | Somers <i>et al.</i> [42]        | Michigan            | Medical records                         | 399                      | 5.5 (5.0, 6.1) <sup>a</sup>                              |
|                 |           | Jarukitsopa <i>et al.</i> [43]   | Minnesota           | Rochester epidemiology project database | 45                       | 2.9 (2.0, 3.7)   |
|                 |           | Nossent [44]                     | Curaçao             | Medical records                         | 68                       | 4.6 (0.4, 8.8)   |
|                 |           | Deligny <i>et al.</i> [45]       | Martinique          | Medical records                         | 180                      | 4.7 (2.5, 6.9)   |
|                 |           | Flower <i>et al.</i> [46]        | Barbados            | National hospital-based SLE registry    | 183                      | 6.3 (5.4, 7.3) <sup>a</sup>                              |
| Africa          | Brazil    | Scolnik [47]                     | Buenos Aires        | Private medical care database           | 68                       | 6.3 (4.9, 7.7)   |
|                 |           | Pereira Vilar <i>et al.</i> [48] | Natal city          | Hospital records                        | 43                       | 8.7 (6.3, 11.7)  |
|                 |           | Nakashima <i>et al.</i> [49]     | Cascavel            | Medical records                         | 14                       | 4.8  |
|                 |           | Taylor <i>et al.</i> [9]         | Bulawayo and Harare | Hospital records                        | 22                       | 0.3  |
|                 |           | Mok <i>et al.</i> [50]           | Hong Kong           | University hospital database            | –                        | 3.1  |
| Asia            | Zimbabwe  | Nasonov <i>et al.</i> [10]       | Semey               | Hospital records                        | 4                        | 1.3 (0.4, 3.4) <sup>a</sup>                              |
|                 |           | Nasonov <i>et al.</i> [10]       | Kursk and Yaroslavl | Hospital records                        | 12                       | 1.2 (0.6, 2.1) <sup>a</sup>                              |
|                 |           | Nasonov <i>et al.</i> [10]       | Vinnitsa            | Hospital records                        | 1                        | 0.3 (0.0, 1.5) <sup>a</sup>                              |
|                 |           | Shim <i>et al.</i> [51]          | National            | National Health Insurance database      | 1398                     | 2.8 (2.7–2.9) <sup>a</sup>                               |
|                 |           | Chiu <i>et al.</i> [52]          | National            | National Health Insurance database      | 12 789                   | 8.1  |
| Australasia     | Australia | Kang <i>et al.</i> [53]          | National            | National Health Insurance database      | 758                      | 3.3  |
|                 |           | Yu <i>et al.</i> [54]            | National            | National Health Insurance database      | 671                      | 8.4 (7.7, 9.0)   |
|                 |           | Yeh <i>et al.</i> [55]           | National            | Catastrophic illness database           | 6675                     | 4.9  |
|                 |           | See <i>et al.</i> [56]           | National            | National Health Insurance database      | 358                      | 7.2 (6.5, 8.0)   |
|                 |           | Anstey <i>et al.</i> [57]        | Northern Territory  | Hospital records                        | 13                       | 11   |

<sup>a</sup>Age standardized. CPRD: UK Clinical Practice Research Datalink.

**Fig. 1** The global incidence (A) and prevalence (B) of SLE (most recent estimates used)

were highest in Black populations and lowest in Caucasians. Asian and Hispanic ethnic groups were intermediate. For example, in the UK, Hopkins *et al.* [59] published race-specific incidence figures for Nottingham, with Afro-Caribbeans highest at 31.9/100 000 person-years, Asians 4.1/100 000 person-years and Whites 3.4/100 000 person-years. In North America, Native American Indians also had higher incidence rates than the White population. This was demonstrated in the study by Feldman *et al.* [8], where the incidence in native American Indians was 30.0/100 000 person-years (95% CI: 22.5, 39.9), which was similar to that of Black or African Americans [31.2/100 000 person-years (95% CI:

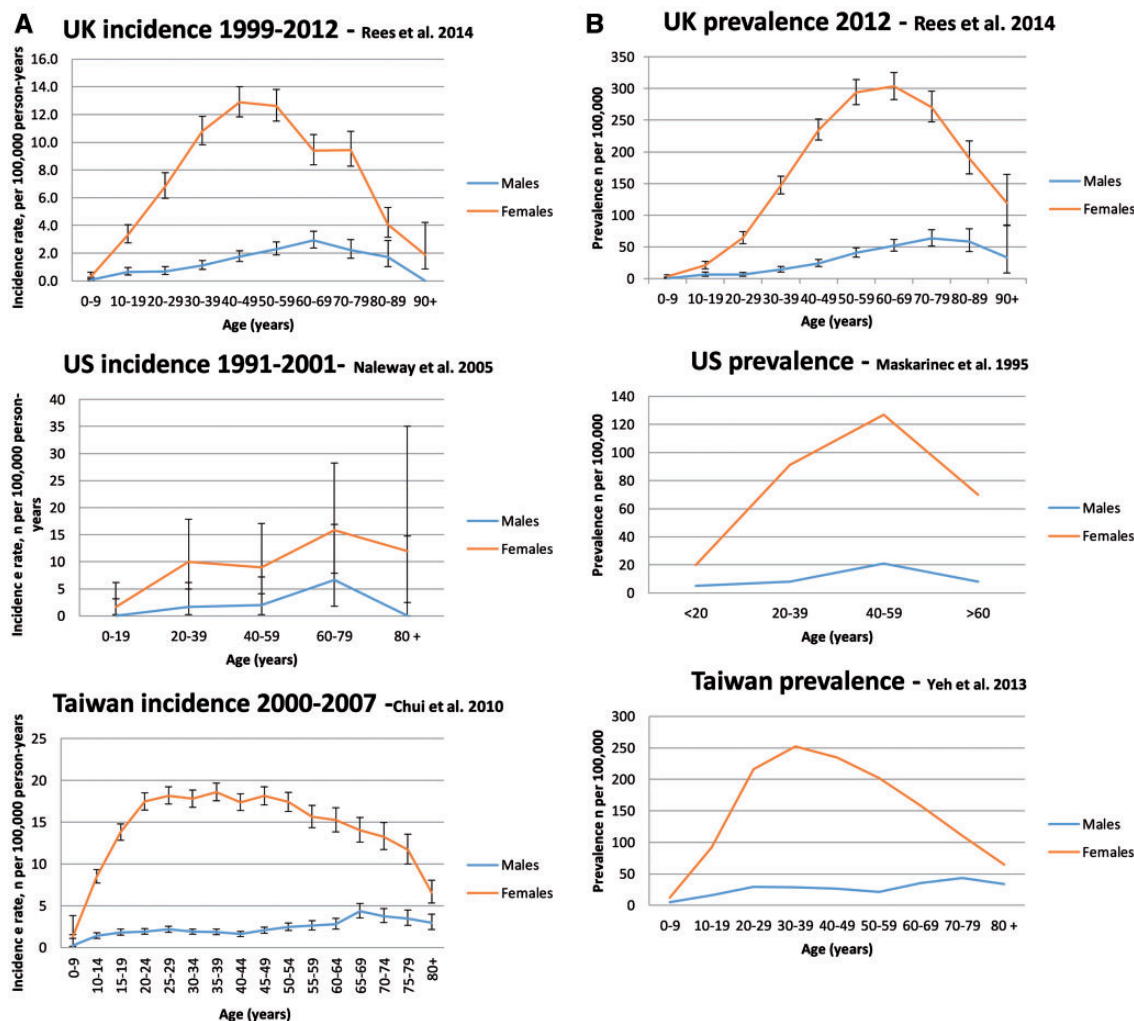
29.6, 32.9)] and significantly higher than for Whites [18.0/100 000 person-years (95% CI: 17.0, 19.0)] and Asians [16.7/100 000 person-years (95% CI: 13.9, 20.0)]. In the same study, the incidence in Hispanics was 22.2/100 000 person-years (95% CI: 20.4, 24.2). A study specifically focusing on native American Indians found that three tribes had a particularly high incidence of SLE, specifically the Crow, Arapahoe and Sioux tribes [60].

#### Temporal trend

There were a number of studies that examined the same population at risk over time, allowing us to examine the temporal trend (Fig. 3A). In the UK, Somers *et al.* [31]



**Fig. 2** The incidence (A) and prevalence (B) of SLE stratified by age and sex in the UK, USA and Taiwan



showed a small but non-significant increase in the incidence in females over the 10-year period 1990–99, but not with males. However, Rees *et al.* [1] found a statistically significant decline in incidence from 1999 to 2012 of 1.8% per year. In the County of Funen in Denmark, Voss *et al.* [5] looked at the time periods 1980–84, 1985–89 and 1990–94. The respective incidence rates were 1.0 (95% CI: 0.6, 1.6), 1.1 (95% CI: 0.7, 1.7) and 2.5 (95% CI: 1.8, 3.3) per 100 000 person-years. Although not linear, there was a significant increase from the first to the last 5-year period. Although this could be a true increase, from 1 January 1993 an additional data source was available, thus increasing the number of cases identified. Alamanos *et al.* [15], in North-West Greece, showed an increasing trend from 1.41/100 000 person-years (95% CI: 0.99, 1.83) in 1982–86 to 2.19/100 000 person-years (95% CI: 1.78, 2.60) in 1997–2001, but this was not statistically significant. Finally, results from the Rochester Epidemiology project in Minnesota were published by

Michet *et al.* [36] for the period 1950–79, when the incidence was 1.8/100 000 person-years (95% CI: 1.1, 2.5), followed by Uramoto *et al.* [38], who published data for 1980–92, when the incidence rate was 5.6/100 000 person-years (95% CI: 3.9, 7.2), and finally, Jarukitsopa *et al.* [43], who examined 1993–2005 and found the incidence rate had declined to 2.9/100 000 person-years (95% CI: 2.0, 3.7).

## Prevalence

### Geography

The prevalence of SLE by country is summarized in Table 3 and Fig. 1B. Figure 1B uses the most recent estimates from Table 3. The lowest prevalence was reported in a community study of 847 people in Yarrabah, North Queensland, Australia [61], where no cases were found. The highest prevalence was in a national survey in the USA [62], which reported a prevalence of 241/100 000

TABLE 3 Worldwide prevalence of SLE

| Continent | Country   | References                         | Study period         | Region            | Case-finding method                   | Prevalent cases | Prevalence, per 100 000 (95% CI) [year of study] |
|-----------|-----------|------------------------------------|----------------------|-------------------|---------------------------------------|-----------------|--|
| Europe    | Denmark   | Voss <i>et al.</i> [5]             | 1 January 1995       | Funen             | Hospital and community records        | 84              | 22.2 <sup>a</sup>                                |
|           |           | Lastrup <i>et al.</i> [11]         | 1 January 2003       | Funen             | Hospital and community records        | 109             | 28.3 (23.3, 34.2)                                |
|           | Finland   | Eaton <i>et al.</i> [63]           | 31 October 2006      | National          | National hospital patient registry    | –               | 48   |
|           |           | Hermansen <i>et al.</i> [12]       | 31 December 2011     | National          | National hospital patient registry    | 1887            | 45.2 (43.3, 47.4)                                |
|           |           | Helve [64]                         | December 1978        | National          | National hospital discharge database  | 1427            | 28   |
|           | France    | Arnaud <i>et al.</i> [13]          | 2010                 | National          | National Health Insurance database    | 27 369          | 40.8 <sup>a</sup>                                |
|           |           | Brinks <i>et al.</i> [65]          | 2002                 | National          | National Health Insurance database    | 845             | 36.7 (34.3, 39.3)                                |
|           | Greece    | Alamanos <i>et al.</i> [15]        | 31 December 2001     | North-West        | Hospital records                      | 193             | 38.1 (36.3, 39.9) <sup>a</sup>                   |
|           |           | Anagnostopoulos <i>et al.</i> [66] | 2008                 | Central           | Postal survey                         | 2               | 110 (110, 370)                                   |
|           | Iceland   | Gudmundsson <i>et al.</i> [16]     | 1975–84              | National          | Hospital registers                    | 86              | 35.9 <sup>a</sup>                                |
|           |           | Benucci <i>et al.</i> [67]         | June 2002            | Florence          | Community survey                      | 23              | 71 (49, 92) <sup>a</sup>                         |
|           | Italy     | Govoni <i>et al.</i> [17]          | 2002                 | Ferrara           | Hospital records                      | 201             | 57.9   |
|           |           | Sardu <i>et al.</i> [68]           | July 2009            | Southern Sardinia | Community records                     | –               | 81 (50, 124)                                     |
|           |           | Tsioni <i>et al.</i> [18]          | 31 December 2012     | Valtrompia        | Hospital and community records        | 44              | 39.2 (28.5, 52.6)                                |
|           | Lithuania | Dadoniene <i>et al.</i> [69]       | 2004                 | Vilnius           | Hospital records and community survey | 76              | 16.2 (12.7, 20.3)                                |
|           | Norway    | Nossent [19]                       | 1996                 | North             | Hospital records                      | 89              | 49.7 (44.3, 55) <sup>a</sup>                     |
|           |           | Eilertsen <i>et al.</i> [20]       | 2007                 | North             | Hospital records                      | 114             | 64.1   |
|           | Spain     | Lerang <i>et al.</i> [21]          | 1 January 2008       | Oslo              | Hospital records                      | 238             | 52.8 (45.2, 58.4)                                |
|           |           | López <i>et al.</i> [22]           | 31 December 2002     | Asturias          | Hospital records                      | 367             | 34.1 (30.6, 37.6)                                |
|           | Sweden    | Gómez <i>et al.</i> [23]           | December 2003        | Asturias          | Hospital records                      | –               | 31.7 (28.3, 35.0)                                |
|           |           | Alonso <i>et al.</i> [24]          | 31 December 2006     | Lugo              | Hospital records                      | 150             | 17.5 (12.6, 24.1) <sup>a</sup>                   |
|           |           | Leonhardt [7]                      | 1955<br>1958<br>1961 | Malmö             | Hospital records                      | –               | 2.9<br>4.5<br>6.0                                |
|           |           | Nived <i>et al.</i> [70]           | 31 December 1982     | Lund and Orup     | Hospital and community records        | 61              | 39 (30, 48)                                      |

(continued)

TABLE 3 Continued

| Continent     | Country | References                         | Study period     | Region                      | Case-finding method                             | Prevalent cases | Prevalence, per 100 000 (95% CI) [year of study] |
|---------------|---------|------------------------------------|------------------|-----------------------------|---|-----------------|--|
| North America | Canada  | Ståhl-Hallengren <i>et al.</i> [6] | 31 December 1986 | Lund and Orup               | Hospital and community records                  | 121             | 42   |
|               |         | Simard <i>et al.</i> [71]          | 31 December 1991 | National                    | National patient register                       | 162             | 68   |
|               |         | Ingvarsson <i>et al.</i> [27]      | 1 January 2010   | Lund and Orup               | Hospital and community records                  | 7929            | (46, 85)   |
|               |         |                                    | 31 December 2006 |                             |   | 174             | 65   |
|               |         | Çakır <i>et al.</i> [72]           | -                | Havsa                       | Community survey                                | 10              | 57 (46, 70) <sup>a</sup>                         |
|               | USA     | Hochberg [73]                      | 1981-82          | Whole UK                    | Community medical record survey                 | 20              | 6.5  |
|               |         | Samanta <i>et al.</i> [74]         | 1986-89          | Leicester                   | Hospital records                                | 50              | 26.1   |
|               |         | Hopkinson <i>et al.</i> [28]       | 30 April 1990    | Nottingham                  | Hospital records                                | 147             | 24.6 (20.6, 28.7) <sup>a</sup>                   |
|               |         | Johnson <i>et al.</i> [29]         | 1992             | Birmingham                  | Hospital records                                | 242             | 27.7 (24.2, 31.2)                                |
|               |         | Gourley <i>et al.</i> [75]         | 1 August 1993    | Northern Ireland            | Hospital records                                | 408             | 25.4 (22.1, 28.7) <sup>a</sup>                   |
|               | USA     | Nightingale <i>et al.</i> [76]     | 1992-98          | Whole UK                    | CPRD  | 1538            | 25.0 (23.4, 26.7) [1992]                         |
|               |         | Rees <i>et al.</i> [1]             | 1999-2012        | Whole UK                    | CPRD  | 1875            | 40.7 (37.6, 43.8) [1998]                         |
|               |         | Peschken <i>et al.</i> [77]        | 1996             | Manitoba                    | Medical records                                 | 257             | 65.0 (62.1, 67.9) [1999] <sup>a</sup>            |
|               |         | Bernatsky <i>et al.</i> [32]       | 2003             | Quebec                      | Physician billing and hospitalization databases | 3825            | 97.0 (94.2, 99.9) [2012] <sup>a</sup>            |
|               |         | Siegel <i>et al.</i> [58]          | 1959             | New York                    | Hospital records                                | -               | 22.1 (13.2, 32.4)                                |
| North America | Canada  | Fessel [34]                        | 1973             | San Francisco               | Hospital records                                | 64              | 54.7 <sup>a</sup>                                |
|               |         | Serdula <i>et al.</i> [78]         | 1975             | Oahu, Hawaii                | Hospital records                                | 81              | 5  |
|               |         | Michet <i>et al.</i> [36]          | 1 January 1980   | Minnesota                   | Hospital records                                | 20              | 50.8   |
|               |         | Uramoto <i>et al.</i> [38]         | 1 January 1993   | Minnesota                   | Hospital records                                | -               | 15.3 <sup>a</sup>                                |
|               |         | Maskarinec <i>et al.</i> [79]      | 1989             | Hawaii                      | Hospital records                                | 20              | 40.0 (23.5, 57.5)                                |
|               | USA     | Post <i>et al.</i> [80]            | 1996             | California                  | Postal survey                                   | 454             | 122 (97, 217) <sup>a</sup>                       |
|               |         | Balluz <i>et al.</i> [81]          | 1997             | Arizona                     | Hospital and community records                  | 20              | 41.8   |
|               |         | Ward [62]                          | 1988-94          | National                    | US National health survey                       | 40              | 68.2   |
|               |         | Naleway <i>et al.</i> [39]         | 2001             | Wisconsin                   | Medical records                                 | 64              | 103 (56, 149)                                    |
|               |         | Chakravarty <i>et al.</i> [82]     | 2000             | California and Pennsylvania | Hospitalization databases                       | -               | 241 (130, 352)                                   |
|               | USA     |                                    |                  |                             |   |                 | 78.5 (59.0, 98.0) <sup>a</sup>                   |
|               |         |                                    |                  |                             |   |                 | California: 107.6 (106.1, 109.2) <sup>a</sup>    |
|               |         |                                    |                  |                             |   |                 |  |
|               |         |                                    |                  |                             |   |                 |  |
|               |         |                                    |                  |                             |   |                 |  |

(continued)



TABLE 3 Continued

| Continent       | Country   | References                            | Study period    | Region                                       | Case-finding method                     | Prevalent cases      | Prevalence, per 100 000 (95% CI) [year of study]                                 |
|-----------------|-----------|---------------------------------------|-----------------|--|---|----------------------|--|
| Central America |           | Feldman <i>et al.</i> [8]             | 2000–04         | National                                     | Medicaid database                       | 34339                | Pennsylvania:<br>149.5 (146.9,<br>152.2) <sup>a</sup><br>143.7 (142.2,<br>145.3) |
|                 |           | Furst <i>et al.</i> [40]              | 2003–08         | National                                     | Medical claims database                 | 15396                | 81.1 (78.5,<br>83.6) [2003]<br>102.9 (100.4,<br>105.5) [2008]                    |
|                 |           | Lim <i>et al.</i> [41]                | 2002            | Georgia                                      | Georgia Lupus registry                  | 1156                 | 73.0 (68.9,<br>77.4) <sup>a</sup>  |
|                 |           | Somers <i>et al.</i> [42]             | 2002–04         | Michigan                                     | Medical records                         | 2139                 | 72.8 (70.8,<br>74.8) <sup>a</sup>  |
|                 |           | Jarukitsopa <i>et al.</i> [43]        | 1 January 2006  | Rochester, MN                                | Rochester epidemiology project database | 72                   | 53.5 (41.1,<br>65.9)   |
|                 |           | Nossent [44]                          | 1 January 1990  | Curaçao                                      | Medical records                         | 69                   | 47.6 (34.1,<br>51.1)   |
|                 |           | Deligny <i>et al.</i> [45]            | 1999            | Martinique                                   | Medical records                         | 245                  | 64.2 (56.2,<br>72.2)   |
|                 |           | Molina <i>et al.</i> [83]             | 2003            | Puerto Rico                                  | Private health insurance database       | 877                  | 159  |
|                 |           | Reyes-Llerena <i>et al.</i> [84]      | –               | Havana, Cuba                                 | WHO-ILAR COPCORD                        | 2                    | 60 (10, 200)   |
|                 |           | Flower <i>et al.</i> [46]             | 31 October 2009 | Barbados                                     | National hospital-based SLE registry    | 226                  | 84.1 (73.5,<br>95.8)   |
| South America   | Mexico    | Peláez-Ballesteras <i>et al.</i> [85] | –               | Five regions in Mexico                       | WHO-ILAR COPCORD                        | –                    | 60 (30, 100) <sup>a</sup>  |
|                 | Argentina | Scolnik <i>et al.</i> [47]            | 1 January 2009  | Buenos Aires                                 | Private medical care database           | 75                   | 58.6 (46.1,<br>73.5)   |
|                 | Brazil    | Rodrigues Senna <i>et al.</i> [86]    | –               | Montes Claros City                           | WHO-ILAR COPCORD                        | 3                    | 98 (20, 280)   |
| Asia            | Venezuela | Granados <i>et al.</i> [87]           | 2011            | Monagos                                      | WHO-ILAR COPCORD                        | 3                    | 70 (10, 200)   |
|                 | China     | Wigley <i>et al.</i> [88]             | –               | North (near Beijing)<br>South (near Shantou) | WHO-ILAR COPCORD                        | North: 3<br>South: 1 | 10<br>20   |
|                 | India     | Li <i>et al.</i> [89]                 | –               | Beijing                                      | Community survey                        | 3                    | 30 (0, 60)   |
|                 |           | Malaviya <i>et al.</i> [90]           | –               | Delhi  | Community survey                        | 3                    | 3.2 (0, 6.86)  |
|                 | Iran      | Davatchi <i>et al.</i> [91]           | September 2005  | Tehran city                                  | WHO-ILAR COPCORD                        | 3                    | 40   |
|                 |           | Davatchi <i>et al.</i> [92]           | September 2006  | Five villages in NW Iran                     | WHO-ILAR COPCORD                        | 1                    | 60 (6, 670)  |

(continued)

TABLE 3 Continued

| Continent   | Country     | References                  | Study period                    | Region                                | Case-finding method                | Prevalent cases             | Prevalence, per 100 000 (95% CI) [year of study] |
|-------------|-------------|-----------------------------|---------------------------------|---------------------------------------|------------------------------------|-----------------------------|--|
| Australasia | Kazakhstan  | Nasonov <i>et al.</i> [10]  | 31 December 2010                | Semey                                 | Hospital records                   | 52                          | 17.3 (12.9, 22.6) <sup>a</sup>                   |
|             | Malaysia    | Wang <i>et al.</i> [93]     | 1974–90                         | Kuala Lumpur                          | Hospital records                   | 539                         | 43   |
|             | Pakistan    | Farooqi <i>et al.</i> [94]  | –                               | North                                 | WHO-ILAR COPCORD study             | 1                           | 50   |
|             | Russia      | Nasonov <i>et al.</i> [10]  | 31 December 2010                | Kursk and Yaroslavl                   | Hospital records                   | 79                          | 7.7 (6.1, 9.7) <sup>a</sup>                      |
|             | South Korea | Ju <i>et al.</i> [95]       | 2004–06                         | National                              | National Health Insurance database | 9000–11000                  | 18.8, 21.7                                       |
|             |             | Shim <i>et al.</i> [51]     | 2006–10                         | National                              | National Health Insurance database | 10080                       | 20.6 (20.2, 21.0) [2006]                         |
|             |             |                             |                                 |                                       |                                    | 13316                       | 26.5 (26.0, 27.0) [2010]                         |
|             | Taiwan      | Chou <i>et al.</i> [96]     | –                               | Cu-Tien                               | Community survey                   | 1                           | 33   |
|             |             | Chiu <i>et al.</i> [52]     | 2000–07                         | National                              | National Health Insurance database | 15463                       | 42.2 [2000]                                      |
|             |             | Kang <i>et al.</i> [53]     | 31 December 2005                | National                              | National Health Insurance database | 15753                       | 67.4 [2007]                                      |
| Ukraine     |             | Yu <i>et al.</i> [54]       | 2000                            | National                              | National Health Insurance database | 356                         | 37.0 (10.0, 41.0)                                |
|             |             | Yeh <i>et al.</i> [55]      | 2003                            | National                              | Catastrophic illness database      | 133488                      | 97.5   |
|             |             | See <i>et al.</i> [56]      | 2008                            | National                              | National Health Insurance database | 435                         | 43.5 (39.4, 47.6)                                |
|             |             | Nasonov <i>et al.</i> [10]  | 31 December 2010                | Vinnitsa                              | Hospital records                   | 45                          | 12.2 (8.9, 16.4) <sup>a</sup>                    |
|             | Australia   | Anstey <i>et al.</i> [57]   | 1 January 1991                  | Northern Territory                    | Hospital records                   | 22                          | 52   |
|             |             | Grennan <i>et al.</i> [97]  | 1993                            | Queensland Sydney                     | Hospital records                   | Queensland: 20<br>Sydney: 3 | 89<br>13   |
|             |             | Bossingham [98]             | 1 August 1996 to 31 August 1998 | Far North                             | Hospital records                   | 108                         | 45.3   |
|             |             | Minaur <i>et al.</i> [61]   | January 2002                    | Queensland Yarrabah, North Queensland | WHO-ILAR COPCORD study             | 0                           | 0  |
|             | New Zealand | Meddings <i>et al.</i> [99] | –                               | Dunedin                               | Hospital records                   | 16                          | 14.7   |
|             |             | Hart <i>et al.</i> [100]    | 1980                            | Auckland                              | Hospital records                   | 136                         | 17.6 <sup>a</sup>                                |

<sup>a</sup>Age standardized. CPRD: clinical practice research datalink; WHO-ILAR COPCORD: World Health Organization-ILAR Community Orientated Program for the Control of Rheumatic Diseases.

people (95% CI: 130, 352). The most frequent methods for case-finding were local secondary care hospital-based outpatient or discharge registries, National Health Insurance databases or community surveys, such as the World Health Organization-ILAR Community Orientated Program for the Control of Rheumatic Diseases (WHO-ILAR COPCORD).

#### Age and sex

In all studies, prevalence was highest among females, with a female to male ratio ranging between 1.2:1 [86] and 15:1 [46]. As an example, in Birmingham in the UK, Johnson *et al.* [29] found estimates of 49.6/100 000 (95% CI: 43.2, 56.1) for women compared with 3.6/100 000 (95% CI: 2.0, 6.0) for men in a hospital-based study. A further study in Birmingham, UK in 1996 aimed to identify undiagnosed cases of SLE in the community via a postal questionnaire sent to a random sample of 3500 women aged 18–65 years. This suggested a much greater prevalence in women of 200/100 000 (95% CI: 80, 412) [101] compared with the hospital-based study.

Prevalence curves by age had a similar distribution to that of the incidence data, but with a later peak age. Figure 2B shows the age- and sex-specific prevalence from three papers from selected countries from around the world. Summarizing studies from the UK, the peak age of prevalence was between 45 and 69 years for females and between 40 and 89 years for males [1, 76]. Most worldwide studies confirmed the delayed peak age of incidence in males apart from two studies from Scandinavia, which found a lower peak age in men [21, 70].

#### Ethnicity

Similar to the incidence data, Black ethnic groups had the highest reported prevalence of SLE, White groups the lowest and Asian and Hispanic groups were intermediate for both males and females. As an example, the prevalence in different ethnic groups in the UK is summarized in Table 4.

In addition to the studies in Table 4, a study of women aged 15–64 years in South London estimated the

prevalence of SLE to be 177/100 000 (95% CI: 135, 220) in Afro-Caribbean people and 110/100 000 (95% CI: 58, 163) in West African people compared with 35/100 000 (95% CI: 26, 43) in White European people [103]. Studies from the USA have also confirmed the difference between Black and White populations [8, 33], with intermediate figures for Hispanic, Asian and native North Americans. A study from Hawaii had the greatest ethnic diversity [78]. Here, Chinese and native Hawaiian groups were most prevalent (24.1 and 20.4/100 000, respectively) and Whites least prevalent (5.8/100 000; 95% CI not given). In the same study, White people had a significantly older mean age of disease prevalence of 38.1 years, compared with 29.7 years overall.

#### Temporal trend

There appeared to be a trend for increasing prevalence with time (Fig. 3B). In the UK, the crude annual prevalence of SLE reported by Nightingale *et al.* [76] increased from 25/100 000 (95% CI: 23.4, 26.7) in 1992 to 40.7/100 000 (95% CI: 37.6, 43.8) in 1998. A subsequent study by Rees *et al.* [1] confirmed this trend and found that prevalence rose annually by 3.1% from 1999 to 2012, which was statistically significant. In Malmö, Sweden the prevalence rose from 2.9/100 000 in 1955 to 6.0/100 000 in 1961 [7] and in Lund and Orup from 39/100 000 (95% CI: 30, 48) on 31 December 1982 [70] to 68/100 000 on 31 December 1991 [6]. The same trend was found in Northern Norway [11, 20] and Minnesota [36, 38].

## Discussion

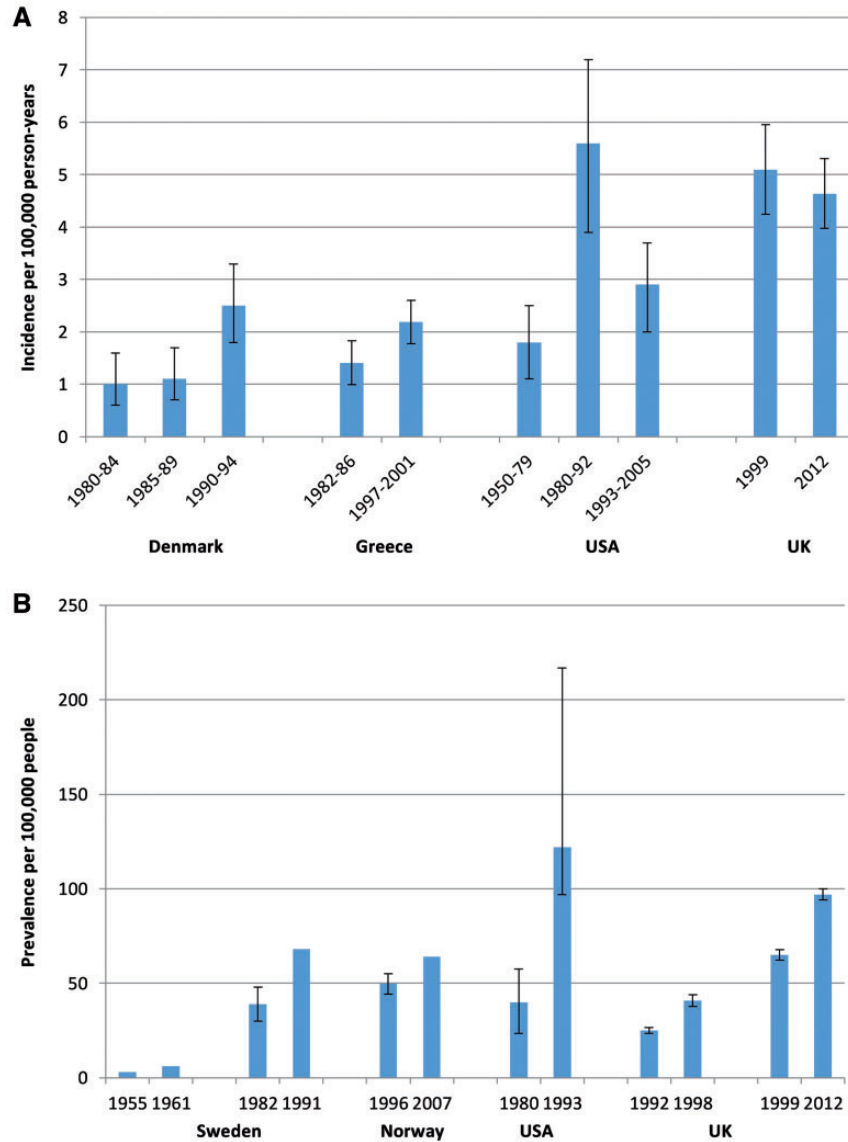
There are five main findings from this systematic review: there is worldwide variation in the reported incidence and prevalence of SLE; in all nationalities, there is a female predominance; there is a peak age of incidence, which occurs in middle-aged adults; Black ethnic groups have the highest incidence and prevalence and White ethnic groups have the lowest; and there appears to be an increasing trend in the prevalence of SLE with time.

The geographical variation could reflect differences in the genetic mix of populations or variation in

**TABLE 4** The prevalence of SLE in the UK by ethnicity

| References                   | Region     | Prevalence per 100 000 (95% CI)  |                                 |                         |                         |
|------------------------------|------------|--|---------------------------------|-------------------------|-------------------------|
|                              |            | Black  | Asian                           | White                   | Chinese                 |
| Samanta <i>et al.</i> [102]  | Leicester  | –  | 40 <sup>a</sup>                 | 20 <sup>a</sup>         | –                       |
| Samanta <i>et al.</i> [74]   | Leicester  | –  | 64.0 <sup>a</sup>               | 20.2                    | –                       |
| Hopkinson <i>et al.</i> [59] | Nottingham | 207.0  | 48.8 <sup>a</sup>               | 20.3 <sup>a</sup>       | 92.9 <sup>a</sup>       |
| Johnson <i>et al.</i> [29]   | Birmingham | 197.2  | 96.5 <sup>a</sup>               | 36.3 <sup>a</sup>       | –                       |
| Rees <i>et al.</i> [1]       | National   | African: 179.8<br>(125.2, 250.1)<br>Caribbean: 517.5<br>(398.5, 660.8) | Indian: 193.1<br>(140.8, 258.4) | 134.5<br>(128.2, 141.1) | 188.39<br>(90.3, 346.5) |

<sup>a</sup>Age-standardized.

**Fig. 3** Temporal trend for the incidence **(A)** and prevalence **(B)** of SLE

environmental exposures; for example, countries nearer the equator are exposed to more ultraviolet radiation, which has been hypothesized to be an environmental trigger for SLE [104, 105]. The variation could also be attributable to differences in the epidemiological study methods used, the diagnosis rates of SLE in each country, the diagnostic criteria used, access to health care, access to immunology laboratory tests and differing thresholds for positive results, the decade the study was carried out, whether the rates were age adjusted and, if not age adjusted, the underlying population structures. For example, the incidence of SLE in Zimbabwe was one of the lowest worldwide. This may have been underestimated because the data were collected retrospectively, relied on the attendance of people with SLE at one of

the study hospitals during the study period, it was not an age-adjusted rate, and life expectancy is lower in Zimbabwe such that the peak age of onset may exceed the average life expectancy. Likewise, the low prevalence found in Australia may be attributable to the fact that it was a small community survey of Australian Aboriginal people in Yarrabah, North Queensland and was underpowered to detect any SLE cases. The North American estimate of SLE incidence of 23.2/100 000 person-years may be overestimated because it is significantly higher than all the other USA estimates. This may be because it is an unadjusted rate or may reflect methodological differences rather than genetic or environmental differences in the population at risk. This study used the Medicaid database, which may have self-selected people with a

chronic disease such as SLE, who may be overrepresented in Medicaid, and hence increased the estimate. It should be emphasized that Fig. 1 used data from different decades and from studies using different case-ascertainment methods so should be interpreted with caution.

In common with other conditions that display autoimmune features, SLE is universally more common in females. This could relate both to possession of the double X chromosome and to differences in oestrogen levels, which modulate immune responses [106, 107]. Hormonal changes have been hypothesized to explain the peak incidence in women in young to middle adulthood compared with childhood and older adulthood. However, this explanation cannot fully explain why the peak in incidence extends into the post-menopausal age group [2] unless there is a longer latency between the rise in oestrogen levels, the triggering of the autoimmune pathway and the development of clinical disease in some women.

Incidence and prevalence peak in middle age. Most worldwide studies confirmed the delayed peak age of prevalence in males. Interestingly, two studies from Scandinavia found a lower peak age in men [21, 70]; however, this could be attributable to the small numbers of males in these studies (24 males in the study by Nived *et al.* [70] and nine males in the study by Lerang *et al.* [21]).

The majority of studies that compared ethnic differences found Black people to have high incidence and prevalence of SLE, White people to have low and Hispanic and Asian people to have intermediate incidence and prevalence of SLE. However, most of these studies were performed in the USA and Europe. Interestingly, the study of Black Africans in Zimbabwe [9] had a low incidence of SLE. As discussed above, this may have been underestimated. Alternatively, it may be that the incidence and prevalence of SLE is higher in Black populations who have emigrated out of Africa because of differences in gene-environment interactions. This is a hypothesis being explored in the Gullah population in South Carolina compared with people from their ancestral origin in Sierra Leone [108, 109]. Further high-quality epidemiological studies in Africa would also help to address this question. This is challenging in a resource-limited system, where health-care systems are constrained, but could be achieved using the approach used by the WHO-ILAR COPCORD [110].

It is not possible directly to compare the change in incidence and prevalence between studies in the same country that have used different study methods or case definitions; for example, in the UK Nightingale *et al.* [76, 30] used a stricter definition of SLE than Somers *et al.* [31] or Rees *et al.* [1]. The majority of those studies that have looked at the same population using the same methods over time have shown an increasing incidence and prevalence, except for the most recent studies from the UK and the USA, which showed a reduction in incidence. These may be true increases in incidence and prevalence over time, for example, because of an increase in risk factors for SLE and improved survival, or they may be artefactual

because of improved diagnosis of people with SLE or better case-ascertainment methods in the study design. Owing to increasing globalization, it is also possibly attributable to net immigration of non-White populations into areas that were previously predominantly White. The recent reductions in incidence in the UK and the USA may therefore reflect changes in environmental risk factors, such as reduced smoking or changes in migration patterns, or perhaps suggest that the risk in later generations of migrants regresses towards the country's mean. It is important to study these temporal changes so that future health services can be planned to meet the needs of the populations.

A potential limitation of this study was that, firstly, for completeness, all eligible studies were included regardless of size or quality. There is therefore a risk of bias affecting the cumulative evidence. In general, earlier studies were less rigorous than more recent studies and there was greater funding of studies in more developed countries. Secondly, as discussed, it is difficult to assess trend over time between studies that have used different methodologies. Future work should consider study design to enable exploration of temporal trends.

## Conclusions

In summary, there is wide geographical variation in the reported incidence and prevalence of SLE. North America had the highest reported incidence and prevalence of SLE, Africa had the lowest incidence and Australia the lowest prevalence. The incidence and prevalence of SLE is higher in females compared with males regardless of age or ethnic origin. The incidence and prevalence are age related, and there is a peak incidence and prevalence for both sex. Males have an older peak age of incidence and prevalence compared with females. In general, people of Black ethnicity have the highest incidence and prevalence of SLE worldwide, followed by Asian and then White ethnic groups. There appears to be a trend of increasing prevalence of SLE with time; the trend for incidence is less clear. Further work to address the lack of epidemiological studies of SLE in Africa, for example using the WHO-ILAR COPCORD approach, may further knowledge underpinning ethnic variation in SLE.

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## Supplementary data

Supplementary data are available at *Rheumatology* Online.

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