LUPUS SCIENCE & MEDICINE™

Age-specific and sex-specific incidence of systemic lupus erythematosus: an estimate from cross-sectional claims data of 2.3 million people in the German statutory health insurance 2002

Ralph Brinks,[1,2] Annika Hoyer,[2] Sergej Weber,[1] Rebecca Fischer-Betz,[1,3] Oliver Sander,[1,3] Jutta G Richter,[1,3] Gamal Chehab,[1,3] Matthias Schneider[1,3]

To cite: Brinks R, Hoyer A, Weber S, *et al*. Age-specific and sex-specific incidence of systemic lupus erythematosus: an estimate from cross-sectional claims data of 2.3 million people in the German statutory health insurance 2002. *Lupus Science & Medicine* 2016;**3**: e000181. doi:10.1136/lupus-2016-000181

► Additional material is available. To view please visit the journal online (http://dx.doi.org/10.1136/lupus-2016-000181).

Received 19 July 2016
Revised 28 October 2016
Accepted 5 November 2016

[1]Hiller Research Unit for Rheumatology, University Hospital Duesseldorf, Duesseldorf, Germany
[2]German Diabetes Center, Institute for Biometry and Epidemiology, Duesseldorf, Germany
[3]Policlinics for Rheumatology, University Hospital Duesseldorf, Duesseldorf, Germany

Correspondence to
Dr Ralph Brinks; ralph.brinks@med.uni-duesseldorf.de

ABSTRACT

Objective: To provide an estimate of age-specific incidence rate of physician-diagnosed systemic lupus erythematosus (SLE) for German men and women.

Methods: The age-specific and sex-specific prevalence of diagnosed SLE in claims data is used to estimate the incidence in the German male and female population. The claims data set stems from a representative sample of the statutory health insurance in 2002 and comprises 2.3 million people. The statutory health insurance covers >85% of the German population.

Results: The estimated incidence rates are 0.9 (95% CI 0.7 to 1.1) per 100 000 person-years for men and 1.9 (95% CI 1.7 to 2.2) per 100 000 person-years for women. The age-specific incidence rate of SLE in the male population has a maximum of 2.2 (95% CI 1.0 to 3.4) per 100 000 person-years at the age of 65–70 years. In women, the incidence is peaking at the rate of 3.6 (95% CI 2.9 to 4.3) cases per 100 000 person-years at the age of 20–25 years, but has a second local maximum (2.6, 95% CI 1.5 to 3.8) at menopausal age.

Conclusions: For the first time, representative data on the incidence of SLE in Germany are provided. The estimated incidence rates of SLE for men and women in Germany are at the lower end of other estimates from comparable European countries.

INTRODUCTION

In descriptive epidemiology, the incidence rate of a chronic disease is an important measure for planning and allocation of healthcare resources.[1] Together with mortality, the incidence is the driving force of the prevalence of the chronic condition.[2 3] Moreover, the pattern of the incidence yields important insights into the underlying causes of the disease. Considering the age-specific incidence rate, one may estimate the individual risk of a newly manifest disease in this age.

Cohort and registry studies are the standard methods for estimating the incidence. In cohort studies, a group of people initially without the disease is followed up over a period of time and regularly examined whether the disease has newly occurred. Particularly in infrequent diseases such as systemic lupus erythematosus (SLE), cohort studies for direct estimation of the incidence are lengthy and need the recruitment of many people. In registry studies, all newly occurring cases of the disease in a well-defined catchment population are reported to the registry. The operation and maintenance of both cohorts and registries are costly.

Hence, in the scientific literature prevalence studies for rare conditions can be found much more frequently than incidence estimates. If, however, the age-specific prevalence is known, it is possible to estimate the age-specific incidence by mathematical relations between incidence and prevalence.[4] To our knowledge, there is no estimate of the incidence of SLE in Germany. The aim of this work is to provide an estimate of age-specific incidence rate for German men and women.

METHODS

For reasons of money transfers between the different sicknesses funds, all funds of the German statutory health insurance (SHI) by law have to collect a comprehensive set of claims data. In 2007, the Federal Statistical Office (FSO) of Germany released parts of this data set for scientific purposes.[5] The

released data set consisted of the anonymised demographic data, medical diagnoses (coded in International Classification of Diseases, Tenth Revision), medical consultations, hospital stays, sick leaves, prescribed drugs and the associated costs of a representative sample of all insurants in 2002. At that time, the SHI covered 85.7% of the total German population.[6] This allows estimating the sex-specific and age-specific prevalence of SLE.[7] We use the age-specific prevalence of SLE in men and women to estimate the incidence by a recently developed method, which makes use of a validated analytical relationship between age-specific prevalence, age-specific incidence rate and mortality.[4] The central idea is to describe a change in the prevalence from one age group to the consecutive age group by balancing incident cases and fatalities in terms of a differential equation. Further details on the method are given in the online supplementary file. All calculations have been stratified by gender.

To determine the overall incidence for SLE in men and women in 2002, we use the estimated age-specific incidence rates for men and women and the age distribution of the German population in 2002.[8]

All calculations have been performed with the statistical software R, V.3.2 (The R Foundation for Scientific Computing).

RESULTS

Of the 2.3 million people in the data set released by the FSO, 845 people (165 men) had a diagnosis of SLE.[7] The resulting incidence estimate for men and women is shown in figure 1. Numerical values are presented in the online supplementary data.

For ages <60 years, the median age-specific incidence rate of women in 2002 is greater than the median rate of men. While in women the incidence is peaking at the rate of 3.6 (95% CI 2.9 to 4.3) cases per 100 000 person-years at the age of 20–25 years, in men the maximum is 2.2 (95% CI 1.0 to 3.4) per 100 000 person-years at the age of 65–70 years. Obviously, there is a second peak in the incidence of women at menopausal age. The apparent third modus of the incidence in women about the age 65–69 possibly is an artefact of the minimum at age 60–64, which has wide confidence bars.

Overall incidence rates in the population are estimated to be 0.9 (95% CI 0.7 to 1.1) per 100 000 person-years for men and 1.9 (95% CI 1.7 to 2.2) per 100 000 person-years for women.

DISCUSSION

Our article presents an estimate of the age-specific incidence rates of SLE for men and women in Germany in 2002 based on claims data from the SHI. For Germany, this is the first presentation of the age-specific incidence rates of SLE. We found a bimodal distribution of the incidence for women. There are indications for this bimodal distribution in German register data,[9] but to our knowledge it has never been described on a representative population-based sample. A possible hypothesis for the two modes could be that those women contracting SLE at ages about the first maximum have a different pathogenesis than those at the second maximum. Indications for varying disease aetiologies are the differences of SLE phenotypes occurring in patients with different ages of disease onset.[10]

There are comparable estimates from other European countries. Data from the French SHI find overall incidence rates of 0.9 and 5.5 per 100 000 person-years in men and women.[11] While the overall incidence rates of men agree, the overall rate of German women is less than half of the French rate. While part of this difference may be explained by a higher incidence rate in the French overseas territories,[11] the German rate for women still appears to be low. This leads to a relatively low female-to-male ratio of the incidence (about 2:1 in Germany and about 6:1 in France). Moreover, the French data show a different course of age-specific incidence rate for women. The curve is unimodal with a maximum in the age group 30–39. Older age-specific incidence data from the UK show a maximum incidence rate of 13 per 100 000 person-years in women at about 50 years of age.[12] The maximum incidence in men from the UK is at the age of about 70 years, which agrees with our data. However, the peak value in the data about

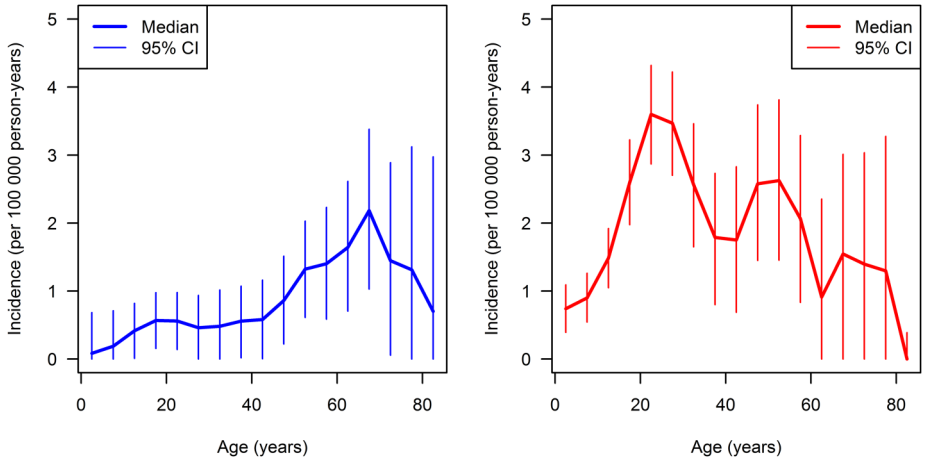

Figure 1 Age-specific incidence of systemic lupus erythematosus (SLE) in German men (left) and women (right) in 2002. The vertical bars indicate the 95% CIs.

British men is twice as high as in Germany. Thus, we may conclude that our estimated incidence rates are at the lower end of existing estimates from comparable European countries. Apart from different ethnic compositions of the German, French and the UK populations, another reason for the differences might be that our data have not been collected for scientific purposes. Thus, the completeness, the quality of the diagnoses and the underlying diagnostic criteria cannot be assessed. Nevertheless, the validity of the claims data for scientific and epidemiological purposes was tested in case of dementia, where the estimates were consistent with several other data sources.[13]

The prevalence data, which our incidence estimates are based upon, are in good agreement with estimates from comparable national data.[7] The estimation of the age-specific incidence is accomplished indirectly via a mathematical method, which has demonstrated higher accuracy compared with all hitherto existing methods of incidence estimation from prevalence data.[14] By the epidemiological rule that the prevalence equals the product of the mean incidence and the mean duration, it can be shown that our estimated incidence rate is consistent with the prevalence data (see the online supplementary file for details).

One limitation of our work is the age of data used for this analysis. All changes in prevalence after the data collection in 2002 have not been captured. Here, more recent data would be helpful. The results of the newer incidence estimates may be compared with the results presented here. This is important to derive secular trends of the incidence, which might reflect a change of the risk factors of SLE in the German population. This may be seen in the light of the joint efforts of the WHO and the United Nations to monitor the risk factors of chronic diseases.[15]

The data this analysis is based upon is a representative sample of all insurants from the German SHI. A drawback is the lack of people who were not insured in the SHI during the survey in 2002. It is unclear how the possible differences regarding health risks between privately and publicly insured people might affect the incidence. However, as the sample underlying this analysis is representative for >85% of the German population, the effect is likely to be low.

Despite these limitations, our study provides evidence about the age-specific and sex-specific incidence rates of SLE in Germany. Our work provides a basis for comparison with future surveys and contributes to regular monitoring of lupus and its risk factors in Germany.

Acknowledgements The authors thank the Forschungsdaten-Zentrum of the German FSO, especially Lydia Spies and Rafael Beier.

Contributors RB developed the methods, drafted the text, and performed the analysis. RB, AH, SW, RF-B, OS, JGR, GC and MS critically revised the text, gave important intellectual contributions and final approval of the version to be published.

Competing interests None declared.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement The data presented in this article are based on the data published in peer-reviewed journals only. These data sources have been properly cited; no unpublished data have been used.

REFERENCES

1. Hennekens CH, Buring JE, Mayrent SL. *Epidemiology in medicine*. New York, NY: Little, Brown and Company, 1987.
2. Keiding N. Age-specific incidence and prevalence: a statistical perspective. *J Royal Statist Soc Series A* 1991;154:371–412.
3. Brinks R, Landwehr S. Age- and time-dependent model of the prevalence of non-communicable diseases and application to dementia in Germany. *Theo Popul Biol* 2014;92:62–8.
4. Brinks R, Landwehr S, Icks A, *et al*. Deriving age-specific incidence from prevalence with an ordinary differential equation. *Statist Med* 2013;32:2070–8.
5. Lugert P. Stichprobendaten von Versicherten der gesetzlichen Krankenversicherung 2007:Arbeitspapier 22, Federal Statistical Office of Germany, Wiesbaden http://www.forschungsdatenzentrum.de/publikationen/veroeffentlichungen/22.asp (accessed May 2016).
6. Federal Ministry of Health. Gesetzliche Krankenversicherung Mitglieder und mitversicherte Angehörige nach Altersgruppen, 2005. http://www.bundesgesundheitsministerium.de/fileadmin/redaktion/pdf_statistiken/krankenversicherung/Versicherte-1992-2004-pdf-6849.pdf (accessed May 2016).
7. Brinks R, Fischer-Betz R, Sander O, *et al*. Age-specific prevalence of diagnosed systemic lupus erythematosus in Germany 2002 and projection to 2030. *Lupus* 2014;23:1407–11.
8. Federal Statistical Office of Germany, Bevölkerung Deutschland. https://www-genesis.destatis.de/genesis/online/link/tabellen/12411* (accessed May 2016).
9. Deutsches Rheuma-Forschungszentrum, Daten der Kerndokumentation 2014, http://www.drfz.de/wp-content/uploads/Ergebnisse_Kerndokumentation_2014.pdf, Slide 12 (accessed Jun 2016).
10. Ambrose N, Morgan TA, Galloway J, *et al*. Differences in disease phenotype and severity in SLE across age groups. *Lupus* 2016;25:1542–50.
11. Arnaud L, Fagot JP, Mathian A, *et al*. Prevalence and incidence of systemic lupus erythematosus in France: a 2010 nation-wide population-based study. *Autoimm Rev* 2014;13:1082–9.
12. Somers EC, Thomas SL, Smeeth L, *et al*. Incidence of systemic lupus erythematosus in the United Kingdom, 1990–1999. *Arthrit Care Res* 2007:57:612–18.
13. Ziegler U, Doblhammer G. Prävalenz und Inzidenz von Demenz in Deutschland—Eine Studie auf Basis von Daten der gesetzlichen Krankenversicherungen von 2002. *Gesundheitswesen* 2009;71:281–90.
14. Landwehr S, Brinks R. A comparative study of prevalence-based incidence estimation techniques with application to dementia data in Germany. *Statist Med* 2016;35:768–81.
15. Beaglehole R, Bonita R, Alleyne G, *et al*. UN high-level meeting on non-communicable diseases: addressing four questions. *Lancet* 2011;378:449–55.

Age-specific and sex-specific incidence of systemic lupus erythematosus: an estimate from cross-sectional claims data of 2.3 million people in the German statutory health insurance 2002

Ralph Brinks, Annika Hoyer, Sergej Weber, Rebecca Fischer-Betz, Oliver Sander, Jutta G Richter, Gamal Chehab and Matthias Schneider

*Lupus Sci Med*2016 3:
doi: 10.1136/lupus-2016-000181