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ORIGINAL ARTICLE

# Incidence of rheumatoid arthritis from 1995 to 2001: impact of ascertainment from multiple sources

**Jens K. Pedersen · Niels K. Kjær · Anders J. Svendsen · Kim Hørslev-Petersen**

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**Abstract** The aim of this study was to describe the mean incidence rate of rheumatoid arthritis over a 7-year period from 1995 to 2001 in a population in the southern part of Denmark, using the data from several sources. Cases fulfilling the 1987 American College of Rheumatology criteria for rheumatoid arthritis were identified at hospitals and private practising rheumatologists (referral centres), and in general practice. The observed incidence was 32/100,000 person-years (95% confidence interval 29–35). Using the ratio between the number of cases known only from general practice and the number known from general practice and referral centres, the estimated incidence was 35/100,000 person-years (95% confidence interval 32–38). We suggest that the estimated rate should be viewed as a plausible upper limit for the incidence of rheumatoid arthritis in the southern part of Denmark.

**Keywords** Rheumatoid arthritis · Incidence · Epidemiology · Registers

## Introduction

When investigating the incidence of rheumatoid arthritis (RA), a frequently used approach has been to identify cases at health care facilities covering the population in a defined region [1]. However, when using data from, for instance, one hospital it is possible that some cases in the population may have been treated at other hospitals or by private practising rheumatologists. When using data from hospitals and rheumatologists, some cases may have been treated only in general practice, and if attempts have been made to identify the cases at all the health care facilities within a region, it is still possible that cases may have been treated outside the region.

Accordingly, to minimise the risk of underestimating the incidence of RA, some studies have been based on data from all or most of the health care facilities covering a population [2–7]. Another approach may be to use data from one or more facilities where the majority of cases are expected to be found and subsequently to estimate the number of cases missing, using data from an independent source. If the completeness of registrations at a facility is known, biased estimates based on the data from the selected facility may then be corrected [8].

On the basis of cases ascertained retrospectively at a rheumatology hospital in the southern part of Denmark, we have previously reported age and sex specific incidence rates of RA over a 7-year period from 1995 to 2001 [9]. The aim of the present study was to re-evaluate the mean annual incidence of RA using data from general practice, hospitals, and private practising rheumatologists working inside and outside the region defining the study population.

## Methods and materials

### Setting

Until a governmental reform in 2007, the County of South Jutland was situated in the southern part of Jutland, Denmark. To the south, the region was delineated by the

J. K. Pedersen (✉) · K. Hørslev-Petersen
Research Unit, King Christian X Hospital for Rheumatic Diseases, Toldbodgade 3, 6300 Graasten, Denmark
e-mail: jensk@dadlnet.dk

N. K. Kjær
General Practice, V. Sottrup, Sønderborg, Denmark

A. J. Svendsen
Institute of Public Health, University of Southern Denmark, Odense, Denmark

Danish–German border, to the east and west by the costal line of Jutland, and to the north by two neighbouring counties (Fig. 1).

Ascertainment of cases

*Rheumatology hospital*

The King Christian X Hospital for Rheumatic Diseases served as a referral centre for patients with rheumatic diseases from the County of South Jutland. From 1995 to 2001 most of the rheumatologic expertise in the region was centred at the hospital. Details about the procedures used for ascertaining incident cases of RA in the hospital register have been reported elsewhere [9]. In short, the hospital medical records were scrutinised to identify the incident cases of RA over a 7-year period from 1995 to 2001, retrospectively. As case definition, we used the list and tree format of the 1987 American College of Rheumatology criteria for RA (1987 ACR) [10]. The criteria were fulfilled cumulatively. Patients were included as cases if they had been classified as having RA for the first time in the study period, if they were older than 15, and if they were residing in the County of South Jutland at the time the criteria were fulfilled.

*Danish National Hospital Register (DNHR)*

When a patient is discharged from a Danish hospital, diagnostic data are transferred to the DNHR. This nationwide register was established in 1977, and from 1995 outpatient contacts were also included [11]. In the register, patients are identified by a unique personal identification number (CPR number) given to all Danish citizens, and diagnoses are registered according to the WHO International Classification of Diseases (ICD). From the DNHR, data were extracted on the residents in the County of South Jutland who for the first time from 1995 to 2001 appeared in the register with a diagnosis of RA (ICD-10 codes: M05.0–M05.9 and M06.0–M06.9). For patients in the register who had not been ascertained as incident cases at the King Christian X Hospital for Rheumatic Diseases [9], the following work-up procedure was used: if a patient had never been to the rheumatology hospital or if a patient had been to the rheumatology hospital prior to the contact where the diagnosis was made, medical records were requested from the hospital where the patient had been diagnosed. Subsequently, all records were scrutinized to see if the patient had fulfilled the 1987 ACR criteria (list and tree format).

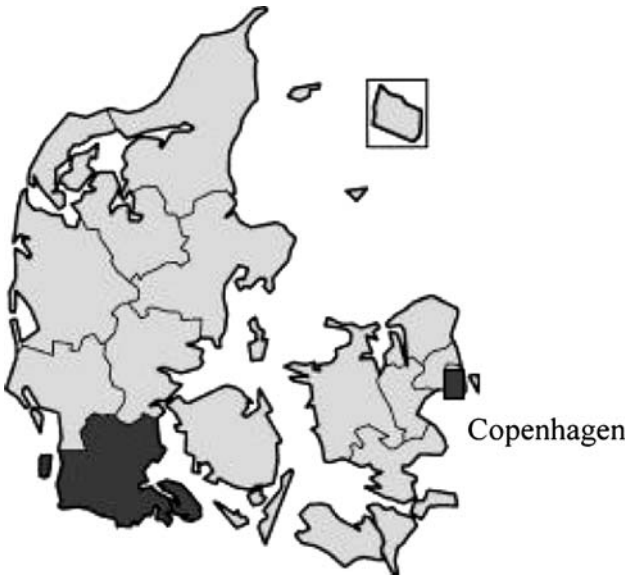


**Fig. 1** The County of South Jutland, Denmark, a region with a mean population from 1995 to 2001 of 204,769 people over the age of 15

*Private practicing rheumatologists*

In the study period, two private practising rheumatologists worked inside the region. We were given access to the local register at one of the private practising rheumatologists who settled in the county in 2001, and the medical records were scrutinized to identify incident cases of RA according to the 1987 ACR criteria.

Using data from the public Health Insurance, we identified patients residing in the county who in the period 1997–2001 had been treated with disease-modifying antirheumatic drugs (DMARD) by rheumatologists working inside and outside the region. Data for the years 1995 and 1996 were not available. A total of six rheumatologists who worked outside the region were identified, and all participated in the study. The six rheumatologists were asked on a mail questionnaire to indicate if and when the patients for the first time had fulfilled the list format of the 1987 ACR criteria. The other rheumatologist who worked half-time inside the region had, according to Health Insurance data, treated seven patients with DMARD, but the rheumatologist did not want to participate in the study. None of these patients were identified as cases in any of the other sources.

*General practice*

In Denmark, the vast majority of patients with rheumatic diseases can only get access to a rheumatologist after having consulted a general practitioner. In theory, general practitioners (GPs) therefore hold key information on the health status of their patients. In 2004, the 170 GPs from 91 practices in the region were asked on a questionnaire to report all patients with incident RA from 1995 to 2001. On the basis of registrations at the King Christian X Hospital for Rheumatic Diseases we knew that more than 95% of the

practices in the region had at least one patient with incident RA in the study period. Since it was assumed that medical records in general practice would not hold information on the involvement of specific joint areas, the GPs were asked to indicate if the patients had ever fulfilled an adapted version of the 1987 ACR list format. In the adapted version, the 1987 ACR criterion referring to the presence of swellings in three or more defined joint areas was substituted for the item "Did the patient have swellings of three joints or more". The criterion referring to symmetrical swellings in 14 defined joint areas was substituted for the item "Did the patient have swellings in the same joints on both the sides of the body (symmetrical joint swelling)".

Before being used, nine GPs found that the questionnaire appeared relevant, clear, and acceptable. By mail, up to four personalised reminders were sent to the GPs in the county and on two occasions the questionnaire and a pre-addressed, stamped return envelope was enclosed. Finally, the non-respondents were contacted by phone. Doctors who tried to ascertain cases were given an incentive of about 30 EUR.

### Statistics and ethics

In the analysis, cases ascertained at the rheumatology hospital, other hospitals (identified through the DNHR), and by private practising rheumatologists were grouped under the name *referral centres*. Duplicate cases from general practice and the referral centres were identified using the CPR number, and it was ensured that no patient appeared more than once within each source. The estimated total number of cases in the population was calculated using the ratio estimator. The Binomial distribution was used for calculating the 95% confidence intervals (95% CI) for incidence rates (crude rates) and the completeness of registrations. Statistics were done using Stata, version 8.2. Population data were provided by Statistics Denmark.

The study was approved by the local ethics committee (Reference No. 2426-02) and the Danish Data Protection Agency (Reference No. 2002-41-2231).

## Results

### Ascertainment of cases

#### *Referral centres*

At the King Christian X Hospital for Rheumatic Diseases 440 cases were ascertained. In the DNHR, we identified 90 patients who had not been ascertained as cases at the rheumatology hospital. In 53 patients, relevant records were available at the rheumatology hospital and none of these patients fulfilled the 1987 ACR criteria. In the remaining 37 patients, information was requested from other hospitals and three patients fulfilled the 1987 ACR criteria. At the private practice of the rheumatologist who settled in the region in 2001, seven patients fulfilled the 1987 ACR criteria. From the private practising rheumatologists working outside the region information was requested on 30 patients treated with DMARD, and 1 patient for the first time in the study period fulfilled the 1987 ACR criteria.

#### *General practice*

A total of 126/170 (74%) of the GPs returned the questionnaire, and 60 GPs (35%) reported at least 1 patient diagnosed with RA in the study period. The doctors worked in 40 (44%) of the 91 practices in the region. The GPs reported a total of 148 patients diagnosed with RA and in 121 patients (108 known at referral centres, 13 only known by GPs) the fulfilment of the classification criteria was documented. Features in the cases ascertained at referral centres and in general practice are seen in Table 1.

### Incidence rates and completeness of registrations

The total number of observed cases at the referral centres and from general practice was 464 (Fig. 1) and the mean observed incidence from 1995 to 2001 was 32/100,000 person-years (*py*) (95% CI 28–34). The observed completeness of registrations at the rheumatology hospital was 95% (95%

**Table 1** Features in patients fulfilling the 1987 ACR classification criteria ascertained at referral centres (hospitals and private practicing rheumatologists) and in general practice (%, unless otherwise stated)

| | Cases fulfilling the 1987 ACR criteria | | |
|---|---|---|---|
| | General practice only ($n$ = 13) | Referral centres and general practice ($n$ = 108) | Referral centres only ($n$ = 343) |
| Age, years, median | 64 | 61 | 63 |
| Females | 69 | 76 | 63 |
| Rheumatoid factor positive | 77 | 79 | 75 |
| Erosions or periarticular osteopenia on radiographs | 8 | 22 | 22 |

CI 92–97%) and the observed completeness at the referral centres was 97% (95% CI 96–99%).

The estimated number of cases in the population not ascertained in general practice or at the referral centres was 41 [(13/108)*343 = 41] and the estimated total number of cases in the population was 505. The mean estimated incidence from 1995 to 2001 was 35/100,000 *py* (95% CI 32–38). At the rheumatology hospital, the estimated mean completeness of registrations was 87% (95% CI 84–90%), and at the referral centres it was 89% (95% CI 86–92) (Fig. 2).

## Discussion

The primary strength of this study is that an extensive search for cases was carried out at hospitals, GPs, and private practising rheumatologists working inside and outside the region defining the study population. In fact, this is the first study attempting to identify the incident RA cases at private practising rheumatologists, using administrative data from the public Danish Health Insurance.

Still, we may not have identified all patients with incident RA from the study period. First, from the public Health Insurance data on patients treated in 1995 and 1996 were not available and one of the two private practising rheumatologists working inside the region did not want to participate in the study. If it is assumed that the seven patients seen by this rheumatologist actually were RA cases, and that one additional patient would have been ascertained if Health Insurance data had been available for 1995 and 1996, we would have missed a maximum of eight cases. Second, it has previously been described that data in the DNHR are not accurate. In one study, up to 22% of the diagnoses for diseases of the musculoskeletal system and connective tissues were not correct [12]. In another study, it was estimated that only 50% of RA cases may have been registered in the DNHR [13]. We may therefore not have identified all patients with incident RA treated at other hospitals than the rheumatology hospital. At the rheumatology hospital a search for cases of RA misclassified with other diagnoses had been performed [9], and we therefore do not think that we have missed any cases at this facility. In our opinion, all RA cases at referral centres may not have been ascertained, but the impact on the rates would have been minimal.

All the GPs in the region were asked to participate in the study, but not all reported patients. It is not possible to discern whether the reported cases were known by the individual general practitioner only or by all the GPs in practices with more than one doctor. Nevertheless, a lower number of cases than expected were reported from general practice. There may be three reasons for this: first, the GPs may have been reluctant to participate in our study as a consequence of the numerous mail questionnaires sent to general practice [14]. Second, some of the GPs may not have received information about the disease status of their RA patients. Third, as the study proceeded we were informed that not all of the GPs had a record system that enabled them effectively to retrieve data on patients with RA. It has previously been estimated that over a 1-year period 18–42% of the patients with RA have not been in contact with their GPs [15], and this would have made it difficult for the GPs to recall the patients with RA.

For the ascertainment of cases from general practice, we used an adapted version of the 1987 ACR criteria. Using this version, it may have been easier to be classified as being a case in general practice. However, the cases ascertained in general practice and at the referral centres had similar features except for the proportion of patients with radiographic changes. This could reflect that in general practice, radiographs may not be taken routinely in patients with arthritis. We believe that the cases ascertained by GPs only, would also have fulfilled the original 1987 ACR criteria.

The number of missing cases was estimated using the ratio estimator, which is based on the same logic as the capture–recapture methodology [16], and although not shown, the two methods gave similar results. Using the ratio estimator, it is implicit that the estimated numbers of missing cases have the same features as the cases identified in the sources used in the analysis. In studies of the occurrence of RA in Oslo, the completeness of registrations in a county register has been evaluated using an independent, random sample of the general population [17, 18]. In a random sample of the general population, however, the majority of RA cases identified will be prevalent and this approach may therefore be suitable for the evaluation of the completeness of registrations of prevalent cases, but not necessarily for incident cases. In our study, there is no way to test the hypothesis whether the GPs and the referral centres were

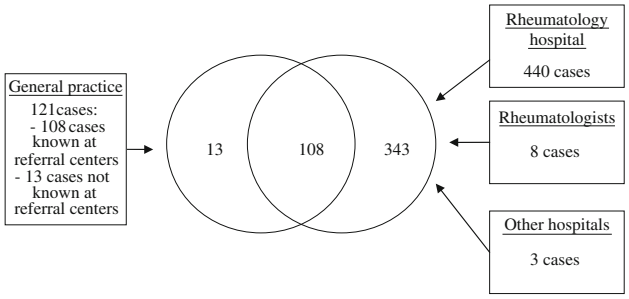


**Fig. 2** Incident cases of rheumatoid arthritis ascertained in general practice and at referral centres (hospitals and private practicing rheumatologists) from 1995 to 2001

independent sources. It may be that the GPs or practices reporting cases were the only ones who knew patients with incident RA not ascertained at the referral centres. In this situation, we may have overestimated the incidence. On the other hand, the GPs who did not report any cases may have known a disproportionately high number of cases not ascertained at any of the other sources in our analysis. In this situation, our analysis would have underestimated the incidence of RA in the population. In our opinion, the latter scenario is less likely in a health care system where patients may be referred for specialist treatment free of charge. Moreover, in the study period we believe that there was a growing awareness among GPs of the importance of early and specific treatment of patients with RA [19], and patients with incident RA may therefore have been referred to a rheumatologist. We therefore believe that the estimated incidence reported here represents a plausible upper limit for the incidence of RA in this population and time period.

In other studies, data have been collected at several health care facilities covering a population in order to ensure a complete enumeration of cases. In this section, the incidence rates described are per 100,000 *py*. In one study from Finland, the incidence rate was 36 [7] and in a study using data from a drug reimbursement register covering the total Finnish population, it was 34 [5]. In Norfolk, UK, the incidence rate was 25 [6]. In Rochester, Minnesota, the incidence rate from 1985 to 1994 was 33 [3], and in a study from Massachusetts, it was 31 [2]. In a study from France, patients with incident RA were identified through press announcements, at hospitals, by rheumatologists and GPs, and the incidence rate was 9 [4]. In the French study, the authors noted that the low rate could indicate that the occurrence of RA in the south of Europe is lower than in the north. Except from the study from France [4], the rates reported in our study is close to that which has been reported in these studies.

In summary, in this study an extensive search for incident RA cases was carried out. The estimated mean incidence rate may be viewed as a plausible upper limit of the incidence of RA in the southern part of Denmark. The high completeness of registrations at a rheumatology hospital serving the population may be important for the impact of future observational studies in patients with incident RA from this facility.

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**Conflict of interest statement** The Authors declare that they have no conflict of interest.

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