Psoriatic arthritis is a significant rheumatologic disorder with health inequity from the patient perspective and large socioeconomic impact for society: Protocol for a Danish nationwide cohort study with general population controls

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Background

Psoriatic arthritis (PsA) is a chronic inflammatory disorder, which is associated with skin psoriasis (PsO) (1). PsA affects approximately 30% of patients with PsO and the typical onset of PsA occurs during the fourth decade of life (2, 3). The clinical presentation of PsA is heterogenetic, but primary characteristics are peripheral joint inflammation, nail involvement, axial skeleton disorders, enthesitis, tenosynovitis and dactylitis (4). Approximately 40 – 60% of patients with PsA may develop erosive and deforming joint complications and the disease may lead to progressive disability and pain (4, 5). Furthermore, PsA is associated with several severe comorbidities, including depression, anxiety, reduced quality of life (QoL), obesity, type II diabetes, osteoporosis, malignancy, and cardiovascular diseases (1, 6). Thus the awareness regarding health economic aspects of PsA have increased. The proportion of work disabled patients with PsA has been reported to be around 40%.[6] Only few studies to date have focused on the impact of disease on a societal perspective on work disability among PsA patients compared to the general population. As well as burden of disease with regard to comorbidities on PsA.

Putting the current research into context

A systematic literature review was performed initially, revealing 109 potentially relevant studies (see search strategy and selection in appendix 1 at the end of the current protocol). Of these only 7 studies could be considered eligible (7-13), after excluding studies based on diagnosis, study design, outcome, and missing comparator group other than PsA.

Actually we did not identify any longitudinal nation-wide population-based register studies with matched comparators covering socioeconomic outcomes or co-morbidities in PsA to data.

Objective:

In a population-wide register-based study, to investigate the possibility of health inequity by studying the health care and public transfer (allowance) costs and income 2 years before and 10 years after a diagnosis of PsA when compared to a matched general population. Also, to study the burden of comorbidities and employment status in this cohort.

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Design and Method:

Study design:

All studies are analytical, epidemiological cohort studies based on national health registries.

Identification of study cohorts:

All residents in Denmark receive a 10-digit personal identification number, which is consistent throughout all national registries, and hence make register linkage possible.

National registries:

The National Patient Register (NPR): has registered diagnosis and surgical codes from Danish hospital departments since 1977. With every discharge, information is provided on up to 20 discharge diagnoses, hospital department etc. Diagnoses are coded according to a modified edition of ICD-8 until 1993 and ICD-10 from 1993 and afterwards.

The Civil Registration System (CRS): Since 1968 the CRS has registered deaths and migrations among all Danish citizens.

Population

Patient cases

All patients registered in with a discharge diagnosis of PsA (ICD-10 L40.5, M07.3, M07.0, M07.1, M07.2) in the period 1998-2014 will be identified. Also all out patients will be identified. Patients with start dates before 1998 will be excluded, since we have no additional information before 1998 (medical, drg, dags etc.).

Control group

Control groups are matched 1:2 on age, gender, married/co-living and municipality.

Follow-up

The populations will be drawn at their first contact in the NPR-register and the index date is the start date of follow-up. For Inpatients the index date is defined as the date of the first discharge form hospital. For out patients the index date is the date of the first hospital contact with PsA. Costs and income before and up till 10 years after the index date will be calculated.

In the cost analysis a patient/control has an index data defined as the in date in the LPR-register. They must be eligible for one whole year after the index date and then in the following after and before periods.

That is an index date can be no later than 31-12-2013 to have at least 1 year eligibility. That is any after period can't start later than 31-12-2013. So we have the first eligible after period starting 1-1-1998 and the last starting 31-12-2013. There can thus be at most 16 1 year periods after the index date (starting index date in 1998).

Patients with index date in 2014 only have before periods and are excluded from the analysis.

A patient/control can die during a period, but they will not be excluded even though they do not have a full 1 year period alive. The definition is that they have to be eligible and alive at the beginning of the period (not necessarily alive the whole period). This could be changed to only including patients/controls alive the whole period, but that would exclude cost the year of death.

Outcomes

Cost

Since we use in-date as index date we also allocate DRG cost on the in-date. Earlier we allocated cost on the out-date since strictly speaking the price is allocated on the out-date. Since almost all hospitalizations are within the same year for in and out date there is little difference in reality, but doing it this way (on in-date) we find the exact costs before and after the index date (index date is included in the first post-year.

Income

There are no income information in 2014, so income covers only 1998-2013.

Since income is stock and the cost are flow data, income is for the calendar year and costs are from the index year and 1 year ahead. That is income is both before and after index date in a given year. Since patients with index date in 2014 are excluded income is set to the index year and thus the missing data for 2014 is not a problem. Persons withno income information will havetheir income set to missing (not 0).

There are some very large incomes that are not considered valid or are outliers. Income over 270.000 €/year are set to missing.

Co-morbidity

Co-morbidity is pooled on the 22 WHO-chapters. We find all diagnosis on in dates 3 years before index date and 3 year after index date (excluding the index date) in the NPR register. Thus the in date has to be in either of the periods. This means, that earlier in dates with an out date in one of the periods are excluded. There has to be eligibility 3 years before and after index date, so index date in the period 2001-2011 are included.

We include all types of diagnosis found in the NPR register, that is both main, action and secondary diagnosis'.

The model estimating the difference between cases and controls for these 22 WHO-chapters will be based on a conditional logistic regression. A regression model is estimated for each of the 22 chapters.

Patient perspective:

The objective and study design has been discussed with a PsA patient after informed consent, Aase Stampe. Her input has been integrated in the current protocol and data presentation.

Research ethics

Data handling and Ethical approval for the study was granted by the Regional Ethics Committee and the dataauthorities, Copenhagen, Denmark (approval number: 2013-54-0410). No informed consent was applicable as the study only involved register linkage, and no actual handling of patients. The ethics committee approved this consent procedure.

Statistical analysis

Demographic and descriptive data will be expressed in absolute numbers and fractions (%).The significance of the income and health care cost estimates for matched case and control groups was assessed by non-parametric bootstrap t test analysis due to the non-normal distribution of the data. The distribution of the data is screwed to the left since there are many 0's in the cost and income data. Odds ratio with 95% CI will be presented for comorbidities at baseline and after 3-year follow-up. In all statistical tests p-values < 0.05 (two-sided) will be considered statistically significant. Calculations will be based on observed data and no imputation of missing data will be performed.

RESULTS

Outline (anticipated)

Table 1: Baseline patient characteristics and comorbidity status at the time of diagnosis.

Figure 2: Total healthcare cost 5 years prior to diagnosis and 10 years after.

Table 2: Comorbidities 3 years before and 3 years after diagnosis of PsA.

Table 3: Average healthcare costs and income from time of diagnosis until end of study period.

Figure 2: Income 5 years prior to diagnosis and 10 years after and Govermental subvention (transfer income) 5 years prior to diagnosis and 10 years after

Figure 3: Employment status 5 years prior diagnosis and 10 years after

Timeline (anticipated)

March-April 2016: Protocol preparation.

Ultimo April 2016: Data extraction.

April-May 2016: Data analysis and interpretation.

May 2016: Manuscript preparation & submission.

Publication

The goal is to publish the obtained results in the Lancet thematic issue: http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(16)00259-2/abstract; with the in the protocol mentioned authors and other participating authors according to involvement. Other rheumatologic specialist journals will be tried if failure in the Lancet.

Additionally, the study results will be presented at national and international professional meetings as well as to professionals and patients, who take an interest in PsA.

CONTRIBUTIONS OF AUTHORS

LEK: will contribute to study conception and design, data collection, the analysis and interpretation of data, drafting the manuscript and approving the final version. LEK takes responsibility for the integrity of the work as a whole.

TSJ: will contribute to study conception and design, the analysis and interpretation of data, revising the manuscript and approving the final version. TSJ had access to data throughout the process and knowledge of roles and responsibilities of each author.

HRG: will contribute to study conception and design, data collection, the analysis and interpretation of data, revising the manuscript and approving the final version. HRG had access to data throughout the process and knowledge of roles and responsibilities of each author.

LD: will contribute to study conception and design, data collection, the analysis and interpretation of data, revising the manuscript and approving the final version. LD had access to data throughout the process and knowledge of roles and responsibilities of each author.

RC: will contribute to study conception and design, data collection, the analysis and interpretation of data, revising the manuscript and approving the final version. RC had access to data throughout the process and knowledge of roles and responsibilities of each author.

ACB: will contribute to study conception and design, data collection, the analysis and interpretation of data, revising the manuscript and approving the final version. ACB had access to data throughout the process and knowledge of roles and responsibilities of each author.

LTHJ: will contribute to interpretation of data, drafting and revising the manuscript and approving the final version. LTHJ had access to data throughout the process and knowledge of roles and responsibilities of each author.

VS: will contribute to interpretation of data, drafting and revising the manuscript and approving the final version. VS had access to data throughout the process and knowledge of roles and responsibilities of each author.

PJM: will contribute to interpretation of data, drafting and revising the manuscript and approving the final version. PJM had access to data throughout the process and knowledge of roles and responsibilities of each author.

JK: will contribute to study conception and design, data collection, the analysis and interpretation of data, drafting the manuscript and approving the final version. JK takes responsibility for the integrity of the work as a whole.

COMPETING INTEREST STATEMENT

LEK, LTHJ, VS, PJM, and RC have received fees for speaking and consultancy by Pfizer, AbbVie, BMS, MSD, Novartis, Eli Lilly, and Janssen pharmaceuticals.

TSJ has received fees for speaking and consultancy by AbbVie, Roche, and Novartis

All other authors have no financial conflicting interests.

All authors declare no non-financial conflicting interests.

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Arthritis Rheumatol. 2014 Jun;66(6):1472-81.

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Ann Rheum Dis. 2012 Aug;71(8):1273-7.

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Feltkode ændret

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APPENDIX 1

Search filter:
Psoriatic Arthritis Prevalence and Disease Impact Survey

PUBMED SEARCH (done the 18 04 2016)
Design:
Nationwide OR Cohort OR Register* OR Registr* OR Register-Based OR "Population based" OR Population-based

Population:
"Arthritis, Psoriatic"[Mesh] OR psoriatic

Outcome:
Burden OR inequity OR comorbidity OR co-morbidity OR "Health-Care Cost" OR "Health Care Cost" OR "Sick leave" OR unemployment

Eligibility criteria:

- Population = PsA
- Design = longitudinal cohort study
- Data (outcome) = socio-economic or co-morbidities
- Contrast/comparator population other than PsA = present

The Search:
109 studies initially retrieved.
34 studies excluded because the study population was other than PsA
39 studies excluded because the design was not longitudinal cohort design
23 studies excluded because the outcome was not co-morbidities and/or health care cost, work disability, or other social costs
6 studies excluded because of no comparator group other than PsA was included

7 studies included after active search:

Gulati AM, Semb AG, Rollefstad S, et al. On the HUNT for cardiovascular risk factors and disease in patients with psoriatic arthritis: population-based data from the Nord-Trøndelag Health Study.
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