EXTENDED REPORT

Societal costs and patients’ experience of health inequities before and after diagnosis of psoriatic arthritis: a Danish cohort study

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ABSTRACT

Objectives To comprehensively study the comorbidities, healthcare and public transfer (allowance) costs in patients with psoriatic arthritis (PsA) before and after diagnosis.

Methods Nationwide cohort study, using data from Danish registries from January 1998 through December 2014. A total of 10 525 patients with PsA and 20 777 matched general population comparator (GPC) subjects were included. Societal costs, employment status and occurrence of comorbidities in patients with PsA both before and after diagnosis were compared with GPC subjects.

Results At baseline, patients with PsA had significantly more comorbidities, including cardiovascular disease (OR 1.70 95% CI 1.55 to 1.86), respiratory diseases (OR 1.73 95% CI 1.54 to 1.96) and infectious diseases (OR 2.03 95% CI 1.69 to 2.42) compared with GPC subjects. At all time points, patients with PsA had higher total healthcare and public transfer costs; they also had lower income (p<0.001) and incurred a net average increased societal cost of £10 641 per patient-year compared with GPC subjects following diagnosis. The relative risk (RR) for being on disability pension 5 years prior to PsA diagnosis was 1.36 95% CI 1.24 to 1.49 compared with GPC subjects. The RR increased to 1.60 (95% CI 1.49 to 1.72) at the time of diagnosis and was 2.69 (95% CI 2.40 to 3.02) 10 years after diagnosis, where 21.8% of the patients with PsA received disability pension.

Conclusions Our findings are suggestive of health inequity for patients with PsA and call for individual preventive measures and societal action.

INTRODUCTION

Psoriatic arthritis (PsA), a chronic inflammatory disorder, is associated with skin psoriasis (PsO).1 PsA affects approximately 30% of patients with PsO, the typical onset of PsA occurring during the fourth decade of life.2-4 The clinical presentation of PsA is heterogeneous, but primary characteristics include peripheral joint inflammation, nail involvement, axial skeleton disorders, enthesitis, tenosynovitis and dactylitis.5 Approximately 40%-60% of patients with PsA may develop erosive and deforming joint complications, and the disease may lead to progressive disability and pain.6-8 Furthermore, PsA is associated with several severe comorbidities, including depression, anxiety, reduced quality of life, obesity, type II diabetes, osteoporosis, malignancy and cardiovascular diseases.1 7 Thus, the awareness regarding cost and health economic aspects of PsA have increased.8-9 The proportion of work disabled patients with PsA has been reported to be approximately 40%.7 10 Few studies to date have focused on the inequities of PsA from a social and economic perspective, comparing patients with PsA with the general population. Likewise, the total burden of PsA with regard to timing and impact of all comorbidities has been scarcely studied.11-16 Health inequities are systematic differences in the health status of different population groups, and there is abundant evidence that the lower an individual’s socioeconomic position, the higher their risk of poor health.17 However, the causality is often bidirectional; poor health also leads to significant individual, social and economic costs, creating a classic downward spiral.18 In a nationwide population-based cohort study, based on prospectively recorded register data, we address the hypothesis that patients with PsA face health inequity by studying the healthcare and public transfer (allowance) costs, employment status as well as personal income 5 years before and 10 years after a diagnosis of PsA. Also, we hypothesise that the burden of various comorbidities will be higher in PsA compared with the general population.

METHODS

Study design and participants
To ascertain the inequities of PsA from an individual, social and economic perspective, our investigation used a nationwide cohort study with data from Danish registries from January 1998 through December 2014. Our study was conducted in accordance with the Strengthening the Reporting of Observational studies in Epidemiology (STROBE) statement and according to a prespecified protocol (see online supplementary file S1) available and published as open-access at the official website of the Parker Institute (http://www.parkerinstitute.dk). Data handling and ethical approval for the study were granted by the Regional Ethics Committee and the Danish Data Protection Agency, Copenhagen, Denmark (approval number: 2013-54-0410). No informed consent was applicable as the study...
involved only linkage of registry-based data, with no actual interaction with patients. The ethics committee approved this consent procedure.

Some background on the Danish healthcare system and information infrastructure follows, as it is necessary to explain our methods. On 31 December 2014, Denmark had a population of approximately 5.7 million. Health and demographic information on all citizens is updated annually in a series of national registries, with a very high degree of completeness. \(^{15,16}\) Linkage of data from these registries is possible using the 10-digit personal identification number automatically assigned to all Danish citizens. \(^{20}\)

The Danish healthcare system is tax funded and offers universal access. Data on healthcare contacts at inpatient and non-primary outpatient facilities are registered in the Danish Patient Registry (DPR), including date of contact and diagnoses given by the treating physician according to the Danish version of the International Statistical Classification of Diseases (ICD-10 starting 1993). \(^{21}\) Reporting of data on each single healthcare contact, excluding primary care visits, is required by the state.

Using data from the DPR, we identified a national population-based cohort of patients with PsA, including those patients who had attended an outpatient clinic during the time period 1 January 1998 through 31 December 2014 and who had received at least one ICD-coded diagnosis corresponding to PsA (ie, ICD-10: L40.5, M07.3, M07.0, M07.1, M07.2). A separate validation study done by LEK and LTHJ revealed a validity of >90% of spondyloarthritis diagnoses in a similar cohort. \(^{22}\)

For each patient with PsA, two general population comparators (GPC) subjects, alive, without PsA and matched on year of birth, gender, time and marital status were identified.

Most patients with PsA are diagnosed by rheumatologists at public outpatient and inpatient facilities. Information on socioeconomic status was obtained from nationwide registries on employment, educational level, income and pensions. Cost of hospital contacts included costs of hospitalisation weighted by use for separate diagnosis-related groups (tariffs) and cost of specific outpatient treatments (DAGS tariffs) based on data from the Danish Ministry of Health. The cost of medicine was derived from the Danish Drug Prescription Registry and consisted of the retail price of each drug multiplied by prescribed quantity. Information on health costs associated with consultation and treatment in the primary sector was collected from the National Health Insurance Service Registry.

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

The PsA population was drawn at the first contact in the DPR after 1998, and the index date was designated as the baseline date. For inpatients, the index date was defined as the date of the first discharge form hospital after January 1998. For outpatients, the index date was defined as the date of the first hospital contact with PsA. Thus, the onset of PsA (index date) is defined as the date of first possible registered PsA diagnosis in DPR. In our cost analysis, subjects had to be eligible for 12 months after the index date; thus, an index date could be no later than 31 December 2013. Consequently, patients with an index date in year 2014 were excluded from our analyses. Healthcare and public transfer (allowance) costs, employment status and personal income 5 years before and 10 years after the index date of patients with PsA were compared with a GPC. Moreover, the burden of various comorbidities was studied 3 years prior to and 3 years after the index date of the patients with PsA. Patients and/or comparators who were registered as deceased were included in the analyses up until the year after their registered date of death. As such, patients/comparators had to be eligible and alive at the beginning of the period but not necessarily alive over the entire period.

Employment status was categorised as regular job/self-employment, unemployment, disability pension, early retirement, age pension retirement, retired on other pensions or not in labour. Average income per patient with PsA and comparators was differentiated into income deriving from employment, social security and unemployment benefit, sick pay, disability pension, early retirement, age pension, other public transfer, other pensions and total income. Very large incomes were not considered valid; income over €270 000/year was set to missing. Yearly healthcare costs for study participants were calculated using information on frequency and cost of hospital contacts (inpatient and outpatient treatments), consultations with general practitioners and other specialists and use and cost of medicine.

Prior to study entry and during follow-up, data on comorbidities registered by physicians in hospital-based inpatient or outpatient somatic care clinics in patients with PsA and GPC subjects were retrieved from the DPR. Comorbidity was pooled on the 22 WHO-chapters (see online supplementary file S2 for definition). We identified all diagnoses 3 years before the baseline date and 3 years after index date (excluding the index date) in the DPR register. Thus, only patients with an index date in the period 2001–2011 were included in the comorbidity analysis. Our study included both main and secondary diagnoses found in the DPR register. The objective and study design were discussed with a patient with PsA after oral and written informed consent and the findings in the current study were shared and discussed with the patient subsequently (see Acknowledgements section for further detail).

### Statistical analysis

Demographic and descriptive data were expressed in crude numbers and fractions (%). The significance of the income and healthcare cost estimates for matched case and comparator groups was assessed by non-parametric bootstrap t-test analysis due to the non-normal distribution of the data. \(^{23}\) The relative risk (RR) to be unemployed, on disability pension or early retired compared with the background population including the 95% CI were calculated at different time points using crude proportions. ORs with 95% CI were presented for comorbidity diagnoses received up to 3 years prior to baseline and during a 3-year follow-up period after diagnosis of PsA. In all statistical tests, p values <0.05 (two-sided) were considered statistically significant. Calculations were based on observed data, and no imputation of missing data was performed.

### RESULTS

A total of 10 525 patients with PsA and 20 777 matched GPC subjects were included in the study.

Median age of patients with PsA and GPC subjects at study entry was 52 years (IQR 40–60 years), 41% were male. Baseline characteristics of patients with PsA and GPC subjects are presented in [table 1](#). The baseline data on demographics and comorbidities split according to organ systems for the PsA group compared with the general population, presented in [table 1](#), showed that already at the time of diagnosis the group of patients with PsA had significantly more comorbidities including neoplasms (OR 1.25 95% CI 1.11 to 1.41), cardiovascular disease (OR 1.7 95% CI 1.53 to 1.86), respiratory diseases (OR 1.8 95% CI 1.69 to 1.96), infectious diseases (OR 2.03 95% CI 1.69 to 2.42) and haematological diseases (OR 1.94 95% CI 1.55 to 2.43).
As illustrated in figure 1, the healthcare costs for the patients with PsA increased from <$2000/year 5 years prior to diagnosis to >$5000/year around the time of PsA diagnosis, reflecting an increased utilisation of healthcare resources associated with reaching a diagnosis. At all time points, the total healthcare costs were higher for patients with PsA compared with the GPC, although the difference was clearly attenuated after time of diagnosis (p<0.001). Figure 2 shows that the average yearly income is lower for patients with PsA at all time points from 5 years prior to diagnosis until 10 years after. However, the difference is markedly increased around and after the year of diagnosis. Likewise, the average public transfer payments are higher for the patients with PsA even before time of diagnosis; again, this difference was attenuated after receiving a diagnosis. In table 2, the average yearly costs and income after date of diagnosis for patients with PsA and GPC are summarised, illustrating a net average increased societal cost of €10 641 per patient-year for patients with PsA compared with GPC.

**Socioeconomic status**

In figure 3, the proportions of employment (or self-employment), disability pension and other socioeconomic status (ie, student, <16 years, unemployment or retired) can be seen at different time points for the patients with PsA and the matched GPC subjects. A detailed view on all the different socioeconomic status proportions can be seen in online supplementary figure S1. The relative risk for being on disability pension 5 years prior to PsA diagnosis was 1.36 (95% CI 1.24 to 1.49) compared with GPC subjects. This figure increased to RR 1.60 (95% CI 1.49 to 1.72) at the time of diagnosis and was RR 2.69 (95% CI 2.40 to 3.02) 10 years after diagnosis, where 21.8% of the patients with PsA received disability pension. Likewise, the relative risk for being unemployed was 1.21 (95% CI 1.09 to 1.34) for patients with PsA compared with GPC 5 years prior to diagnosis, increasing to RR 1.72 (95% CI 1.58 to 1.87) at the time of diagnosis, where 9.1% of the patients with PsA were unemployed. The RR then decreases to 0.95 (95% CI 0.74 to 1.21). The RR for being employed 5 years prior to diagnosis was 0.95 (95% CI 0.93 to 0.97) compared with GPC subjects. This figure decreased to RR 0.87 (95% CI 0.85 to 0.89) at the time of diagnosis and further decreased to 0.76 (95% CI 0.72 to 0.80) 10 years after diagnosis, where 40.9% of the patients with PsA were working.

**Comorbidities**

In table 3, the ORs for various comorbidities in the 3-year period prior to diagnosis and the 3-year period after diagnosis are displayed for subjects diagnosed with PsA and for matched GPC subjects. Subjects diagnosed with PsA have an increased risk of also receiving other diagnoses prior to diagnosis of PsA. However, the ORs are also significantly increased in the 3 years following a PsA diagnosis. Notably, the OR for having mental or behavioural disorders (1.21 95% CI 1.09 to 1.34) became significant after receiving a PsA diagnosis compared with GPC subjects.

**DISCUSSION**

This study demonstrates increased healthcare costs, lower income, higher unemployment rates, higher risk for disability pension and more comorbidities for patients with PsA compared with the general population both in the period prior to diagnosis and with accentuating differences in the years following a PsA diagnosis, confirming our prespecified hypothesis of health inequity from a patient’s perspective and significant socioeconomic impact of PsA from a societal perspective.

The findings are consistent with previous studies reporting increased comorbidities, costs and work disability. To our knowledge, however, this is the first study to assess healthcare and societal cost as well as comorbidities at large in a population of patients with PsA compared with a matched general population based on nationwide prospective data. Some potential limitations of the study design should be considered. The DPR consisting of the Inpatient Register and the Outpatient Register is a substantial data source in this study. All physicians in the country working in healthcare units are obliged to report data, including personal identity number and ICD-coded diagnosis, on all inpatient and specialist outpatient visits.

Evaluations of data in the Inpatient Registry have shown validity between 85% and 95% across different diagnoses and coverage of >99%. Regarding data on specialist outpatient visits, the overall coverage of 80% is somewhat lower. This is primarily explained by missing data from private caregivers, whereas coverage from public non-primary care outpatient units is almost 100%.

Thus, nationwide register-based studies like the present have the apparent strength of being population-based reducing the risk of selection bias. However, some degree of residual confounding and bias cannot be ruled out.

**Table 1** Baseline characteristics and comorbidities at the time of diagnosis for patients with PsA and matched general population comparator

<table>
<thead>
<tr>
<th>Comorbidity</th>
<th>PsA (n=10 525)</th>
<th>GPC (n=20 777)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender, no. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>6222 (59.1)</td>
<td>12 311 (59.3)</td>
</tr>
<tr>
<td>Age, no. (%)</td>
<td>&lt;20</td>
<td>20 (1.9)</td>
</tr>
<tr>
<td></td>
<td>20–29</td>
<td>715 (6.8)</td>
</tr>
<tr>
<td></td>
<td>30–39</td>
<td>1707 (16.2)</td>
</tr>
<tr>
<td></td>
<td>40–49</td>
<td>2431 (23.1)</td>
</tr>
<tr>
<td></td>
<td>50–59</td>
<td>2812 (26.7)</td>
</tr>
<tr>
<td></td>
<td>60–69</td>
<td>1686 (16.0)</td>
</tr>
<tr>
<td></td>
<td>70–79</td>
<td>765 (7.3)</td>
</tr>
<tr>
<td></td>
<td>&gt;80</td>
<td>208 (2.0)</td>
</tr>
<tr>
<td>Married/cohabiting, no. (%)</td>
<td>7320 (69.5)</td>
<td>14 395 (69.3)</td>
</tr>
<tr>
<td>Comorbidities, no. (%)</td>
<td>PsA (n=7508*)</td>
<td>GPC (n=14 800*)</td>
</tr>
<tr>
<td>Endocrine and metabolic disorders, no. (%)</td>
<td>658 (8.8)</td>
<td>816 (5.5)</td>
</tr>
<tr>
<td>Digestive tract disorders, no. (%)</td>
<td>965 (12.9)</td>
<td>1075 (7.3)</td>
</tr>
<tr>
<td>Cardiovascular disorders, no. (%)</td>
<td>1060 (14.1)</td>
<td>1340 (9.1)</td>
</tr>
<tr>
<td>Mental disorders, no. (%)</td>
<td>220 (2.9)</td>
<td>379 (2.6)</td>
</tr>
<tr>
<td>Neuronal system, no. (%)</td>
<td>489 (6.5)</td>
<td>602 (3.4)</td>
</tr>
<tr>
<td>Musculoskeletal system, no. (%)</td>
<td>2884 (38.4)</td>
<td>1936 (13.1)</td>
</tr>
<tr>
<td>Infections, no. (%)</td>
<td>251 (3.3)</td>
<td>249 (1.7)</td>
</tr>
<tr>
<td>Neoplasms, no. (%)</td>
<td>502 (6.7)</td>
<td>805 (5.4)</td>
</tr>
<tr>
<td>Haematological disorders, no. (%)</td>
<td>156 (2.1)</td>
<td>161 (1.1)</td>
</tr>
<tr>
<td>Genitourinary disorders, no. (%)</td>
<td>796 (10.6)</td>
<td>1210 (8.2)</td>
</tr>
<tr>
<td>Skin disorders, no. (%)</td>
<td>778 (10.4)</td>
<td>335 (2.3)</td>
</tr>
<tr>
<td>Respiratory disorders, no. (%)</td>
<td>522 (7.0)</td>
<td>613 (4.1)</td>
</tr>
<tr>
<td>Nervous system, no. (%)</td>
<td>778 (10.4)</td>
<td>335 (2.3)</td>
</tr>
<tr>
<td>Digestive tract disorders, no. (%)</td>
<td>965 (12.9)</td>
<td>1075 (7.3)</td>
</tr>
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<td>796 (10.6)</td>
<td>1210 (8.2)</td>
</tr>
</tbody>
</table>

*Please note that comorbidities required at least 3 years of observation prior and after inclusion date.

GPC, general population comparator; PsA, psoriatic arthritis.

**Costs analysis**

As illustrated in figure 1, the healthcare costs for the patients with PsA increased from <$2000/year 5 years prior to diagnosis to >$5000/year around the time of PsA diagnosis, reflecting an increased utilisation of healthcare resources associated with reaching a diagnosis. At all time points, the total healthcare costs were higher for patients with PsA compared with the GPC, although the difference was clearly attenuated after time of diagnosis (p<0.001). Figure 2 shows that the average yearly income is lower for patients with PsA at all time points from 5 years prior to diagnosis until 10 years after. However, the difference is markedly increased around and after the year of diagnosis. Likewise, the average public transfer payments are higher for the patients with PsA even before time of diagnosis; again, this difference was attenuated after receiving a diagnosis. In table 2, the average yearly costs and income after date of diagnosis for patients with PsA and GPC are summarised, illustrating a net average increased societal cost of €10 641 per patient-year for patients with PsA compared with GPC.
Selection of patients with PsA in this study is based on ICD codes recorded by a selection bias towards more severe cases being included while missing patients with mild disease who are managed entirely at primary care units. However, according to a previous study in Sweden (a Scandinavian country closely resembling Denmark), this is a minor problem and would only increase the number of cases by <4%, at the expense of a larger degree of misclassification.27 Regarding the case definitions of

Figure 1 Illustrates the annual total healthcare costs in Euros for patients with psoriatic arthritis (PsA) and matched general population comparator (GPC) 5 years before diagnosis and 10 years after (p<0.001).

Figure 2 Illustrates the annual income in Euros from employment and annual public transfer allowance in Euros for patients with psoriatic arthritis (PsA) and matched general population comparator (GPC) (p<0.001).
PsA used in this study data and results from another group, spondyloarthritis and ankylosing spondylitis, data suggest that misclassification occurs in <10%. Concerning comorbidities such as acute coronary events, misclassification is estimated to be <5%.19 25

Moreover, the onset of PsA (index date) is defined as the date of first registered PsA diagnosis, thus introducing a risk of diagnostic delay in the current study. However, the majority of ICD codes comes from outpatient clinic and are registered at the time the patient is seen in the clinic. Moreover, the differences are apparent 5 years prior to the index date and a diagnostic delay of >5 years is highly unlikely.

The increased socioeconomic burden and increased frequency of comorbidities many years prior to diagnosis of PsA raise the possibility that these factors may contribute to the development of PsA. However, it should be noted that patients with PsA often suffers from psoriasis of the skin prior to the joint involvement. Further studies are encouraged in order to clarify these mechanisms and to establish effective prophylaxis. Notably, the differences in socioeconomic and health status are accentuated in the years after diagnosis of PsA, illustrating a potential bidirectional causality. Thus, poor health contributes to significant individual, social and economic costs and the lower an individual’s socioeconomic position, the higher their risk of poor health.17 18

Further studies are needed to disentangle the relative role of poor health and lower socioeconomic position or an interaction of the two with regard to risk for developing PsA. Nonetheless, these mechanisms together create a classic downward spiral. At present, close monitoring and preventive measures for various comorbidities including, but not restricted to, cardiovascular diseases should be undertaken when dealing with patients with PsA in the clinic.28 29 Moreover, early diagnosis and sufficient and aggressive treatment, including antitumour necrosis factor

Table 2  Presents average yearly costs and income in Euros for patients with PsA and matched GPC during a 10-year period after date of diagnosis

<table>
<thead>
<tr>
<th></th>
<th>Patients with PsA</th>
<th>GPC</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of persons (N)</td>
<td>10 525</td>
<td>20 777</td>
<td></td>
</tr>
<tr>
<td>Health cost total</td>
<td>€ 4336</td>
<td>2170</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Outpatient services</td>
<td>€ 1074</td>
<td>449</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Inpatient admissions</td>
<td>€ 1914</td>
<td>1062</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Prescription drugs</td>
<td>€ 790</td>
<td>379</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Primary health sector</td>
<td>€ 559</td>
<td>279</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Home care*</td>
<td>€ 483</td>
<td>337</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Income</td>
<td>€ 26 429</td>
<td>31 879</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Income from employment</td>
<td>25 083</td>
<td>30 673</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Other income private pension</td>
<td>1346</td>
<td>1206</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Public transfer income total</td>
<td>€ 11 525</td>
<td>8646</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Sick pay (public funded)</td>
<td>€ 790</td>
<td>357</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Disability pension</td>
<td>3978</td>
<td>1941</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Early retirement</td>
<td>814</td>
<td>1079</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age pension</td>
<td>€ 3974</td>
<td>3861</td>
<td>0.040</td>
</tr>
<tr>
<td>Other public transfers</td>
<td>€ 1970</td>
<td>1408</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Direct health costs</td>
<td>€ 4336</td>
<td>2170</td>
<td></td>
</tr>
<tr>
<td>Home care costs</td>
<td>€ 483</td>
<td>337</td>
<td></td>
</tr>
<tr>
<td>Indirect costs, foregone earnings</td>
<td>€ 5450</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sum of direct and indirect costs</td>
<td>€ 10 269</td>
<td>2507</td>
<td></td>
</tr>
<tr>
<td>Net costs</td>
<td>€ 7762</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Social transfer payments</td>
<td>€ 11 525</td>
<td>8646</td>
<td></td>
</tr>
<tr>
<td>Net costs including transfers</td>
<td>€ 10 641</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Home care cost data are only available from 2009.

GPC, general population comparator; PsA, psoriatic arthritis. Bold signifies the value derived from the sum of other values.

Figure 3  Illustrates socioeconomic status (ie, employment p<0.001, disability pension p<0.001 and other) for the patients with psoriatic arthritis (PsA) and matched general population comparator (GPC) 5 years prior to diagnosis and 10 years after.
therapy, seems to have an impact on the risk for developing work disability and thus diminishing the burden of disease from a patient's perspective and societal perspective. It is evident from this study that the management of the overall burden of disease in patients with PsA is indeed needed and that a successful holistic handling of patients' health may have an impact on both a personal and societal level.

In conclusion, this is the first study to document increased healthcare costs, lower income, higher unemployment rates, higher risk for disability pension and more comorbidities for patients with PsA compared with the general population both in the period prior to diagnosis and with even larger consequences in the years following a PsA diagnosis. This finding is suggestive of health inequity for patients with PsA and calls for preventive measures for the individual as well as an overall societal action.

Acknowledgements We thank Aase Stampe (patient with PsA) for her valuable input to the study design and conception, ensuring the patient's perspective in this article. Her input led to lumping of comorbidities into organ system according to WHO chapters, and omission of some comorbidities (eye and ear diseases; external causes of morbidity and mortality; pregnancy, childbirth and the newborn period). Each author has had full access to all the data in the study, had final responsibility for the decision to submit the publication and take responsibility for all coauthors and the integrity of the work as a whole.

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Competing interests LEK, LTH, VS, PIM, and RC have received fees for speaking and consultancy by Pfizer, AbbVie, Amgen, UCB, Celgene, BMS, MSD, Novartis, Eli Lilly and Janssen Pharmaceuticals. HG has received fees for speaking and consultancy by AbbVie, Roche and Novartis. HG has received fees for speaking by Pfizer. LD has received fees for speaking and consultancy by UCB, MSD and Janssen.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement Unidentified and additional raw data making the basis for this work can be requested after proper correspondence with LEK, and under the extent possible according to national Danish law.

Transparency statement LEK affirms that the manuscript is honest, accurate and in accordance with the prespecified protocol, which can be accessed in the online supplementary material or as open access at http://www.parkerinstitute.dk. No important aspects of the study have been omitted in the current manuscript.

**REFERENCES**

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

Protocol version 1.2
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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 larserik_kristensen@yahoo.com

**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 heterogeneous, 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.
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 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 with no income information will have their 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.
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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 data authorities, 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 skewed 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.
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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)

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.
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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.
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. All authors have no financial conflicting interests.
All authors declare no non-financial conflicting interests.

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References:
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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-morbidity 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:


Supplementary file S2 – WHO ICD10 classification of diseases.

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<tr>
<th>Chapter</th>
<th>Blocks</th>
<th>Title</th>
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<td>Certain infectious and parasitic diseases</td>
</tr>
<tr>
<td>II</td>
<td>C00–D48</td>
<td>Neoplasms</td>
</tr>
<tr>
<td>III</td>
<td>D50–D89</td>
<td>Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism</td>
</tr>
<tr>
<td>IV</td>
<td>E00–E90</td>
<td>Endocrine, nutritional and metabolic diseases</td>
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<td>V</td>
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<tr>
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<tr>
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<td>H60–H95</td>
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<td>XV</td>
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<td>Certain conditions originating in the perinatal period</td>
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<td>XVII</td>
<td>Q00–Q99</td>
<td>Congenital malformations, deformations and chromosomal abnormalities</td>
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<tr>
<td>XVIII</td>
<td>R00–R99</td>
<td>Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified</td>
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<tr>
<td>XIX</td>
<td>S00–T98</td>
<td>Injury, poisoning and certain other consequences of external causes</td>
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<td>V01–Y98</td>
<td>External causes of morbidity and mortality</td>
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<td>Factors influencing health status and contact with health services</td>
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<td>XXII</td>
<td>U00–U99</td>
<td>Codes for special purposes</td>
</tr>
</tbody>
</table>
Supplementary figure S1
Socio status at different years before and after

Socio status
- Employed/self employed
- Public transfer (unemployed)
- Disability pension
- Early retirement
- Retired on age pension
- Student
- Under 16 years
- Other

Year - 15
Case
Year - 10
Control
Year - 5
Case
Year - 2
Control
Year 0
Case
Year 2
Control
Year 5
Case
Year 10
Control
Year 15
Case
Control
Health inequity for people with psoriatic arthritis (PsA) before and after diagnosis

People with psoriatic arthritis have healthcare costs, lower income, higher unemployment rates, higher risk for disability pension and more comorbidities than the general population.

**INTRODUCTION**
Psoriatic arthritis is a chronic inflammatory disease that affects a person’s joints, causing pain and disability. The disease often causes swelling of the fingers and toes, mainly because of joint inflammation. It gets its name from the link between this type of arthritis and a skin condition called psoriasis, which causes skin redness and scaling.

**WHAT DID THE AUTHORS HOPE TO FIND?**
The authors wanted to get a better understanding of what was going on before people developed psoriatic arthritis – for example, whether they had other disease or were unable to work.

**WHO WAS STUDIED?**
The study looked at 10,525 people with psoriatic arthritis and 20,777 people in the general population. There was no restriction on people’s age or gender. Everyone was living in Denmark. Data was collected from 1998 to 2014.

**HOW WAS THE STUDY CONDUCTED?**
This was a longitudinal nationwide study using information from databases in Denmark. This means there was no treatment or intervention being studied. The authors used the information in the databases to see how the societal costs, employment status, and occurrence of other disease in people with psoriatic arthritis both before and after diagnosis compared to people without psoriatic arthritis in the general population.

**WHAT WERE THE MAIN FINDINGS OF THE STUDY?**
The study found that people with psoriatic arthritis have higher healthcare costs, lower income, higher unemployment, and higher risk of being on a disability pension than people in the general population without psoriatic arthritis. 10 years after diagnosis, people with psoriatic arthritis were almost three-times more likely to be on a disability pension compared with people in the general population. They also found that before people with psoriatic arthritis are diagnosed, they have more other diseases than normal people in the general population. Once people have been diagnosed with psoriatic arthritis, they have higher healthcare and social costs, and more difficulty working than people without the disease.

**ARE THESE FINDINGS NEW?**
The authors think that this is the first study of its kind in people with psoriatic arthritis.

**WHAT ARE THE LIMITATIONS OF THE STUDY?**
The study collected data from national databases. All doctors in Denmark are obliged to report data, including personal identity number and a coded diagnosis, on all inpatient and specialist outpatient visits. It is thought that the majority of entries are accurate, although figures for completing data are not as good for specialist outpatient visits to private clinics compared to public clinics. This could mean that there is information missing in these study results. However, the authors are confident that the large number of people included means that the results are reliable.

**WHAT DO THE AUTHORS PLAN ON DOING WITH THIS INFORMATION?**
This information has been presented at meetings and conferences, and more studies are planned to look at whether there is a link with other risks such as dying early.
WHAT DOES THIS MEAN FOR ME?

If you have psoriatic arthritis, you may have also been diagnosed with other diseases (sometimes called comorbidities), and you may find it difficult to work or to do the things you used to.

There are treatments for psoriatic arthritis than can help you to function better. If you have concerns about your disease or your treatment, you should speak to your doctor.

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