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 173 95% CI 154 to 196) 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 patientyear 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.⁵ ⁶ 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.parkerinst.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

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Clinical and epidemiological research

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.¹⁹ 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 nonprimary 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 populationbased 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 comparator (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/selfemployment, 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 \notin 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 1.55 to 1.86), respiratory diseases (OR 1.73 95% CI 1.54 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). **Table 1**Baseline characteristics and comorbidities at the time ofdiagnosis for patients with PsA and matched general populationcomparator

	PsA (n=10 525)	GPC (n=20 777)
Female, no. (%)	6222 (59.1)	12 311 (59.3)
Age, no. (%)		
<20	201 (1.9)	403 (1.9)
20–29	715 (6.8)	1414 (6.8)
30–39	1707 (16.2)	3392 (16.3)
40–49	2431 (23.1)	4831 (23.3)
50–59	2812 (26.7)	5572 (26.8)
60–69	1686 (16.0)	3298 (15.9)
70–79	765 (7.3)	1472 (7.1)
>80	208 (2.0)	395 (1.9)
Married/coliving, no. (%)	7320 (69.5)	14 395 (69.3)
Comorbidities	PsA (n=7508*)	GPC (n=14 800*)
Infections, no. (%)	251 (3.3)	249 (1.7)
Neoplasms, no. (%)	502 (6.7)	805 (5.4)
Haematological disorders, no. (%)	156 (2.1)	161 (1.1)
Endocrine and metabolic disorders, no. (%)	658 (8.8)	816 (5.5)
Mental disorders, no. (%)	220 (2.9)	379 (2.6)
Nervous system, no. (%)	489 (6.5)	502 (3.4)
Cardiovascular disorders, no. (%)	1060 (14.1)	1340 (9.1)
Respiratory disorders, no. (%)	522 (7.0)	613 (4.1)
Digestive tract disorders, no. (%)	965 (12.9)	1075 (7.3)
Skin disorders, no. (%)	778 (10.4)	335 (2.3)
Musculoskeletal system, no. (%)	2884 (38.4)	1936 (13.1)
Genitourinary disorders, no. (%)	796 (10.6)	1210 (8.2)

*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 $< \varepsilon 2000/year 5$ 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 selfemployment), 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 1.04 to 1.41) 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.¹⁰ ^{12–16} ²⁴ To our knowledge, however, this is the first study to assess health-care 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%.¹⁹ 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.²⁵ ²⁶ However, some degree of residual confounding and bias cannot be ruled out.

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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).



Total Healthcare Costs

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).

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

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 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

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

*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.

PsA used in this study data and results from another group, spondyloarthritis and ankylosing spondylitits, data suggest that misclassification occurs in <10%.²² 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 socio-18 economic position, the higher their risk of poor health.¹⁷ 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 3	ORs for	comorbidities	before and	after	diagnosis	of PsA
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Comorbidities	Baseline (PsA: n=7508*; GPC; n=14 800) OR (95% CI)	Follow-up (PsA: n=7508*; GPC: n=14 800) OR (95% CI)
Infections	2.03 (1.69 to 2.42)	2.20 (1.89 to 2.55)
Neoplasms	1.25 (1.11 to 1.41)	1.26 (1.14 to 1.40)
Haematological disorders	1.94 (1.55 to 2.43)	2.13 (1.77 to 2.56)
Endocrine and metabolic disorders	1.65 (1.48 to 1.84)	1.89 (1.72 to 2.07)
Mental disorders	1.15 (0.97 to 1.36)	1.21 (1.14 to 1.40)
Nervous system	1.99 (1.75 to 2.26)	1.78 (1.58 to 2.00)
Cardiovascular disorders	1.70 (1.56 to 1.86)	1.70 (1.57 to 1.85)
Respiratory disorders	1.73 (1.54 to 1.96)	1.75 (1.57 to 1.95)
Digestive tract disorders	1.89 (1.73 to 2.08)	1.98 (1.82 to 2.16)
Skin disorders	4.99 (4.37 to 5.71)	10.86 (9.58 to 12.32)
Musculoskeletal system	4.23 (3.94 to 4.54)	8.37 (7.76 to 9.02)
Genitourinary disorders	1.33 (0.75 to 1.04)	1.49 (1.36 to 1.63)

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

GPC, general population comparator; PsA, psoriatic arthritis.

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.¹⁰ ²⁴ ³⁰ 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.

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Contributors LEK: contributed to study conception and design, literature search, data collection, the analysis and interpretation of data, figures, drafting the manuscript and approving the final version. LEK takes responsibility for all coauthors and the integrity of the work as a whole. TSJ: contributed to study conception and design, the analysis and interpretation of data, figures, 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. HG: contributed to study conception and design, data collection, the analysis and interpretation of data, revising the manuscript and approving the final version. HG had access to data throughout the process and knowledge of roles and responsibilities of each author. LD: contributed 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. LD: contributed 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: contributed to study conception and design, literature search, data collection, the analysis and interpretation of data, revising the manuscript and approving the manuscript and externs throughout the analysis and interpretation of data, revising the manuscript and approving the final version. LD had access to data throughout the study conception and design, literature search, data collection, the analysis and interpretation of data, revising the manuscript and

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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.parkerinst.dk. No important aspects of the study have been omitted in the current manuscript.

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