Incremental Costs for Psoriasis and Psoriatic Arthritis in a Population-based Cohort in Southern Sweden: Is It All Psoriasis-attributable Morbidity?

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ABSTRACT. ***Objective.*** To estimate incremental costs for patients with psoriasis/psoriatic arthritis (PsO/PsA) compared to population-based referents free from PsO/PsA and estimate costs attributable specifically to PsO/PsA.

Methods. Patients were identified by International Classification of Diseases, 10th ed., codes for PsO/PsA using information from 1998 to 2007 in the Skåne Healthcare Register, covering healthcare use for the population of the Skåne region of Sweden. For each patient, 3 population-based referents were selected. Data were retrieved from Swedish registers on healthcare, drugs, and productivity loss. The human capital method was used to value productivity losses. Mean annual costs for 2008 to 2011 were assessed from a societal perspective.

Results. We identified 15,283 patients fulfilling the inclusion criteria for PsO [n = 12,562, 50% women, mean age (SD) 52 (21) yrs] or PsA [n = 2721, 56% women, mean age 54 (16) yrs] and included 45,849 referents. Mean annual cost per patient with PsO/PsA was 55% higher compared to referents: €10,500 vs €6700. The cost was 97% higher for PsA compared to PsO. Costs due to productivity losses represented the largest share of total costs, ranging from 52% for PsO to 60% for PsA. Biological drug costs represented 10% of the costs for PsA and 1.6% for PsO. The proportion of cost identified as attributable to PsO/PsA problems was greatest among the patients with PsA (drug costs 71% and healthcare costs 31%).

Conclusion. Annual mean incremental societal cost per patient was highest for PsA, mainly because of productivity losses and biological treatment. A minor fraction of the costs were identified as attributable to PsO/PsA specifically, indicating an increased morbidity in these patients that needs to be further investigated. (First Release January 15 2016; J Rheumatol 2016;43:640–7; doi:10.3899/jrheum.150406)

Key Indexing Terms:
PSORIASIS PSORIATIC ARTHRITIS DIRECT COSTS
INDIRECT COSTS INCREMENTAL ANALYSIS

Psoriasis (PsO) is a chronic inflammatory disease affecting the skin and nails, with reported worldwide prevalence between 0.7% and 3.2%[1,2]. The disease has systemic features and it is characterized by a relapsing course. Most people with PsO have mild to moderate symptoms managed in primary care with topical emollients or phototherapy. Pharmaceutical treatment including systemic treatments are indicated for moderate and severe PsO and prescribed by dermatologists[3]. Psoriatic arthritis (PsA) is manifested as pain, stiffness, and swelling in and around the joints or in the back. The prevalence of PsA is lower than that of PsO; between 0.1% and 0.42%[1,4] in the general population, or between 7% and 31% as proportion of people with PsO[1,5]. The level of skin involvement varies in PsA and there seems to be no obvious correlation between the degree of the joint and skin problems[6]. PsO and PsA have multiple effects on society including the health and well-being of the individual, the need for healthcare resources for disease management, and the loss of productivity[7,8,9,10].

The annual mean cost of PsO and PsA ranges between €2866 and €11,928, according to a recent international

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review[11]. The economic burden of PsO and PsA increase with disease severity[12,13], and for PsO, direct costs exceed indirect costs in some studies[14,15,16], but there are other studies reporting differently[17]. PsA seems to incur greater cost compared with PsO because of the added burden of joint involvement[18,19], with estimates of mean annual direct costs €5574 and indirect costs €55,600[20]. Most studies find that loss of productivity is a main cost driver even when costs for biological treatment are included[21,22]. Studies to date have been restricted by data availability and limited time frames for observation. This may be especially true concerning mild cases of PsO with irregular healthcare needs[23]. Moreover, few studies have considered the relatively high degree of comorbidities among people with PsO and PsA[19,24,25].

The aims of our study were to estimate the incremental societal cost per person for PsO alone and for PsA compared to a matched population-based referent group free from PsO and PsA, and to estimate the costs attributable to specific PsO and PsA problems.

MATERIALS AND METHODS

Study design and subject identification. Mean annual resource use and associated costs for healthcare and work loss were estimated for people with PsO and PsA resident in the Skåne region of Sweden, with 1.2 million inhabitants in 2011. Patients of any age were identified by diagnostic codes associated with PsO and PsA according to the Swedish version of the International Classification of Diseases and Related Health Problems system, version 10 (ICD-10) using information from 1998 to 2007 in the Skåne Healthcare Register (SHR), which covers healthcare use by the Skåne region population.

Patient cohort: PsO alone and PsO with PsA. Patients were classified as having PsO alone (hereby PsO) if they had at least 1 of the ICD-10 codes L40.0, L40.1, L40.2, L40.4, and L40.8, but not L40.5. Patients with ICD-10 diagnostic code L40.5 alone or at least 1 code for PsO in combination with any of codes M07.1, M07.2, M07.3, or M09.0 were classified as having PsA. When analyzed jointly, we used PsO/PsA for writing convenience. Patients who fulfilled these diagnostic criteria and were residents of the Skåne region as of December 31, 2007, were included. PsO alone patients turning into PsA patients after the index date were excluded (Figure 1).

Population-based referent cohort. We created a population-based referent cohort from the Swedish Population Register by matching 3 referents on year of birth, sex, and residential area for each included patient. Referents were alive and resident in Skåne region on December 31, 2007, and were required to have no history of registered healthcare use consistent with PsO or PsA in the SHR during 1998-2011.

Followup period of outcome variables. Data on healthcare resource use, filled drug prescriptions, and productivity losses for PsO/PsA patients and the referent cohort were included in the 4 years of followup (2008–2011). Data were retrieved from Swedish national and regional registers and linked by personal identification numbers. We calculated the mean annual cost per patient over this period and adjusted estimates for patients and referents dropping out of the study because of relocation from the region or death from January 1, 2008, to December 31, 2011.

Healthcare use. The SHR continuously registers all primary care, secondary outpatient, and inpatient care contacts (including visits and non-visits such as telephone contacts or letters) for residents in the Skåne region. Data include age, sex, healthcare provider, date of consultation, and diagnostic codes according to ICD-10. Private and public healthcare providers are registered in exactly the same way in SHR, apart from private healthcare providers' exemption from forwarding diagnostic codes to the SHR.

To attach monetary value to each individual's healthcare consultation and inpatient care we used individual center-specific unit costs, which are available from the SHR. These costs are calculated based on each specific unit's share of the total costs for healthcare for that specific healthcare provider. Costs are allocated using Diagnosis-related Groups weights including pharmaceuticals used at hospital during inpatient episodes.

Drugs. Data on filled drug prescriptions were collected from the Swedish Prescribed Drug Register, a national individual-level register, where all dispensed prescribed outpatient drugs to the entire Swedish population are registered except for drugs given in hospitals[26]. The cost variable in the register refers to the pharmacy wholesale prices including costs paid by the patient and subsidy paid by the county council.

Productivity losses. Data on work loss were obtained from the Swedish Social Insurance Agency (SSIA). Information includes 1 main diagnosis (ICD-10 diagnostic code) for sick leave and 2 main diagnoses for disability pension. All sickness benefits exceeding 14 days and disability pensions are registered by the SSIA. Both sick leave and disability pension can be full-time (100%) or part-time (e.g., 25%, 50%, or 75%). The number of days with part-time compensation was adjusted to days of full compensation. We valued the loss of productivity following the human capital approach and each day lost from work by the average wage for women and men including social insurance fees[27].

Incremental costs and costs attributable to PsO/PsA. Two strategies for analyzing costs of PsO and PsA were applied. First, the incremental annual costs as the mean difference in costs of healthcare resource use and productivity loss for the PsO and PsA cohort compared to the referent cohort. The incremental cost approach is a preferred method when there is reason to believe that non–disease-related morbidity costs are present[28]. Second, we were also interested in estimating the amount of the costs specifically attributable to PsO/PsA problems and in analyzing whether these costs were equivalent to the incremental costs. We defined healthcare consultations and work loss episodes as attributable to PsO/PsA problems if registered with an ICD-10 diagnostic code associated with PsO/PsA. Within healthcare, the calculation of costs attributable to PsO/PsA problems was possible to perform for publicly provided healthcare (physician consultations in primary and secondary outpatient care and inpatient care), but we lack information about ICD-10 diagnostic codes for private healthcare providers. For filled prescriptions we used drug Anatomical Therapeutic Chemical Classification System codes related to PsO and PsA diseases (Supplementary Table 1 for list of drugs, available at jrheum.org) to identify costs attributable to PsO/PsA problems.

All costs were expressed in 2011 Euros (1 Euro = 9.03 Swedish krona in 2011). All costs were inflated to the 2011 price level using the consumer price index[29]. Cost calculations had a societal perspective.

Statistical analysis. We report arithmetic mean and SD of costs. Additional reports on nonparametric statistics are available on request from the authors. Differences between groups (PsO and PsA patients vs referents and PsO patients vs PsA patients) were analyzed with 2-sample t tests. P values < 0.05 were considered statistically significant. We used STATA software v 13.0 (Stata Corp.) for statistical analysis.

Ethical considerations. Our study was conducted according to the Declaration of Helsinki and approved by the Regional Ethical Review Board in Lund, Sweden (Dnr 301/2007, Dnr 406/2008, and supplement to Dnr 2012/359).

RESULTS

Patient and referent characteristics. Patient and referent characteristics are shown in Table 1. A total of 15,283 patients fulfilled the inclusion criteria for PsO (n = 12,562) or PsA (n = 2721) and there were 45,849 referents matched for year of birth, sex, and residential area. While PsO had equal proportion of sexes, the proportion of women was slightly higher (56%) in the PsA group. For both sexes, the mean age

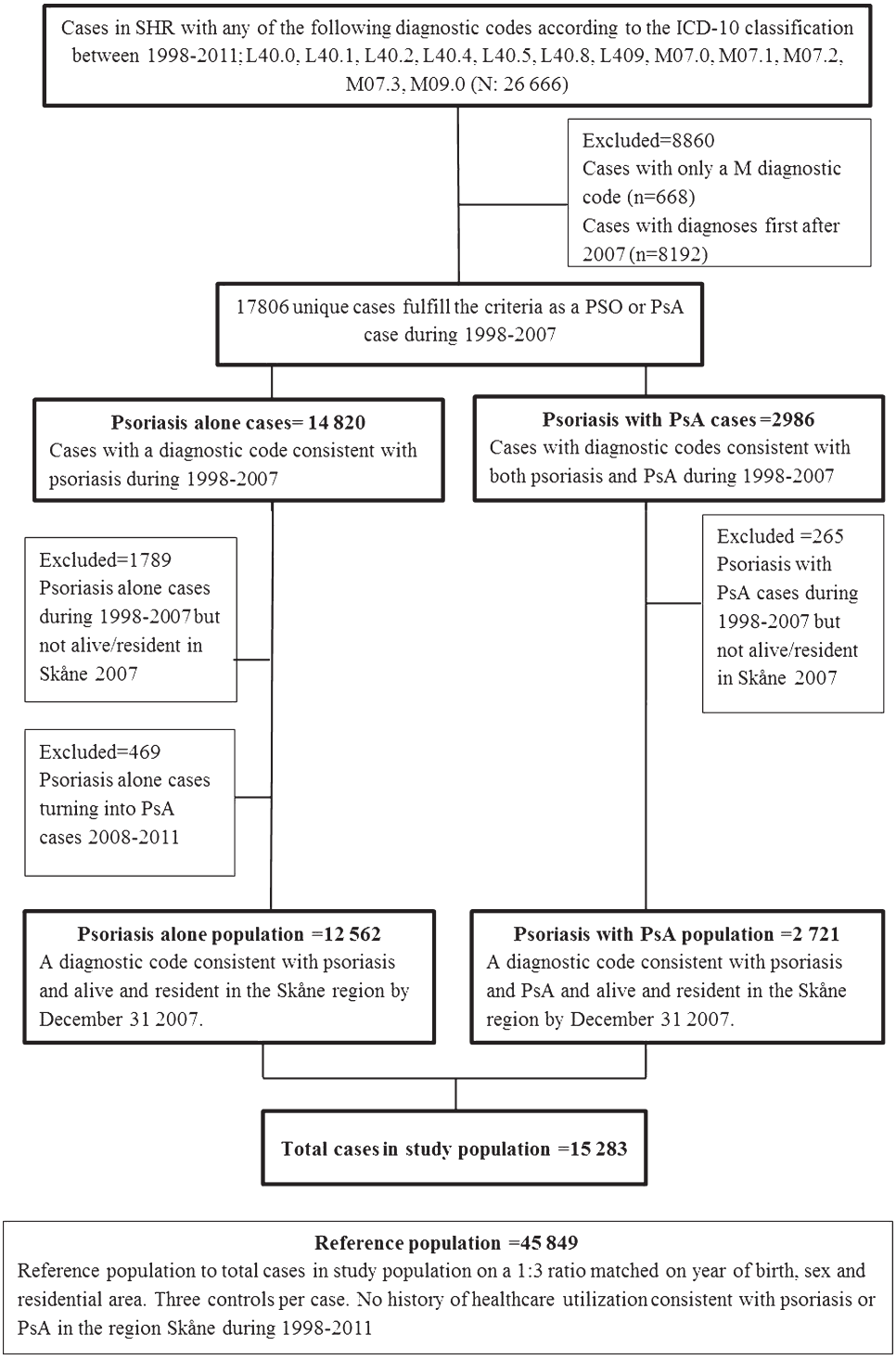

Figure 1. Flowchart of inclusion of patients and referent population. SHR: Skåne [Sweden] Healthcare Register; ICD-10: International Classification of Diseases, 10th ed; PsO: psoriasis; PsA: psoriatic arthritis.

was somewhat lower for PsO compared to PsA. The majority of both patients and referents had at least 1 healthcare consultation or use of drugs, while a minority had episodes of sick leave or disability pension. The exit rate due to deaths and relocations ranged from 6% (PsA) to 10% (PsO).

Cost comparisons. The incremental mean annual societal cost was 55% higher for patients with PsO/PsA compared to referents (€10,500 vs €6700, $p < 0.001$; Figure 2), and the costs were significantly higher for patients with PsO/PsA through all cost components (all $p < 0.001$; for detailed

Table 1. Characteristics of patients with PsO, patients with PsA, and referents.

Characteristics	Patients w/PsO alone	Patients w/PsO and PsA	All Patients	Referents
N*	12,562	2721	15,283	45,849
Women, n (%)*	6292 (50)	1522 (56)	7814 (51)	23,442 (51)
Age, yrs**				
Women, mean (SD), median (25th–75th, min–max)	52 (21), 54 (35–68)	54 (16), 56 (43–65)	52 (20), 55 (37–67)	52 (20), 55 (37–67)
Men, mean (SD), median (25th–75th, min–max)	51 (19), 53 (38–65)	54 (15), 55 (44–64)	52 (18), 53 (39–65)	52 (18), 53 (39–65)
Age group**				
< 20 yrs	769 (6)	64 (3)	833 (5)	2499 (5)
20–64 yrs	7896 (63)	1891 (70)	9787 (64)	29,361 (64)
≥ 65 yrs	3897 (31)	766 (28)	4663 (31)	13,989 (31)
Followup duration, in yrs, mean (SD)	3.8 (0.63)	3.9 (0.52)	3.8 (0.61)	3.8 (0.61)
Exit during followup, n (%)	1215 (10)	174 (6.0)	1389 (9)	4169 (9)
Deaths, n (%)	885 (7.0)	135 (5.0)	1020 (7.0)	2508 (5.0)
Relocation out of Skåne, n (%)	330 (3.0)	39 (1.0)	369 (2.0)	1661 (4.0)
No healthcare consultations during followup, n (%)***	242 (1.9)	18 (0.7)	260 (1.7)	2376 (5.1)
No drug use at all during followup, n (%)#	458 (3.6)	27 (1.0)	485 (3.2)	4649 (10.1)
No sick leave or disability pension during followup, n (%)†	9400 (75)	1475 (54)	10,875 (71)	36,016 (79)
No sick leave or disability pension during followup, n (%), age 20–64 yrs†	4887 (62)	700 (37)	5587 (57)	20,021 (68)

*At the end of 2007. ** During the first cost-calculation year (2008). ***As registered in SHR. #As registered in SPDR. †As registered in SSIA Register. PsO: psoriasis; PsA: psoriatic arthritis; SHR: SHR: Skåne [Sweden] Healthcare Register; SPDR: Swedish Prescribed Drug Register; SSIA: Swedish Social Insurance Agency.

Table 2. Mean annual cost per patient due to all-resource use and cost attributable to resource use associated specifically with PsO- and PsA-diagnosed consultations (first and secondary diagnosis) or pharmaceuticals. All costs are in Euros.

	Patients with PsO, n = 12,562			Patients with PsA, n = 2721		
	Mean Costs			Mean Costs		
	All Resource Use*	Mean Cost due to Resource Use**	Mean Cost due to Skin and Joint Problems (% of all costs)	All Resource Use*	Mean Cost due to Resource Use**	Mean Cost due to Skin and Joint Problems (% of all costs)
Healthcare						
Primary care physician	271	214	15 (7)	286	225	25 (11)
Secondary outpatient care — dermatologist, rheumatologist or internist	217	155	31 (20)	714	598	395 (66)
Secondary outpatient care — other specialist	635	499	3 (0.6)	760	589	31 (5)
Inpatient care	1778	1778	135 (8)	1841	1841	571 (31)
Total	2901	2646	184 (7)	3601	3253	1022 (31)
Drugs	816	816	216 (26)	2585	2585	1844 (71)
Productivity losses***	4666	4666	3803 (82)	10,566	10,566	9390 (89)

* Mean cost due to all resource use (i.e., public and private healthcare).** For healthcare; mean cost due to resource use (both primary and secondary diagnoses) within public healthcare providers (about 70% of all outpatient physician consultations) because we do not have information about ICD-10 diagnostic codes for private healthcare providers. All inpatient care is within public healthcare providers. *** Productivity losses include both sick leave and disability pension. PsO: psoriasis; PsA: psoriatic arthritis.

results, Supplementary Table 2A, available at jrheum.org). A higher cost for patients with PsO/PsA was identified regardless of sex and age with the greatest absolute difference compared to referents observed among people aged 20-64 years (Figure 3, panel A).

Compared to the PsO group, the PsA group had 97% higher mean annual societal cost per patient (€17,600 vs €8900, $p < 0.001$) during followup (Figure 2). This difference was driven by higher costs in all cost components except inpatient care. The difference in costs within primary care was mainly due to more physiotherapist/occupational therapist consultations for patients with PsA. The use of disease-modifying antirheumatic drugs (DMARD) differed with 10-fold higher proportion of patients using biologic DMARD, and 6-fold for nonbiologic DMARD among patients with PsA (Supplementary Table 2B, available at jrheum.org). The difference between PsA and PsO was present in all groups by sex and age. However, it was most pronounced among women (Figure 3, panel B).

Distribution of cost sources. Costs due to productivity losses

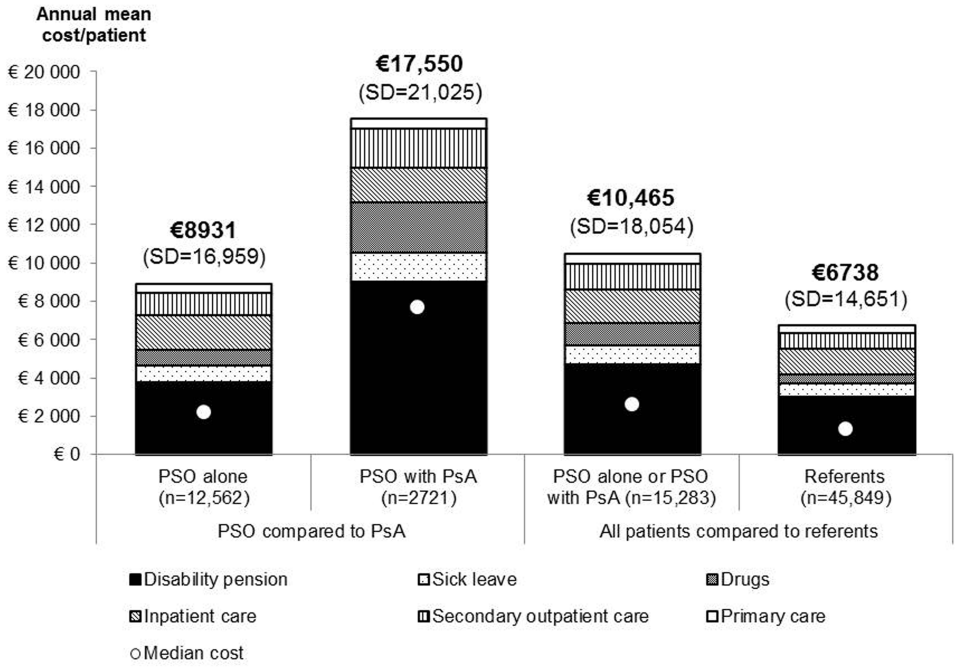

Figure 2. Mean annual societal cost over different cost components for patients with PsO and PsA compared to referents and for patients with PsO compared to patients with PsA. The white bullet represents median annual cost per patient. PsO: psoriasis; PsA: psoriatic arthritis.

represented the largest share of the total societal costs in all groups, with the highest share for PsA (60%). Annual mean drug cost represented 15% (biologics 10%) of the costs for PsA. The corresponding values for PsO was 9% (biologics 1.6%) and for referents 7% (biologics < 1%).

Costs attributable to morbidity associated with PsO and PsA. The overall proportion of costs identified as attributable to PsO/PsA problems was greatest among the patients with PsA (Table 2). For both PsO and PsA, cost due to work loss accounted for the highest proportion of costs attributable to PsO/PsA problems (82% for PsO and 89% for PsA). The proportion of healthcare costs and drug costs attributable to PsO/PsA was highest for patients with PsA (31% and 71%, compared to 7% and 26% for patients with PsO).

DISCUSSION

Our results show that patients with PsO/PsA incurred higher societal costs compared to referents; and that being diagnosed with PsA doubled the societal cost compared with being diagnosed with PsO alone. Irrespective of sex and age, patients with PsA incurred greater societal costs than those in patients with PsO; the cost difference was most pronounced for women and individuals under the age of 20. Cost-driving components in the PsO/PsA group compared to referents and in patients with PsA vs patients with PsO were primarily drug use, especially biological DMARD, and productivity losses.

Only a minor part of the healthcare costs was attributable to PsO/PsA using primary and secondary diagnoses. In addition, our estimated incremental healthcare costs exceeded those with the more narrow diagnosis-based definition. There are a number of studies on the prevalence of different comorbidities and associated costs in patients with PsO/PsA[19,24,25], and because we did not want to ignore costs due to comorbidity on the causal pathway, often defined by the secondary diagnoses, we also included these diagnoses. The greater proportion of costs due to work loss (80%) attributable to PsO/PsA problems may be overestimated as a consequence of the infrequent updating of the ICD-10 diagnostic codes for new work loss episodes in the SSIA register[30]. Mustonen, *et al*[31] used an alternative strategy for attributing costs — patient assessed attribution. Their results, based on questionnaires from 262 patients with PsO/PsA, attributed 35% out of the total work loss to PsO or other medical reasons. Another study by the same group and same data reported that PsO was the reason for the exit from working life for 17% of retired patients with PsO/PsA[32].

Because of differences in cost perspective, methodologies, and healthcare systems, comparisons between cost studies can be done only cautiously[33]. There are 3 recent Swedish studies estimating the mean annual cost for PsO/PsA using data from 2008–2011. Two register-based studies, our own and Norlin, *et al*[17], found lower annual direct costs of PsO/PsA compared to direct costs reported in 2 dermatology clinic–based questionnaire studies (by Ghatnekar, *et al* and Ekelund, *et al*[12,34]). These differences may be explained by case-mix differences in which register-based studies included milder cases and thus a larger proportion of the target population. Other factors are different cost components and

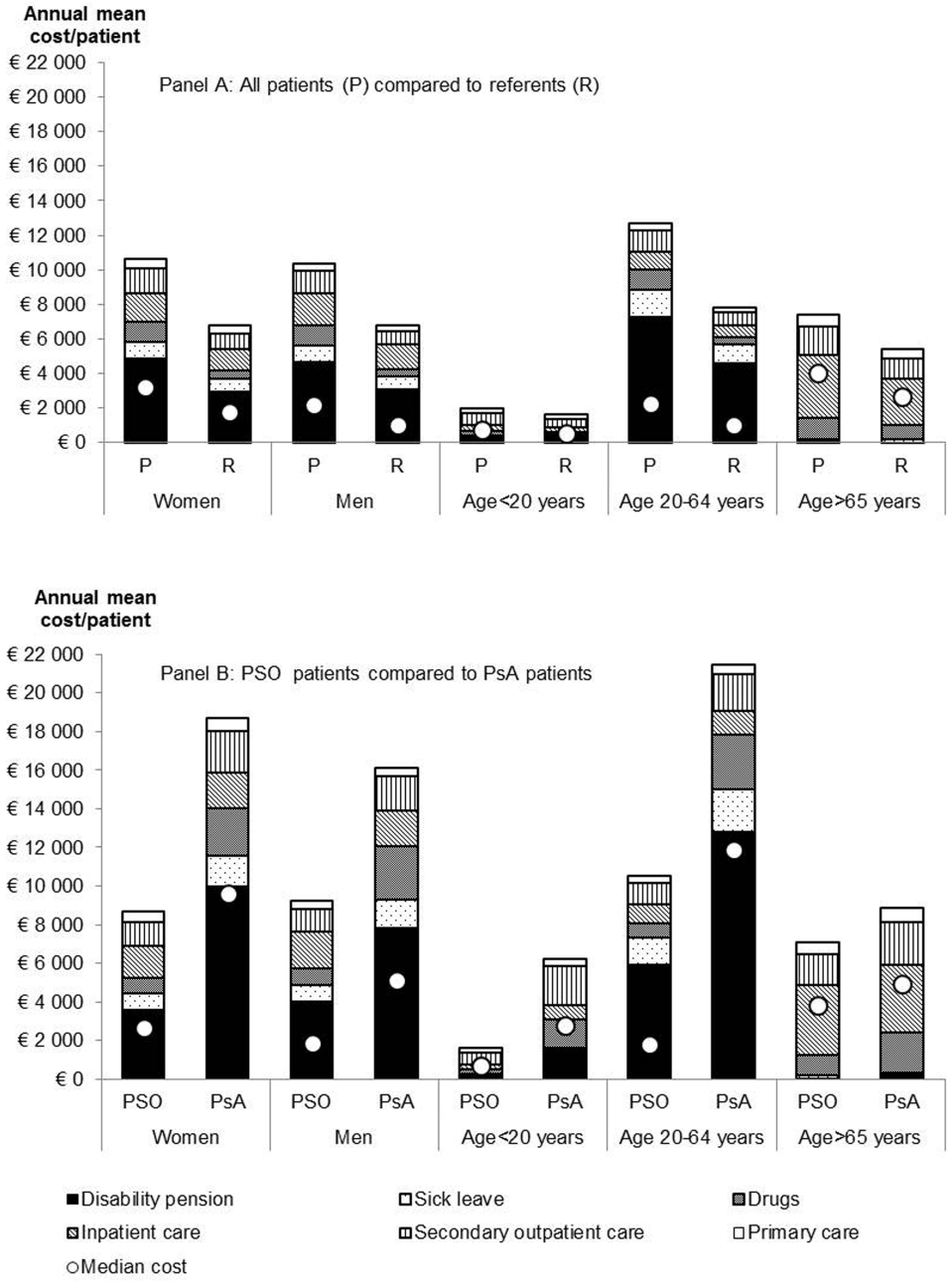

Figure 3. Mean annual cost per patient over different cost components, 2008–2011. A. Comparison between all patients (P) and referents (R). B. Comparison between patients with psoriasis alone (PsO) and psoriasis patients with psoriatic arthritis (PsA). The white bullet represents median annual cost per patient.

different data collection periods (the latter study was conducted during fall/winter, when PsO tends to flare). Our study reported lower indirect cost compared to Norlin, *et al* and Ghatnekar, *et al*. These cost differences may be explained by use of different data sources for collection of data on productivity losses. Our study and Norlin, *et al* did not have information on short-term sick leave and this limitation of the SSIA register is further elaborated below.

In contrast to the comparison to other Swedish studies, our results are in the upper range of mean annual total cost for patients with PsO/PsA compared with studies outside Sweden[11,20]. In accordance with the Swedish study by Norlin, *et al*[17] but contrary to studies from the United States[14], Canada[15], and Italy[16], indirect costs exceeded direct costs. In our study the difference was marginal for patients with PsO alone while the difference was clearly pronounced for patients with PsA. Studies, including this, do consistently report higher costs of PsA compared to PsO[18,19] and reported cost drivers are primarily biological drugs and productivity losses [21,22].

One strength of our study is the use of individual-based data for a large population over 4 years, which means that we identified rare health consumers[23], which facilitates robust cost estimates. Another strength is that we provided data on resource use and associated costs over different types of healthcare providers and care levels. This is the first Swedish study estimating costs of primary care in a larger setting, to our knowledge. We found that primary care accounts for a limited but non-negligible proportion of societal costs — 5% and 3% for PsO and PSA, respectively. A previous validation study from our group showed limited misclassification of patients with PsO and PsA in SHR (i.e., high positive predicted value for the diagnostic codes), which suggests that problems associated with misclassification are small in this register-based study[1]. Although our data are from 1 healthcare region, it covers 13% of the Swedish population, and the Skåne region resembles Sweden as a whole on key socioeconomic and demographic variables[35]. This facilitates national generalization, and for comparisons beyond the national level we provide detailed and transparent results on resource use and costs in supplementary information (available at jrheum.org). Further results are available on request from the authors.

Our study design may have underestimated costs. First, only individuals consulting a healthcare provider (physician) for their PsO/PsA problems were included. However, the long inclusion period of 10 years is likely to reduce this problem. Second, our register-based approach did not include direct costs such as the patients' out-of-pocket payment for over-the-counter drugs and transportation. In 2 studies on costs from the patient's perspective, the mean annual cost per person associated with patient and family ranged from about €500 to €2100, indicating that such costs may be non-negligible[36,37]. Also, time spent on skin care at home and on performing household chores are important factors to take into account when studying the overall burden of PsO/PsA[38]. Third, we did not record short-term sick leave because the SSIA register does not include sick leave periods shorter than 14 days. In a report of doctors who prescribed sick leave in the Skåne region during 2009-2010, the short-term sick leave (8-14 days) within all musculoskeletal disorders and skin disorders accounted for 15% and 13% of the total number of sick leave periods, respectively[39]. In a Finnish questionnaire study, patients with PsO reported an average sick leave period of 4.5 h per month[32]. These studies show that short-term sick leave is present among patients with PsO/PsA, but the magnitude of the occurrence is still uncertain. There is a strong need for more research on short-term sick leave using a population-based perspective. In the absence of population-based register data, the Finnish questionnaire study[32] is a good example of another method for collection of sick leave data. However, the caveats of survey studies are often small sample sizes with less representativeness. Costs due to reduced productivity while at work were also not included. Haglund, *et al* reported a mean productivity reduction of 20% while at work because of disease-related problems for patients with PsA[40]. Reduced productivity at work has also been reported for patients with PsO/PsA; Mustonen, *et al*[31] reported a mean productivity reduction of 45%. Fourth, we did not measure costs due to premature death. However, studies on the risk of mortality in patients with PsO/PsA compared with the general population show inconsistent results; there is a tendency of an increased mortality in patients with severe PsO (DMARD users) but not in patients with mild PsO or PsA[41,42].

There are also some other limitations. Private healthcare providers (about 30% of all physician consultations were within private care during 2008-2011) are registered in SHR but without diagnostic codes. This means that there may be referents misclassified as free from PsO/PsA if they received a PsO/PsA diagnosis only at private healthcare providers during the inclusion period. There may also be an underestimation of the costs attributable to specific PsO/PsA problems if the studied patients are more likely to seek private healthcare providers for their PsO/PsA problems compared to other morbidity. The magnitude of this shortcoming is difficult to estimate, but there is reason to believe that the problem is less severe as physician healthcare contacts are not the main cost driver for total costs. An underestimation of the cost attributable to specific PsO/PsA problems may also result from the less complete coverage of ICD-10 diagnostic codes for non-physician consultations (e.g., nurse, physiotherapist, occupational therapist, and others) in the SHR. Concerning drug cost, we could have overestimated the proportion of cost attributable to PsO/PsA, because the included drugs could have been prescribed for indications other than PsO/PsA.

The present results indicate an incremental cost of nearly 55% for patients with PsO/PsA compared to population-based referent subjects. Patients with PsA incurred twice as much cost as patients with PsO. However, only a small fraction of the costs were identified as attributable to PsO/PsA, indicating an increased morbidity in these patients that needs to be further investigated.

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ONLINE SUPPLEMENT

Supplementary data for this article are available online at jrheum.org.

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