Time Trends in Epidemiology and Characteristics of Psoriatic Arthritis Over 3 Decades: A Population-based Study

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ABSTRACT. Objective. To determine time trends in incidence, prevalence, and clinical characteristics of psoriatic arthritis (PsA) over a 30-year period.

Methods. We identified a population-based incidence cohort of subjects aged 18 years or over who fulfilled Classification of Psoriatic Arthritis (CASPAR) criteria for PsA between January 1, 1970, and December 31, 1999, in Olmsted County, Minnesota, USA. PsA incidence date was defined as the diagnosis date of those who fulfilled CASPAR criteria. Age- and sex-specific incidence rates were estimated and age- and sex-adjusted to the 2000 US White population.

Results. The PsA incidence cohort comprised 147 adult subjects with a mean age of 42.7 years, and 61% were men. The overall age- and sex-adjusted annual incidence of PsA per 100,000 was 7.2 [95% confidence interval (CI) 6.0, 8.4] with a higher incidence in men (9.1, 95% CI 7.1, 11.0) than women (5.4, 95% CI 4.0, 6.9). The age- and sex-adjusted incidence of PsA per 100,000 increased from 3.6 (95% CI 2.0, 5.2) between 1970 and 1979 to 9.8 (95% CI 7.7, 11.9) between 1990 and 2000 (p for trend < 0.001). The point prevalence per 100,000 was 158 (95% CI 132, 185) in 2000, with a higher prevalence in men (193, 95% CI 150, 237) than women (127, 95% CI 94, 160). At incidence, most PsA subjects had oligoarticular involvement (49%) with enthesopathy (29%).

Conclusion. The incidence of PsA has been rising over 30 years in men and women. Reasons for the increase are unknown, but may be related to a true change in incidence or greater physician awareness of the diagnosis. (First Release Jan 15 2009; J Rheumatol 2009;36:361–7; doi:10.3899/jrheum.080691)

Key Indexing Terms:
EPIDEMIOLOGY PSORIATIC ARTHRITIS POPULATION-BASED STUDY

Few population-based studies exist documenting the incidence and prevalence of psoriatic arthritis (PsA)². Annual incidence estimates of PsA range from 3 to 23 per 100,000, while prevalence estimates vary widely from 0.02% to 0.25%, with higher estimates in recent years¹,³,¹³. These variations may be due to secular trends in epidemiology of PsA, increased recognition of the condition over time, or differences in case ascertainment methods in individual studies¹,³,⁸,¹³. Several classification criteria with widely variable sensitivity and specificity have been used, but none has been universally accepted. Hence, the comparability of the published incidence and prevalence estimates of PsA is problematic.

The recently validated classification criteria set for PsA from the ClASsification of Psoriatic A Rthritis (CASPAR) group offers a unique opportunity to assess time trends in incidence and prevalence rates of PsA using the same criteria consistently over time, irrespective of patients’ assigned diagnoses at the time of their medical care¹⁴. Further, the sensitivity and specificity of the CASPAR criteria are high in established and early PsA¹⁴,¹⁵. Therefore, criteria can readily be applied retrospectively to ascertain subjects with PsA through review of the original medical records.

In addition, the clinical manifestations of PsA have been heterogeneous in reported case series⁸,¹². One reason for this may be inclusion of subjects with established PsA. The disease course of early PsA differs from late PsA given the tendency of an oligoarticular pattern to evolve into a polyarticular pattern⁸. We sought to determine the time trends in incidence, prevalence, and the clinical and radiographic features of PsA over a 30-year period using the recently validated CASPAR criteria.

MATERIALS AND METHODS

Study setting. Our study was designed as a retrospective, population-based study in Olmsted County, Minnesota, USA, using the data resources of the Rochester Epidemiology Project (REP). According to the 2000 Olmsted
County census, the total population is 124,277, and 90% of individuals are White. The socioeconomic characteristics of the source population are similar to US Whites generally, except that a higher percentage of the population is employed in healthcare-related services, with a high proportion of college or advanced degrees. The REP is a diagnostic indexing and medical-records linkage system and its potential for population-based studies has been described in detail.\textsuperscript{16,17} Population-based epidemiologic research in this community is enhanced due to relative geographic isolation from urban centers. In addition, nearly all medical care is delivered to local residents by a small number of healthcare providers, including the Mayo Clinic and its affiliated hospitals, the Olmsted Medical Center, the Olmsted Community Hospital, local nursing homes, and a few private practitioners. All medical, surgical, and histological diagnoses and other key information are abstracted and entered into computerized indices to facilitate case identification. This unique population-based data resource ensures virtually complete ascertainment and followup of all clinically diagnosed cases of PsA in a geographically defined community. Further, data from all providers are contained in a single comprehensive medical-records linkage system. Availability of the original medical records, including results of all laboratory and radiographic tests, allows identification and reclassification of potential subjects with PsA based on contemporary diagnostic criteria.

Data collection. Using the resources of the REP, we identified all subjects aged 18 years and over with a diagnosis suggestive of PsA or both psoriasis and arthritis from January 1, 1969, through December 31, 1999. The complete medical records (from all healthcare providers) of all potential subjects with PsA were identified and reviewed by a clinical rheumatology fellow (FCW) using a standardized, computerized, pretested data abstraction form. Data collection included information on demographics, clinical manifestations, laboratory data, and radiographic characteristics. For inclusion into the study as a subject with incident PsA, subjects must have demonstrated inflammatory articular disease (joint, spinal, enthesal) documented by either a primary care physician or a rheumatologist, and have met the CASPAR criteria\textsuperscript{14} at that visit by attaining a score ≥ 3 among the following 5 categories: (1) current psoriasis (score of 2), a personal history of psoriasis, or a family history of psoriasis (does not score if current psoriasis present); (2) nail dystrophy such as onycholysis, pitting, or hyperkeratosis; (3) a negative rheumatoid factor (RF); (4) current dactylitis or a personal history of dactylitis as recorded by a rheumatologist; and (5) radiographic evidence of psoriatic bone changes of the hand or foot such as joint space narrowing, juxtaarticular new bone formation, ankylosis, spondylitis, joint erosions, peristitis, osteolysis, and sacroiliitis on plain radiographs at time of PsA diagnosis\textsuperscript{14}. Hard copies of approximately 75% of radiographs were available for review. We recorded the date of first radiographs (irrespective of findings) and the date, site, and findings of the first positive radiographs. The final incidence cohort comprised subjects aged ≥ 18 years who first fulfilled CASPAR criteria between January 1, 1970, through December 31, 1999. Subjects who did not fulfill CASPAR criteria or who were diagnosed outside the study time period were excluded. All subjects were followed up until January 1, 2007, for vital status.

Statistical analysis. Age- and sex-specific incidence rates were calculated assuming individuals aged ≥ 18 years were at risk for PsA. Age- and sex-specific incidence rates were calculated by using the number of incident cases as the numerator and population estimates based on decennial census counts as the denominator, with linear interpolation between census years as described.\textsuperscript{18} Only subjects who were residents of Olmsted County at disease onset and who fulfilled the CASPAR criteria for PsA were included in the incidence calculations. Overall incidence rates were age- and sex-adjusted to the US White population. Ninety-five percent confidence intervals (95% CI) for the incidence rates were constructed using the assumption that the number of incident cases per year follows a Poisson distribution. Incidence trends were examined using Poisson regression models. Smoothing splines were used to model the age effect and obtain the smoothed curves shown in Figure 1. The prevalence of PsA in 2000 was estimated by using the number of prevalence cases on January 1, 2000, as the numerator and the Olmsted County population in 2000 as the denominator. We accepted a p value of less than 0.05 as significant for data analysis.

Kaplan-Meier methods were used to estimate survival. Expected survival in the general population was obtained from the Minnesota White population life tables, according to the age and sex distribution of the PsA cohort. A one-sample log-rank test was used to compare observed and expected survival. Age- and sex-specific incidence and prevalence rates were applied to the total US population in 2000 to estimate the number of affected individuals in the US population.

RESULTS

We identified a total of 357 Olmsted County residents with a potential diagnosis of PsA. Of these, 147 subjects aged ≥ 18 years fulfilled the CASPAR criteria for inclusion into the study and composed the final PsA incidence cohort. Reasons for exclusion of the remaining subjects were as follows: prevalent PsA subjects with disease onset outside of Olmsted County or disease onset before/after the study time period, or age < 18 years (62, 17.4%), subjects who were not residents of Olmsted County (19, 5.3%), subject refusal of authorization to use medical records for research (1, 0.3%), or did not fulfill CASPAR criteria (128, 35.9%). Of the 128 subjects who did not fulfill CASPAR criteria, 40 were confirmed to have psoriasis but presented with noninflammatory arthropathies, including osteoarthritis, rheumatoid arthritis (RA), or other mechanical or trauma-associated musculoskeletal pain.

Table 1 shows the demographic characteristics of the 147 incident subjects with PsA according to decades of PsA incidence. Overall, there were 90 men (61%). The mean age at incidence was 42 years (± 14) for men and 44 years (± 17) for women. We did not observe significant trends in sex distribution or the mean age of the incident PsA subjects over time. Although mean age at incidence appeared to have declined over time, this was not significant.

Incidence of PsA. Figure 1 and Table 2 illustrate the age- and
sex-specific annual incidence of PsA. The overall age- and sex-adjusted annual incidence of PsA was 7.2 per 100,000 (95% CI 6.0, 8.4). The overall age-adjusted incidence in men (9.1 per 100,000, 95% CI 7.1, 11.0) was higher than in women (5.4 per 100,000, 95% CI 4.0, 6.9). In men, the annual incidence was highest in the 30–39 age range (12.2 per 100,000) and declined thereafter. In women, the annual incidence was highest in the 50–59 age range (10.5 per 100,000) and then declined thereafter. After the sixth decade, incidence in women was similar to incidence in men (Figure 1).

Figure 2 and Table 3 illustrate the overall age- and sex-adjusted incidence over 3 decades. During the 1970-79 period, the incidence of PsA per 100,000 was 3.6 (95% CI 2.0, 5.2). The incidence increased to 7.0 per 100,000 (95% CI 4.9, 9.1) in 1980-89 and 9.8 per 100,000 (95% CI 7.6, 11.9) in 1990-99. This increasing trend was apparent in both men and women and was statistically significant (p < 0.001 for trend). We also examined survival in this population in comparison to expected survival. Over a mean followup of 13.6 years (total 2003 person-yrs), the survival of subjects with PsA did not differ from that of the general population, with a standardized mortality ratio of 0.91 (95% CI 0.58, 1.37; p = 0.66) over the entire period.

Prevalence of PsA. The overall, estimated point prevalence of PsA on January 1, 2000, was 158 per 100,000 (95% CI 132, 185). The sex-specific prevalence per 100,000 was 193 for men (95% CI 150, 237) and 127 for women (95% CI 94, 160).

Clinical characteristics of incident PsA subjects. The clinical characteristics of the subjects with PsA at incidence are shown in Table 4. A total of 126 (86%) subjects presented with inflammatory joint disease, followed by enthesopathy in 43 (29%) subjects, and inflammatory back pain in 12

Table 1. Characteristics of 147 subjects with psoriatic arthritis* between January 1, 1970, and December 31, 1999, in Olmsted County, Minnesota.

<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Total no. (%) of subjects</td>
<td>20</td>
<td>46</td>
<td>81</td>
<td>147</td>
</tr>
<tr>
<td>Male</td>
<td>12 (60)</td>
<td>28 (61)</td>
<td>50 (62)</td>
<td>90 (61)</td>
</tr>
<tr>
<td>Female</td>
<td>8 (40)</td>
<td>18 (39)</td>
<td>31 (38)</td>
<td>57 (39)</td>
</tr>
<tr>
<td>Age at incidence, mean (± SD) yrs</td>
<td>44.1 ± 18.3</td>
<td>43.6 ± 17.8</td>
<td>41.8 ± 12.8</td>
<td>42.7 ± 15.2</td>
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<tr>
<td>Male</td>
<td>42.8 ± 15.7</td>
<td>44.3 ± 18.4</td>
<td>39.9 ± 10.1</td>
<td>41.7 ± 13.9</td>
</tr>
<tr>
<td>Female</td>
<td>46.0 ± 22.7</td>
<td>42.6 ± 17.4</td>
<td>44.8 ± 15.9</td>
<td>44.3 ± 17.1</td>
</tr>
</tbody>
</table>

* According to the CASPAR criteria. SD: standard deviation.

Table 2. Annual incidence (per 100,000) of psoriatic arthritis* by age and sex between January 1, 1970, and December 31, 1999, in Olmsted County, Minnesota.

<table>
<thead>
<tr>
<th>Age Group, yrs</th>
<th>Male</th>
<th>Rate</th>
<th>Female</th>
<th>Total</th>
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<tbody>
<tr>
<td>20–29</td>
<td>20</td>
<td>7.6</td>
<td>14</td>
<td>4.5</td>
</tr>
<tr>
<td>30–39</td>
<td>29</td>
<td>12.2</td>
<td>10</td>
<td>4.1</td>
</tr>
<tr>
<td>40–49</td>
<td>17</td>
<td>9.5</td>
<td>9</td>
<td>4.9</td>
</tr>
<tr>
<td>50–59</td>
<td>11</td>
<td>8.6</td>
<td>14</td>
<td>10.5</td>
</tr>
<tr>
<td>60–69</td>
<td>8</td>
<td>9.4</td>
<td>5</td>
<td>5.0</td>
</tr>
<tr>
<td>70–79</td>
<td>5</td>
<td>10.0</td>
<td>4</td>
<td>5.2</td>
</tr>
<tr>
<td>80+</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1.8</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>90</td>
<td>9.1</td>
<td>147</td>
<td>7.2</td>
</tr>
</tbody>
</table>

* According to the CASPAR criteria. † Age-adjusted to the 2000 US White population. †† Age- and sex-adjusted to the 2000 US White population.

Figure 2. Annual incidence (per 100,000) of PsA by calendar year and sex, January 1, 1970, to December 31, 1999, Olmsted County, Minnesota.

Figure 3. Annual incidence rate (per 100,000) of PsA by sex and age, Olmsted County, Minnesota.
The most common enthesopathy and/or sites of tenosynovitis were in the plantar fascia (28%), fingers (28%), and shoulder (21%). Some PsA patients with enthesopathy presented with a combination of inflammatory sites (21%). At PsA incidence, 49% of subjects had oligoarticular and 39% had polyarticular involvement. Asymmetrical joint pattern of incident PsA was more common (78%) than symmetrical involvement (22%).

The majority of subjects with PsA (138, 94%) had psoriasis at PsA incidence. Additionally, 30 (21%) subjects had a family history of psoriasis. However, a family history of psoriasis was not consistently documented in the medical records (60% missing). There were 122 (98%) subjects with a negative RF test among the 124 subjects who received RF testing. Nail dystrophy was present in 40% of the subjects. Out of 108 subjects with documentation, active dactylitis was present in 33 (24%) subjects.

A total of 133 subjects had radiographs, and 73 (55%) subjects had findings consistent with inflammatory joint disease. There were 44 (33%) subjects with evidence of radiological features typical of PsA in hand and wrist radiographs. The most common radiographic changes were erosions in 42 (32%) subjects, including erosions at the distal interphalangeal joints in 14 subjects (11%). Seventeen subjects had osteolysis and 5 had periostitis. Additionally, 13 (10.7%) subjects had radiological findings of inflammatory spinal disease. Four subjects had unilateral sacroiliitis and 9 had bilateral sacroiliitis.

**DISCUSSION**

We are the first to report on the time trends in the incidence and prevalence of PsA using the CASPAR criteria over a 30-year period in a geographically defined population. Our findings indicate that there is a progressive increase in the incidence of PsA between 1970 and 2000. We have estimated that by the year 2000, the age- and sex-adjusted incidence rate for PsA was 10 per 100,000, with a prevalence of 158 per 100,000. Using these findings, we have extrapolated that between 162,000 to 589,000 adults aged ≥18 years were affected with PsA in the US in 2000, and 8,000 to 27,000 new cases occur each year.

There are only a limited number of incidence studies of PsA. Ours is the first study that examines PsA incidence trends using the same classification criteria consistently over an extended period. Although our PsA incidence estimates are broadly consistent with previous estimates, the most significant finding is the increasing incidence over time. This is in contrast to RA, a Th1-mediated disease, which has shown a decline in incidence over the same period. Previous studies have suggested a birth-cohort effect to explain the decline in RA, which had a higher incidence in the beginning of the 20th century, suggesting infectious or environmental triggers. Reasons for the change in PsA incidence are also unclear, but may be due to greater physician awareness, the changing nature of the disease, or unknown environmental or genetic risk factors. Of note, the incidence of psoriasis also has increased in this population during the same period, and thus the increase in incidence of PsA may parallel the increasing psoriasis trend.
Intriguingly, our findings also demonstrate a difference in the age-specific incidence of PsA between men and women. Contrary to prevailing belief that PsA occurs equally in both sexes, our findings indicate that the incidence of PsA in women is less than the incidence in men until the sixth decade of life. A similar pattern was observed in the incidence of psoriasis in the Olmsted County population and in a recent database study from the United Kingdom. These findings suggest a possible hormonal influence in the onset of PsA. Pregnancy has been associated with a reduced likelihood of PsA. Further, PsA improves during pregnancy, but disease flares are common during the postpartum period when estrogen levels are in flux. Also, patients treated with estrogen-modifying drugs were less likely to develop PsA. Although evidence is limited in PsA, research in RA and systemic lupus erythematosus has demonstrated that changes in cortisol, estrogen, progesterone, and glucocorticoids levels and the androgen/estrogen balance result in a downregulation of the Th1 response and a shift toward a Th2 cytokine profile. In summary, our sex-specific incidence patterns provide indirect evidence of the potential role of sex hormones in the etiology of PsA. Further research is needed to elucidate the complex role of sex hormones in the pathogenesis of PsA in men and women.

Our findings mostly agree with Shbeeb, et al, who examined the incidence and prevalence of PsA within the Olmsted County population between 1982 and 1991 using the resources from the REP. They found an overall incidence of 6.59 per 100,000 and a point prevalence of 1 per 1000. This is very similar to our 1980-89 estimate of 7.0 per 100,000. In contrast to our study, the PsA case definition used by Shbeeb, et al excluded subjects without psoriasis. In our study, we identified 30 subjects who had no evidence of psoriasis and yet fulfilled CASPAR criteria based on family history of psoriasis. Further, the clinical characteristics of the PsA cohort reported by Shbeeb, et al are similar to ours, with an average age at diagnosis of 40.7 years, and the majority of subjects presenting with oligoarthritis as well. One notable difference is sex differences in incidence. In that earlier cohort, the incidence of PsA was approximately equal in both sexes, while we found a higher incidence in men than in women. However, we had the advantage of examining trends over a 30-year period, which may also account for the sex difference. Another significant study examining the prevalence of PsA in the US population is the 2001 telephone survey conducted by the National Psoriasis Foundation. In that cross-sectional, self-reported survey, the overall point prevalence of PsA was 0.25%, reaching 11% among patients with psoriasis. Despite the differences in ascertainment methodology, this estimate based on self-reports is surprisingly similar to ours.

Our study also provides further evidence on the clinical and radiographic features in early PsA. First, most subjects in our incidence cohort satisfied CASPAR criteria based on the presence of psoriasis and a negative RF. This is consistent with patterns seen at other centers. Second, our study demonstrates an oligoarticular pattern with predominance of enthesopathy, similar to other early PsA case series. In contrast, studies of prevalent PsA subjects have documented the predominance of polyarticular involvement. As suggested by Gladman, et al, PsA begins as an oligoarticular disease that may evolve into a polyarticular phenotype. Third, a common radiographic feature in our incidence cohort was erosions, especially at the distal interphalangeal joints. Uncommon findings were osteolysis, fluffy periostitis, and bony proliferation or ankylosis. Potential reasons for less severe radiographic features in this inception cohort include underrecording of certain radiographic features by the general radiologists or ascertainment of subjects during early stages of PsA. Most previous studies included prevalent PsA subjects who may have prolonged exposure to the proinflammatory cytokines that are responsible for promoting the cascade that leads to bone destruction and new bone formation. Development of radiological damage is related to duration of clinically evident joint inflammation, and the number of actively inflamed joints is associated with the progression of radiological joint destruction. Alternatively, erosive disease or severe radiographic changes of bony deformation are more frequent in PsA subjects who have symmetrical, polyarticular disease, a group not common in our study.

In contrast to previous studies, we did not observe an increase in overall mortality in this cohort over an average followup of 13.6 years. This was also reported by an earlier study in this population. During the 30 years of the study, the underlying Olmsted County population was stable, without any major changes in demographics or major population shifts. As recently addressed by Ali and colleagues, one of the reasons for the discrepant findings may be an early, less severe stage of the disease in our incidence cohort, with the potential for exposure to sustained treatment that dampens the inflammatory state in later years. In other words, subjects with severe PsA are underrepresented in our inception cohort, whereas they are overrepresented especially in the earlier years of the Canadian clinic-based cohort, where the average PsA disease duration was 4.5 years. Alternatively, our PsA inception cohort is not large enough to detect a small excess in mortality. Indeed, our confidence intervals indicate that, if there is a small increase in risk of death, we cannot exclude a risk less than 37%.

Our study has several potential limitations. First, because of the variable disease course, there is the possibility that we missed PsA cases that presented with minimal or no psoriatic skin lesions, as inflammatory arthritis may precede the diagnosis of PsA in roughly 15%–19% of subjects. The sensitivity of the CASPAR criteria is only 91% and therefore, some true-PSA cases may not have fulfilled the CAS-
PAR criteria. However, over the course of 30 years, we expected that most PsA cases and psoriasis lesions would have been ascertained due to the comprehensive medical-records linkage system provided by the REP. Also, PsA subjects who never seek medical care would be missed in our study, leading to an underestimation of the true incidence of PsA. We assume that most patients with PsA will be diagnosed, albeit with a delay, during the 30-year study period. In addition, the CASPAR criteria were validated in hospital patients with inflammatory arthritis and not tested yet in a community-based setting. Community-based physicians may not be as vigilant in documenting clinical findings specific to PsA such as dactylitis. Nevertheless, referral to a rheumatologist is relatively easy in the Mayo health system and clinical findings missed on initial examinations would be documented by the rheumatologists and/or dermatologists.

Second, there is the concern of reviewer/detection bias due to the retrospective design of the study. However, the majority of data abstraction was performed with a standardized, pretested data abstraction form that included explicit variable definitions provided by the CASPAR criteria. Questions regarding individual PsA diagnosis were discussed with the other coinvestigators and resolved by consensus.

Third, the availability of information in the medical records may be subject to clinician variability; information on clinical variables, such as nail pitting, dactylitis, or the number of affected joints, may have been incompletely documented. Hence, it is plausible that the 128 subjects excluded may have had PsA (especially 40 with psoriasis), but documentation was inadequate in the medical record to have satisfied the CASPAR classification criteria. Similarly, radiographic results in the earlier years of the study were available only as paper copies with reports of “erosions typical of psoriatic arthritis” without further elaboration. Hard copies of radiographs were not reviewed for detailed confirmation of the presence or absence of individual radiographic features. Nevertheless, radiographic evidence was not necessary if a patient already accumulated 3 points to achieve the CASPAR criteria. Further, patients diagnosed with psoriasis prior to arthritis and treated with longterm methotrexate for the skin disease may have had suppression of an inflammatory arthritis, thus underrepresenting PsA in this population. In addition, although we found no difference in survival among subjects with PsA than in the general population, it is possible that not enough subjects were studied for an adequate period.

Finally, the population of Olmsted County is primarily White (90%) and thus limits the generalization of our incidence estimates to racially diverse populations.

Nevertheless, strengths of our study include the unique medical-records linkage system provided by the REP that allows near-complete ascertainment of all clinically recognized cases of PsA in a well defined population. In addition, ours is the first study that examines not only the time trends in the epidemiology of PsA, but also relies on the newly validated CASPAR criteria, which have been shown to have a sensitivity of 91.4% and specificity of 98.7%. The CASPAR criteria thus can be used in retrospective studies, provided that documentation of clinical and radiographic characteristics are available.

Our findings indicate that the incidence of PsA has been rising over 30 years in men and women. Incidence patterns in men and women follow different patterns, suggesting the potential role of sex hormones in the development of PsA. Further research is needed to elucidate the reasons for the increase in PsA incidence and the sex-specific patterns, including the potential role of environmental and hormonal risk factors.

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