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Risk of Uveitis Among People With Psoriasis
A Nationwide Cohort Study

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IMPORTANCE Uveitis has been associated with psoriatic arthritis, but to our knowledge, the relationship between uveitis and psoriasis is unsettled among researchers.

OBJECTIVE To evaluate the risk of incident uveitis among people with psoriasis.

DESIGN, SETTING, AND PARTICIPANTS This nationwide, retrospective cohort study conducted in Taiwan from January 1, 2000, to December 31, 2012 included 147 954 people with psoriasis (including 10 107 with concomitant psoriatic arthritis and 137 847 without psoriatic arthritis) and 147 954 nonpsoriatic controls.

EXPOSURE Psoriasis.

MAIN OUTCOMES AND MEASURES Risk of incident uveitis.

RESULTS The mean (SD) age of the 295 908 study participants was 44.4 (19.8) years, and 41.2% (n = 121 878) were women. We found that the group with severe psoriasis with psoriatic arthritis had the greatest risk of incident uveitis compared with the nonpsoriatic controls (adjusted hazard ratio, 2.40; 95% CI, 1.90-3.02). The group with severe psoriasis without psoriatic arthritis and the group with mild psoriasis with psoriatic arthritis also had an increased risk of incident uveitis (adjusted hazard ratio, 1.42; 95% CI, 1.23-1.64; and 1.42; 95% CI, 1.03-1.96; respectively). However, an increased risk for incident uveitis with mild psoriasis without psoriatic arthritis was not identified (adjusted hazard ratio, 1.09; 95% CI, 1.00-1.20).

CONCLUSIONS AND RELEVANCE People with severe psoriasis and those with mild psoriasis have an increased risk of uveitis. Clinicians may use this finding as a guide for uveitis risk stratification among patients with different inflammatory presentations on the spectrum of psoriatic disease.

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Invited Commentary page 422
Journal Club Slides

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Psoriasis is a chronic inflammatory dermatosis that affects 0.1% to 3% of the adult population worldwide and results in a heavy economic burden.[1-6] Psoriasis has been associated with various comorbidities, including cardiovascular disease, stroke, diabetes mellitus, renal diseases, and arthritis.[7,8] Various studies reported that 6% to 42% of participants with psoriasis had concomitant psoriatic arthritis, while the percentage was lower among Asian people.[9] Psoriatic arthritis is an inflammatory joint disease that may lead to joint destruction and disability.[9]

Uveitis is characterized by inflammation involving the uveal tract and associated ocular structures including the iris, ciliary body, and choroid tissue.[10] When affecting the anterior chamber, uveitis may present with pain and redness of the eye. When affecting the posterior chamber, eye pain and redness may not appear, but compromised visual acuity may occur.[11] Uveitis has been associated with psoriatic arthritis[12] and was more frequent and severe in the presence of human leukocyte antigen B27.[13] By contrast, the relationship between uveitis and psoriasis is still under investigation.[11] There have been a few studies examining the association between uveitis and psoriasis without psoriatic arthritis. A US case series reported that 9 patients with psoriasis without psoriatic arthritis had uveitis.[14] A cross-sectional study of 100 Singaporean patients with psoriasis found that the severity of psoriasis assessed by the Global Assessment score of the Lattice System Physician appeared to be higher among patients with uveitis than those without uveitis, although the difference did not reach statistical significance.[15] However, the Singaporean study did not find an association between uveitis and psoriatic arthritis.[15] A Turkish case-control study among 100 patients

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with psoriasis and 100 healthy individuals found no association between uveitis and psoriasis.[16] However, the validity of these studies was confined by their study design being case series, cross-sectional, or case-control with a limited sample size. Although a recent Danish retrospective cohort study showed an increased risk of uveitis associated with psoriasis, the association appeared only in mild psoriasis and psoriatic arthritis but not in severe psoriasis,[17] and there were no other cohort studies to confirm their findings. The relationship between psoriasis and uveitis thus remains unsettled to our knowledge.

To evaluate the respective risk estimates of uveitis among people with psoriasis with and without concomitant psoriatic arthritis, we conducted a retrospective nationwide population-based cohort study. We further evaluated the risk of uveitis among those with mild and severe psoriasis, respectively.

Key Points

Question Do people with psoriasis have an increased risk of incident uveitis?

Findings In this cohort study including 147 954 participants with psoriasis and 147 954 nonpsoriatic controls from Taiwan, people with concurrent severe psoriasis and psoriatic arthritis had the greatest risk of developing incident uveitis, followed by those with severe psoriasis but without psoriatic arthritis and those with mild psoriasis and psoriatic arthritis. There was not an increased risk for incident uveitis with mild psoriasis but without psoriatic arthritis.

Meaning The risk of incident uveitis differs with different inflammatory presentations on the spectrum of psoriatic disease.

Methods

Data Source

The National Health Insurance (NHI) is a compulsory single-payer health care system that covers more than 99% of the Taiwanese population. The National Health Insurance Research Database (NHIRD) provides anonymized linked data from the NHI for epidemiologic research, encompassing the registration and demographic data of enrollees, health care services data from hospitals and general practices, and medication dispensation data from hospitals, general practices, and community pharmacies. The NHIRD provides diagnosis data coded using the *International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9-CM*). The accuracy and completeness of the claim data of the NHIRD, including the *ICD-9-CM* diagnoses and medication records, have been validated.[18,19] The NHIRD has been extensively used in thousands of published epidemiological studies.[20]

We identified psoriatic patients from a specialized data set that contained all people with psoriasis from 2000 to 2011 in the NHIRD. The nonpsoriatic controls were selected from the 2005 Longitudinal Health Insurance Database that provides longitudinally linked anonymized data of 1 000 000 enrollees (nearly 5% of Taiwan's population) randomly sampled from the 2005 Registry for Beneficiaries of the NHIRD. The Longitudinal Health Insurance Database has been validated as a representative sample of the Taiwanese population in terms of age, sex, and average payroll bracket.[21] This study was approved by the institutional review board of the Chang Gung Medical Foundation (104-3810B). As all the data were anonymized, informed consent was exempted.

Study Population

The selection of study participants is shown in **Figure 1**. Participants with psoriasis were identified from the NHIRD by using *ICD-9-CM* codes 696, 696.1, and 696.8. These codes have been adopted in previous epidemiological studies that used the NHIRD.[7,22-24] We excluded people for whom psoriasis was diagnosed before 2000 to prevent overestimating the risk of incident uveitis (if the risk of uveitis rises with a longer disease duration of psoriasis, including those who received a diagnosis of psoriasis before 2000 would have overestimated the risk of incident uveitis) and excluded those for whom psoriasis was diagnosed after 2011 to ensure an at least 1-year follow-up duration. The nonpsoriatic control group consisted of people who had never received a diagnosis of psoriasis from the 2005 Longitudinal Health Insurance Database.

We also excluded people with a history of uveitis or the lifetime comorbidities that might have caused uveitis: human immunodeficiency virus infection (*ICD-9-CM* codes 042-044), ankylosing spondylitis (*ICD-9-CM* code 720.0), Behçet syndrome (*ICD-9-CM* codes 136.1, 711.1, 711.2), cytomegalovirus infection (*ICD-9-CM* code 078.5), herpes zoster ophthalmicus (*ICD-9-CM* code 053.2), histoplasmosis (*ICD-9-CM* codes 115.x), Kawasaki disease (*ICD-9-CM* code 446.1), juvenile rheumatoid arthritis(*ICD-9-CM* codes 714.x), sarcoidosis (*ICD-9-CM* codes 135.x, 321.4), syphilis (*ICD-9-CM* codes 090-097, 647.0), toxoplasmosis (*ICD-9-CM* codes 130.x), tuberculosis of the eye (*ICD-9-CM* code 017.3), ulcerative colitis (*ICD-9-CM* codes 556.x), Crohn disease (*ICD-9-CM* codes 555.x), and systemic lupus erythematosus (*ICD-9-CM* code 710.0).[25]

We mitigated potential selection bias between the psoriasis and nonpsoriatic groups via 1 to 1 matching by age (±180 days) and sex. Each participant with psoriasis was matched with 1 nonpsoriatic control who had not received a diagnosis of uveitis before the index date. The index date for the group with psoriasis was the date when psoriasis was diagnosed for the first time, whereas the index date for the nonpsoriatic control was the psoriasis-diagnosed date of the matched patient with psoriasis.

We divided the group with psoriasis into 2 groups according to the presence or absence of concomitant psoriatic arthritis: the group with psoriasis with psoriatic arthritis and the group with psoriasis without psoriatic arthritis. The *ICD-9-CM* code 696.0 was used to identify people who had received diagnoses of psoriatic arthritis. The 2 groups were further divided into 2 subgroups based on treatment patterns: the group with severe psoriasis was composed of people who had received systemic therapy (including acitretin, methotrexate, cyclosporine, etanercept, adalimumab, and ustekinumab) and/or phototherapy, and the group with mild psoriasis consisted of people who had not received systemic therapy or phototherapy. The classification of psoriasis based on treatment patterns has been widely adopted in previous epidemiological studies.[7,22-24,26-30]

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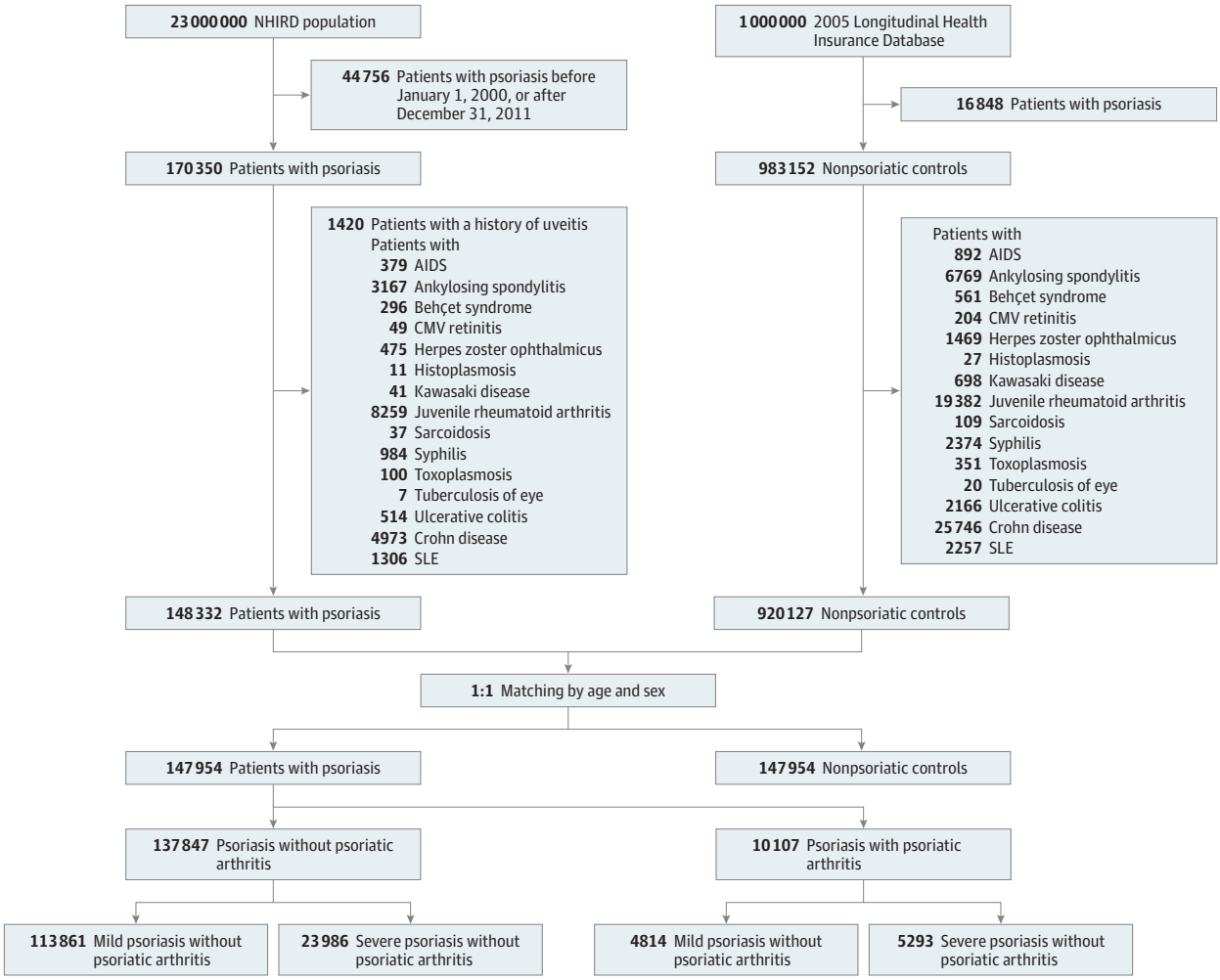
Figure 1. Flowchart of the Selection of the Study Population



CMV indicates cytomegalovirus; NHIRD, National Health Insurance Research Database; SLE, systemic lupus erythematosus.

Outcomes

The outcome of our interest was incident uveitis (*ICD-9-CM* codes 360.01, 360.02, 360.03, 360.1, 360.11, 360.12, 360.14, 360.19, 362.18, 363.0x, 363.1x, 363.2x, 364.0, 364.00, 364.01, 364.02, 364.04, 364.05, 364.1x, 364.2x, and 364.3). Uveitis related to infections, such as syphilis, was excluded.

The length of follow-up for people who developed incident uveitis was the period from the index date to the date of first diagnosis of uveitis in inpatient or outpatient records. The censored time of people who did not have uveitis was the period from the index dates to either December 31, 2012, or the date of withdrawal from the NHI. To enhance the accuracy of outcomes, we confirmed the end point by requiring records of the diagnosis on at least 2 outpatient visits or 1 hospital admission.

Statistical Analysis

We examined the baseline characteristics that included age, sex, comorbidity, and medication of psoriasis among the matched cohort. The categorical and continuous data were compared by using the χ^2 test and an analysis of variance test, respectively. We calculated the incidence (per 100 000 person-years) by dividing the number of people with incident uveitis by the person-years of each group. The Poisson distribution was used to obtain the confidence interval and compare the incidence between groups.[31] We used the Kaplan-Meier method for survival analysis and the log-rank test to compare the risk of incident uveitis between various groups with psoriatic disease.

In the primary analysis, we used univariate and multivariate Cox proportional hazard models to estimate the hazard ratios (HR) and 95% confidence intervals for the association between psoriasis status and incident uveitis using the nonpsoriatic control group as the reference. In the multivariate analysis, we adjusted potential confounders including age, sex, type 2 diabetes mellitus, hypertension, and hyperlipidemia.

Some of the *ICD-9-CM* codes of outcomes may refer to subtypes of uveitis that are not considered associated with psoriasis or psoriatic arthritis. Therefore, we conducted a sensitive analysis by using more selective *ICD-9-CM* codes (including 360.11, 360.12, 362.18, 363.0x, 363.1x, 363.2x, 364.0. 364.00,

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364.01, 364.02, 364.05, 364.1x, 364.2x, and 364.3) to confirm the associations between psoriasis and uveitis.

All statistical analyses were performed by using the SAS software, version 9.4 (SAS Institute). A *P* value of <.05 and a CI not containing 1 were considered statistically significant.

Results

The characteristics and confounders of the study participants are shown in **Table 1**. Of the data collected from January 1, 2000, to December 31, 2012, we included 147 954 people with psoriasis (including 10 107 with concomitant psoriatic arthritis and 137 847 without psoriatic arthritis) and 147 954 matched nonpsoriatic controls. The study population was predominantly Han Chinese. Because of the use of matching among selected study participants, the age and sex distribution was comparable across all groups. The mean (SD) age in the group with psoriasis and the control groups was 44.4 (19.8) years, and women accounted for 41.2% (n = 121 878) of both groups. Compared with the nonpsoriatic controls, a higher proportion of participants with psoriasis had type 2 diabetes mellitus, hypertension, and hyperlipidemia (*P* < .001).

As demonstrated in **Table 2**, the group with psoriasis with psoriatic arthritis and the group with psoriasis without psoriatic arthritis had a higher incidence of uveitis compared with the control group (160.88 and 103.99 vs 87.23 per 10^5 person-years). When further stratified by the severity of psoriasis, the group with severe psoriasis with psoriatic arthritis had the highest incidence of uveitis compared with other groups with psoriasis (185.55 vs 125.11, 126.39, and 99.08 per 10^5 person-years). The Kaplan-Meier curves of cumulative incidence of uveitis are illustrated in **Figure 2**. The group with psoriasis with psoriatic arthritis and the group with psoriasis without psoriatic arthritis had a higher risk for incident uveitis than the nonpsoriatic controls (*P* < .01, Figure 2A). When further stratified according to the severity of psoriasis, all 4 groups had a higher risk for incident uveitis than the nonpsoriatic controls (*P* < .05, Figure 2B).

As shown in Table 2, the primary analysis demonstrated that the group with psoriasis with psoriatic arthritis had an increased risk of incident uveitis (crude HR, 1.84; 95% CI, 1.52-2.24), as well as the group with psoriasis without psoriatic arthritis (crude HR, 1.19; 95% CI, 1.09-1.30) when compared with nonpsoriatic controls. After adjustment for potential confounders, the group with psoriasis with psoriatic arthritis and psoriasis and the group without psoriatic arthritis had a higher risk for incident uveitis (adjusted HR, 1.95; 95% CI, 1.61-2.37; and 1.16; 95% CI, 1.06-1.26, respectively) compared with nonpsoriatic controls. We found a stepwise increase in the risk of incident uveitis from nonpsoriatic controls to psoriasis alone to psoriasis with concomitant psoriatic arthritis (*P* < .001, χ^2 test for trend).

When further stratified by the severity of psoriasis, the group with severe psoriasis with concomitant psoriasis arthritis had the greatest risk of incident uveitis compared with the nonpsoriatic controls (crude HR, 2.14; 95% CI, 1.70-2.70; adjusted HR, 2.40; 95% CI, 1.90-3.02), and the group with severe psoriasis without psoriatic arthritis and the group with mild psoriasis with concomitant psoriatic arthritis had a higher risk of incident uveitis than the nonpsoriatic controls (adjusted HR, 1.42; 95% CI, 1.23-1.64; and 1.42; 95% CI, 1.03-1.96, respectively). However, an increased risk for incident uveitis with mild psoriasis without psoriatic arthritis was not identified after adjusting for potential confounders (adjusted HR, 1.09; 95% CI, 1.00-1.20). An increasing trend for incident uveitis across these groups was found (*P* < .001, χ^2 test for trend).

As illustrated in **Table 3**, the sensitivity analysis confirmed both psoriatic patients with and without concomitant psoriatic arthritis had an increased risk of incident uveitis (adjusted HR, 1.88; 95% CI, 1.54-2.31; and 1.15; 95% CI, 1.05-1.26, respectively). The sensitivity analysis also identified an increasing trend for uveitis from nonpsoriatic controls to psoriasis alone to psoriasis with concomitant psoriatic arthritis (*P* < .001, χ^2 test for trend). The sensitivity analysis also found that when compared with nonpsoriatic controls, the group with severe psoriasis with psoriatic arthritis had the highest risk of incident uveitis (adjusted HR, 2.38; 95% CI, 1.87-3.03), followed by the group with severe psoriasis without psoriatic arthritis (adjusted HR, 1.46; 95% CI 1.26-1.70) and the group with mild psoriasis with psoriatic arthritis (adjusted HR, 1.29; 95% CI 0.91-1.84). However, an increased risk for incident uveitis among the group with mild psoriasis without psoriatic arthritis was not found (adjusted HR, 1.08; 95% CI, 0.98-1.19). The sensitivity analysis also found an increasing trend for incident uveitis across these groups (*P* < .001, χ^2 test for trend).

Discussion

Over the past decade, there has been an increasing awareness of the comorbidities of psoriasis.[7] The term *psoriatic disease* was introduced to highlight its multiorgan involvement.[32] Although the association between psoriatic arthritis and uveitis is well-known, the relation between uveitis and psoriasis without psoriatic arthritis, to our knowledge, was rarely examined.[11] This study adds evidence for this previously unsettled question. We found that people with concurrent severe psoriasis and psoriatic arthritis (ie, those with the most severe inflammatory presentation of psoriatic disease) have the highest risk for incident uveitis. People with severe psoriasis but without psoriatic arthritis and people with mild psoriasis and psoriatic arthritis (ie, those with a moderately inflammatory presentation on the spectrum of psoriatic disease) also have an increased risk of incident uveitis. By contrast, an increased risk for incident uveitis among people with mild psoriasis but without psoriatic arthritis (ie, those with the mildest inflammatory presentation on the spectrum of psoriatic disease) was not found. The sensitivity analysis adopting more selective diagnostic codes for uveitis confirmed the results of the primary analysis. These findings suggest that the risk of incident uveitis, a condition of intraocular inflammation, increases with the degree of inflammation of psoriatic disease that may present either on the skin or a joint.

Our study results are incongruent with a previous Turkish study that found no association between uveitis and psoriasis.[16] However, our study has the strength of the cohort study design, which provides a higher level of causality evidence than the

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Table 1. Characteristics and Potential Confounders in the Study Population

Characteristic	Nonpsoriatic Controls[a] (n = 147 954)	Total[a] (n = 295 908)	Psoriasis[a] (n = 147 954)	P Value[b]	Psoriasis With Psoriatic Arthritis[a] (n = 10 107)	Psoriasis Without Psoriatic Arthritis[a] (n = 137 847)	P Value[b]	Severe Psoriasis With Arthritis[a] (n = 5293)	Severe Psoriasis Without Arthritis[a] (n = 23 986)	Mild Psoriasis With Arthritis[a] (n = 4814)	Mild Psoriasis Without Arthritis[a] (n = 113 861)	P Value[b]
Mean (SD) age, y	44.4 (19.8)	44.4 (19.8)	44.4 (19.8)	1.00	42.7 (18.1)	44.5 (19.9)	<.001	41.4 (16.2)	44.4 (18.6)	44.3 (19.8)	44.5 (20.1)	<.001
Women	60 938 (41.2)	121 876 (41.2)	60 938 (41.2)	1.00	3808 (37.7)	57 130 (41.4)	<.001	1756 (33.2)	7629 (31.8)	2052 (42.6)	49 501 (43.5)	<.001
Mean (SD) follow-up, y	7.1 (3.4)	7.1 (3.4)	7.1 (3.4)	.54	7.1 (3.6)	7.1 (3.4)	.83	7.9 (3.5)	7.7 (3.5)	6.2 (3.4)	7.0 (3.4)	<.001
Median follow-up, (IQR), y	7.3 (5.9)	7.3 (5.9)	7.2 (5.9)	NA	7.1 (6.3)	7.3 (5.9)	NA	8.4 (6.0)	8.1 (6.10)	6.0 (5.7)	7.1 (5.8)	NA
Type 2 diabetes mellitus	14 782 (10.0)	34 429 (11.6)	19 647 (13.3)	<.001	1200 (11.9)	18 447 (13.4)	<.001	540 (10.2)	3178 (13.3)	660 (13.7)	15 269 (13.4)	<.001
Hypertension	31 304 (21.2)	69 191 (23.4)	37 887 (25.6)	<.001	2372 (23.5)	35 515 (25.8)	<.001	1122 (21.2)	6062 (25.3)	1250 (26.0)	29 453 (25.9)	<.001
Hyperlipidemia	19 992 (13.5)	46 197 (15.6)	26 205 (17.7)	<.001	1795 (17.8)	24 410 (17.7)	<.001	836 (15.8)	4226 (17.6)	959 (19.9)	20 184 (17.7)	<.001

Abbreviations: IQR, interquartile range; NA, not applicable.

[a] No. (%).

[b] Compared with nonpsoriatic controls.

Turkish case-control study.[33] Also, the Turkish study did not examine the risk for different severities of psoriasis.

Our study indicates that besides psoriatic arthritis, severe psoriasis is an important marker of inflammation associated with incident uveitis. In this aspect, our study is in congruent with the Singaporean study that found that the severity of psoriasis correlated with the presence of uveitis.[15]

A recent Danish study found that the risk of uveitis increased in mild psoriasis without arthritis (adjusted incidence rate ratio, 1.38; 95% CI, 1.11-1.70), but not in severe psoriasis without arthritis (adjusted incidence rate ratio, 1.40; 95% CI, 0.70-2.81),[17] which appears to contradict the well-recognized greater degree of systemic inflammation in severe psoriasis.[34] While the Danish study only adjusted for 3 comorbidities (herpes zoster, inflammatory bowel disease, and sarcoidosis) in its statistical analysis,[17] our study controlled for a variety of confounding comorbidities by limitation to obtain a less biased estimate of the risk of uveitis (see Study Population in the Methods section).

Limitations

There are a few limitations in this study. First, we used the *ICD-9-CM* codes to identify cases of psoriasis and psoriatic arthritis; so did other epidemiological studies.[17,22-24,26,27,30] One previous study demonstrated that the sensitivity of the *ICD-9-CM* code for detecting psoriatic arthritis was 73%.[35] Therefore, some patients with psoriasis with psoriatic arthritis might have been misclassified and included in the group with psoriasis without psoriatic arthritis. However, this misclassification only led to an underestimation of the risk of incident uveitis in the group with psoriasis with psoriatic arthritis. Second, similar to other claim databases for epidemiological studies,[26,27,30] the data source of this study, the NHIRD, did not provide direct clinical data to determine the severity of psoriasis. As has been widely adopted in previous studies on psoriasis,[7,22-24,26-30] we used treatment patterns to identify mild and severe psoriasis. If we misclassified cases of severe psoriasis as mild psoriasis, the association found between uveitis and severe psoriasis would have been underestimated. Third, when we excluded psoriasis diagnosed before 2000 to avoid overestimating the risk of incident uveitis, it is likely that people with early-onset psoriasis (eg, adults who first presented with psoriasis in childhood) were also excluded. However, we adopted a survival analysis and have considered the duration of psoriasis as a factor in the development of uveitis. Fourth, the exclusion of patients with a history of uveitis from the cohort with psoriasis presumably has led to an underestimation of the overall uveitis burden in the group with psoriasis. Fifth, the definition of severe psoriasis was a history of receiving phototherapy and/or systemic treatments, including cyclosporine and biologics. The 2 latter kinds of drugs are also indicated for treating established uveitis, and thus might well have reduced the risk of uveitis among this group and led to an underestimation of the "true" risk of uveitis among the group with severe psoriasis. Sixth, the study participants were censored after their first attack of uveitis. These participants may have had further attacks and a higher disease burden than detected in this study. Seventh, human leukocyte antigen B27 has been associated with uveitis,[13] but we were unable to adjust for it because the NHIRD does not

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Table 2. Risk of Incident Uveitis in Patients With Psoriasis

	No. of Incident Uveitis	No. of Person-years	Incidence per 10^5 Person-years (95%CI)	*P* Value[a]	Crude HR (95% CI)	Adjusted HR[b] (95% CI)
Nonpsoriatic controls	922	1 057 030.21	87.23 (81.7-93.0)	NA	1.00	1.00
Psoriasis without psoriatic arthritis	1023	983 787.37	103.99 (97.7-110.6)	.001	1.19 (1.09-1.30)[c]	1.16 (1.06-1.26)[c]
Psoriasis with psoriatic arthritis	116	72 102.51	160.88 (132.9-193.0)	<.001	1.84 (1.52-2.24)[d]	1.95 (1.61-2.37)[d]
P_{trend}, nonpsoriatic controls to psoriasis without psoriatic arthritis to psoriasis with psoriatic arthritis	NA	NA	NA		<.001	<.001
Nonpsoriatic controls	922	1 057 030.21	87.23 (81.7-93.0)		1 (Reference)	1 (Reference)
Mild psoriasis without psoriatic arthritis	791	798 348.13	99.08 (92.2-106.2)	.001	1.14 (1.03-1.25)[c]	1.09 (1.00-1.20)
Mild psoriasis with psoriatic arthritis	38	30 065.03	126.39 (89.4-173.5)	.02	1.44 (1.04-1.99)[e]	1.42 (1.03-1.96)[e]
Severe psoriasis without psoriatic arthritis	232	185 439.24	125.11 (109.5-142.3)	<.001	1.44 (1.25-1.66)[d]	1.42 (1.23-1.64)[d]
Severe psoriasis with psoriatic arthritis	78	42 037.47	185.55 (146.7-231.6)	<.001	2.14 (1.70-2.70)[d]	2.40 (1.90-3.02)[d]
P_{trend}, nonpsoriatic controls to mild psoriasis without psoriatic arthritis to mild psoriasis with psoriatic arthritis to severe psoriasis without psoriatic arthritis to severe psoriasis with psoriatic arthritis	NA	NA	NA	NA	<.001	<.001

Abbreviations: HR, hazard ratio; NA, not applicable.

[a] Compared with nonpsoriatic controls.

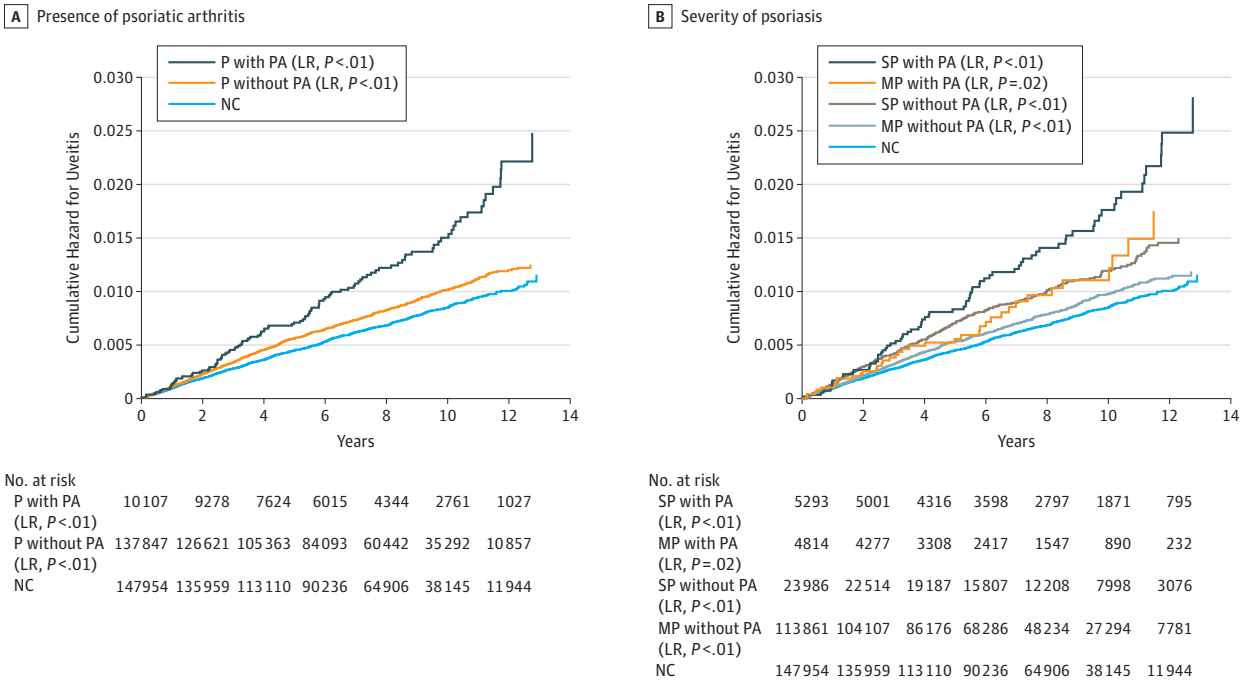
[b] Adjusted for age, sex, type 2 diabetes mellitus, hypertension, and hyperlipidemia.

[c] $P < .01$.

[d] $P < .001$.

[e] $P < .05$.

Figure 2. Cumulative Incidence Curves for Uveitis



Classified based on the presence of psoriatic arthritis (A), and further classified according to the severity of psoriasis (B). LR indicates log rank; MP, mild psoriasis; NC, nonpsoriatic controls; P, psoriasis; PA, psoriatic arthritis; SP, severe psoriasis.

contain relevant data. Eighth, there might have been residual unknown confounding, although we have applied limitation and adjustment to control known confounding. Ninth, we originally planned to analyze the risk of complications following uveitis—

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Table 3. Sensitivity Analysis

	No. of Incident Uveitis	No. of Person-years	Incidence per 10^5 Person-years (95% CI)	*P* Value[a]	Crude HR (95% CI)	Adjusted HR[b] (95% CI)
Nonpsoriatic controls	848	1 057 340.41	80.20 (74.9-85.8)		1 (Reference)	1 (Reference)
Psoriasis without psoriatic arthritis	939	984 107.66	95.42 (89.4-101.7)	.001	1.19 (1.08-1.30)[c]	1.15 (1.05-1.26)[c]
Psoriasis with psoriatic arthritis	103	72 148.53	142.76 (116.5-173.1)	<.001	1.78 (1.45-2.18)[d]	1.88 (1.54-2.31)[d]
P_{trend}, nonpsoriatic controls to psoriasis without psoriatic arthritis to psoriasis with psoriatic arthritis	NA	NA	NA	NA	<.001	<.001
Nonpsoriatic controls	848	1 057 340.41	80.20 (74.9-85.8)		1 (Reference)	1 (Reference)
Mild psoriasis without psoriatic arthritis	719	798 628.41	90.03 (83.6-96.9)	.02	1.12 (1.02-1.24)[e]	1.08 (0.98-1.19)
Mild psoriasis with psoriatic arthritis	32	30 088.27	106.35 (72.7-150.1)	.12	1.31 (1 0.92-1.87)	1.29 (0.91-1.84)
Severe psoriasis without psoriatic arthritis	220	185 479.25	118.61 (103.5-135.4)	<.001	1.48 (1.28-1.72)[d]	1.46 (1.26-1.70)[d]
Severe psoriasis with psoriatic arthritis	71	42 060.26	168.81 (131.8-212.9)	<.001	2.12 (1.67-2.71)[d]	2.38 (1.87-3.03)[d]
P_{trend}, nonpsoriatic controls to mild psoriasis without psoriatic arthritis to mild psoriasis with psoriatic arthritis to severe psoriasis without psoriatic arthritis to severe psoriasis with psoriatic arthritis	NA	NA	NA	NA	<.001	<.001

Abbreviations: HR, hazard ratio; NA, not applicable.

[a] Compared with nonpsoriatic controls.

[b] Adjusted for age, sex, type II diabetes mellitus, hypertension, and hyperlipidemia.

[c] $P < .01$.

[d] $P < .001$.

[e] $P < .05$.

for example, cataracts and glaucoma—but the number of events was too few for analysis. Finally, the study participants were predominantly Han Chinese and therefore, as with other population-specific studies, the findings may not be generalizable.

Conclusions

This study found that people with concurrent severe psoriasis and psoriatic arthritis have the highest risk of incident uveitis, while those with mild psoriasis and psoriatic arthritis and those with severe psoriasis but without psoriatic arthritis have a moderately increased risk of incident uveitis. An increased risk of incident uveitis with mild psoriasis but without psoriatic arthritis was not found. Clinicians may use this finding as a guide for uveitis risk stratification among patients with different inflammatory presentations on the spectrum of psoriatic disease. Patients with psoriasis should be educated about the increased risk and manifestations of uveitis. An ophthalmological consultation is needed when patients present with eye symptoms.

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Invited Commentary

The Draw(backs) of Big Data

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The association between psoriatic arthritis and uveitis is well-known. Intraocular inflammation in psoriatic arthritis is found among up to 25% of patients seen at tertiary rheumatology centers.[1] To our knowledge, however, less is known about the association between uveitis and psoriasis without arthritis. Some have noted differences in the onset and clinical features of uveitis between patients with psoriasis and psoriatic arthritis.[2] This is interesting given that while psoriatic arthritis is a seronegative spondyloarthropathy, psoriasis without arthritis is not. However, among patients with psoriasis, the prevalence of psoriatic arthritis is certainly higher than in the general population.[3] Interestingly, 1 epidemiologic study noted that the presence of uveitis in a patient with psoriasis increased the risk of that patient developing psoriatic arthritis substantially more than the severity of the psoriasis or the presence of nail pitting.[4]

Related article page 415

In this issue of *JAMA Ophthalmology*, Chi and colleagues[5] evaluate the incidence of uveitis among Taiwanese patients with psoriasis using its National Health Insurance Research Database. The power of this study is appreciated when considering that Taiwan's National Health Insurance program covers more than

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