Psoriasis and the risk of diabetes: A prospective population-based cohort study

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Background: Data evaluating the impact of objectively measured psoriasis severity on type 2 diabetes mellitus (T2DM) risk are lacking.

Objective: To determine the risk for T2DM in patients with psoriasis compared with that in adults without psoriasis, stratified by categories of directly assessed body surface area (BSA) affected by psoriasis.

Methods: A prospective, population-based, cohort study from the United Kingdom in which 8124 adults with psoriasis and 76,599 adults without psoriasis were followed prospectively for approximately 4 years.

Results: There were 280 incident cases of diabetes in the psoriasis group (3.44%) and 1867 incident cases of diabetes in those without psoriasis (2.44%). After adjustment for age, sex and body mass index, the hazard ratios for development of incident diabetes were 1.21 (95% confidence interval [CI], 1.01-1.44), 1.01 (95% CI, 0.81-1.26), and 1.64 (95% CI, 1.23-2.18) in the groups with 2% or less of their BSA affected, 3% to 10% of their BSA affected, and 10% or more of their BSA affected compared with in the groups without psoriasis, respectively (P = .004 for trend). Worldwide, we estimate an additional 125,650 new diagnoses of T2DM per year in patients with psoriasis as compared with in those without psoriasis.

Limitations: Relatively short-term follow-up and exclusion of prevalence cases, which may have masked associations in patients with less extensive psoriasis.

Conclusion: Clinicians may measure BSA affected by psoriasis to target diabetes prevention efforts for patients with psoriasis. (J Am Acad Dermatol 2018;78:315-22.)

Key Words: body surface area; cohort study; diabetes; epidemiology; psoriasis.

Psoriasis is a common, chronic inflammatory disease affecting more than 125 million people worldwide.[1,2] A vast and growing body of literature links psoriasis to an excess risk for major medical morbidities, and even mortality.[3-10] Of special interest is the association of psoriasis and

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diabetes,[11,12] as genetic studies have identified shared susceptibility loci and inflammatory cytokines that are up-regulated in psoriasis and known to promote insulin resistance.[13-17] A recent, small meta-analysis identifying 5 articles (4 of which did not measure psoriasis severity) assessing incidence showed that psoriasis is associated with a relative risk of 1.27 (95% confidence interval [CI], 1.16-1.40) for development of type 2 diabetes mellitus (T2DM).[4] Beyond the systematic review, we identified 1 additional study that used treatment patterns to establish a higher risk for T2DM.[18] Despite current knowledge, data from population-based, prospective studies evaluating the impact of objectively measured disease severity on T2DM risk are still lacking. Only a handful of studies have assessed risk (incidence) of T2DM while adjusting for confounding variables,[11,18-20] and even fewer have been able to evaluate the effects of psoriasis severity (all of which used treatment patterns) on T2DM association.[18,19]

Therefore, a better understanding of how physician-reported psoriasis severity affects the risk for development of T2DM is essential to determine which patients have a clinically important increased risk for diabetes and therefore should be targeted for augmented prevention efforts. Although a variety of approaches have been used to define psoriasis severity, categories of body surface area (BSA) affected have been commonly used in epidemiologic studies and are clinically intuitive. The National Psoriasis Foundation[21,22] and the Centers for Disease Control[23] categorize extent of BSA affected into 2% or less (mild), 3% to 10% (moderate), and more than 10% (severe). Furthermore, we have previously shown that these simple categories are positively associated with prevalence of psoriatic arthritis and major medical comorbidities in a dose-response manner.[12,24] The goal of this study was to determine the risk for development of T2DM in patients with psoriasis compared with in adults without psoriasis, stratified by categories of directly assessed BSA affected by psoriasis.

CAPSULE SUMMARY

- Psoriasis is associated with diabetes.
- Increasing body surface area affected by psoriasis is associated with a greater risk for diabetes independent of risk factors.
- Body surface area affected by psoriasis should be routinely measured. Patients with psoriasis, especially those with a BSA greater than 10%, should be targeted for diabetes prevention.

METHODS

Study design and data source

We conducted a prospective, population-based cohort study nested within The Health Improvement Network (THIN) to determine the incidence of diabetes in patients with psoriasis. THIN is a United Kingdom (UK) electronic medical record database containing patient demographics, diagnostic information, clinical measurements, and prescriptions from general practitioners (GPs) using Vision software (In Practice Systems, Ltd, London, UK). GPs coordinate almost all patients' care in the UK health care system; hence, medical information from specialists and hospitals is routinely recorded in patients' electronic medical record. Diagnoses are recorded in THIN through a READ diagnostic code system,[25] and documented prescriptions are linked to the British National Formulary.[26] This study's version of THIN included longitudinal data on 7.5 million registered patients from 415 practices, with demographics broadly representative of the general UK population.[27] Studies have validated the accuracy of THIN data for use in large-scale epidemiology research, particularly in psoriasis research.[28,29] This study was conducted in compliance with the Declaration of Helsinki,[30] and the manuscript was prepared in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology statement.[31] The research was approved by the University of Pennsylvania Institutional Review Board and the Cambridgeshire Research Ethics Committee. No consent was required, as de-identified data were used.

Study population

The Incident Heath Outcomes and Psoriasis Events cohort, which was previously described by our group,[12] comprises individuals randomly sampled from THIN who, at the time of sampling, were between the ages of 25 to 64 years, had at least 1 psoriasis READ diagnostic code within 2 years before survey administration, and were registered in a practice that was participating in THIN's Additional Information Services (58% of the THIN practices), which involves participants' GPs completing questionnaires in exchange for financial compensation. As psoriasis was the exposure of interest, GPs were prospectively sent a research survey,[29] which was collected in the subsequent 12 months and involved GPs confirming psoriasis diagnosis and evaluating severity of disease. GPs assessed the extent of psoriasis by evaluating the amount of BSA involved

Abbreviations used:

BMI: body mass index
BSA: body surface area
CI: confidence interval
GP: general practitioner
T2DM: type 2 diabetes mellitus
THIN: The Health Improvement Network

and provided this as a continuous estimate (0%-100%) and as separate categories as follows: mild (limited disease with ≤2% of BSA affected), moderate (scattered disease with 3%-10% of BSA affected), or severe (extensive disease with >10% of BSA affected).[32]

Each patient with psoriasis was individually matched with up to 10 randomly selected patients without psoriasis (defined by no history of psoriasis READ diagnostic codes) by practice, visit date, and age (within 10-year age categories). The exposed group in our primary analyses required GP confirmation of psoriasis diagnosis and severity assessment by BSA affected from the survey. The unexposed group was also required to be actively registered, with at least 1 visit to their GP within 2 years before the time of random sampling. Subjects with and without psoriasis were excluded from analyses if there was a history of T2DM at baseline, which corresponds to the index date.

T2DM outcome and covariate definitions

The primary outcome, namely, the incidence of T2DM, was defined by a composite of 1 T2DM READ diagnostic code *plus* a second READ diagnostic code, 1 T2DM pharmacologic therapy, or 1 laboratory confirmation, whichever occurred first. This identification approach was adapted from a validation study using THIN by Sharma et al with 100% PPV.[33] Furthermore, according to the UK National Institute for Clinical Excellence and GP Notebook clinical guidelines, T2DM was defined as a glycosylated hemoglobin level of 6.5% or higher or 48 mmol/mol or higher.[34,35] T2DM antidiabetic drugs were identified according to the British National Formulary that corresponded with the observation period.[36]

Multiple potential confounders were identified a priori: age, sex, body mass index (BMI), smoking and alcohol use, medical comorbidities (hyperlipidemia and hypertension), use of prescription oral and inhaled corticosteroids, and the Townsend deprivation score (which correlates with socioeconomic status). These were measured before survey sampling or the corresponding visit date for matched controls. Age was treated as a continuous variable, whereas the other covariates were categorical.

Person-time calculation

For psoriasis-exposed individuals, the index date (cohort entry) was defined by the date the GP survey[29] was sent. The index date for unexposed individuals was the corresponding date for the exposed individual to whom they were matched. The event of interest was the incidence of T2DM. Patients were censored at end of follow-up as a result of patient death or transfer out of practice, end of practice participation in THIN, or the end of the observation period (February 5, 2015).

Statistical analysis

Baseline patient demographics were summarized with descriptive statistics for patients with and without psoriasis. Differences in baseline demographic and clinical characteristics were assessed using the Student *t* test for continuous variables and χ^2 tests for categorical variables. A raw incidence rate for T2DM was estimated by dividing the number of events (new diagnoses of T2DM) by the total person-time under observation. Cox proportional hazards models were used to estimate hazard ratios (HRs) comparing the exposed and unexposed cohorts. We identified covariates for inclusion in a final, adjusted Cox proportional hazards model utilizing a purposeful selection approach. Our initial model included all covariates in Table I. Variables were then eliminated from the model by sequentially removing covariates, starting with the largest *P* value ($P > .05$). If the HR point estimates for psoriasis did not change by more than 10% in the reduced model as compared with in the prior multivariable model, then the covariate was removed. Our final model was adjusted for age, sex, and BMI. The likelihood ratio test was used to evaluate significance of covariates, determining best model fit. Log-log survival plots for psoriasis were constructed to assess the proportional hazards assumption, which was not violated. All effect measures were reported with 95% CIs. Our sample size provided power in excess of 98% for HRs of 1.2 or greater, assuming a 2-sided α level of 0.05. Analyses were performed with STATA 13.1 software (StatCorp LP, College Station, TX).

RESULTS

Patient characteristics

Of the 10,474 eligible patients with psoriasis READ codes sampled for survey mailing, 10,026 had surveys returned from their GPs, of whom 9069 had a confirmed diagnosis of psoriasis by their GP. A total of 652 subjects had a history of T2DM, and

Table I. Baseline Characteristics of Patients with and without psoriasis (N = 84,723)

Characteristic	Without psoriasis (n = 76,599)		With psoriasis (n = 8124)		*P* value*	Standardized difference
Sex						
Male	35,711	46.62%	4088	50.32%	<.001	0.07
Female	40,888	53.38%	4036	49.68%		
Age, y						
Mean	44.54		44.86		.015	0.03
Median (IQR)	45 (36-54)		45 (36-54)			
BMI, kg/m^2						
<18.5	1435	2.11%	127	1.74%	<.001	0.14
≥18.5 to <25	27,355	40.14%	2547	34.99%		
≥25 to <30	23,759	34.87%	2547	34.99%		
≥30 to <35	10,313	15.13%	1284	17.64%		
>35	5280	7.75%	774	10.63%		
Missing	8457	11.04%	845	10.40%		
Smoking						
Never	37650	49.98%	3025	37.58%	<.001	0.25
Current	18,744	24.88%	2582	32.05%		
Former	18,934	25.14%	2442	30.34%		
Missing	1271	1.66%	75	0.92%		
Alcohol						
Never	7420	11.04%	654	9.09%	<.001	0.07
Current	55565	82.70%	6026	83.76%		
Former	4206	6.26%	514	7.14%		
Missing	9408	12.28%	930	11.45%		
History of hyperlipidemia						
Yes	5351	6.99%	663	8.16%	<.001	0.04
No	71,248	93.01%	7461	91.84%		
History of hypertension						
Yes	9444	12.33%	1084	13.34%	.008	0.03
No	67,155	87.67%	7040	86.66%		
History of systemic corticosteroids						
Yes	4861	6.35%	636	7.83%	<.001	0.06
No	71,738	93.65%	7488	92.17%		
History of inhaled corticosteroids						
Yes	3941	5.14%	449	5.53%	.140	0.02
No	72,658	94.86%	7675	94.47%		
Townsend score						
1	19,159	26.00%	1856	23.72%	<.001	0.06
2	16,024	21.75%	1689	21.59%		
3	15,407	20.91%	1668	21.32%		
4	13,228	17.95%	1469	18.78%		
5	9865	13.39%	1141	14.59%		
Missing	2916	3.81%	301	3.71%		
History of biologic/systemic drugs	151	0.19%	353	4.35%		
History of phototherapy	70	0.09%	560	6.89%		

BMI, Body mass index; *IQR*, interquartile range.

*The χ^2 test was used for analyses of categoric variables, and the *t* test was used for analyses of continuous variables. *P* values are based on comparisons of the group of patients with psoriasis compared with matched individuals without psoriasis.

17 had missing medical records and were therefore excluded from analyses. Our entire study cohort consisted of 84,723 individuals of whom 8124 had psoriasis and 76599 did not. After stratification by physician-reported BSA, 4216 (51.90%), 2915 (35.88%), and 993 (12.22%) had 2% or less of their BSA affected, 3% to 10% of their BSA affected, and more than 10% of their BSA affected, respectively (Fig 1). Compared with patients without psoriasis, those in the group with psoriasis had the same

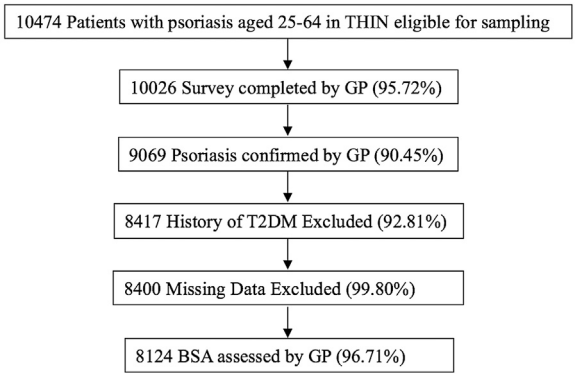

Fig 1. Selection of the exposed population. *BSA*, Body surface area; *GP*, general practitioner; *T2DM*, type 2 diabetes mellitus; *THIN*, The Health Improvement Network.

median age, slightly more male patients, and similar follow-up duration. Standardized differences (Table I), a measure not influenced by sample size, indicated meaningful differences (>0.1) between patients with and without psoriasis for BMI and smoking status.[37]

Incidence of T2DM in patients with psoriasis

There were 280 (3.44%) and 1867 (2.44%) incident outcomes of T2DM in patients with and without psoriasis, respectively. The unadjusted incidence rate of T2DM was 5.97 new diagnoses of T2DM per 1000 person-years in the unexposed group. The highest incidence rate of T2DM was in patients with more than 10% of their BSA affected by psoriasis (12.22 per 1000 person-years) (Table II). After adjustment for age, sex, and BMI, the HRs for development of incident T2DM were 1.21 (95% CI, 1.01-1.44), 1.01 (95% CI, 0.81-1.26), and 1.64 (95% CI, 1.23-2.18) in the groups with 2% or less of their BSA affected, 3% to 10% of their BSA affected, and more than 10% of their BSA affected compared with in patients without psoriasis, respectively (P = .004 for trend; Table III). As patients with more than 10% of their BSA affected by psoriasis may be heterogeneous in their disease burden, we further evaluated increases in BSA affected in this group (on the basis of a continuous measure provided by GPs) and determined that for every 10% increase in BSA affected with the fully adjusted model, the hazard of incident T2DM increased by a factor of 1.193 (95% CI, 1.025-1.390). Interactions between age and psoriasis and sex and psoriasis were not statistically significant ($P < .1$). Findings were similar when robust standard errors were used to account for clustering within matched sets of observations.

Sensitivity analyses and multiple imputation

Our observations were robust across a variety of sensitivity analyses and after use of multiple imputation for missing BMI data (Supplemental Table I; available at http://www.jaad.org). The results changed little in response to varying outcome (T2DM) definitions, varying definitions of exposure (psoriasis) group, and alternative handling of missing data in BMI. Investigating observation bias and treatment pattern effects did not affect our findings significantly (Supplemental Table I, lines 11, 7, and 8). To ensure that incident T2DM outcomes were not prevalent outcomes, sensitivity analyses excluding patients who had registered with the practice within 9 months before the index date[38] and those with diagnoses of T2DM within 1 year after index date were conducted, and the results were essentially unchanged.

Attributable risk

On the basis of our data, we estimate that in individuals with psoriasis, there are 3 additional diagnoses of diabetes per 1000 patient-years compared with in patients without psoriasis, after accounting for traditional risk factors such as age, sex, and BMI identified in routine medical practice. Furthermore, the excess risk, or number of extra cases of T2DM, attributable to psoriasis is most clinically significant in patients with more than 10% of their BSA affected, with 6.25 extra cases per 1000 person-years as compared with in those without psoriasis versus in those with 2% or less of their BSA affected, in which case the excess risk is 1.99 per 1000 person-years. When standardized cumulative incidence estimates based on our adjusted Cox model[39] are used, an additional estimated 125,650 new diagnoses of T2DM per year worldwide are seen in patients with psoriasis as compared with in those without psoriasis, of whom approximately 25,000 have psoriasis affecting more than 10% of their BSA.

DISCUSSION

In our large, population-based, prospective cohort study from the United Kingdom, we found a positive dose-response relationship between an objective measure of psoriasis severity and the incidence of T2DM. Patients with more than 10% of their BSA affected by psoriasis had the highest risk for development of T2DM compared with that in adults without psoriasis. Moreover, for every 10% increase in BSA affected by psoriasis (ie, 20%, 30%, etc) there is approximately a 20% higher hazard of diabetes, which emphasizes the dose-response relationship between burden of skin psoriasis and risk for development of diabetes. Our results accounted

Table II. Incidence of type 2 diabetes mellitus in patients with psoriasis compared with in controls and by psoriasis severity

Characteristic	Without psoriasis (n = 76,599)	With psoriasis (n = 8124)	≤2% BSA (n = 4216)	3%-10% BSA (n = 2915)	>10% BSA (n = 993)
Number of new DM cases	1867 (2.44%)	280 (3.44%)	139 (3.30%)	92 (3.16%)	49 (4.93%)
Number of person-years	312,682.34	33,788.32	17,471.24	12,308.72	4008.36
Average length of follow-up, y	4.08	4.16	4.14	4.22	4.04
Incident T2DM rate, per 1000 person-years (95% CI)	5.97 (5.71-6.25)	8.29 (7.37-9.32)	7.96 (6.74-9.40)	7.47 (6.09-9.17)	12.22 (9.24-16.17)

Type 2 diabetes mellitus defined by (1) 2 diagnostic READ codes (2) 1 diagnostic READ code and 1 diabetic drug code, or (3) 1 diagnostic READ code and 1 laboratory value of HbA1c 6.5% or higher or 48 mmol/mol or higher.
BSA, Body surface area; *CI*, confidence interval; *DM*, diabetes mellitus; *HbA1c*, glycosylated hemoglobin; *T2DM*, type 2 diabetes mellitus.

Table III. Hazard of type 2 diabetes mellitus in patients with psoriasis compared with in patients without psoriasis

		Psoriasis, hazard ratio (95% CI)			
Adjustment	n	≤2% BSA	3% to 10% BSA	>10% BSA	*P* value*
Unadjusted	84,723	1.33 (1.12-1.58)	1.25 (1.02-1.54)	2.05 (1.55-2.73)	<.001
Fully adjusted†	75,421	1.21 (1.01-1.44)	1.01 (0.81-1.26)	1.64 (1.23-2.18)	.004

BSA, Body surface area.
**P* value for test for trend conducted by coding psoriasis severity as a linear variable (0, no psoriasis; 1, mild psoriasis; 2, moderate psoriasis; 3, severe psoriasis).
†Fully adjusted model includes age, sex, and body mass index. Type 2 Diabetes Mellitus defined by (1) 2 diagnostic READ codes (2) 1 diagnostic READ code and 1 diabetic drug code, or (3) 1 diagnostic READ code and 1 laboratory value of HbA1c of 6.5% higher or 48 mmol/mol or higher.

for major diabetic risk factors (age, sex, and BMI) routinely collected in clinical practice, were robust across multiple sensitivity analyses, and suggest that psoriasis and its severity are important predictors of diabetes risk. We estimate, on the basis of our data, that patients with psoriasis affecting 10% or more of their BSA have about a 60% higher risk per year for development of T2DM, which translates into an extra 25,000 new cases of diabetes annually worldwide that are attributable to severe psoriasis. We also observed an increased risk for diabetes in patients with 2% or less of their BSA affected by psoriasis, and although this association was smaller and of lower clinical significance, it was still important to note. Interestingly, we did not observe a statistically significantly increased risk in the group with 3% to 10% of their BSA affected. We note that on the basis of the 95% CIs and Kaplan-Meier curves (Fig 2), we cannot exclude that this finding is statistically different from that for the group with 2% or less of their BSA affected by psoriasis, although the risk is evidently lower than that for the group with more than 10% of their BSA affected. Furthermore, we have previously demonstrated a dose-response relationship between BSA and prevalent diabetes,[12] so it is conceivable that our findings with incident T2DM were diluted by prevalent T2DM in patients with varying levels of psoriasis severity. Additionally, the sample size and duration of follow-up may not have been sufficient to detect a prospective association in this subgroup.

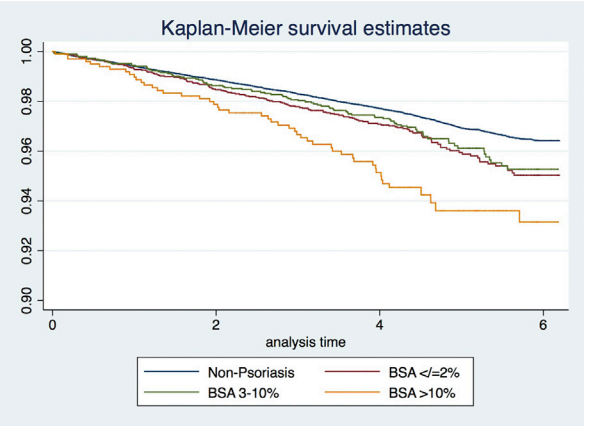

Fig 2. Kaplan-Meier survival estimates of time to T2DM diagnosis for patients in the psoriasis cohort stratified according to body surface area (BSA) as follows: 2% or less (mild), 3% to 10% (moderate), and more than 10% (severe); and matched patients without psoriasis.

Our study advances existing literature by demonstrating that a simple phenotypic objective measure of disease severity has clinical significance beyond the skin in that it predicts risk for development of T2DM. It also builds on our recent work in which we demonstrated that mortality risk among patients with psoriasis followed prospectively for a period of approximately 4 years is restricted to patients with more than 10% of their BSA affected.[10] Current literature uses treatment patterns (ie, systemic therapy) to define severity, which is problematic, as treatment may alter the risk for diabetes (either positively or negatively), and it is well known that psoriasis is widely undertreated.[21] Thus, it is necessary to determine whether the findings generalize to patients with extensive psoriasis who are not receiving systemic agents or phototherapy. Most studies that assessed incidence[4,18,19] did not adjust for confounders, and all used psoriasis treatment as a surrogate marker for psoriasis severity. Moreover, our broadly representative, population-based study design and high GP survey response rate suggest that our findings are likely generalizable to the psoriasis population (ie, that they have strong external validity).

Overall limitations of our study include selection bias and information bias. However, exposed and unexposed matched individuals were randomly drawn from the same population (minimizing selection bias), and data were collected by the same practices within a similar time frame (minimizing information bias). It is possible that patients with severe psoriasis visit their GP more frequently, especially with existing comorbidities, although our findings were robust to observation bias (Supplemental Table 1, line 11). Finally, as with all observational studies, the possibility of unmeasured or unknown confounders exist. However, we tested and accounted for numerous confounders in our primary analyses, and our findings were robust to multiple sensitivity analyses.

CONCLUSION

Our findings demonstrate that psoriasis is a significant risk factor for incident T2DM beyond age, sex, and BMI and that the risk for development of T2DM increases with increasing BSA affected. Clinicians may consider measuring BSA affected by psoriasis as part of the standard of care because it has important prognostic implications. Patients with psoriasis affecting more than 10% of their BSA should be targeted for diabetes prevention efforts.

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Supplemental Table I. Sensitivity analyses using varying definitions of the outcome (1-5), specific exclusion criteria (6-12), and multiple imputation (13-16) from the fully adjusted model

		Psoriasis, hazard ratio (95% CI)		
Characteristic	**n**	**≤2% BSA**	**3%-10% BSA**	**>10% BSA**
Varying definitions of T2DM*				
(1) 2 diagnostic codes	75,421	1.25 (1.05-1.48)	1.02 (0.81-1.27)	1.60 (1.19-2.15)
(2) 1 diagnostic code + 1 diabetic drug code	75,421	1.32 (0.93-1.89)	1.208 (0.79-1.86)	2.21 (1.31-3.70)
(3) 1 diagnostic code + 1 laboratory value	75,421	1.22 (1.00-1.48)	0.99 (0.77-1.27)	1.64 (1.19-2.26)
(4) 1 diagnostic code	75,421	1.18 (1.02-1.37)	0.98 (0.81-1.19)	1.53 (1.18-1.98)
(5) any 1 of the following: diagnostic code, diabetic drug code, or laboratory value	75,421	1.14 (0.98-1.31)	1.06 (0.89-1.26)	1.61 (1.27-2.05)
Excluding patients				
(6) With any history of psoriatic arthritis	74,743	1.22 (1.02-1.47)	0.94 (0.74-1.20)	1.42 (1.00-2.23)
(7) With any history of systemic corticosteroids	68,243	1.22 (1.01-1.48)	0.99 (0.78-1.26)	1.57 (1.15-2.16)
(8) With any history or use during observation period of biologic, systemic, or phototherapy	74,433	1.19 (1.00-1.43)	0.99 (0.79-1.26)	1.42 (0.98-2.04)
(9) Registered within 9 months before index date	73,084	1.20 (1.01-1.44)	1.03 (0.83-1.29)	1.61 (1.20-2.15)
(10) With T2DM diagnosed within 1 year after index date	70,456	1.21 (1.01-1.44)	1.01 (0.81-1.26)	1.64 (1.23-2.18)
(11) With ≤1 GP visit per year, on average	73,595	1.20 (1.01-1.43)	1.01 (0.81-1.26)	1.63 (1.22-2.17)
(12) With any history or use during observation period of biologic or systemic therapies	74,786	1.19 (1.00-1.43)	1.00 (0.79-1.25)	1.47 (1.06-2.04)
BMI missing data handling				
(13) Exclude missing BMI data	75,421	1.21 (1.01-1.44)	1.01 (0.81-1.26)	1.64 (1.23-2.18)
(14) Multiple imputation of missing BMI	84,723	1.21 (1.018-1.44)	1.10 (0.89-1.36)	1.67 (1.26-2.22)
(15) Missing BMI data as separate category	84,723	1.18 (1.00-1.41)	1.08 (0.87-1.33)	1.60 (1.20-2.12)
(16) BMI as a continuous measure (vs categoric)	75,421	1.21 (1.02-1.44)	1.00 (0.80-1.25)	1.65 (1.24-2.20)

Fully adjusted model was adjusted for age, sex, and body mass index.

BMI, Body mass index; *BSA*, body surface area; *CI*, confidence interval; *GP*, general practitioner; *HbA1c*, glycosylated hemoglobin; *T2DM*, type 2 diabetes mellitus.

*Type 2 diabetes mellitus defined by (1) 2 diagnostic READ codes; (2) 1 diagnostic READ code and 1 diabetic drug code; or (3) 1 diagnostic READ code and 1 laboratory value of HbA1c 6.5% or higher or 48 mmol/mol or higher.