Published in final edited form as:
JAMA Dermatol. 2013 October 1; 149(10): 1173–1179. doi:10.1001/jamadermatol.2013.5015.

Psoriasis severity and the prevalence of major medical co-morbidities: a population-based study

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Abstract

Importance—Despite the growing literature on co-morbidity risks in psoriasis, there remains a critical knowledge gap on the degree to which objectively measured psoriasis severity may affect the prevalence of major medical co-morbidities.

Objective—To examine the prevalence of major medical co-morbidities in patients with mild, moderate, and severe psoriasis, classified objectively based on body surface area involvement, compared to patients without psoriasis.

Design—Population-based, cross-sectional study.

Setting—United Kingdom-based electronic medical records.

Participants—9,035 patients aged 25 to 64 years with psoriasis and 90,350 age- and practice-matched patients without psoriasis.

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Author Attribution: Mr. Yeung and Dr. Gelfand have full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design:* Gelfand; *Acquisition of data:* Yeung, Shin, Gelfand; *Analysis and interpretation of data:* Yeung, Takeshita, Mehta, Kimmel, Ogdie, Margolis, Shin, Attor, Troxel, Gelfand; *Drafting of the manuscript:* Yeung; *Critical revision of the manuscript for important intellectual content:* Yeung, Takeshita, Mehta, Kimmel, Ogdie, Margolis, Shin, Attor, Troxel, Gelfand; *Statistical analysis:* Yeung, Takeshita, Margolis, Shin, Troxel, Gelfand; *Obtained funding:* Gelfand; *Administrative, technical, or material support:* Attor, Shin; *Study supervision:* Gelfand.

Role of the Sponsors: The sponsors had no role in the design and conduct of the study; in the collection, analysis, and interpretation of data; or in the preparation, review, or approval of the manuscript.

No other authors have disclosed relevant conflicts of interests.

The abstract was presented at the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) Annual Meeting in Stockholm, Sweden on June 26–27, 2012.

Exposures—Psoriasis diagnosis and severity, based on body surface area involvement, as determined by provider-based questionnaires.

Main Outcomes and Measures—Prevalence of major co-morbidities comprising the Charlson co-morbidity index.

Results—Among patients with psoriasis, 51.8%, 35.8%, and 12.4% respectively had mild, moderate, and severe disease. Mean Charlson co-morbidity index was increasingly higher in patients with mild (0.375 vs. 0.347), moderate (0.398 vs. 0.342), and severe psoriasis (0.450 vs. 0.348) compared to respective controls (each $p < 0.05$). Psoriasis overall was associated with higher prevalence of chronic pulmonary disease (adjusted odds ratio 1.08; 95% CI, 1.02–1.15), diabetes (1.22; 1.11–1.35), diabetes with systemic complications (1.34; 1.11–1.62), mild liver disease (1.41; 1.12–1.76), myocardial infarction (1.34; 1.07–1.69), peptic ulcer disease (1.27; 1.03–1.58), peripheral vascular disease (1.38; 1.07–1.77), renal disease (1.28; 1.11–1.48), and rheumatologic disease (2.04; 1.71–2.42). Trend analysis revealed significant associations between psoriasis severity and each of above co-morbidities (each $p < 0.05$).

Conclusions and Relevance—The burdens of overall medical co-morbidity and of specific co-morbid diseases are greater among psoriasis patients with increasing disease severity. Physicians should be aware of these associations in providing comprehensive care to patients with psoriasis, especially those presenting with more severe disease.

Introduction

Psoriasis is a common T helper type-1 and -17-mediated chronic inflammatory disease, affecting 2–3% of the general population.[1, 2] While traditionally considered a disease limited to the skin and joints, increasing evidence suggests that psoriasis has far-reaching systemic effects.[3–15] Research characterizing co-morbidities risk in patients with psoriasis may advance our understanding of the natural history of psoriasis and improve clinical practice. In particular, the presence of co-morbid diseases may affect psoriasis treatment choice and monitoring, as well as inform the provision of comprehensive care with proper health screening, evaluation, and management.[16, 17]

Multiple observational studies have demonstrated that patients with psoriasis, particularly those receiving systemic treatments or phototherapy, have higher incidences of myocardial infarction, stroke, diabetes, and cardiovascular mortality independent of traditional risk factors for these outcomes.[3–12] Associations with other co-morbidities such as metabolic syndrome, chronic obstructive pulmonary disease, asthma, peptic ulcer disease, liver disease, renal failure, and rheumatoid arthritis, have also emerged.[13–15]

Despite the growing literature on psoriasis co-morbidities, there is a critical knowledge gap on the degree to which psoriasis severity may affect the prevalence of co-morbidities. Previous studies have relied on indirect measures of psoriasis severity, such as treatment utilization pattern, rather than direct and objective measures. Moreover, few epidemiologic investigations have been conducted using a validated co-morbidity index on a wide array of major co-morbidities that may confer prognostic information on mortality risks.[13] Therefore, our objective was to examine the prevalence of major co-morbidities in patients with mild, moderate, and severe psoriasis as assessed by objective measures of body surface area (BSA) involvement, compared to those without psoriasis in a broadly representative patient population.

Methods

Study Design

We conducted a population-based, cross-sectional study in The Health Improvement Network (THIN) to determine the prevalence of medical co-morbidities in psoriasis patients. THIN is an electronic medical records database of patient demographics, diagnostic, referral, and prescribing data from general practices using the In Practice Systems Vision software. The version of THIN used in this study included longitudinal data on 7.5 million registered patients from 415 general practices, with demographics broadly representative of the population in the United Kingdom (UK). Most aspects of medical care in the UK, including specialist care, are coordinated by the general practitioner (GP) and captured in THIN as part of ongoing patient management. Studies have validated the accuracy of THIN data for epidemiologic research and for studying psoriasis in particular.[18, 19] This study was approved by the University of Pennsylvania Institutional Review Board and the Cambridgeshire Research Ethics Committee.

Study Cohort

Eligible case patients in the study cohort were identified from individuals aged 25 to 64 with at least one psoriasis diagnostic Read code within the two years before survey administration using a validated algorithm.[19] At the time of sampling, eligible patients must be registered with one of 228 practices (55% of THIN practices) that were actively responding to questionnaires through THIN's Additional Information Services. Eligible patients with psoriasis were randomly sampled within age categories and questionnaires were mailed to their GPs to verify the presence of psoriasis and assess the extent of disease. Completed questionnaires were collected over the subsequent 12 months.

Patients were defined as having psoriasis if their diagnosis was confirmed in the questionnaire. The questionnaire also determined the severity of psoriasis, namely mild (limited disease with ≤2% BSA affected), moderate (scattered disease with 3–10% BSA) and severe psoriasis (extensive disease with >10% BSA).[2, 20] Face and construct validity of this approach has been demonstrated in previous studies showing that non-dermatologists rated degrees of skin involvement accurately and that patients categorized with higher BSA are more likely to require frequent visits for psoriasis and require systemic therapies or phototherapy for psoriasis.[19, 21, 22] Case patients with missing medical records were excluded. Ten patients with no history of psoriasis diagnostic codes ever (i.e. control patients) were randomly matched to each psoriasis patient based on age category and general practice. Controls must be alive and actively registered with at least one practice visit within 2 years prior to sampling.

Outcomes

Major co-morbid disease burden was evaluated using the Charlson co-morbidity index, a prognostic index designed to predict the risk of mortality attributable to co-morbid diseases by measuring 17 major systemic co-morbidities.[23] Read codes for defining Charlson co-morbidities were translated by the first author from validated ICD-10 coding algorithms by Quan et al.[25] This approach was previously used by Khan et al. to validate that the Charlson index is a strong predictor of 5-year mortality in a UK general practice medical records database analogous to THIN.[24] Our codes were cross-checked with those from Khan et al. to ensure completeness in capturing diagnoses. Under this algorithm, psoriatic arthritis was not included under "rheumatologic disease" of the Charlson index. Co-morbid diseases were identified by the presence of diagnostic Read codes or recordings in the Additional Health Details part of the database. Assessment of co-morbid diseases occurred from the patients' start date (defined as the latest of the Vision software or computerization in the practice and

registration dates of the patient) to the end date (defined as earliest date of transfer out of practice, death, or date of survey sampling). Cardiovascular co-morbidities (cerebrovascular disease, myocardial infarction, and peripheral vascular disease) were aggregated and presented as a combined outcome.

Sample size

With 4,500 mild, 3,000 moderate, and 1,000 severe psoriasis cases and baseline co-morbidity prevalence of 3%, we estimated to have 80% power in detecting increased co-morbidity prevalence odds ratios of 1.29, 1.36, and 1.70 for mild, moderate, and severe psoriasis, respectively, in two-sided tests at a significance level of 0.05.

Statistical analysis

Sample characteristics and Charlson co-morbidity index scores were summarized descriptively. Characteristics of patients with psoriasis and patients without psoriasis were compared using Wilcoxon rank-sum test for continuous variables and either χ^2 or Fisher's exact test for categorical variables, as appropriate. The associations between psoriasis severity and co-morbidities were modeled using conditional logistic regression, with adjustment for age, sex, and years of follow-up. We did not consider interaction terms or nonlinear effects. The Benjamini-Hochberg procedure was used to adjust for multiple comparisons of 17 outcomes, with significance defined as $p < 0.05$ in two-sided tests.

As sensitivity analysis, we excluded patients with psoriatic arthritis to exclude potential confounding from known independent association between psoriatic arthritis and psoriasis severity. We also excluded all patients who, on average, had less than 1 average annual visit to the GP to assess for detection bias. Statistical analyses were conducted with Stata 12.1 (College Station, TX).

Results

Patient Characteristics

Of 10,474 eligible patients with psoriasis codes sampled for survey mailing, 10,026 surveys were returned by their GPs (response rate 95.7%) and confirmed psoriasis diagnoses in 9,056 patients (90.3%). After exclusion of 21 patients with missing medical records, 9,035 (90.1%) patients were included in the analysis. Psoriasis severity was determined in 8,747 patients (96.8%), among which 4,523 (51.8%) had mild psoriasis, 3,122 (35.8%) had moderate psoriasis, and 1,081 (12.4%) had severe psoriasis (Table 1). Comparing to 90,350 matched controls, patients with psoriasis had similar median age and follow up duration, but were more often male. Systemic therapy and/or phototherapy use was recorded prior to disease severity assessment in 137 (3.0%), 278 (8.9%), and 322 (29.8%) patients with mild, moderate, and severe psoriasis, respectively. Psoriatic arthritis was diagnosed in 172 (3.8%), 250 (8.0%), and 180 (16.7%) patients with mild, moderate, and severe psoriasis, respectively.

Co-morbidity Prevalence

Mean Charlson co-morbidity index scores were higher in patients with psoriasis than controls across all categories of psoriasis severity (Table 2; all $p < 0.001$). Trend analysis of Charlson index scores by disease severity (0 = no psoriasis to 3 = severe psoriasis) was also significant (p for trend < 0.001). After adjusting for age, sex, and follow-up duration, patients with mild psoriasis (odds ratio (OR) 1.11, 95% confidence interval (CI) 1.03–1.19), moderate psoriasis (OR 1.15, 95% CI 1.05–1.25), and severe psoriasis (OR 1.35, 95% CI 1.16–1.56) had higher odds of having one or more major co-morbidities compared to patients without psoriasis (p for trend < 0.001).

Prevalence odds ratios of co-morbid diseases comprising the Charlson index were individually analyzed (Table 3). After adjusting for age, sex, and follow-up duration, significant associations were found between psoriasis and the following prevalent co-morbidities: chronic pulmonary disease (odds ratio (OR) 1.08, 95% confidence interval (CI) 1.02–1.15), diabetes (OR 1.22, 95% CI 1.11–1.35), diabetes with systemic complications (OR 1.34, 95% CI 1.11–1.62), mild liver disease (OR 1.41, 95% CI 1.12–1.76), myocardial infarction (OR 1.34, 95% CI 1.07–1.69), peptic ulcer disease (OR 1.27, 95% CI 1.03–1.58), peripheral vascular disease (OR 1.38, 95% CI 1.07–1.77), renal disease (OR 1.28, 95% CI 1.11–1.48), and rheumatologic disease (OR 2.04, 95% CI 1.71–2.42). Significant associations were not observed between psoriasis and prevalence of cancer, metastatic tumor, and congestive heart failure.

Significant positive trends were demonstrated between psoriasis severity and increased co-morbidity prevalence for each of the co-morbidities shown above to have significantly higher prevalence among psoriasis patients overall (each adjusted p for trend < 0.05). For example, strong dose-response relationships were demonstrated with 22% and 32% increases in diabetes, 36% and 87% increases in diabetes with complications, and 39% and 81% increases in aggregated atherosclerotic outcomes among patients with moderate and severe psoriasis as compared to respective controls. There was also a non-significant trend showing modest increases in prevalence of these outcomes in patients with mild psoriasis. There was a trend for association between cerebrovascular disease with psoriasis severity (adjusted p for trend = 0.03), but its association with psoriasis overall was not significant (adjusted p = 0.21).

Sensitivity Analyses

After excluding patients with psoriatic arthritis, point estimates for most co-morbidity associations remained similar, with the notable exception for rheumatologic disease. Its association with psoriasis overall was attenuated (OR 1.29, 95% CI 1.03–1.61) and with psoriasis severity was no longer significant (p for trend = 0.20). After excluding all patients who, on average, had less than 1 average annual visit to the GP, all co-morbidity associations point estimates also remained similar (data not shown).

Discussion

These results provided novel evidence supporting a positive dose-response relationship between objectively measured psoriasis severity and the burden of major co-morbid diseases in a broadly representative patient sample. We demonstrated that psoriasis severity is associated with higher mean Charlson co-morbidity index and higher odds of having at least one major co-morbid disease. Given the prognostic significance of the Charlson co-morbidity index in predicting short-term mortality,[24] the higher disease burden associated with more severe psoriasis may in part explain the excess mortality previously seen in psoriasis patients receiving systemic therapies.[10, 26]

While previous studies have suggested higher prevalence of co-morbidities in patients with psoriasis, most relied on treatment with systemic therapies or phototherapy as a surrogate marker for moderate-to-severe disease.[3–10, 12–14] This approach may not accurately reflect psoriasis severity as patients with severe psoriasis are often under-treated and systemic treatments for psoriasis may themselves either increase or decrease the risk of developing co-morbid conditions.[20, 27–29] Our results confirmed that patients with psoriasis have higher odds of numerous major systemic co-morbidities, with a positive dose-response relationship demonstrated between objectively measured psoriasis severity and prevalence of specific co-morbidities.

Dose-response trends were demonstrated between psoriasis severity and cardiovascular co-morbidities, including myocardial infarction and peripheral vascular disease. Prior studies have also shown that moderate to severe psoriasis, estimated from treatment pattern and/or affected body sites as proxy measures, is an independent risk factor for cardiovascular disease.[3, 6, 13] Shared inflammatory pathways between psoriasis and atherosclerosis, including the activation of inflammatory cells and the expression of pro-inflammatory cytokines, may link psoriasis with cardiovascular disease.[30–33] Indeed, an experimental mouse model of psoriasis has shown that sustained cutaneous inflammation is sufficient for promoting vascular inflammation and thrombosis.[33] Of note, the association between cerebrovascular disease and psoriasis overall was not statistically significant despite the presence of a significant trend with severity. This lack of association is found in one population-based study,[13] but contrasts with others showing that psoriasis patients had higher stroke incidence, independent of traditional risk factors.[4, 5] Given the limited number of cases detected in our relatively young patient samples, the lack of association with cerebrovascular disease may be attributable to inadequate statistical power.

Strong dose-response relationships were seen between psoriasis severity and prevalent diabetes. In particular, a novel association with diabetes-associated systemic complications – including nephropathy, retinopathy, neuropathy, and vasculopathy – was revealed. Higher risk of diabetes has been shown in patients with psoriasis, particularly those receiving systemic treatments, independent of obesity and other risk factors.[7, 12] Independent associations between objectively measured psoriasis severity and metabolic syndrome components, including hyperglycemia, were also demonstrated.[15] Diabetes, insulin resistance, and obesity have been linked to psoriatic inflammation through common cytokines and adipokines mediators.[31] Overlapping disease susceptibility loci between psoriasis and both type 1 (IFIH1 and TYK2) and type 2 diabetes (CDKAL1) have been identified and lend additional biologic plausibility.[32] Given the higher burden of prevalent diabetes among patients with psoriasis, the newly identified association between psoriasis severity and risk of chronic diabetic complications warrant confirmation in future studies.

Psoriasis severity was also associated with mild liver disease, a category including chronic hepatitis, alcoholic liver disease and non-alcoholic fatty liver disease. Studies have previously linked psoriasis with increased risks non-alcoholic fatty liver disease independent of alcohol intake, obesity, and hepatotoxic medications,[34, 35] but yielded inconsistent results with chronic hepatitis B and C risks.[13, 36–38] Subclinical hepatic inflammation noted on advanced imaging studies in patients with psoriasis also provided potential mechanisms for liver dysfunction.[30] Our data did not reveal any association with moderate to severe liver disease, such as cirrhosis and liver failure, but the small number of detected cases precluded our ability to reach firm conclusions.

We also detected higher prevalence of renal disease related to psoriasis severity. Psoriasis has been associated with microalbuminuria, a sign of subclinical glomerular dysfunction and a marker of cardiovascular risk, independent of risk factors such as hypertension and diabetes.[39–43] While higher mortality attributed to renal disease was demonstrated among patients with psoriasis, mixed results have been shown regarding the prevalence of renal failure in psoriasis.[10, 13, 44] Potential confounding factors, such as hypertension, diabetes, and the use of nephrotoxic psoriasis treatments, should to be scrutinized to assess whether psoriasis is independently associated with the development of chronic kidney disease.

Our data also provide further evidence to support previous associations between psoriasis and chronic obstructive pulmonary disease,[45, 46] peptic ulcer disease,[13] and autoimmune rheumatologic diseases beyond psoriatic arthritis.[47] Future studies need to examine these associations with psoriasis severity after adjustment for disease-specific risk factors.

This study should be reviewed in light of its strengths and limitations. The major strength of this study lies in its population-based methods with very high survey response rate for assessing psoriasis severity, thus minimizing selection bias and enhancing generalizability of the findings. Misclassification of psoriasis severity by GPs can be a potential source of error; however, we have previously demonstrated that untrained psoriasis patients can reliably classify psoriasis severity using a similar approach.[22] While patients with severe disease that is well controlled by systemic therapy and/or phototherapy may be classified as having mild disease based on our methods, only a small portion (3.0%) of patients with ≤2% BSA had a history of such treatment use. Moreover, such misclassification would likely bias our dose-response results toward the null. GPs may have determined psoriasis severity at any time up to 12 months after survey mailing, thus our cross-sectional design precluded the establishment of temporal relationships between psoriasis severity and co-morbidities. Detection bias cannot be excluded but is unlikely to account for our results, since our hypotheses were unknown to GPs who routinely cared for psoriasis and control patients and our study findings were robust to the exclusion of patients with low levels of GP follow-up care. The lack of association found between psoriasis and prevalent internal malignancy may also argue against the presence of detection bias. Our study may be underpowered in detecting associations with co-morbidities for which the overall prevalence in our sample is low. Lastly, we did not evaluate the degree to which these associations are due primarily to psoriasis or confounding factors such as smoking, obesity, or treatment. Therefore, our results should be considered hypothesis-generating and require confirmation in prospective studies.

In conclusion, our study demonstrated increases in major co-morbid disease burden in psoriasis patients according to objectively measured disease severity, which may have implications in the excess mortality risks from severe psoriasis. Moreover, dose-response relationships between psoriasis severity and prevalence of cardiovascular disease and diabetes were demonstrated and confirmed previous epidemiologic findings. Several less well-characterized co-morbid associations were also recognized and might warrant further research. Physicians should be aware of these co-morbid disease associations to provide comprehensive medical care to patients with psoriasis, especially those presenting with more severe disease.

Acknowledgments

Funding / Support: This study was supported by the NIH T32-AR07465 training grant (HY, DBS), NIH T32-GM075766-6 training grant and National Psoriasis Foundation Fellowship (JT), American College of Rheumatology Investigator Award (AO), and NIH R01-HL089744 grant (JMG).

Financial Disclosures:

1. **Relevant to this manuscript:** Dr. Gelfand has served as a consultant for Abbott, Amgen, Celgene, Centocor, Merck, Novartis, and Pfizer; had grants from Abbott, Amgen, Genentech, Novartis, and Pfizer; and received payment for continuing medical education work related to psoriasis. No other authors have disclosed relevant conflicts of interests.
2. **All other relationships:** Dr. Kimmel has served as a consultant for Centocor, Merck, Novartis, and Pfizer, all unrelated to the subject of this manuscript.

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Table 1

Demographic characteristics.

N (%)	Psoriasis (N = 9,035)	Controls (N = 90,350)	*P* value
Psoriasis extent			
Mild (≤ 2% BSA)	4,523 (51.8)	N/A	
Moderate (3–10% BSA)	3,122 (35.8)	N/A	
Severe (> 10% BSA)	1,081 (12.4)	N/A	
Age, median (IQR), y	46 (37–55)	46 (36–55)	0.66
Age group, y			
25–34	1,838 (20.3)	18,375 (20.3)	0.29
35–44	2,316 (25.6)	23,162 (25.6)	
45–54	2,514 (27.8)	25,849 (28.6)	
55–64	2,367 (26.2)	22,964 (25.4)	
Sex			
Male	4,569 (50.6)	42,548 (47.1)	< 0.001
Female	4,466 (49.4)	47,802 (52.9)	
Follow-up duration, median (IQR), y	10.7 (4.7–16.2)	10.7 (4.7–16.2)	0.98
Psoriatic arthritis diagnosis	630 (7.0)	4 (0.0)	< 0.001

IQR, interquartile range; BSA, body surface area

Table 2

Charlson Co-morbidity Index by psoriasis extent.

	Any Psoriasis			By Psoriasis Extent								
CCI, N (%)	**Cases**	**Controls**	***P* value**	**Mild**	**Controls**	***P* value**	**Moderate**	**Controls**	***P* value**	**Severe**	**Controls**	***P* value**
0	6,679 (73.9)	69,066 (76.4)	<0.001[a]	3,376 (74.6)	34,596 (76.5)	0.02[a]	2,316 (74.2)	23,911 (76.6)	0.001[a]	773 (71.5)	8,274 (76.5)	<0.001[a]
1	1,658 (18.4)	15,195 (16.8)		821 (18.2)	7,639 (16.9)		570 (18.3)	5,279 (16.9)		215 (19.9)	1,796 (16.6)	
2	363 (4.0)	3,628 (4.0)		177 (3.9)	1,753 (3.9)		122 (3.9)	1,244 (4.0)		44 (4.1)	445 (4.1)	
3	218 (2.4)	1,582 (1.8)		104 (2.3)	805 (1.8)		74 (2.4)	506 (1.6)		29 (2.7)	194 (1.8)	
4+	117 (1.3)	879 (1.0)		45 (1.0)	437 (1.0)		40 (1.3)	280 (0.9)		20 (1.9)	101 (0.9)	
Mean (SD)	0.399 (0.855)	0.349 (0.787)	<0.001[b]	0.375 (0.796)	0.347 (0.784)	0.02[b]	0.398 (0.876)	0.342 (0.772)	<0.001[b]	0.450 (0.918)	0.348 (0.786)	<0.001[b]

CCI, Charlson Co-morbidity Index; SD, standard deviation

[a]Chi-square test

[b]*t*-test

Table 3

Association between psoriasis severity and prevalent co-morbidities[a]

Co-morbidities	Psoriasis, N (%)	Controls, N (%)	Psoriasis OR (95% CI)	Adjusted *P*[b]	Mild OR (95% CI)	Moderate OR (95% CI)	Severe OR (95% CI)	Adjusted *P* /for trend[b,c]
Cancer	142 (1.6)	1719 (1.9)	0.85 (0.71–1.02)	0.11	0.91 (0.72–1.16)	0.83 (0.61–1.14)	0.66 (0.38–1.15)	0.06
Cerebrovascular disease	98 (1.1)	844 (0.9)	1.17 (0.94–1.45)	0.21	0.98 (0.71–1.35)	1.14 (0.80–1.64)	2.50 (1.46–4.26)	0.03
Chronic pulmonary disease	1,368 (15.1)	12,877 (14.3)	1.08 (1.02–1.15)	0.02	1.08 (0.99–1.18)	1.06 (0.95–1.18)	1.18 (0.98–1.40)	0.03
Congestive heart failure	34 (0.4)	303 (0.3)	1.08 (0.75–1.56)	0.71	0.93 (0.54–1.61)	0.77 (0.37–1.59)	2.98 (1.37–6.49)	0.30
Dementia	7 (0.1)	47 (0.1)	1.32 (0.57–3.04)	0.59	2.18 (0.77–6.11)	0.76 (0.17–3.41)	N/A	0.78
Diabetes	476 (5.3)	3,844 (4.3)	1.22 (1.11–1.35)	<0.001	1.14 (0.99–1.32)	1.22 (1.03–1.46)	1.32 (1.00–1.74)	0.004
Diabetes with complications	130 (1.4)	944 (1.0)	1.34 (1.11–1.62)	0.006	1.17 (0.89–1.54)	1.36 (0.97–1.89)	1.87 (1.16–2.99)	0.003
Hemiplegia	7 (0.1)	100 (0.1)	0.70 (0.32–1.50)	0.44	0.70 (0.25–1.93)	0.65 (0.15–2.76)	1.06 (0.13–8.43)	0.53
Metastatic tumor	5 (0.1)	66 (0.1)	0.81 (0.32–2.08)	0.67	0.65 (0.15–2.77)	1.27 (0.35–4.52)	N/A	0.78
Mild liver disease	88 (1.0)	616 (0.7)	1.41 (1.12–1.76)	0.008	1.29 (0.93–1.79)	1.46 (0.97–2.18)	1.69 (0.96–2.97)	0.007
Moderate to severe liver disease	4 (0.0)	43 (0.1)	0.91 (0.33–2.55)	0.81	0.87 (0.21–3.72)	0.64 (0.08–4.84)	N/A	0.50
Myocardial infarction	95 (1.1)	693 (0.77)	1.34 (1.07–1.69)	0.03	1.39 (1.01–1.91)	1.39 (0.93–2.07)	1.28 (0.68–2.44)	0.03
Peptic ulcer disease	98 (1.1)	771 (0.9)	1.27 (1.03–1.58)	0.04	1.18 (0.85–1.63)	1.54 (1.11–2.12)	1.08 (0.54–2.17)	0.03
Peripheral vascular disease	75 (0.8)	554 (0.6)	1.38 (1.07–1.77)	0.02	1.05 (0.71–1.55)	1.92 (1.29–2.85)	1.85 (0.95–3.61)	0.003
Renal disease	251 (2.8)	2,026 (2.2)	1.28 (1.11–1.48)	0.005	0.97 (0.77–1.21)	1.41 (1.11–1.79)	1.83 (1.26–2.68)	<0.001
Rheumatologic disease	161 (1.8)	845 (0.9)	2.04 (1.71–2.42)	<0.001	2.01 (1.56–2.58)	1.85 (1.36–2.50)	2.89 (1.84–4.53)	<0.001
Atherosclerotic outcomes[d]	250 (2.8)	1,961 (2.2)	1.28 (1.11–1.47)	0.004	1.14 (0.93–1.39)	1.39 (1.11–1.76)	1.81 (1.25–2.63)	<0.001

OR, odds ratio; CI, confidence interval; N/A, not applicable due to small numbers of detected cases.

[a]Models are conditioned on matching criteria and adjusted for age, sex, and years of follow-up. Acquired immune deficiency syndrome was not modeled due to the low detected prevalence.

[b]*P* values corrected for multiple comparisons using the Benjamini-Hochberg procedure.

[c]Trend analysis was conducted by coding psoriasis severity as a linear variable (0 = no psoriasis, 1 = mild, 2 = moderate, 3 = severe).

[d]Atherosclerotic outcomes were aggregated from cerebrovascular disease, myocardial infarction, and peripheral vascular disease.