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Rates of Cancers and Opportunistic Infections in Patients With Psoriatic Arthritis Compared With Patients Without Psoriatic Arthritis

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Objectives: This study aimed to estimate rates of cancer or opportunistic infection in patients with psoriatic arthritis (PsA) compared with patients without PsA.

Methods: Using the Clinical Practice Research Datalink, we conducted a cohort study of patients with a PsA diagnosis and patients without such diagnosis, matched on age, sex, general practice, and calendar time, to assess the incidence of cancers (solid, hematologic, and nonmelanoma skin cancer) and opportunistic infections. We estimated incidence rates (IRs) and IR ratios (IRRs) with 95% confidence intervals (CIs) for each outcome and stratified results in the PsA cohort by receipt of systemic PsA drugs.

Results: The rate of hematologic cancer was slightly higher in the PsA cohort compared with the non-PsA cohort (IRR, 1.52; 95% CI, 1.10–2.10), whereas the rates of solid cancer and of nonmelanoma skin cancer were similar between the PsA and non-PsA cohorts (IRR, 1.01; 95% CI, 0.90–1.13; and IRR, 0.97; 95% CI, 0.82–1.14, respectively). Incidence rates were higher for PsA patients who received prescriptions for PsA drugs compared with those who did not. The IRs for infection were higher in the PsA compared with the non-PsA cohort (IRR, 1.39; 95% CI, 1.31–1.47) and were significantly higher in patients who received prescriptions (IRR, 1.71; 95% CI, 1.52–1.91).

Conclusions: The rates of solid and nonmelanoma skin cancers were similar in patients with PsA compared with patients without PsA, but the rates of hematologic cancer and opportunistic infections were higher in patients with PsA. In patients with PsA, rates of all outcomes were higher among those who received prescriptions for systemic PsA therapy.

Key Words: cancer, malignancy, opportunistic infection, psoriatic arthritis
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Increased risks for malignancy and infections in patients with rheumatoid arthritis and psoriasis have been reported extensively in the literature. However, less is known regarding the frequency of malignancies or infections in patients with psoriatic arthritis (PsA).

There are a limited number of published studies that report rates of malignancy in patients with PsA to date. These studies report similar rates of cancer in patients with PsA compared with the

general population¹ or compared with patients with rheumatoid arthritis.^{2,3} One study reported that the risk of lymphoma in patients with PsA who used anti-tumor necrosis factor (anti-TNF) drugs was not elevated in comparison with patients with rheumatoid arthritis, but not much is known about the risk of cancer with the use of other PsA treatments.²

The rate of opportunistic infections in the PsA population is unknown, but several published studies have estimated the rate of infections in patients with psoriasis or rheumatoid arthritis. A recent analysis of a US health care database reported serious hospital infection rates in patients with psoriasis ranging from 165/10,000 person-years (PYs) for patients receiving phototherapy to 262/10,000 PYs for patients receiving anti-TNF.⁴ A biological therapy registry in France reported 45 events of opportunistic infection among 43 patients receiving anti-TNF for several indications, including PsA,⁵ of which, 40% of the infections were viral, 33% were bacterial, 22% were fungal, and 4% were parasitic. Ten patients (23%) were admitted to intensive care units, and 4 patients (9%) died. A retrospective analysis of treated patients with rheumatoid arthritis and spondyloarthritis (which included PsA) at one medical center in Rome found a high proportion of infection (52%) with incidence rates (IRs) of 36.3/100 PYs, which varied depending on the treatment received, from 12.4/100 person-years for patients receiving disease-modifying antirheumatic drugs (DMARDs) to 62.7/100 PYs for patients receiving anti-TNF, with a mean incidence of 36.3/100 PYs.⁶

The objective of this study was to estimate the rate of solid, hematologic, and nonmelanoma skin cancers and of opportunistic infections among patients with PsA compared with matched patients without PsA or psoriasis using the UK Clinical Practice Research Datalink (CPRD). For patients with PsA, we also estimated rates of these diseases by type of systemic PsA drugs received.

METHODS

Data Source

The UK CPRD is a large, longitudinal, population-based electronic medical record database that contains data on approximately 10 million people. The UK National Health Service provides universal coverage; therefore, the database contains a representative sample of the UK general population.⁷ Participating general practitioners (GPs) contribute data in an anonymous format including medical diagnoses, physical findings, symptoms, details of hospital stays and specialist visits, and deaths. Several validation studies have been published on the accuracy of information recorded in the CPRD,^{8–10} which indicate that the data are of high accuracy with regard to recorded clinical diagnoses with more than 90% of information from the manual medical records present in the GP's office recorded on the computer.

Study Design and Cohort Identification

This cohort study was conducted using the CPRD data from January 1, 1988, through December 31, 2012. The PsA cohort

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included all patients in the CPRD with a diagnosis of PsA who had at least 1 year of medical information in their record before the first PsA diagnosis code. One year of history was required to ensure that we identified patients with new diagnoses of PsA that were not diagnosed before the start of the patient record. The cohort entry date was the date of the first recorded PsA diagnosis. For each PsA patient, we identified up to 10 patients with no recorded diagnoses of psoriasis or PsA (henceforth referred to as the non-PsA cohort) matched on age, sex, and general practice attended. All patients without PsA were required to be present in the database on the cohort entry date of their matched patient with PsA, and the cohort entry date of each patient with PsA was assigned to the matched patient without PsA.

Separate subcohorts were identified for each outcome of interest (ie, solid and hematologic cancer, nonmelanoma skin cancer, and opportunistic infections). For solid and hematologic cancers, any patient who had a diagnosis of a solid or hematologic cancer before the cohort entry date was excluded from that subcohort. We did not exclude any patients from the nonmelanoma skin cancer subcohort or patients from the opportunistic infection subcohort because previous diagnoses were not thought to influence development of these outcomes at a later date. In each subcohort, patient follow-up began at the cohort entry date and continued until the end of the study period, end of registration with the practice, death, or until they developed the outcome of interest. The accumulated time was expressed as PYs either exposed to PsA or not exposed.

Case Identification

Diagnoses of interest were identified using automated searches of the electronic records of all patients in each subcohort. For each outcome included in the study, we reviewed samples of electronic medical records to review the accuracy of our case selection process. A patient was identified as a case if he or she had a diagnosis of the outcome of interest (solid, hematologic, nonmelanoma skin cancer or opportunistic infection) recorded after the cohort entry date. If a patient had more than one diagnosis of the outcome of interest under study, we included the first to occur. Opportunistic infections under evaluation were pneumocystis pneumonia, cryptosporidiosis, tuberculosis, diseases caused by mycobacteria, bartonellosis, leukoencephalopathy, candidiasis, cryptococcus, other mycoses, cytomegaloviral disease, herpes simplex, herpes zoster, human papilloma virus, viral hepatitis, Epstein-Barr virus, histoplasmosis, or toxoplasmosis.

Stratification by Receipt of PsA Systemic Therapy

Among those with PsA, we further evaluated the effects of having treated versus untreated PsA. For each patient in the PsA cohort, we accumulated person time on any PsA systemic therapy and for nonexposed time. Systemic therapies included DMARDs/biologics (eg, methotrexate, sulfasalazine, and adalimumab), immunosuppressants (eg, azathioprine and leflunomide), and corticosteroids (codes are available upon request). For the analysis of the cancer outcome, person time of exposure to PsA therapy was accrued from the date of the first prescription through the end of follow-up or until the date of the cancer diagnosis minus 1 year (the induction period) for cancer cases. People who received only 1 prescription were considered unexposed. We conducted a sensitivity analysis to assess the appropriateness of this induction period definition by expanding the induction period to 2 years before the cancer diagnosis date. Analyses were further stratified by type of PsA therapy prescribed. A patient could be exposed to more than 1 type of therapy.

For the analysis of the opportunistic infection outcome, person time of exposure to these drugs was accrued starting at the

date of the prescription for a PsA therapy through the end of the supply (based on the amount prescribed divided by the number of times per day) plus 30 days. Time during follow-up was treated as not exposed to systemic therapy when no drug prescriptions were issued. To assess the appropriateness of this exposure time window definition, we conducted sensitivity analyses where the period after the end of supply was extended to 90 days. Analyses were further stratified by type of PsA therapy prescribed. A patient contributed person time to 1 type of therapy until the end of supply plus 30 days for each therapy separately, and a patient could be exposed to more than 1 type of therapy at a time.

Statistical Analysis

Within each subcohort, we estimated IRs per 1000 PYs and IR ratios (IRRs) with 95% confidence intervals (CIs) for PsA compared with non-PsA cohorts and stratified by sex and age (<30, 30–49, 50–69, ≥70 years). We estimated the risk (cumulative hazard function) of each study outcome using the Kaplan-Meier method and tested the differences using log rank test. We stratified the rates of nonmelanoma skin cancer by whether patients had a previous nonmelanoma skin cancer diagnosis and, separately, if they had a diagnosis of solid or hematologic tumor before cohort entry. In the PsA cohort, the results were stratified by receipt or nonreceipt of prescriptions for systemic PsA therapy and by the type of drug prescribed. Statistical analyses were performed using SAS release 9.2 (SAS Institute Inc, Cary NC).

The protocol for this study was reviewed and approved by the Independent Scientific Advisory Committee of the CPRD.

RESULTS

Solid and Hematologic Cancers

We identified 8493 patients with PsA and 82,601 patients without PsA in the solid and hematologic cancer subcohorts after exclusions. These two cohorts are composed of the same individuals because in both we excluded any person with a diagnosis of solid or hematologic cancer before cohort entry. Their characteristics are presented in Table 1.

The rate of incident solid cancer was similar between the PsA cohort and the non-PsA cohort (5.4/1000 PYs [95% CI, 4.8–6.0] vs 5.3/1000 PYs [95% CI, 5.2–5.5]; IRR, 1.01 [95% CI, 0.90–1.13]) (Table 2). Rates were lowest for the youngest age group (<30) and increased with increasing age in both PsA and non-PsA cohorts. The analysis of cumulative hazards demonstrated that there was no statistically significant difference between the PsA and non-PsA cohorts in the solid cancer analysis ($P > 0.9$) (Fig. 1).

The rate of incident hematologic cancer was slightly higher in the PsA cohort compared with the non-PsA cohort (0.7/1000 PYs [95% CI, 0.5–0.9] vs 0.4/1000 PYs [95% CI, 0.4–0.5]; IRR, 1.52 [95% CI, 1.10–2.10]) (Table 2). Rates were lowest for the youngest age group (<30) and increased with increasing age in both PsA and non-PsA cohorts. The difference in risk/hazard was very small but significant in the hematologic cancer analysis of cumulative hazards ($P = 0.011$) (Fig. 2).

In the PsA cohort, rates of incident solid cancer were higher in patients who received prescriptions for PsA drugs compared with those who did not (IRs, 8.4/1000 PYs [95% CI, 6.9–10.1] and 4.7/1000 PYs [95% CI, 4.1–5.3], respectively; IRR, 1.80 [95% CI, 1.44–2.27]) (Table 3). Similarly, rates of incident hematologic cancer were higher in patients with PsA who received prescriptions for PsA drugs compared with those who did not (IRs, 1.6 [95% CI, 0.9–2.4] and 0.4 [95% CI, 0.3–0.7], respectively; IRR, 3.50 [95% CI, 1.92–6.36]) (Table 3). For both solid and

TABLE 1. Distribution of Characteristics of Patients With and Without PsA: Cancer Subcohorts

	Solid and Hematologic Cancer Cohorts ^a		Nonmelanoma Skin Cancer Cohort	
	PsA n = 8493 (%)	No PsA n = 82,601 (%)	PsA n = 8677 (%)	No PsA n = 86,413 (%)
Age (years)				
Mean (SD)	47.11 (14.49)	46.76 (14.35)	47.40 (14.61)	47.35 (14.56)
<10	16 (0.19)	160 (0.19)	17 (0.20)	170 (0.20)
10–19	142 (1.67)	1413 (1.71)	143 (1.65)	1426 (1.65)
20–29	775 (9.13)	7712 (9.34)	779 (8.98)	7773 (9.00)
30–39	1812 (21.34)	17,972 (21.76)	1821 (20.99)	18,165 (21.02)
40–49	2065 (24.31)	20,341 (24.63)	2081 (23.98)	20,782 (24.05)
50–59	1959 (23.07)	18,964 (22.96)	2015 (23.22)	20,078 (23.23)
60–69	1140 (13.42)	10,759 (13.03)	1184 (13.65)	11,759 (13.61)
70–79	473 (5.57)	4331 (5.24)	512 (5.90)	5082 (5.88)
80+	111 (1.31)	949 (1.14)	125 (1.44)	1178 (1.36)
Sex				
Female	4245 (49.98)	41,035 (49.68)	4352 (50.16)	43,373 (50.19)
Male	4248 (50.02)	41,566 (50.32)	4325 (49.84)	43,040 (49.81)
Smoking status				
Current	1769 (20.83)	17,407 (21.07)	1806 (20.81)	18,072 (20.91)
Former	1655 (19.49)	12,307 (14.90)	1717 (19.79)	13,227 (15.31)
Never	3339 (39.31)	34,312 (41.54)	3403 (39.22)	35,979 (41.64)
Unknown	1730 (20.37)	18,575 (22.49)	1751 (20.18)	19,135 (22.14)
Body mass index				
<18.5	92 (1.08)	1250 (1.51)	94 (1.08)	1311 (1.52)
18.5–24.99	2377 (27.99)	28,713 (34.76)	2431 (28.02)	30,014 (34.73)
25.0–29.99	2762 (32.52)	24,996 (30.26)	2819 (32.49)	26,236 (30.36)
≥30	2331 (27.45)	14,805 (17.92)	2384 (27.47)	15,574 (18.02)
Unknown	931 (10.96)	12,837 (15.54)	949 (10.94)	13,278 (15.37)
Year of cohort entry				
1988–1994	1336 (15.73)	13,039 (15.79)	1360 (15.67)	13,486 (15.61)
1995–1999	1618 (19.05)	15,772 (19.09)	1642 (18.92)	16,345 (18.91)
2000–2004	2310 (27.20)	22,489 (27.23)	2355 (27.14)	23,481 (27.17)
2005–2009	2347 (27.63)	22,783 (27.58)	2407 (27.74)	24,011 (27.79)
2010–2012	882 (10.39)	8518 (10.31)	913 (10.52)	9090 (10.52)
Length of medical history before cohort entry, y				
Mean (SD)	7.04 (5.86)	7.44 (5.66)	7.04 (5.86)	7.44 (5.66)
Length of medical history after cohort entry, y				
Mean (SD)	7.64 (5.72)	7.25 (5.64)	7.60 (5.71)	7.20 (5.61)
Died				
Yes	584 (6.88)	5124 (6.20)	630 (7.26)	5797 (6.71)
No	7909 (93.12)	77,477 (93.80)	8047 (92.74)	80,616 (93.29)

^aThe same exclusion criteria were applied to the solid and hematologic cohorts; thus, the same individuals were included in these cohorts.

hematologic cancer, patients who were prescribed DMARDs/biologics had the lowest rates of these cancers. The results did not differ when we expanded the induction period to 2 years before the cancer diagnosis in the sensitivity analyses.

Nonmelanoma Skin Cancer

We identified 8677 patients with PsA and 86,413 patients without PsA in the nonmelanoma skin cancer subcohort. Their characteristics are presented in Table 1. The rate of nonmelanoma skin cancer was similar between the PsA cohort and non-PsA cohort ([2.5/1000 PYs [95% CI, 2.1–2.9] vs 2.5/1000 PYs [95% CI,

2.4–2.7]; IRR, 0.97 [95% CI, 0.82–1.14]) (Table 2). Rates were lowest for the youngest age group (<30) and increased with increasing age in both PsA and non-PsA cohorts. Rates of nonmelanoma skin cancer were highest among patients with a history of solid or hematologic cancer or a history of previous nonmelanoma skin cancer; however, these rates were not significantly different between the PsA and non-PsA cohorts. The analysis of cumulative hazards demonstrated that there was no statistically significant difference between the PsA and non-PsA cohorts in the nonmelanoma skin cancer analysis ($P = 0.61$) (Fig. 3).

In the PsA cohort, rates of nonmelanoma skin cancer were higher in patients who received prescriptions for PsA drugs

TABLE 2. Incident Rates of Cancers in Patients With and Without PsA

	PsA Cohort			Non-PsA Cohort		
	Cases	PY	IR/1000 PYs (95% CI)	Cases	PY	IR/1000 PYs (95% CI)
Solid cancer						
All	344	63,698	5.4 (4.8–6.0)	3139	587,863	5.3 (5.2–5.5)
Female	191	31,625	6.0 (5.2–7.0)	1616	295,461	5.5 (5.2–5.7)
Male	153	32,073	4.8 (4.0–5.6)	1523	295,402	5.2 (5.0–5.5)
Age < 30 y	6	6589	0.9 (0.3–2.0)	31	60,715	0.5 (0.3–0.7)
Age, 30–49 y	74	29,956	2.5 (1.9–3.1)	659	276,194	2.4 (2.2–2.6)
Age, 50–69 y	206	23,733	8.7 (7.5–9.9)	1939	219,751	8.8 (8.4–9.2)
Age, 70+ y	58	3421	17.0 (12.9–21.9)	510	31,203	16.3 (15.0–17.8)
Hematologic cancer						
All	43	64,683	0.7 (0.5–0.9)	261	597,608	0.4 (0.4–0.5)
Female	17	32,200	0.5 (0.3–0.8)	107	301,140	0.4 (0.3–0.4)
Male	26	32,483	0.8 (0.5–1.2)	154	296,468	0.5 (0.4–0.6)
Age < 30 y	2	6594	0.3 (0.0–1.1)	6	60,812	0.1 (0.0–0.2)
Age, 30–49 y	10	30,238	0.3 (0.2–0.6)	63	278,628	0.2 (0.2–0.3)
Age, 50–69 y	26	24,307	1.1 (0.7–1.6)	146	225,830	0.6 (0.5–0.8)
Age, 70+ y	5	3544	1.4 (0.5–3.3)	46	32,338	1.4 (1.0–1.9)
Nonmelanoma skin cancer						
All	160	65,135	2.5 (2.1–2.9)	1561	613,936	2.5 (2.4–2.7)
Female	88	32,481	2.7 (2.2–3.3)	743	312,718	2.4 (2.2–2.6)
Male	72	32,654	2.2 (1.7–2.8)	818	301,218	2.7 (2.5–2.9)
Age < 30 y	1	6628	0.2 (0.0–0.8)	16	61,247	0.3 (0.1–0.4)
Age, 30–49 y	32	30,314	1.1 (0.7–1.5)	276	281,898	1.0 (0.9–1.1)
Age, 50–69 y	94	24,489	3.8 (3.1–4.7)	933	235,029	4.0 (3.7–4.2)
Age, 70+ y	33	3704	8.9 (6.1–12.5)	336	35,762	9.4 (8.4–10.5)
History of solid or hematologic cancer						
Yes	16	1144	14.0 (8.0–22.7)	177	12,706	13.9 (12.0–16.1)
No	144	63,991	2.3 (1.9–2.6)	1384	601,230	2.3 (2.2–2.4)
History of nonmelanoma skin cancer						
Yes	15	384	39.1 (21.9–64.5)	162	4841	33.5 (28.5–39.0)
No	145	64,751	2.2 (1.9–2.6)	1399	609,096	2.3 (2.2–2.4)

compared with those who did not (IRs, 4.6/1000 PYs [95% CI, 3.5–6.0] and 1.9/1000 PYs [95% CI, 1.6–2.3], respectively; IRR, 2.42 [95% CI, 1.76–3.34]) (Table 3). Rates were highest among those treated with corticosteroids (8.0/1000 PYs [95% CI, 0.9–29.0]) and similar among patients who were prescribed DMARDs/biologics or immunosuppressants (4.9/1000 PYs [95% CI, 3.7–6.3] and 5.0/1000 PYs [95% CI,

1.6–11.7]). The results did not differ when we expanded the induction period to 2 years before the cancer diagnosis in the sensitivity analyses.

Opportunistic Infections

We identified 8677 patients with PsA and 86,413 patients without PsA in the opportunistic infection subcohort. Their

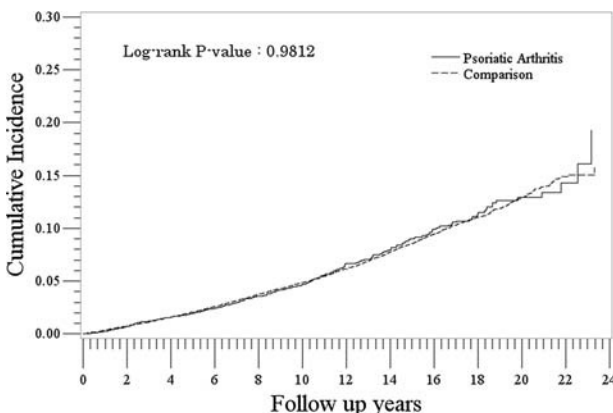


FIGURE 1. Cumulative incidence of solid cancer in the PsA and comparison cohorts.

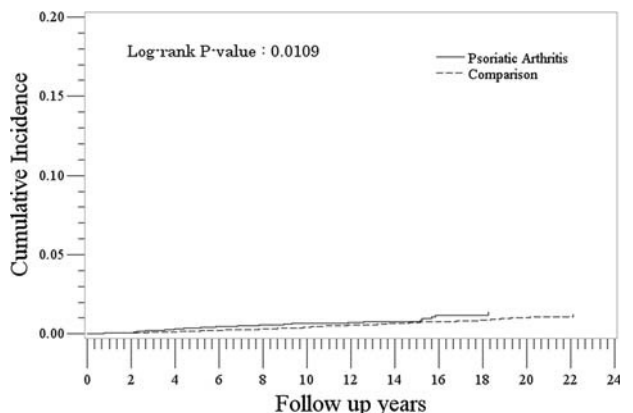


FIGURE 2. Cumulative incidence of hematologic cancer in the PsA and comparison cohorts.

TABLE 3. Rates of Solid, Hematologic, and Nonmelanoma Skin Cancer in Patients With PsA, Stratified by Receipt of PsA Drug Prescriptions

	Cancer Cases ^a	PY	IR/1000 PYs (95% CI)	IRR (95% CI)
Solid cancer				
PsA treatment ^b				
No PsA drug Rx	237	50,967	4.7 (4.1–5.3)	1.00 (reference)
PsA drug Rx	107	12,754	8.4 (6.9–10.1)	1.80 (1.44–2.27)
DMARDs/biologics	101	11,799	8.6 (7.0–10.4)	1.84 (1.46–2.32)
Immunosuppressant	9	973	9.2 (4.2–17.6)	1.99 (1.02–3.87)
Corticosteroid	4	233	17.2 (4.6–43.9)	3.69 (1.37–9.91)
Hematologic cancer				
PsA treatment ^b				
No PsA drug Rx	23	51,816	0.4 (0.3–0.7)	1.00 (reference)
PsA drug Rx	20	12,890	1.6 (0.9–2.4)	3.50 (1.92–6.36)
DMARDs/biologics	19	11,910	1.6 (1.0–2.5)	3.59 (1.96–6.60)
Immunosuppressant	3	995	3.0 (0.6–8.8)	6.79 (2.04–22.62)
Corticosteroid	0	242	0.0 (0.0–15.1)	^c
Nonmelanoma skin cancer				
PsA treatment ^b				
No PsA drug Rx	100	52,232	1.9 (1.6–2.3)	1.00 (reference)
PsA drug Rx	60	12,926	4.6 (3.5–6.0)	2.42 (1.76–3.34)
DMARDs/biologics	58	11,942	4.9 (3.7–6.3)	2.54 (1.84–3.51)
Immunosuppressant	5	994	5.0 (1.6–11.7)	2.63 (1.07–6.45)
Corticosteroid	2	249	8.0 (0.9–29.0)	4.19 (1.03–17.01)

^aCases could have received more than 1 category of PsA drug and therefore be counted more than once.

^bCase considered exposed if first PsA drug prescription occurred at least 1 year before the date of cancer diagnosis.

^cCould not be calculated because of 0 exposed cases.

characteristics are presented in Table 4. The rate of infection was higher in the PsA cohort compared with the non-PsA cohort (24.6/1000 PYs [95% CI, 23.3–25.9] vs 17.7/1000 PYs [95% CI, 17.1–18.1]; IRR, 1.39 [95% CI, 1.31–1.47]) (Table 5). In both PsA and non-PsA cohorts, rates were more than double for females compared with males and highest in the youngest and oldest age categories. Rates of infection were consistently higher in the PsA cohort compared with the non-PsA cohort at each time point after cohort entry ($P < 0.0001$) (Fig. 4). Most infections were cryptosporidiosis, cryptococcosis, or other mycoses.

In the PsA cohort, rates of opportunistic infection were significantly higher in patients who received prescriptions for PsA drugs compared with those who did not (IRs, 36.1/1000 PYs

[95% CI, 33.3–40.4] and 21.5/1000 PYs [95% CI, 20.2–22.9], respectively; IRR, 1.71 [95% CI, 1.52–1.91]) (Table 6). Rates for users of DMARDs/biologics were similar to the rates in users of immunosuppressants, but the rate was higher in current users of corticosteroids. The results did not differ when we redefined the exposure window to 90 days in the sensitivity analyses.

DISCUSSION

Rates of hematologic cancer were higher in patients with PsA compared with patients without PsA, whereas rates of solid cancers and nonmelanoma skin cancers were similar for the 2 groups. Rates of all cancers were higher in patients with PsA who received prescriptions for systemic treatments (DMARDs/biologics, immunosuppressants, and corticosteroids), although the rates did not differ by type of treatment prescribed. These results are similar to other studies. Rohekar et al¹ also reported similar rates of all cancer compared with the general population; however, their results suggested more breast cancers (standardized incidence ratio, 1.55; 95% CI, 0.92–2.62) and fewer hematologic cancers (standardized incidence ratio, 0.69; 95% CI, 0.26–1.83) among PsA patients. Similar to our study, a study in Sweden reported a slightly higher hazard ratio (1.2; 95% CI, 0.9–1.7) of lymphoma in PsA patients compared with the general population.² A recent analysis of a US population reported similar incidence of malignancies in both patients with PsA and patients with rheumatoid arthritis (5.6/1000 PYs).³ Reported IRs of solid, hematologic, and nonmelanoma skin cancers in patients with PsA in this US study (2.8/1000 PYs, 0.7/1000 PYs, and 3.5/1000 PYs, respectively) were similar to those we found in our analysis.

In our study, rates of opportunistic infection were higher in patients with PsA compared with patients without PsA and highest among PsA patients who received prescriptions for systemic therapy.

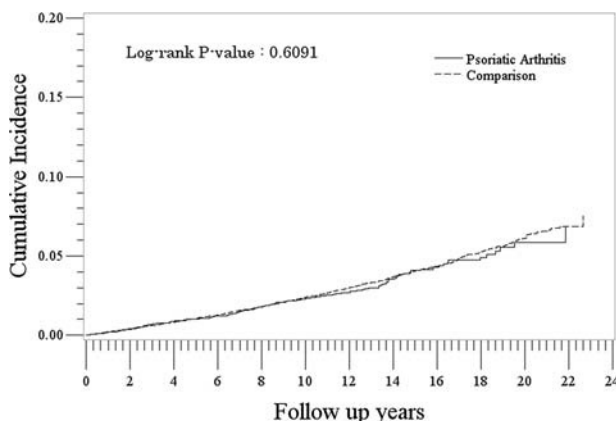


FIGURE 3. Cumulative incidence of nonmelanoma skin cancer in the PsA and comparison cohorts.

TABLE 4. Distribution of Characteristics of Patients With and Without PsA—Opportunistic Infection Subcohort

	PsA n = 8677 (%)	No PsA n = 86,413 (%)
Age, y		
Mean (SD)	47.40 (14.61)	47.35 (14.56)
<10	17 (0.20)	170 (0.20)
10–19	143 (1.65)	1426 (1.65)
20–29	779 (8.98)	7773 (9.00)
30–39	1821 (20.99)	18,165 (21.02)
40–49	2081 (23.98)	20,782 (24.05)
50–59	2015 (23.22)	20,078 (23.23)
60–69	1184 (13.65)	11,759 (13.61)
70–79	512 (5.90)	5082 (5.88)
80+	125 (1.44)	1178 (1.36)
Sex		
Female	4352 (50.16)	43,373 (50.19)
Male	4325 (49.84)	43,040 (49.81)
Smoking status		
Current	1806 (20.81)	18,072 (20.91)
Former	1717 (19.79)	13,227 (15.31)
Never	3403 (39.22)	35,979 (41.64)
Unknown	1751 (20.18)	19,135 (22.14)
Body mass index		
<18.5	94 (1.08)	1311 (1.52)
18.5–24.99	2431 (28.02)	30,014 (34.73)
25.0–29.99	2819 (32.49)	26,236 (30.36)
≥30	2384 (27.47)	15,574 (18.02)
Unknown	949 (10.94)	13,278 (15.37)
Year of cohort entry		
1988–1994	1360 (15.67)	13,486 (15.61)
1995–1999	1642 (18.92)	16,345 (18.91)
2000–2004	2355 (27.14)	23,481 (27.17)
2005–2009	2407 (27.74)	24,011 (27.79)
2010–2012	913 (10.52)	9090 (10.52)
Length of medical history before cohort entry, y		
Mean (SD)	7.04 (5.86)	7.44 (5.66)
Length of medical history after cohort entry, y		
Mean (SD)	7.60 (5.71)	7.20 (5.61)
Died		
Yes	630 (7.26)	5797 (6.71)
No	8047 (92.74)	80,616 (93.29)

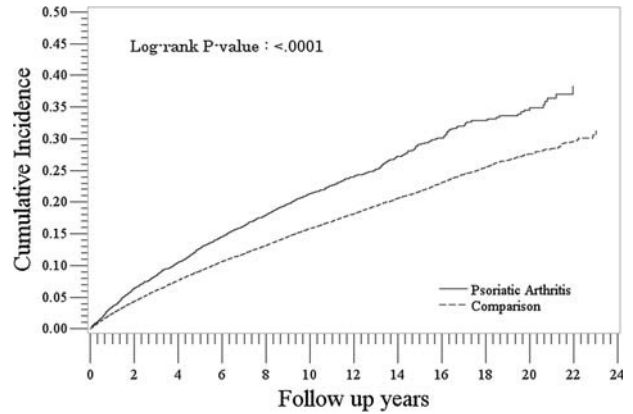


FIGURE 4. Cumulative incidence of opportunistic infections in the PsA and comparison cohorts.

Rates were similar in current users of DMARDs/biologics and immunosuppressants but were higher among current users of corticosteroids. These results suggest that exposure to systemic treatment increases the rate of opportunistic infection, yet untreated patients with PsA also had a higher rate of infection compared with that of patients without PsA (21.5/1000 PYs non-treated PsA, 17.7/1000 PYs non-PsA). Our results are similar to published results of a cohort of patients with psoriasis in an administrative database where hospital infection events ranged from 16.5/1000 PYs in phototherapy exposed to 26.2/1000 PYs for anti-TNF-α exposed.⁴ The finding of the highest IRR in the corticosteroid group is similar to the results from Germano et al,⁶ where the highest IRR for opportunistic infection (3.6; 95% CI, 1.58–8.20) was found among patients treated with DMARDs and corticosteroids compared with DMARDs alone. Combined with our results, this suggests that patients with PsA treated with corticosteroids have the highest risk for opportunistic infection.

Our population-based study had a number of strengths. We used a very large and well-established, validated, longitudinal primary care database, the CPRD, which is known for its high accuracy and completeness of diagnoses. The mean length of follow-up was more than 7 years in both the PsA and non-PsA cohorts for each outcome of interest. By excluding patients who had less than 1 year in their history before the index date, we reduced the risk of including patients with prevalent, rather than incident, PsA.

There were a few potential limitations to consider. First, it is possible that we included some people who did not actually have PsA. Results of validation studies have indicated that the diagnosis of psoriasis and PsA in the CPRD has high positive predictive value.^{11,12} In addition, we reviewed the electronic medical records

TABLE 5. Rates of Incident Opportunistic Infection in Patients With and Without PsA

	PsA Cohort			Non-PsA Cohort		
	Cases	PY	IR/1000 PYs (95% CI)	Cases	PYs	IR/1000 PYs (95% CI)
Opportunistic infection						
All	1410	57,417	24.6 (23.3–25.9)	9946	561,535	17.7 (17.1–18.1)
Female	995	26,829	37.1 (34.8–39.5)	7054	272,067	25.9 (25.3–26.5)
Male	416	30,587	13.6 (12.3–14.9)	2892	289,468	10.0 (9.6–10.4)
Age < 30 y	153	5629	27.2 (23.0–31.8)	1165	53,766	21.7 (20.4–22.9)
Age, 30–49 y	594	26,582	22.3 (20.6–24.2)	4238	255,660	16.6 (16.1–17.1)
Age, 50–69 y	558	21,882	25.5 (23.4–27.7)	3816	217,852	17.5 (17.0–18.1)
Age, 70+ y	105	3323	31.6 (25.8–38.2)	727	34,257	21.2 (19.7–22.8)

TABLE 6. Rates of Opportunistic Infection in Patients With PsA, Stratified by Receipt of PsA Drug Prescriptions

	Cases ^a	PY	IR/1000 PYs (95% CI)	IRR (95% CI)
PsA treatment ^b				
No PsA drug Rx	989	45,979	21.5 (20.2–22.9)	1.00 (reference)
PsA drug Rx	421	11,461	36.7 (33.3–40.4)	1.71 (1.52–1.91)
DMARDs/TNF- α	377	10,624	35.5 (32.0–39.3)	1.65 (1.47–1.86)
Immunosuppressant	34	841	40.4 (28.0–56.5)	1.88 (1.34–2.65)
Corticosteroid	23	211	109.1 (69.1–163.7)	5.07 (3.35–7.66)

^aCases could have received more than 1 category of PsA drug and therefore be counted more than once.

^bCase considered exposed if last PsA drug prescription occurred 1 month or less before infection diagnosis date.

of the patients with PsA and assessed the presence of and number of PsA diagnoses, codes for PsA symptoms, and treatments for PsA to provide confidence in the PsA diagnosis. We found that approximately 98% of potential patients with PsA identified had at least one of these supporting codes, so we are confident that the vast majority of people in the PsA cohort did have the disease. To be eligible for inclusion in the PsA cohort, a patient had to have a recorded diagnosis of PsA; thus, if a GP did not record the diagnosis, the patient was not included in the study. Therefore, the results of this study are generalized to patients with diagnosed PsA that comes to the attention of the GP. Second, the CPRD does not contain information on PsA severity or activity. Patients with PsA who receive treatments are likely to have more severe or active disease than patients with PsA who do not; thus, the elevated risks of observed among treated patients with PsA compared with patients with PsA who did not receive treatment may be explained by disease severity or activity. Third, it is possible that some patients with PsA stopped taking systemic PsA therapies sooner than was assumed in our estimation of person time. To assess this, we conducted sensitivity analyses where we extended and shortened the exposure time window, and there were no material differences in the rates of opportunistic infection in these analyses. Finally, in the United Kingdom, biologics are often prescribed by consultants (specialists) and thus may not be captured in the GP record; thus, it is possible that we misclassified some exposed person time as nonexposed. The incomplete capture of exposure to biologics also limits our ability to separate independent effects of biologics from DMARDs.

In summary, we found that the rates of solid and nonmelanoma skin cancer were similar in patients with PsA compared with patients without PsA, but rates of hematologic cancer and opportunistic infections were higher in patients with PsA. In patients with PsA, rates of all outcomes were higher among those who received prescriptions for systemic PsA therapy.

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