Association between Systemic Treatments and COVID-19 Infection Risk in Patients with Psoriasis

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BACKGROUND, OBJECTIVE, AND PATIENTS

Background

- Psoriasis affects 2.8% of the adult population[1]; Psoriasis patients may have a higher risk of serious infection and more commonly display risk factors for more severe COVID-19 pneumonia such as obesity, and diabetes[2-3].
- Systemic therapies for moderate-to-severe psoriasis have been linked to increased risk of upper respiratory tract viral infection[4].
- It is uncertain if having psoriasis itself, having comorbidities associated with psoriasis, or systemic treatments for psoriasis explain this association.
- The Symphony dataset is one of the largest existing repositories of patient-level integrated data, covering 92% of retail pharmacy claims, >280 million patients, >1.8 million prescribers and >16,000 health plans.

Objective

1. To assess risk of incident COVID-19 infection in adult psoriasis patients compared to the general population.
2. To assess risk of incident COVID-19 infection in adult psoriasis patients treated with systemic therapies compared to patients on topical therapies.

Key Inclusion Criteria

- At least 2 *ICD-10* codes for psoriasis or psoriatic arthritis (L40.x) between May 1, 2019, and January 1, 2020 (n=167,027)
- Allowed concomitant therapy: oral systemic agents and biologics; most proximal treatment was selected for cohort categorization.
- General population controls selected in 1:6 ratio (n=1,002,162).

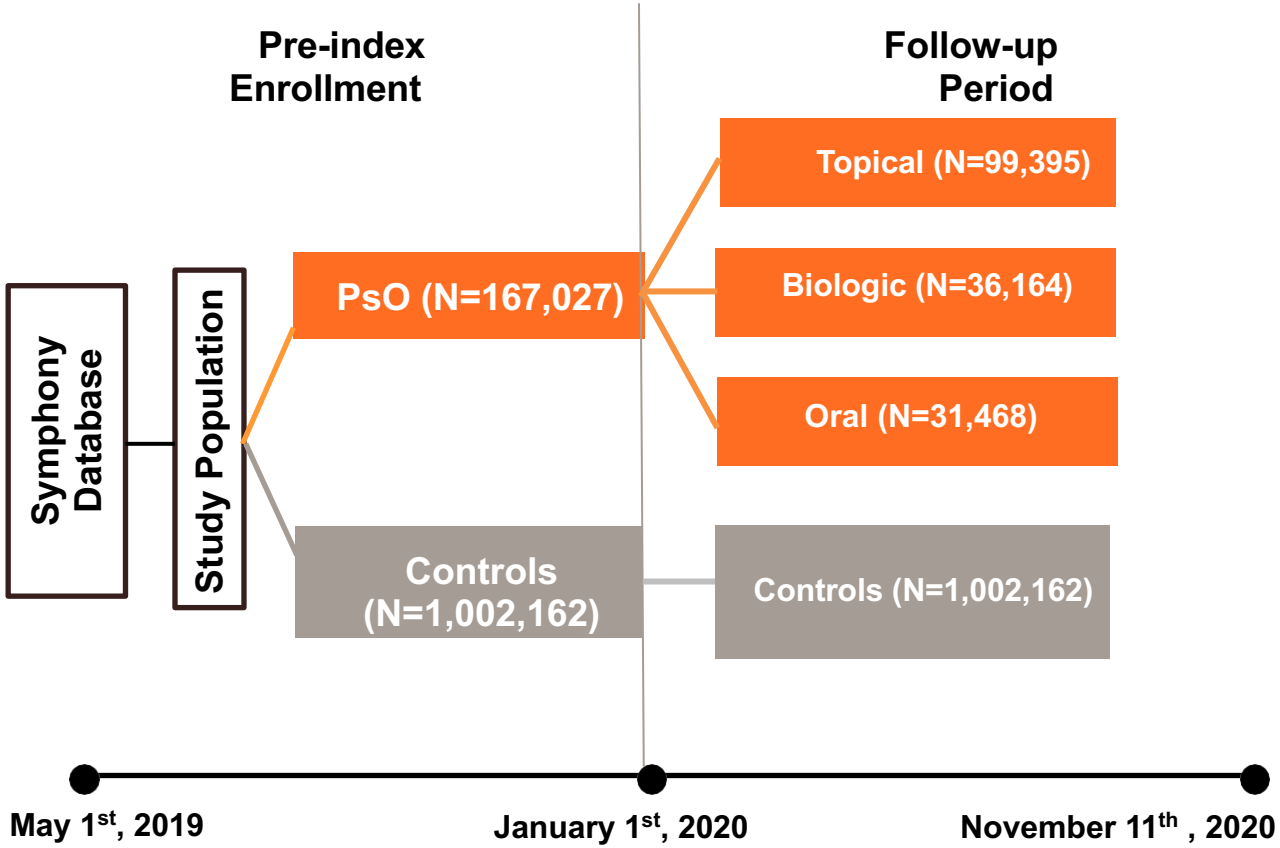
Key Exclusion Criteria

- Under the age of 20
- Enrolled after the index date, January 1st, 2020

1 Liu J, Thatiparthi A, Martin A, Egeberg A, Wu JJ. Prevalence of psoriasis among adults in the US 2009-2010 and 2013-2014 National Health and Nutrition Examination Surveys. J Am Acad Dermatol. 2021 Mar;84(3):767-769. **2.** Gisondi P et al. The impact of the COVID-19 pandemic on patients with chronic plaque psoriasis being treated with biological therapy: the Northern Italy experience. *Br J Dermatol*. 2020;183(2):373-374. **3.** Amin M, Lee EB, Tsai TF, Wu JJ. Psoriasis and Co-morbidity. Acta Derm Venereol. 2020 Jan 30;100(3):adv00033. **4.** Wan MT, Shin DB, Winthrop KL, Gelfand JM. The risk of respiratory tract infections and symptoms in psoriasis patients treated with interleukin 17 pathway-inhibiting biologics: A meta-estimate of pivotal trials relevant to decision making during the COVID-19 pandemic. *J Am Acad Dermatol*. 2020;83(2):677-679. doi:10.1016/j.jaad.2020.05.035

STUDY DESIGN AND ANALYSES

Study Design, (CORONAVIRUSHUB-00060-R1)



- Patients with psoriasis were classified as receiving topical agents only if the patients never received a code consistent with moderate-to-severe disease (i.e. treatment with acitretin, methotrexate, cyclosporine, apremilast or any biologic
- Patients who received any biologic were analyzed as the biologic cohort, stratified by class, regardless of use combined with any oral agent.
- The biologic-naïve patients who received oral agents were stratified by medication class into acitretin, cyclosporine, methotrexate, and apremilast cohorts

Analyses

- Prespecified outcome of incident COVID infection include the number of participants who received a medical code (U07.1) consistent with this diagnosis during follow-up.

1. Demographic and clinical characteristics of the 3 PsO cohorts (topical, oral, biologic) and controls were summarized by frequency for categorical variables and mean for continuous variables.

2. Poisson regression was used to examine the incidence rates of COVID in psoriasis patients and controls. Age and sex-adjusted incidence rates were compared pairwise between the 3 PsO cohorts and controls with adjusted incidence rate ratios (aIRR).

3. Multivariable logistic regression was used to examine the association between psoriasis and COVID infection with adjusted odds ratios (aOR). Subset analyses was performed on the total PsO cohort.

1. RESULTS: BASELINE CHARACTERISTICS

Baseline Demographics and Disease Characteristics

	Psoriasis (n=167,027)	No Psoriasis (n=1,002,162)	Total (n=1,169,189)
Female sex. No (%)	89,302 (53.5)	557,690 (55.7)	646,992 (55.3)
Age, mean (SD), y	58.1 (13.6)	57.7 (16.1)	57.7 (15.7)
Race. No (%)			
Caucasian	132,036 (79.1)	748,490 (74.7)	880,526 (75.3)
Hispanic	15,568 (9.3)	90,413 (9.0)	105,981 (9.1)
African American	13,848 (8.3)	130,392 (13.0)	144,240 (12.3)
Asian	2,894 (1.7)	17,171 (1.7)	20,065 (1.7)
Other	2,681 (1.6)	15,696 (1.6)	18,377 (1.6)
COVID-19 risk factors No. (%)			
Congestive heart failure	10,354 (6.2)	48,025 (4.8)	58,379 (5.0)
Type-2 Diabetes mellitus	37,975 (22.7)	158,987 (15.9)	196,962 (16.9)
Obesity	44,557 (26.7)	145,347 (14.5)	189,904 (16.2)
COPD	16,514 (9.9)	64,145 (6.4)	80,659 (6.9)
Psoriasis treatment			
Topical	99,395 (59.5)	NA	NA
Oral	31,468 (18.8)	NA	NA
Biologics	36,164 (21.7)	NA	NA

Treatments Received

	Oral Cohort (n=31,468)	Biologics (n=36,164)	Total Moderate-to-Severe Psoriasis (n=67,632)
Oral systemics. No (%)			
Methotrexate	21,478 (68.3)	230 (0.6)	21,708 (32.1)
Apremilast	7,398 (23.5)	99 (0.3)	7,497 (11.1)
Cyclosporine	1,573 (5.0)	7 (0.02)	1,580 (2.3)
Acitretin	1072 (3.4)	5 (0.01)	1,077 (1.6)
Biologics. No (%)			
TNF-α inhibitors			
Adalimumab	0	9,553 (26.4)	9,553 (14.1)
Infliximab	0	3,366 (9.3)	3,366 (5.0)
Etanercept	0	4,201 (11.6)	4,201 (6.2)
Certolizumab	0	1,438 (4.0)	1,438 (2.1)
IL-12/23 inhibitor			
Ustekinumab	0	5,085 (14.1)	5,085 (7.5)
IL-17 inhibitors			
Secukinumab	0	6,266 (17.3)	6,266 (9.3)
Ixekizumab	0	3,135 (8.7)	3,135 (4.6)
Brodalumab	0	142 (0.4)	142 (0.2)
IL-23 inhibitors			
Guselkumab	0	1,687 (4.7)	1,687 (2.5)
Risankizumab	0	1,021 (2.8)	1,021 (1.5)
Tildrakizumab	0	312 (0.9)	312 (0.5)

2. RESULTS: POISSON REGRESSION

Factor	Adjusted Incidence Rate Ratios (95% CI)	P Value
Psoriasis vs. No Psoriasis	1.33 (1.23- 1.38)	<0.0001
Biologics vs Topical		
TNFi vs Topical	0.82 (0.69 – 0.95)	<0.0029
Ustekinumab vs Topical	0.96 (0.74 – 1.18)	<0.7282
IL-17i vs Topical	1.06 (0.90-1.22)	<0.4848
IL-23i vs Topical	0.72 (0.40-1.05)	<0.0510
Oral Agents vs Topical		
Acitretin vs. Topical	0.86 (0.53-1.41)	<0.5630
Cyclosporine vs. Topical	0.94 (0.64-1.39)	<0.7569
Methotrexate vs. Topical	0.75 (0.67-0.86)	<0.0001
Apremilast vs. Topical	0.69 (0.55-0.85)	<0.0006
Biologics vs Oral Agents		
TNFi vs Oral Agents	1.07 (0.91-1.25)	<0.4221
Ustekinumab vs Oral Agents	**1.25 (0.99 – 1.59)**	**<0.0604**
IL-17i vs Oral Agents	1.36 (1.13-1.63)	<0.0009
IL-23i vs Oral Agents	0.93 (0.66-1.31)	<0.6784
Biologics vs No Psoriasis		
TNFi vs No Psoriasis	1.17 (1.03 – 1.32)	<0.0127
Ustekinumab vs. No Psoriasis	1.37 (1.07 - 1.70)	<0.0041
IL-17i vs No Psoriasis	1.51 (1.06 – 1.76)	<0.0001
IL-23i vs No Psoriasis	1.03 (0.85– 1.42)	<0.8521

Age and Sex-Adjusted Incidence Rate Ratios (aIRR):

- Psoriasis patients had a 33% increase in COVID incidence compared to controls.
- TNF-α inhibitor use was associated with a 18% reduction in COVID incidence vs. topical cohort and a 17% increase vs. controls.
- Methotrexate use was associated with a 25% reduction in COVID incidence vs. topical cohort.
- Apremilast use was associated with a 31% reduction in COVID incidence vs. topical cohort.
- IL-17 inhibitor use was associated with a 36% increase in COVID incidence vs. the oral cohort and a 51% increase vs. controls.
- Ustekinumab use was associated with a 37% increase in COVID incidence vs. controls and a non-significant 25% increase vs. the oral cohort.

3. RESULTS: MULTIVARIATE LOGISTIC REGRESSION

Factor	Adjusted Odds Ratio (95% CI)	P Value
Psoriasis	1.182 (1.132 – 1.234)	<0.0001
Age	0.997 (0.996-0.998)	<0.0001
Sex: Male vs. Female	0.977 (0.945-1.009)	<0.1605
Race: Caucasian vs. Non-Caucasian	0.519 (0.501-0.537)	<0.0001
Congestive heart failure	2.087 (1.978-2.202)	<0.0001
COPD	1.519 (1.441-1.600)	<0.0001
Type-2 Diabetes mellitus	1.722 (1.656-1.790)	<0.0001
Obesity	1.588 (1.529-1.640)	<0.0001
TNFi vs. Topical	0.874 (0.766-0.998)	<0.0469
Ustekinumab vs. Topical	1.028 (0.823-1.285)	<0.8070
IL-17i vs. Topical	1.081 (0.921-1.269)	<0.3395
IL-23i vs. Topical	**0.739 (0.532-1.026)**	**<0.0709**
Acitretin vs. Topical	0.834 (0.507-1.372)	<0.4745
Cyclosporine vs. Topical	0.914 (0.617-1.353)	<0.6535
Methotrexate vs. Topical	0.808 (0.712-0.919)	<0.0011
Apremilast vs. Topical	0.702 (0.565-0.873)	<0.0014
Age	0.996 (0.993-0.999)	<0.0095
Sex: Male vs. Female	0.935 (0.865-1.010)	<0.0896
Race: Caucasian vs. Non-Caucasian	0.531 (0.489-0.576)	<0.0001
Congestive heart failure	1.934 (1.711-2.186)	<0.0001
COPD	1.338 (1.194-1.499)	<0.0001
Type-2 Diabetes mellitus	1.551 (1.421-1.692)	<0.0001
Obesity	1.391 (1.280-1.512)	<0.0001

Comorbidity and Demographic Adjusted Odds Ratios (aOR):

- Adjusting for demographic variables and comorbidities, psoriasis patients were 18% more likely to have an incident COVID infection (aOR, 1.18; 95% CI, 1.13-1.23) compared to controls.
- Decreasing age, non-Caucasian ethnicity, and comorbidities were strongly associated with a greater risk of COVID infection in patients and controls.

Subset Analyses:

- TNF-α inhibitor users were 13% less likely to have an incident COVID-infection (aOR, 0.87; 95% CI, 0.77-1.00) compared to patients on topical therapy.
- Though non-significant, IL-23 inhibitor users were 26% less likely to have an incident COVID-infection compared to patients on topical therapy (aOR, 0.74; 0.53-1.03).
- Methotrexate users were 19% less likely to have an incident COVID-infection (aOR, 0.81; 0.71-0.92) compared to patients on topical therapy.
- Apremilast users were 30% less likely to have an incident COVID-infection compared to patients on topical therapy (aOR, 0.70; 0.57-0.87).

CONCLUSION

- In this large EHR claims database, patients with psoriasis are more likely to have an incident COVID-19 infection compared to the general population.

- Biologics:
  - TNF-**α** inhibitor use may be associated with **lower odds** of contracting COVID-19 in patients with psoriasis.
  - On age and sex-adjusted incidence rates, ustekinumab and IL17-inhibitor use may be associated with **higher odds** of contracting COVID-19 in patients with psoriasis.

- Oral Systemics:
  - Methotrexate and apremilast use may be associated with **lower odds** of contracting COVID-19 in patients with psoriasis.