

# Real World Studies of Psoriasis and Mental Illness in Newfoundland and Labrador



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## Abstract

**Background:** Psoriasis is a chronic, immune-mediated inflammatory disease with an implied connection to psychiatric disorders.

**Objective:** This study aims to illustrate an association between psoriasis and psychiatric disorders using real world data gathered from the Newfoundland and Labrador population.

**Methods:** Data on 15,100 patients with psoriasis and 75,500 controls (1:5) was collected from the Newfoundland and Labrador Centre for Health Information's Electronic Health Records. The cases and controls were matched for age, sex, and geography. Indicators for psychiatric disorders include diagnosis of mental illnesses from physician's visits and hospitalization records (all coded for mental health using ICD-9 and ICD-10 codes).

**Results:** 9,991 (66.2%) cases were identified to have at least one visit with a diagnostic code for mental illness compared to 42,276 (56.0%),  $P < .0001$  in the control group. The percentage of people coded for anxiety was 36.50% compared to 28.95%,  $P < .0001$ ; depression was 37.04% compared to 30.19%,  $P < .0001$ ; and adjustment disorder was 6.89% versus 5.48%,  $P < .0001$ , among those with and without psoriasis, respectively. The greatest risk for anxiety [OR 1.4 (1.20, 1.67)] and depression [OR 1.65 (1.36, 2.00)] among psoriasis patients was between the 0 to 20 age group. Women with psoriasis are more likely to have anxiety [OR 1.08 (1.03, 1.13)], depression [OR 1.04 (1.01, 1.09)] and adjustment disorder [OR 1.07 (0.98, 1.17)] compared to female controls.

**Conclusion:** Our result shows that patients with psoriasis have an increased prevalence of mental illness. Using real world data to carry out further investigations will better elucidate this association and provide an increased understanding of the association between psoriasis and mental disorders.

## Keywords

psoriasis, real world data, depression, anxiety, adjustment disorders, suicide, newfoundland and labrador

## Introduction

Psoriasis is a chronic, immune-mediated inflammatory disease. While manifestation of the skin and joints are the primary disease characteristics, psoriasis is a multisystem inflammatory disorder.<sup>1</sup> The most common type of psoriasis is psoriasis vulgaris, or plaque psoriasis, which is characterized by thick, inflamed, scaly plaques on the patients' skin. Other forms of psoriasis include guttate, pustular, and inverse psoriasis.<sup>2</sup> This disease can be classified as mild, moderate, or severe based on the amount of psoriasis a patient has (body surface area) and the location of psoriasis lesions on the patient's body.<sup>1</sup>

Psoriasis is also associated with several comorbidities, including psoriatic arthritis, inflammatory bowel disease,

psychological disorders, cardiovascular disease, and metabolic syndrome.<sup>3</sup> This has been confirmed and well documented in the Newfoundland and Labrador (NL) population.<sup>4-6</sup> The

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presence and severity of these comorbidities may also increase in patients with more severe disease.<sup>7</sup> As a result, patients with psoriasis can experience significant physical, sociological, and psychological burdens that negatively affect their overall quality of life.

Psoriasis is known to have undesirable effects on mental health. As a result of skin hyperpigmentation, stigmatization, and constant medication and subjection to treatment, coupled with the fact that psoriasis typically commences at a young age, psoriasis patients are prone to psychological distress.<sup>8,9</sup> To demonstrate an association between psoriasis and mental illness, previously collected data from the NL health care system is used to carry out a Real-World Experience (RWE) study.

RWE studies rely on Real World Data (RWD), which is data gathered in a real-world context outside of a clinical trial setting<sup>10</sup> and often involving a population that has received an intervention or therapy in the clinical environment.<sup>11</sup> In this case, the RWD relies on patient information gathered in the context of healthcare provision from patients, clinicians, hospitals, and payers,<sup>12,13</sup> and not necessarily reuse of a previously collected research dataset.

The importance of RWE studies has been increasingly acknowledged by regulatory bodies such as Health Canada and the United States Food and Drug Administration. RWE-based research can be invaluable in interrogating a common complex disease such as psoriasis as this approach is known to be more efficient, less expensive, and have better generalizability than traditional clinical trials.<sup>14</sup>

This study aims to show an association between psoriasis and mental health, therefore strengthening the existing theory that implies the presence of such connection and highlighting the importance of RWD for further psoriatic studies.

## Materials and Methods

The ability to carry out this study is feasible because of the unique Janssen and Newfoundland and Labrador Health Innovation Partnership (JANL-HIP), which is comprised of the Government of Newfoundland and Labrador, the Eastern Health regional health authority, the Newfoundland and Labrador Centre for Health Information (NLCHI), Janssen Inc., and Memorial University of Newfoundland. This partnership intends to lay a foundation for RWE studies and interrogate RWD regarding psoriatic disease in NL. The study received full ethical approval from the NL Health Research Ethics Board (HREB).

### Data Sources and Study Population

Under the Newfoundland and Labrador public healthcare plan, citizens of NL are provided with a Medical Care Plan (MCP) number as each patient's primary identifier. Although many patients with very mild psoriasis might not seek medical services for this condition, and others might be attended to by their

primary care provider, a psoriasis diagnosis is primarily made following confirmation by a dermatologist. Once a dermatologist diagnoses a patient with psoriasis—and after further consultations, generates a diagnostic code—prescription details and other vital health-related information are then entered into the Newfoundland and Labrador Centre for Health Information - Electronic Health Records (NLCHI-EHR), which the NLCHI curates. This client registry contains the health information of all people with an MCP number and visits to a Regional Health Authority and pharmacy connected to the Pharmacy Network.<sup>15</sup> Other datasets compiled by the Data and Information Services Department NLCHI for this study were derived from the MCP Fee-for-Service (FFS) Physician Claims data, MCP Beneficiary Registration data, NLCHI Mortality System, NLCHI Suicide Database and the Provincial Discharge Abstract Database (PDAD).

Patients with psoriasis were identified through *International Classification of Diseases 9th revision (ICD-9) code 696* from dermatologists in NL and medical information on these patients during the period of January 1, 2009, to March 31, 2019, was collected from the NLCHI-EHR, using MCP FFS data. The psoriasis cases were matched with five unexposed controls (1:5 ratio) drawn from the databases with similar study period based on age, sex, and geography. Cases born before the study start date (January 1, 2009) were age-matched to controls based on their age at the start of the study period. Cases born within the study period were age-matched to controls based on their age at the end of the study period (March 31, 2019). The Primary Healthcare (PHC) Service Area of residence was used to match for geography. The PHC Service Areas are subdivisions of each of the four Regional Health Authorities in NL. Outcome data, including healthcare utilization data, indicators of mental health status, cardiovascular outcomes, and age and sex of patients, were extracted from NLCHI health records. On their own, the measures listed exclude medication data; hence, the need to link to Newfoundland and Labrador Prescription Drug Program data or the physician record data.

To identify patients with mental health conditions, information on patients with the ICD-9 diagnostic codes 290 – 319 was extracted from the FFS database. The outcomes were general practitioner visits (coded for mental health), emergency room visits and hospitalizations (coded for mental health), psychologists and psychiatrists visits, diagnosis of depression excluding bipolar disorder, diagnosis of anxiety including anxiety-related disorders, and Electroconvulsive Therapy (ECT) use among psoriasis patients. ECT was identified with ICD-10 Canadian Classification of Interventions (CCI) code- 1.AN.09.^.^ . Information on attempted suicide was ascertained by identifying a flag that indicates that the individual was hospitalized for suicide attempt during the study period. According to Kurd et al.,<sup>16</sup> suicidality is defined as suicidal ideation, suicide attempt or suicide. In this study, only attempted suicide and suicide are used as the parameters of suicidality. Information on suicide was drawn from the NLCHI mortality system database.

**Table 1.** Summary of Cases and Controls With Mental Health Information Using the FFS Records.

	Cases	Control	P-value
Number of Patients	15100	75500	NA
Sex	F-8462 (56%) M-6638 (44%)	F-42310 (56%) M-33190 (44%)	NA
Location (Urban or Rural)	Rural-6220 (41.2%) Urban-8864 (58.6%)	Rural- 31432(41.6%) Urban- 43804 (58.0%)	NA
Average study age	N/A- 34 (0.2%) 52.7 (18.7SD)	N/A-264 (0.3%) 52.5 (19.3SD)	NA
Number of patients with at least one visit with a diagnosis code for mental illness	9991 (66.2%)	42276 (56.0%)	<.0001 OR 1.53 95 CI (1.48, 1.59)
Average number of visits among patients with at least one visit for mental illness	17.5	16.6	0.0654

Abbreviations: CI, Confidence Interval; FFS, Fee for Service; N/A, Not available; OR, Odds Ratio.

<sup>a</sup>NA – as the samples were matched

### Statistical Analysis

Descriptive analyses were used to compare for age, sex, geography, number of visits and hospitalizations for mental health illnesses (particularly depression and anxiety, suicidality and ECT) between case and controls using SPSS software. The two data sets were compared using the two sample t-test,  $\chi^2$ , and Fischer's exact test, when appropriate. At this stage of the analysis, no corrections were made for multiple testing.

### Results

After identifying patients with psoriasis within the study period after a dermatologist diagnosis, the numbers of cases were 15100. Matching the cases 1:5 of the general NL population based on age, sex, and geography, 75500 controls were established. Overall, there were more women than men at 56% to 44% for all participants. The average age for cases is 52.7 years (18.7SD), and for controls, 52.5 (19.4SD) years. Over half of the cases and controls are located in urban areas

at 58.6% and 58.0%, respectively. The characteristics of these cases and control are shown in Table 1.

Upon analyzing the FFS physician visit records, patients with psoriasis were found to have a higher prevalence of mental health conditions when compared with controls. As seen in Table 1, 9991 (66.2%) cases were identified to have at least one visit with a diagnostic code for mental illness compared to 42276 (56.0%) for the control group ( $P < .001$ ).

Comparing the prevalence of specific mental health conditions such as anxiety, depression, and adjustment disorder among psoriasis patients and controls, a statistically significant difference was recorded. The difference for anxiety was 5512 (36.50%) cases to 21861(28.95%) controls ( $P < .001$ ; OR 1.41; 95% CI, 1.36-1.46); depression was 5593 (37.04%) cases to 22798 (30.19%) controls ( $P < .001$ ; OR 1.35; 95% CI, 1.31-1.41) and adjustment disorder was 1040 (6.89%) cases to 4142 (5.48%) controls ( $P < .001$ ; OR 1.27; 95% CI, 1.18-1.36) respectively (Tables 2 and 3). Patients with psoriasis were more likely to have these mental health conditions than controls (Figure 1).

**Table 2.** Using FFS and PDAD Records to Determine the Prevalence of Several Mental Health Conditions and Outcome- Suicidality Among Psoriatic and Control Population.

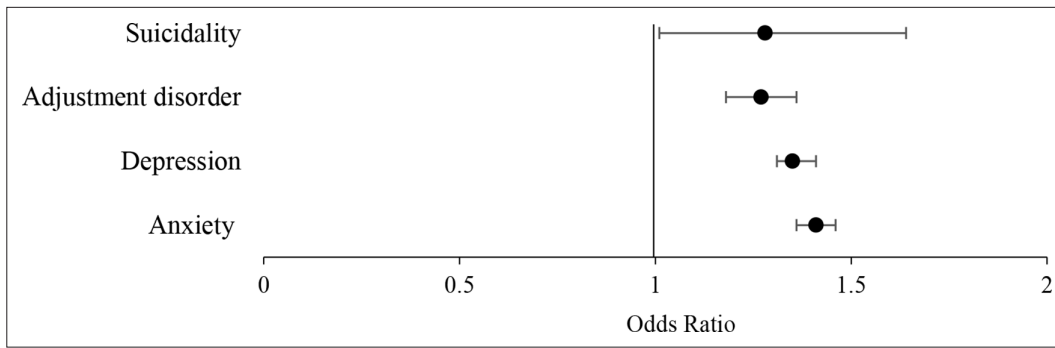
	Cases	Control	P-value	OR (95 CI)
Number of Patients	15100	75500		
Patient diagnosed with Anxiety	5512 (36.50%)	21861 (28.95%)	<.0001	OR 1.41 (1.36, 1.46)
Patient diagnosed with Depression	5593 (37.04%)	22798 (30.19%)	<.0001	OR 1.35 (1.31, 1.41)
Patient diagnosed with Adjustment disorder	1040 (6.89%)	4142 (5.48%)	<.0001	OR 1.27 (1.18, 1.36)
Patients with known suicide attempts (Using PDAD records)	84 (0.55%)	326 (0.43%)	0.0375	OR 1.28 (1.01, 1.64)

Abbreviations: CI, Confidence Interval; FFS, Fee for Service; OR, Odds Ratio; PDAD, Provincial Discharge Abstract Database.

**Table 3.** Using FFS Records to Determine the Prevalence of Mental Health Conditions.

	Cases	Control	P-value	OR (95 CI)
Number of patients with at least one visit with a diagnosis code for mental illness	9991	42275		
Sex	F-6170(61.75%) M-3821 (38.25%)	F-26581(62.88%) M-15694 (37.12%)	0.037	OR 0.95 (0.91, 0.98)
Average Age	53.95	54.87		
0-20	407 (4.07%)	1381 (3.27%)	<.001	OR 1.25 (1.12, 1.40)
21-40	1854 (18.56%)	7365 (17.42%)	<.001	OR 1.08 (1.02, 1.14)
41-60	3861 (38.64%)	16353 (38.68%)	0.94458	OR 0.99 (0.95, 1.04)
61+	3869 (38.73%)	17176 (40.63%)	<.001	OR 0.92 (0.88, 0.96)
Patients coded for Anxiety	5512 (55.16%)	21861 (51.71%)	<.001	OR 1.15 (1.1, 1.20)
Sex	F-3603(36.06%) M-1909(19.10%)	F- 14440 (35.16%) M-7421 (17.55%)	<.001	OR 1.08 (1.03, 1.13) OR 1.10 (1.04, 1.17)
Ages				
0-20	191 (1.91%)	573 (1.35%)	<.001	OR 1.41 (1.20, 1.67)
21-40	1164 (11.65%)	4227 (10.00%)	<.001	OR 1.18 (1.10, 1.27)
41-60	2151(21.53%)	8588 (20.31%)	0.006	OR 1.07 (1.02, 1.13)
61+	2006 (20.07%)	8473(20.04%)	0.936	OR 1.00 (0.94, 1.05)
Patients coded for Depression	5593 (55.98%)	22798 (53.93%)	0.00021	OR 1.08 (1.04, 1.13)
Sex	F- 3757(37.60%) M-1836(18.38%)	F-15442 (36.53%) M- 7356 (17.40%)	0.044	OR 1.04 (1.01, 1.09)
Ages			<.001	OR 0.22 (0.21, 0.23)
0-20	145(1.45%)	374 (0.88%)	<.001	OR 1.65 (1.36, 2.00)
21-40	1060(10.61%)	3970 (9.39%)	<.001	OR 1.14 (1.06, 1.23)
41-60	2231(22.33%)	9193(21.74%)	0.203	OR 1.03 (0.98, 1.09)
61+	2157(21.59%)	9261(21.90%)	0.490	OR 0.98 (0.93, 1.03)
Patients coded for Adjustment Disorder	1040 (10.40%)	4142 (9.79%)	0.06571	OR 1.15 (1.1, 1.20)
Sex	F-724 (7.25%) M-316 (3.16%)	F-2864 (6.77%) M-1278 (3.02%)	0.093	OR 1.07 (0.98, 1.17)
Ages			<.001	OR 0.18 (0.16, 0.21)
0-20	15 (0.15%)	71 (0.17%)	0.692	OR 0.89 (0.51, 1.56)
21-40	176 (1.76%)	712 (1.68%)	0.590	OR 1.04 (0.88, 1.23)
41-60	470 (4.70%)	1835 (4.34%)	0.111	OR 1.08 (0.98, 1.20)
61+	379 (3.79%)	1524 (3.60%)	0.365	OR 1.05 (0.94, 1.18)

Abbreviations: CI, Confidence Interval; FFS, Fee for Service; OR, Odds Ratio.



**Figure 1.** Odds ratio of having several mental health conditions and suicidality between psoriasis patients and controls in the Newfoundland and Labrador population.

After adjusting for sex across the three mental illnesses groups individually (anxiety, depression and adjustment disorder) among cases and controls, women were more likely to be diagnosed with any of these three disorders. Women had higher odds of having anxiety, depression, and adjustment disorder if they had psoriasis compared to controls [OR 1.08 (1.03, 1.13); OR 1.04 (1.01, 1.09) and OR 1.07 (0.98, 1.17)] respectively (Table 3). On the other hand, an association between sex with psoriasis and mental illness was only seen in the anxiety patient group for the men cohorts [anxiety OR 1.10 (1.04, 1.17)]. There were no increased odds found for depression and adjustment disorder among men with psoriasis compared to controls [depression OR 0.22 (0.21, 0.23) and adjustment disorder OR 0.18 (0.16, 0.21)] (Table 3).

An association between age, mental illness and psoriasis was observed in the younger patient groups. Patients between the ages 0-20 and 21-40 were more likely to have a mental illness diagnosis, especially for anxiety and depression. The association was statistically significant at  $P < .001$  (Table 3). The FFS records also show that the average number of visits among patients with at least one mental illness visit was 17.5 for cases and 16.6 for controls ( $P < .0654$ ).

To determine the rate of suicidality, we compared the number of psoriasis patients with recorded suicide attempts to controls and the overall number of suicides. 84 (0.55%) people among the cases attempted suicide compared to 326 (0.43%) ( $P < .0375$ ) of the controls, and 7(0.73%) people out of the psoriasis population were documented to have died by suicide compared to 50(0.86%) among the controls ( $P < .6807$ ) (Tables 2 and 4). These results were not statistically significant, suggesting no difference in the prevalence of

suicidality in patients with psoriasis and controls, however, the total number of completed suicides was small.

## Discussion

It has already been suggested that there is an epidemiological association between psoriatic and mental illnesses.<sup>17,18</sup> Several studies have also noted an increased risk for psychiatric disorders such as anxiety and depression (Table 5).<sup>9,16</sup> For example, a study carried out by Gupta et al.<sup>8</sup> showed that there is a strong association between depressive symptoms, suicidal ideation, and psoriasis. Our study strengthens this claim by demonstrating an association between psoriasis and mental illness, specifically depression, anxiety, and adjustment disorder. These psychiatric disorders, while incredibly complex, could be partially attributed to the stress that accompanies the changes in the skin, medication use, change in lifestyle, and general discomfort.

Our study shows that women with psoriasis are at a higher prevalence for depression, anxiety and adjustment disorder than controls, whereas such association was only found among men with anxiety (Table 3). This is consistent with various other studies showing a higher prevalence of mental illness in women with psoriasis than controls and men.<sup>19-21</sup> Future study is important to expand on the specific association between psoriasis and mental illness in women. Our results also highlighted an association between age and the prevalence of mental disorders. Young psoriasis patients are more likely to have a mental illness diagnosis compared to controls. This observation aligns with previous studies findings that psoriasis has a significant effect on the psychological state of younger patients.<sup>16,20</sup>

Regarding the prevalence of psychiatric disorders, particularly depression, what is important to note is the relative difference between the cases and controls. The number of patients with depression might be overstated in the information received from the databases as the presence of depressive symptoms alone (not necessarily a diagnosis of depression) may be sufficient for physicians to code for

**Table 4.** Using NLCHI Mortality system to determine the Prevalence of Suicide.

	Cases	Control	P-value
Number of Deaths	955	5783	
Suicide numbers	7 (0.73%)	50(0.86%)	0.6807

**Table 5.** Comparing the Data From Our Study to Other Studies That Have Assessed the Link Between Psoriasis to Psychiatric Disorders.

Location	Newfoundland and Labrador (This study)	United Kingdom (Kurd et al., 2010)	Turkey (Devrimci-Ozguven et al., 2000)	United Kingdom (Parisi et al., 2019)	Denmark (Egeberg et al., 2016)
Time frame	2009-2019	1987-2002	Not Provided	1998-2014	1997-2011
Source of Mental Health Diagnosis	Used diagnostic code to collect data from patients EMR	Used diagnostic code to collect data from patients EMR	The HADS questionnaire was used for the assessment of mental health.	Delineated Clinical Practice Research Datalink, with linkage to Hospital Episode Statistics and Office for National Statistics mortality records	Previous diagnosis of self-harm or a nonfatal suicide attempt, or completed suicide
Matches	Age, Sex and Geography	Age, sex, follow-up time, history of depression, anxiety, and suicidality and reason for censorship.	Age, Sex and Education	Age, sex and general practice	Age, sex, and calendar time
Aim of study	To investigate the association between psoriasis and the prevalence of mental illnesses.	To determine the incidence of depression, anxiety and suicidality in patients with psoriasis compared with the general population	To determine the effect of psoriasis on depression and anxiety	To investigate psychiatric comorbidity, psychotropic medication prescribing, and risk of suicidality in people with psoriasis	Association between psoriasis and the risk of self-harm, suicide attempts and suicides
Control Matches	1:5	1:5	1:1	1:20	1:5
No of patients	15100:75500	150000:766950	50:50	56961: 876919	68511: 340152
Sex (M)	6,638 (44%); 33,190 (44%)	71151(47.82%); 366238(48%)	36 (72%) cases	27 363 (48.0%); 390086 (44.5%)	33207 (48.5%); 164565 (48.4%)
(F)	8,462 (56%); 42,310 (56%)	-	14 (28%) Cases	29 598 (52.0%); 486833 (55.5%)	35304 (51.5%); 175587 (51.6%)
Average study age	52.7: 52.5	40 (26. 57); 33 (18, 53)	35.42 (cases)	47(33-62); 46(32-61)	51.2: 51.2
Mortality (suicide)	7 (0.9%); 50 (1.0%)	Mild psoriasis 2946 (0.39%); 1041 (0.71%)	-	35 (0.1%); 679 (0.1%)	Mild psoriasis 168 (0.24%); 688 (0.20%)
Results	Psoriasis patients present with an increased risk of mental disorders. No increased risk of suicidality between cases and controls	Severe psoriasis 76 (0.38%); 40 (1.01%) Patients with psoriasis have an increased risk of depression, anxiety, and suicidality.	Patients with psoriasis have an significantly higher levels of depression than controls.	There is a small increased risk for self-harm associated with psoriasis.	Severe psoriasis 29 (0.04%); 134 (0.040%) Patients with mild psoriasis had no increased risk of self-harm or suicide attempts. Patients with severe psoriasis are at a significantly increased risk of self-harm.

Abbreviations: EMR, Electronic Medical Records; HADS, Hospital Anxiety and Depression Scale.

depression in the EHR. The relative differences (percentages) between the two patient groups are valuable indicators of prevalence.

This study was unable to ascertain that there is an association between psoriasis and suicidality. Other studies aiming to prove this association have provided inconsistent results (Table 5).<sup>16,22,23</sup> In our future studies using RWD, analyzing suicidality in relation to psoriasis severity might yield different results.

This study's strengths include its length of the study period and large sample size with representation from various age groups and different demographics, which allowed us to efficiently determine who had been suffering from mental illness together with psoriasis. It also is the first province wide study of mental disorders in Newfoundland, which is a founder population with an increased prevalence of psoriasis. We are also confident about psoriasis diagnoses among cases as the ICD9 codes were retrieved solely from dermatologists. However, its limitations include a lack of nuanced information directly from patients that might indicate undiagnosed and undocumented psychiatric disorders. Further studies are warranted to assess the impact of disease duration, demographic variables, and cutaneous and articular severity on the various aspects of mental health. In addition, the NL population is primarily Caucasian, so generalization of these results to other ethnicities might be tenuous. While this RWE study has provided some valuable information surrounding mental illness in psoriasis patients, it is still subject to the inherent limitations of RWD analysis.<sup>13</sup> Data from clinical charts will augment further exploration and study of our RWD derived from the NLCHI databases. The clinical charts will provide disease-specific information such as psoriasis and severity index (PASI), disease life quality index (DLQI) and body surface area (BSA), which will allow us to assess the impact of disease severity on mental illness in future studies. Finally, this study highlights and emphasizes the incredible accomplishments that can be made because of innovative collaborations such as the JANL-HIP partnership. The limitations of RWE studies such as lack of internal validity and risk of using biased data, have led to calls for caution and transparency when working with RWD.<sup>13</sup>

In conclusion, our initial interrogation of RWD has demonstrated an increased prevalence of mental illnesses in psoriatic patients. As noted in this paper, further interrogation will provide good value for the health care system as it can better elucidate the association between psoriasis and mental disorders, particularly the temporal sequence, assess the impact of disease burden and treatment response, as well investigate other aspects of psoriatic disease such as metabolic disease, drug effectiveness, persistence, adverse events, and economic evaluation. All these insights are essential to guide dermatologists and primary care physicians in providing the right mental health referral and care to psoriasis patients.

## Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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