

# Increased Risk of Dermatomyositis in Patients with Psoriasis: A Retrospective Cohort Study

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**Purpose:** This study aimed to investigate the risk of dermatomyositis among patients with psoriasis in a large population.

**Patients and Methods:** Individuals aged  $\geq 20$  years with records in the TriNetX database from January 1, 2002 to December 31, 2022 were included. Diagnoses of psoriasis, non-psoriasis, dermatomyositis, and associated comorbidities were established using the International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM) code. Patients who were diagnosed with dermatomyositis before the index date were excluded. Propensity score matching (PSM) was performed in a 1:1 ratio between the psoriasis group and non-psoriasis group. Kaplan–Meier curves were used to determine the cumulative incidence of dermatomyositis, and the Cox proportional hazard model was used to estimate the hazard ratio between the two groups.

**Results:** After PSM, 301018 individuals were included in the psoriasis and non-psoriasis groups, respectively. A higher risk of dermatomyositis was identified in patients with psoriasis than in those without (HR: 2.41, 95% CI: 2.01–2.89). This elevated risk was further confirmed in various subgroup analyses. Specifically, patients with PsA exhibited a higher incidence of dermatomyositis than those without PsA (HR, 1.73; 95% CI, 1.32–2.28). Patients treated with interleukin-17 inhibitors (IL-17i) showed a significantly higher risk of developing dermatomyositis compared to those naïve to biological agents (HR, 5.79; 95% CI, 1.57–21.31). In the European, Middle East, and Africa network and Asia-Pacific network, the risk of dermatomyositis in patients with psoriasis was higher than that in patients without psoriasis (HR (95% CI): 4.77 (1.40–16.10) and 2.50 (1.33–4.66), respectively).

**Conclusion:** This study revealed a higher risk of dermatomyositis in patients with psoriasis than in those without. The psoriatic patients with PsA or those who had received IL-17i treatment demonstrated a significantly higher risk of developing dermatomyositis.

**Keywords:** dermatomyositis, psoriasis, psoriatic arthritis, biological agents, incidence

## Introduction

Idiopathic inflammatory myopathies (IIM) encompass a collection of autoimmune inflammatory muscle diseases involving the skin and visceral organs. Dermatomyositis is one of the most common phenotypes of IIM, accounting for 35–50% of IIM cases.<sup>1</sup> Dermatomyositis is characterized by proximal muscle weakness, a typical rash, systemic manifestations, and the presence of myositis-specific antibodies (MSAs). Typical rashes of dermatomyositis consist of a periorbital heliotrope rash with edema, Gottron papules over extensor surfaces, and photosensitive erythema on the face, neck, and anterior chest (V sign).<sup>2</sup> The prevalence of dermatomyositis is estimated to be 1–6 per 100,000 adults in the United States.<sup>3</sup> Dermatomyositis affects both sexes, but it is more common in females, with a 2:1 ratio of females to males.<sup>4</sup> The pathogenesis of dermatomyositis is complex and involves genetic, environmental, and immune mechanisms.<sup>1</sup> The multifactorial genetic background, particularly human leukocyte antigen (HLA) class; and

environmental stimuli as a trigger result in the inflammatory cascade in dermatomyositis, including type 1 interferon (IFN) response, activation of T and B cells, and overexpression of major histocompatibility complex (MHC) class 1.<sup>5</sup>

Psoriasis is a chronic immune-mediated inflammatory skin disease that affects over 60 million individuals worldwide.<sup>6</sup> Plaque psoriasis is the most common form of psoriasis, characterized by symmetric, well-demarcated, pink plaques covered with silvery scales. Psoriasis can manifest on any skin surface; however, the knee and elbow extensors, lumbosacral area, and scalp are the most commonly affected sites. Psoriasis impacts not just the skin, but also internal organs like the digestive, metabolic, and cardiovascular systems.<sup>7</sup> Consequently, the notion of a psoriatic syndrome has been introduced in recent years. The pathogenesis of psoriasis is multifactorial, and includes genetic, environmental, and immune factors. According to genetic and immunological studies, the T helper 17 (Th17) cells and interleukin-23 (IL-23) pathways are the main drivers of psoriasis pathogenesis, and immunological studies.<sup>8</sup> As an autoimmune disease itself, psoriasis has been reported to coexist with other autoimmune disorders. Various autoimmune diseases have been reported in psoriatic patients, like Hashimoto thyroiditis, Crohn's disease, diabetes mellitus, vitiligo, and connective tissue diseases (CTD) including systemic lupus erythematosus (SLE), systemic sclerosis (SSc), Sjögren syndrome, and dermatomyositis.<sup>9</sup>

Psoriasis and dermatomyositis are both autoimmune diseases that can affect the skin. Keratotic erythema on the extensor surfaces of joints, such as the elbows and knees, is a common feature observed in both diseases. Common underlying immune mechanisms, including plasmacytoid dendritic cell (pDC) activation, type 1 IFN response, and the IL-17-IL-23 pathway, may be involved in both psoriasis and dermatomyositis.<sup>5,7</sup> There were isolated case-reports on the concurrence of psoriasis and dermatomyositis.<sup>10</sup> The risk of dermatomyositis in the psoriasis patient population remains to be thoroughly investigated on a larger scale. Biological agents are commonly used medications for psoriasis therapy, including tumor necrosis factor inhibitors (TNFi), interleukin 17 inhibitors (IL-17i) and interleukin 12/23 inhibitors (IL-12/23i). Individual cases have been reported regarding the onset of dermatomyositis following biological therapy in patients with psoriasis.<sup>11,12</sup> Given the role of these cytokines in both conditions, these findings appear contradictory, and it is crucial to determine whether this paradoxical phenomenon is prevalent in the general population. To address these issues, we conducted this study in a large population based on the TriNetX database to investigate the association between psoriasis and the incidence of dermatomyositis. The association of biological therapy for psoriasis and the risk of dermatomyositis has also been investigated.

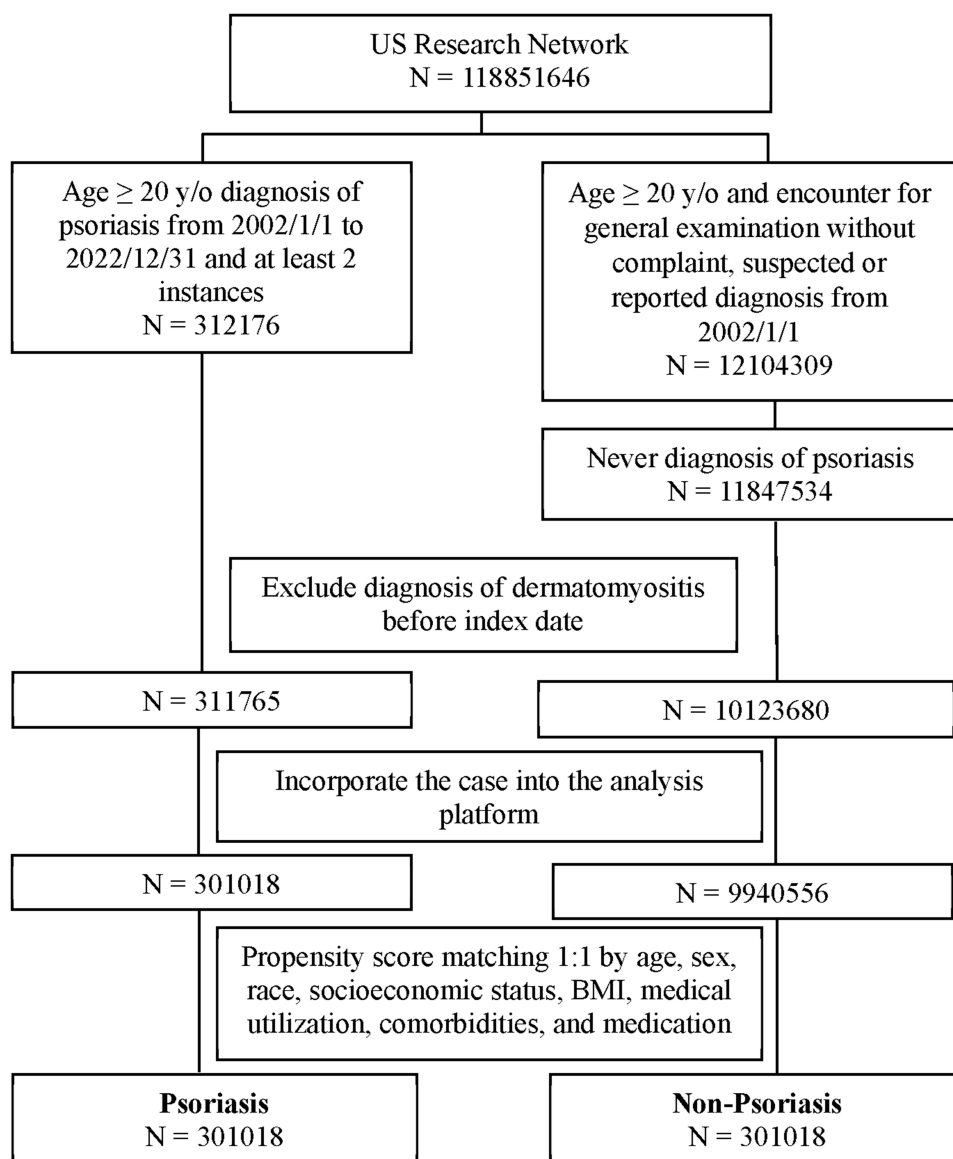
## Materials and Methods

### Data Sources

This retrospective study was conducted using the TriNetX network database (<https://trinetx.com/>). It is a large global federated health research network that contains over 250 million patient records from over 120 health-care organizations (HCOs). The database is updated in real-time, meaning that data is continuously and instantaneously refreshed as new information becomes available. This real-time database is built upon real-world data (RWD) periodically synchronized from the servers of participating HCOs. It incorporates updates on demographics, diagnoses, laboratory values, medications, and vital status, ensuring a comprehensive and current resource for research and clinical analysis. No protected health information or personal privacy is available on the TriNetX platform. Informed consent was not required in the present study because only de-identified information and statistical summaries were obtained from the database. The use of the TriNetX platform in this study was approved by the Institutional Review Board of Chung Shan Medical University Hospital (No. CS2-21176).

### Subjects and Study Design

This retrospective cohort study utilized de-identified electronic health records from the TriNetX platform, a US-based collaborative network that includes approximately 118 million patients.<sup>13</sup> The exposed group consisted of patients aged 20 years and older with psoriasis, identified between January 1, 2002, and December 31, 2022. Psoriasis was defined using the International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM) code L40, with at least two recorded diagnoses during the study period. The comparison group was defined as individuals aged 20 and



**Figure 1** Flowchart of study design.

**Abbreviations:** US, United States; BMI, body mass index.

older who underwent a general examination without complaint, suspected, or reported diagnosis (ICD-10-CM = Z00) and who have never been diagnosed with psoriasis. The index date for the psoriasis group was defined as the date of the initial diagnosis of psoriasis. For the non-psoriasis group, the index date was defined as the date of the first general examination. Additionally, individuals who had been diagnosed with dermatomyositis prior to the index date were excluded from both groups (Figure 1). The primary outcome was the initial diagnosis of dermatomyositis with ICD-10-CM code M33, as well as the related diagnoses, including M33 for dermatopolymyositis, M33.0 for juvenile dermatomyositis, M33.1 for other dermatomyositis, and M33.9 for unspecified dermatopolymyositis. M33.2 for polymyositis without skin eruptions was excluded. The amyopathic dermatomyositis (ADM) was included under M33.1. Individuals were followed until the onset of dermatomyositis or the last recorded event in the US collaborative network.

## Covariates Definitions

The following comorbidities were identified using the ICD-10-CM code within one year before the index date: hypertensive disease (I10-I16), ischemic heart disease (I20-I25), cerebrovascular diseases (I60-I69), diabetes mellitus

(E08-E13), disorders of lipoprotein metabolism (E78), liver disease (K70-K77), depressive disease (F32), and history of nicotine dependence (Z87.891). Medication within one year prior to the index date was stratified into hormones/synthetics/modifiers and antirheumatic drugs. The biological therapies included etanercept, adalimumab, ustekinumab, secukinumab, ixekizumab and infliximab ([Supplementary Table 1](#)). Socioeconomic status was identified using problems related to education and literacy (ICD-10-CM = Z55), problems related to employment and unemployment (ICD-10-CM = Z56), occupational exposure to risk factors (ICD-10-CM = Z57), and problems related to housing and economic circumstances (ICD-10-CM = Z59).

## Statistical Analysis

Statistical analyses were conducted using the built-in tools of the TriNetX platform. To reduce the impact of confounding factors, propensity score matching (PSM) was performed at a one-to-one ratio between the psoriasis and non-psoriasis groups by demographic parameters, including age, sex, race, socioeconomic status, BMI, medical utilization, comorbidities, and medication. In the match, a greedy nearest neighbor matching with a caliper of 0.1 pooled standard deviations of the two groups were used. The standardized mean difference (SMD) was used to compare the baseline characteristics of the two cohorts after PSM. A SMD <0.1 is considered well matched. Kaplan–Meier curves were used to determine the cumulative incidence of dermatomyositis, and the log rank test was used to test significance. The Cox proportional hazards model was used to estimate hazard ratios between the two groups. In addition, to further investigate the association between different psoriasis subgroups and dermatomyositis, this study conducted the following subgroup analyses: the presence of psoriatic arthritis (ICD-10-CM = L40.5), the use of biological agents categorized into TNFi, IL-17i and IL-12/23i. To examine the effects of biologics on the occurrence of dermatomyositis in psoriasis patients, we included psoriasis patients on the index date and excluded individuals who were diagnosed with dermatomyositis either prior to or within six months of the psoriasis index date. The biologics-treated group was set as psoriasis patients with treatment history of biologics on the index date. The control group was set as psoriasis patients without biologics treatment history on the index date as well as during the follow-up period. All statistical analyses were performed on the TriNetX platform, which utilizes R 4.0.2 as its underlying statistical software.

## Results

### Demographic Characteristics of the Subjects

A total of 312176 psoriatic patients aged 20 years or older with records of at least two instances' records from January 1, 2002 to December 31, 2022 were identified in the TriNetX database. Individuals in the same age range, without a diagnosis of psoriasis counted for 12104309 were identified as the control group. After excluding individuals diagnosed with dermatomyositis before the index date, PSM was performed for the psoriasis and non-psoriasis groups. Finally, 301018 individuals were selected from each group ([Figure 1](#)). After PSM, the demographic characteristics of patients with and without psoriasis were comparable. All SMDs between the two groups were <0.1 ([Table 1](#)).

### Risk of Dermatomyositis in Psoriasis and Non-Psoriasis Groups and Subgroup Analyses

Four hundred and thirty-six patients with psoriasis developed dermatomyositis during the follow-up period. The risk of dermatomyositis in the psoriasis and non-psoriasis groups was compared using three models adjusted for different variables in the PSM. There were respectively 143, 141, and 159 individuals who developed dermatomyositis in the non-psoriasis group in Models 1–3 ([Table 2](#)). After PSM based on variables such as age, sex, race, socioeconomic status, BMI, medical utilization, comorbidities, and medication use, the risk of dermatomyositis in the psoriasis group remained significantly higher than that in the non-psoriasis group (HR: 2.41, 95% CI: 2.01–2.89) ([Table 2](#)). Kaplan–Meier curves also showed a significantly higher incidence of dermatomyositis in the psoriasis group than that in the non-psoriasis group ( $P < 0.001$  in the Log rank test ([Figure 2](#))). The higher risk of dermatomyositis among patients with psoriasis was further confirmed by subgroup analysis ([Figure 3](#) and [Supplementary Table 2](#)).

**Table 1** Demographic Characteristics of Psoriasis Patients and Non-Psoriasis Patients

	Before PSM		P	SMD	After PSM		P	SMD
	Psoriasis N = 301,018	Non-Psoriasis N = 9,940,556			Psoriasis N = 301,018	Non-Psoriasis N = 301,018		
Age, years	51.54 ± 15.35	47.63 ± 17.05	<0.001	0.241	51.54 ± 15.35	51.54 ± 15.35	0.982	<0.001
Sex								
Female	159440 (52.97)	5,345,864 (53.78)	<0.001	0.016	159,440 (52.97)	163,407 (54.29)	<0.001	0.026
Male	126991 (42.19)	4,012,384 (40.36)	<0.001	0.037	126,991 (42.19)	121,342 (40.31)	<0.001	0.038
Race								
White	227078 (75.44)	6,242,497 (62.80)	<0.001	0.276	227,078 (75.44)	227,080 (75.44)	0.995	<0.001
Black or African American	14393 (4.78)	1,265,043 (12.73)	<0.001	0.284	14,393 (4.78)	14,403 (4.79)	0.952	<0.001
Asian	9277 (3.08)	401,613 (4.04)	<0.001	0.052	9277 (3.08)	9518 (3.16)	0.074	0.005
Socioeconomic status								
Problems related to education and literacy	70 (0.02)	2249 (0.02)	0.821	<0.001	70 (0.02)	65 (0.02)	0.667	0.001
Problems related to employment and unemployment	159 (0.05)	7033 (0.07)	<0.001	0.007	159 (0.05)	221 (0.07)	0.001	0.008
Occupational exposure to risk factors	65 (0.02)	4444 (0.05)	<0.001	0.013	65 (0.02)	116 (0.04)	<0.001	0.010
Problems related to housing and economic circumstances	420 (0.14)	20,146 (0.20)	<0.001	0.015	420 (0.14)	655 (0.22)	<0.001	0.018
BMI								
<18.5	2369 (0.79)	94,067 (0.95)	<0.001	0.017	2369 (0.79)	2345 (0.78)	0.726	0.001
18.5–24.9	26,000 (8.64)	1,030,146 (10.36)	<0.001	0.059	26,000 (8.64)	26,001 (8.64)	0.996	<0.001
25–29.9	37,405 (12.43)	1,260,843 (12.68)	<0.001	0.008	37,405 (12.43)	37,394 (12.42)	0.966	<0.001
≥30	56,089 (18.63)	1,495,561 (15.05)	<0.001	0.096	56,089 (18.63)	56,072 (18.63)	0.955	<0.001
Medical utilization								
Outpatient	176236 (58.55)	5,000,375 (50.30)	<0.001	0.166	176,236 (58.55)	176,241 (58.55)	0.990	<0.001
Emergency	26163 (8.69)	807,020 (8.12)	<0.001	0.021	26,163 (8.69)	25,873 (8.60)	0.183	0.003
Hospitalization	17062 (5.67)	530,451 (5.34)	<0.001	0.015	17,062 (5.67)	19,665 (6.53)	<0.001	0.036
Comorbidities								
Hypertensive disease	56120 (18.64)	1,672,198 (16.82)	<0.001	0.048	56,120 (18.64)	56,125 (18.65)	0.987	<0.001
Ischemic heart disease	13008 (4.32)	366,346 (3.69)	<0.001	0.032	13,008 (4.32)	13,013 (4.32)	0.975	<0.001
Cerebrovascular diseases	5317 (1.77)	170,194 (1.71)	0.024	0.004	5317 (1.77)	5717 (1.90)	<0.001	0.010
Diabetes mellitus	26415 (8.78)	714,631 (7.19)	<0.001	0.059	26,415 (8.78)	27,322 (9.08)	<0.001	0.011
Disorders of lipoprotein metabolism	47160 (15.67)	1,374,473 (13.83)	<0.001	0.052	47,160 (15.67)	50,420 (16.75)	<0.001	0.029
Liver disease	8393 (2.79)	169,567 (1.71)	<0.001	0.073	8393 (2.79)	6620 (2.20)	<0.001	0.038
Depressive disease	16713 (5.55)	464,827 (4.68)	<0.001	0.040	16,713 (5.55)	16,776 (5.57)	0.723	0.001
History of nicotine dependence	9235 (3.07)	265,332 (2.67)	<0.001	0.024	9235 (3.07)	9625 (3.20)	0.004	0.007
Medication								
Hormones/synthetics/ modifiers	91807 (30.50)	2,138,608 (21.51)	<0.001	0.206	91,807 (30.50)	91,810 (30.50)	0.993	<0.001
Antirheumatics	47409 (15.75)	1,043,390 (10.50)	<0.001	0.156	47,409 (15.75)	37,161 (12.35)	<0.001	0.098

**Abbreviations:** BMI, body mass index; PSM, propensity score matching; SMD, standardized mean difference.

**Table 2** Risk of Dermatomyositis in Psoriasis Patients Compared to Non-Psoriasis Patients

	<b>Psoriasis N = 301018</b>	<b>Non-Psoriasis N = 301018</b>	<b>HR (95% CI)</b>
Model 1	436	143	2.69 (2.23–3.25)
Model 2	436	141	2.73 (2.26–3.30)
Model 3	436	159	2.41 (2.01–2.89)

**Notes:** Model 1: Propensity matching by age, sex, race, socioeconomic status, BMI (body mass index), and medical utilization. Model 2: Propensity matching by age, sex, race, socioeconomic status, BMI, medical utilization, and comorbidities. Model 3: Propensity matching by age, sex, race, socioeconomic status, BMI, medical utilization, comorbidities, and medication.

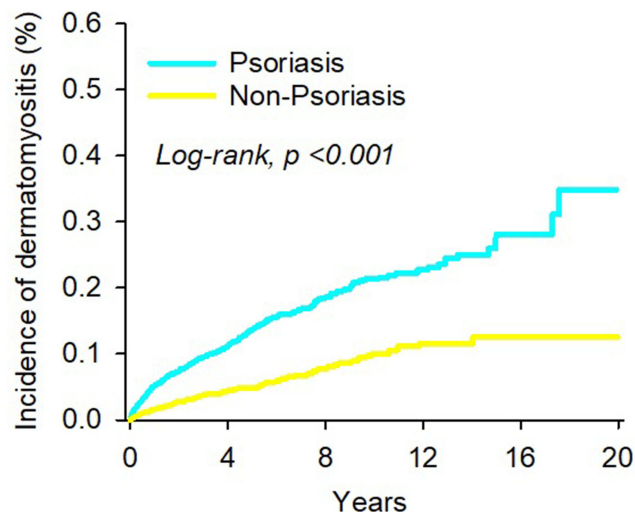
**Abbreviations:** HR, hazard ratio; CI, confidence intervals.

## Influence of PsA and Biological Agents Use on Dermatomyositis Risk

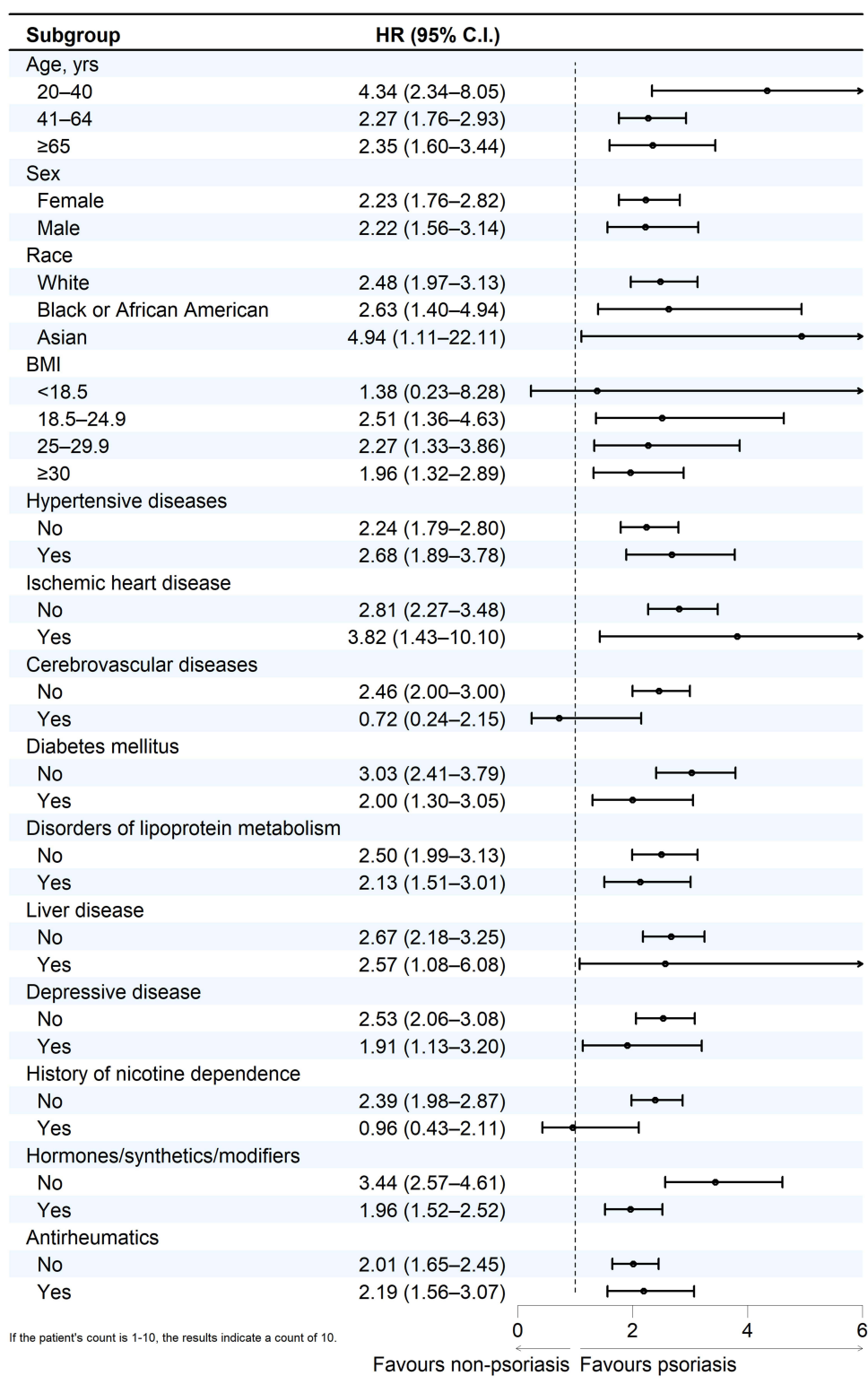
Patients with PsA exhibited a significantly increased risk of developing dermatomyositis compared to those without PsA (HR, 1.73; 95% CI: 1.32–2.28). There was no significant difference in the risk of developing dermatomyositis between psoriatic patients who had been treated with biological agents, including TNFi, IL-17i, and IL-12/23i, and those who were naïve to such treatments (HR, 1.35; 95% CI, 0.85–2.13). Despite this, Kaplan-Meier survival analysis revealed a significantly higher incidence of dermatomyositis among psoriatic patients who had undergone biological agent therapy ( $P < 0.001$  in the Log rank test) compared to those who were biological agent-naïve (Figure 4). Among the different types of biological agents, psoriatic patients treated with IL-17i showed a significantly elevated risk of developing dermatomyositis (HR, 5.79; 95% CI, 1.57–21.31) (Table 3).

## Risk of Dermatomyositis in Different TriNetX Network Database

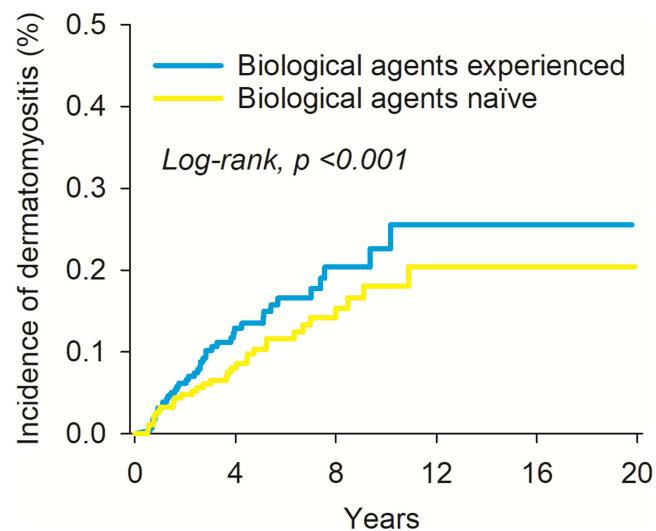
The risk of dermatomyositis in patients with psoriasis compared with that in patients without psoriasis was further explored in different racial population databases. In the European, Middle East, and Africa (EMEA) network, including Bulgaria, Germany, Italy, Lithuania, Malaysia, Poland, Spain, and the UK, as well as the APAC (Asia-Pacific) network, including Australia, India, Malaysia, Singapore, and Taiwan, patients with psoriasis showed a significantly higher risk of developing dermatomyositis than those without psoriasis (HR (95% CI): 4.77 (1.40–16.10) and 2.50 (1.33–4.66), respectively) (Table 4).



**Figure 2** Kaplan–Meier analysis for risk of dermatomyositis among patients with psoriasis compared with the non-psoriasis group.



**Figure 3** Forest plots for subgroup analysis of risk of dermatomyositis exposed to psoriasis compared to the non-psoriasis group.  
**Abbreviation:** BMI, body mass index.



**Figure 4** Kaplan–Meier analysis for risk of dermatomyositis between psoriatic patients experienced biological agent treatment and those naïve to biological agents. The biological agents included tumor necrosis factor inhibitors (TNFi), interleukin 17 inhibitors (IL-17i) and interleukin 12/23 inhibitors (IL-12/23i).

## Discussion

In this retrospective study, the effect of psoriasis on the incidence of dermatomyositis was investigated using a propensity score-matched cohort from the TriNetX network. The risk of dermatomyositis in patients with psoriasis was significantly higher than that in patients without psoriasis, after adjusting for various potential confounding variables. The psoriatic patients with PsA or those experienced treatment of IL-17i exhibited a higher risk of developing dermatomyositis compared to those who did not use biologics.

**Table 3** Risk of Dermatomyositis in Different Groups of Psoriasis Patients

	N	No. of Event	HR (95% CI)
Group			
Without PsA	76802	83	Reference
With PsA	76802	138	1.73 (1.32–2.28)
Group			
Biological agents naïve	30191	33	Reference
Biological agents experienced	30191	41	1.35 (0.85–2.13)
Group			
Biological agents naïve	24113	23	Reference
TNFi	24113	29	1.29 (0.75–2.23)
Group			
Biological agents naïve	5190	10	Reference
IL-17i	5190	12	5.79 (1.57–21.31)
Group			
Biological agents naïve	4093	10	Reference
IL-12/23i	4093	10	2.56 (0.66–9.93)

**Notes:** TNFi: Etanercept, Adalimumab, Infliximab; IL-17i: Secukinumab, Ixekizumab; IL-12/23i: Ustekinumab. If the patient's count is 1–10, the results indicate a count of 10.

**Abbreviations:** HR, hazard ratio; CI, confidence intervals; PsA, psoriatic arthritis; TNFi, tumor necrosis factor inhibitors; IL-17i, interleukin 17 inhibitors; IL-12/23i, interleukin 12/23 inhibitors; N/A, not applicable.



**Table 4** Risk of Dermatomyositis in Psoriasis Patients Compared to Non-Psoriasis Patients in Different TriNetX Network Database

	Psoriasis		Non-Psoriasis		HR (95% CI)
	N	Number of Events	N	Number of Events	
EMEA network	21206	19	21,206	10	4.77 (1.40–16.10)
APAC network	10099	41	10,099	13	2.50 (1.33–4.66)

**Notes:** If the patient's count is 1–10, the results indicate a count of 10. EMEA (Europe, Middle East, and Africa) includes the countries/regions of Bulgaria, Germany, Italy, Lithuania, Malaysia, Poland, Spain, and United Kingdom. APAC (Asia-Pacific) includes the countries/regions of Australia, India, Malaysia, Singapore, and Taiwan.

**Abbreviations:** HR, hazard ratio; CI, confidence intervals.

The occurrence of dermatomyositis in patients with psoriasis has been previously reported in separated cases.<sup>10</sup> This is the first study to provide evidence that patients with psoriasis have an elevated risk of dermatomyositis based on a large population cohort. Both psoriasis and dermatomyositis are systemic autoimmune inflammatory diseases, with cutaneous manifestations serving as primary indicators of both disorders. Clinically, both psoriasis and dermatomyositis can present with a rash accompanied by cutaneous keratosis on the extended sides of the knee and elbow. The pathogenesis of psoriasis and dermatomyositis remains incompletely understood, but genetic background, environment stimuli and immune imbalance were thought to play important roles in it.<sup>1,6</sup> Genome-wide association studies have identified numerous susceptible loci for psoriasis and dermatomyositis.<sup>14,15</sup> Although there is no reported overlap in susceptible loci for these two diseases, the MHC was found to be the major genetic region associated with both psoriasis and dermatomyositis.<sup>14,15</sup> In terms of external triggers for induction of skin lesions, Koebner phenomenon which describes the onset of skin lesions resulting from physical stress, injury or trauma would be stimuli for onset both of the two diseases.<sup>9</sup> In addition, drug and viral infection have been identified as established environmental trigger factors to both diseases.<sup>2,6</sup> For dermatomyositis, ultraviolet (UV) radiation is proposed as a trigger for the occurrence of skin lesions.<sup>1</sup> UV exposure or sunlight exposure was found to be associated with dermatomyositis flares.<sup>16</sup> However, the UV-based phototherapy, including UVB or psoralen UVA (PUVA) is effective for psoriasis treatment and widely applied clinically.<sup>17</sup> Consequently, it is proposed that the UV exposure may be imputed to the occurrence of dermatomyositis among patients with psoriasis under UV phototherapy.

Aberrant immune response plays a crucial role in the pathogenesis of dermatomyositis, psoriasis, and autoimmune inflammatory diseases. Common cellular and cytokine imbalances, such as dendritic cells and IFN, are shared by these two diseases. In psoriasis, dendritic cells play a key role in both the onset and maintenance stages of psoriasis.<sup>18</sup> Increased infiltration of pDC has been identified in the skin lesions of psoriasis patients compared to the normal skin of healthy controls.<sup>19</sup> In the early phase of psoriasis, pDCs produce IFN and TNF- $\alpha$ , which causes the maturation of resident dermal DC and the differentiation of monocytes into inflammatory DC (iDC). Increased iDCs produce cytokines, such as IL-23, IL-12, and TNF- $\alpha$ , which activate the differentiation of naive T cells into Th17 and Th22 cells. The secretion of IL-17 and IL-22 from Th-17 and Th-22 can induce the proliferation and abnormal differentiation of keratinocytes, which act as the main immune cells in psoriasis.<sup>18</sup> Similar to psoriasis, IFNs and DCs play a pivotal role in triggering and perpetuating dermatomyositis.<sup>20</sup> Various subsets of dendritic cells have been recently identified in skeletal muscle and skin lesions in dermatomyositis. IFN-inducible proteins, such as CXC chemokines (CXCL9, CXCL10, and CXCL11), are commonly overexpressed in dermatomyositis skin and muscle.<sup>21</sup> In addition, these two diseases share signaling pathways, such as the IL-17-IL-23 axis. The central role of the IL-17-IL-23 axis in the pathogenesis of psoriasis has been established in many previous studies. Biological agents targeting inflammatory cytokines, including IL-17 and IL-23, have been widely used in psoriasis therapy.<sup>8,22</sup> Recent studies have reported IL-17-IL-23 axis also participates in the onset of dermatomyositis. The infiltration of Th17 cells in cutaneous lesions of dermatomyositis implies an activating role of IL-17.<sup>23</sup> Increased serum IL-17 levels have been identified in dermatomyositis and are associated with disease activity.<sup>24</sup> In a murine model of myositis, IL-23 was found to mediate the muscle damage in myositis.<sup>25</sup> The IL-17-IL-23 axis is also recognized for its significant role in the pathogenesis of PsA. Targeting this axis has been shown to ameliorate

both musculoskeletal and cutaneous symptoms in patients with PsA. Prior research indicates that severe psoriasis is associated with a higher prevalence of PsA.<sup>26</sup> The heightened activity of the IL-17-IL-23 axis in psoriatic patients with PsA, as compared to those without PsA, potentially confers an increased risk of developing dermatomyositis, which was observed in the present study.

The psoriatic patients who had been treated with biological agents, especially IL-17i, showed a higher risk of developing dermatomyositis than those who did not. As mentioned above, psoriasis and dermatomyositis share common inflammatory cytokines such as IL-17 and TNF- $\alpha$ . Biologics targeting these cytokines have been used to treat both diseases. Paradoxically, the application of biologics in patients with psoriasis increases the risk of dermatomyositis. There have been several previous reports on the association of biologic treatments, such as IL-17i or TNFi, with the occurrence or exacerbation of dermatomyositis in patients with psoriasis.<sup>11,12</sup> Similar contradictory reactions have also been observed with the use of IL-17 inhibitors to induce systemic lupus erythematosus. The mechanism by which biological use increases the risk of dermatomyositis remains elusive. Biologics targeting one cytokine can alter the balance of the inflammatory circuit, leading to the accumulation of other inflammatory cytokines. This is so-called “cytokine shift” or “paradoxical reaction” hypothesis. For example, the TNFi or IL-17i targeting TNF or IL-17 may indirectly influence other cytokines that interact with these targets, including type I IFN. This interaction could potentially elevate the risk of developing dermatomyositis. On the other hand, the psoriasis patients experience biological agent therapy may have severe disease condition and have higher activities of IL-17-IL-23 axis, and thus have higher risk to develop dermatomyositis. However, since the dosage and duration of biological agent use could not be adjusted, the results based on whether biological agents experience may not be reliable. Furthermore, the relatively small sample sizes within different categories of biological agents can also affect the reliability of the results.

The present study has some limitations. First, psoriasis and dermatomyositis were diagnosed according to the International Classification of Diseases codes in the TriNetX network. Miscoding of these two diseases is occasionally observed in the clinical setting. Some dermatomyositis patients present without muscle involvement and only show cutaneous manifestations, which are called clinically amyopathic dermatomyositis (CADM). Under these circumstances, the cutaneous symptoms of dermatomyositis, especially those affecting the extensor surface of the joint (Gottron’s sign), may be misdiagnosed as psoriasis. Second, the severity of psoriasis was not adjusted for in the subgroup analysis, which may have affected the risk of dermatomyositis.

## Conclusion

In conclusion, the current study is the first to revealed that psoriasis increased the risk of dermatomyositis development based on a large population. The psoriatic patients with PsA or those who had received IL-17i treatment demonstrated a significantly higher risk of developing dermatomyositis. These findings suggest the need for clinicians to screen patients with psoriasis for dermatomyositis, especially when they present with atypical rashes. The mechanism underlying the association between these two diseases needs to be explored in the future.

## Funding

This study was supported by Shanghai Sixth People’s Hospital Fund (ynts202307) and Bethune Charity Foundation (J202301E036).

## Disclosure

The authors report no conflicts of interest in this work.

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