Beyond the Skin

Navigating the Association of Obesity and Other Comorbidities in Psoriasis

KEY TAKEAWAYS

for Dermatology Providers

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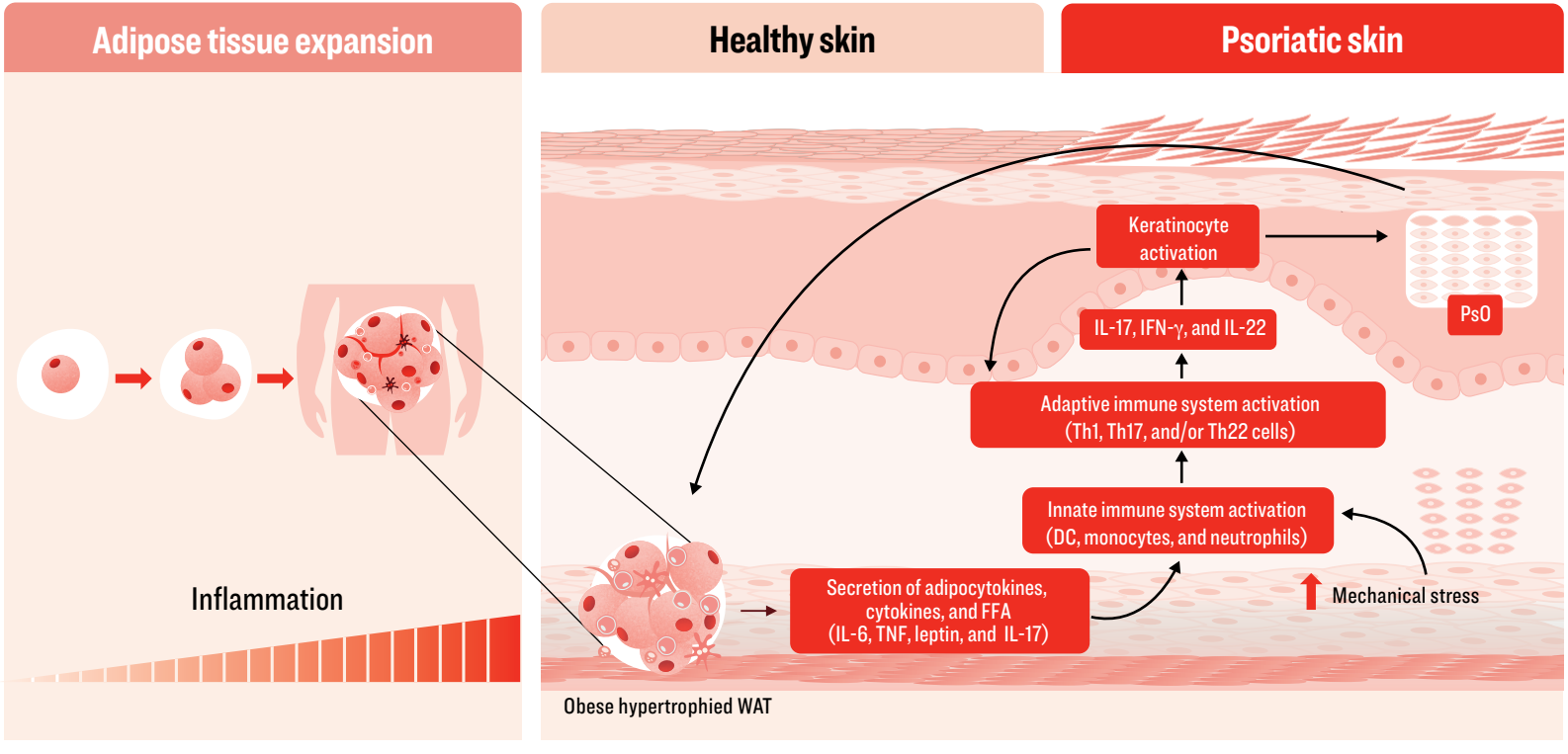
Obesity

Among patients with PsO, approximately 38%-50% have comorbid obesity[a-c,1-3]

Patients With Comorbid Obesity Are More Likely to Have

- A lower response to some biologics for PsO[b,4,5]
- 1.5× to 3× higher risk of PsA[c,6]
- High-impact area involvement[d,7,8,14]
- Impaired QoL[e,9]

Obesity-Associated Low-Grade Inflammation May Have a Role in the Pathogenesis of PsO[10-13,22]

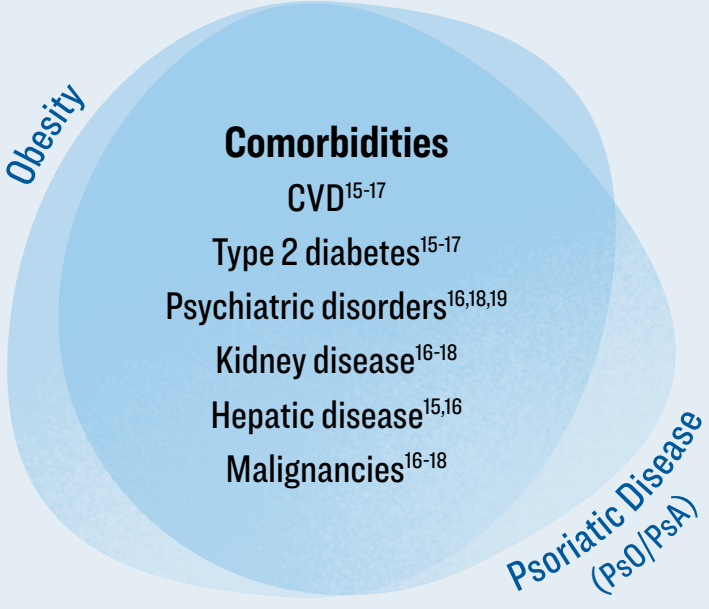


[a]NHANES is a nationally representative survey of the US civilian, non-institutionalized population conducted by the CDC NCHS. The cross-sectional survey includes an in-home interview to obtain sociodemographic characteristics, medical history, and a physical examination and laboratory measures, including BMI, taken at a mobile examination center. Patients self-reported being diagnosed with PsO; [b]Obesity defined as BMI ≥30 kg/m² [21]; [c]Obesity definition ranged from BMI ≥30 kg/m² to <35 kg/m²; [d]Definition of obesity varied between studies. Some studies involved a small number of patients; [e]Obesity defined as BMI ≥28 kg/m².

Obesity, Inflammation, and Shared Comorbidities in PsO

Obesity and Psoriatic Disease Have Overlapping Comorbidities

Worsening of disease[14]



Note: Additional comorbidities may exist beyond those listed here.

Adipose Tissue Dysregulation Contributes to Systemic Inflammation

Qualitative and quantitative changes in adipose tissue signal production lead to the impairment of multiple organs and their functions[19,20]

- Type 2 diabetes[20]
- MAFLD[a,20,21]
- Hepatocarcinoma[20]
- Coronary heart disease[18]
- CV risk[22]
- Atherosclerosis/ atherothrombosis[23,24]
- **Dermatological diseases** (eg, PsO,[25] AD,[25] and HS[24])
- Altered hematopoiesis[20]
- Osteoporosis[20]
- Arthritis[23]
- Sarcopenia[20]
- Altered food intake and energy expenditure[20]

[a]Also known as NAFLD.[14]

Obesity, Inflammation, and Shared Comorbidities in PsO

In Patients With Clear Skin (PASI ≤2) Following Biologic Therapy, There is Residual Inflammation Associated With Obesity and Fatty Liver Disease

A prospective observational study of 3 international cohorts evaluated "residual inflammation"—hsCRP ≥2 mg/L—in patients with high-risk atherosclerosis whose inflammatory markers remained elevated despite biologic therapy[26]

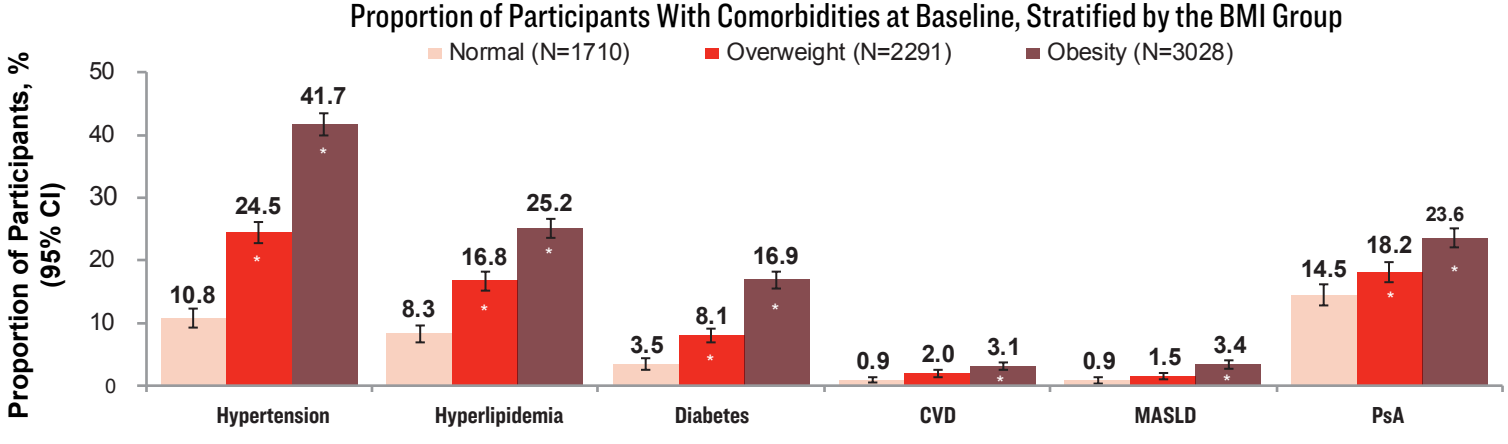
Spanish cohort	American cohort	Swedish cohort	OVERALL RESIDUAL INFLAMMATION
EDSAP N=71	**PACI** N=71	**DermaReg** N=67	
42.3%	35.2%	26.4%	36.3%

In patients with residual inflammation in the 3 cohorts:

- BMI was higher
- Hepatic Steatosis Index was significantly higher

Residual inflammation was observed in 36.3% of patients and was significantly associated with higher BMI, MASLD, increased baseline systemic inflammation, and visceral adipose tissue

Untreated Obesity and Overweight Are Associated With a Higher Prevalence of Comorbidities in Patients With PsO[27]



Managing Obesity in Patients With PsO

Evidence-Based Tools and Guidelines for Weight Management in PsO

The AAD/NPF recommendations[a,28]

- INFORM patients regarding the association between metabolic syndrome components and PsO
- Advise on lifestyle interventions
- Encourage engagement with the patient's PCP
- Communicate with the patient's PCP for appropriate evaluation and treatment

Specific interventions that are available for patients include[16,29,31-33]:

Diet and Exercise (eg, calorie reduction, diet composition, aerobic exercise, and resistance training)[29,31,32]	Pharmacological Interventions (eg, weight-loss medications)[16,29]
Psychological and Behavioral Interventions (eg, self-monitoring, and motivational interviewing)[29,31,32]	Surgical Interventions (eg, gastric bypass)[29,33]

Consensus statements developed by dermatology providers, offers guidance for PsO treatment and optimizing weight management[b,30]

Strength A Statements

Consistent, good quality, and patient-oriented evidence

PsO is associated with obesity	Obesity is an independent risk factor for the development of PsO
Patients with PsO and obesity have a higher risk of diabetes, metabolic syndrome, and CVD	Obesity decreases efficacy of PsO treatment with biologics
Obesity may decrease efficacy and potentiate side effects of conventional oral PsO therapies	Obesity impacts drug survival for PsO therapies

Strength B Statements

Inconsistent, limited quality, and patient-oriented evidence

Weight control is an important part of PsO management	Treatment of obesity may improve efficacy of PsO therapies

Strength C Statements

Consensus, opinion, etc

Limited data exist for the potential impact of obesity on PDE4i and TYK2i efficacy	Patients with PsO and obesity may require larger quantities of topical therapies and may experience increased difficulty in applying medications and side effects

Dermatology providers should be encouraged to take ownership of weight management

[a]Based on the 2019 AAD/NPF guidelines, which are expected to be updated in 2025; [b]The content does not represent a complete list of all expert consensus statements.

Managing Obesity in Patients With PsO

USE THE 5As MODEL[34,35]

ASK	for permission to discuss weight and explore readiness to change
ASSESS	obesity-related risks and potential root causes of weight gain
ADVISE	on health risks and treatment options
AGREE	on health outcomes and behavioral goals
ASSIST	in accessing appropriate resources and providers and arranging follow-up appointments

Accurate Coding for Obesity Among Patients With PsO is Important for Patient Care and Overcoming Hurdles to Access[36,37]

Challenges
Long-held misconceptions hinder appropriate support and care[37,38]

Access to Care
Diagnostic coding and medical billing complexities may block access to obesity care[40]

Opportunities for Change
New advancements in obesity care offer a chance to enhance its visibility[39,41]

Obesity Medical Coding Essentials[42-44]

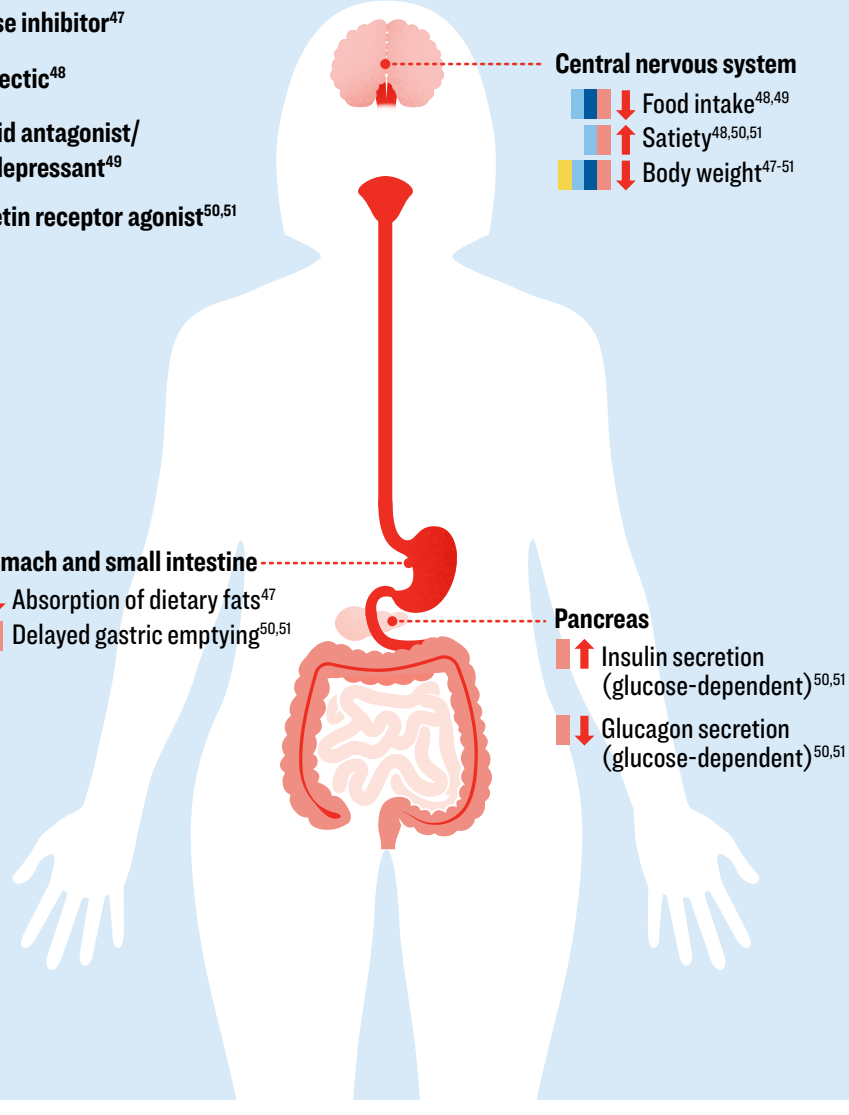
1. **ICD-10 Diagnostic code**
2. **Appropriate BMI code**
3. **Additional Z codes** (eg, for SDOH, screening, or counseling)
4. **CPT code for visit/counseling**

Diagnosis of obesity may help patients achieve optimal weight loss and meet other clinical outcomes[45,46]

Managing Obesity in Patients With PsO

Weight Management Therapies
Primary Physiological Actions

- Lipase inhibitor[47]
- Anorectic[48]
- Opioid antagonist/ antidepressant[49]
- Incretin receptor agonist[50,51]



Central nervous system
- ↓ Food intake[48,49]
- ↑ Satiety[48,50,51]
- ↓ Body weight[47-51]

Stomach and small intestine
- ↓ Absorption of dietary fats[47]
- Delayed gastric emptying[50,51]

Pancreas
- ↑ Insulin secretion (glucose-dependent)[50,51]
- ↓ Glucagon secretion (glucose-dependent)[50,51]

Common Adverse Reactions

Lipase inhibitor[a,47]
- Oily spotting
- Flatus with discharge
- Fecal urgency
- Fatty/oily stool
- Oily evacuation
- Increased defecation
- Fecal incontinence

Anorectic[b,48]
In adults:
- Paresthesia
- Dizziness
- Dysgeusia
- Insomnia
- Constipation
- Dry mouth

Opioid antagonist/ antidepressant[c,49]
- Nausea
- Constipation
- Headache
- Vomiting
- Dizziness
- Insomnia
- Dry mouth
- Diarrhea

Incretin receptor agonist[d,50,52-55]
- Nausea
- Diarrhea
- Vomiting
- Constipation
- Abdominal pain

Note: Not a comprehensive list of all physiological actions of the listed therapies and not all actions have been studied in humans.

[a]Adverse reactions occurring at ≥5% and at least 2 times that of placebo; [b]Adverse reactions occurring at ≥5% and at least 1.5 times that of placebo; [c]Adverse reactions occurring at ≥5%; [d]Adverse reactions typically occurring at a rate of >10%.

Cardiovascular Disease

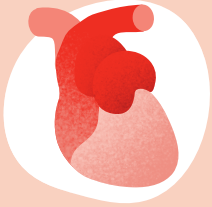
PsO is an Independent Risk Factor for CVD[56,57]

Patients with PsO are up to 50% more likely to develop CVD compared to those without PsO[58]

Severe PsO confers the highest CV risk
(compared with control subjects), including up to:[58]

- *3-fold* increased odds of myocardial infarction
- *60%* higher odds of stroke
- *40%* higher odds of CV-related mortality

Biologic therapy for PsO is associated with *reduced coronary inflammation*[59]



Premature Mortality in Severe PsO: CVD

Patients with severe PsO[a] have a reduced life expectancy, *dying ~5 years earlier than expected*[60,61]

CVD is the most common cause of this premature mortality[61]

This increased mortality persists independent of traditional CV risk factors[61]

PsO and cardiometabolic disorders may be associated with each other via **systemic inflammation**[62]

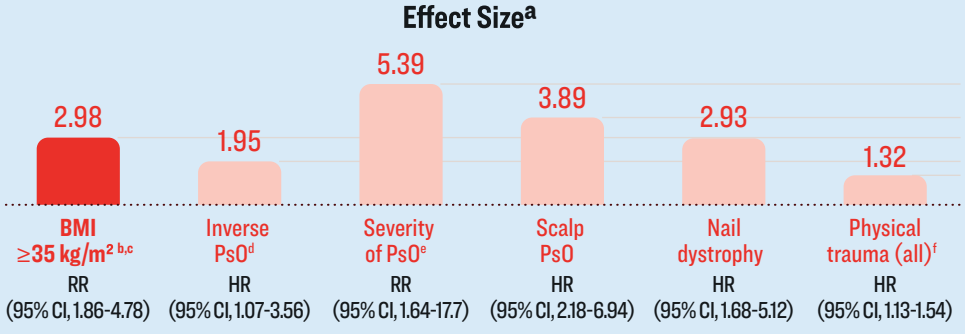
Obesity increases the risk of CVD in PsO[63]

Weight loss may improve PsO while also reducing markers of CV risk[64]

[a]Requiring systemic therapy or phototherapy.

Psoriatic Arthritis

Risk Factors for PsA[6]



Note: Risk factors for the development of PsA in patients with PsO are from cohort studies, unless otherwise stated.

Other risk factors may include family history of PsA, smoking, and duration of PsO

Treatment Considerations[65]

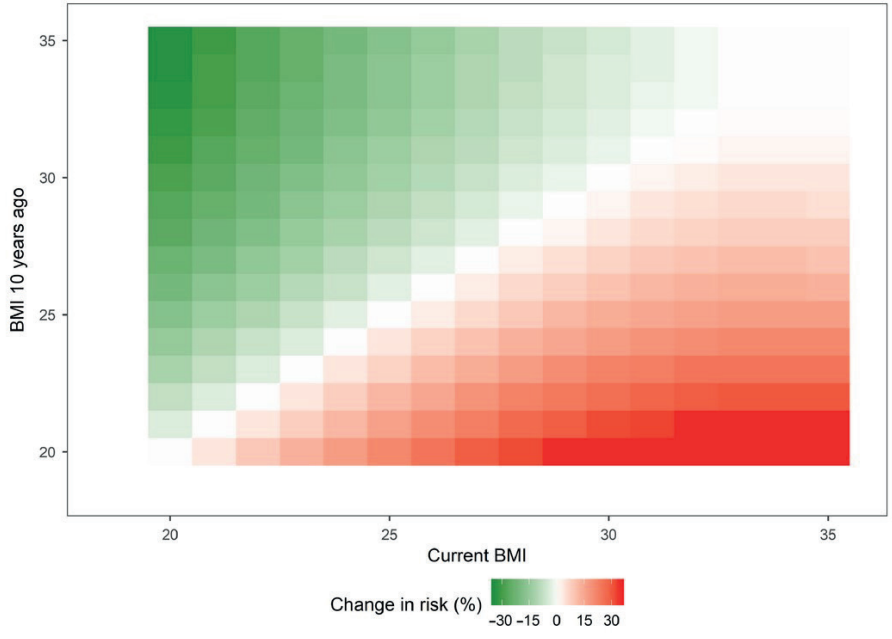
In PsA, irreversible joint damage can:

- happen with a **delay in diagnosis of just** *6 months*
- lead to **worse long-term physical function**

Treatment of PsA leads to improvements in QoL for patients[66]

Weight Loss Reduces the Cumulative Risk of Developing PsA in Patients With PsO[68]

Risk Calculator for BMI and Developing PsA in Patients With PsO



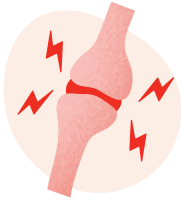
A Simple Mnemonic: PsA[67]

Joint

PAIN • STIFFNESS • AXIAL

after waking in the morning, or after a period of inactivity. Swelling/Sausage digit (dactylitis)

involvement



[a]Adjusted for other covariates; [b]BMI ≥35.0 kg/m2 vs. normal (BMI <25.0 kg/m2); [c]Time varying exposure; dIntergluteal/perianal involvement; [e]PASI score >20 vs. <10; [f]Values based on the general population.

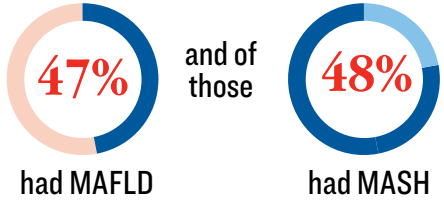
Hepatic Disease

Patients With PsO Are at an Increased Risk of Developing Hepatic Disease

MAFLD encompasses a spectrum of liver diseases ranging from steatosis, which is relatively benign, to MASH — a severe form where fatty infiltration is accompanied by inflammation and hepatocellular ballooning[69]

There may be an interplay between **PsO and MAFLD** in their **pathogenic mechanisms**[28,69-71]

Patients with PsO and PsA (N=103) are at an **increased risk of MASH**[72]



Patients with PsO have a **higher risk** of MAFLD compared with non-PsO controls[71]: **OR, 1.67 (95% CI, 1.03-2.70), p=.04**[71]

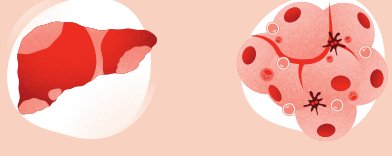
- Patients with MASH are **at risk** of progressing to advanced liver disease[69,70]
- MASH can result in **cirrhosis in 12%-25% of cases**[70]

Obesity and Hepatic Disease

Obesity is one of the **most important risk factors** for MAFLD[73,74]

It affects **~75%** of people with a BMI of 25.0-29.9 kg/m^2 and **>90%** of people with a BMI of ≥40.0 kg/m^2 [75,76]

Patients with psoriasis who also have diabetes (OR, 2.56; 95% CI, 0.53–12.49) or obesity (OR, 1.74; 95% CI, 0.96–3.15) are at an increased risk of developing NAFLD[77]



Depression

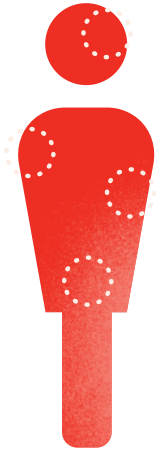
Patients With PsO are at Increased Risk of Developing Depression[78,79]



Social stigmatization is one possible cause of the association between PsO and depression[80,81]

Visible physical symptoms may result in low self-esteem, depression, and social isolation[80,81]

Sleep disturbance from PsO and pruritus is linked to depression and reduced QoL[82]



The interplay between stress and PsO creates a cycle where stress triggers PsO flares, which then elevate stress levels[80]

Levels of **pro-inflammatory cytokines** such as IL-17 and TNF-α **are elevated in both PsO and depression**[83-86]

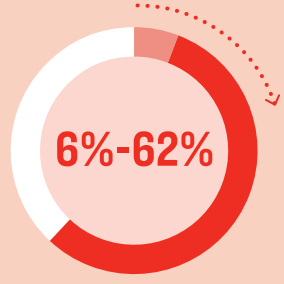
Impacts of Obesity on Depression in Patients with PsO

Obesity is associated with an increased risk of depression[88]

Shared inflammatory pathways between PsO and obesity may lead to **higher prevalence of depression**, and risk is highest in individuals with elevated BMI (BMI ≥30kg/m^2)[89-92]

Patients with PsO are about **1.5 times more likely** to have depression than those without PsO **(odds ratio 1.57; 95% CI: 1.40–1.76)**[87]

The **prevalence of depression** in patients with PsO ranges from **6%-62%**[87]



The risk of depression increases with severity of PsO[78]

Patients with severe PsO are **2.2× more likely** to have depression than patients with mild PsO[78]



Abbreviations

AAD=American Academy of Dermatology
AD=Atopic Dermatitis
BMI=Body Mass Index
BSA=Body Surface Area
cDAPSA=Clinical Disease Activity Index for Psoriatic Arthritis
CDC=Centers for Disease Control and Prevention
CHD=Coronary Heart Disease
CI=Confidence Interval
CPT=Current Procedural Terminology
CRP=C-Reactive Protein
CV=Cardiovascular
CVD=Cardiovascular Disease
DC=Dendritic Cells
EDSAP=Early Detection and Progression of Subclinical Atherosclerosis in Psoriasis
FFA=Free Fatty Acid
HAQ-DI=Health Assessment Questionnaire Disability Index
hsCRP=High-Sensitivity C-Reactive Protein
HR=Hazard Ratio
HS=Hidradenitis Suppurativa
HSI=Hepatic Steatosis Index
ICD-10=International Classification of Diseases, 10th Revision
IFN=Interferon
IL=Interleukin
MAFLD=Metabolic Dysfunction-Associated Fatty Liver Disease
MASH=Metabolic Dysfunction-Associated Steatohepatitis
MASLD=Metabolic Dysfunction-Associated Steatotic Liver Disease
NAFLD=Non-Alcoholic Fatty Liver Disease
NCHS=National Center for Health Statistics
NHANES=National Health and Nutrition Examination Survey
NPF=National Psoriasis Foundation
OR=Odds Ratio
PACI=Psoriasis Atherosclerosis and Cardiometabolic Disease Initiative
PAD=Peripheral Arterial Disease
PASI=Psoriasis Area and Severity Index
PCP=Primary Care Provider
PDE4i=Phosphodiesterase-4 Inhibitor
PsA=Psoriatic Arthritis
PsO=Psoriasis
PSOLAR=Psoriasis Longitudinal Assessment and Registry
QoL=Quality of Life
RR=Relative Risk
SD=Standard Deviation
SDOH=Social Determinants of Health
Th=T Helper
TNF-α=Tumor Necrosis Factor Alpha
TYK2i=Tyrosine Kinase 2 Inhibitor
WAT=White Adipose Tissue

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