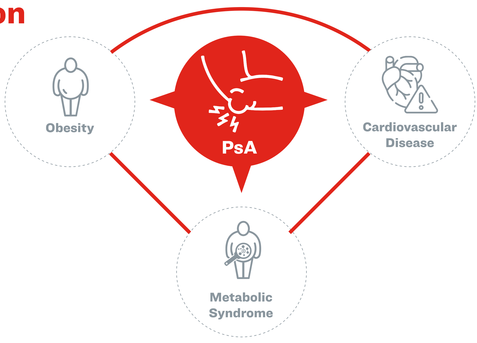
The Role of Systemic Inflammation in Psoriatic Arthritis and Its Metabolic and Cardiovascular Comorbidities

The Inflammatory Connection

At the center of PsA and some of its comorbidities is an association with inflammation. Both obesity and metabolic syndrome are characterized by persistent low-grade inflammation, largely due to the activity of visceral adipose tissue, which secretes proinflammatory cytokines.[1]

These overlapping inflammatory pathways involving **IL-2, IL-6, IL-17, IL-23, TNF-α,** and **IFN-γ** are believed to link PsA with metabolic and vascular dysfunction.[1]



Obesity

Up to **48% of patients with PsA** also have obesity [a,2,3]

In patients with PsA, comorbid obesity is associated with:

- Higher disease activity[4,5]
- Reduced response to some biologic therapies[1,6]
- Persistent inflammation, insulin resistance, and lipid abnormalities[1]

PsA patients with obesity are 2.5 to 3-fold less likely to be in remission/LDA[b,5]

Metabolic Syndrome

Affects **29%-46% of patients with PsA** – 1.6x more than in RA[1,7,8]

Persistent low-grade inflammation is a key driver, with increased adipose tissue promoting impaired[1,9]:

- Glycemic control
- Lipid metabolism

Metabolic syndrome is defined by the presence of visceral obesity, hyperlipidemia, hypertension, and/or dysglycemia[1,10]

Patients with metabolic syndrome are 44% less likely to achieve minimal disease activity[c,11]

Cardiovascular Disease

Affects **~19% of patients with PsA**

- PsA and metabolic syndrome are both **pro-inflammatory conditions that increase MACE risk[1]**
- Patients with PsA have a **43% higher CVD risk** vs. the general population[12,13]
  - **68%** increased risk of MI[12,13]
  - **22%** increased risk of cerebrovascular disease[12,13]

Drivers of CV risk in PsA:

High inflammatory burden[13,14]

High prevalence of traditional CV risk factors included in metabolic syndrome (hypertension, glucose intolerance, dyslipidemia, obesity)[13-15]

IL-6, IL-17, and TNF-α, are key cytokines contributing to endothelial dysfunction and vascular damage[15,16]

Obesity, metabolic syndrome, and cardiovascular disease share several inflammatory mediators and pathways with PsA.[1,15,16] These overlapping mechanisms may contribute to increased disease burden, variable treatment responses, and long-term outcomes.[1,4-6,11]

For your patients with PsA and comorbidities, consider a management approach that integrates treatment of both their rheumatic disease and associated comorbidities.

[a]The National Health and Nutrition Examination Survey (NHANES) is a nationally representative survey of the US civilian, non-institutionalized population conducted by the CDC National Center for Health Statistics (NCHS). The cross-sectional survey includes an in-home interview to obtain sociodemographic characteristics and medical history, and a physical examination and laboratory measures, including BMI, taken at a mobile examination center. Patients self-reported being diagnosed with psoriatic arthritis; [b]Remission/LDA was defined as Very Low Disease Activity (VLDA)/minimal disease activity (MDA) or Disease Activity in PSoriatic Arthritis (DAPSA) ≤4/≤14; [c]Based on multivariate regression (OR 0.56, p<.001) from an observational study in patients treated with anti-TNF-α.

Abbreviations: BMI=Body Mass Index; **CDC**=Centers for Disease Control and Prevention; **CV**=Cardiovascular; **CVD**=Cardiovascular Disease; **IFN-γ**=Interferon Gamma; **IL**=Interleukin; **LDA**=Low Disease Activity; **MACE**=Major Adverse Cardiovascular Event; **MI**=Myocardial Infarction; **OR**=Odds Ratio; **PsA**=Psoriatic Arthritis; **RA**=Rheumatoid Arthritis; **TNF-α**=Tumor Necrosis Factor Alpha.

References: 1. Williams JC, et al. *Ther Adv Musculoskelet Dis.* 2024;16:1759720X241271886. **2.** CDC NHANES Questionnaires, Datasets, and Related Documentation. https://wwwn.cdc.gov/nchs/nhanes/Default.aspx (2009-2020). Accessed January 30, 2024. **3.** Data on file. Lilly USA LLC. DOF-IX-US-0341. **4.** Galarza-Delgado DA, et al. *Int J Dermatol.* 2024;63(1):e1-e2. **5.** Leung Y, et al. *RMD Open.* 2023;9(3):e003157. **6.** Tournadre A, Beauger M. *Joint Bone Spine.* 2024;91(3):105647. **7.** Gupta S, et al.*Rheumatol Int.* 2021;41(2):275-284. **8.** Loganathan A, et al. *Int J Rheum Dis.* 2021;24(9):1112-1120. **9.** Atzeni F, et al. *Front Med (Lausanne).* 2021;8:735150. **10.** Grundy SM, et al. *Circulation.* 2005;112(17):2735-2752 (updated 112(17):e297-e298). **11.** Costa L, et al. *Immunol Res.* 2015;61(1-2):147-153. **12.** Polachek A, et al. *Arthritis Care Res.* 2017;69: 67-74. **13.** Karmacharya P, et al. *Ther Adv Musculoskelet Dis.* 2021;13:1759720X21998279. **14.** Eder L, et al. *Ann Rheum Dis.* 2016;75:1680-1686. **15.** Verhoeven F, et al. *Joint Bone Spine.* 2020;87(5):413-418. **16.** Radić M, et al. *Metabolites.* 2025;15(3):206.