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Beyond the Skin: Addressing Obesity & Cardiometabolic Risk in Psoriasis Management

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Disclosures

- **Alexa Hetzel, DMSc, PA-C:** Consulting/Speaking – AbbVie, Arcutis, BMS, Eli Lilly, Galderma, Incyte, Johnson & Johnson, Leo, Novartis, Pfizer, Regeneron/Sanofi, UCB; Clinical Research – AbbVie, Actelion, Amgen, Arcutis, BI Pharma, BMS, Brickell Biotech, Castle Bioscience, Celgene, CorEvitas, Dow Pharma, Eli Lilly, Incyte, Janssen, Leo Pharma, Menlo Therapeutics, Mindera, Novartis, PCORI, Pfizer, PSOLAR, Regeneron, Sanofi, Sun Pharma, Takeda, Target Derm, UCB

- **Michael Garshick, MD, MS:** Consulting – Kiniksa, Novo Nordisk; Funding – National Psoriasis Foundation, NIH, Pfizer

This activity may include discussion of off-label, investigational, or unapproved uses of drugs.

Learning Objectives

- Assess the shared pathophysiologic mechanisms linking obesity and PsO, and their impact on response to biologic therapies
- Implement evidence-based screening strategies (eg, BMI, waist circumference) for obesity and overweight in patients with PsO
- Evaluate available and emerging treatment strategies for PsO that also consider obesity and overweight to improve response and overall outcomes
- Address cardiometabolic risk in patients with comorbid PsO and obesity, including diabetes, metabolic syndrome, and cardiovascular disease, through comprehensive, multidisciplinary care

PsO = psoriasis; BMI = body mass index.

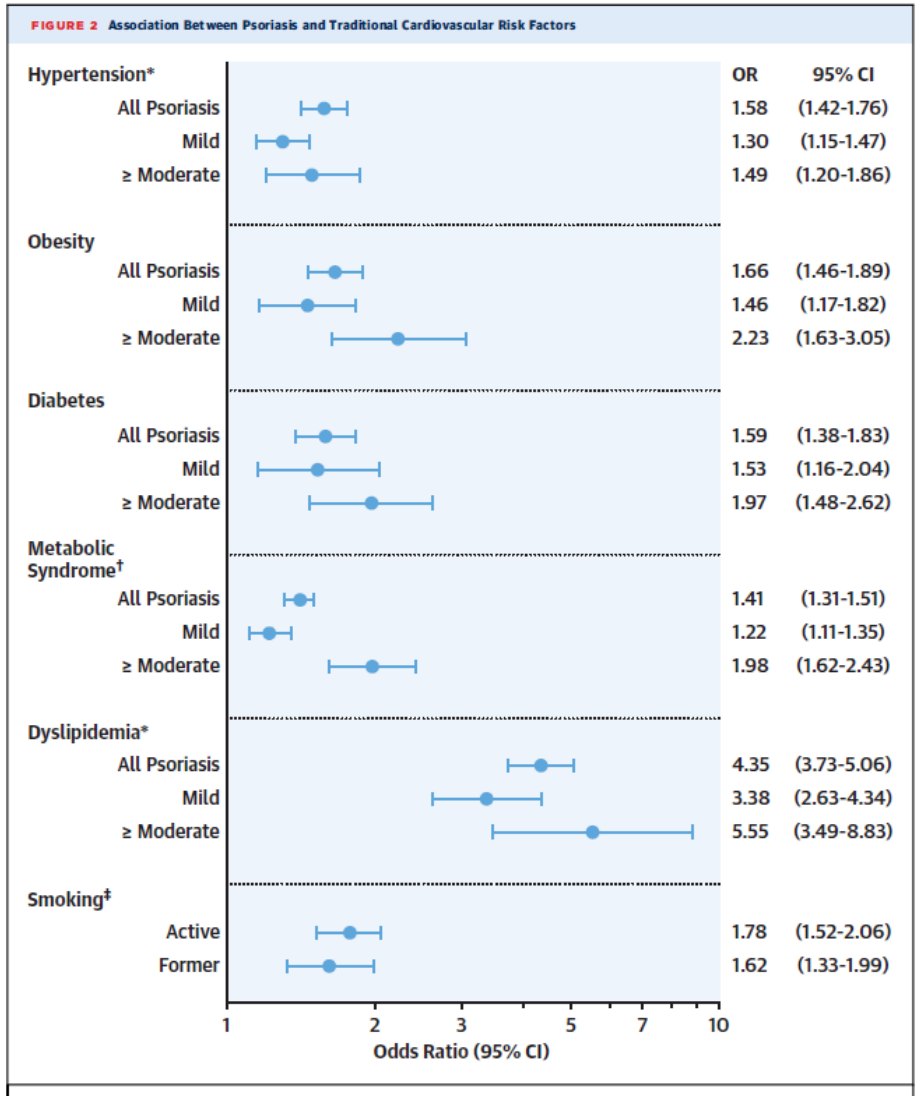
Introduction



- Psoriasis as a systemic disease
  - What is overweight?
  - What is obesity?
  - What roles do both play?
- How are these conditions connected?
- Clinical burden of obesity in psoriasis

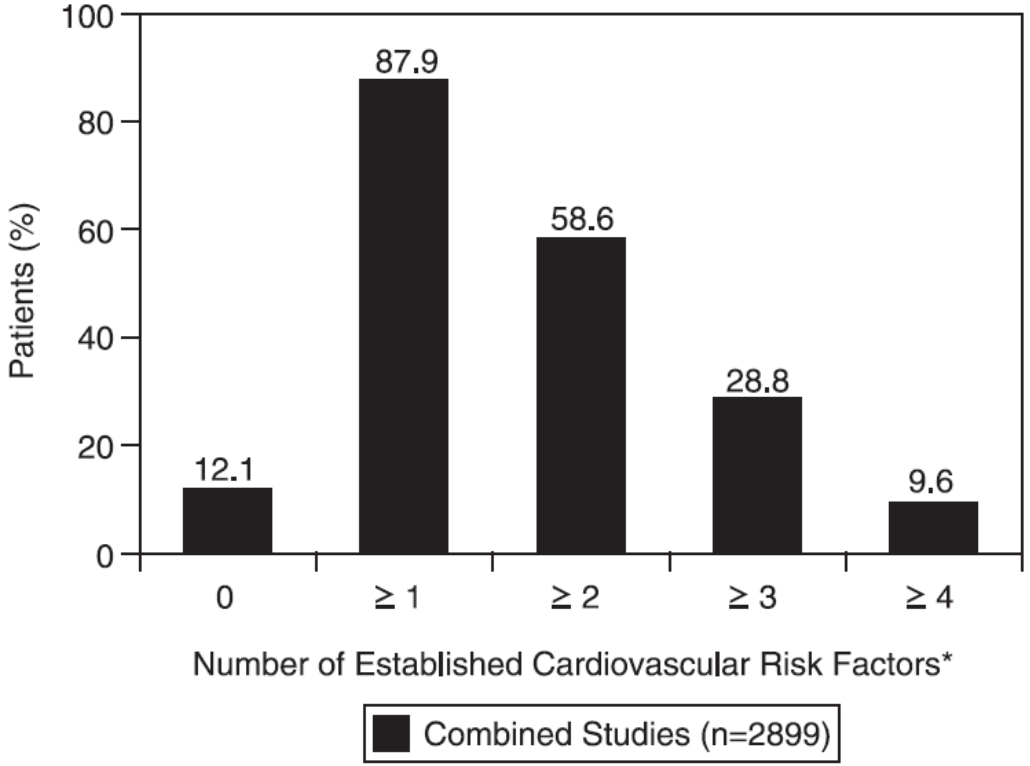
De Brandt E, Hillary T. *Psoriasis* (Auckl). 2022;12:113-126.

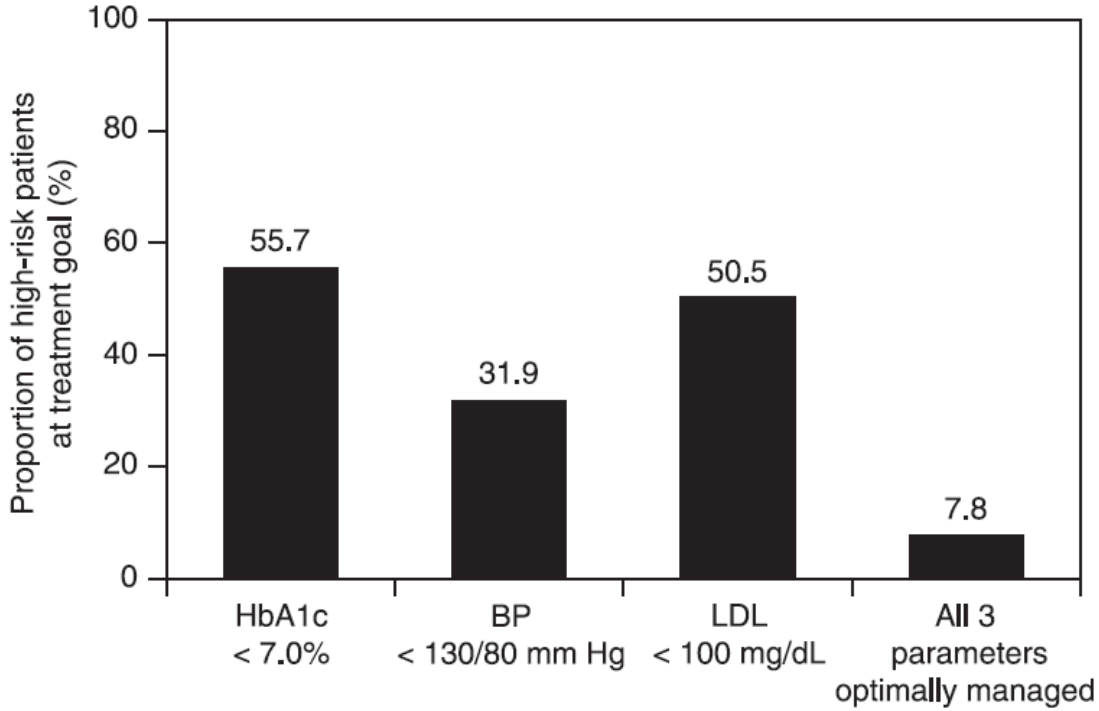
Traditional Cardiovascular Disease Risk Factors Are Elevated in Psoriasis



Garshick MS, et al. *J Am Coll Cardiol*. 2021;77(13):1670-1680.

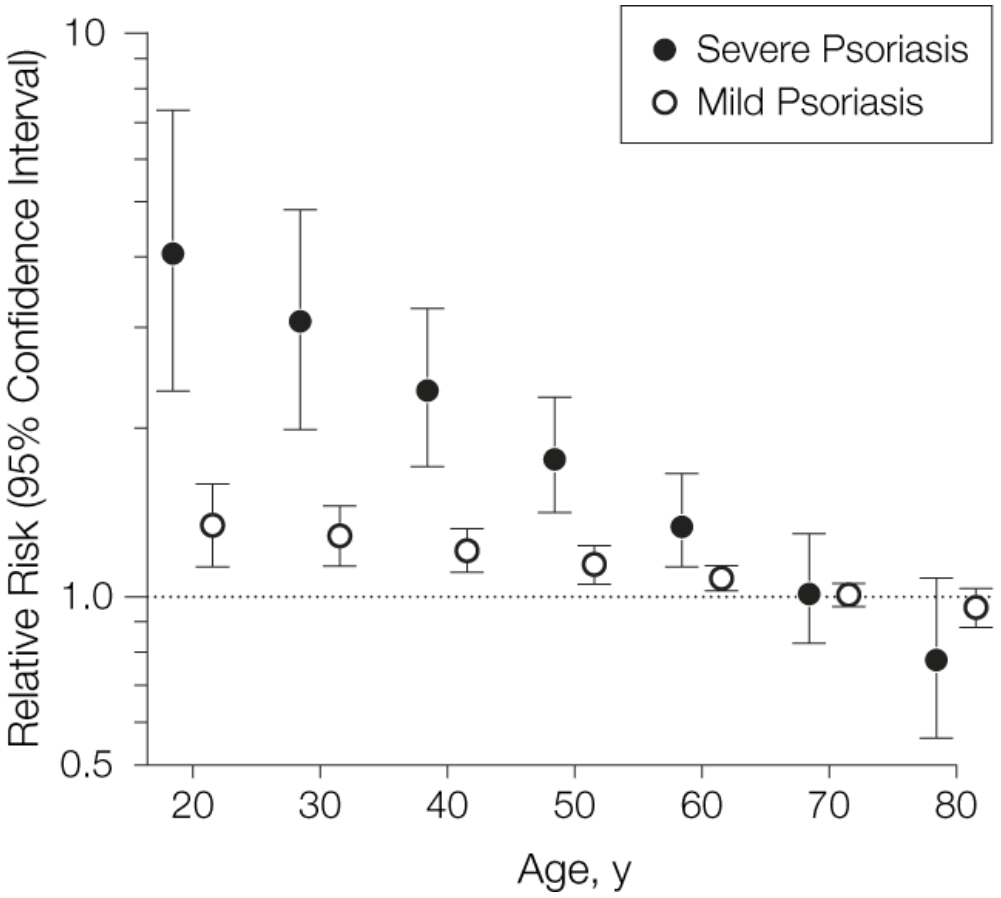
Recognize and Treat Traditional Cardiovascular Risk Factors

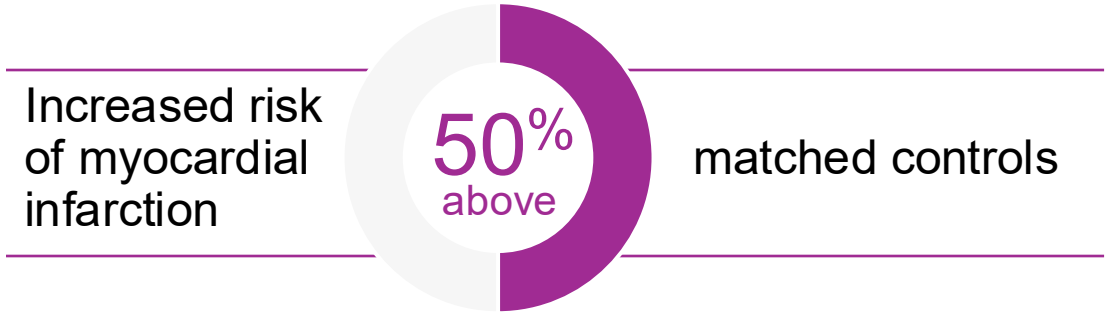




Kimball AB, et al. *J Am Acad Dermatol*. 2012;67(1):76-85.

Psoriasis Increases the Risk of Myocardial Infarction





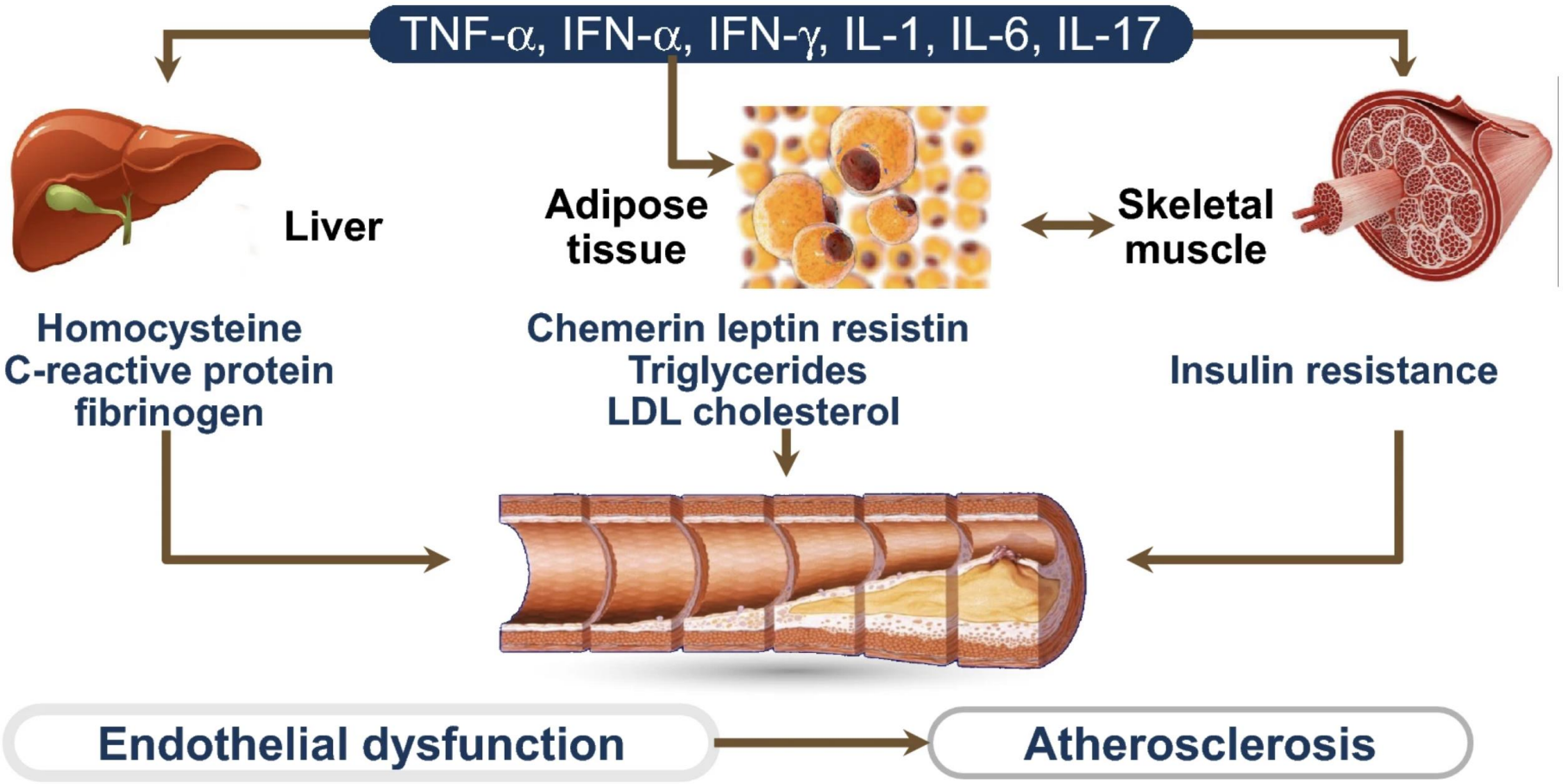
Young patients with severe psoriasis,



MI = myocardial infarction.

Gelfand JM, et al. *JAMA*. 2006;296(14):1735-1741.

Inflammatory Mediators Released from Psoriatic Lesions into the Systemic Circulation



TNF = tumor necrosis factor; IFN = interferon; IL = interleukin.

Bellinato F, et al. *Am J Clin Dermatol*. 2024;25(4):527-540.

Impact of Obesity on PsO Disease Severity and Progression

- Clinical consequences
  - Reduced biologic response
  - Suboptimal skin clearance
  - Drug survival

Kaushik SB, Lebwohl MG. *J Am Acad Dermatol*. 2019;80(1):27-40. Burshtein J, et al. *J Am Acad Dermatol*. 2025;92(4):807-815.

Obesity May Reduce Biologic Response in Psoriasis

2026 systematic review & meta-analysis | 12 studies | 4,200 patients

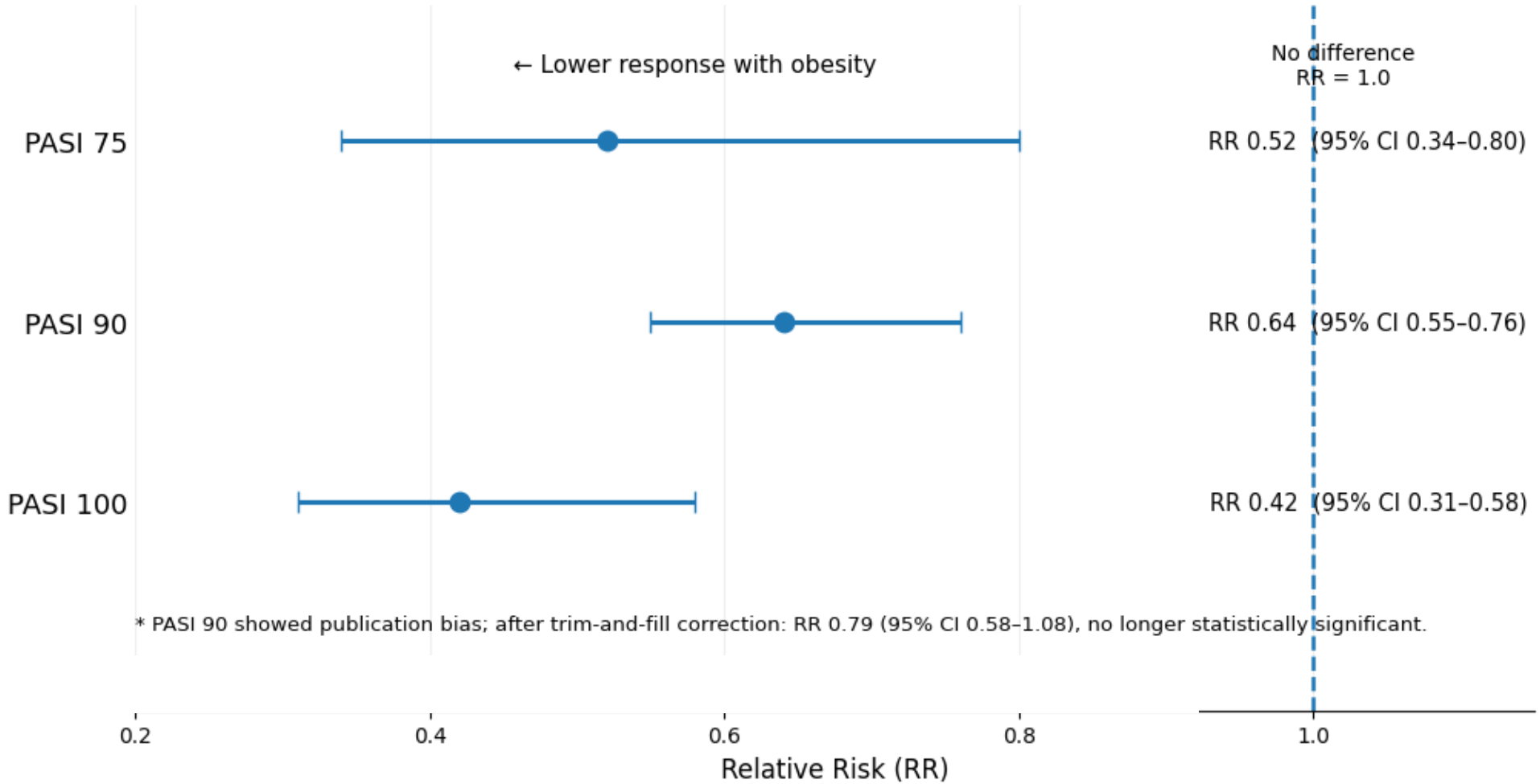
Psoriasis Outcome	Relative Response in Patients with Obesity	Key Finding
PASI 75	RR 0.52	↓ response
PASI 90	RR 0.64	↓ response*
PASI 100	RR 0.42	↓ complete clearance

Obesity may be a modifiable factor influencing psoriasis treatment response – not simply a comorbidity

PASI = Psoriasis Area and Severity Index.

Zhou W, et al. *J Dermatolog Treat*. 2026;37(1):2705161.

Impact of Obesity on Biologic Response in Psoriasis



Zhou W, et al. *J Dermatolog Treat*. 2026;37(1):2705161.

Underrecognition and Undertreatment of Obesity in PsO

- Importance of integrating weight management into PsO
  - GLP-1
  - Tirzepatide
  - Surgery

GLP-1 = glucagon-like peptide-1.

Typical Psoriasis and Primary Cardiovascular Prevention Case

- 52 y/o male
  - Obese (32 kg/m^2)
  - Sedentary
- Past medical history
  - Blood pressure 145/85 mm Hg
  - No diabetes
  - Past smoker

<u>Lipid panel</u>
Total chol: 197 mg/dL
HDL-C: 33 mg/dL
LDL-C: 110 mg/dL
Triglycerides: 270 mg/dL

Hemoglobin A1c: 5.8%

High sensitivity C-reactive protein: 1.5 mg/L

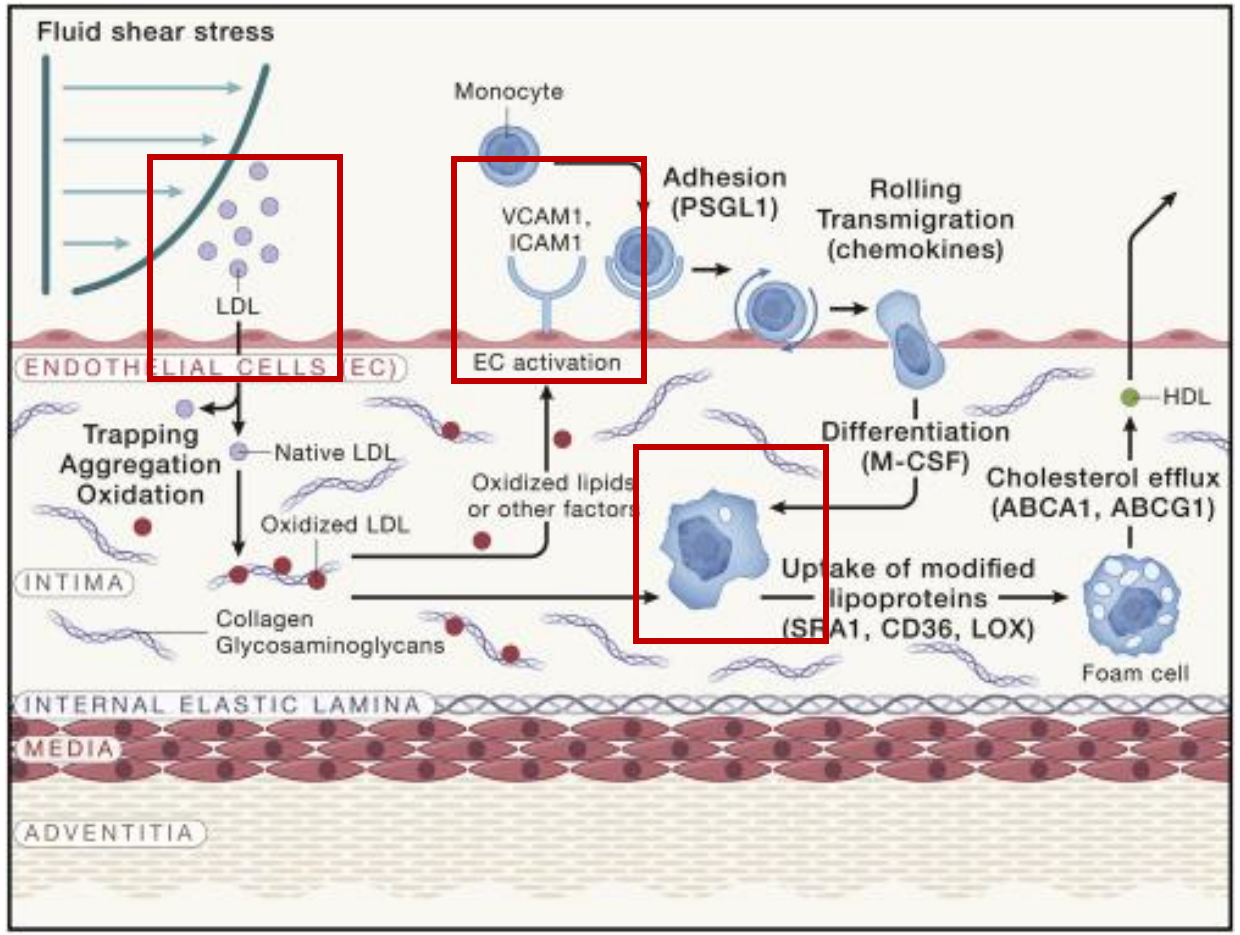
HDL = high-density lipoprotein; LDL = low-density lipoprotein.

Typical Psoriasis and Primary Cardiovascular Prevention Case

- Plaque psoriasis
  - 15 years
  - >10% of his body surface area
- Psoriatic arthritis



Atherosclerosis: Dyslipidemia, Endothelial Damage, Inflammation



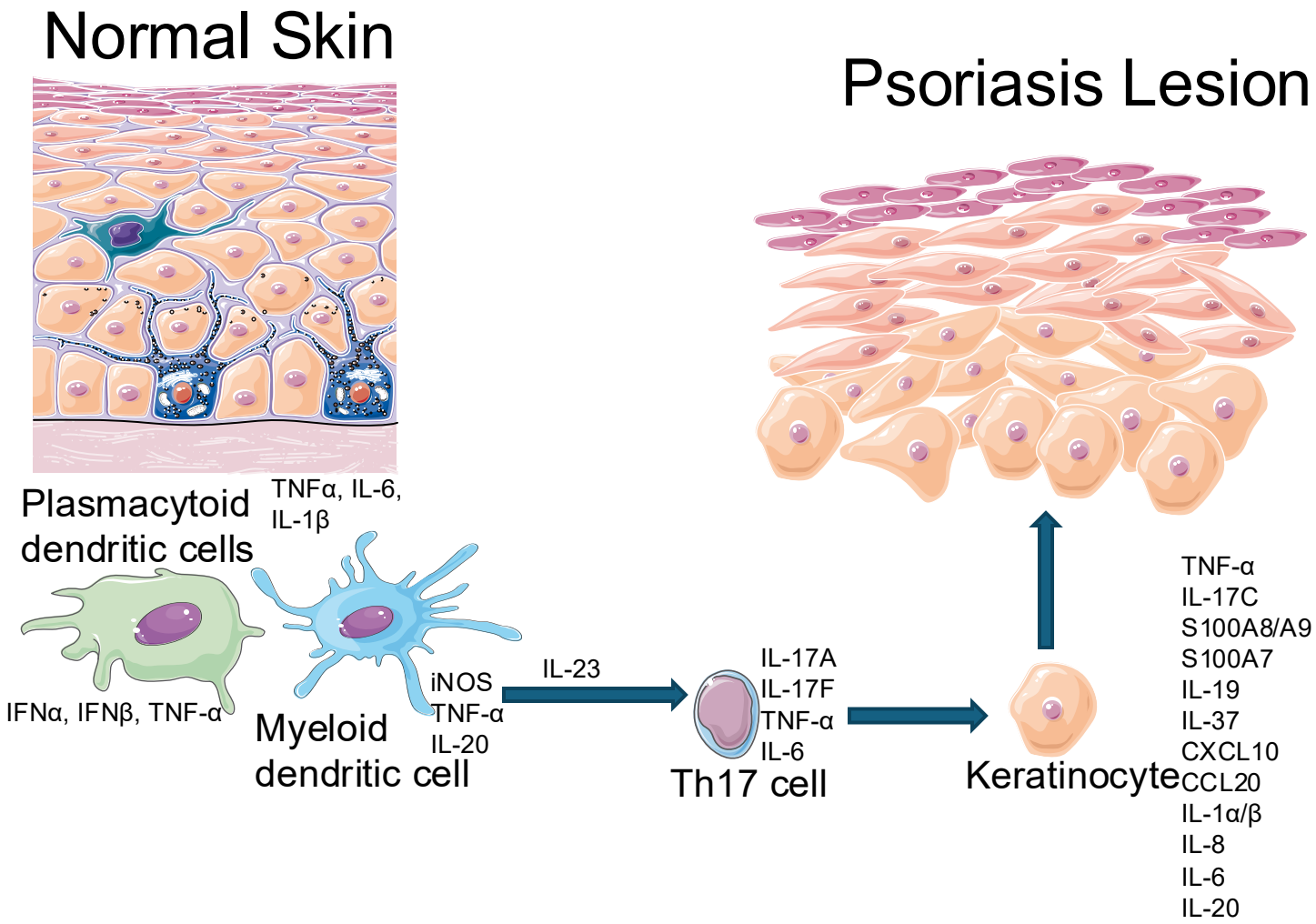
You still fundamentally need a lipid exposure

Endothelial damage

Phagocytosis of modified lipoproteins by macrophages

Bjorkegren JM, Lusis AJ. *Cell*. 2022;185(10):1630-1645.

Psoriasis Is an Inflammatory Skin Condition



Garshick MS, et al. *J Am Coll Cardiol*. 2021;77(13):1670-1680.

Examples of Drivers of Inflammation Promoting Atherosclerosis Inflammation within Adipose Tissue

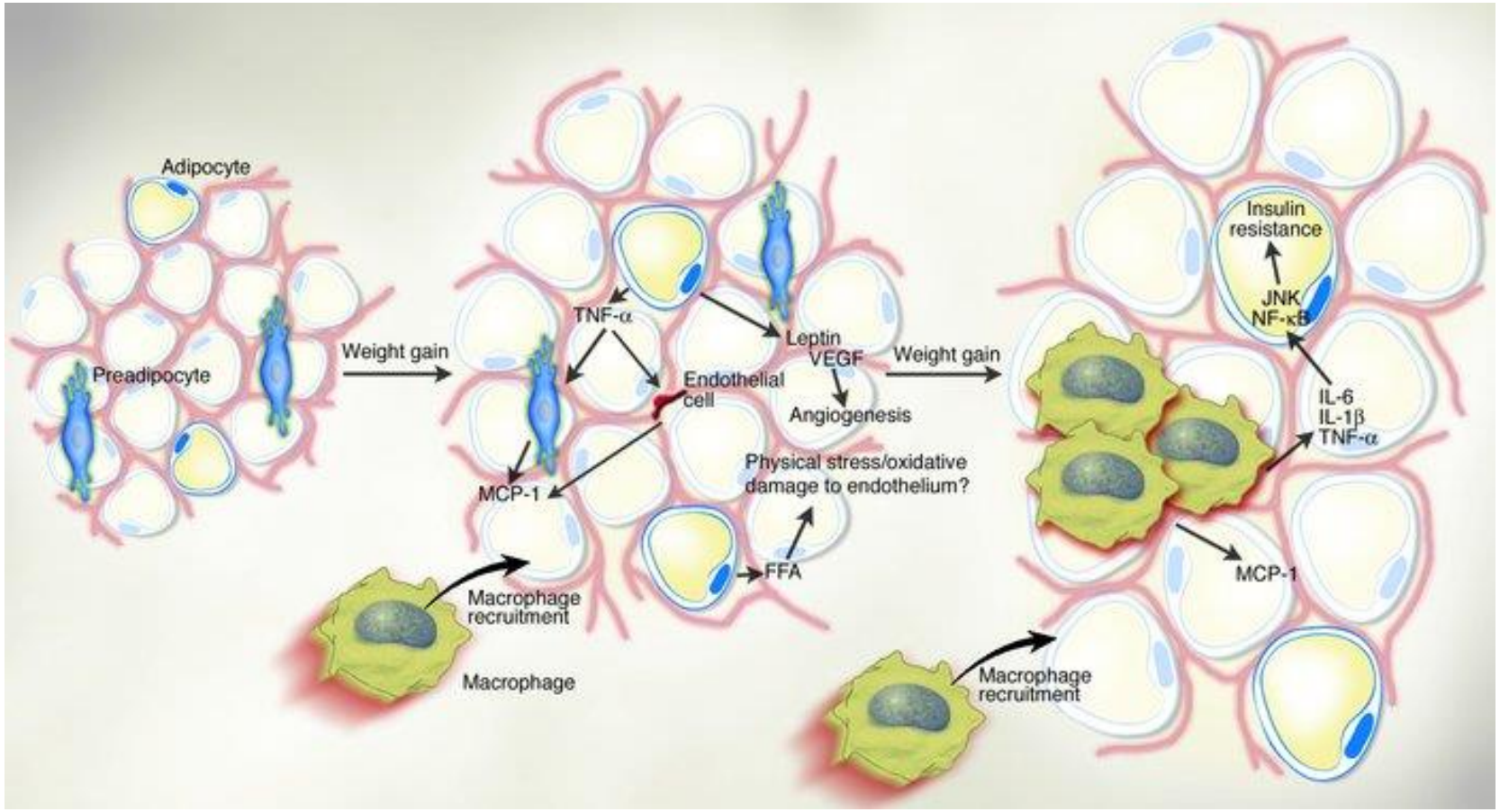
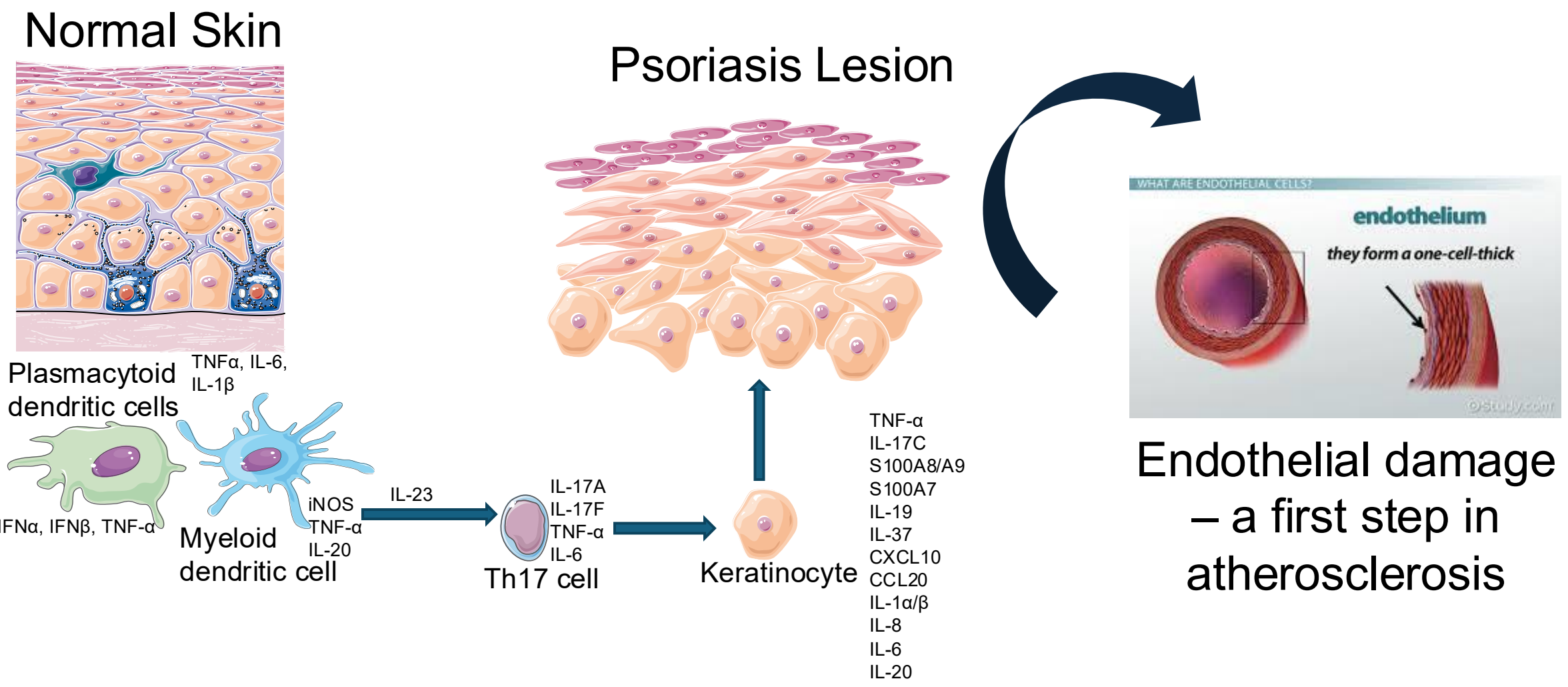


Figure obtained from Wellen KE, Hotamisligil GS. *J Clin Invest*. 2003;112(12):1785-1788.

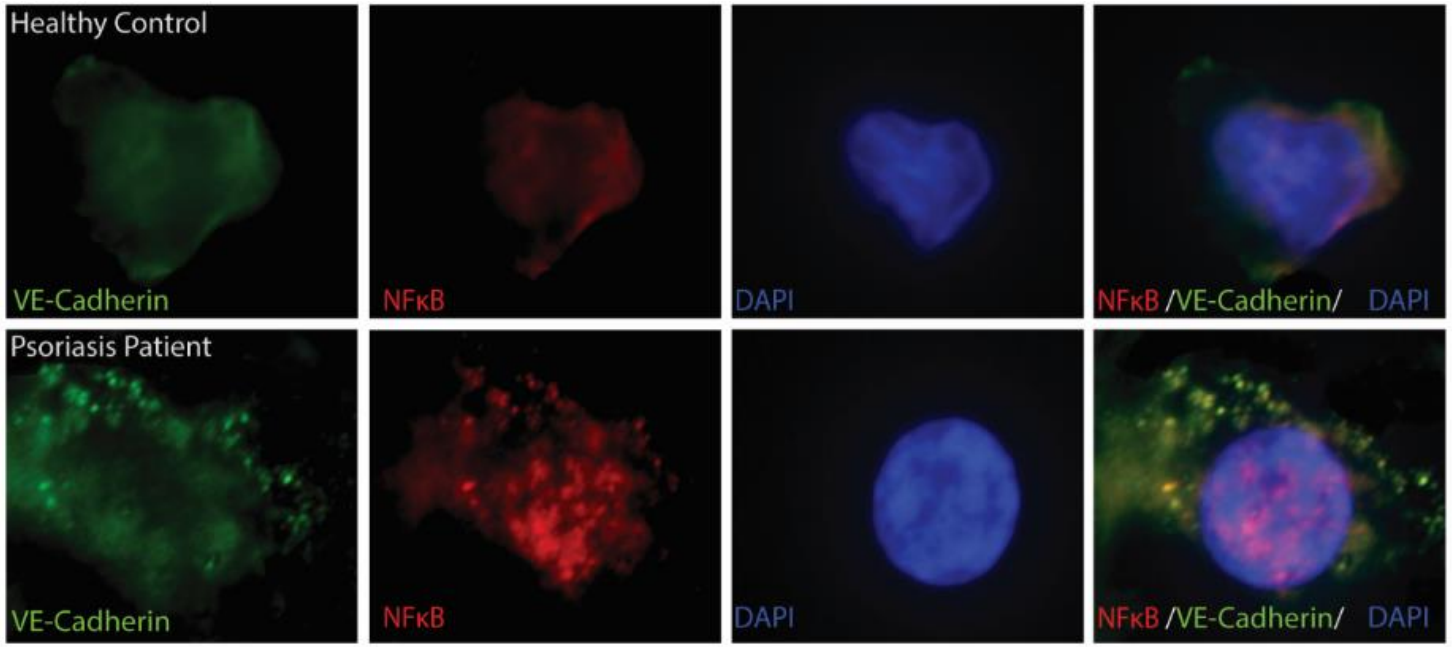
Does Psoriasis Promote Endothelial Damage as a Key Step in Promoting Atherosclerosis?



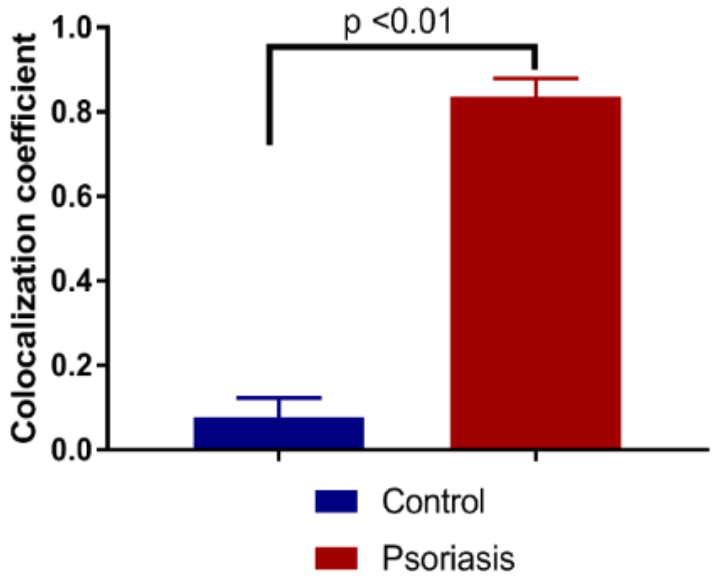
Endothelial damage – a first step in atherosclerosis

Garshick MS, et al. *J Am Coll Cardiol*. 2021;77(13):1670-1680.

Large Vessel Endothelial Inflammation Is Present in Psoriasis



NFκB Nuclear Colocalization



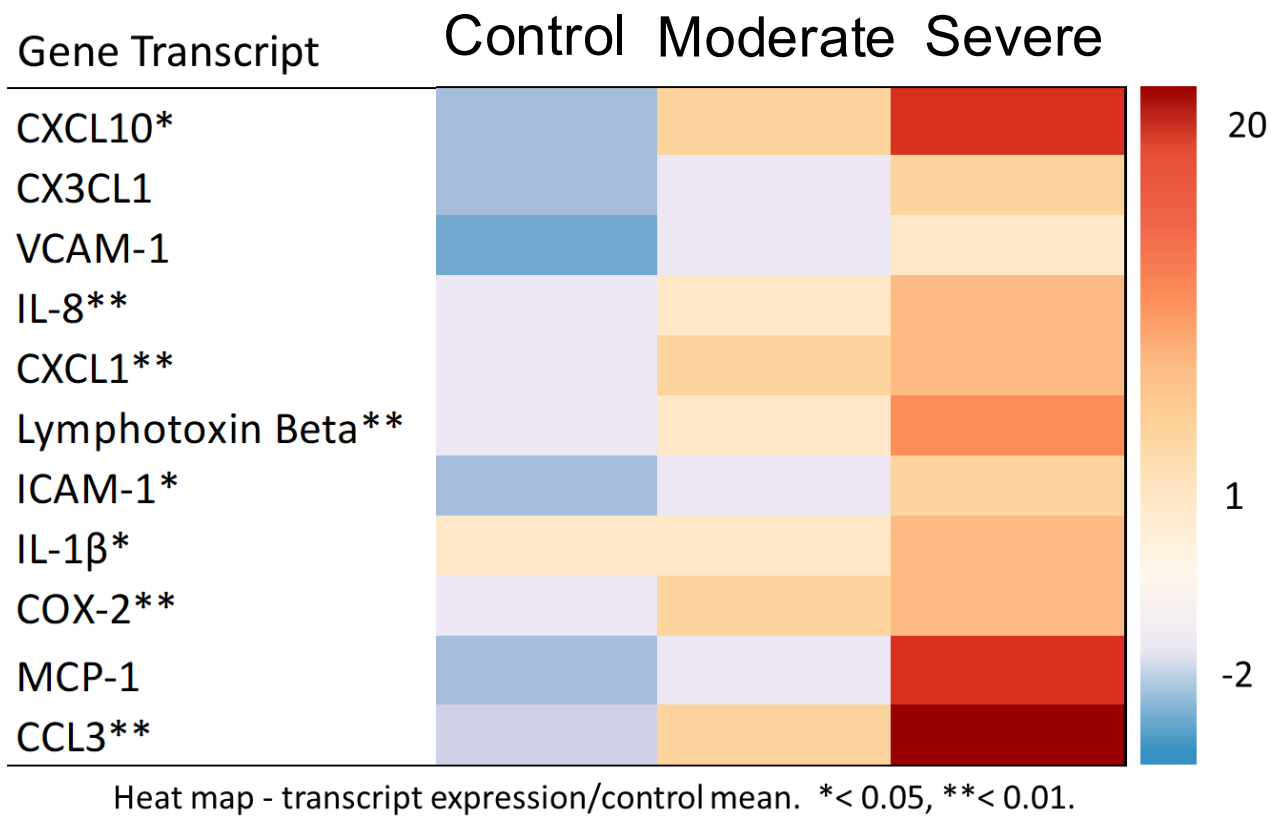
Endothelial Cell Membrane

NFκB (inflammation)

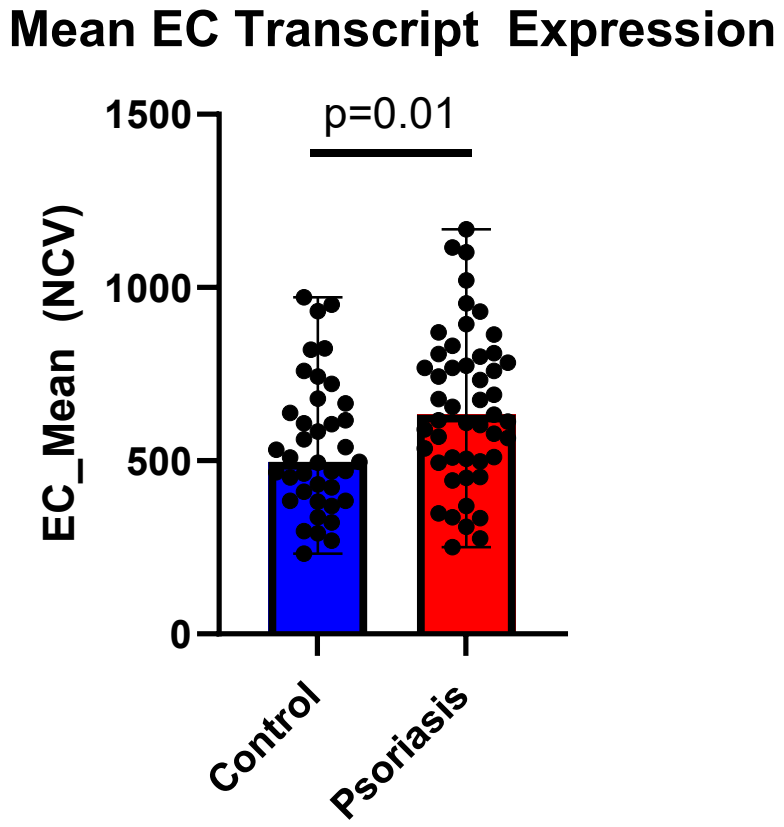
DAPI - Nucleus

Garshick MS, et al. *Arterioscler Thromb Vasc Biol*. 2019;39(4):787-798.

Endothelial Inflammatory Genes Are Upregulated in Patients with Psoriasis



Heat map - transcript expression/control mean. *< 0.05, **< 0.01.

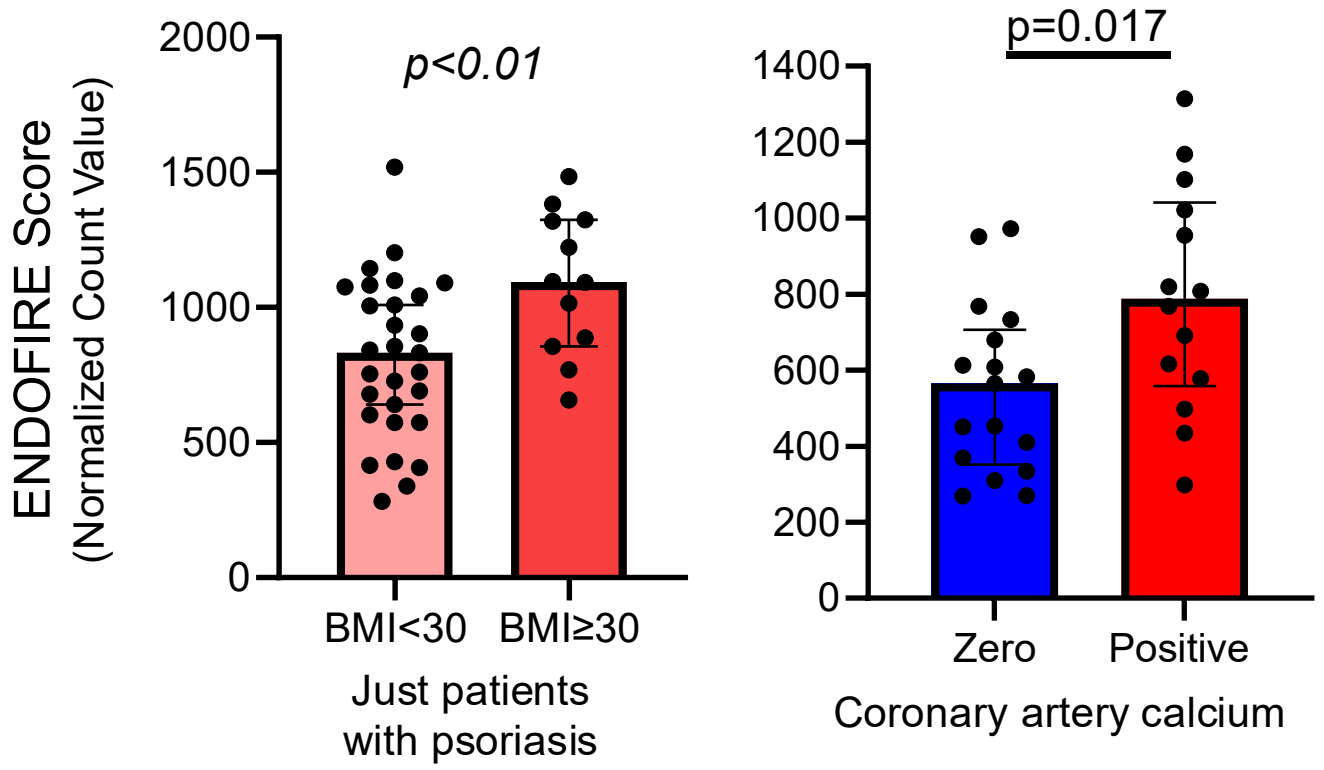


EC = endothelial cell; NCV = normalized count value.

Garshick MS, et al. *Arterioscler Thromb Vasc Biol*. 2019;39(4):787-798.

Endothelial Damage in Psoriasis Is Directly Associated with Cardiometabolic Disease in Psoriasis

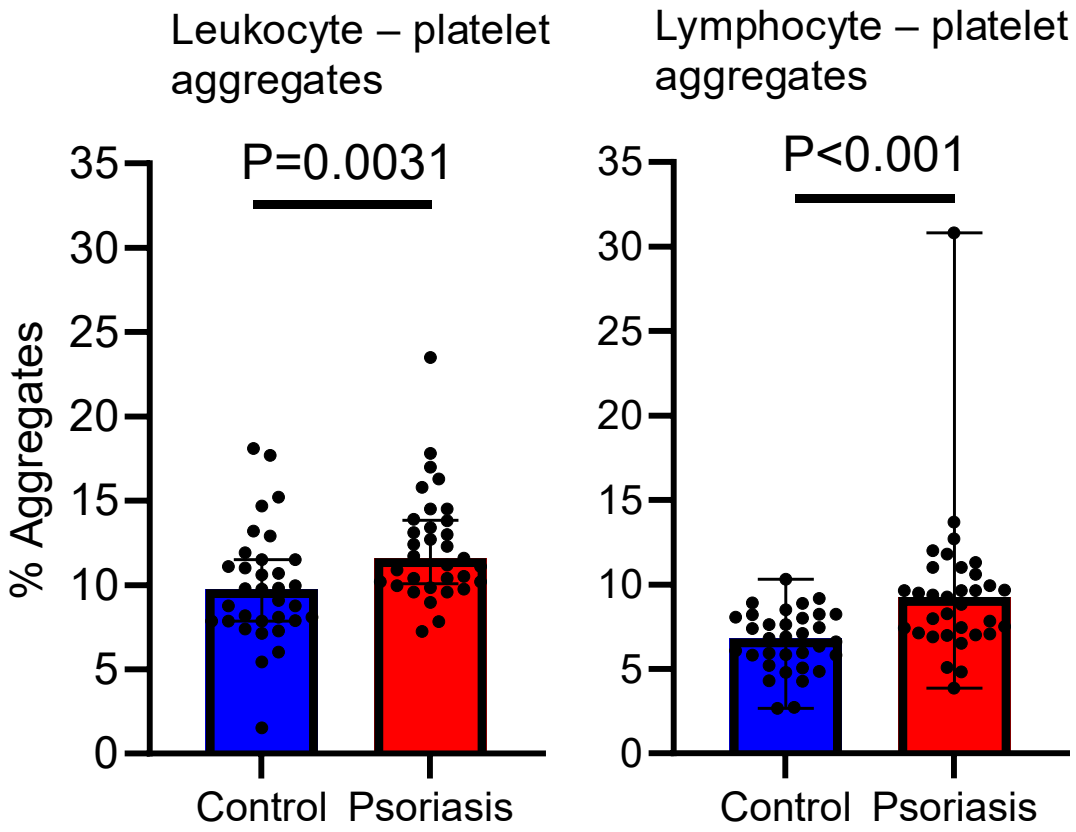
ENDOFIRE Score	*ρ*	*p*-value
Age	0.029	0.78
Women	-0.17	0.094
BMI	0.21	0.042
HOMA-IR	0.26	0.041
10-year ASCVD Risk	0.12	0.23
Non-HDL Cholesterol	-0.12	0.26
Hs-CRP	0.27	0.0091
Percent BSA	0.32	0.029

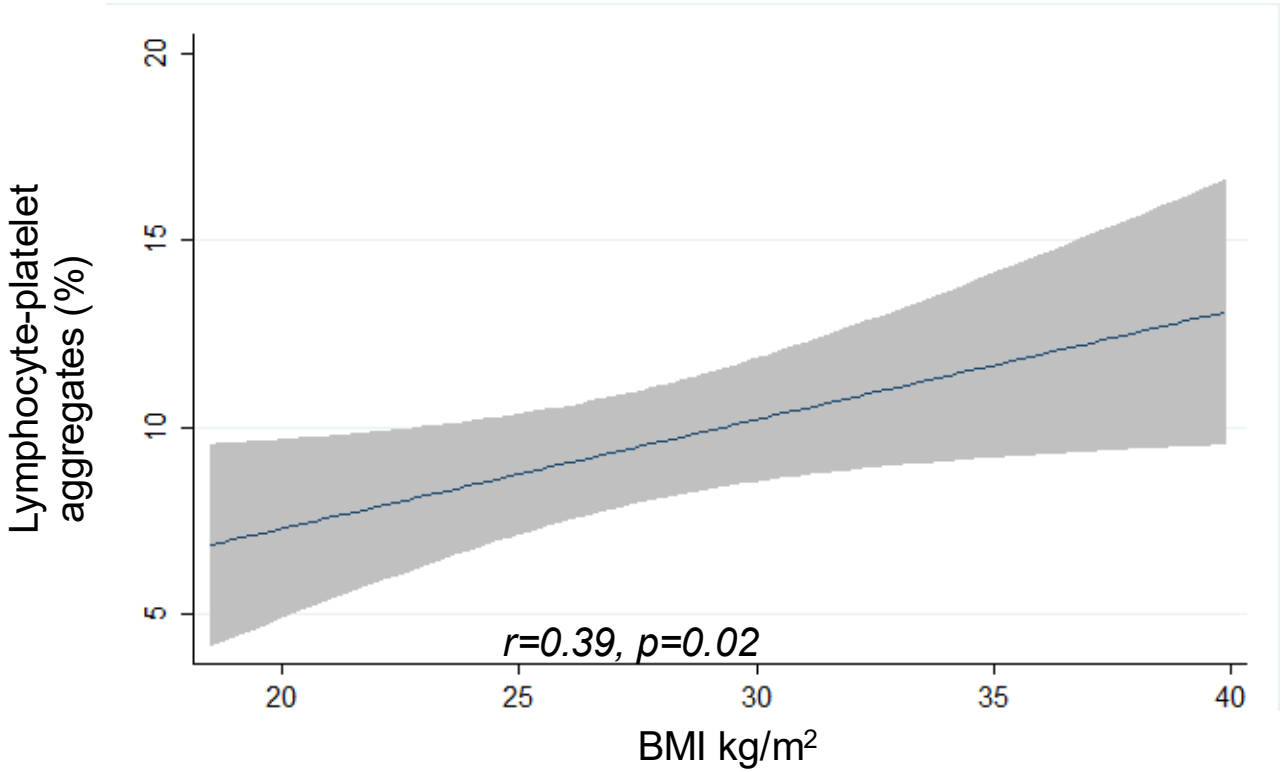


ENDOFIRE = Endothelial Inflammatory Index from RNA-seq Expression; HOMA-IR = homeostatic model assessment for insulin resistance; ASCVD = atherosclerotic cardiovascular disease; CRP = C-reactive protein; BSA = body surface area.

Garshick MS, et al. *Circ Res*. 2026;139(2):e328283.

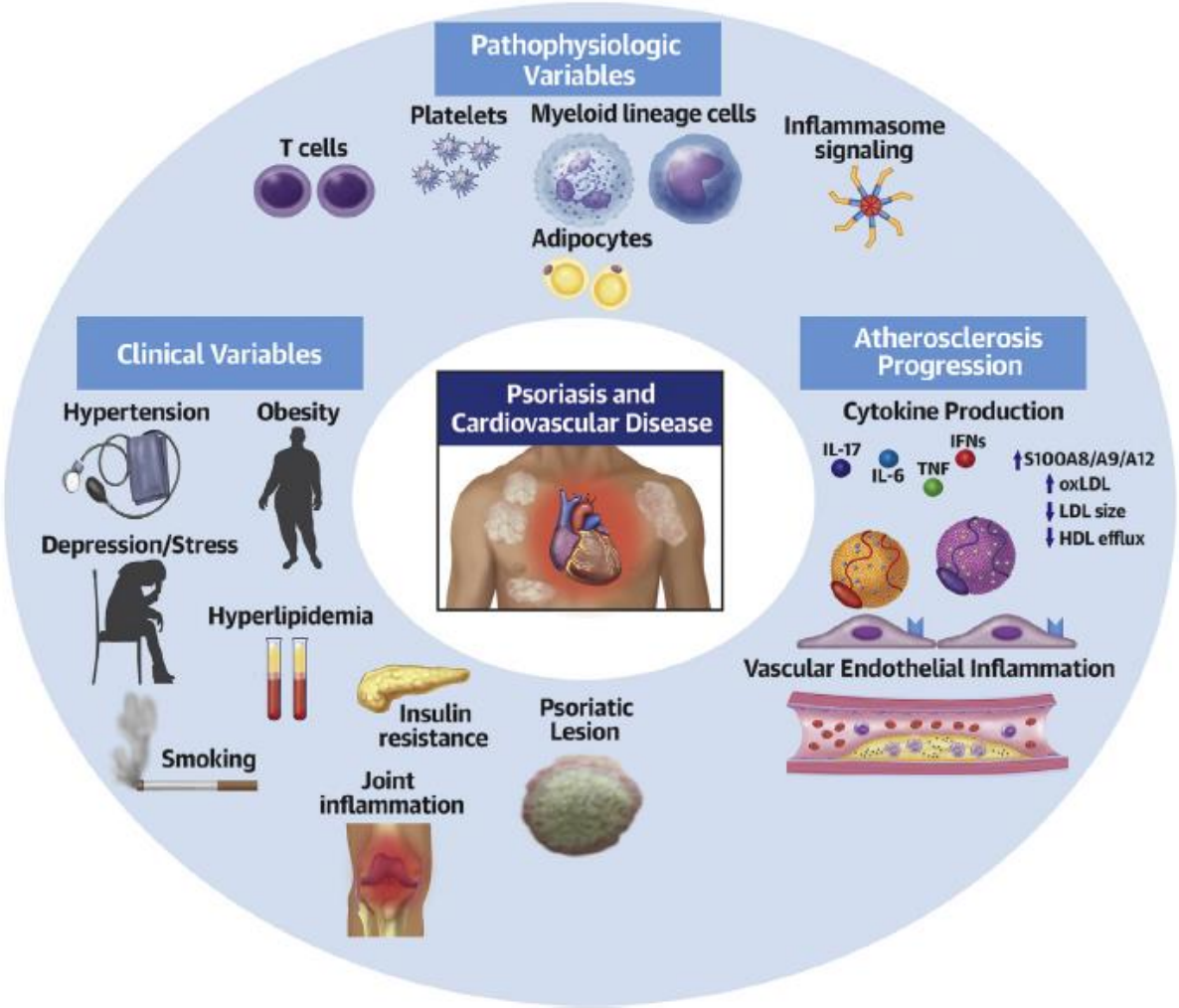
Patients with Psoriasis and Obesity Harbor Activated Platelets





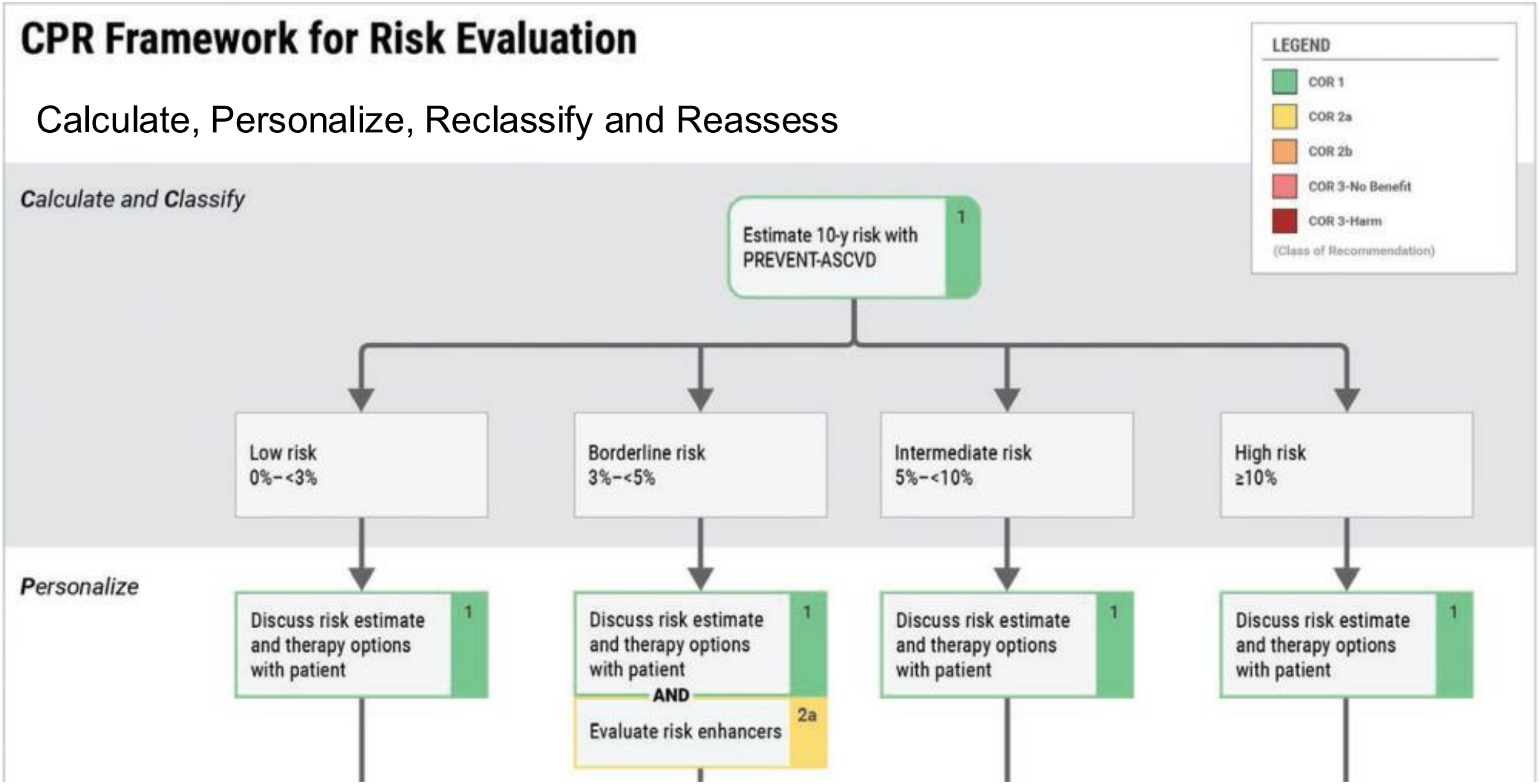
Garshick MS, et al. *Arterioscler Thromb Vasc Biol*. 2025;45(11):2086-2096.

Cardiovascular Disease Risk in Psoriasis Is a Combination of Traditional CV Risk Factors and Underlying Systemic Inflammation



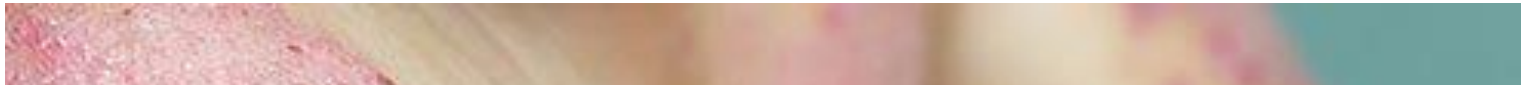
Garshick MS, et al. *J Am Coll Cardiol*. 2021;77(13):1670-1680.

Primary Cardiovascular Disease Prevention



Arnett DK, et al. *Circulation*. 2019;140(11):e596-e646.

Typical Psoriasis and Primary Cardiovascular Prevention Case



- 52 y/
  - O
  - S
- Past
  - B
  - N
  - P

10-year risk of a heart attack or stroke
6% “intermediate risk”

30-year risk of a CV event – 29.4%



Clinical Cardiovascular Risk Assessment in Inflammatory Conditions



VERY LIMITED DATA

Challenges exist in appropriate cardiovascular risk assessment

Challenges

- Traditional cardiovascular risk scores are inaccurate
- History of severe psoriasis, add 6.2% to a calculated 10-year cardiovascular risk

Mehta NN, et al. *J Am Acad Dermatol*. 2012;67(4):796-798.

Inflammation Has Been Incorporated into New Cardiovascular Disease Primary Prevention Guidelines

Risk-Enhancing Factors for
Clinician-Patient Risk Discussion

- **Primary hypercholesterolemia** (LDL-C, 160–189 mg/dL [4.1–4.8 mmol/L); non–HDL-C 190–219 mg/dL [4.9–5.6 mmol/L])*
- **Metabolic syndrome** (increased waist circumference, elevated triglycerides [>175 mg/dL], elevated blood pressure, elevated glucose, and low HDL-C [<40 mg/dL in men; <50 in women mg/dL] are factors; tally of 3 makes the diagnosis)
- **Chronic kidney disease** (eGFR 15–59 mL/min/1.73 m^2 with or without albuminuria; not treated with dialysis or kidney transplantation)
- **Chronic inflammatory conditions** such as psoriasis, RA, or HIV/AIDS
- **History of premature menopause (before age 40 y) and history of pregnancy-associated conditions that increase later ASCVD risk such as preeclampsia**
- **High-risk race/ethnicities** (e.g., South Asian ancestry)

AMERICAN COLLEGE of CARDIOLOGY

American Heart Association.

Grundy SM, et al. *J Am Coll Cardiol*. 2019;73(24):e285-e350.

What Are the Treatment Considerations and How Do We Reduce Risk in Autoimmune Conditions?



Guidelines and Guidance Statement Recommendations for the Identification and Management of Cardiovascular Risk in Psoriasis

Joint AAD-NPF guidelines of care for the management and treatment of psori

Table XVIII. Psoriasis and metabolic syndrome comorbidity level

Recommendation	Recomme numl
Education	
Association between psoriasis and metabolic syndrome plus screen for metabolic syndrome	3.1
Screening and referral	
Obesity screen and referral to primary care physician for proper follow-up and management of disease.	3.2
Blood pressure screen and referral to primary care physician for proper follow-up and management of disease.	3.3
Lipid status screen with referral to primary care physician for proper follow-up and management of disease.	3.4
Blood glucose screen and referral to primary care physician for proper follow-up and management of disease	3.5

Ronald Prussick, MD[4]; Jensen Y
Bolden, MD[9,10]; Elizabeth Walla
M. Cohen, MD, MPH[15]; Andrew

Author Affiliations

Steps for initial cardiovascular risk evaluation of patients with Psoriasis and Psoriatic Arthritis

1

Perform a CV risk assessment in all patients with PsO at the time of diagnosis by measuring:

- Blood pressure
- Body Mass Index
- Fasting blood glucose or Hemoglobin A1c
- Lipid panel
- Creatinine and Glomerular Filtration Rate (GFR)
- Screen for tobacco use and alcohol use
- Check for CV risk enhancers, including Lp(a) and hsCRP, at least once.

2

a. Counsel all patients on the importance of:

a. Regular physical activity

b. A healthy diet

c. Smoking cessation

b. Follow-up on CV risk factors on Step 1 and manage according to current guidelines of care.

3

Calculate the ASCVD risk score with the data obtained and classify based on the 10-year risk for ASCVD.

*If the ASCVD risk is high, or if management of CV risk factors is complex, refer to a cardiologist, who can discuss indications for additional medications (e.g.statins, GLP-1) and CV imaging.

4

Low-risk (<5%): screen yearly or sooner if comorbidities change. Assess CV risk enhancers to aid in decision about statin use

Borderline risk (5% to 7.4%): moderate-intensity statin should be considered with shared-decision making

Intermediate risk (7.5% to 19.9%): initiate a moderate-intensity statin to reduce LDLc by 30%-49%

High risk (≥20%): initiate a high intensity statin with the goal of lowering LDLc by ≥ 50%

Sheth S, et al. *J Psoriasis Psoriatic Arthritis*. 2025;10(4):124-130. Elmets CA, et al. *J Am Acad Dermatol*. 2019;80(4):1073-1113. Sheth S, et al. *JAMA Dermatol*. 2026;162(6):619-630.

Awareness of Cardiometabolic Risk in Patients with Psoriasis

- Most participants had **seen a PCP** within the past year and **underwent screening for CVD risk factors** within the past 2 years
- **2/3 of participants** were ***not*** **aware** of the **connection between psoriasis and CVD**
- **Male participants** were **more likely to be told about psoriasis/CVD connection** and **recommended to undergo screening** for risk of CVD
- **Most participants (83.2%) desired more education** regarding cardiometabolic risk in psoriasis and **preferred this counseling from their dermatologist (72.3%)**

		Screening recommended		Aware of psoriasis/CVD connection	
Variable	***n***	**Adjusted odds ratio [95% CI]**	***P* value**	**Adjusted odds ratio [95% CI]**	***P* value**
Location					
Phototherapy clinic	36	1.00 [ref]	-	1.00 [ref]	-
Psoriasis specialty clinic	65	0.96 [0.33, 2.85]	.95	1.35 [0.48, 3.94]	.57
Age					
18-49	36	1.00 [ref]	-	1.00 [ref]	-
50-69	38	4.19† [1.32, 14.88]	.02*	1.51 [0.50, 4.72]	.47
70-89	27	2.11 [0.59, 7.97]	.26	2.03 [0.62. 6.96]	.25
Race					
White	65	1.00 [ref]	-	1.00 [ref]	-
Black	6	0.84 [0.09, 6.59]	.87	1.21 [0.14, 8.15]	.85
Other	30	0.51 [0.13, 1.77]	.31	0.82 [0.24, 2.71]	.76
Sex					
Female	41	1.00 [ref]	-	1.00 [ref]	-
Male	60	3.10‡ [1.07, 9.95]	.04*	3.80‡ [1.36, 11.82]	.01*
Ethnicity					
Hispanic	14	1.16 [0.23, 5.81]	.85	1.21 [0.26, 5.43]	.80
Primary care provider					
Seen within 1 year	79	1.65 [0.47, 6.54]	.45	0.66 [0.19, 2.22]	.49
Rheumatologist					
Seen within 1 year	32	0.78 [0.26, 2.21]	.64	1.73 [0.65. 4.72]	.28
Primary dermatologist					
Seen within 1 year	33	0.96 [0.30, 3.00]	.94	1.18 [0.38, 3.66]	.78

Kearney CA, et al. *JAAD Int*. 2024;16:72-74.

Patients with Psoriasis: Characteristics

Table 1. Participant demographics.

Variable (*N* = 101)	No. (%)
Age (Mean, Range)	50.7 (20 – 100)
Sex (*n* = 100)	
Male	50 (50)
Female	50 (50)
Race (*n* = 100)	
Asian	12 (12)
Black or African American	11 (11)
White	55 (54)
Other	21 (21)
Unknown	2 (2)
Ethnicity (*n* = 98)	
Hispanic or Latino	23 (23)
Insurance (*n* = 99)	
Private or commercial	60 (59)
Medicaid	30 (30
Medicare	16 (16)
None	1 (1)
Don't know	3 (4)
Education (*n* = 99)	
High school or below	29 (29)
Some college or college degree	52 (53)
Postgraduate degree	18 (18)

Table 2. Participant-reported psoriasis history.

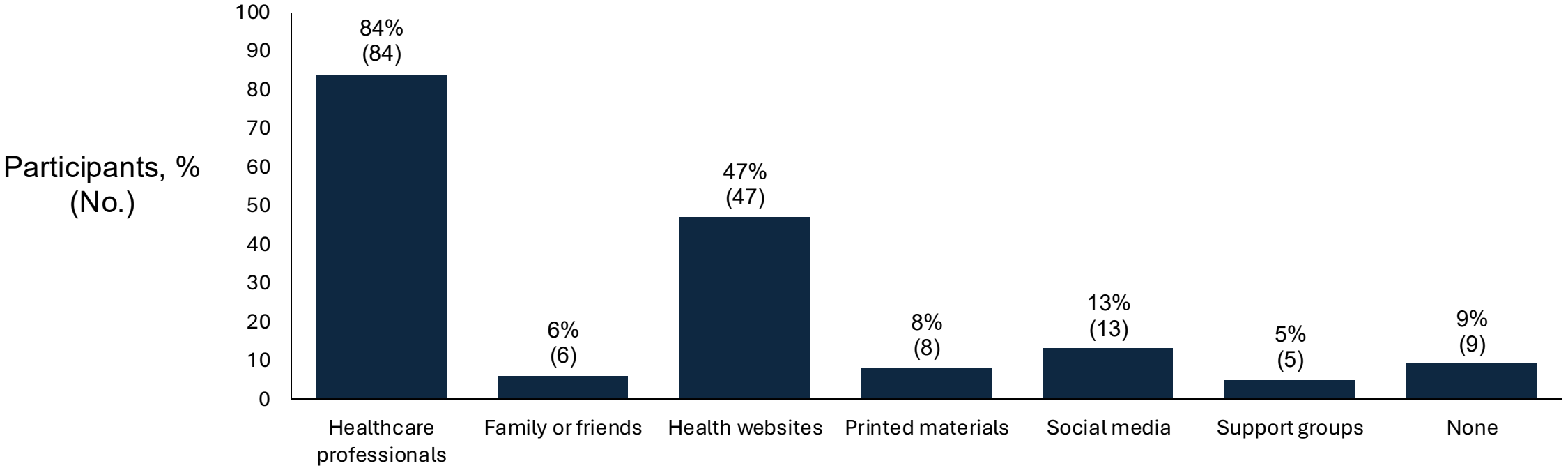
Variable (*N* = 101)	No. (%)
Length of Psoriasis Diagnosis (*n* = 100)	
Less than 3 years	20 (20)
5-10 years	27 (27)
Greater than 10 years	52 (52)
Don't know	1 (1)
Current Psoriasis Treatment (*n* = 99)	
No current therapy	3 (3)
Topical therapy	40 (40)
Phototherapy	16 (16)
Systemic therapy (oral, injection)	69 (69)
Psoriatic Arthritis	
Yes	35 (35)
No	52 (52)
Not sure/don't know	12 (12)

Table 3. Participant-reported cardiometabolic history.

Variable (*N* = 101)	No. (%)
Diabetes	15 (15)
Borderline or pre-diabetes	28 (28)
Hyperlipidemia	36 (36)
Hypertension	36 (36)
Obesity	28 (28)
CAD and/or MACE	11 (11)
Tobacco use:	
Current smoker	9 (9)
Former smoker (quit > 2 weeks ago)	30 (30)

Kearney CA, et al. Presented at: AAD Annual Meeting; March 7-11, 2025; Orlando, FL.

Patients with Psoriasis: Current Sources of Information



Participants with a high school education or less were less likely to report use of healthcare providers or health websites for information than those with some college or a college degree

Kearney CA, et al. Presented at: AAD Annual Meeting; March 7-11, 2025; Orlando, FL.

Patients with Psoriasis: Baseline Knowledge

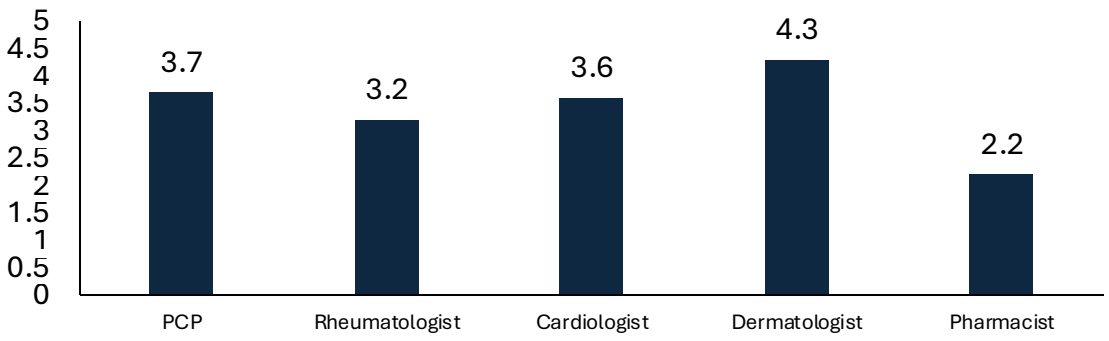
Statement	Average Likert Score	No. (%)		
		Disagree or Strongly Disagree	Neutral/Don't Know	Agree or Strongly Agree
PsO is exclusively a disease of the skin.	2.7	53 (53)	16 (16)	28 (28)
Treatment for PsO only benefits the skin.	2.8	48 (48)	20 (20)	29 (29)
PsO may affect my heart health.	3.5	6 (6)	44 (44)	47 (47)
Moderate-severe PsO increases heart attack risk.	3.3	7 (7)	59 (59)	32 (32)
Cardiometabolic risk screening is important for PsO patients.	3.6	2 (2)	46 (46)	50 (50)
CVD is the leading cause of death in the US.	3.8	6 (6)	27 (27)	65 (65)
High cholesterol causes symptoms.	3.1	22 (22)	44 (44)	32 (32)

- High school education or less was associated with a lower psoriasis knowledge score than those with some college or a college degree
- Psoriasis diagnosis <3 years ago or >10 years ago were associated with a lower psoriasis-CVD knowledge score than those with a diagnosis 5-10 years ago

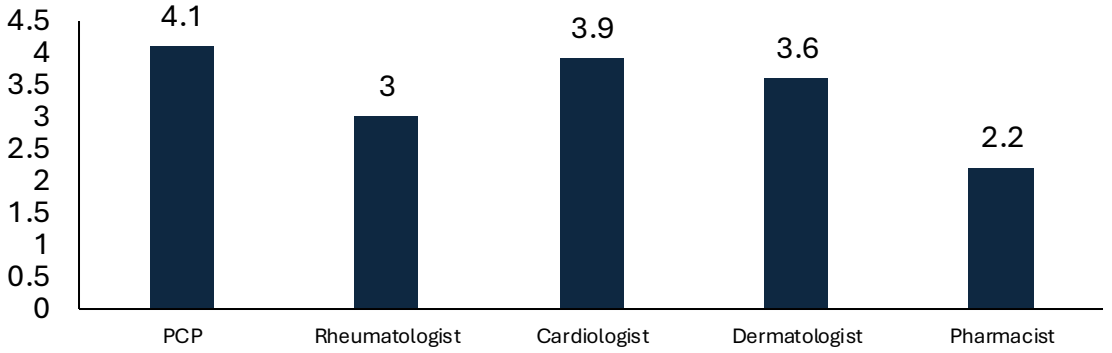
Kearney CA, et al. Presented at: AAD Annual Meeting; March 7-11, 2025; Orlando, FL.

Patients with Psoriasis: Education Preferences

- Most participants prefer to receive health information directly from their doctor (average Likert score 4.3)



Preferred physician or provider to educate on the connection between psoriasis and CVD (average Likert score)



Preferred physician or provider to educate on CVD risk reduction strategies (average Likert score)

- Participants who had previously seen a cardiologist or rheumatologist were more likely to indicate they would seek education from these specialists
- Male participants and those with postgraduate education were more likely to prefer education from a specialist in a certain health problem than from their regular doctor, whom they know well

Kearney CA, et al. Presented at: AAD Annual Meeting; March 7-11, 2025; Orlando, FL.

Quality Improvement: Barriers to Education

- 30% of participants reported that their doctor or other healthcare provider had discussed the connection between psoriasis and CVD with them
  - 17% phototherapy or psoriasis specialty clinic dermatologist
  - 11% PCP
  - 7% cardiologist
  - 4% rheumatologist

- Time for appointments, transportation, language, or finances were not perceived as significant barriers to education

- Participants endorsed some concerns about the side effects of treatments for psoriasis and heart disease (average Likert score 3.5)

Kearney CA, et al. Presented at: AAD Annual Meeting; March 7-11, 2025; Orlando, FL.

Does Treatment of Psoriasis Reduce Cardiovascular Risk?

Observational data suggest yes!

- TNFα inhibitor therapy over 3 years – 50% reduction in myocardial infarction
- Those who undergo psoriasis treatment show
  - Reduced vascular aortic inflammation
  - Improved myocardial strain
  - Reduced coronary plaque burden

Randomized, placebo-controlled clinical trials of biologic therapy in psoriasis to reduce CV risk are inconclusive

- TNFα inhibitor
  - NCT01722214 – adalimumab
  - NCT01553058 – adalimumab
- IL-12/23 inhibitor
  - NCT02187172 – ustekinumab
- IL-17A inhibitor
  - NCT02690701 – secukinumab
  - NCT02559622 – secukinumab
- PDE4 inhibitor
  - NCT03082729 – apremilast (not RCT)

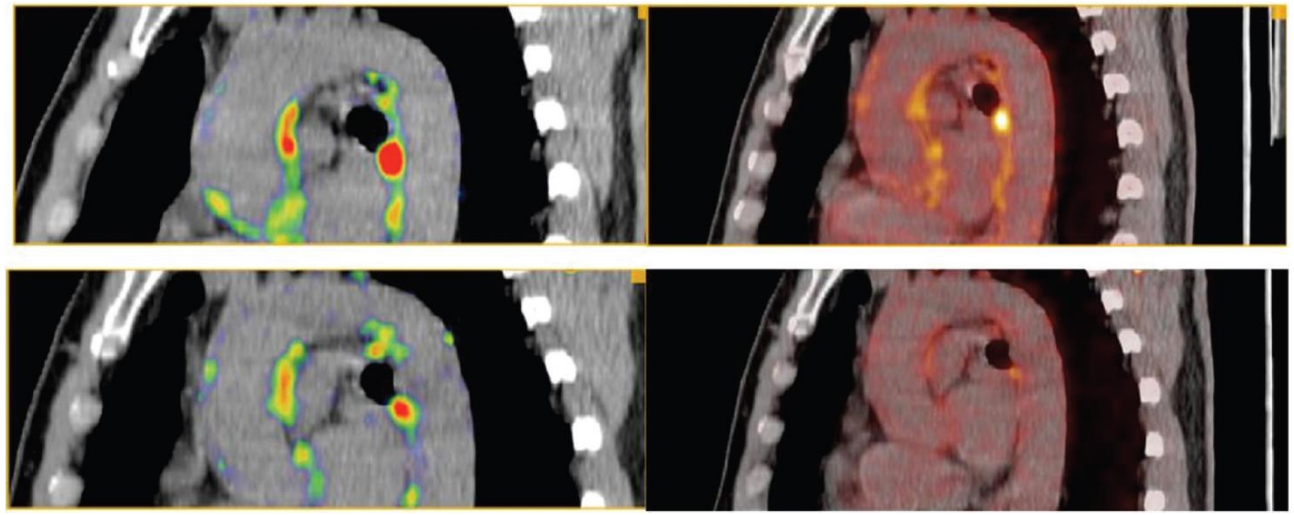
RCT = randomized controlled trial.

Wu JJ, et al. *Arch Dermatol*. 2012;148(11):1244-1250. Groenendyk JW, et al. *Eur J Nucl Med Mol Imaging*. 2019;46(12):2488-2495. Dey AK, et al. *JAMA Cardiol*. 2017;2(9):1013-1018. Ikonomidis I, et al. *Circ Cardiovasc Imaging*. 2017;10(9):e006283. Choi H, et al. *Circ Cardiovasc Imaging*. 2020;13(9):e011199. Elnabawi YA, et al. *Cardiovasc Res*. 2019;115(4):721-728. ClinicalTrials.gov. Accessed September 9, 2026. https://clinicaltrials.gov.

In Observational Studies, TNF Inhibitor Therapy Reduces Aortic Inflammation in Rheumatoid Arthritis

- 17 patients with RA treated with either adalimumab or etanercept

- FDG PET CT at baseline and after 8 weeks of therapy
  - Aortic inflammation (assessed via target-to-blood pool ratio) significantly reduced
    - 2.02 to 1.90; *P*=0.03

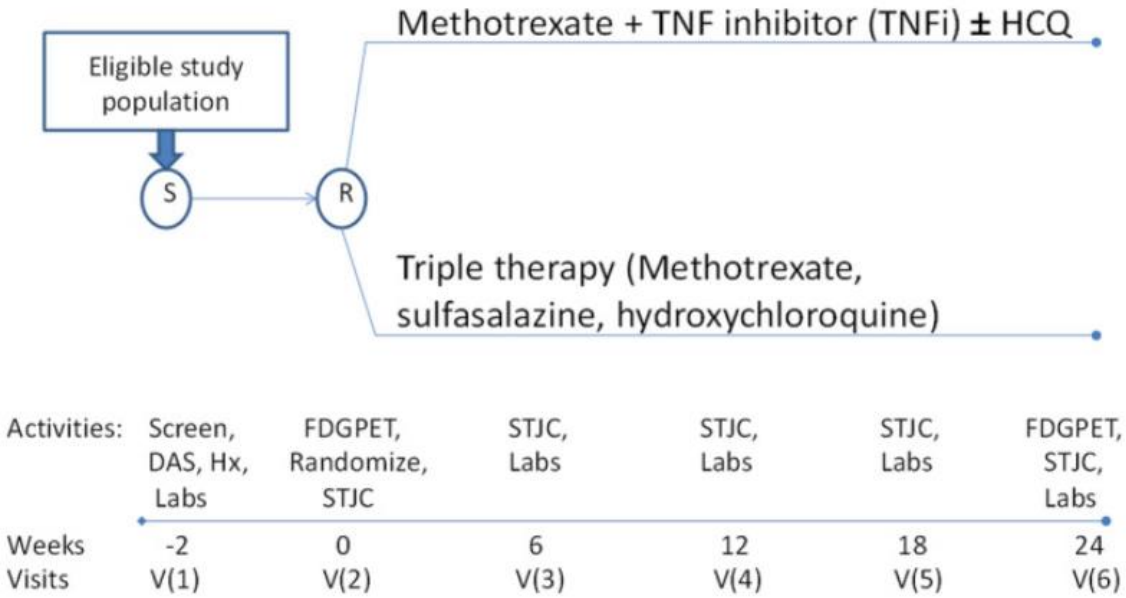


RA = rheumatoid arthritis; FDG = fluorodeoxyglucose; PET = positron emission tomography.

Maki-Petaja KM, et al. *Circulation*. 2012;126(21):2473-2480.

The TARGET Trial: DMARDs vs Triple Therapy to Reduce Aortic Inflammation

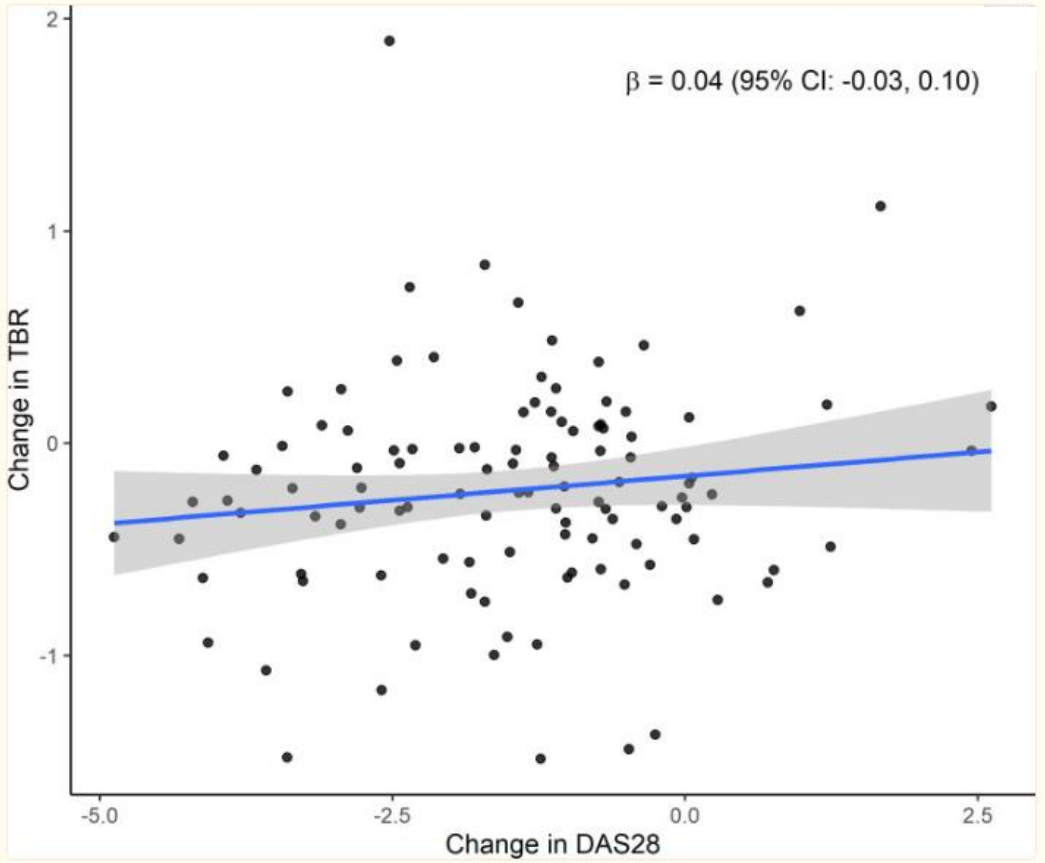
- Patients with RA without CVD (n=115 for baseline and f/u measures)
  - Inadequate response to methotrexate with DAS28-CRP >3.2
  - Mean age 58 years, 71% women, 57% seropositive
  - Randomized to TNF inhibitor + methotrexate or triple therapy (methotrexate/sulfasalazine, hydroxychloroquine)
  - Primary outcomes aortic and carotid inflammation by FDG-PET
    - Initial scan and follow-up scan at 24 weeks



DMARDs = disease-modifying antirheumatic drugs; DAS = Disease Activity Score; HCQ = hydroxychloroquine; STJC = swollen/tender joint count.
Solomon DH, et al. *Ann Rheum Dis*. 2023;82(3):324-330. Giles JT, et al. *ACR Open Rheumatol*. 2021;3(6):371-380.

TARGET Results

- 8% decrease in vascular inflammation overall (in the most diseased vessel – carotid or aorta), *P*=0.001
- No statistical difference in change between MTX+ TNFi group vs triple therapy
- No subgroup differences according to age, sex, steroid use, statin use, seropositivity, or RA duration



MTX = methotrexate; TBR = target-to-background ratio.
Solomon DH, et al. *Ann Rheum Dis*. 2023;82(3):324-330.

Some Treatments May Actually Increase Thrombotic Risk in Psoriatic (and Other Immune-Mediated) Diseases



WARNING: SERIOUS INFECTIONS, MORTALITY, MALIGNANCY, MAJOR ADVERSE CARDIOVASCULAR EVENTS (MACE), and THROMBOSIS

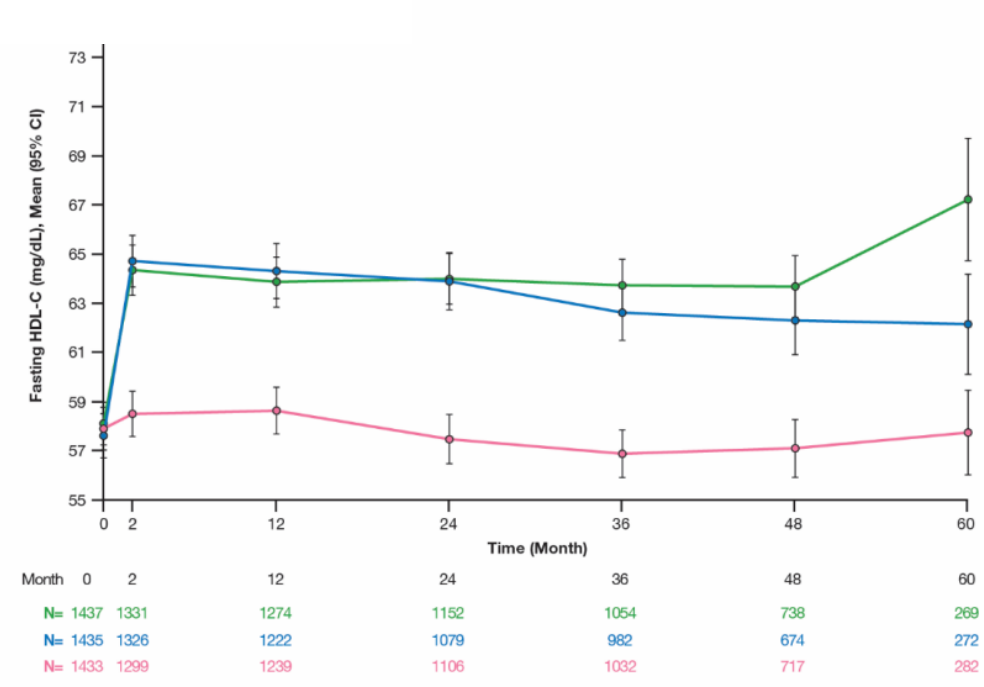
See full prescribing information for complete boxed warning.

- **Increased risk of serious bacterial, fungal, viral, and opportunistic infections leading to hospitalization or death, including tuberculosis (TB). Interrupt treatment with upadacitinib if serious infection occurs until the infection is controlled. Test for latent TB before and during therapy; treat latent TB prior to use. Monitor all patients for active TB during treatment, even patients with initial negative, latent TB test. (5.1)**
- **Higher rate of all-cause mortality, including sudden cardiovascular death with another Janus kinase (JAK) inhibitor vs. tumor necrosis factor (TNF) blockers in rheumatoid arthritis (RA) patients. (5.2)**
- **Malignancies have occurred in patients treated with upadacitinib. Higher rate of lymphomas and lung cancers with another JAK inhibitor vs. TNF blockers in RA patients. (5.3)**
- **Higher rate of MACE (defined as cardiovascular death, myocardial infarction, and stroke) with another JAK inhibitor vs. TNF blockers in RA patients. (5.4)**
- **Thrombosis has occurred in patients treated with upadacitinib. Increased incidence of pulmonary embolism, venous and arterial thrombosis with another JAK inhibitor vs. TNF blockers. (5.5)**

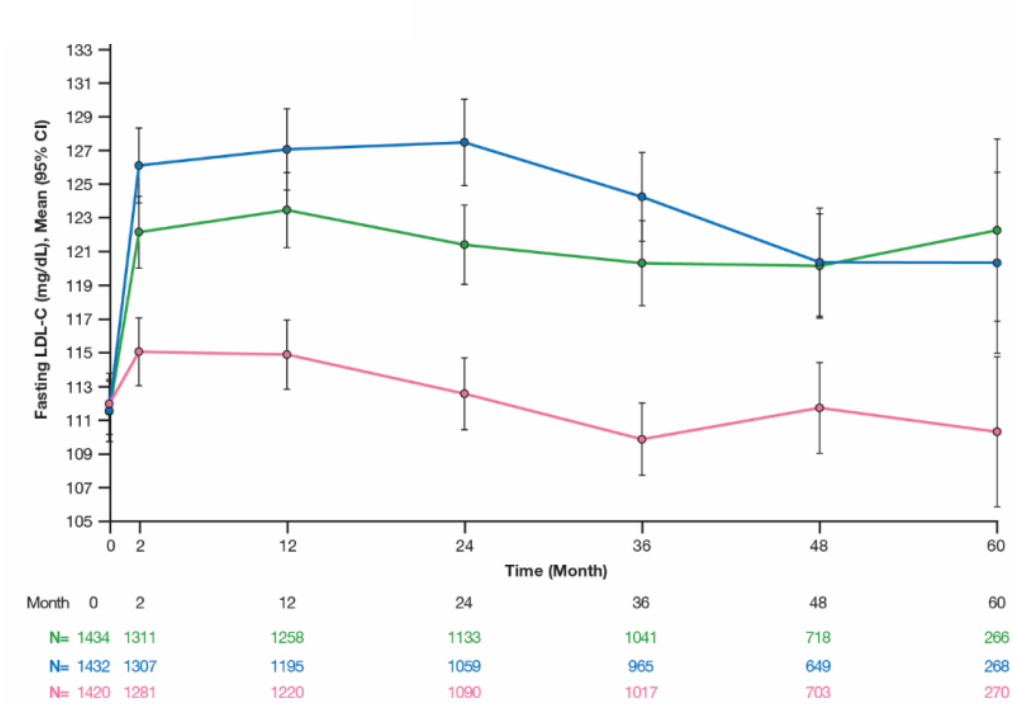
FDA. Accessed September 10, 2026. https://www.accessdata.fda.gov/drugsatfda_docs/label/2026/218347Orig1s008,211675Orig1s034lbl.pdf.

JAK Inhibitors Increase Lipoproteins

HDL-C



LDL-C



TNF inhibitor
Tofacitinib 5 mg BID
Tofacitinib 10 mg BID

JAK = Janus kinase.

Ytterberg SR, et al. *N Engl J Med*. 2022;386(4):316-326.

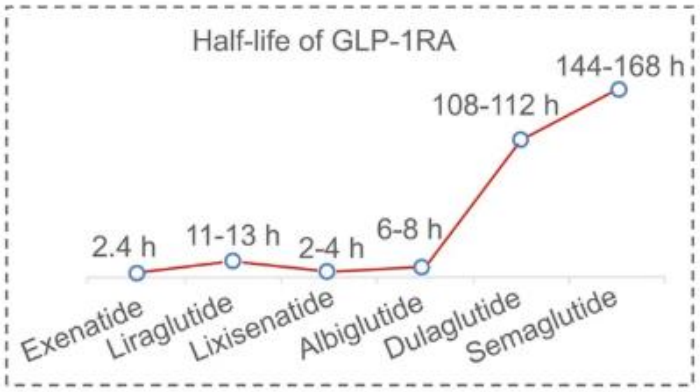
Part of the Story: FDA Mandate to Investigate CV Risk Reduction Strategies in Patients with Diabetes

- Before 2008 – new diabetes medications were approved based on reductions in HbA1c

- The Food and Drug Administration (FDA) is announcing the availability of a guidance for industry entitled “Diabetes Mellitus—Evaluating Cardiovascular Risk in New Antidiabetic Therapies to Treat Type 2 Diabetes”
  - This guidance makes recommendations about how to demonstrate that a new antidiabetic therapy to treat type 2 diabetes is not associated with an unacceptable increase in cardiovascular risk

FDA. Accessed September 10, 2026. https://downloads.regulations.gov/FDA-2008-D-0118-0029/content.pdf.

Timeline of GLP-1 Agonists



1981–82: Cloning of anglerfish proglucagon cDNAs

1983–84: Cloning of mammalian proglucagon cDNAs

1987: GLP-1 stimulates insulin secretion

1992: Isolation of exendin-4

2005: First twice-daily GLP-1RA (exenatide) for diabetes

2006: First DPP-4 inhibitor (sitagliptin) approved for diabetes

2010: First once-daily GLP-1RA (liraglutide) for diabetes

2012: First once-weekly GLP-1RA (once-weekly exenatide) for diabetes

2014: First once-daily GLP-1RA (liraglutide) for obesity

2016: First positive CVOT for a GLP-1RA in diabetes (liraglutide)

First GLP-1:insulin combinations for diabetes (insulin degludec/liraglutide; insulin glargine/lixisenatide)

2022: First approval for a GLP-1R co-agonist (tirzepatide) for T2D

2023: First GLP-1:co-agonist (tirzepatide) approval for obesity

First positive phase III trials for GLP-1 medicines (tirzepatide and semaglutide) in sleep apnoea, heart failure, osteoarthritis and metabolic liver disease

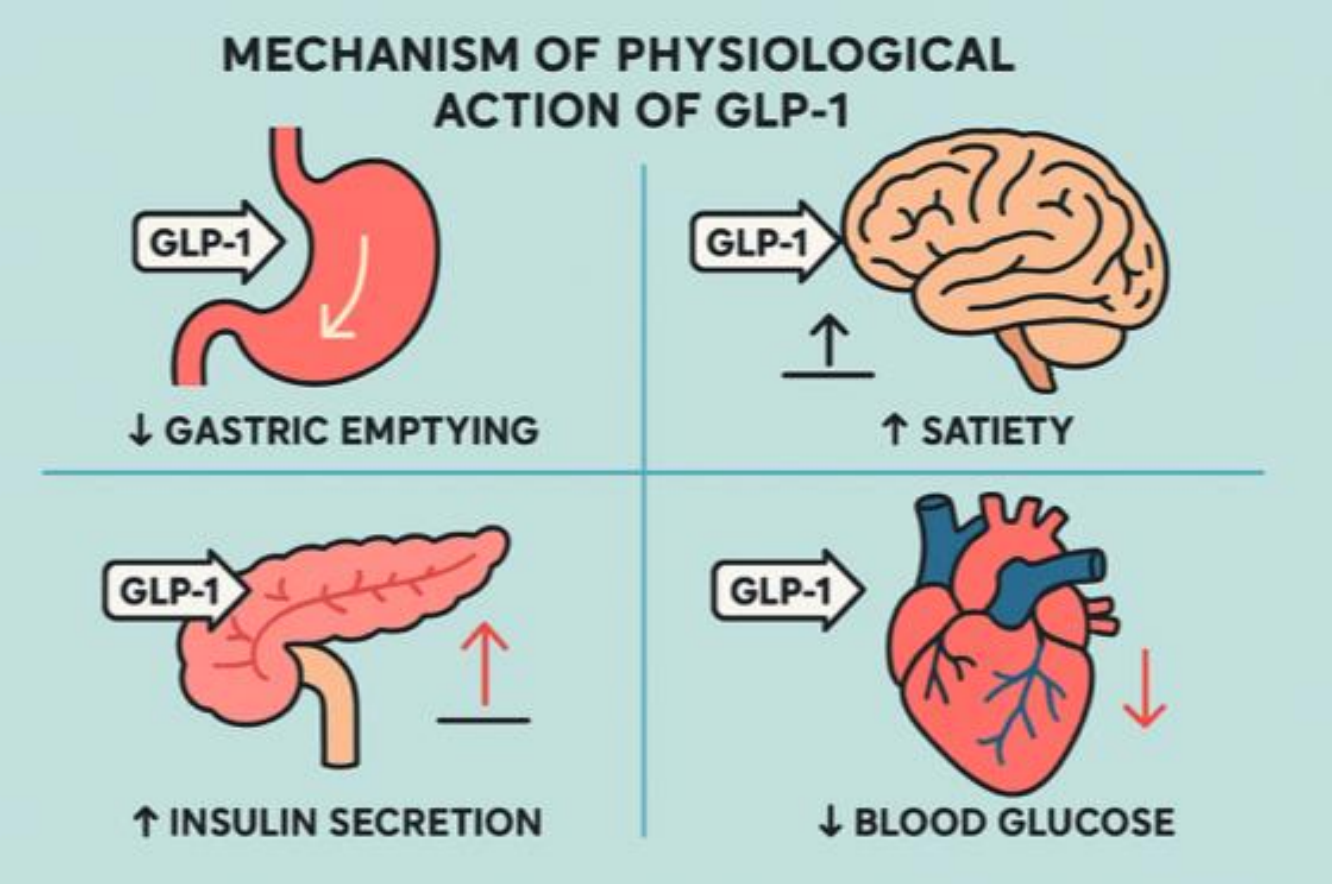
2024: First positive CVOT for a GLP-1RA (semaglutide) in obesity

CVOT = cardiovascular outcomes trial.

Drucker DJ, et al. *Nat Rev Drug Discov*. 2025;24(8):631-650.

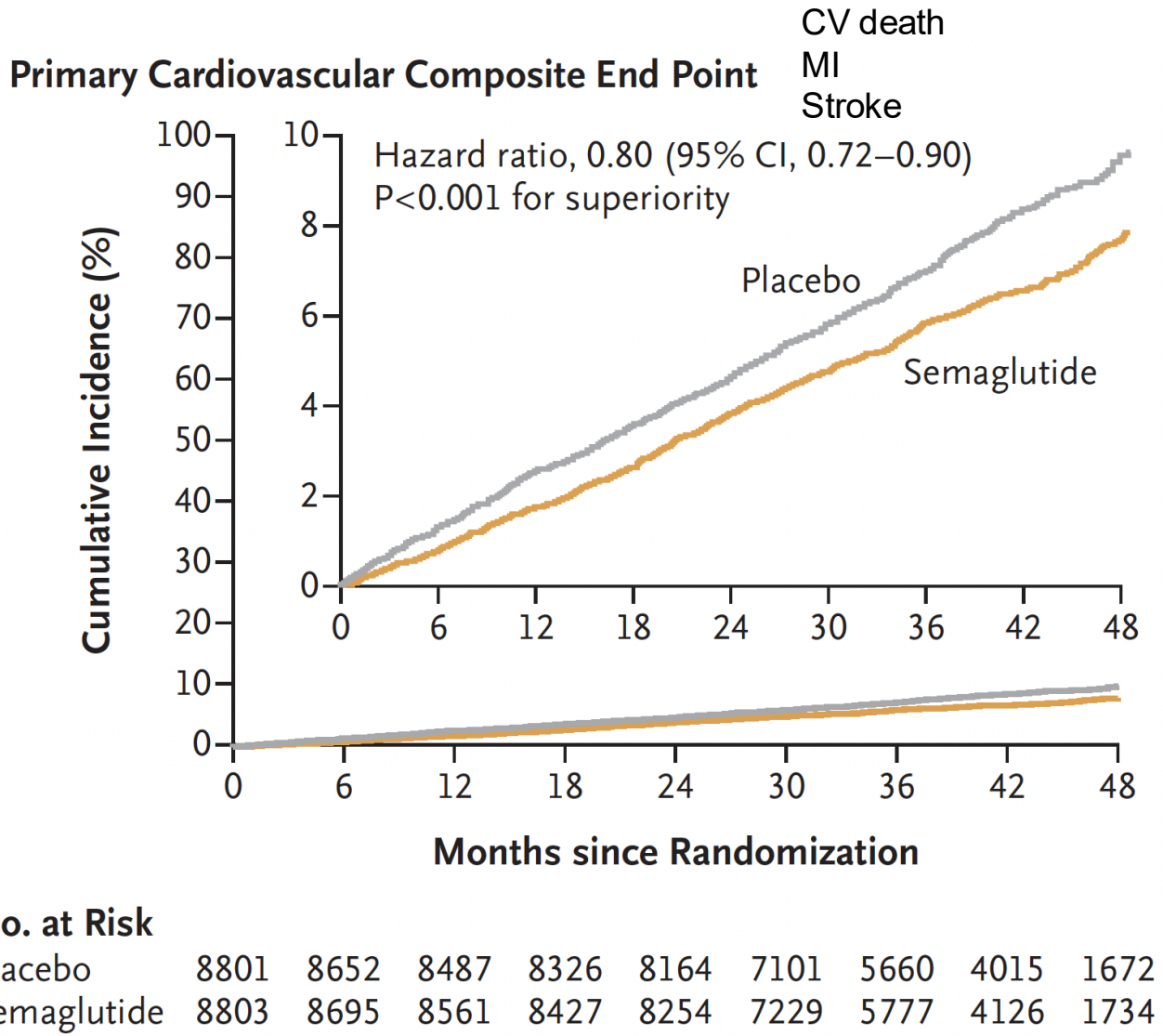
What Is GLP-1?

Naturally occurring hormone that is produced in the intestine with broad physiologic functions



Persson C, et al. *Diseases*. 2025;13(5):127.

SELECT Trial: ASCVD + Overweight/Obesity



20%

Other risk factors that improved

- Waist circum
- SBP/DBP
- Hs CRP
- LDL-C
- Triglycerides

SBP/DBP = systolic blood pressure / diastolic blood pressure.

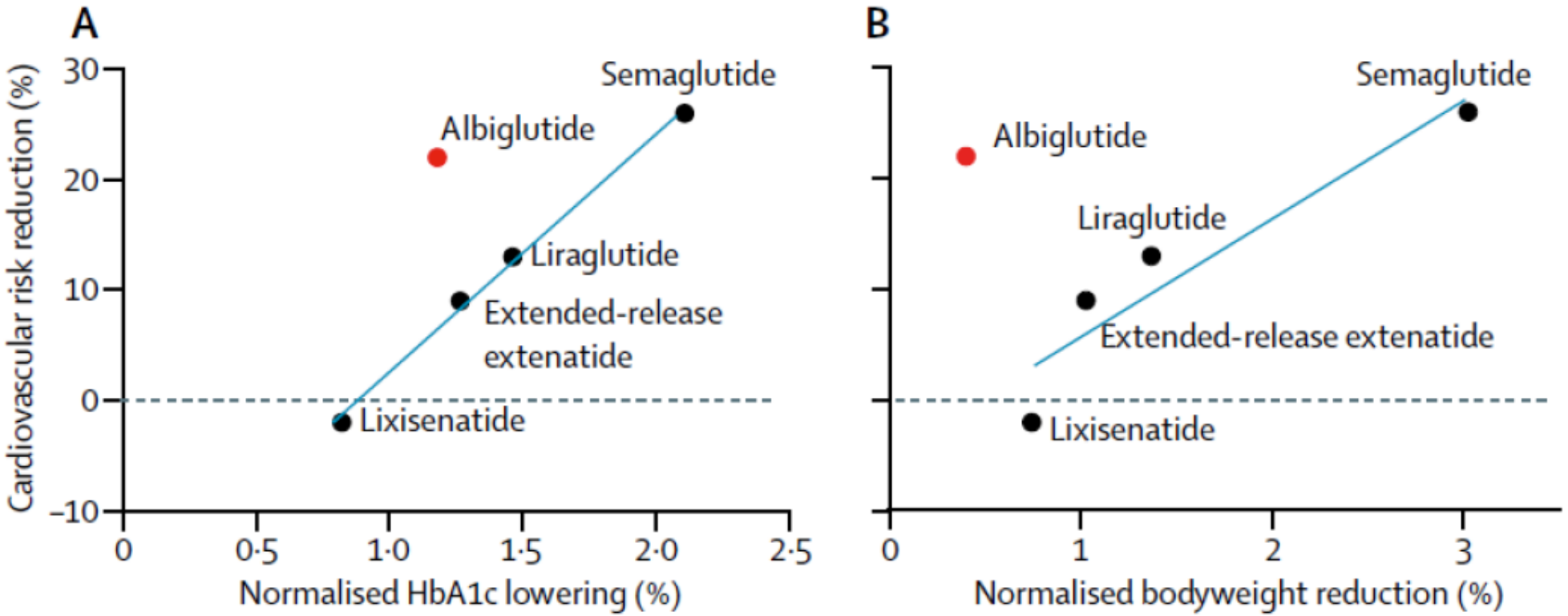
Lincoff AM, et al. *N Engl J Med*. 2023;389(24):2221-2232.

Changes in Cardiometabolic Parameters: SELECT Trial

Mean change from randomization to week 104			
Body weight — %	−9.39±0.09	−0.88±0.08	−8.51 (−8.75 to −8.27)
Waist circumference — cm	−7.56±0.09	−1.03±0.09	−6.53 (−6.79 to −6.27)
Glycated hemoglobin level — percentage points	−0.31±0.00	0.01±0.00	−0.32 (−0.33 to −0.31)
Systolic blood pressure — mm Hg	−3.82±0.16	−0.51±0.16	−3.31 (−3.75 to −2.88)
Diastolic blood pressure — mm Hg	−1.02±0.10	−0.47±0.10	−0.55 (−0.83 to −0.27)
Heart rate — beats/min	3.79±0.11	0.69±0.11	3.10 (2.80 to 3.39)
EQ-5D-5L index score§	0.01±0.00	−0.01±0.00	0.01 (0.01 to 0.02)
EQ-5D-VAS score§	2.52±0.16	0.92±0.16	1.60 (1.16 to 2.04)
High-sensitivity CRP level — %	−39.12	−2.08	−37.82 (−39.70 to −35.90)
Total cholesterol level — %	−4.63	−1.92	−2.77 (−3.37 to −2.16)
HDL cholesterol level — %	4.86	0.59	4.24 (3.70 to 4.79)
LDL cholesterol level — %	−5.25	−3.14	−2.18 (−3.22 to −1.12)
Triglyceride level — %	−18.34	−3.20	−15.64 (−16.68 to −14.58)

Lincoff AM, et al. *N Engl J Med*. 2023;389(24):2221-2232.

Relationship between GLP1 Agonists, HbA1c, and Body Weight Reduction



Zweck E, Roden M. *Lancet Diabetes Endocrinol*. 2019;7(2):89-90.

Future Directions in Psoriasis and Psoriatic Arthritis: TOGETHER-PsA Study

- 271 adults with PsA and obesity/overweight
- IL-17A antagonist/GLP-1/GIP RA vs IL-17A
- Primary endpoint: ACR50 AND >10% weight reduction

At 36 weeks, the TOGETHER-PsA study met its primary endpoint of 50% improvement in psoriatic arthritis activity based on ACR50 in addition to ≥10% weight reduction

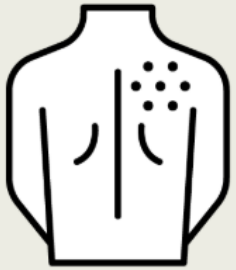
PsA = psoriatic arthritis; GIP RA = glucose-dependent insulinotropic polypeptide receptor agonist; ACR = American College of Rheumatology.
Merola JF, et al. *Arthritis Rheumatol*. 2026 [Epub ahead of print].

TOGETHER-PsO Phase 3b Clinical Trial

RCT: Ixekizumab With or Without Tirzepatide in Adults With Psoriasis and Overweight or Obesity

POPULATION

151 Male, 123 Female



Adults with psoriasis and overweight with ≥1 weight-related comorbidity or obesity

Mean (SD) age, 45.6 (12.7) y

SETTINGS / LOCATIONS

72 Sites in the US

INTERVENTION

274 Patients randomized and analyzed



136 Ixekizumab
Subcutaneous ixekizumab as adjunct to diet and exercise



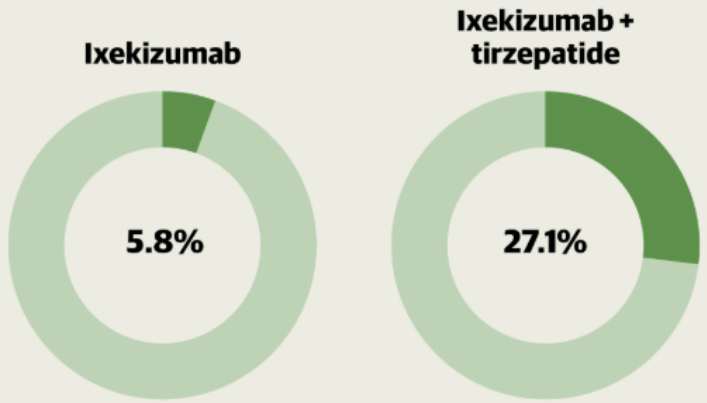
138 Ixekizumab plus tirzepatide
Subcutaneous ixekizumab plus tirzepatide as adjunct to diet and exercise

PRIMARY OUTCOME

Simultaneous achievement of Psoriasis Activity and Severity Index improvement from baseline of 100% (PASI 100) and ≥10% weight reduction at week 36

FINDINGS

Overall, 27.1% of participants receiving ixekizumab + tirzepatide vs 5.8% receiving ixekizumab achieved PASI 100 and ≥10% weight reduction at week 36



Response rate
Ixekizumab group: 5.8% (95% CI, 1.9% to 9.8%)
Ixekizumab plus tirzepatide group: 27.1% (95% CI, 19.6% to 34.5%)
Risk difference: 21.2% (95% CI, 12.8% to 29.7%); *P* < .001

Lebwohl M, et al. *JAMA Dermatol*. 2026;162(7):709-719.

How I Use GLP-1 RAs in Clinical Practice

- First of all, get them approved
  - In patients with type II diabetes
  - Medicare patients with obesity who have had an atherosclerotic cardiovascular event
  - Insurance coverage is getting better
  - Injectable: Tirzepatide/semaglutide self-pay program → $350 to $450/month
  - Oral: Semaglutide pill/orforglipron self-pay program → up to $350/month
  - Medicare GLP-1 Bridge Program ($50/month)

- Counsel patients on side effects, utility, and duration
  - Contraindicated in patients with medullary thyroid cancer, pregnancy, and breastfeeding
  - Start at low doses, increase slowly
  - Accompanied by lifestyle changes, low saturated fat diets…please
  - Dose adjustment/holding may be required before surgery

In the Right Patient, I Consider GLP-1 Agonists an Anti-Hypertensive

- Patient I saw several weeks ago in clinic

- 54 years old
  - Idiopathic pericarditis
  - Obesity (BMI 35 kg/m^2)
  - Hypertension
  - Pre-DMII

- Clinic notes 3/2025
  - Olmesartan 40 mg, amlodipine 2.5 mg
  - Blood pressure 120/78 mm Hg
  - Just uptitrated to 5 mg of tirzepatide

- Clinic notes 9/2025
  - Lost 35 pounds
  - Blood pressure 108/60 mm Hg
  - Stopped amlodipine

DMII = diabetes mellitus type 2.

I Don’t Really Consider Them to Be Lipid-Lowering, and Certainly Should Not Preclude a Statin…with Some Exceptions

- **7/2022**
- 37-year-old female
- Obesity – 286 lbs
- Pregnancy-induced HTN
- LDL 192 mg/dL
- BP 138/88 mm Hg
- Food recall
  - High in saturated fat
- Started tirzepatide

- **8/2025**
- Technically still overweight – 155 lbs
- LDL – 77 mg/dL
- Exercises daily – 45 minutes to 1 hour
  - Runs, soul cycle
- BP 116/80 mm Hg

HTN = hypertension.

Case-Based Discussion: Treatment Selection in Patients with PsO/PsA

A 52-year-old man presents for evaluation of worsening plaque psoriasis. He has had psoriasis for 15 years and reports increasing pruritus, scaling, and joint pain despite treatment with high-potency topical corticosteroids and intermittent phototherapy.

PMHx
- Psoriatic arthritis
- New pre-diabetes
- New hypertension
- Obesity (BMI 32 kg/m^2)

Medications
- Olmesartan 40 mg
- Amlodipine 2.5 mg

Relevant labs
- LDL-c 110 mg/dL
- Triglycerides 270 mg/dL
- Hemoglobin A1c 5.8%

PMHx = past medical history.

Case Continued

- **Physical exam**
  - **Blood pressure: 145/85 mm Hg**
  - **BSA:** 25%
  - **Investigator's Global Assessment (IGA):** 4 (Severe)
  - Thick, well-demarcated erythematous plaques with overlying silvery scale involving the scalp, trunk, upper and lower extremities
  - Nail pitting and onycholysis
  - Swollen and tender MCP and PIP joints consistent with active psoriatic arthritis

MCP = metacarpophalangeal; PIP = proximal interphalangeal.

What Do We Do?

- Which of the following biologic therapies is the **most appropriate initial treatment** for this patient?
  - **A. Adalimumab (TNF-α inhibitor)**
  - **B. Ixekizumab (IL-17A inhibitor)**
  - **C. Guselkumab (IL-23 inhibitor)**
  - **D. Ustekinumab (IL-12/23 inhibitor)**

B. Ixekizumab (IL-17A inhibitor)

Patient was also up-titrated to 5 mg of tirzepatide



Multidisciplinary Management

- How to identify metabolic comorbidities
  - Be the “Playmaker”!

Table 1.

Recommended targeted medical history, physical examination, and laboratory tests for a patient with psoriasis and obesity

Directed anamnesis
Dietary habits (type of diet, regular meal times, changes on holidays)
Physical exercise (type, duration/week)
Onset of obesity
Drugs with harmful metabolic profiles (glucocorticoids, paroxetine, antipsychotics, etc.)
Presence of other metabolic complications (diabetes, hypertension, dyslipidemia, hyperuricemia, etc.)
Presence of mechanical complications (psoriatic arthritis, OSAHS, etc.)
Presence of psychological complications (depression, binge eating disorder, emotional eating, etc.)
Personal history of cardiovascular events (AMI, stroke, etc.)
Family history of obesity
Previous attempts at weight loss
Previous use of weight loss drugs

Physical examination
Weight, height, BMI, waist circumference
Blood pressure
Acanthosis nigricans
Hirsutism
Goiter
Red–purple stretch marks

Recommended laboratory tests
Fasting glucose, HbA1c
Creatinine, glomerular filtration rate
Lipid profile (LDLc, HDLc, triglycerides)
Insulin, HOMA
Liver profile
TSH
If clinically suspected: plasma cortisol

OSAHS = obstructive sleep apnea-hypopnea syndrome; AMI = acute MI; TSH = thyroid-stimulating hormone.
Nicolau J, et al. *Dermatol Ther* (Heidelb). 2026;16(2):687-700.

Multidisciplinary Management

- How to manage them
  - What counseling strategies can we use to address weight?



Multidisciplinary Management

- Referral pathways and multidisciplinary care models

Mitigating CV Risk in Psoriasis: Role of Dermatology/Rheumatology/Cardiology Collaborators

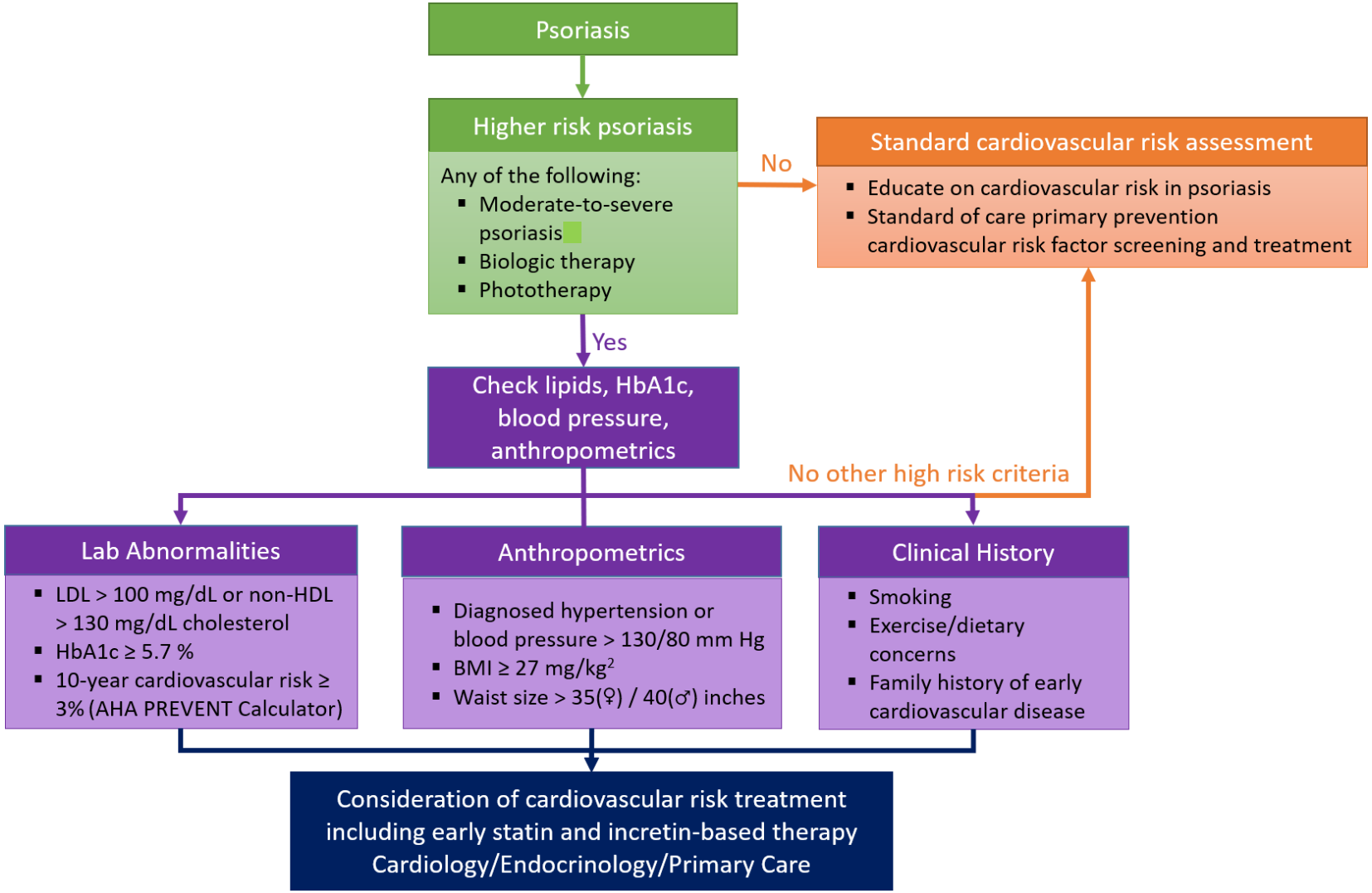
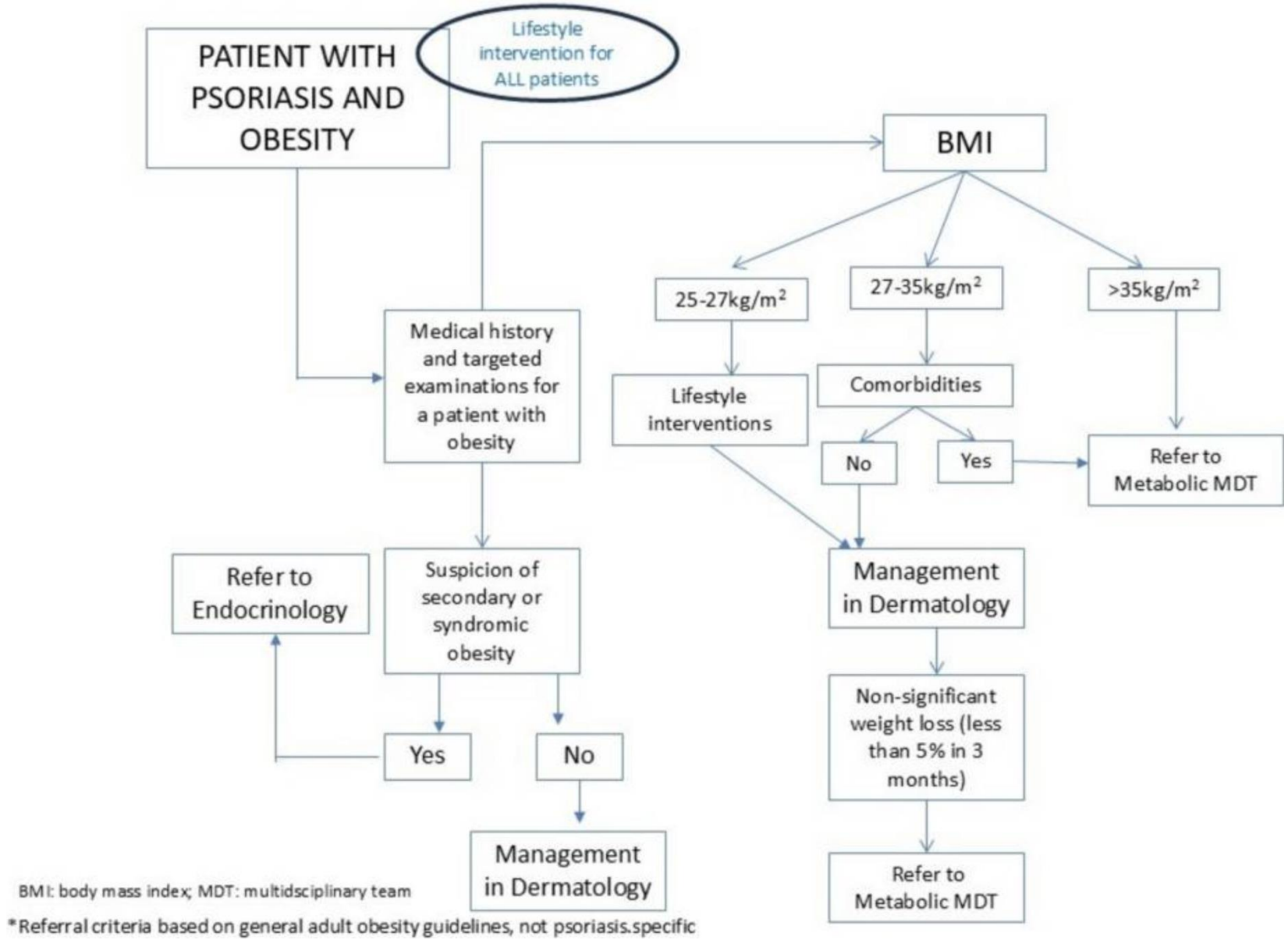


Image generated by Dr. Garshick.



Nicolau J, et al. *Dermatol Ther* (Heidelb). 2026;16(2):687-700.

Out with the Old, in with the New

The **old** psoriasis visit

- How is your skin?
- Any side effects?

The new psoriasis visit

- Skin disease
- Joint disease
- Diabetes risk
- Cardiovascular risk
- Mental health
- Lifestyle
- Preventive care

Clear skin is no longer the only outcome that matters

Every Patient with Moderate-Severe PsO



- **MEASURE**
  BP • Weight • BMI • Waist circumference
- **SCREEN**
  A1c/glucose • Lipids
- **ASK**
  Smoking • Activity • Diet • Family/CV history
- **ACT**
  Counsel • Treat PsO • Refer/coordinate when indicated

Case-Based Application

A 48-year-old woman presents with a 12-year history of **moderate-to-severe plaque psoriasis** involving approximately **22% BSA with an IGA of 4**. She has obesity (BMI 36 kg/m²), hypertension, type 2 diabetes mellitus, and hyperlipidemia. She reports worsening psoriasis despite topical therapy and intermittent joint stiffness, but has never been formally evaluated for psoriatic arthritis.

Although controlling her skin disease is important, her visit provides an opportunity to address psoriasis as a **systemic inflammatory disease** and evaluate health risks that may accompany it.

Screening and Counseling Considerations Include

- **Psoriatic arthritis:** Ask about joint pain, morning stiffness, swelling, dactylitis, heel pain, and inflammatory back pain; consider a validated screening tool such as PEST
- Cardiometabolic disease: Review blood pressure, BMI/weight trajectory, lipid profile, and glycemic control, and ensure appropriate primary care follow-up
- Mental health: Screen for depression/anxiety and discuss the effect psoriasis has on relationships, work, sleep, and quality of life (DLQI)
- Lifestyle: Discuss nutrition, physical activity, smoking, and alcohol use without making weight loss a prerequisite for appropriate psoriasis treatment
- Preventive health: Review age-appropriate cancer screening, vaccination status, and infectious-disease screening relevant to the systemic therapy being considered
- Psoriasis treatment: Discuss systemic/biologic therapy capable of achieving meaningful skin clearance while considering her joint symptoms, obesity, comorbidities, treatment preferences, and overall health

PEST = Psoriasis Epidemiology Screening Tool; DLQI = Dermatology Life Quality Index.

Key Learning Points



- Obesity and psoriasis share inflammatory pathways – and obesity measurably reduces biologic response (lower PASI 75/90/100, shorter drug survival)
- Screen every patient with moderate-to-severe PsO for obesity: BMI plus waist circumference, at every visit
- Weight-directed therapies – GLP-1s, tirzepatide, bariatric surgery – are emerging adjuncts to biologics, with combination approaches improving skin, joint, and metabolic outcomes
- PsO carries independent cardiometabolic risk beyond traditional factors – manage it through coordinated, multidisciplinary care

Questions?

Mark your calendar
for what's coming up next!

masterclasses in dermatology annual meeting

February 18–21, 2027
Signia by Hilton
Orlando Bonnet Creek

masterclasses in dermatology NP/PA institute

September 11–12, 2027
New York Marriott Marquis

October 23–24, 2027
Thompson Dallas by Hyatt

masterclasses in dermatology saturday morning live

Two 2026 dates remaining:
November 14, 2026
December 19, 2026



Click on Polling in the app to participate in this session

AMPHITHEATER

You can also scan this QR code: