

51 **Abstract**

52 Psoriasis is a common chronic inflammatory disease of the skin that is increasingly being
53 recognized as a systemic inflammatory disorder. Psoriatic arthritis is a well-known comorbidity
54 of psoriasis. A rapidly expanding body of literature in various populations and settings supports
55 additional associations between psoriasis and cardiometabolic disease, gastrointestinal disease,
56 kidney disease, malignancies, infections, and mood disorders. The pathogenesis of comorbid
57 disease in psoriasis patients remains unknown; however, shared inflammatory pathways, cellular
58 mediators, genetic susceptibility, and common risk factors are hypothesized to be contributing
59 elements. As additional psoriasis comorbidities continue to emerge, education of healthcare
60 providers is essential to ensuring comprehensive medical care for patients with psoriasis.

61 **Introduction**

62 Psoriasis is a common chronic inflammatory disease that affects over 7.5 million people
63 in the United States (U.S.) and approximately 125 million people worldwide.¹⁻³ It has significant
64 impacts on both physical and emotional health-related quality of life comparable to other major
65 illnesses.⁴ In the last decade, tremendous progress has been made in furthering our understanding
66 of the genetics, pathophysiology, and treatment of psoriasis. Epidemiologic and basic scientific
67 evidence contributing to our knowledge of the natural history and biology of psoriasis,
68 respectively, have led to the recognition of psoriasis as a disorder with important health
69 implications that extend beyond the skin.

70 The first observation of comorbid disease among patients with psoriasis was made in
71 1897 when Strauss⁵ reported an association between psoriasis and diabetes. In 1961, Reed, et al.⁶
72 described a high prevalence of heart disease including coronary thrombosis and myocardial
73 infarction (MI) in postmortem examinations of psoriasis patients with psoriatic arthritis (PsA).
74 Subsequently, in 1978, McDonald, et al.⁷ observed an increased prevalence of venous and
75 arterial vascular disease in hospitalized psoriasis patients. Now many years later, a quickly
76 evolving body of literature using modern epidemiological techniques has demonstrated that
77 psoriasis, particularly severe disease, is associated with increased mortality⁸ and comorbid
78 disease burden^{9,10} that are hypothesized to be the result of chronic inflammation associated with
79 the skin disease.

80 We review the epidemiologic data supporting associations between psoriasis and
81 cardiometabolic diseases, gastrointestinal diseases, kidney disease, malignancy, infection, mood
82 disorders, PsA, and other emerging comorbid diseases. Recognition of the comorbid disease

83 burden associated with psoriasis is essential for comprehensive medical care for patients with
84 this chronic skin disorder.

85

86 **Cardiometabolic Disease**

- 87 • Cardiometabolic disease is prevalent among patients with psoriasis, especially those with
88 more severe skin disease.
- 89 • Psoriasis may be an independent risk factor for diabetes and major adverse cardiovascular
90 events (MACE); risk of MACE is greatest among those with severe psoriasis.
- 91 • Chronic systemic, specifically vascular, inflammation may be increased in patients with
92 psoriasis and may contribute to atherogenesis.

93

94 *Major Adverse Cardiovascular Events*

95 Cardiovascular (CV) risk factors are prevalent among patients with psoriasis, thus, an
96 increased risk of CV disease (CVD) may be expected. However, in 2006, a large, population-
97 based cohort study in the United Kingdom (U.K.) demonstrated that psoriasis was associated
98 with an increased risk of MI, independent of traditional risk factors such as body mass index
99 (BMI), smoking, hypertension, diabetes, and dyslipidemia.¹¹ Moreover, a dose-response was
100 demonstrated with stronger, more clinically significant risks in patients with more severe disease
101 as defined by receipt of phototherapy or systemic therapies indicated for severe psoriasis.
102 Subsequently, numerous epidemiologic studies have similarly suggested psoriasis to be an
103 independent risk factor for MI, stroke, and death due to CVD, collectively termed MACE. While
104 a few studies have reported non-statistically significant associations between psoriasis and
105 MACE¹²⁻¹⁵ as discussed in detail elsewhere,¹⁶⁻¹⁸ results from these studies remain consistent with

106 the larger body of work that have found statistically significant associations. Many of the studies,
107 to date, have been summarized in at least one of eight meta-analyses of psoriasis and CVD
108 (Table I).¹⁹⁻²⁶ Two meta-analyses^{19,25} specifically examined the risks of MI, stroke, and CV
109 mortality according to psoriasis severity and reported the greatest risks to be among those with
110 severe disease. Risk of MI among patients with mild psoriasis was found to be significantly
111 increased in both meta-analyses,^{19,25} albeit to a lesser extent, suggesting that CV risk is not
112 limited to those with severe disease. Longer duration of psoriasis has also been associated with
113 increased risk of CVD.^{27,28} Collectively, these data provide evidence for psoriasis as an
114 independent risk factor for CVD.

115 Additional analyses have identified the clinical importance of and provided practical
116 measures for the increased risk of MACE associated with psoriasis.^{29,30} In a cohort study of
117 severe psoriasis patients in the U.K., Mehta, et al.²⁹ found the attributable risk of severe psoriasis
118 on MACE over a 10 year period to be 6.2%. Importantly, in a study to determine the impact of
119 psoriasis on the Framingham Risk Score (FRS), adding psoriasis to the FRS resulted in
120 reclassification of a majority of patients to a higher CV risk category whereby 73% of patients at
121 low risk were reclassified as intermediate risk and 53% of patients at intermediate risk as high
122 risk.³¹ Putting the psoriasis-associated CV risk into context with other chronic inflammatory
123 diseases, Ahlehoff, et al.³⁰ found the increased risk of MACE associated with severe psoriasis to
124 be nearly identical to that conferred by diabetes alone. Similarly, a single observational study of
125 patients with rheumatoid arthritis (RA) and psoriasis suggests that patients treated with similar
126 systemic treatments (e.g., methotrexate) each have similarly elevated risks of MACE,
127 independent of traditional risk factors.³²

128 Shared pathophysiologic pathways between psoriasis and CVD including chronic type 1
129 helper (Th1) T cell- and Th17-mediated inflammation³³⁻³⁸, monocyte and neutrophil
130 modulation³⁹⁻⁴¹, increased oxidative stress³⁵, endothelial cell dysfunction⁴², increased uric
131 acid^{43,44}, angiogenesis³⁵, and increased circulating microparticles⁴⁵⁻⁴⁸ may explain the increased
132 CVD risk associated with psoriasis. Additionally, persistent pathophysiologic processes that
133 drive psoriasis (e.g., epidermal hyper-proliferation, inflammation,^{49,50} and angiogenesis) may
134 also exert pleiotropic adverse effects on the CV system that contribute to atherogenesis. Mouse
135 models of psoriasis have demonstrated that chronic skin-specific inflammation has systemic
136 effects including arterial hypertension⁵¹, endothelial dysfunction⁵¹, and vascular inflammation
137 and thrombosis.³⁸ Studies in psoriasis patients yield similarly consistent findings using [18F]-
138 fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT), a
139 sensitive tool for measuring vascular inflammation and visualizing macrophage activity *in vivo*.
140 Aortic inflammation measured by PET/CT is a predictor of future CV events and has been
141 shown to rapidly decrease when patients are exposed to interventions known to lower CV risk
142 (i.e., statins), thus making it an attractive surrogate endpoint to study.⁵² Aortic inflammation has
143 been observed to be increased in psoriasis patients in a manner that is independent of CV risk
144 factors and correlates with severity of skin disease,⁵³ lending further support to the idea that
145 inflammatory pathways in psoriasis exert systemic effects. Lastly, common genetics between
146 psoriasis, diabetes, and CVD such as CDKAL1, ApoE4, and others have been suggested,⁵⁴⁻⁶⁴
147 and genes relevant to metabolic disease and CVD have been found to be dysregulated in lesional
148 skin and in the serum of psoriasis patients.⁶⁴⁻⁶⁶ On the other hand, other work suggests that
149 shared genetic pathways are unlikely to explain the association between psoriasis and CVD.⁶⁷
150

151 *Obesity*

152 Obesity is an independent risk factor for psoriasis. In studies of incident psoriasis,⁶⁸⁻⁷⁰ the
153 risk of psoriasis was found to increase with higher BMI.⁶⁹ A meta-analysis of 16 observational
154 studies found a pooled odds ratio [OR] for the association between psoriasis and obesity to be
155 1.66 (95% confidence interval [CI] 1.46-1.89) (Table II).⁷¹ Among studies that accounted for
156 psoriasis severity, generally defined by treatment patterns, the pooled ORs for the association
157 between obesity and mild and severe psoriasis were 1.46 (95%CI 1.17-1.82) and 2.23 (95% CI
158 1.63-3.05), respectively. As further support for a relationship between psoriasis severity and
159 obesity, Langan, et al. performed a cross-sectional study of patients with psoriasis in the U.K. for
160 whom information on body surface area (BSA) involvement by psoriasis was available and
161 found a positive dose-dependent relationship between objective measures of psoriasis severity
162 and obesity.⁷²

163

164 *Hypertension*

165 Hypertension is more prevalent among patients with versus without psoriasis. A meta-
166 analysis of 24 observational studies found a pooled OR for the association between psoriasis and
167 hypertension to be 1.58 (95% CI 1.42-1.76).⁷³ The odds of hypertension among patients with
168 psoriasis increased with greater disease severity with ORs of 1.30 (95% CI 1.15-1.47) for mild
169 and 1.49 (95% CI 1.20-1.86) for severe psoriasis as defined by treatment patterns.⁴² Two cohort
170 studies also observed psoriasis to be associated with an increased risk of incident hypertension.

171 ^{74,75}

172 Importantly, studies of patients with hypertension suggest more severe hypertension and
173 poorly controlled blood pressure among patients with psoriasis compared with those without

174 psoriasis.^{76,77} Furthermore, the likelihood of poorly controlled hypertension appears to increase
175 with more severe skin disease, independent of BMI and other risk factors⁷⁷.

176

177 *Diabetes*

178 Psoriasis is associated with an increased risk of diabetes, independent of traditional risk
179 factors. A meta-analysis of five cohort studies assessing the risk of incident diabetes among
180 patients with psoriasis found a pooled relative risk (RR) for diabetes of 1.27 (95% CI, 1.16-
181 1.40).⁷⁸ The risk of diabetes and likelihood of insulin resistance and diabetic complications are
182 suggested to increase with greater psoriasis severity as defined by treatment patterns or BSA
183 affected, respectively, independent of traditional risk factors such as BMI.^{72,79} Moreover,
184 diabetic patients with psoriasis appear to be more likely to require pharmacological
185 management⁷⁹ and suffer from micro- and macrovascular diabetes complications than diabetic
186 patients without psoriasis.⁸⁰

187

188 *Dyslipidemia*

189 Dyslipidemia may be more prevalent among patients with than without psoriasis. In a
190 systematic review, 20 of 25 included studies found significant associations between psoriasis and
191 dyslipidemia with ORs ranging from 1.04 to 5.55.⁸¹ Among three of the studies included in the
192 systematic review, the ORs for dyslipidemia ranged from 1.10 to 3.38 for patients with mild
193 psoriasis and from 1.36-5.55 for patients with severe psoriasis. The directionality of the
194 association between the two conditions remains unclear as some studies suggest dyslipidemia
195 may be a risk factor for developing psoriasis.^{82,83}

196 Advanced lipid testing techniques have demonstrated a more atherogenic lipid profile and
197 decreased high density lipoprotein (HDL) cholesterol efflux capacity (CEC) among patients with
198 versus without psoriasis, beyond CV risk factors.^{84,85} Increasing psoriasis severity has also been
199 found to correlate negatively with HDL CEC in both adults and children with psoriasis.^{85,86}
200 Furthermore, HDL CEC is directly related to coronary artery disease burden in patients with
201 psoriasis⁸⁷ and is suggested to be an important proxy for vascular disease.

202

203 *Metabolic Syndrome*

204 Metabolic syndrome is generally defined by the presence of a combination of central
205 obesity, hypertension, insulin resistance, and dyslipidemia.⁸⁸ Studies have found metabolic
206 syndrome as well as its individual components to be more prevalent among patients with than
207 without psoriasis in both adult and pediatric populations.^{89,90} A meta-analysis of 12 observational
208 studies found a pooled OR of 2.26 (95% CI 1.70-3.01) for the association between psoriasis and
209 metabolic syndrome, though the analysis was limited by presence of publication bias and
210 absence of small studies in the published literature.⁸⁹ Importantly, in Langan, et al.'s cross-
211 sectional study in the U.K., the prevalence of metabolic syndrome correlated directly with BSA
212 affected by psoriasis.⁷²

213

214 **Gastrointestinal Disease**

- 215 • Psoriasis may be associated with an increased incidence and prevalence of inflammatory
216 bowel disease (IBD), particularly Crohn's disease (CD).
- 217 • Few studies suggest that psoriasis is associated with an increased prevalence of hepatic
218 diseases, particularly nonalcoholic fatty liver disease (NAFLD).

219

220 *Inflammatory Bowel Disease*

221 Common genetic and inflammatory pathways have been implicated in psoriasis and IBD
222 which includes CD and ulcerative colitis (UC).^{59,91-94} The epidemiology of this relationship
223 remains poorly defined. Several studies have observed increased prevalence and incidence of
224 IBD among patients with psoriasis^{95,96} and vice versa⁹⁷⁻⁹⁹ with varying degrees of association,
225 and a Taiwanese study suggested an absence of association.¹⁰⁰ Cohen, et al.⁹⁵ observed that
226 psoriasis may be more strongly associated with CD than UC (OR 2.49 [95% CI, 1.71-3.62] and
227 1.64 [95% CI, 1.15-2.23], respectively). Similarly, a cohort study of U.S. women found an
228 increased risk of CD among patients with psoriasis (RR 3.86 [95% CI, 2.23-6.67]) while the risk
229 of UC was attenuated and not statistically significant (RR 1.17 [95% CI, 0.41-3.36]).⁹⁶

230

231 *Hepatic Disease*

232 NAFLD is a common chronic liver disease in Western industrialized countries¹⁰¹ and
233 encompasses a spectrum of liver disorders from mild hepatic steatosis to nonalcoholic
234 steatohepatitis (NASH). Associations between psoriasis and NAFLD have been reported in the
235 literature. In a meta-analysis of seven observational studies which were considered low to
236 moderate quality and, for the most part, did not adjust for potential confounding factors such as
237 metabolic syndrome, NAFLD was found to be more prevalent among patients with versus
238 without psoriasis (pooled OR 2.15 [95% CI, 1.57-2.94]).¹⁰² Beyond NAFLD, a cross-sectional
239 study in the U.K. found that psoriasis is associated with a higher prevalence of “mild” liver
240 disease including chronic hepatitis, alcoholic liver disease, and NAFLD (OR 1.41 [95% CI 1.12-

241 1.76]).⁹ A positive dose-response relationship between psoriasis severity based on BSA
242 involvement and “mild” liver disease was also observed.

243

244 **Chronic Kidney Disease**

- 245 • Moderate-to-severe psoriasis may be an independent risk factor for chronic kidney
246 disease (CKD) and end-stage renal disease (ESRD).
- 247 • The odds of CKD increase in a dose-dependent manner with greater psoriasis severity.

248

249 The term “psoriatic nephropathy” was first introduced based on case reports of
250 glomerulonephritides in patients with psoriasis.¹⁰³ Until recently, most studies assessing the
251 association between psoriasis and kidney disease have been small and cross-sectional with
252 varying results. In a U.K. cohort study of cause-specific mortality among patients with psoriasis,
253 severe psoriasis was associated with a four-fold increased risk of death from nephritic or non-
254 hypertensive kidney disease.¹⁰⁴ A Swedish cohort study also found mild psoriasis to be
255 associated with more than a two-fold increased risk of death from kidney disease.¹⁰⁵ In 2013,
256 another U.K. cohort study found that severe psoriasis may, in fact, be a risk factor for CKD and
257 ESRD, independent of traditional risk factors such as age, sex, BMI, CVD, diabetes,
258 hypertension, hyperlipidemia, and nephrotoxic medications (hazard ratio [HR] for CKD 1.93,
259 95% CI 1.79-2.08, and HR for ESRD 4.15, 95% CI 1.70-10.11).¹⁰⁶ A nested cross-sectional
260 analysis of patients with psoriasis for whom information on BSA involvement was available
261 found the prevalence of CKD to increase in a dose-dependent manner with more severe
262 psoriasis. A cohort study in Taiwan similarly found severe psoriasis to be associated with nearly
263 two- and three-fold increased risks of CKD and ESRD, respectively.¹⁰⁷

264

265 **Malignancy**

- 266 • Psoriasis, particularly severe disease, may be associated with an increased risk of cancer.
- 267 • Lymphoma has been most consistently associated with psoriasis, and risk for cutaneous T
- 268 cell lymphoma is suggested to be the highest.

269

270 Patients receiving treatments for severe psoriasis have a 41% increased risk of dying
271 from malignancy than patients without psoriasis.¹⁰⁴ Risk of malignancy due to psoriasis, itself,
272 remains uncertain. A meta-analysis of 11 observational studies evaluating the risk of malignancy
273 among patients with psoriasis suggests that overall risk of cancer, excluding non-melanoma skin
274 cancers (NMSC), is increased (standardized incidence ratio 1.16 (95% CI, 1.07-1.25)).¹⁰⁸ Greater
275 risks of upper aerodigestive tract, respiratory tract, liver, pancreas, and urinary tract cancers, and
276 lymphoma were also suggested.¹⁰⁸ The level of heterogeneity among the included studies was
277 high, though, making interpretation challenging. Furthermore, many studies did not account for
278 important confounding factors such as smoking and drinking and/or assess psoriasis treatment
279 effects on the risk of subsequent malignancy calling into question the validity of attributing the
280 increased risk of cancer to psoriasis, alone. A subsequent cohort study of cancer risk among
281 patients with psoriasis in the U.K. that included information on BMI, smoking, and drinking also
282 found increased risks of lung cancer, NMSC, and lymphoma, supporting some of Pouplard, et
283 al.'s findings.¹⁰⁹ The greatest risks of cancer were among those receiving treatments for severe
284 psoriasis. The association between psoriasis and lung cancer was lost, however, after
285 stratification by smoking status. Additional studies¹¹⁰⁻¹¹² assessing lymphoma risk in patients
286 with psoriasis also found persistently increased risks of lymphoma (1.3 to 2-fold increased risk)

287 even among those without a history of immunosuppressive therapy, though absolute risks
288 remained low. Of the specific lymphoma types, the association between psoriasis and cutaneous
289 T cell lymphoma (CTCL) was suggested to be the strongest.^{109,112} It remains unclear what role
290 psoriasis therapies and/or misdiagnosis of CTCL as psoriasis may play in explaining this
291 observation.

292

293 **Infection**

- 294 • Streptococcal pharyngitis is a trigger of guttate psoriasis, and exacerbation of psoriasis in
295 the setting of Human Immunodeficiency Virus (HIV) infection is known.
- 296 • Psoriasis may be associated with an increased risk of serious infection (i.e., infection
297 requiring hospitalization), especially respiratory infections.

298

299 Infection is the second leading cause of excess death among patients receiving therapies
300 for severe psoriasis, and patients with severe psoriasis have a 65% increased risk of dying from
301 infection than patients without psoriasis.¹⁰⁴ With the advent of targeted biologic therapies, much
302 attention has been paid to measuring the risk of infection associated with these therapies for
303 psoriasis. However, infection risk attributable to psoriasis itself remains poorly understood. The
304 most well-recognized association between psoriasis and infection is that of guttate psoriasis and
305 streptococcal pharyngitis which is thought to be caused by molecular mimicry of streptococcal
306 M peptides and human keratins.^{113,114} Exacerbation of psoriasis in the setting of HIV infection
307 has also been documented.^{115,116} The risk of serious infection among patients with psoriasis has
308 only more recently been evaluated.^{117,118} A Dutch cohort study found psoriasis to be an
309 independent risk factor for serious infection (HR 1.54, 95% CI 1.44-1.65) whereby the greatest

310 risk was among patients with severe psoriasis as defined by treatment patterns (HR 1.81, 95% CI
311 1.57-2.08).¹¹⁷ Respiratory tract, abdominal, and skin infections were the most common infections
312 among psoriasis patients. Similarly, a cohort study in Taiwan reported an increased risk of
313 hospitalized pneumonia among patients with psoriasis, independent of other potential risk factors
314 for pneumonia (HR 1.40, 95% CI 1.12-1.73). Severe psoriasis was associated with the greatest
315 risk of hospitalized pneumonia (HR 1.68, 95% CI 1.12-2.52).¹¹⁸ While neither study had access
316 to information on potential confounders such as obesity, smoking, and drinking, subsequent
317 cohort studies in the U.K. including this information confirmed that psoriasis is associated with
318 increased risks of serious infection¹¹⁹ including hospitalized pneumonia,¹²⁰ and further suggested
319 that the risks may increase with greater BSA involvement by psoriasis.

320

321 **Mood Disorders**

- 322 • Mood disorders are common among patients with psoriasis.
- 323 • Psoriasis is associated with an increased risk of depression, anxiety, and suicidal ideation.

324

325 Psoriasis has a major impact on patients' physical and emotional health-related quality of
326 life comparable to other major illnesses⁴ that may predispose patients to the development of
327 mood disorders such as depression, anxiety, and suicidality. Mood disorders, particularly
328 depression, have been suggested to be more prevalent in patients with psoriasis than in the
329 general population (up to 62% prevalence).¹²¹ In a meta-analysis of 98, mostly cross-sectional,
330 studies examining the association between psoriasis and depression, patients with psoriasis had
331 more depressive symptoms (pooled standardized mean difference 1.16; 95% CI 0.67-1.66) and

332 were nearly 1.6-fold more likely to experience depression (pooled OR 1.57; 95% CI 1.40-1.76)
333 than patients without psoriasis.¹²¹

334 The risk of depression in psoriasis has been evaluated in two cohort studies. In a U.K.
335 study, psoriasis was found to be associated with increased risks of depression (HR 1.39; 95% CI
336 1.37-1.41), anxiety (HR 1.31; 95% CI 1.29-1.34), and suicidality (HR 1.44; 95% CI 1.32-
337 1.57).¹²² The risk of depression was greatest among patients receiving therapies for severe
338 psoriasis (HR 1.72; 95% CI 1.57-1.88). Similarly, a study of women in the Nurses' Health
339 Study¹²³ found psoriasis to be associated with a nearly 30% increased risk of depression (RR
340 1.29; 95% CI 1.10-1.52), independent of age, BMI, lifestyle factors, and comorbid conditions.

341

342 **Psoriatic Arthritis**

- 343 • PsA is an inflammatory arthritis that is present in 6-42% of patients with psoriasis.
- 344 • PsA is more prevalent among patients with more extensive skin disease.
- 345 • Approximately 15% of patients with psoriasis have undiagnosed PsA.

346

347 PsA is the most well-recognized comorbidity of psoriasis and is a heterogeneous
348 inflammatory arthritis characterized by joint and/or enthesial inflammation and extra-articular
349 manifestations.¹²⁴ The prevalence of inflammatory arthritis in psoriasis patients ranges between
350 6-42% depending on the definitions used and populations studied.¹²⁵⁻¹³⁸ The prevalence of PsA
351 increases with greater psoriasis severity^{125,133,139} and duration,^{125,140} however, the severity of skin
352 disease is only weakly associated with severity of joint disease. PsA has been associated with the
353 distribution of psoriasis involvement (i.e., scalp, intergluteal, perianal)¹⁴¹ and the presence of nail
354 dystrophy, which is suggested to indicate early enthesial inflammation^{124,141,142}.

355 The diagnosis of PsA can be especially challenging. The differential diagnosis includes
356 osteoarthritis, RA, crystal arthropathy (e.g., gout or calcium pyrophosphate disease), and
357 fibromyalgia.^{124,143-147} Undiagnosed PsA among psoriasis patients seen in the dermatology
358 setting is prevalent and estimated at 15.5%.¹⁴⁸ PsA generally occurs after the onset of
359 psoriasis^{142,148} and can be progressive and result in permanent joint damage. Therefore, early
360 detection is essential as early treatment improves outcomes.^{124,149,150} The varied clinical features
361 of and classification criteria for PsA as well as associations with cardiometabolic and other
362 comorbid diseases are reviewed elsewhere.^{124,151}

363

364 **Emerging Comorbidities**

- 365 • Other emerging comorbidities of psoriasis include chronic obstructive pulmonary disease,
366 peptic ulcer disease, sexual dysfunction, and obstructive sleep apnea.

367

368 Additional epidemiologic studies have suggested associations between psoriasis and
369 other emerging comorbid conditions including chronic obstructive pulmonary disease,^{9,152,153}
370 peptic ulcer disease,^{9,154} sexual dysfunction,¹⁵⁵ and obstructive sleep apnea,¹⁵⁶⁻¹⁵⁸ among others.
371 Further characterization of known comorbidities and identification of new comorbid disease
372 associations with psoriasis are anticipated as research efforts continue.

373 In summary, it is essential for both clinicians and patients to recognize the potentially
374 heightened risk of CVD and other comorbidities associated with psoriasis which may increase
375 with greater disease severity and duration. Particularly as psoriasis remains largely
376 undertreated^{159,160}, the disease remains active for decades in most patients, potentially placing
377 them at increased risk for associated comorbidities and mortality. Patient and provider education

378 as well as increased awareness of psoriasis comorbidities are critical to improving the care and
379 quality of life for those living with psoriasis.

380 **Acknowledgement**

381 We are indebted to Jina Chung, MD for her early contributions to preparation of the manuscript.

382 **Abbreviations and Acronyms**

BMI	Body mass index
BSA	Body surface area
CAD	Coronary artery disease
CD	Crohn's disease
CEC	Cholesterol efflux capacity
CHD	Coronary heart disease
CI	Confidence interval
CKD	Chronic kidney disease
CTCL	Cutaneous T cell lymphoma
CV	Cardiovascular
CVD	Cardiovascular disease
ESRD	End-stage renal disease
FDG	Fluorodeoxyglucose
FRS	Framingham Risk Score
HDL	High density lipoprotein
HIV	Human immunodeficiency virus
HR	Hazard ratio
IBD	Inflammatory bowel disease
IHD	Ischemic heart disease
IRR	Incidence rate ratio
MACE	Major adverse cardiovascular event
MI	Myocardial infarction
NAFLD	Nonalcoholic fatty liver disease

NASH	Nonalcoholic steatohepatitis
NMSC	Non-melanoma skin cancer
OR	Odds ratio
PET/CT	Positron emission tomography/computed tomography
PsA	Psoriatic arthritis
RA	Rheumatoid arthritis
RR	Relative risk or risk ratio
Th	T helper
UC	Ulcerative colitis

384 **References**

- 385 1. National Psoriasis Foundation. https://www.psoriasis.org/cure_known_statistics.
386 Accessed October 1, 2015.
- 387 2. Kurd SK, Gelfand JM. The prevalence of previously diagnosed and undiagnosed
388 psoriasis in US adults: results from NHANES 2003-2004. *J Am Acad Dermatol*.
389 2009;60(2):218-224.
- 390 3. Rachakonda TD, Schupp CW, Armstrong AW. Psoriasis prevalence among adults in the
391 United States. *J Am Acad Dermatol*. 2014;70(3):512-516.
- 392 4. Rapp SR, Feldman SR, Exum ML, et al. Psoriasis causes as much disability as other
393 major medical diseases. *J Am Acad Dermatol*. 1999;41(3 Pt 1):401-407.
- 394 5. Strauss H. Zur Lehre von der neurogenen und der thyreogenen Glykosurie. *Dtsch Med*
395 *Wochenschr*. 1897;20:309-312.
- 396 6. Reed WB, Becker SW, Rohde R, et al. Psoriasis and arthritis. Clinicopathologic study.
397 *Arch Dermatol*. 1961;83:541-548.
- 398 7. McDonald CJ, Calabresi P. Psoriasis and occlusive vascular disease. *Br J Dermatol*.
399 1978;99(5):469-475.
- 400 8. Gelfand JM, Troxel AB, Lewis JD, et al. The risk of mortality in patients with psoriasis:
401 results from a population-based study. *Arch Dermatol*. 2007;143(12):1493-1499.
- 402 9. Yeung H, Takeshita J, Mehta NN, et al. Psoriasis severity and the prevalence of major
403 medical comorbidity: a population-based study. *JAMA Dermatol*. 2013;149(10):1173-
404 1179.
- 405 10. Tsai TF WT, Hung ST, Tsai PI, et al. Epidemiology and comorbidities of psoriasis
406 patients in national database in Taiwan. *J Dermatol Sci*. 2011;63(1):40-46.

- 407 11. Gelfand JM, Neimann AL, Shin DB, et al Risk of myocardial infarction in patients with
408 psoriasis. *JAMA*. 2006;296(14):1735-1741.
- 409 12. Brauchli YB, Jick SS, Miret M, et al. Psoriasis and risk of incident myocardial infarction,
410 stroke or transient ischaemic attack: an inception cohort study with a nested case-control
411 analysis. *Br J Dermatol*. 2009;160(5):1048-1056.
- 412 13. Wakkee M, Herings RM, Nijsten T. Psoriasis may not be an independent risk factor for
413 acute ischemic heart disease hospitalizations: results of a large population-based Dutch
414 cohort. *J Invest Dermatol*. 2010;130(4):962-967.
- 415 14. Dowlatshahi EA, Kavousi M, Nijsten T, et al. Psoriasis is not associated with
416 atherosclerosis and incident cardiovascular events: the Rotterdam Study. *J Invest*
417 *Dermatol*. 2013;133(10):2347-2354.
- 418 15. Parisi R, Rutter MK, Lunt M, et al. Psoriasis and the risk of major cardiovascular events:
419 cohort study using the Clinical Practice Research Datalink. *J Invest Dermatol*.
420 2015;135(9):2189-2197.
- 421 16. Gelfand JM, Azfar RS, Mehta NN. Psoriasis and cardiovascular risk: strength in
422 numbers. *J Invest Dermatol*. 2010;130(4):919-922.
- 423 17. Gelfand JM, Mehta NN, Langan SM. Psoriasis and cardiovascular risk: strength in
424 numbers, part II. *J Invest Dermatol*. 2011;131(5):1007-1010.
- 425 18. Ogdie A, Troxel AB, Mehta NN, et al. Psoriasis and Cardiovascular risk: strength in
426 numbers part 3. *J Invest Dermatol*. 2015;135(9):2148-2150.
- 427 19. Armstrong EJ, Harskamp CT, Armstrong AW. Psoriasis and major adverse
428 cardiovascular events: a systematic review and meta-analysis of observational studies. *J*
429 *Am Heart Assoc*. 2013;2(2):e000062.

- 430 20. Gaeta M, Castelvechio S, Ricci C, et al. Role of psoriasis as independent predictor of
431 cardiovascular disease: a meta-regression analysis. *Int J Cardiol.* 2013;168(3):2282-
432 2288.
- 433 21. Gu WJ, Weng CL, Zhao YT, Liu QH, Yin RX. Psoriasis and risk of cardiovascular
434 disease: a meta-analysis of cohort studies. *Int J Cardiol.* 2013;168(5):4992-4996.
- 435 22. Horreau C, Pouplard C, Brenaut E, et al. Cardiovascular morbidity and mortality in
436 psoriasis and psoriatic arthritis: a systematic literature review. *J Eur Acad Dermatol*
437 *Venereol.* 2013;27 Suppl 3:12-29.
- 438 23. Miller IM, Ellervik C, Yazdanyar S, et al. Meta-analysis of psoriasis, cardiovascular
439 disease, and associated risk factors. *J Am Acad Dermatol.* 2013;69(6):1014-1024.
- 440 24. Pietrzak A, Bartosinska J, Chodorowska G, et al. Cardiovascular aspects of psoriasis: an
441 updated review. *Int J Dermatol.* 2013;52(2):153-162.
- 442 25. Samarasekera EJ, Neilson JM, Warren RB, et al. Incidence of cardiovascular disease in
443 individuals with psoriasis: a systematic review and meta-analysis. *J Invest Dermatol.*
444 2013;133(10):2340-2346.
- 445 26. Xu T, Zhang YH. Association of psoriasis with stroke and myocardial infarction: meta-
446 analysis of cohort studies. *Br J Dermatol.* 2012;167(6):1345-1350.
- 447 27. Armstrong AW, Harskamp CT, Ledo L, et al. Coronary artery disease in patients with
448 psoriasis referred for coronary angiography. *Am J Cardiol.* 2012;109(7):976-980.
- 449 28. Li WQ, Han JL, Manson JE, et al. Psoriasis and risk of nonfatal cardiovascular disease in
450 U.S. women: a cohort study. *Br J Dermatol.* 2012;166(4):811-818.
- 451 29. Mehta NN, Yu Y, Pinnelas R, et al. Attributable risk estimate of severe psoriasis on
452 major cardiovascular events. *Am J Med.* 2011;124(8):775 e771-776.

- 453 30. Ahlehoff O, Gislason GH, Charlott M, et al. Psoriasis is associated with clinically
454 significant cardiovascular risk: a Danish nationwide cohort study. *J Intern Med.*
455 2011;270(2):147-157.
- 456 31. Mehta NN, Krishnamoorthy P, Yu Y, et al. The impact of psoriasis on 10-year
457 Framingham risk. *J Am Acad Dermatol.* 2012;67(4):796-798.
- 458 32. Ogdie A, Yu Y, Haynes K, et al. Risk of major cardiovascular events in patients with
459 psoriatic arthritis, psoriasis and rheumatoid arthritis: a population-based cohort study.
460 *Ann Rheum Dis.* 2015;74(2):326-332.
- 461 33. Nestle FO, Kaplan DH, Barker J. Psoriasis. *N Engl J Med.* 2009;361(5):496-509.
- 462 34. Packard RR, Lichtman AH, Libby P. Innate and adaptive immunity in atherosclerosis.
463 *Semin Immunopathol.* 2009;31(1):5-22.
- 464 35. Armstrong AW, Voyles SV, Armstrong EJ, et al. Angiogenesis and oxidative stress:
465 common mechanisms linking psoriasis with atherosclerosis. *J Dermatol Sci.*
466 2011;63(1):1-9.
- 467 36. Armstrong AW, Voyles SV, Armstrong EJ, et al. A tale of two plaques: convergent
468 mechanisms of T-cell-mediated inflammation in psoriasis and atherosclerosis. *Exp*
469 *Dermatol.* 2011;20(7):544-549.
- 470 37. Spah F. Inflammation in atherosclerosis and psoriasis: common pathogenic mechanisms
471 and the potential for an integrated treatment approach. *Br J Dermatol.* 2008;159 Suppl
472 2:10-17.
- 473 38. Wang Y, Gao H, Loyd CM, et al. Chronic skin-specific inflammation promotes vascular
474 inflammation and thrombosis. *J Invest Dermatol.* 2012;132(8):2067-2075.

- 475 39. Davidovici BB, Sattar N, Prinz J, et al. Psoriasis and systemic inflammatory diseases:
476 potential mechanistic links between skin disease and co-morbid conditions. *J Invest*
477 *Dermatol.* 2010;130(7):1785-1796.
- 478 40. Mehta NN, Reilly MP. Monocyte mayhem: do subtypes modulate distinct atherosclerosis
479 phenotypes? *Circ Cardiovasc Genet.* 2012;5(1):7-9.
- 480 41. Noels H, Weber C. Catching up with important players in atherosclerosis: type I
481 interferons and neutrophils. *Curr Opin Lipidol.* 2011;22(2):144-145.
- 482 42. Alexandroff AB, Pauriah M, Camp RD, et al. More than skin deep: atherosclerosis as a
483 systemic manifestation of psoriasis. *Br J Dermatol.* 2009;161(1):1-7.
- 484 43. Puig JG, Mateos FA, Jimenez ML, et al. Uric acid metabolism in psoriasis. *Adv Exp Med*
485 *Biol.* 1986;195 Pt A:411-416.
- 486 44. Cassano N, Carbonara M, Panaro M, et al. Role of serum uric acid in conditioning the
487 association of psoriasis with metabolic syndrome. *Eur J Dermatol.* 2011;21(5):808-809.
- 488 45. Martínez-Sales V, Vila V, Ricart JM, et al. Increased circulating endothelial cells and
489 microparticles in patients with psoriasis. *Clin Hemorheol Microcirc.* 2015;60(3):283-290.
- 490 46. Pelletier F, Garnache-Ottou F, Angelot F, et al. Increased levels of circulating
491 endothelial-derived microparticles and small-size platelet-derived microparticles in
492 psoriasis. *J Invest Dermatol.* 2011;131(7):1573-1576.
- 493 47. Tamagawa-Mineoka R, Katoh N, Kishimoto S. Platelet activation in patients with
494 psoriasis: increased plasma levels of platelet-derived microparticles and soluble P-
495 selectin. *J Am Acad Dermatol.* 2010;62(4):621-626.

- 496 48. Takeshita J, Mohler ER, Krishnamoorthy P, et al. Endothelial cell-, platelet-, and
497 monocyte/macrophage-derived microparticles are elevated in psoriasis beyond
498 cardiometabolic risk factors. *J Am Heart Assoc.* 2014;3(1):e000507.
- 499 49. Rose S, Stansky E, Dagur PK, et al. Characterization of immune cells in psoriatic adipose
500 tissue. *J Transl Med.* 2014;12:258.
- 501 50. Cheung L, Fisher RM, Kuzmina N, et al. Psoriasis Skin Inflammation-Induced
502 microRNA-26b Targets NCEH1 in Underlying Subcutaneous Adipose Tissue. *J Invest*
503 *Dermatol.* 2016;136(3):640-648.
- 504 51. Karbach S CA, Oelze M, Schüler R, et al. Interleukin 17 drives vascular inflammation,
505 endothelial dysfunction, and arterial hypertension in psoriasis-like skin disease.
506 *Arterioscler Thromb Vasc Biol.* 2014;34(12):2658-2668.
- 507 52. Mehta NN, Yu Y, Saboury B, et al. Systemic and vascular inflammation in patients with
508 moderate to severe psoriasis as measured by [18F]-fluorodeoxyglucose positron emission
509 tomography-computed tomography (FDG-PET/CT): a pilot study. *Arch Dermatol.*
510 2011;147(9):1031-1039.
- 511 53. Naik HB, Natarajan B, Stansky E, et al. Severity of psoriasis associates with aortic
512 vascular inflammation detected by FDG PET/CT and neutrophil activation in a
513 prospective observational study. *Arterioscler Thromb Vasc Biol.* 2015;35(12):2667-2676.
- 514 54. Bowden DW, Rudock M, Ziegler J, et al. Coincident linkage of type 2 diabetes,
515 metabolic syndrome, and measures of cardiovascular disease in a genome scan of the
516 diabetes heart study. *Diabetes.* 2006;55(7):1985-1995.

- 517 55. Parker A, Meyer J, Lewitzky S, et al. A gene conferring susceptibility to type 2 diabetes
518 in conjunction with obesity is located on chromosome 18p11. *Diabetes*. 2001;50(3):675-
519 680.
- 520 56. Park MH, Kwak SH, Kim KJ, et al. Identification of a genetic locus on chromosome
521 4q34-35 for type 2 diabetes with overweight. *Exp Mol Med*. 2013;45:e7.
- 522 57. Ng MC, So WY, Lam VK, et al. Genome-wide scan for metabolic syndrome and related
523 quantitative traits in Hong Kong Chinese and confirmation of a susceptibility locus on
524 chromosome 1q21-q25. *Diabetes*. 2004;53(10):2676-2683.
- 525 58. Ng MC, So WY, Cox NJ, et al. Genome-wide scan for type 2 diabetes loci in Hong Kong
526 Chinese and confirmation of a susceptibility locus on chromosome 1q21-q25. *Diabetes*.
527 2004;53(6):1609-1613.
- 528 59. Wolf N, Quaranta M, Prescott NJ, et al. Psoriasis is associated with pleiotropic
529 susceptibility loci identified in type II diabetes and Crohn disease. *J Med Genet*.
530 2008;45(2):114-116.
- 531 60. Campalani E, Allen MH, Fairhurst D, et al. Apolipoprotein E gene polymorphisms are
532 associated with psoriasis but do not determine disease response to acitretin. *Br J*
533 *Dermatol*. 2006;154(2):345-352.
- 534 61. Nair RP, Ruether A, Stuart PE, et al. Polymorphisms of the IL12B and IL23R genes are
535 associated with psoriasis. *J Invest Dermatol*. 2008;128(7):1653-1661.
- 536 62. Genetic Analysis of Psoriasis Consortium & the Wellcome Trust Case Control
537 Consortium 21 SA, Capon F, Spencer CC, et al. A genome-wide association study
538 identifies new psoriasis susceptibility loci and an interaction between HLA-C and
539 ERAP1. *Nat Genet*. 2010;42(11):985-990.

- 540 63. Fung EY, Smyth DJ, Howson JM, et al. Analysis of 17 autoimmune disease-associated
541 variants in type 1 diabetes identifies 6q23/TNFAIP3 as a susceptibility locus. *Genes*
542 *Immun.* 2009;10(2):188-191.
- 543 64. Suarez-Farinas M, Li K, Fuentes-Duculan J, Hayden K, et al. Expanding the psoriasis
544 disease profile: interrogation of the skin and serum of patients with moderate-to-severe
545 psoriasis. *J Invest Dermatol.* 2012;132(11):2552-2564.
- 546 65. Eiris N, Gonzalez-Lara L, Santos-Juanes J, et al. Genetic variation at IL12B, IL23R and
547 IL23A is associated with psoriasis severity, psoriatic arthritis and type 2 diabetes
548 mellitus. *J Dermatol Sci.* 2014;75(3):167-172.
- 549 66. Mehta NN, Li K, Szapary P, et al. Modulation of cardiometabolic pathways in skin and
550 serum from patients with psoriasis. *J Transl Med.* 2013;11:194.
- 551 67. Adler BL, Krausz AE, Tian J, et al. Modifiable lifestyle factors in psoriasis: screening
552 and counseling practices among dermatologists and dermatology residents in academic
553 institutions. *J Am Acad Dermatol.* 2014;71(5):1028-1029.
- 554 68. Setty AR, Curhan G, Choi HK. Obesity, waist circumference, weight change, and the risk
555 of psoriasis in women: Nurses' Health Study II. *Arch Int Med.* 2007;167(15):1670-1675.
- 556 69. Kumar S, Han J, Li T, et al. Obesity, waist circumference, weight change and the risk of
557 psoriasis in US women. *J Eur Acad Dermatol Venereol.* 2013;27(10):1293-1298.
- 558 70. Naldi L, Chatenoud L, Linder D, et al. Cigarette smoking, body mass index, and stressful
559 life events as risk factors for psoriasis: results from an Italian case-control study. *J Invest*
560 *Dermatol.* 2005;125(1):61-67.

- 561 71. Armstrong AW, Harskamp CT, Armstrong EJ. The association between psoriasis and
562 obesity: a systematic review and meta-analysis of observational studies. *Nutr Diabetes*.
563 2012;2:e54.
- 564 72. Langan SM, Seminara NM, Shin DB, et al. Prevalence of metabolic syndrome in patients
565 with psoriasis: a population-based study in the United Kingdom. *J Invest Dermatol*.
566 2012;132(3 Pt 1):556-562.
- 567 73. Armstrong AW, Harskamp CT, Armstrong EJ. The association between psoriasis and
568 hypertension: a systematic review and meta-analysis of observational studies. *J*
569 *Hypertens*. 2013;31(3):433-442.
- 570 74. Qureshi AA, Choi HK, Setty AR, et al. Psoriasis and the risk of diabetes and
571 hypertension: a prospective study of US female nurses. *Arch Dermatol*. 2009;145(4):379-
572 382.
- 573 75. Kaye JA, Li L, Jick SS. Incidence of risk factors for myocardial infarction and other
574 vascular diseases in patients with psoriasis. *Br J Dermatol*. 2008;159(4):895-902.
- 575 76. Armstrong AW, Lin SW, Chambers CJ, et al. Psoriasis and hypertension severity: results
576 from a case-control study. *PLoS ONE*. 2011;6(3):e18227.
- 577 77. Takeshita J, Wang S, Shin DB, et al. Effect of psoriasis severity on hypertension control:
578 a population-based study in the United Kingdom. *JAMA Dermatol*. 2015;151(2):161-169.
- 579 78. Armstrong AW, Harskamp CT, Armstrong EJ. Psoriasis and the risk of diabetes mellitus:
580 a systematic review and meta-analysis. *JAMA Dermatol*. 2013;149(1):84-91.
- 581 79. Azfar RS, Seminara NM, Shin DB, et al. Increased risk of diabetes mellitus and
582 likelihood of receiving diabetes mellitus treatment in patients with psoriasis. *Arch*
583 *Dermatol*. 2012;148(9):995-1000.

- 584 80. Armstrong AW, Guerin A, Sundaram M, et al. Psoriasis and risk of diabetes-associated
585 microvascular and macrovascular complications. *J Am Acad Dermatol.* 2015;72(6):968-
586 977.e2.
- 587 81. Ma C, Harskamp CT, Armstrong EJ, et al. The association between psoriasis and
588 dyslipidaemia: a systematic review. *Br J Dermatol.* 2013;168(3):486-495.
- 589 82. Wu S, Li WQ, Han J, et al. Hypercholesterolemia and risk of incident psoriasis and
590 psoriatic arthritis in US women. *Arthritis Rheum.* 2014;66(2):304-310.
- 591 83. Mallbris L, Granath F, Hamsten A, et al. Psoriasis is associated with lipid abnormalities
592 at the onset of skin disease. *J Am Acad Dermatol.* 2006;54(4):614-621.
- 593 84. Mehta NN, Li R, Krishnamoorthy P, et al. Abnormal lipoprotein particles and cholesterol
594 efflux capacity in patients with psoriasis. *Atherosclerosis.* 2012;224(1):218-221.
- 595 85. Holzer M, Wolf P, Curcic S, et al. Psoriasis alters HDL composition and cholesterol
596 efflux capacity. *J Lipid Res.* 2012;53(8):1618-1624.
- 597 86. Tom WL, Playford MP, Admani S, et al. Characterization of Lipoprotein Composition
598 and Function in Pediatric Psoriasis Reveals a More Atherogenic Profile. *J Invest*
599 *Dermatol.* 2016;136(1):67-73.
- 600 87. Salahuddin T, Natarajan B, Playford MP, et al. Cholesterol efflux capacity in humans
601 with psoriasis is inversely related to non-calcified burden of coronary atherosclerosis. *Eur*
602 *Heart J.* 2015;36(39):2662-2665.
- 603 88. Kassi E, Pervanidou P, Kaltsas G, et al. Metabolic syndrome: definitions and
604 controversies. *BMC Med.* 2011;9:48.

- 605 89. Armstrong AW, Harskamp CT, Armstrong EJ. Psoriasis and metabolic syndrome: a
606 systematic review and meta-analysis of observational studies. *J Am Acad Dermatol.*
607 2013;68(4):654-662.
- 608 90. Gutmark-Little I, Shah, KN. Obesity and the metabolic syndrome in pediatric psoriasis.
609 *Clin Dermatol.* 2015;33(3):305-315.
- 610 91. Najarian DJ, Gottlieb AB. Connections between psoriasis and Crohn's disease. *J Am*
611 *Acad Dermatol.* 2003;48(6):805-821; quiz 822-804.
- 612 92. Skroza N, Proietti I, Pampena R, et al. Correlations between psoriasis and inflammatory
613 bowel diseases. *Biomed Res Int.* 2013;2013:983902.
- 614 93. Wellcome Trust Case Control Consortium. Genome-wide association study of 14,000
615 cases of seven common diseases and 3,000 shared controls. *Nature.* 2007;447(7145):661-
616 678.
- 617 94. Ellinghaus D, Ellinghaus E, Nair RP, et al. Combined analysis of genome-wide
618 association studies for Crohn disease and psoriasis identifies seven shared susceptibility
619 loci. *Am J Hum Genet.* 2012;90(4):636-647.
- 620 95. Cohen AD, Driehar J, Birkenfeld S. Psoriasis associated with ulcerative colitis and
621 Crohn's disease. *J Eur Acad Dermatol Venereol.* 2009;23(5):561-565.
- 622 96. Li WQ, Han JL, Chan AT, et al. Psoriasis, psoriatic arthritis and increased risk of incident
623 Crohn's disease in U.S. women. *Ann Rheum Dis.* 2013;72(7):1200-1205.
- 624 97. Bernstein CN, Wajda A, Blanchard JF. The clustering of other chronic inflammatory
625 diseases in inflammatory bowel disease: a population-based study. *Gastroenterology.*
626 2005;129(3):827-836.

- 627 98. Yates VM, Watkinson G, Kelman A. Further evidence of an association between
628 psoriasis, Crohn's disease and ulcerative colitis. *Br J Dermatol*. 1982;106(3):323-330.
- 629 99. Lee FI, Bellary SV, Francis C. Increased occurrence of psoriasis in patients with Crohn's
630 disease and their relatives. *Am J Gastroenterol*. 1990;85(8):962-963.
- 631 100. Tsai TF, Wang TS, Hung ST, et al. Epidemiology and comorbidities of psoriasis patients
632 in a national database in Taiwan. *J Dermatol Sci*. 2011;63(1):40-46.
- 633 101. Younossi ZM, Stepanova M, Afendy M, et al. Changes in the prevalence of the most
634 common causes of chronic liver diseases in the United States from 1988 to 2008. *Clin*
635 *Gastroenterol Hepatol*. 2011;9(6):524-530 e521; quiz e560.
- 636 102. Candia R, Ruiz A, Torres-Robles R, et al. Risk of non-alcoholic fatty liver disease in
637 patients with psoriasis: a systematic review and meta-analysis. *J Eur Acad Dermatol*
638 *Venereol*. 2015;29(4):656-662.
- 639 103. Singh NP, Prakash A, Kubba S, et al. Psoriatic nephropathy--does an entity exist? *Renal*
640 *Failure*. 2005;27(1):123-127.
- 641 104. Abuabara K, Azfar RS, Shin DB, et al. Cause-specific mortality in patients with severe
642 psoriasis: a population-based cohort study in the U.K. *Br J Dermatol*. 2010;163(3):586-
643 592.
- 644 105. Svedbom A, Dalen J, Mamolo C, et al. Increased cause-specific mortality in patients with
645 mild and severe psoriasis: a population-based Swedish register study. *Acta Derm*
646 *Venereol*. 2015;95(7):809-815.
- 647 106. Wan J, Wang S, Haynes K, et al. Risk of moderate to advanced kidney disease in patients
648 with psoriasis: population based cohort study. *Br J Dermatol*. 2013;347:f5961.

- 649 107. Chi CC, Wang J, Chen YF, et al. Risk of incident chronic kidney disease and end-stage
650 renal disease in patients with psoriasis: a nationwide population-based cohort study. *J*
651 *Dermatol Sci.* 2015;78(3):232-238.
- 652 108. Pouplard C, Brenaut E, Horreau C, et al. Risk of cancer in psoriasis: a systematic review
653 and meta-analysis of epidemiological studies. *J Eur Acad Dermatol Venereol.* 2013;27
654 Suppl 3:36-46.
- 655 109. Chiesa Fuxench ZC, Shin DB, Ogdie Beatty A, et al. The risk of cancer in patients with
656 psoriasis: a population-based cohort study in The Health Improvement Network. *JAMA*
657 *Dermatol.* 2016;152(3):282-290.
- 658 110. Brauchli YB, Jick SS, Miret M, et al. Psoriasis and risk of incident cancer: an inception
659 cohort study with a nested case-control analysis. *J Invest Dermatol.* 2009;129(11):2604-
660 2612.
- 661 111. Margolis D, Bilker W, Hennessy S, et al. The risk of malignancy associated with
662 psoriasis. *Arch Dermatol.* 2001;137(6):778-783.
- 663 112. Gelfand JM, Shin DB, Neimann AL, et al. The risk of lymphoma in patients with
664 psoriasis. *J Invest Dermatol.* 2006;126(10):2194-2201.
- 665 113. Naldi L, Peli L, Parazzini F, et al. Family history of psoriasis, stressful life events, and
666 recent infectious disease are risk factors for a first episode of acute guttate psoriasis:
667 results of a case-control study. *J Am Acad Dermatol.* 2001;44(3):433-438.
- 668 114. Telfer NR, Chalmers RJ, Whale K, et al. The role of streptococcal infection in the
669 initiation of guttate psoriasis. *Arch Dermatol.* 1992;128(1):39-42.
- 670 115. Patel RV, Weinberg JM. Psoriasis in the patient with human immunodeficiency virus,
671 part 1: review of pathogenesis. *Cutis.* 2008;82(2):117-122.

- 672 116. Morar N, Willis-Owen SA, Maurer T, et al. HIV-associated psoriasis: pathogenesis,
673 clinical features, and management. *Lancet Infect Dis*. 2010;10(7):470-478.
- 674 117. Wakkee M, de Vries E, van den Haak P, et al. Increased risk of infectious disease
675 requiring hospitalization among patients with psoriasis: a population-based cohort. *J Am*
676 *Acad Dermatol*. 2011;65(6):1135-1144.
- 677 118. Kao LT, Lee CZ, Liu SP, et al. Psoriasis and the risk of pneumonia: a population-based
678 study. *PLoS ONE*. 2014;9(12):e116077.
- 679 119. Takeshita J, Shin DB, Ogdie A, Gelfand JM. Increased risk of serious infection among
680 patients with psoriasis: a population-based cohort study in the United Kingdom. *J Invest*
681 *Dermatol*. 2016;136(5S, Suppl 1):S34.
- 682 120. Takeshita J, Shin DB, Ogdie A, Gelfand JM. Increased risk of pneumonia among patients
683 with psoriasis: a population-based cohort study in the United Kingdom. *J Invest*
684 *Dermatol*. 2015;135(5S, Suppl 1):S50.
- 685 121. Dowlatshahi EA, Wakkee M, Arends LR, et al. The prevalence and odds of depressive
686 symptoms and clinical depression in psoriasis patients: a systematic review and meta-
687 analysis. *J Invest Dermatol*. 2014;134(6):1542-1551.
- 688 122. Kurd SK, Troxel AB, Crits-Christoph P, et al. The risk of depression, anxiety, and
689 suicidality in patients with psoriasis: a population-based cohort study. *Arch Dermatol*.
690 2010;146(8):891-895.
- 691 123. Dommasch ED, Li T, Okereke OI, et al. Risk of depression in women with psoriasis: a
692 cohort study. *Br J Dermatol*. 2015;173(4):975-980.
- 693 124. Ogdie A, Weiss P. The epidemiology of psoriatic arthritis. *Rheum Dis Clin North Am*.
694 2015;41(4):545-568.

- 695 125. Ogdie A, Langan S, Love T, et al. Prevalence and treatment patterns of psoriatic arthritis
696 in the UK. *Rheumatology (Oxford)*. 2013;52(3):568-575.
- 697 126. Li R, Sun J, Ren LM, et al. Epidemiology of eight common rheumatic diseases in China:
698 a large-scale cross-sectional survey in Beijing. *Rheumatology (Oxford)*. 2012;51(4):721-
699 729.
- 700 127. Yang Q, Qu L, Tian H, et al. Prevalence and characteristics of psoriatic arthritis in
701 Chinese patients with psoriasis. *J Eur Acad Dermatol Venereol*. 2011;25(12):1409-1414.
- 702 128. Carneiro JN, Paula AP, Martins GA. Psoriatic arthritis in patients with psoriasis:
703 evaluation of clinical and epidemiological features in 133 patients followed at the
704 University Hospital of Brasília. *An Bras Dermatol*. 2012;87(4):539-544.
- 705 129. Henes JC, Ziupa E, Eisfelder M, et al. High prevalence of psoriatic arthritis in
706 dermatological patients with psoriasis: a cross-sectional study. *Rheumatol Int*.
707 2014;34(2):227-234.
- 708 130. Ibrahim G, Waxman R, Helliwell PS. The prevalence of psoriatic arthritis in people with
709 psoriasis. *Arthritis Rheum*. 2009;61(10):1373-1378.
- 710 131. Jamshidi F, Bouzari N, Seirafi H, et al. The prevalence of psoriatic arthritis in psoriatic
711 patients in Tehran, Iran. *Arch Iran Med*. 2008;11(2):162-165.
- 712 132. Love TJ, Gudbjornsson B, Gudjonsson JE, et al. Psoriatic arthritis in Reykjavik, Iceland:
713 prevalence, demographics, and disease course. *J Rheumatol*. 2007;34(10):2082-2088.
- 714 133. Haroon M, Kirby B, FitzGerald O. High prevalence of psoriatic arthritis in patients with
715 severe psoriasis with suboptimal performance of screening questionnaires. *Ann Rheum*
716 *Dis*. 2013;72(5):736-740.

- 717 134. Love TJ, Gudjonsson JE, Valdimarsson H, et al Psoriatic arthritis and onycholysis --
718 results from the cross-sectional Reykjavik psoriatic arthritis study. *J Rheumatol.*
719 2012;39(7):1441-1444.
- 720 135. Mease PJ, Gladman DD, Papp KA, et al. Prevalence of rheumatologist-diagnosed
721 psoriatic arthritis in patients with psoriasis in European/North American dermatology
722 clinics. *J Am Acad Dermatol.* 2013;69(5):729-735.
- 723 136. Khraishi M, Chouela E, Bejar M, et al. High prevalence of psoriatic arthritis in a cohort
724 of patients with psoriasis seen in a dermatology practice. *J Cutan Med Surg.*
725 2012;16(2):122-127.
- 726 137. Radtke MA, Reich K, Blome C, et al. Prevalence and clinical features of psoriatic
727 arthritis and joint complaints in 2009 patients with psoriasis: results of a German national
728 survey. *J Eur Acad Dermatol Venereol.* 2009;23(6):683-691.
- 729 138. Reich K, Kruger K, Mossner R, et al. Epidemiology and clinical pattern of psoriatic
730 arthritis in Germany: a prospective interdisciplinary epidemiological study of 1511
731 patients with plaque-type psoriasis. *Br J Dermatol.* 2009;160(5):1040-1047.
- 732 139. Tey HL, Ee HL, Tan AS, et al. Risk factors associated with having psoriatic arthritis in
733 patients with cutaneous psoriasis. *J Dermatol.* 2010;37(5):426-430.
- 734 140. Ficco HM, Citera G, Cocco JA. Prevalence of psoriatic arthritis in psoriasis patients
735 according to newer classification criteria. *Clin Rheumatol.* 2014;33(10):1489-1493.
- 736 141. Wilson FC, Icen M, Crowson CS, et al. Incidence and clinical predictors of psoriatic
737 arthritis in patients with psoriasis: a population-based study. *Arthritis Rheum.*
738 2009;61(2):233-239.

- 739 142. Raposo I, Torres T. Nail psoriasis as a predictor of the development of psoriatic arthritis.
740 *Actas Dermosifiliogr.* 2015;106(6):452-457.
- 741 143. Merola JF, Wu S, Han J, et al. Psoriasis, psoriatic arthritis and risk of gout in US men and
742 women. *Ann Rheum Dis.* 2015;74(8):1495-1500.
- 743 144. Mody E, Husni ME, Schur P, et al. Multidisciplinary evaluation of patients with psoriasis
744 presenting with musculoskeletal pain: a dermatology: rheumatology clinic experience. *Br*
745 *J Dermatol.* 2007;157(5):1050-1051.
- 746 145. Marchesoni A, Atzeni F, Spadaro A, et al. Identification of the clinical features
747 distinguishing psoriatic arthritis and fibromyalgia. *J Rheumatol.* 2012;39(4):849-855.
- 748 146. De Marco G, Cattaneo A, Battafarano N, et al. Not simply a matter of psoriatic arthritis:
749 epidemiology of rheumatic diseases in psoriatic patients. *Arch Dermatol Res.*
750 2012;304(9):719-726.
- 751 147. Tan AL, Grainger AJ, Tanner SF, et al. A high-resolution magnetic resonance imaging
752 study of distal interphalangeal joint arthropathy in psoriatic arthritis and osteoarthritis:
753 are they the same? *Arthritis Rheum.* 2006;54(4):1328-1333.
- 754 148. Villani AP, Rouzaud M, Sevrain M, et al. Prevalence of undiagnosed psoriatic arthritis
755 among psoriasis patients: systematic review and meta-analysis. *J Am Acad Dermatol.*
756 2015;73(2):242-248.
- 757 149. Gladman DD, Thavaneswaran A, Chandran V, et al. Do patients with psoriatic arthritis
758 who present early fare better than those presenting later in the disease? *Ann Rheum Dis.*
759 2011;70(12):2152-2154.
- 760 150. Theander E, Husmark T, Alenius GM, et al. Early psoriatic arthritis: short symptom
761 duration, male gender and preserved physical functioning at presentation predict

- 762 favourable outcome at 5-year follow-up. Results from the Swedish Early Psoriatic
763 Arthritis Register (SwePsA). *Ann Rheum Dis*. 2014;73(2):407-413.
- 764 151. Ogdie A, Schwartzman S, Husni ME. Recognizing and managing comorbidities in
765 psoriatic arthritis. *Curr Opin Rheumatol*. 2015;27(2):118-126.
- 766 152. Dreiherr J, Weitzman D, Shapiro J, et al. Psoriasis and chronic obstructive pulmonary
767 disease: a case-control study. *Br J Dermatol*. 2008;159(4):956-960.
- 768 153. Chiang YY, Lin HW. Association between psoriasis and chronic obstructive pulmonary
769 disease: a population-based study in Taiwan. *J Eur Acad Dermatol Venereol*.
770 2012;26(1):59-65.
- 771 154. Yang YW, Keller JJ, Lin HC. Medical comorbidity associated with psoriasis in adults: a
772 population-based study. *Br J Dermatol*. 2011;165(5):1037-1043.
- 773 155. Molina-Leyva A, Jimenez-Moleon JJ, Naranjo-Sintes R, et al. Sexual dysfunction in
774 psoriasis: a systematic review. *J Eur Acad Dermatol Venereol*. 2015;29(4):649-655.
- 775 156. Papadavid E, Vlami K, Dalamaga M, et al. Sleep apnea as a comorbidity in obese
776 psoriasis patients: a cross-sectional study. Do psoriasis characteristics and metabolic
777 parameters play a role? *J Eur Acad Dermatol Venereol*. 2013;27(7):820-826.
- 778 157. Yang YW, Kang JH, Lin HC. Increased risk of psoriasis following obstructive sleep
779 apnea: a longitudinal population-based study. *Sleep Med*. 2012;13(3):285-289.
- 780 158. Cohen JM, Jackson CL, Li TY, et al. Sleep disordered breathing and the risk of psoriasis
781 among US women. *Arch Dermatol Res*. 2015;307(5):433-438.
- 782 159. Horn EJ, Fox KM, Patel V, et al. Are patients with psoriasis undertreated? Results of
783 National Psoriasis Foundation survey. *J Am Acad Dermatol*. 2007;57(6):957-962.

- 784 160. Armstrong AW, Robertson AD, Wu J, Schupp C, Lebwohl MG. Undertreatment,
785 treatment trends, and treatment dissatisfaction among patients with psoriasis and psoriatic
786 arthritis in the United States: findings from the National Psoriasis Foundation surveys,
787 2003-2011. *JAMA Dermatol.* 2013;149(10):1180-1185.

788 **CME Questions:**

789

790 1. A 25 year-old man presents to your clinic for evaluation of his severe plaque psoriasis of
791 6 months duration that affects 15% of his body surface area. His is not on any treatment
792 and denies joint pain. He denies any other known medical issues.

793 Which of the following conditions have been strongly associated with psoriasis in
794 numerous epidemiological studies:

795 a. Colon cancer

796 b. Addison's disease

797 c. Metabolic syndrome

798 d. Peptic ulcer disease

799 e. Schizophrenia

800

801 **Answer: c**

802

803 2. You are discussing the cardiovascular disease risk of a patient with severe psoriasis with
804 her primary care provider. You are asked how the risk of cardiovascular disease
805 associated with severe psoriasis compares to that associated with other risk factors.

806

807 You explain that the risk of cardiovascular disease that is associated with severe psoriasis
808 is similar to that conferred by which of the following:

809

810 a. Diabetes

- 811 b. Dyslipidemia
- 812 c. Hypertension
- 813 d. Inflammatory bowel disease
- 814 e. Smoking
- 815
- 816 Answer: a