Supplementary material

Appendix					
Author	Study design	Participants	Aim	Main findings	Comment/Conclusion
Cheung et al ⁴⁶ , 2016	Case-series	7 PsO	Link PsO and comorbidities using miRNA	Cholesterol efflux miRNA upregulated in lesional skin	MiRNA may serve as a mechanistic link between psoriatic skin inflammation and systemic PsO comorbidities
Henseler et al ⁴⁰ , 1995	Case-control	2,941 PsO 355 ODD	Comorbidities in PsO	More systemic conditions, including T2D (observed and expected frequency, O/E = 1.47)	Fewer other dermatological conditions in patients with PsO
Sommer et al ²⁵ , 2006	Case-control	581 PsO 1,044 C	Elucidate association of PsO with chronic vascular and metabolic disorders	T2D OR in PsO: 2.24 for early onset, 2.63 for late onset MS unadjusted OR = 5.29	PsO is potentially life-threatening due to insulin resistance syndrome cluster of disorders
Ucak et al ¹⁹ , 2006	Case-control	70 PsO 40 C	Glucose tolerance in PsO vs. C	Impaired glucose tolerance significantly more in PsO, mainly late onset	
Naldi et al ²⁸ , 2008	Case-control	560 PsO 690 C	PsO risk based on medical conditions and drugs used prior to diagnosis	T2D OR=1.1.	
Solomon et al ³³ , 2010	Case-control	48,718 RA 40,346 PsA/PsO 442,033 C	Risk of DM in RA and PsA/PsO compared to non- rheumatic C	Adjusted HR for T2D: 1.5 for RA 1.4 for PsA/PsO	
Husted et al ³⁶ , 2011	Case-control	449 PsO 611 PsA	Prevalence of CV risk factors in PsO with and without PsA	T2D prevalence PsA vs. PsO: 12.0% vs. 6.7% T2D OR PsA vs. PsO was 1.90, p=0.0045 No difference in adjusted T2D OR	More prevalent HT in PsA suggest role of inflammatory arthritis in cardiovascular risk
Mehta et al ³⁸ , 2011	Case-control	3,603 PsO 14,330 C	Cardiovascular event and risk factors in PsO vs. C	T2D PsO vs. C: 7.5 vs 5. 1%, p<0.01	PsO significant history of stroke, MI, HL, HT, smoking, and elevated BMI
Karoli et al ³⁰ , 2013	Case-control	96 PsO 100 C	Cardiovascular risk factors between PsO and C	T2D PsO vs. C: 9 vs. 2%, p=0.02 PsO more prevalent: HT, MS, HL Longer disease duration in PsO+MS	Otherwise healthy PsO should be encouraged to reduce modifiable risk factors
Bang et al ²⁴ , 2014	Case-control	154 PsO 6,945 C	Risk of atrial fibrillation	T2D baseline PsO v. C; 18.1 vs. 12.3%, p=0.015	PsO predict new-onset atrial fibrillation. Studies should delineate association and determine the need for screening
Bostoen et al ³⁹ , 2014	Case-control	49 PsO 55 PsA	Metabolic disease burden in PsA and PsO	MS in PsO vs. PsA: 44.9 vs. 25.5%, p=0.037 AO in PsO vs. PsA: 83.7 vs. 65.5%, p=0.034	Recommend patient education about lifestyle
Dubreuil et al ³² , 2014	Case-control	59,281 PsO 4,196 PsA	Diabetes incidence in cohorts	Diabetes incidence PsA vs. PsO: 7.3 vs. 6.4 pr.1000 person-years	
Gerdes et al ⁵¹ , 2014	Case-control	20 lean PsO 20 obese PsO 20 lean C 20 obese C	Wnt5a contribution to metabolic complications	Wnt5a significantly higher PsO groups. Wnt5a significantly higher in obese PsO compared to lean PsO	Wnt5a suggested to play a role in PsO comorbidity. Data support influence of diet and/or obesity on comorbidity
Labitigan et al ⁵³ , 2014	Case-control	4,105 PsA 25,976 RA	Comorbidity prevalence PsA vs. RA	T2D in PsA vs. RA: 15 vs. 11%, p=0.02	

Lee et al ²⁶ , 2014	Case-control	6,611PsO 6,806 C	Medication and comorbidity severity n PsO, impact on T2D risk.	HR T2D Severe PsO vs. mild PsO: 2.06 vs. 1.28. PsO significantly more: HT, HL and Cushings	PsO risk of T2D is modulated by PsO severity, comorbidities and concomitant medication
Edson-Heredia et al ³⁴ , 2015	Case-control	27,672 mild PsO 22,174 moderate PsO 5,498 severe PsO 1952 PSA	Comorbidity risk in PsO vs. PsA	PsO T2D prevalence 5%, incidence rate 0.57 per 100 person-years. Severe PsO and RA T2D HR compared to mild PsO: 1.23 and 2.88 PSA more HT compared to severe PsO	PsA with larger comorbid burden compared to overall PsO, but inconsistent for severe PsO. Mild PsO less affected than severe PsO
Feldman et al ⁵² , 2015	Case-control	1,230 PsO+PsA 1,230 C	Comorbidities and health care utilization in PsO+PSA vs. C	PsO+PSA significantly more HT (35.8 vs. 23.5%), HL (34.6 vs. 28.5%), T2D (15.8 vs. 10.0%) – all p<0.01	Substantial economic and comorbidity burden among moderate-severe PsO+PsA despite availability of biologic treatments
Nas et al ³⁵ , 2015	Case-control	67 PsO 173 PsA 138 RA	Comorbidities in PsO vs. PsA vs. RA	HT OR PsA vs. PsO: 4.26 BMI higher in PsA vs. PsO, p=0.007 No difference in comorbidity prevalence	
Parisi et al ²³ , 2015	Case-control	48,523 PsO 208,187 C	Comorbidity risk, hazard ratio	PsO significantly more HT (15.39 vs. 14.93%, p=0.011), higher mean BMI (p<0.001)	Inflammatory arthritis in PsO is an independent risk factor for major CV events
Puig et al ⁵⁴ , 2015	Case-control	189 PsO 84 PsA	PsO compared to PsA during 24 weeks of etanercept treatment	No difference in PASI. Prevalence of HT (61.9 vs. 26.5%) and T2D (21.4 vs. 9.0%) significantly higher in PsA	Screening for PsA and cardiovascular risk factors is important. Early detection may help guide treatment decisions and reduce overall disease risk
Jacob et al ²² , 2016	Case-control	72,148 T2D 72,148 C	Risk of PsO diagnosis in T2D	T2D increased risk of PsO over 10 year- period (HR= 1.12 (1.08-1.29))	T2D positively associated with PsO. Study design limits reliability. No conclusions regarding causal relationship between T2D and PsO
Lee et al ²¹ , 2016	Case-control	135 PsO 73 C	Relationship between childhood PsO and metabolic syndrome, and obesity.	No difference in mean WtHR between groups. Elevated WtHR more prevalent in PsO. BMI based overweight not different between groups	Increased cardiometabolic risk warrants discussion of lifestyle choices in PsO patients
Buquicchio et al ⁴⁷ , 2017 (abstract)	Case-control	15 PsO (unknown) C	Serum levels of clusterin	PsO significantly higher levels (p<0.001)	Clusterin suggested as pathogenic marker in PsO.
Kwa et al ¹⁷ , 2017	Case-control	185,803 PsO compared to BPP	Comorbidity OR in inflammatory skin diseases	PsO vs. C: HT (OR:1.61), T2D (OR:1.22), obesity (OR: 2.36)	PsO associated with increased CV risk, particularly at younger age
Radtke et al ⁴³ , 2017	Case-control	37,456 PsO 48,140 AD	Comorbidity prevalence in PsO vs. AD	T2D, HT, HL and obesity significantly more common in PsO	
Wan et al ³⁷ , 2018	Case-control	8,124 PsO 76,599 C	T2D risk in PsO vs. C	HR for T2D (PsO vs. C): increases with BSA (trend p=0.004)	BSA >10% should be targeted for diabetes prevention efforts
Mahé et al ²⁹ , 2013	Cross-sectional Cohort	545 COP 1656 AOP	CV and metabolic comorbidities	T2D AOP vs. COP: 12.9 vs. 4.6%, p<0.0001 AOP significantly more HT, HL and mean BMI	
Baeta et al ⁵ , 2014	Cross-sectional cohort	190 PsO	Comorbidities in PsO	T2D in PsO: 15.3%	PsO may manifest as a multisystem disease.
Mahé et al ⁵⁰ , 2014	Cross-sectional cohort	191 PsO	Risk of factors for weight increment in PsO treated with infliximab	T2D prevalence independent of weight was 10.5%	Weight monitoring in PsO on infliximab due to increased prevalence of comorbidities and risk of weight increment

Sanchez-Carazo et al ⁹ ,	Cross-sectional	1,022 PsO	Correlation between quality of	Diabetes in 8%, >90% was T2D.	
2014	cohort		life and comorbidities in PsO		
Armstrong et al ²⁰ , 2015	Cross-sectional cohort	6,164 D 6,164 D+PsO	Risk of vascular complications D vs. D+PsO	D+PsO increased risk of microvascular events overall and by PsO severity	
Phan et al ⁸ , 2016	Cross-sectional cohort	212 PsO (≥70 years of age) 1,998 PsO (<70 years of age)	Comorbidities in PsO	PsO >70 years significantly higher prevalence of comorbidities, except obesity	
Pongpit et al ¹¹ , 2016	Cross-sectional cohort	165 PsO	Comorbidities in PsO	T2D: 50.3% MS: 18.8%	
Rutter et al ⁵⁵ , 2016	Cross-sectional cohort	287 PsO	Investigate if risk factor screening augments their prevalence	Difference between known and screen- detected risk factors	Screening identified high proportion of patients with high CVD risk and suboptimal management of known risk factors
Theodorakopoulou ⁴² et al, 2016	Cross-sectional cohort	17 PsO EOP 14 PsO LOP 340 PsO from different cohort	Phenotypical comparison between groups	EOP: Greater lymphocytic infiltration (p=0.03), LOP: greater CD4+:CD8+ ratio (p=0.002). In different cohort, LOP more likely to have T2D	Findings support differences between EOP and LOP
Dregan et al ¹² , 2017	Cross-sectional cohort	6,286 PsO	Morbidity and mortality in PsO	T2D: 6% CHD: 6% T2D+CHD: 1%	
Kojanova et al ¹³ , 2017	Cross-sectional cohort	1,412 PsO	Characteristics and risk profile in PsO treated with biologics	T2D: 11.4%, PsA: 41.0%, HT: 35.2%, HL: 27.7%, Obese: 15.2%, CHD: 4.9%	Found prevalence's were either similar or higher compared to other European registries
Xu et al ¹⁴ , 2017	Cross-sectional cohort	27 PsO COP 229 PsO EOP 183 PsO LOP	Comorbidities in PsO	Fatty liver, HL and MS most prevalent in EOP, whereas T2D most in LOP	EOP have MS mainly related to lipid disorders. Glucose metabolism and diabetes, often not involved
Ardisen et al ¹⁵ , 2018	Cross-sectional cohort	563 PsO	Prevalence of CV risk factors	MS: 12.6%, Central obesity: 38.7%, HT: 14.3%, DL: 18.6%, T2D: 9.2%	MS+PsO had longer disease duration and were women. Central obesity and T2D associated to severe disease
Mihai et al ¹⁶ , 2018	Cross-sectional cohort	82 PsO	Association of selected single- nucleotide polymorphisms (SNPs) to PsO	PsO severity not significantly influenced by any of the studied SNPs. Two SNPs associated with T2D	The influence of SNP's on multiple organ systems justifies research on its relation to MS development in PsO
Gisondi et al ⁶ , 2013	Prospective cohort	10,539 PsO	Laboratory measures and new diagnoses: 16 weeks of systemic treatment, 8 groups.	Average prevalence of T2D in treatment groups was 7.1% During treatment average new diagnosis of T2D was 0.18%	Benefits and risks of systemic therapy must be weighed carefully for each patient to ensure optimal management of PsO symptoms and minimization of acute and cumulative toxicities
Kimbal et al ¹⁸ , 2014	Prospective cohort	11,900 PsO	Demographic and disease characteristics	T2D: 11.4%. Mean BMI of 30.9kg/m2	Cardiovascular risk factors, incl. T2D, increased substantially with age. Patient age should be considered when evaluating PsO comorbidities
Phan et al ⁷ , 2014 (abstract)	Multicenter prospective cohort	2,210 PsO	Metabolic comorbidities in PsO compared to background population	Obese: 24.5%, HT: 26.0%, DL: 27.5%, T2D: 11.0% T2D incidence higher in PsO than BPP, particularly after age of 35 years	PsO associated with significant metabolic comorbidities and hypertension compared to general population
Vanaclocha et al ¹⁰ , 2014	Multicenter prospective cohort	528 PsO	Comorbidities and risk factors in PsO	Smoking: 40.5%, obesity: 26.0%, DL: 24.8%, HT: 24.3%, T2D: 12.3%	Almost ¾ PsO had ≥1 CV risk factor Dermatologist to take active role. Patients are often young and with little knowledge of CV risk

P; Patients, C; Controls, BPP; Background Population PsO; Psoriasis, AO; Abdominal obesity, CHD; Coronary heart Disease, MI; Myocardial Infarction, PsA; Psoriatic Arthritis, OR; Odds Ratio, HR; Hazard Ratio, T2D; Type-2-diabetes mellitus, HT; Hypertension, HL; Hyperlipidemia, DL; Dyslipidemia, MS; Metabolic Syndrome, BSA; Body Surface Area, BMI; Body Mass Index, WtHR; Waist to Height Ratio, ODD; Other dermatological diseases, PASI; Psoriasis Activity and Severity Index, IQR; Inter Quartile Range, PGA; Physicians Global Assessment, EOP; Early onset PsO (18-39 years), LOP; late onset PsO (>40 years), COP; childhood onset PsO (<18 years).

References

- 1. Mahé E, Reguiai Z, Barthelemy H, et al. Evaluation of risk factors for body weight increment in psoriatic patients on infliximab: a multicentre, crosssectional study. *J Eur Acad Dermatol Venereol*. 2014;28(2):151–159.
- 2. Gerdes S, Laudes M, Neumann K, Baurecht H, Mrowietz U. Letter to the editor Wnt5a a potential factor linking psoriasis to metabolic complications. *Exp Dermatol*. 2014:438–441.
- 3. Feldman SR, Zhao Y, Shi L, Tran MH, Lu J. Economic and comorbidity burden among moderate-to-severe psoriasis patients with comorbid psoriatic arthritis. *Arthritis Care Res.* 2015;67(5):708–717.
- 4. Monalyn Labitigan M, Bahce-Altuntas A, Kremer JM, et al. Higher rates and clustering of abnormal lipids, obesity, and diabetes in psoriatic arthritis compared with rheumatoid arthritis. *Arthritis Care Res.* 2014;66(4):600–607.
- 5. Puig L, Strohal R, Husni ME, et al. Cardiometabolic profile, clinical features, quality of life and treatment outcomes in patients with moderate-to-severe psoriasis and psoriatic arthritis. *J Dermatolog Treat*. 2015;26(1):7–15.
- 6. Rutter MK, Kane K, Lunt M, et al. Primary care-based screening for cardiovascular risk factors in patients with psoriasis. *Br J Dermatol*. 2016;175(2):348–356.