

David Plunkert "5 Biggest Heart Risks for Men"

Psoriasi e rischio CV

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Projections of Global Mortality and Burden of Disease from 2002 to 2030

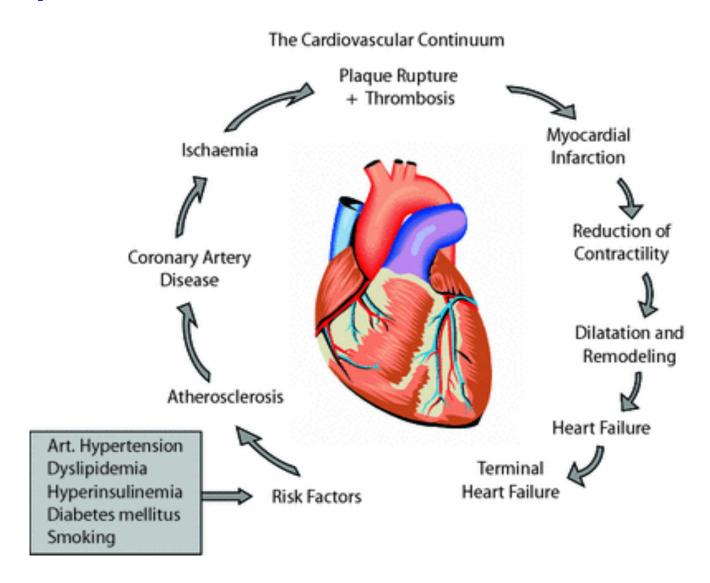
Colin D. Mathers*, Dejan Loncar

Evidence and Information for Policy Cluster, World Health Organization, Geneva, Switzerland

Category	Disease or Injury	2002 Rank	2030 Ranks	Change in Rank
Within top 15	Ischaemic heart disease	1	1	0
	Cerebrovascular disease	2	2	0
	Lower respiratory infections	3	5	-2
	HIV/AIDS	4	3	+1
	COPD	5	4	+1
	Perinatal conditions	6	9	-3
	Diarrhoeal diseases	7	16	-9
	Tuberculosis	8	23	-15
	Trachea, bronchus, lung cancers	9	6	+3
	Road traffic accidents	10	8	+2
	Diabetes mellitus	11	7	+4
	Malaria	12	22	-10
	Hypertensive heart disease	13	11	+2
	Self-inflicted injuries	14	12	+2
	Stomach cancer	15	10	+5
Outside top 15	Nephritis and nephrosis	17	13	+4
	Colon and rectum cancers	18	15	+3
	Liver cancers	19	14	+5

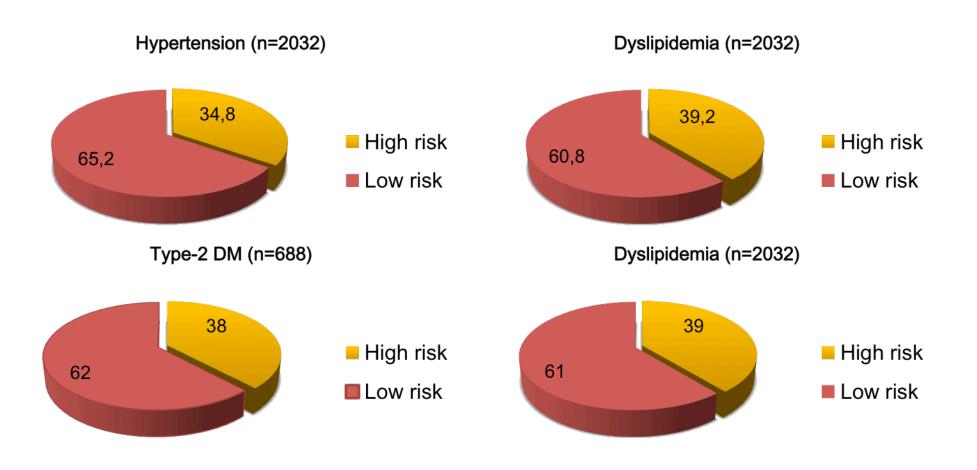
DOI: 10.1371/journal.pmed.0030442.t002

Sequenza di eventi che causano malattie CV



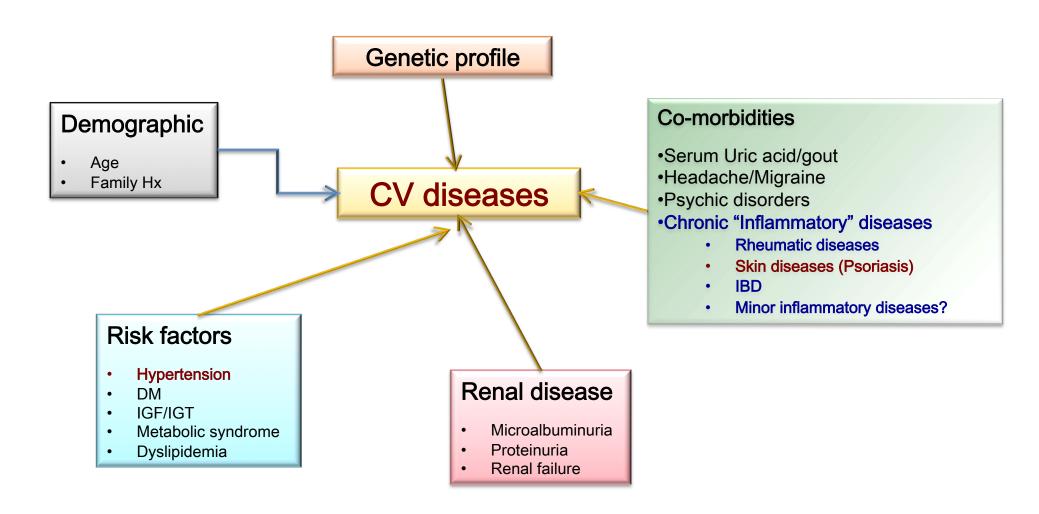
Patients remaining at high CV risk* after achieving treatment goals for selected RF's

*10-year risk of CVD death ≥ 5% based on the Systematic Coronary Risk Evaluation (SCORE)

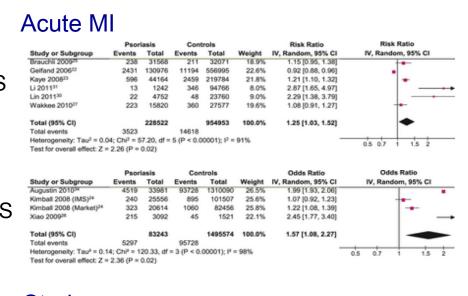


Banegas J, Borghi C et al, Eur Heart J, 2011

Factors contributing to CV disease



Cardiovascular morbidity and mortality in psoriasis and psoriatic arthritis: a systematic literature review



CS=Cohort Studies CSS=Cross-sectional studies MA=Metanalysis

CHD Psoriasis Controls Risk Ratio Risk Ratio Study or Subgroup Events Total Events Weight IV, Fixed, 95% CI IV, Fixed, 95% CI Kaye 2008²³ 1006 219784 69.9% 1.20 [1.12, 1.28] Wakkee 2010? 583 15820 846 27577 30.1% 1.20 [1.08, 1.33] Total (95% CI) 1.20 [1.13, 1.27] Total events 1589 5032 Heterogeneity: Chi2 = 0.00, df = 1 (P = 0.94); I2 = 0% 0.5 0.7 1.5 2 Test for overall effect: Z = 6.21 (P < 0.00001)

		Fauti	10010	COIN	1010		Occus resuc		-	39 150		
	Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI		IV, Rano	dom, t	95% CI	
	Al-Mutairi 2010 ³⁶	79	1790	26	1831	31.1%	3.21 [2.05, 5.02]			т	_	$\overline{}$
	Han 200638	224	3066	675	12264	39.0%	1.35 [1.16, 1.58]			1.		
	Sommer 2006 ¹⁰	32	581	38	1044	30.0%	1.54 [0.95, 2.50]			+	•	
CS	Total (95% CI)		5437		15139	100.0%	1.84 [1.09, 3.09]			-	•	
$C_{\mathcal{O}}$	Total events	335		739								
	Heterogeneity: Tau ² = 0	.17; Chi ² = 1	2.70, df =	2 (P = 0.0	$02); I^2 = 8$	4%			_	-	_	_
	Test for overall effect: Z	= 2.30 (P =	0.02)					0.2	0.5	1	2	5

Outdo Patio

Odds Patio

	Psor	iasis	Con	trois		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	N, Random, 95% CI	IV, Random, 95% CI
Brauchli 2009 ²⁵	264	32930	271	33209	22.2%	0.98 [0.83, 1.16]	-
Gelfand 2009 ⁴⁰	2174	132746	8747	510996	43.7%	0.96 [0.91, 1.00]	=
Kaye 2008 ²³	388	44164	1724	219784	32.1%	1.12 [1.00, 1.25]	-
Li 2011 ³¹	7	1242	351	94766	2.0%	1.52 [0.72, 3.21]	
Total (95% CI)		211082		858755	100.0%	1.02 [0.92, 1.14]	*
Total events	2833		11093				
Heterogeneity: Tau ² = 0	.01; Chi ² = 8	3.05, df = 3	3 (P = 0.04)	4); I ² = 63%			0.5 0.7 1 1.5 2
Test for overall effect: Z	= 0.39 (P =	0.70)					

Stroke

Test for overall effect: Z = 5.27 (P < 0.00001)

CS

CSS

	Psori	asis	Cont	rols		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	N, Random, 95% CI	IV, Random, 95% CI
Brauchli 2009 ⁷⁵	264	32930	271	33209	22.2%	0.98 [0.83, 1.16]	-
Gelfand 2009 ⁴⁰	2174	132746	8747	510996	43.7%	0.96 [0.91, 1.00]	-
Kaye 2008 ²³	388	44164	1724	219784	32.1%	1.12 [1.00, 1.25]	
Li 2011 ³¹	7	1242	351	94766	2.0%	1.52 [0.72, 3.21]	-
Total (95% CI)		211082		858755	100.0%	1.02 [0.92, 1.14]	+
Total events	2833		11093				
Heterogeneity: Tau ^a = 0.0	1; Chi ² = 8	.05, df = 3	(P = 0.04)); 12 = 63%			0.5 0.7 1 1.5 2
Test for overall effect: Z =	0.39 (P =	0.70)					
	Pso	riasis	Cor	ntrois		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Han 2006 ³⁸	95	3066	380	12264	4.3%	1.00 [0.80, 1.26]	
Kimball 2008 (IMS) ²⁴	784	25556	2655	101507	34.2%	1.18 [1.09, 1.28]	-
Kimball 2008 (Market) ²⁴	1344	20614	4812	82456	57.2%	1.13 [1.06, 1.20]	
Yang 2011 ³⁷	109	1685	304	5055	4.4%	1.08 [0.86, 1.36]	
Total (95% CI)		50921		201282	100.0%	1.14 [1.08, 1.19]	
Total events	2332		8151				
Heterogeneity: $Chi^2 = 2.2$	6. df = 3 (P	= 0.52): F	$^{2} = 0\%$				05 07 1 15

Horreau C et al, J of the Eur Academy of Dermatology and Venereology, 2013

MA



Psoriasis and Major Adverse Cardiovascular Events: A Systematic Review and Meta-Analysis of Observational Studies

Ehrin J. Armstrong, MD, MAS, MSc; Caitlin T. Harskamp, BA; April W. Armstrong, MD, MPH

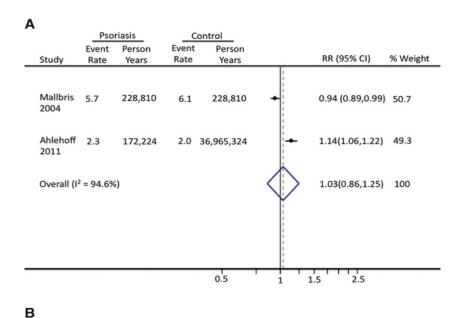
Background—Psoriasis is a chronic inflammatory disease that may be associated with increased risk of cardiovascular events, including cardiovascular mortality, myocardial infarction, and stroke.

Methods and Results—We searched the MEDLINE, EMBASE, and Cochrane Central Register databases for relevant studies in English between January 1, 1980, and January 1, 2012. Extraction was by 3 independent reviewers. Summary incidence, risk ratios (RRs), and confidence intervals (CIs) were calculated using fixed-effects and random-effects modeling. Meta-regression was also performed to identify sources of between-study variation. Nine studies were included, representing a total of 201 239 patients with mild and 17 415 patients with severe psoriasis. The level of covariate adjustment varied among studies, leading to the possibility of residual confounding. Using the available adjusted effect sizes, mild psoriasis remained associated with a significantly increased risk of myocardial infarction (RR, 1.29; 95% CI, 1.02 to 1.63) and stroke (RR, 1.12; 95% CI, 1.08 to 1.16). Severe psoriasis was associated with a significantly increased risk of cardiovascular mortality (RR, 1.39; 95% CI, 1.11 to 1.74), myocardial infarction (RR, 1.70; 95% CI, 1.32 to 2.18), and stroke (RR, 1.56 95% CI, 1.32 to 1.84). Based on these risk ratios and the background population event rates, psoriasis is associated with an estimated excess of 11 500 (95% CI, 1169 to 24 407) major adverse cardiovascular events each year.

Conclusions—Mild and severe psoriasis are associated with an increased risk of myocardial infarction and stroke. Severe psoriasis is also associated with an increased risk of cardiovascular mortality. Future studies should include more complete covariate adjustment and characterization of psoriasis severity. (J Am Heart Assoc 2013;2:e000062 doi: 10.1161/JAHA.113.000062)

Key Words: cardiovascular diseases • epidemiology • meta-analysis • myocardial infarction • psoriasis

Cardiovascular death among patients with psoriasis.

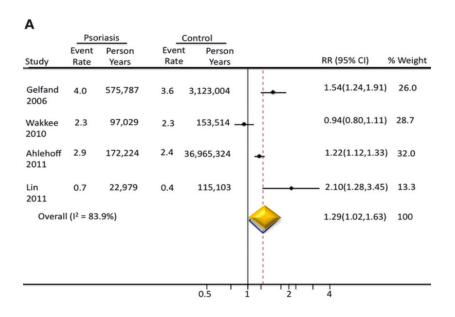




	Event	riasis Person	Event	ntrol Person			
Study	Rate	Years	Rate	Years		RR (95% CI)	% Weigh
Mallbris 2004	16.2	94,583	10.6	94,583		▲ 1.52(1.44,1	.60) 28.3
Abuabara 2010	8.7	12,346	6.2	48,662		1.57(1.26,1	.96) 22.5
Ahlehoff 2011	3.1	13,146	2.0 3	6,965,324		1.57(1.27,1	.94) 22.9
Stern 2011	8.0	30,817	7.8	30,817	+	1.02(0.90,1	.16) 26.3
Overall (I ²	= 91.1%	6)				1.39(1.11,1	.74) 100

Armstrong E J et al. J Am Heart Assoc 2013;2:e000062

Myocardial infarction among patients with psoriasis.





Mild

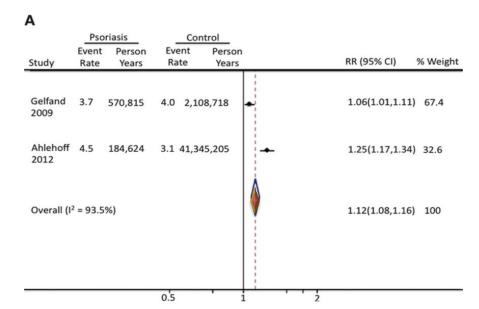
	Pso Event	riasis Person	Eve	Control nt Person	
Study	Rate	Years	Rat		RR (95% CI) % Weight
Gelfand 2006	5.1	21,845	3.6	3,123,004	7.08(3.06,16.37) 9.0
Ahlehoff 2011	3.4	13,146	2.4	36,965,324	1.45(1.10,1.91) 84.3
Lin 2011	1.7	2,940	0.4	115,10 <u>3</u>	1.81(0.69,4.74) 6.8
Overall (I	2 = 83.99	%)			1.70(1.32,2.18) 100
				0.5	1 2 6

В

Severe

Armstrong E J et al. J Am Heart Assoc 2013;2:e000062

Stroke among patients with psoriasis.





В					
	Psoi	riasis	Cc	ntrol	
Study	Event Rate	Person Years	Event Rate	Person Years	RR (95% CI) % Weigh
Gelfand 2009	6.1	12,222	4.4	48,248	1.43(1.10,1.86) 39.9
Ahlehoff 2012	6.8	13,261	3.1 41	,345,205	1.65(1.33,2.05) 60.1
Overall (I	2 = 0.0%)			1.56(1.32,1.84) 100
			0.5		2.5

Armstrong E J et al. J Am Heart Assoc 2013;2:e000062

Mild psoriasis and rate of major CV events

Reference	Study Country	Number of Patients	Mean Age, Years	Events	Event Rate, Control	Event Rate, Psoriasis	Mean Follow-Up Time, Years	Effect Measure	Definition of Outcomes	Adjusted Effect Size	Adjustment Variables
Cardiovascular morta	lity										
Mallbris et al ¹⁸	Sweden	19 757	NR	1302	6.1	5.7	11.6	SMR	Death registry; ICD-7, ICD-8, and ICD-9 codes	0.94 (0.89 to 0.99)	A, G
Ahlehoff et al ²⁰	Denmark	34 371	47.2	393	2.0	2.3	5.0	RR	Cardiovascular death using ICD-10 code	1.14 (1.06 to 1.22)	A, G, M
Myocardial infarction											
Gelfand et al ¹¹	United Kingdom	127 129	46.4	2319	3.6	4.0	3.8	HR	Diagnostic code using READ or OXMIS	1.54 (1.24 to 1.91)	H, D, C, A, G, S, MI, BMI
Wakkee et al ³⁴ ∗	Netherlands	15 820	48.9	223	2.3	2.3	6.0	HR	Hospitalization for MI	0.94 (0.8 to 1.11)	H, D, C, A, G, U
Ahlehoff et al ²⁰	Denmark	34 371	47.2	494	2.4	2.9	5.0	RR	MI using ICD-10 code	1.22 (1.12 to 1.33)	A, G, M
Lin et al ³⁵	Taiwan	4162	NR	17	0.4	0.7	5.0	HR	New MI, using insurance database	2.10 (1.27 to 3.43)	H, D, C, A, G, SD
Stroke											-
Gelfand et al ¹²	United Kingdom	129 143	45.1	2100	4.0	3.7	3.7	HR	Diagnostic code using Read or OXMIS	1.06 (1.01 to 1.11)	A, G, H, D, C, S, N
Ahlehoff et al ³⁶	Denmark	36 765	46.1	838	3.1	4.5	5.0	RR	Ischemic stroke using ICD-9 codes	1.25 (1.17 to 1.34)	A, G, SD, M

Event rates are reported as events/1000 person-years. NR indicates not reported; SMR, standardized mortality ratio; ICD, International Classification of Diseases; RR, risk ratio; HR, hazard ratio; A, age; G, gender; M, medical comorbidities (individual comorbidities not reported); OXMIS, Oxford Medical Information System; H, hypertension; D, diabetes; C, cholesterol; S, smoking; U, healthcare utilizatior; N, neurovascular disease; MI, prior myocardial infarction; BMI, body mass index; SD, social demographics.

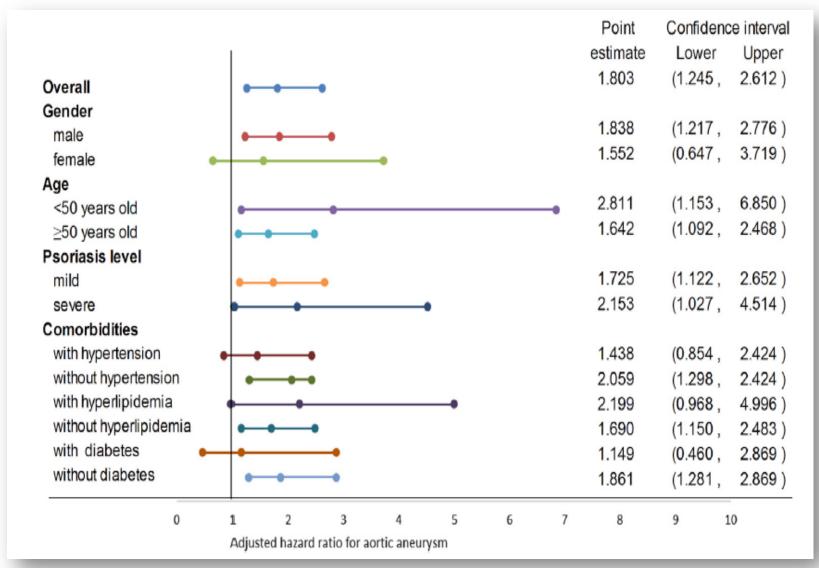
^{*}Authors did not distinguish mild from severe psoriasis.

Severe psoriasis and rate of major CV events

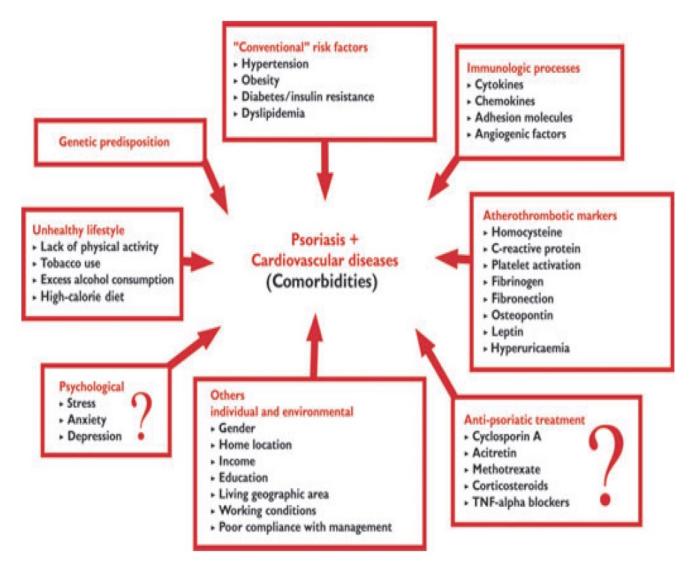
Reference	Study Country	Number of Patients	Mean Age, Years	Events	Event Rate, Control	Event Rate, Psoriasis	Mean Follow-Up Time, Years	Effect Measure	Definition of Outcomes	Adjusted Effect Size	Adjustment Variables
Cardiovascular	Cardiovascular mortality										
Mallbris et al ¹⁸	Sweden	8991	NR	1529	10.6	16.2	10.5	SMR	Death registry; ICD-7, ICD-8, and ICD-9 codes	1.52 (1.44 to 1.60)	A, G
Abuabara et al ³³	United Kingdom	3603	52.2	108	6.2	8.7	2.7	HR	Diagnostic code using READ or OXMIS	1.57 (1.26 to 1.96)	A, G
Ahlehoff et al ²⁰	Denmark	2621	46.9	41	2.0	3.1	5.0	RR	Cardiovascular death using ICD-10 code	1.57 (1.27 to 1.94)	A, G, M
Stem et al ¹⁹	USA	1376	46	246	7.8	8.0	22.4	SMR	Telephone interviews and national death index	1.02 (0.90 to 1.16)	A, G
Myocardial infar	ction		_			_					
Gelfand et al ¹¹	United Kingdom	3837	49.8	112	3.6	5.1	5.4	HR	Diagnostic code using READ or OXMIS	7.08 (3.06 to 16.36)	H, D, C, A, G, S, MI, BMI
Ahlehoff et al ²⁰	Denmark	2621	46.9	45	2.4	3.4	5.0	RR	MI using ICD-10 code	1.45 (1.10 to 1.90)	A, G, M
Lin et al ³⁵	Taiwan	590	NR	5	0.4	1.7	5.5	HR	New MI, using insurance database	1.81 (0.69 to 4.74)	H, D, C, A, G, SD
Stroke											
Gelfand, 2009 ¹²	United Kingdom	3603	52.2	74	4.4	6.1	2.7	HR	Diagnostic code using READ or OXMIS	1.43 (1.10 to 1.87)	A, G, H, D, C, S, N
Ahlehoff et al ³⁶	Denmark	2793	46.0	90	3.1	6.8	4.7	RR	Ischemic stroke using ICD-9 codes	1.65 (1.33 to 2.05)	A, G, SD, M

NR indicates not reported; SMR, standardized mortality ratio; ICD, International Classification of Diseases; RR, risk ratio; HR, hazard ratio; A, age; G, gender; M, medical comorbidities (individual comorbidities not reported); H, hypertension; D, diabetes; C, cholesterol; S, smoking; U, healthcare utilization; MI, prior myocardial infarction; BMI, body mass index; SD, social demographics; N, neurovascular disease, including prior stroke or transient ischemic attack.

Overall adjusted hazard ratios for *aortic aneurysm* in all patients with psoriasis and subgroups of psoriasis



Factors that may contribute towards the co-occurrence of psoriasis and CVD



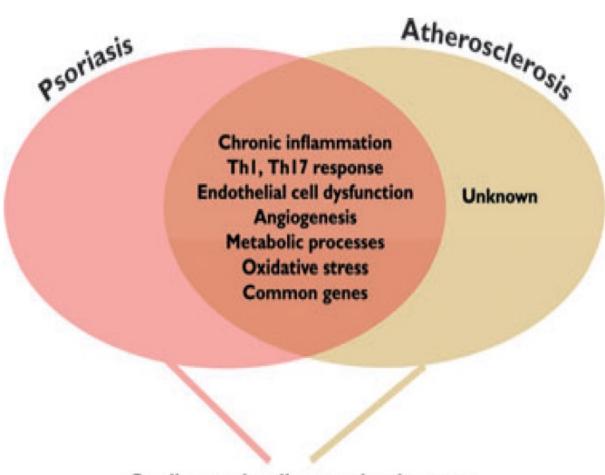
Pietrzak A et Al., International Journal of Dermatology 2013;52:153–162

Odds ratios (95 % CI) for CV risk factors for patients with psoriasis, mild psoriasis, and severe psoriasis compared to the general population

Cardiovascular risk factors	Psoriasis	Mild psoriasis	Moderate-to-severe psoriasis
Obesity ^a	1.66 (1.46–1.89)	1.46 (1.17–1.82)	2.23 (1.63–3.05)
Hypertension ^a	1.58 (1.42–1.76)	1.30 (1.15–1.47)	1.49 (1.20–1.86)
Type 2 diabetes mellitus ^a	1.59 (1.38–1.83)	1.53 (1.16–2.04)	1.97 (1.48–2.62)
Metabolic syndrome	2.26 (1.70–3.01) ^a	1.22 (1.11–1.35) ^b	1.98 (1.62–2.43) ^b

a From Armstrong et al., meta-analyses synthesizing the global epidemiologic associations between psoriasis or psoriasis disease severity and obesity, hypertension, type 2 diabetes mellitus, and metabolic syndrome, from January 1980 to January 2012 b From Langan et al., a primary investigation of the association between psoriasis disease severity and metabolic syndrome in the UK in February 2009

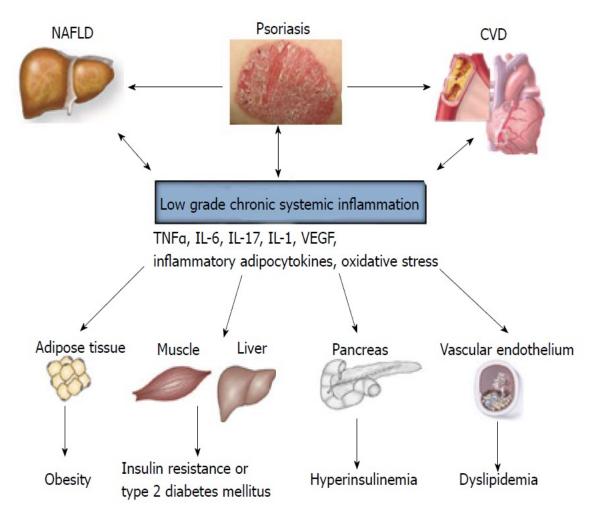
Pathogenetic mechanisms in psoriasis and atherosclerosis with the potential to trigger CVD



Cardiovascular diseases development

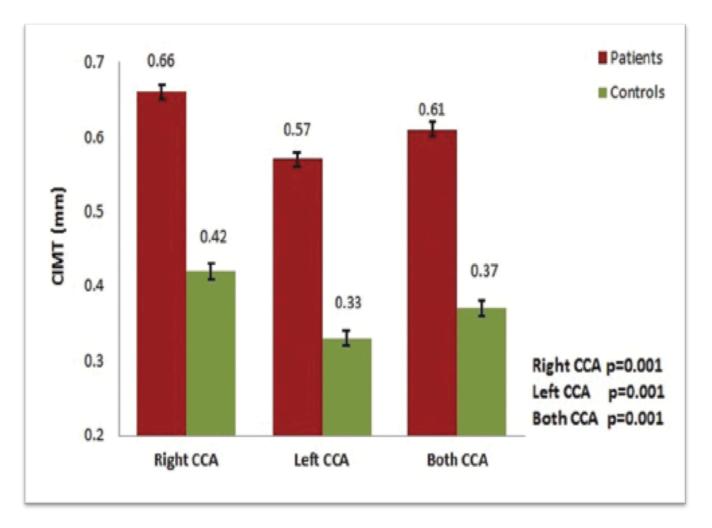
Pietrzak A et Al., International Journal of Dermatology 2013;52:153–162

Psoriasis, non-alcoholic fatty liver disease, CV diseases and CV risk factors: a unique inflammatory background

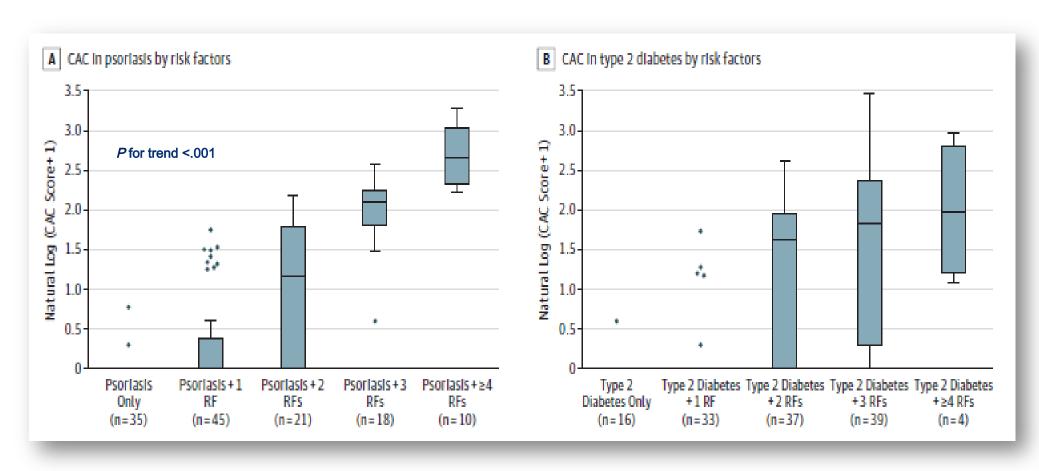


Ganzetti G et Al., *World J Cardiol* 2016;8(2):120-131

Mean intima-media thickness of the right and left common carotid artery in 30 patients with chronic plaque psoriasis and 30 controls (CIMT: Carotid intima-media thickness, CCA: Common carotid artery)

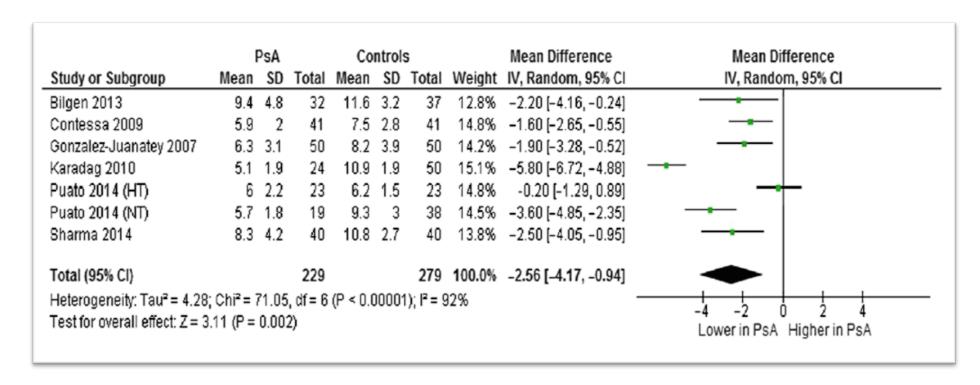


Median Coronary Artery Calcium (CAC) as Assessed by Mean Agatston Scores in Psoriasis and Diabetes Mellitus



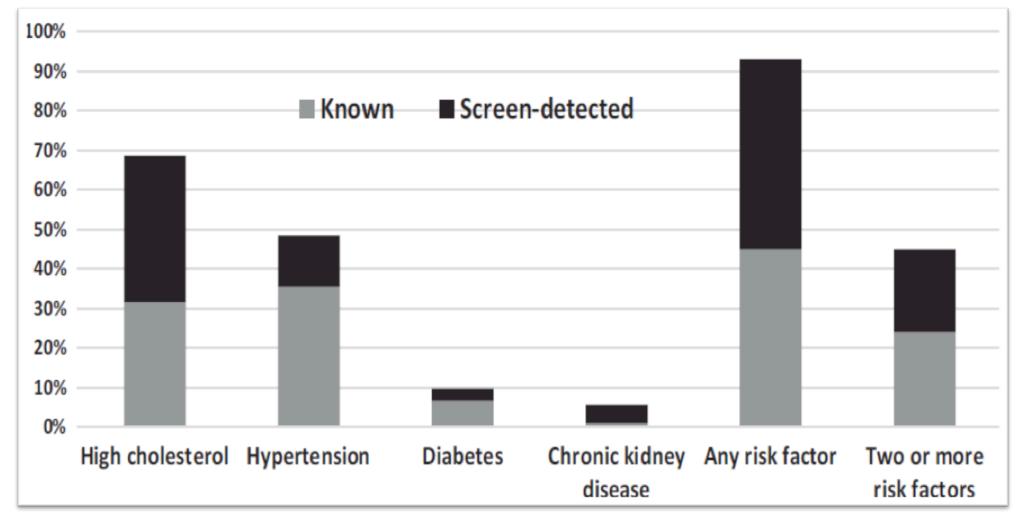
Mansouri B et Al., JAMA Dermatol 2016; doi:10.1001/jamadermatol.2016.2907

Flow-mediated dilation (FMD) in psoriatic arthritis patients and controls



Di Minno MND et Al., *Annals* of *Medicine*, 2015;1–8

Proportion of Identification and Management of Psoriasis Associated ComorbidiTy (IMPACT) study participants with known and screen-detected CVD risk factors



Data are proportions of IMPACT study participants. 'Known' is the sum of (i) self-report, (ii) medical or nursing staff knowing about this RF and (iii) medication for this RF. HBP was defined as SBP \geq 140 mmHg or DPB \geq 90 mmHg. High cholesterol was defined as T-chol \geq 5 mmol/L. Diabetes was defined by high glycated Hb \geq 48 mmol/mol. CKD was defined by low estimated GFR < 60 mL/min.

Cardiovascular disease in patients with psoriasis: key point

- Psoriasis is a systemic inflammatory skin disorder associated with a significantly increased of CV risk profile
- Traditional CV risk scores underestimates the CV risk in patients with psoriasis.
- Systemic inflammation is probably involved in the genesis of atherosclerosis and CV diseases associated with psoriasis.
- A significant under-treatment of CV risk factors is an issue in patients with psoriasis compared with the general population
- Anti-psoriatic treatment may modify CV risk, however, results from randomized clinical trials are awaited
- The importance of screening and effective management of CV risk factors, should be emphasized for patients with psoriasis