H.5 Identification of comorbidities

H.5.1 Myocardial infarction

Reference	Study type	Number of patients	Patient characteristics	Intervention	Length of follow-up	Outcome measures	Source of funding
Gelfand et al. (2006) Risk of Myocardial infraction in patients with psoriasis Ref ID: GELFAND2006A	**Observational:** Prospective population-based cohort 1987-2002 **Representative population sample:** yes the data was collected from the electronic general Practice Research Database which has data on more than 8 million people. **Prognostic factor adequately measured:** yes **Confounders adjusted for:** age, diabetes, history of MI, hyperlipidemia,	N: 130976 psoriasis patients; 556995 corresponding control patients (127139 in mild psoriasis group and 3837 in severe psoriasis group)	**Inclusion criteria:** Patients with psoriasis aged 20 -90 years with at least 1 day of observation time. Each patient was matched to up to 5 control patients who did not have psoriasis diagnostic codes and were observed in the same practice on the latest date of when the psoriasis patient registered with the practice or when the practice was designated 'up to standard' within 60 days. **Exclusion criteria:** None stated. Mean age in years: Control: 45.72 Mild psoriasis:46.35	GPRD used. They either received a medical code consistent with the diagnosis or not. Severe psoriasis was based on history of having had systemic therapies, the majority of whom had MTX.	Mean 5.4 years **Note**: study ended due to: death, end of up to standard or transfer out.	Incidence of myocardial infarction	Grant from the National Institutes of Health/ National Institute of Arthritis and musculoskeletal and Skin Diseases and an unrestricted grant to the Trustees of the University of Pennsylvania from Biogen Idec. Biogen Idec assisted in interpretin

	hypertension, sex, smoking. **Attrition bias:** No. Patients who died without MI were considered as censored for the primary analysis and they conducted sensitivity analyses for the composite outcome of the earlier of MI and death. **Outcomes adequately measured:** Yes **Appropriate statistical analysis:** yes		Severe psoriasis: 49.75 Note: all groups had <2% with a history of MI				g the data.

Effect size:

	Control	Mild	Severe
No. of new MI cases (%)	**11 194 (2.0)**	**2319 (1.8)**	**112 (2.9)**
Incidence of per 1000 person-years (95% CI)	**3.58 (3.52-3.65)**	**4.04 (3.88-4.21)**	**5.13 (4.22-6.17)**

Univariable and multivariable cox proportional hazard regression models of the risk of MI in patients with mild and severe psoriasis compared with control patients*

	Model Hazard Ratio (95% CI)		**P value**
Covariate	**Mild psoriasis**	**Severe psoriasis**	**<0.001**
Psoriasis (unadjusted)	1.11 (1.07-1.17)	1.43 (1.18-1.72)	<0.001
Psoriasis	1.54 (1.24-1.91)**	7.08 (3.06-16.36)**	<0.001
Age per year	1.077 (1.076-1.079)	1.077 (1.076-1.078)	<0.001
Age x psoriasis (interaction term)	0.994 (0.991-0.997)	0.97 (0.96-0.99)	<0.001
Diabetes	1.61 (1.53-1.70)	1.62 (1.53-1.71)	<0.001
History of MI	3.24 (3.07-3.41)	3.31 (3.13-3.51)	<0.001
Hyperlipidemia	3.08 (2.93-3.23)	3.18 (3.02-3.36)	<0.001
Hypertension	1.11 (1.07-1.16)	1.12 (1.07-1.17)	<0.001
Male sex	2.12 (2.04-2.19)	2.14 (2.05-2.22)	<0.001
Smoking	1.15 (1.10-1.20)	1.16 (1.11-1.21)	<0.001

*Body mass index was not included in the primary model because it was available for only 61% of the patients.

** The point estimate of the hazard ratio for MI due to mild or severe psoriasis is not directly interpretable as this hazard ratio was modified by age (**ie age x psoriasis interaction term was significant**). Age was categorised in years.

Sensitivity analyses hazard ratio point estimates for patients aged 30 and 60 years:

	Hazard Ratio (95% CI)	
	Mild Psoriasis	Severe Psoriasis

	Age 30 years	Age 60 years	Age 30 years	Age 60 years
Primary analysis	1.29 (1.14 -1.46)	1.08 (1.03-1.13)	3.10 (1.98-4.86)	1.36 (1.13-1.64)
At least 6 months of follow-up (to ensure capture of incident, not prevalent MIs)	1.27 (1.12-1.45)	1.08 (1.03-1.14)	2.11 (1.95-4.94)	1.45 (1.20-1.76)
Last prescription or diagnosis as end date (to ensure that patients are actively followed up and censored for the same reason)	1.28 (1.13-1.44)	1.07 (1.02-1.13)	2.90 (1.86-4.54)	1.32 (1.09-1.59)
Inclusion of patients observed >/= time/y by the general practitioner (to ensure that patients are actively followed up)	1.20 (1.06-1.36)	1.04 (0.99-1.09)	2.82 (1.81-4.40)	1.29 (1.07-1.56)
Primary model but also adjusting for BMI (excluded approximately 40% of patients for whom there was no BMI)	1.36 (1.17-1.58)	1.07 (1.01-1.13)	2.65 (1.53-4.59)	1.56 (1.25-1.93)
Primary model excluding approximately 40% of patients for whom there was no BMI; in this model, BMI was not included	1.37 (1.18-1.59)	1.08 (1.02-1.14)	2.70 (1.56-4.66)	1.58 (1.27-1.96)
Exclusion of patients	NA	NA	4.12 (2.24-7.58)	1.45 (1.11-1.91)

treated with methotrexate				
Exclusion of patients treated with oral retinoids or ciclosporine*	NA	NA	2.06 (1.16-3.67)	1.28 (1.03-1.58)
Composite end point of MI or death	1.44 (1.34-1.55)	1.20 (1.17-1.24)	2.08 (1.54-2.82)	1.42 (1.27-1.58)

*Age x psoriasis interaction term was of borderline statistical significance (p=0.06).

Author's conclusion:

Psoriasis may confer an independent risk for MI. The risk was greatest in young patients with severe psoriasis, is attenuated with age and is still increased after controlling for traditional cardiovascular risk factors.

H.5.2 MYOCARDIAL INFARCTION

Reference	Study type	Number of patients	Patient characteristics	Intervention	Length of follow-up	Outcome measures	Source of funding
Lin et al. (2011) Title: Increased risk of acute myocardial infarction in patients with	**Observational:** retrospective population-based cohort study from 1999-2005 **Representative population sample:**	N: 28,512. Psoriasis diagnosis n=4752; without Psoriasis diagnosis n=23,760.	**Inclusion criteria:** all patients who visited ambulatory care centres for treatment of psoriasis (International Classification of Disease, Ninth Revision, Clinical Modification codes 696, 696.0, 696.1, and 696.8) from January 1 1999 to December 31, 2001).	Longitudinal Health insurance database 2005 from the Taiwan National Health Research Institute (NHRI), released in 2006.	5 years.	Incidence of acute myocardial infarction;	None.

psoriasis: A 5-year population-based study in Taiwan Ref ID: LIN2011	Yes **Prognostic factor adequately measured:** yes **Confounders adjusted for:** stratified by sex and age and adjustments made for patient's hospital clustering, hypertension, diabetes, hyperlipidemia, monthly income, geographic region and urbanisation level **Attrition bias:** not reported. **Outcomes adequately measured:** yes **Appropriate statistical analysis:** yes – Pearson's X^2 tests for differences between two cohorts.		**Exclusion criteria:** Younger than 18 years (n=2093); diagnosis of AMI (international classification of disease, ninth revision, clinical modification code 410 or 412) before their index ambulatory care visit (n=54).	They randomly selected patients and 5 control patients for every one patient diagnosed, matched by age (<30, 30-59, and >59 years) and sex.			

	5-year AMI-free survival estimated with Kaplan-Meier method. Stratified Cox proportional hazard regressions for clustering and confounders.						

Baseline:

	Patients with psoriasis	**Control group**	
Variable	**Number (%)**	**Number (%)**	**P value**
Male	2361 (49.7%)	11,805 (49.7%)	1.00
Aged 18-29	1568 (33%)	7840 (33%)	1.00
Aged 30-59	2429 (51.1%)	12,145 (51.1%)	1.00
>59	755 (15.9%)	3775 (15.9%)	1.00
Hypertension	1054 (22.2%)	4823 (20.3%)	0.003
Diabetes	567 (11.9%	2401 (10.1%)	<0.001
Hyperlipidemia	564 (11.9%)	2296 (9.7%)	<0.001

Effect size:

Crude and adjusted hazard ratios for psoriasis among patients during 5-year follow-up period starting from index ambulatory care visit (n=28,512)

			Psoriasis	

Presence of AMI	Control group	Patients with psoriasis	Receiving systemic therapy* for >/= 90 days (n=590)	Receiving systematic therapy* for < 90 days (n=475)	Others (n=4162)
Yes	48 (0.2%)	22 (0.5%)	5 (0.8%)	0 (0%)	17 (0.4%)
Crude HR (95% CI)	1.00	2.30** (1.38-3.80)	4.22*** (1.68-10.65)	-	2.03**** (1.16-3.53)
Adjusted*** HR (95% CI)**	1.00	2.10 (1.27-3.43)	1.81 (0.69-4.74)	-	2.0 (1.13-3.54)

*Patients who receive systemic therapy in our study include those who received ultraviolet B phototherapy and systemic agents.

**P<0.001,

***p<0.01;

****p<0.05.

*****Stratified by patient's sex and age and adjustments were made for patient's hospital clustering, hypertension, diabetes, hyperlipidemia, monthly income, geographic region and urbanisation level.

Author's conclusion: Psoriasis may confer an independent risk of AMI in Asian populations.

H.5.3 MYOCARDIAL INFARCTION AND STROKE

Reference	Study type	Number of	Patient characteristics	Prognostic factors	Length of follow-up	Outcome measures	Source

		patients					**of** **funding**
Brauchli 2009 Psoriasis and risk of incident myocardial infarction, stroke or transient ischaemic attack: an inception cohort study with a nested case-control analysis. Ref ID: BRAUCHLI 2009A	**Observational:** inception cohort study with a nested case-control analysis **Representative population sample:** Yes - UK based General practice Research Database **Prognostic factor adequately measured:** yes **Confounders adjusted for:** Matched on calendar time, age (same year of birth), sex, general practice, and years of history in the GPRD. **Attrition bias:** not reported.	N: 73,404. 36,702 with psoriasis and 36,702 matched psoriasis-free.	**Inclusion criteria:** all patients with a first-time recorded diagnosis of psoriasis between 1st January 1994 and 31st December 2005 and a comparison group of the same number of psoriasis-free patients. **Exclusion criteria:** excluded those with <3 years of history in the database prior to the first-time psoriasis diagnosis (or the corresponding date in the comparison group); history of ischaemic heart disease or cerebrovasulcar diseases, cancer or human immunodeficiency virus (HIV) prior to the psoriasis diagnosis (or corresponding date in the control group).	The comparison group was matched to the psoriasis patients on date of psoriasis diagnosis, age (same year of birth), sex, general practice, and years of history in the GPRD. All patients with a recorded psoriasis diagnosis in the analyses. Validated all potential cases with a recorded code for incident MI, stroke or TIA using a computer-based algorithm and manual computer profile review. Validation process done blinded as to whether cases had psoriasis or not.	**Mean 4.6 years** **Note**: followed up until they developed a first-time diagnosis of MI, stroke or TIA, they died or follow-up in the medical record ended.	Incidence of MI; incidence of stroke; incidence of transient ischaemic attach	Funded by an unrestricted grant from Merck Serono International SA. One author was supported by a grant from the Senglet Foundation, Switzerland.

	Outcomes adequately measured: yes **Appropriate statistical analysis:** not multivariable/regression **Notes:** nested case-control analysis involved matching at random up to four control patients from the study population on age, sex and calendar time and applied same exclusion criteria to controls as did cases.						

Incidence rates of myocardial infarction (MI), stroke and transient ischaemic attack (ITA)

Outcome	Group	Events	Person-years	IR/1000 person-years (95% CI)	IRR (95% CI)
MI					
Psoriasis	All	238	150972.2	1.58 (1.39-1.79)	1.07 (0.89-1.29)
	Men	151	68503.1	2.20 (1.88-2.58)	1.06 (0.84-1.33)
	Women	82	82469.0	1.05 (0.86-1.30)	1.09 (0.80-1.48)

	Age 0-29 years	0	40383.7	NA	NA	
	Age 30-59 years	76	70212.8	1.08 (0.86-1.35)	1.99 (1.37-2.88)	
	Age 60-80+ years	162	40375.7	4.01 (3.44-4.68)	0.92 (0.75-1.14)	
No psoriasis	All	211	143231.5	1.47 (1.29-1.69)	1.0	
	Men	135	64707.2	2.09 (1.76-2.47)	1.0	
	Women	76	78524.3	0.97 (0.77-1.21)	1.0	
	Age 0-29 years	1	37068.7	0.03 (0.00-0.15)	1.0	
	Age 30-59 years	36	66180.7	0.54 (0.39-0.75)	1.0	
	Age 60-80+ years	174	39982.1	4.35 (3.75-5.05)	1.0	
Stroke						
Psoriasis	All	264	156492.8	1.69 (1.50-1.90)	0.92 (0.77-1.09)	
	Men	135	72208.3	1.87 (1.58-2.21)	1.02 (0.80-1.31)	
	Women	129	84284.5	1.53 (1.29-1.82)	0.83 (0.65-1.05)	
	Age 0-29 years	1	40392.1	0.02 (0.00-0.14)	NA	
	Age 30-59 years	37	71800.5	0.52 (0.37-0.71)	0.75 (0.49-1.16)	
	Age 60-80+ years	226	44300.3	5.10 (4.48-5.81)	0.98 (0.81-1.18)	
No psoriasis	All	271	147287.7	1.84 (1.63-2.07)	1.0	
	Men	123	67279.2	1.83 (1.53-2.18)	1.0	
	Women	148	80008.5	1.85 (1.58-2.17)	1.0	
	Age 0-29 years	0	37076.6	NA	NA	

	Age 30-59 years	46	67094.7	0.69 (0.51-0.91)	1.0
	Age 60-80+ years	225	43116.3	5.22 (4.58-5.94)	1.0
TIA					
Psoriasis	All	205	156492.8	1.31 (1.14-1.50)	0.98 (0.81-1.19)
	Men	92	72208.3	1.27 (1.04-1.56)	0.88 (0.66-1.18)
	Women	113	84284.5	1.34 (1.12-1.61)	1.07 (0.82-1.40)
	Age 0-29 years	0	40392.1	NA	NA
	Age 30-59 years	28	71800.5	0.39 (0.27-0.56)	1.14 (0.66-1.97)
	Age 60-80+ years	177	44300.3	4.00 (3.45-4.63)	0.99 (0.80-1.22)
No psoriasis	All	197	147287.7	1.34 (1.16-1.54)	1.0
	Men	97	67279.2	1.44 (1.18-1.76)	1.0
	Women	100	80008.5	1.25 (1.03-1.52)	1.0
	Age 0-29 years	0	37076.6	NA	NA
	Age 30-59 years	23	67094.7	0.34 (0.23-0.51)	1.0
	Age 60-80+ years	174	43116.3	4.04 (3.48-4.68)	1.0

Author's conclusion: they did not find an increased risk for developing a cardiovascular outcome with early psoriasis. Subanalyses however found a suggestion of an increased (but low absolute) MI risk of patients with psoriasis aged <60 years.

H.5.4 MYOCARDIAL INFARCTION

Reference	Study type	Number of patients	Patient characteristics	Prognostic factors	Length of follow-up	Outcome measures	Source of funding
Kaye (2008) Incidence of risk factors for myocardial infarction and other vascular diseases in patients with psoriasis Ref ID: KAYE2008	**Observational:** retrospective cohort study. **Representative population sample:** Yes - General practice research database **Prognostic factor adequately measured:** yes **Confounders adjusted for:** Matched on age, sex and index date. **Attrition bias:** not reported	N: 44,164 with psoriasis and 219,784 without psoriasis.	**Inclusion criteria:** all patients with a first-time diagnosis of psoriasis after 1st January 1991 The psoriasis cohort was restricted to those with at least 1 year of medical history recorded in the database before their index date (the date of the first-time diagnosis of psoriasis). The index date defined the start of follow-up for estimating the cumulative incidences of the outcomes of interest in the psoriasis group. The comparison cohort was randomly selected and matched in a 5:1 ratio by year of birth, sex, general practice and index date. **Exclusion criteria:** none stated.	GPRD used. S standard OXMIS and READ codes for diagnosis.	**1, 3, 5 and 10 year follow-ups.** **Note**: follow-up ended when a patient developed an outcome of interest, transferred out of their practice or died.	Incidence of diabetes, hypertension, obesity, hyperlipidaemia, myocardial infarction, angina, atherosclerosis, peripheral vascular disease and stroke.	Amgen, Inc.

	Outcomes adequately measured: yes **Appropriate statistical analysis:** yes - Kaplan-Meier to estimate cumulative incidences for each of outcomes at specific times. Cox regression to estimate hazard ratio for each outcome comparing psoriasis cohort with comparison group.						

Baseline characteristics:

Variable	**Psoriasis**	**Comparison**
	N (%)	**N (%)**
Male	21,121 (47.8%)	105, 045 (48.8%)
Age (years)		
< 10	1887 (4.3%)	9418 (4.3%)

10-19	5058 (11.5%)	25,248 (11.5%)
20-29	5848 (13.2%)	29, 198 (13.3%)
30-39	7079 (16%)	35,363 (16.1%)
40-49	6415 (14.5%)	32,021 (14.6%)
50-59	6648 (15.1%)	33,193 (15.1%)
60-69	5740 (13%)	28,607 (13%)
70-79	3938 (8.9%)	19,520 (8.9%)
80-89	1389 (3.2%)	6679 (3.0%)
90+	162 (0.4%)	537 (0.2%)
Treatment	41,790 (94.6%)	N/A

Effect size:

Incident diabetes cases in the psoriasis and comparison cohorts

	Psoriasis n=44164	**Comparison n=219784**
	N (%)	**N (%)**
Total	1198 (2.7)	4482 (2.0)
Sex		
Male	661 (55.2)	2532 (56.5)

Female	537 (44.8)	1950 (43.5)
Age (years)		
< 10	4 (0.3)	13 (0.3)
10-19	7 (0.6)	27 (0.6)
20-29	24 (2.0)	91 (2.0)
30-39	86 (7.2)	264 (5.9)
40-49	191 (15.9)	638 (14.2)
50-59	325 (27.1)	1160 (25.9)
60-69	356 (29.7)	1357 (30.3)
70-79	168 (14.0)	774 (17.3)
80-89	35 (2.9)	151 (3.4)
90+	2 (0.2)	7 (0.2)

Estimated cumulative incidence of diabetes at specified time after the index date in the psoriasis and comparison cohorts

	Cases	**Cumulative incidence (per 1000)**	**95% CI (per 1000)**
Psoriasis			
1 year	**207**	**5.2**	**4.5-5.9**
3 years	**337**	**15.9**	**14.6-17.3**
5 years	**210**	**25.4**	**23.6-27.3**

10 years	**360**	**57.3**	**53.5-61.2**
Comparison			
1 year	**686**	**3.4**	**3.2-3.7**
3 years	**1169**	**10.9**	**10.4-11.4**
5 years	**886**	**19.0**	**18.3-19.7**
10 years	**1363**	**43.9**	**42.4-45.5**

Incident hypertension cases in the psoriasis and comparison cohorts

	Psoriasis n=44164	**Comparison n=219784**
	N (%)	**N (%)**
Total	**2765 (6.3)**	**12754 (5.8)**
Sex		
Male	**1332 (48.2)**	**6147 (48.2)**
Female	**1433 (51.8)**	**6607 (51.8)**
Age (years)		
< 10	**1 (0.0)**	**4 (0.0)**
10-19	**14 (0.5)**	**70 (0.6)**
20-29	**59 (2.1)**	**327 (2.)**
30-39	**206 (7.5)**	**955 (7.5)**
40-49	**515 (18.6)**	**2124 (16.7)**

50-59	**717 (25.9)**	**3340 (26.2)**
60-69	**724 (26.2)**	**3542 (27.8)**
70-79	**435 (15.7)**	**2003 (15.7)**
80-89	**93 (3.4)**	**368 (2.9)**
90+	**1 (0.0)**	**21 (0.2)**

Estimated cumulative incidence of hypertension at specified time after the index date in the psoriasis and comparison cohorts

	Cases	**Cumulative incidence (per 1000)**	**95% CI (per 1000)**
Psoriasis			
1 year	**501**	**14.0**	**12.9-15.3**
3 years	**796**	**42.2**	**39.9-44.5**
5 years	**521**	**68.2**	**65.2-71.4**
10 years	**732**	**138.5**	**132.7-144.6**
Comparison			
1 year	**2211**	**12.1**	**11.6-12.6**
3 years	**3440**	**36.1**	**35.2-37.1**
5 years	**2441**	**60.4**	**49.0-61.7**
10 years	**3610**	**129.4**	**126.9-132.1**

Incident obesity cases in the psoriasis and comparison cohorts

	Psoriasis n=44164	**Comparison n=219784**
	N (%)	**N (%)**
Total	**2760 (6.3)**	**11996 (5.5)**
Sex		
Male	**1183 (42.9)**	**5274 (44.0)**
Female	**1577 (57.1)**	**6722 (56.0)**
Age (years)		
< 10	**16 (0.6)**	**85 (0.7)**
10-19	**225 (8.2)**	**903 (7.5)**
20-29	**342 (12.4)**	**1560 (13.0)**
30-39	**415 (15.0)**	**2007 (16.7)**
40-49	**531 (19.2)**	**2307 (19.2)**
50-59	**561 (20.3)**	**2388 (19.9)**
60-69	**453 (16.4)**	**1856 (15.5)**
70-79	**191 (6.9)**	**785 (6.5)**
80-89	**25 (0.9)**	**103 (0.9)**
90+	**1 (0.0)**	**2 (0.0)**

*Obesity is defined as body mass index>/=30kgm^{-2}

Estimated cumulative incidence of obesity at specified time after the index date in the psoriasis and comparison cohorts

	Cases	Cumulative incidence (per 1000)	95% CI (per 1000)
Psoriasis			
1 year	**525**	**14.8**	**13.6-16.1**
3 years	**776**	**42.1**	**39.9-44.5**
5 years	**515**	**67.7**	**64.7-70.9**
10 years	**745**	**139.0**	**133.2-145.1**
Comparison			
1 year	**2191**	**11.8**	**11.3-12.3**
3 years	**3335**	**34.6**	**33.8-35.6**
5 years	**2299**	**57.0**	**55.7-58.3**
10 years	**3241**	**118.0**	**115.5-120.5**

*Obesity is defined as body mass index>/=30kgm^{-2}

Incident hyperlipidaemia cases in the psoriasis and comparison cohorts

	Psoriasis n=44164	Comparison n=219784
	N (%)	**N (%)**
Total	**1900 (4.3)**	**8111 (3.7)**
Sex		

Male	**978 (51.5)**	**4074 (50.2)**
Female	**922 (48.5)**	**4037 (49.8)**
Age (years)		
< 10	**0 (0.0)**	**3 (0.0)**
10-19	**1 (0.1)**	**13 (0.2)**
20-29	**35 (1.8)**	**126 (1.6)**
30-39	**112 (5.9)**	**539 (6.7)**
40-49	**319 (16.8)**	**1354 (16.7)**
50-59	**572 (30.1)**	**2337 (28.8)**
60-69	**580 (30.5)**	**2502 (30.9)**
70-79	**257 (13.5)**	**1105 (13.6)**
80-89	**21 (1.1)**	**130 (1.6)**
90+	**3 (0.2)**	**2 (0.0)**

Estimated cumulative incidence of hyperlipidaemia at specified time after the index date in the psoriasis and comparison cohorts

	Cases	**Cumulative incidence (per 1000)**	**95% CI (per 1000)**
Psoriasis			
1 year	**305**	**7.8**	**7.0-8.8**
3 years	**495**	**23.8**	**22.2-25.5**

5 years	**377**	**41.0**	**38.7-43.5**
10 years	**570**	**91.1**	**86.5-96.0**
Comparison			
1 year	**1223**	**6.2**	**5.9-6.6**
3 years	**2172**	**20.3**	**19.7-21.0**
5 years	**1526**	**34.4**	**33.5-35.4**
10 years	**2388**	**77.7**	**75.7-79.7**

Incident myocardial infarction cases in the psoriasis and comparison cohorts

	Psoriasis n=44164	**Comparison n=219784**
	N (%)	**N (%)**
Total	**596 (1.4)**	
Sex		
Male	**378 (63.4)**	**1596 (64.9)**
Female	**218 (36.6)**	**863 (35.1)**
Age (years)		
< 10	**0 (0.0)**	**0 (0.0)**
10-19	**1 (0.2)**	**3 (0.1)**
20-29	**3 (0.5)**	**4 (0.2)**
30-39	**21 (3.5)**	**55 (2.2)**

40-49	**52 (8.7)**	**187 (7.6)**
50-59	**128 (21.5)**	**472 (19.2)**
60-69	**176 (29.5)**	**744 (30.3)**
70-79	**164 (27.5)**	**719 (29.2)**
80-89	**42 (7.1)**	**262 (10.7)**
90+	**9 (1.5)**	**13 (0.5)**

Estimated cumulative incidence of myocardial infarction at specified time after the index date in the psoriasis and comparison cohorts

	Cases	**Cumulative incidence (per 1000)**	**95% CI (per 1000)**
Psoriasis			
1 year	103	2.6	2.1-3.1
3 years	177	8.2	7.3-9.2
5 years	113	13.3	12.0-14.7
10 years	165	27.7	25.2-30.4
Comparison			
1 year	440	2.2	2.0-2.4
3 years	719	6.7	6.3-7.1
5 years	459	10.9	10.4-11.5

10 years	679	22.6	21.6-23.7

Hazard ratios

Outcome	**HR (95% CI)**
Diabetes	1.33 (1.25-1.42)
Angina	1.20 (1.12-1.29)
Hypertension	1.09 (1.05-1.14)
Hyperlipidaemia	1.17 (1.11-1.23)
Obesity	1.18 (1.14-1.23)
Myocardial infarction	1.21 (1.10-1.32)
Atherosclerosis	1.28 (1.10-1.48)
Peripheral vascular disease	1.29 (1.13-1.47)
Stroke	1.12 (1.00-1.25)

Author's conclusion: risk factor for cardiovascular disease as well as myocardial infarction and other vascular disease occurred with higher incidence in patients with psoriasis than in the general population. Further investigations needed as to whether these associations involve causal factors related to psoriasis or its treatment.

H.5.5 MYOCARDIAL INFARCTION – systemic therapy vs phototherapy for psoriasis

Reference	Study type	Number of patients	Patient characteristics	Prognostic factors	Length of follow-up	Outcome measures	Source of funding
K. Abuabara, H. Lee, and A. B. Kimball. The effect of systemic psoriasis therapies on the incidence of myocardial infarction: a cohort study. Br.J.Dermatol. 165 (5):1066-1073, 2011. Ref ID: ABUABARA2011	**Observational:** population-based cohort study from May 2000 to Sept 2008. **Representative population sample:** yes – large database covering 50% of US hospitals **Prognostic factor adequately measured:** yes – at least one ICD code and at least 2 prescriptions a minimum of 30 days apart for systemic psoriasis treatment or UVB phototherapy **Confounders adjusted for:** Age and sex plus comorbid diagnoses of depression,	N 25,554: phototherapy group n=4220; systemics group (n=20094)	**Inclusion criteria:** open cohort of all patients aged ≥18 years with age and sex data available and moderate-to-severe psoriasis (defined as at least one ICD code and at least 2 prescriptions a minimum of 30 days apart for systemic psoriasis treatment or UVB phototherapy) **Exclusion criteria:** none reported. Note: Of the patients receiving systemic treatment 25% received traditional systemics (methotrexate or ciclosporin), 57% received a biologic (alefacept, efalizumab, adalimumab, etanercept or infliximab) and 18% received both	Data from medical and pharmacy administrative claims database – traditional or biologic systemic agents vs UVB phototherapy	Mean unclear Mean duration of treatment ranged from 243 to 591 days **Note**: follow-up began at first prescription and continued until patients developed the outcome of interest, left the health plan or reached the end of the study period.	Acute MI – ICD code in any position after the first prescription date for systemic or phototherapy	Abbot Inc and the American Academy of Dermatology (Minority Student Mentorship Program)

	hypertension, hyperlipidaemia and diabetes, history of MI **Attrition bias:** not reported **Outcomes adequately measured:** yes **Appropriate statistical analysis:** Cox adjusted models		93% of those receiving biologics took TNF-α inhibitors The mean duration of treatment ranged from 243 to 591 days				

Patient characteristics:

	Phototherapy group	**Systemic group**	**p-value**
N	**4220**	**20094**	
Follow-up data (mean ± SD)			
Age at enrolment	44.2 ± 14.0	44.1 ± 12.1	0.553
Duration of enrolment (years)	3.8 ± 2.2	3.6 ± 2.2	<0.001
Number of visits	96 ± 87	65 ± 69	<0.001

Demographics and comorbidities			
Male (%)	49%	53%	<0.001
PsA (%)	6%	42%	<0.001
Depression	12	15	<0.001
Hypertension	21	25	<0.001
Diabetes	7	11	<0.001
Hyperlipidaemia	27	33	<0.001
Obesity	8	11	<0.001
Tobacco use	10	12	0.003
Outcomes			
Acute MI	30 (0.7%)	187 (0.9%)	-
Total person years	7872	39,931	-
Incidence per 1000 person years (95% CI)	3.81 (2.57-5.44)	4.68 (4.04-5.40)	-

Effect size:

Adjusted hazard ratio (systemic therapy vs phototherapy)

	Cox model HR (95% CI)
Unadjusted	1.22 (0.83-1.80)
Adjusted for cardiovascular risk factors	1.33 (0.90-1.96)

Final model – primary analysis (treatment type)	0.18 (0.03-1.09)

There was a significant interaction between treatment type and age:

Adjusted hazard ratio under different assumptions (systemic therapy vs phototherapy)

	N	**All subjects aged 18-70 years**	**Subjects aged 18-49 years**	**Subjects aged 50-70 years**
Primary analysis	23,785	1.10 (0.74-1.64)	0.65 (0.32-1.34)	1.37 (0.79-2.38)
Exclusion of patients with a history of MI	23,466	1.20 (0.74-1.94)	0.60 (0.28-1.30)	1.61 (0.83-2.80)
Exclusion of patients with PsA	15,157	1.10 (0.70-1.73)	0.59 (0.28-1.24)	1.40 (0.79-2.49)

Author's conclusion: Overall, there appears to be a trend towards an increased risk of MI in patients with psoriasis receiving systemic therapy compared with a group undergoing phototherapy. The risk of MI may vary by age – risk reduction in younger people receiving systemics but risk increase in older people on systemics

H.5.6 STROKE

Reference	Study type	Number of patients	Patient characteristics	Prognostic factors	Length of follow-up	Outcome measures	Source of funding
Gelfand et al (2009) The risk of stroke in patients with psoriasis Ref ID: GELFAND 2009	**Observational:** population-based cohort study from 1987-2002. **Representative population sample:** yes - used GPRD (which has been validated). **Prognostic factor adequately measured:** yes **Confounders adjusted for:** age, sex, hypertension, diabetes, hyperlipidemia, atrial fibrillation, and smoking (current, former, none).	N: 129,143 with mild psoriasis; 3603 with severe psoriasis; 496,666 and 14,330 matched controls.	**Inclusion criteria:** all patients defined as having mild or severe psoriasis, aged >/=18 years old at index date and had at least 1 day of observation time. Up to 4 control subjects were randomly selected for each psoriasis patient, matched on practice, date of registration in the practice and psoriasis index date (so evaluated by same physicians during same time period). **Exclusion criteria:** not reported.	General Practice Research Database used. Mild psoriasis was those with a diagnostic code of psoriasis but no history of systemic therapy at any time point. Severe psoriasis was defined as those with a diagnostic code of psoriasis and a history of systemic therapy consistent with severe psoriasis. Index date first date on or after registration in practice in which a diagnosis was recorded. For severe the index date was first date on or after	3-4.4 years mean and standard deviation 2-3.3 years. Notes: ended due to: death, end of UTS, transfer out.	Stroke occurring after the start date. Stroke identified using diagnostic codes (READ or OXMIS) entered by the GP into the medical record.	Grant from the National Institute of arthritis, musculos keletal, and skin diseases. Authors state that the funding sources had no role in the design and conduct of the study. The lead author receives grant support or is an investigat or for AMGEN, Centocor, and Pfizer and is a consultant

	Attrition bias: not reported. **Outcomes adequately measured:** yes **Appropriate statistical analysis:** yes - dichotomous variables tested with Fisher's exact test and continuous with t-test. Adjusted Cox models for overall HR of stroke in psoriasis patients. **Notes:** mild psoriasis patients defined as those with a diagnostic code of psoriasis, but no history of systemic therapy at any time point. Severe psoriasis patients were defined as those with a diagnostic code of psoriasis and			first diagnosis of psoriasis in which the patient received a code for treatment consistent with severe psoriasis. If psoriasis occurred before registration the registration date was the index date.			for Pfizer, Genentech, Celgene, AMGEN, Centocor and Luitpold.

	a history of systemic therapy consistent with severe psoriasis. Systemic therapy included phototherapy, PUVA, methotrexate, azathioprine, ciclosporine, oral retinoids (etretinate, acitretin), hydroxyurea, and mycophenolate mofetil. It was noted that during the time period that the study was conducted, biological therapies were not approved for psoriasis in the UK. The control group had no history of a psoriasis diagnostic code.						

Patient characteristics:

	Mild group		Severe group	
Characteristics	**Control (n=496,666)**	**Psoriasis (n=129,143)**	**Control (n=14,330)**	**Psoriasis (n=3,603)**
Male	**198.498 (40%)**	**61,956 (48%)**	**5,783 (40.4%)**	**1,750 (48.6%)**

		P<0.001		**P<0.001**	
Age (years) mean+/- SD	**46.1 (19.1)**	**45.1 (17.8)**	**49.7 (19.3)**	**52.2 (16.7)**	
Age (years) median (IQR)	43,30, 61	42,30, 59 P<0.001 Wilcoxon test	48, 33, 65	52, 39, 66 P<0.001 Wilcoxon test	
Diabetes mellitus	22,296 (4.5%)	5,858 (4.5%) P=0.470	737 (5.1%)	270 (7.5%) P<0.001	
History of stroke	7,401 (1.5%)	1,648 (1.3%) P<0.001	268 (1.9%)	89 (2.5%) P=0.023	
History of TIA	5637 (1.1%)	1254 (1.0%) P<0.001	243 (1.7%)	68 (1.9%) P=0.432	
History of stroke or TIA	11,883 (2.4%)	2,655 (2.1%) P<0.001	450 (3.1%)	140 (3.9%) P=0.028	
Hyperlipidemia	22,839 (4.6%)	6,775 (5.2%) P<0.001	842 (5.9%)	250 (6.9%) P=0.019	
Hypertension	88,397 (17.8%)	22,829 (17.7%) P=0.313	3,049 (21.3%)	858 (23.8%) P=0.001	
Smoking never	383,824 (77.3%)	96,944 (75.1%)	10,465 (73%)	2,488 (69.1%)	
Smoking current	19,839 (4%)	5,866 (4.5%)	755 (5.3%)	241 (6.7%)	
Smoking former	93,003 (18.7%)	26,333 (20.4%)	3,110 (21.7%)	874 (24.3%)	

		P<0.001		P<0.001
BMI <25	166,470 (53.2%)	40,606 (49.6%)	5,057 (51.2%)	1,025 (42.1%)
BMI>/=25 & <30	100,551 (32.1%)	27,701 (33.8%)	3,291 (33.3%)	860 (35.4%)
BMI>/=30	45,977 (14.7%)	13,618 (16.6%) P<0.001	1,522 (15.4%)	548 (22.5%) P<0.001
Reason for study end				
Death	32,677 (6.6%)	7,302 (5.6%)	790 (5.5%)	297 (8.2%)
End of UTS	353,565 (71.2%)	95, 275 (73.8%)	11,247 (78.5%)	2,860 (79.4%)
Transfer out	110,424 (22.2%)	26,566 (20.6%) P<0.001	2,293 (16%)	446 (12.4%) P<0.001
Atrial fibrillation	12,861 (2.6%)	3,046 (2.4%) P<0.01	428 (3%)	99 (2.8%) P=0.507

BMI, body mass index (calculated as weight in kilograms divided by height in meters squared);

IQR, interquartile range, SD, standard deviation; TIA, transient ischemic attack; UTS, up-to-standard.

Data for BMI were available for 67% of the patients.

Unless noted otherwise, p-values are derived using Fisher exact test.

Systemic therapies received by patients with severe psoriasis (n=3603)

Systemic therapy	**No. of patients with severe psoriasis (%)***

Methotrexate	2,114 (58.7%)
Psoralen	607 (16.9%)
Azathioprine	582 (16.2%)
Ciclosporine	390 (10.8%)
Etretinate or acetretin	333 (9.2%)
Hydroxyurea	208 (5.8%)
Mycophenolate mofetil	9 (0.3%)

***percentages do not add up to 100 because patients could have received more than one systemic therapy.**

Effect size:

Incidence of stroke in patients with psoriasis compared with control patients

	Mild group		**Severe group**	
Variable	**Control (n=496,666)**	**Psoriasis (n=129,143)**	**Control (n=14,330)**	**Psoriasis (n=3,603)**
Follow up time (years) mean +/SD	4.2 (3.3)	4.4 (3.3)	3.4 (2.7)	3.4 (2.7)
Follow up time median (IQR)	3.5 (1.5, 6.6)	3.7 (1.6, 6.9)	2.6 (1.2, 5.0)	2.7 (1.2, 5.0)
No of person-years	2,108,718	570,814.5	48,248.4	12,222.1

No of new stroke cases (%)	8,535 (1.72%)	2,100 (1.63%)	212 (1.48%)	74 (2.05%)
Incidence per 1,000 person-years (95% CI)	4.05 (3.96, 4.13)	3.68 (3.52, 3.84)	4.39 (3.82, 5.03)	6.05 (4.76, 7.60)

CI, confidence interval; IQR, interquartile range; SD, standard deviation

Unadjusted and adjusted Cox proportional hazard regression models of the risk of stroke in patients mild and severe psoriasis compared with control patients

	Model hazard ratio (95% CI)	
Covariate	**Mild psoriasis**	**Severe psoriasis**
Unadjusted analysis Psoriasis	0.91 (0.86, 0.95)	1.38 (1.05, 1.80)
Adjusted for age and sex		
Psoriasis	1.07 (1.02, 1.12)	1.44 (1.10, 1.88)
Age per year	1.089 (1.087, 1.090)	1.09 (1.08, 1.10)
Sex (male)	1.27 (1.22, 1.32)	1.51 (1.20, 1.91)
Primary model (adjusted for major cardiovascular risk factors)*		
Psoriasis	1.06 (1.01, 1.11)	1.43 (1.10, 1.87)
Age per year	1.082 (1.081, 1.084)	1.08 (1.07, 1.09)
Diabetes	1.78 (1.69, 1.87)	1.60 (1.16, 2.19)
HX of Stroke	4.26 (4.01, 4.51)	3.65 (2.57, 5.18)

HX of TIA	2.01 (1.87, 2.16)	2.05 (1.40, 3.01)
Hyperlipidemia	1.12 (1.04, 1.20)	1.35 (0.92, 1.98)
Hypertension	1.49 (1.43, 1.55)	1.72 (1.35, 2.18)
Sex (male)	1.20 (1.16, 1.25)	1.42 (1.12, 1.80)
Smoking (current vs never)	0.97 (0.89, 1.06)	1.09 (0.71, 1.68)
Smoking (former vs never)	1.10 (1.03, 1.17)	1.24 (0.89, 1.73)

BMI, body mass index; CI, confidence interval; HR, hazard ratio; TIA, transient ischemic attack.

*BMI was not included in the primary analysis as these data are only available in about 65% of patients.

Atrial fibrillation was not included in the primary analysis as this is not a common stroke risk factor.

Interaction terms for sex and age were not statistically significant (p>0.05).

Author's conclusion: Patients with psoriasis, particularly if severe, have an increased risk of stroke that is not explained by major stroke risk factors identified in routine medical care.

H.5.7 ACUTE ISCHAEMIC HEART DISEASE

Reference	Study type	Number of patients	Patient characteristics	Prognostic factors	Length of follow-up	Outcome measures	Source of funding

Wakkee (2010) Psoriasis may not be an independent risk factor for acute ischemic heart disease hospitalisations: results of a large population-based Dutch cohort. Ref ID: WAKKEE2010	**Observational:** prospective population-based cohort from 1997 to 2008. **Representative population sample:** yes – PHARMO record linking system which includes database of hospital discharge information, drug dispensing and clinical laboratory records for 2.5 million individuals in the Netherlands. **Prognostic factor adequately measured:** yes **Confounders adjusted for:** Matched for age and sex; adjusted for healthcare consumption proxy, metabolic drugs and an interaction term between psoriasis and healthcare consumption in IHD model	N: 15,820 (36.5%) psoriasis cohort; 25,577 (63.5%) reference cohort.	**Inclusion criteria:** An algorithm that categorised individuals by the likelihood of psoriasis diagnosis (none, possible, probable or definite) from which only those with definite were selected. Those with a hospital discharge diagnosis of psoriasis and/or psoriatic arthritis, dispensings for psoralen, calcipotriol, calcitriol or dithranol, fumaric acid, and/or efalizumab were considered as definite psoriasis patients. **Exclusion criteria:** patients were classified as possibly or probably having psoriasis if they did not meet any of the above criteria of definite but had prescriptions for topical corticosteroids, coal tar, systemic glucocorticosteroids, retinoids, methotrexate, ciclosporin, adalimumab, etanercept, and/or infliximab; definite	Used data from the PHARMO record linkage system, which links various medical databases. Coded according to the international classification of diseases, ninth revision (WHO, 1987) – medical procedures, dates of hospital admission and discharge; The Anatomical Therapeutic Chemical Classification (WHO, 1999) – dispensing date, amount dispensed and prescription dose regimens and length.	Median follow-up 6 years in both cohorts. First available date of an active treatment or hospitalisation for psoriasis between 1998 and 2007. Matched controls followed from random drug dispensing or hospitalisation occurring within 30 days of the start of follow-up of their matched psoriasis patient. **Note**: follow-up ended with the last drug dispensing before 2008, an IHD or death, whichever was first.	Primary outcome was hospitalisation for acute IHD (acute MI, other acute IHD and angina pectoris); acute MI was also studied separately.	Grant from Wyeth Pharmaceuticals.

	Attrition bias: not reported. **Outcomes adequately measured:** yes **Appropriate statistical analysis:** yes – student t-test and Mann-Whitney for continuous variables. Incidence rates and 95% CIs from Byar's approximation. Kaplan-Meier and Cox proportional hazard analyses were used.		psoriasis patients were excluded if hospitalised for skin conditions other than psoriasis, had < 6 months history before start of follow-up (which is twice the maximum prescription time allowed in the Netherlands) and/or were <18 years of age at index date; also those with a history of diseases that could, theoretically affect the development of psoriasis or its severity (HIV, immune disorders, inflammatory bowel diseases, hepatitis B and C, multiple sclerosis, rheumatoid arthritis, and status after organ transplant). Reference subjects selected and matched in a 1:2 ratio for age, gender, and presence of a database record within 30 days of cohort entry of a definite psoriasis				

			patient. Excluded if < 6 months history was available or if they were hospitalised for dermatological diseases or other conditions above.				

Baseline characteristics

Variable	**Psoriasis cohort**	**Reference cohort**
Male (%)	7,583 (47.9%)	13,306 (48.3%)
Female (%)	8,237 (52.1)	14,271 (51.7
Age years Mean (SD)	48.9 (16.1)	48.1 (16.1)
Earlier hospitalisations[1]		
Yes (%)	1,130 (7.1)[2]	1,415 (5.1)[2]
Total	1,676	1,979
Unique	1,447	1,802
Medical history		
Lipid-lowering drugs (%)	1,102 (7.0)[3]	1,701 96.2)[3]
Antihypertensive drugs (%)	3,076 (19.4)[4]	4,519 (16.4)[4]
Antidiabetic drugs	699 (4.4)[4]	993 (3.6)[4]

(%)		
Psoriasis therapies		
Topicals only	13,851 (87.5)	
Systemic therapy and/or hospitalisation[5]	1,969 (12.5)	
Specific therapies ever used since start of follow-up[6]		
Topical antipsoriatic therapies[7]	15,646 (98.9)	
PUVA therapy	505 (3.2)	
Methotrexate	122 (0.8)	
Ciclosporin	424 (2.7)	
Acitretin	789 (5.0)	
Fumarates	14 (0.1)	
Biologics	84 (0.5)	

PUVA, psoralen plus ultraviolet light A; SD, standard deviation;

[1] In 6 months before cohort entry (excluding hospitalisations for cardiovascular diseases, n=100 and n=124 for the psoriasis and control cohorts, respectively).

[2] $p<0.001$.

[3] $p=0.001$.

[4] $p<0.001$.

[5] Systemic drugs include PUVA therapy, and hospitalisation should be specific for psoriasis.

[6] Total adds up to more than 100% because of the possibility of multiple therapies per patient.

[7] Coal tar, topical corticosteroids, dithranol, calcipotriol, calcitriol, tacrolimus, and pimecrolimus.

[8] Adalimumab (n=19), efalizumab (n=8), etanercept (n=65), infliximab (n=2).

Effect size:

Incidence rates of ischemic heart disease (IHD) and acute myocardial infarction (MI) in patients with psoriasis and the reference cohort, and the crude and adjusted hazard ratios (HRs)

Outcome	**Events**	**Person-years**	**Incidence rate[1]**	**95% CI**	**Crude HR[2]**	**95% CI**	**Adjusted HR[3]**	**95% CI**
IHD[4]								
Reference cohort	846	151,303	559	522,598	1		1	
Psoriasis cohort	583	95,437	611	562,663	1.10	0.99, 1.23	1.05	0.95, 1.17
Acute MI								
Reference cohort	360	153,514	235	211,260	1		1	
Psoriasis cohort	223	97,029	234	201,262	0.99	0.84, 1.17	0.94	0.80, 1.11

CI, confidence interval.

[1] Incidence rate per 100,000 person-years.

[2] HR adjusted for age and gender by matching.

[3] Adjusted for age, gender, earlier use of antihypertensive, antidiabetic, and lipid-lowering drugs, the number of earlier non-cardiovascular hospitalisations in 180 days before cohort entry, and significant interaction terms.

[4] IHD includes hospitalisations for acute myocardial infarction, angina pectoris, and other acute IHDs.

Author's conclusion: The risk of IHD tended to be increased in their study but the analyses of their data suggest that other factors, eg referral bias for other disease are important for interpreting the results. The age and gender-adjusted risk of IHD was comparable between the cohorts. Adjusting for the increased antihypertensive, antidiabetic and lipid-lowering drugs and more hospitalisations that the psoriasis group had the risk remained comparable between both groups. There was no difference between the subgroup that only used topicals versus those who received systemic therapies or inpatient care for psoriasis. Therefore they suggest that psoriasis is not a clinically relevant risk factor for IHD hospitalisations on the population level.

H.5.8 VENOUS THROMBOEMBOLISM

Reference	Study type	Number of patients	Patient characteristics	Prognostic factors	Length of follow-up	Outcome measures	Source of funding
O. Ahlehoff, G. H. Gislason, J. Lindhardsen, M. G. Charlot, C. H. Jorgensen, J. B. Olesen, D.-M. Bretler, L. Skov, C. Torp-	**Observational:** retrospective Danish population-based cohort from 1997 to 2006 (data gathered prospectively). **Representative population sample:** yes – entire adult Danish population (reduced surveillance bias [people	N: 38,664 (1%) psoriasis cohort (35,138 mild and 3526 severe); 4,126,075 (99%) reference cohort.	**Inclusion criteria:** age ≥18 years **Exclusion criteria:** prevalent psoriasis; history of previous VTE; receiving vitamin K antagonist treatment	Used data from the Danish National Patient Register, National Prescription Registry, Central Population Register and National Causes of Death Register Individual-level linkage across all nationwide	Maximum follow-up 10 years in both cohorts. New-onset psoriasis **Note**: follow-up ended on December 31st 2006 or death	Primary outcome was first-time in-hospital discharge diagnosis of VTE (VTE diagnoses made in Emergency Departments were not included)	Department of Cardiology, Copenhagen University Hospital

Pedersen, and P. R. Hansen. Psoriasis carries an increased risk of venous thromboembolism: a Danish nationwide cohort study. PLoS ONE 6 (3), 2011. Ref ID: AHLEHOFF2011	with psoriasis being more likely to visit the GP and therefore be diagnosed with CVD] and avoids selection bias) **Prognostic factor adequately measured:** yes **Confounders adjusted for:** age, calendar year, concomitant medication, comorbidity, socioeconomic data, and gender. **Attrition bias:** not reported. **Outcomes adequately measured:** yes **Appropriate statistical analysis:** yes – Unadjusted event rates are summarized as		**Note:** psoriasis patients were identified by claims of prescriptions for vitamin D analogues according to the comprehensive National Prescription registry and included on their second prescription Severe psoriasis was identified by hospitalisations (including out-patient visits) for psoriasis or psoriatic arthritis – this classification has been validated Note: unable to identify patients treated with topical corticosteroids alone and also unable to address the potential impact of various systemic treatment strategies Comorbidity at study entry was described by Charleson's Index (19	prospectively recorded registers was possible Coded according to the international classification of diseases, 8th-10th revision (WHO, 1987)		Secondary outcome was hospitalisations with the specific diagnosis of pulmonary embolism	

	events per 1000 person-years. The rate ratios (RRs) and 95% confidence interval (CI) of VTE were estimated by time-dependent Poisson regression models adjusted for age, calendar year, concomitant medication, comorbidity (according to Charlton Comorbidity Index), socioeconomic data (surrogate for obesity and smoking), and gender. Psoriasis status was included as a time-dependent variable, i.e., patients were only considered at risk from the time they complied with the inclusion criteria. Age and calendar year were also included as time-dependent variables. Comorbidity, socioeconomics, and concomitant medication were included as fixed variables obtained at baseline.		pre-specified diagnoses at study entry and up to 1 year previously) and modified to ICD-10				

Baseline characteristics							
Characteristic	**Controls** **n = 4,126,075**		**Mild psoriasis** **n = 35,138**		**Severe psoriasis** **n = 3526**		
Age, years (SD)	46.8 (18)		47.7 (16)		48.4 (16)		
Men (%)	48.9%		50.0%		51.9%		
No. of person-years	38,503,356		175,384		22,135		
Comorbidity (%)							
Peripheral vascular disease	0.14%		0.12%		0.23%		
Cerebrovascular disease	0.3%		0.26%		0.23%		
Coronary heart disease	0.47%		0.54%		1.05%		
Congestive heart failure	0.16%		0.11%		0.32%		
Hepatic disease	0.06%		0.06%		0.88%		
Chronic obstructive pulmonary disease	0.27%		0.16%		0.28%		
Cardiac dysrhythmia	0.27%		0.19%		0.45%		

Renal disease	0.06%	0.03%	0.14%
Cancer	0.6%	0.44%	0.99%
Rheumatological disease	0.09%	0.08%	0.26%
Treatment (%)			
Platelet inhibitor	2.32%	2.4%	2.01%
Beta-blocker	3.27%	4.27%	4.74%
ACEI/ARB	2.82%	3.54%	3.77%
Loop diuretic	2.98%	2.45%	4.28%
Statin	0.68%	1.06%	0.94%
Spironolactone	0.35%	0.29%	0.77%
Glucose-lowering drug	1.74%	1.83%	2.72%

Effect Size

Incidence rates of venous **thromboembolism (VTE)** in patients with psoriasis and the reference cohort, and the adjusted incidence rate ratios (RR)

Outcome	**Incidence rate per 1000 person years (95% CI)[1]**		**Adjusted RR (95% CI)**		
	< 50 years	**≥ 50 years**	**< 50 years**	**≥ 50 years**	**All ages**
Controls	0.58 (0.57-0.59)	2.03 (2.01-2.05)	1	1	**1**

Mild psoriasis	0.73 (0.56-0.95)	2.74 (2.45-3.06)	1.24 (0.97-1.58)	1.26 (1.13-1.42)	**1.35 (1.21-1.49)**
Severe psoriasis	2.10 (1.32-3.33)	3.93 (3.01-5.13)	3.14 (1.98-4.97)	1.74 (1.32-2.28)	**2.06 (1.63-2.61)**

Incidence rates of venous **pulmonary embolism** (PE) in patients with psoriasis and the reference cohort, and the adjusted incidence rate ratios (RR)

Outcome	**Adjusted RR (95% CI)**
	All ages
Controls	**1**
Mild psoriasis	**1.14 (0.95-1.37)**
Severe psoriasis	**1.88 (1.22-2.89)**

Sensitivity analyses for VTE risk

Outcome	**Adjusted RR (95% CI)**	
	Excluding those with a history of cancer or rheumatological disease	**Censoring patients undergoing a surgical procedure**
Controls	1	1
Mild psoriasis	1.34 (1.21-1.49)	1.20 (0.96-1.51)
Severe	1.99 (1.56-2.53)	2.55 (1.53-4.24)

psoriasis		

Note: results were not different if the diagnostic criteria for psoriasis were less restrictive (first Vit D prescription or first diagnosis); neither did exclusion of all patients with in- or out-patient hospital contacts up to 1 year prior to study start significantly alter the results

Author's conclusion:

- This first nationwide cohort study indicates that patients with psoriasis are at increased risk of VTE.
- The risk was highest in young patients with severe disease.
- Further prospective studies are needed to confirm this association, but physicians should be aware that patients with psoriasis may be at increased risk of both venous and arterial thromboembolic events

H.5.9 CARDIOVASCULAR RISK

Reference	Study type	Number of patients	Patient characteristics	Prognostic factors	Length of follow-up	Outcome measures	Source of funding
O. Ahlehoff, G. H. Gislason, M. Charlot, C. H. Jorgensen, J. Lindhardsen, J. B. Olesen, S. Z. Abildstrom, L. Skov, C. Torp-Pedersen,	**Observational:** retrospective Danish population-based cohort from 1997 to 2006 (data gathered prospectively). **Representative population sample:** yes – entire adult Danish population (reduced surveillance bias and avoids selection bias)	N: 36,992 (1%) psoriasis cohort (34,371 mild and 2621 severe, including 607 with PsA); 4,003,265 (99%) reference cohort.	**Inclusion criteria:** age ≥18 years **Exclusion criteria:** prevalent psoriasis, diabetes mellitus or atherosclerotic disease (including prior stroke or MI) **Note:** psoriasis patients	Used data from the: Danish National Patient Register for mortality (records all hospital admissions, diagnoses, and invasive procedures according the World Health Organisations International Classification of	Maximum follow-up 10 years in both cohorts. New-onset psoriasis **Note**: follow-up ended on December 31st 2006 or death	All-cause mortality, cardiovascular mortality and hospitalisations for MI, stroke and coronary revascularisation (PCI and CABG)	Department of Cardiology, Copenhagen University Hospital

and P. R. Hansen. Psoriasis is associated with clinically significant cardiovascular risk: A Danish nationwide cohort study. J.Intern.Med 270 (2):147-157, 2011. Ref ID: AHLEHOFF2011D	**Prognostic factor adequately measured:** yes **Confounders adjusted for:** age, calendar year, concomitant medication, comorbidity, socioeconomic data, and gender. **Attrition bias:** not reported. **Outcomes adequately measured:** yes **Appropriate statistical analysis:** yes – Unadjusted event rates are summarized as events per 1000 person-years. The rate ratios (RRs) and 95% confidence interval (CI) were estimated by time-dependent Poisson regression models	In the adjusted analysis patients with psoriasis were matched for age and gender with 4 controls from the general population for sensitivity analyses	were identified by claims of prescriptions for vitamin D analogues according to the comprehensive National Prescription registry and included on their second prescription Severe psoriasis was identified by hospitalisations (including out-patient visits) for psoriasis or psoriatic arthritis – this classification has been validated Diabetes was identified by first prescription of glucose-lowering drugs or insulin Note: unable to identify patients treated with topical corticosteroids alone and also unable to address the potential impact of various systemic treatment strategies	Diseases (ICD), 8th-10th revision (WHO, 1987). Danish Registry of Medicinal Product Statistics (the National Prescription Registry), for medications (records all dispensed prescriptions since 1995) Central Population Register for mortality (records all deaths within 2 weeks). National Causes of Death Register for cause of death (records immediate, contributory, and underlying causes of death were recorded using ICD-10 codes) Individual-level linkage across all nationwide prospectively recorded registers was possible			

	adjusted for age, calendar year, concomitant medication, comorbidity (according to Charlton Comorbidity Index), socioeconomic data (surrogate for obesity and smoking), and gender. Psoriasis status was included as a time-dependent variable, i.e., patients were only considered at risk from the time they complied with the inclusion criteria. Age and calendar year were also included as time-dependent variables. Comorbidity and concomitant medication were included as fixed variables obtained at baseline.		Comorbidity at study entry was described by Charleson's Index (19 pre-specified diagnoses at study entry and up to 1 year previously) and modified to ICD-10				

Baseline characteristics

Characteristic	**Controls**	**Mild psoriasis**	**Severe psoriasis**

	n = 4,003,265	**n = 34,371**	**n = 2621**
Age, years (SD)	47.3 (15.8)	47.2 (15.9)	46.9 (15.4)
Men (%)	48.5%	49.4%	51.6%
No. of person-years	36,965,324	172,224	13,146
Comorbidity (%)			
Congestive heart failure	0.17%	0.1%	0.15%
Chronic obstructive pulmonary disease	0.24%	0.13%	0.23%
Cardiac dysrhythmia	0.27%	0.24%	0.38%
Renal disease	0.05%	0.03%	0.08%
Cancer	0.57%	0.46%	0.61%
Rheumatological disease	0.09%	0.06%	0.11%
Treatments			
Platelet inhibitor	0.17%	1.61%	1.34%
Beta-blocker	2.86%	3.83%	4.08%
ACEI/ARB	2.25%	2.88%	2.82%
Vitamin K antagonist	0.38%	0.38%	0.27%
Loop diuretic	2.43%	2.07%	3.24%
Statin	0.44%	0.67%	0.65%

Spironolactone	0.29%	0.26%	0.38%

Effect Size

Adjusted incidence rate ratios in patients with psoriasis compared with the reference cohort

Outcomes	**Mild psoriasis**				**Severe psoriasis**			
	Overall (n=43,371)	**18-50 yr (n=16,150)**	**51-70 yr (n=13,714)**	**>70 yr (n=4507)**	**Overall (n=2621)**	**18-50 yr (n=1296)**	**51-70 yr (n=1031)**	**>70 yr (n=294)**
All cause mortality								
RR (CI)	1.16 (1.11-1.20)	1.26 (1.08-1.47)	1.23 (1.15-1.31)	1.13 (1.08-1.19)	1.73 (1.54-1.94)	2.87 (2.04-4.02)	2.32 (1.96-2.74)	1.24 (1.05-1.48)
p-value	<0.001	0.003	<0.001	<0.001	<0.001	<0.001	<0.001	0.01
Cardiovascular death								
RR (CI)	1.14 (1.06-1.22)	1 (0.66-1.50)	1.2 (1.05-1.36)	1.14 (1.06-1.24)	1.57 (1.27-1.94)	2.98 (1.32-6.73)	2.22 (1.59-3.10)	1.18 (0.89-1.57)
p-value	<0.001	0.99	0.01	0.001	<0.001	0.001	<0.001	0.26
Composite end-point								
RR (CI)	1.2 (1.14-1.25)	1.4 (1.20-1.63)	1.21 (1.12-1.29)	1.16 (1.09-1.24)	1.58 (1.36-1.82)	2.04 (1.35-3.09)	1.85 (1.51-2.26)	1.19 (0.95-1.50)
p-value	<0.001	<0.001	<0.001	<0.001	<0.001	0.001	<0.001	0.13

Stroke								
RR (CI)	1.25 (1.16-1.33)	1.61 (1.32-1.97)	1.22 (1.10-1.35)	1.15 (1.05-1.20)	1.71 (1.39-2.11)	1.64 (0.88-3.07)	1.87 (1.41-2.49)	1.47 (1.07-1.26)
p-value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Myocardial infarction								
RR (CI)	1.22 (1.12-1.33)	1.17 (0.89-1.54)	1.12 (0.99-1.26)	1.3 (1.16-1.45)	1.45 (1.10-1.9)	2.32 (1.19-4.50)	1.44 (0.99-2.09)	1.00 (0.63-1.45)
p-value	<0.001	0.63	0.06	<0.001	0.01	0.01	0.05	0.97
Coronary revascularisation								
RR (CI)	1.37 (1.26-1.49)	1.62 (1.26-2.07)	1.26 (1.13-1.40)	1.45 (1.24-1.69)	1.77 (1.35-2.32)	2.27 (1.17-4.42)	1.63 (1.16-2.27)	1.58 (0.92-1.45)
p-value	<0.001	<0.001	<0.001	<0.001	<0.001	0.02	0.01	0.10

Adjusted incidence rate ratios in patients with psoriasis affecting the skin only or also the joints compared with the reference cohort

Note that there were no significant differences in baseline characteristics between these two subgroups

Outcome	**Severe psoriasis (skin only) N=2014**				**Psoriatic arthritis N=607**				**Wald Chi-square test between overall estimates**
	Overall	**18-50 yr**	**51-70 yr**	**>70 yr**	**Overall**	**18-50 yr**	**51-70 yr**	**>70 yr**	**P-value**
All cause mortality									
RR (CI)	1.81 (1.60-	3.33 (2.30-	2.59 (2.15-	1.27 (1.05-	1.74 (1.32-	2.23 (1.06-	1.87 (1.27-	1.43 (0.88-	0.79

	2.05)	4.84)	3.12)	1.54)	2.30)	4.69)	2.74)	2.34)	
p-value	<0.001	<0.001	<0.001	<0.001	<0.001	0.03	0.001	0.15	
Cardiovascular death									
RR (CI)	1.56 (1.22-1.98)	3.58 (1.47-8.77)	2.18 (1.45-3.26)	1.25 (0.91-1.72)	1.84 (1.11-3.06)	1.87 (0.26-13.3)	2.68 (1.40-5.16)	1.19 (0.49-2.85)	0.55
p-value	<0.001	0.01	<0.001	0.16	0.02	0.53	0.003	0.7	
Composite end-point									
RR (CI)	1.56 (1.32-1.84)	1.77 (1.04-3.00)	1.93 (1.52-2.47)	1.24 (0.96-1.60)	1.79 (1.31-2.45)	3.27 (1.70-6.31)	1.79 (1.17-2.75)	1.20 (0.62-2.30)	0.44
p-value	<0.001	0.04	<0.001	0.1	<0.001	<0.001	0.01	0.59	

Sensitivity analyses

Note: results were not different if the diagnostic criteria for psoriasis were less restrictive (first Vit D prescription or first diagnosis); neither did exclusion of all patients with in- or out-patient hospital contacts up to 1 year prior to study start significantly alter the results. The results were also similar when using a control cohort matched for age and gender from the full population

Author's conclusion:

- Psoriasis is associated with increased risk of adverse cardiovascular events and all-cause mortality (independent of age, gender, comorbidity, concomitant medication and socio-economic status).
- Young age, severe skin affection and/or psoriatic arthritis carry the most risk.
- The risk was similar among those with severe skin psoriasis and PsA
- Patients with psoriasis may be candidates for early cardiovascular risk factor modification

H.5.10 ATRIAL FIBRILLATION AND ISCHAEMIC STROKE

Reference	Study type	Number of patients	Patient characteristics	Prognostic factors	Length of follow-up	Outcome measures	Source of funding
Ole Ahlehoff, Gunnar H. Gislason, Casper H. Jorgensen, Jesper Lindhardsen, Mette Charlot, Jonas B. Olesen, Steen Z. Abildstrom, Lone Skov, Christian Torp-Pedersen, and Peter Riis Hansen. Psoriasis and risk of atrial fibrillation and ischaemic stroke: a Danish Nationwide Cohort Study. European	**Observational:** retrospective Danish population-based cohort from 1997 to 2006 (data gathered prospectively). **Representative population sample:** yes – entire adult Danish population (reduced surveillance bias and avoids selection bias) **Prognostic factor adequately measured:** yes **Confounders adjusted for:** age, calendar year, concomitant medication, comorbidity, socioeconomic data, and gender. A calculation was also	N: 39,558 (0.9%) psoriasis cohort (36,765 mild and 2793 severe; 4,478,926 (99.1%) reference cohort. In a sensitivity analysis patients with psoriasis were matched for age and gender with 4 controls from the general populatio n	**Inclusion criteria:** age ≥18 years **Exclusion criteria:** prevalent psoriasis, AF and/or stroke **Note:** psoriasis patients were identified by claims of prescriptions for vitamin D analogues according to the comprehensive National Prescription registry and included on their second prescription (approximately 70% of psoriasis patients who require continuing topical treatment will receive vitamin D analogues)	Used data from the: Danish National Patient Register for mortality (records all hospital admissions, diagnoses, and invasive procedures according the World Health Organisations International Classification of Diseases (ICD), 8th-10th revision (WHO, 1987). Danish Registry of Medicinal Product Statistics (the National Prescription Registry), for medications (records all dispensed prescriptions since 1995) Central Population	Maximum follow-up 10 years in both cohorts. New-onset psoriasis **Note**: follow-up ended on December 31st 2006, emigration or death	First-time atrial fibrillation and ischemic stroke	Departme nt of Cardiolog y, Copenhag en University Hospital

Heart Journal, 2011. Ref ID: AHLEHOFF2011E	made that showed that the estimated magnitude of any unmeasured confounder that could nullify the results would have to be greater than the effects and distribution of any of the measured confounders (e.g. valvular heart disease or prior MI) **Attrition bias:** <4% **Outcomes adequately measured:** yes **Appropriate statistical analysis:** yes – Unadjusted event rates are summarized as events per 1000 person-years. The rate ratios (RRs) and 95% confidence interval (CI) were estimated by time-dependent Poisson regression models adjusted for age		Severe psoriasis was identified by hospitalisations (including out-patient visits) for psoriasis or psoriatic arthritis – this classification has been validated Diabetes was identified by first prescription of glucose-lowering drugs or insulin Note: unable to identify patients treated with topical corticosteroids alone and also unable to address the potential impact of various systemic treatment strategies Comorbidity at study entry was described by valvular heart disease and Charleson's Index (19 pre-specified diagnoses at study entry and up to 1 year previously) and modified	Register for mortality (records all deaths within 2 weeks). National Causes of Death Register for cause of death (records immediate, contributory, and underlying causes of death were recorded using ICD-10 codes) Individual-level linkage across all nationwide prospectively recorded registers was possible			

	calendar year, concomitant medication, comorbidity (according to Charlton Comorbidity Index), socioeconomic data (surrogate for obesity and smoking), and gender. Psoriasis status was included as a time-dependent variable, i.e., patients were only considered at risk from the time they complied with the inclusion criteria. Age and calendar year were also included as time-dependent variables. Comorbidity and concomitant medication were included as fixed variables obtained at baseline.		to ICD-10				

Baseline characteristics

Characteristic	**Controls** **n = 4,478,926**	**Mild psoriasis** **n = 36,765**	**Severe psoriasis** **n = 2793**
Age, years (SD)	43.7 (19.7)	46.1 (16.9)	46.0 (16.4)

Men (%)	51.0%	50.4%	48.8%
Mean follow-up time (years)	9.2	5.0	4.7
No. of person-years	41,345,205	184,624	13,261
Effect Size **Adjusted incidence rate ratios** in patients with psoriasis compared with the reference cohort			

Outcomes	**Mild psoriasis**			**Severe psoriasis**		
	Overall (n=36,765)	**18-50 yr**	**≥50 yr**	**Overall (n=2793)**	**18-50 yr**	**≥50 yr**
Atrial fibrillation						
RR (CI)	1.22 (1.14-1.30)	1.50 (1.21-1.86)	1.16 (1.08-1.24)	1.53 (1.23-1.91)	2.98 (1.80-4.92)	1.29 (1.01-1.65)
Attributable risk percentage	18.0%			34.6%		
Ischaemic stroke						
RR (CI)	1.25 (1.17-1.34)	1.97 (1.66-2.34)	1.13 (1.04-1.21)	1.65 (1.33-2.05)	2.80 (1.81-4.34)	1.34 (1.04-1.71)
Attributable risk percentage	20.0%			39.4%		

Sensitivity analyses

Note: results were not different if the diagnostic criteria for psoriasis were less restrictive (first Vit D prescription or first diagnosis); neither did exclusion of all patients with prior MI or censoring of patients at the time of surgical procedure, valvular heart disease or anti-thyroid treatment significantly alter the results. The results were also similar when using a control cohort matched for age and gender from the full population

Author's conclusion:

- Psoriasis is associated with increased risk of adverse cardiovascular events
- Young age, and severe psoriasis carry the most risk.

H.5.11 ALL-CAUSE MORTALITY AND CARDIOVASCULAR EVENTS (following first-time MI)

Reference	Study type	Number of patients	Patient characteristics	Prognostic factors	Length of follow-up	Outcome measures	Source of funding
O. Ahlehoff, G. H. Gislason, J. Lindhardsen, J. B. Olesen, M. Charlot, L. Skov, C. Torp-Pedersen, and P. R. Hansen.	**Observational:** retrospective Danish population-based cohort from 1997 to 2006 (data gathered prospectively). **Representative population sample:** yes (but indirect) – entire adult Danish population who experienced first-	N: 462 (0.9%) psoriasis cohort; 48935 (99.1%) reference cohort.	**Inclusion criteria:** first-time MI during 2002-2006; age ≥10 years **Exclusion criteria:** not stated	Used data from the: Danish National Patient Register for mortality (records all hospital admissions, diagnoses, and invasive procedures according the World	Short-term prognosis evaluated as 30-day outcome **Note**: follow-up ended on December 31st 2006, emigration, death or an event	Primary end-points: all-cause mortality and a composite of recurrent MI, stroke and cardiovascular death Invasive coronary	Department of Cardiology, Copenhagen University Hospital

Prognosis following first-time myocardial infarction in patients with psoriasis: A Danish nationwide cohort study. J.Intern.Med 270 (3):237-244, 2011. Ref ID: AHLEHOFF2011B	time MI during 2002-2006 (reduced surveillance bias and avoids selection bias) **Prognostic factor adequately measured:** yes **Confounders adjusted for:** age, gender, year of inclusion, concomitant medication, comorbidity and socioeconomic data **Attrition bias:** <2% **Outcomes adequately measured:** yes **Appropriate statistical analysis:** yes – Unadjusted event rates are summarized as events per 1000 person-years. The hazard ratios (HRs) and 95% confidence interval (CI)		**Note:** psoriasis patients were identified by claims of prescriptions for vitamin D analogues according to the comprehensive National Prescription registry and included on their second prescription (approximately 70% of psoriasis patients who require continuing topical treatment will receive vitamin D analogues) Note: unable to identify patients treated with topical corticosteroids alone and also unable to address the potential impact of various systemic treatment strategies Comorbidity at study entry was assessed according to the Ontario acute MI mortality prediction rules	Health Organisations International Classification of Diseases (ICD), 8th-10th revision (WHO, 1987). Danish Registry of Medicinal Product Statistics (the National Prescription Registry), for medications (records all dispensed prescriptions since 1995) Central Population Register for mortality (records all deaths within 2 weeks). National Causes of Death Register for cause of death (records immediate, contributory, and underlying causes of death were recorded using ICD-10 codes) Individual-level linkage across all nationwide		revascularisation was defined as percutaneous coronary intervention (PCI) or coronary artery bypass grafted (CABG)	

	were estimated by Cox regression models controlling for age, gender, year of inclusion, concomitant medication, comorbidity and socioeconomic data (surrogate for obesity and smoking).			prospectively recorded registers was possible			

Baseline characteristics

Characteristic	**Controls** **n = 48,935**	**Psoriasis** **n = 462**	**p-value for difference**
Age, years (SD)	70.6 (13.5)	69.5 (12.1)	0.06
Men (%)	61.3%	63.4%	0.35
Comorbidity (%)			
Shock	2.7	2.8	0.9
Pulmonary oedema	1.6	0.4	0.05
Cardiac dysrhythmia	13.9	13.4	0.78
Peripheral atherosclerosis	3.65	2.6	0.23
Congestive heart failure	15.4	16.5	0.52

Chronic obstructive pulmonary disease	7.8	8.9	0.41
Acute renal failure	1.7	1.5	0.75
Cancer	3.6	5.2	0.07
Treatments			
Platelet inhibitor	34.1	37.9	0.09
Beta-blocker	30.7	33.6	0.18
ACEI/ARB	**29.5**	**34.9**	**0.01**
Statin	**22.8**	**27.5**	**0.02**
Loop diuretic	22.9	25.5	0.18
Spironolactone	5.5	5.5	0.93
Glucose-lowering	11.8	13.2	0.35
Note: at baseline patients with psoriasis had a higher rate of ischemic heart disease other than MI (p=0.01)			

Effect Size

Adjusted hazard ratios in patients with psoriasis compared with the reference cohort

Outcomes	**Incidence rate per 1000**	**HR (95% CI)**
All cause mortality		
Complete follow-up	Psoriasis: 138.3 (114.1-167.7)	1.18 (0.97-1.43)

	Control: 119.4 (117.2-138.8)	
1 year follow-up	-	1.15 (0.95-1.40)
30-day follow-up	-	1.20 (0.99-1.46)
Sensitivity analysis – differences in post-MI treatment	-	1.15 (0.93-1.44)
Sensitivity analysis – less stringent classification of psoriasis	-	1.18 (1.03-1.34)
Composite outcome		
Complete follow-up	Psoriasis: 185.6 (155.8-221.0) Control: 149.7 (147.1-152.4)	1.26 (1.06-1.54)
1 year follow-up		1.24 (1.04-1.48)
30-day follow-up		1.24 (1.04-1.49)
Sensitivity analysis – differences in post-MI treatment		1.26 (1.03-1.53)
Sensitivity analysis – less stringent classification of psoriasis		1.25 (1.11-1.42)
Author's conclusion: • After first-time MI people with psoriasis have a significantly impaired prognosis		

H.5.12 CARDIOVASCULAR DISEASE

Reference	Study type	Number of patients	Patient characteristics	Prognostic factors	Length of follow-up	Outcome measures	Source of funding
N. N. Mehta, Y. Yu, R. Pinnelas, P. Krishnamoorthy, D. B. Shin, A. B. Troxel, and J. M. Gelfand. Attributable risk estimate of severe psoriasis on major cardiovascular events. Am.J.Med. 124 (8):775, 2011. Ref ID: METHA2011	**Observational:** cohort study from 1987-2002. **Representative population sample:** yes GPRD used. **Prognostic factor adequately measured:** yes **Confounders adjusted for:** cardiovascular risk factors including age, sex, hypertension, diabetes, hyperlipidaemia, and smoking (current, former, never). BMI calculated from the data available in medical record.	N: severe psoriasis group n=3603; control group n=14330)	**Inclusion criteria:** 18 years or older at index date and had at least 1 day of observation time; severe psoriasis patients their index date was first date on or after the first diagnosis of psoriasis in which they received a code for treatment consistent with severe disease. Patients without psoriasis the index date was date of medical record entry within 60 days of the psoriasis index date. Up to 4 unexposed subjects were randomly selected, matched on practice, date of registration in practice and psoriasis index date. **Exclusion criteria:** history of cardiovascular disease, defined as ischemic heart disease, MI, TIA, stroke or peripheral arterial disease on or before the	General Practice Research Database. Severe psoriasis defined as code of psoriasis and history of systemic therapy consistent with severe psoriasis (e.g., UVB, PUVA, MTX, azathioprine, CSA, retinoids, hydroxyurea and myconphenolate mofetil	Mean 3.4 ± 2.8 years for non-psoriasis and 3.4 ± 2.7 years for psoriasis group. For psoriasis cohort follow-up started at the latest date when they could be defined as having severe psoriasis For all groups follow-up ended at death, event, transfer out of practice or end of 'up-to-standard' status	First recorded major adverse cardiac event (nonfatal MI, nonfatal stroke or death due to CV cause)	National Psoriasis Foundation Award, Doris Duke Charitable Foundation grant, Psoriasis Research Foundation in honour of Herman Beerman and grant from the National Institute of Arthritis, Musculoskeletal, and Skin Diseases and the Heart Lung Blood Institute.

	Attrition bias: not reported **Outcomes adequately measured:** yes **Appropriate statistical analysis:** yes – age and sex adjusted Cox proportional hazards model		start date				

Patient characteristics:

Characteristics	**Unexposed group(n=14330)**	**Psoriasis group (n=3603)**	**P values**
Sex (male)	5783 (40.4%)	1750 (48.6%)	P<0.001
Age (year)[1]		P<0.001	
Mean (SD)	49.7 (19.3)	52.2(16.7)	
Median (IQR)	48 (33-65)	52 (39-66)	
Diabetes mellitus	737 (5.1%)	270 (7.5%)	P<0.001
History of MI	375 (2.6%)	116 (3.2%)	P=0.052
History of stroke	268 (1.9%)	89 (2.5%)	P=0.023
History of TIA	243 (1.7%)	68 (1.9%)	P=0.432

Hyperlipidaemia	842 (5.9%)	250 (6.9%)	P=0.019
Hypertension	3049 (21.3%)	858 (23.8%)	P=0.001
Smoking			
Never	10465 (73%)	2488 (69.1%)	
Current	755 (5.3%)	241 (6.7%)	
Former	3110 (21.7%)	874 (24.3%)	P<0.001
BMI[2]			
<25	5057 (51.2%)	1025 (42.1%)	
>/=25 and <30	3291 (33.3%)	860 (35.4%)	
>/=30	1522 (15.4%)	548 (22.5%)	P<0.001
Reason for end of study			
Death	790 (5.5%)	297 (8.2%)	
End of UTS	11247 (78.5%)	2860 (79.4%)	
Transfer out	2293 (16%)	446 (12.4%)	P<0.001

MI, myocardial infarction; TIA, transient ischaemic attach; BMI, body mass index; SD, standard deviation; IQR, interquartile range.

[1] Wilcoxon test.

[2] Data for BMI were available for 69% of the patients.

Effect size:

Variable	Unexposed	Psoriasis
Mean follow-up, years (SD)	3.4 (2.8)	3.4 (2.7)
Number of person years	48661.8	12346.3
Number of MACEs	148 (2.9%)	384 (4.5%)
Incidence per 1000 person-years (95% CI)	11.6 (10.7-12.6)	16.4 (14.3-18.9)

Adjusted Cox proportional hazard regression models of the risk of MACE in severe psoriasis compared with unexposed patients (plus sensitivity analyses)

Covariate	N Psoriasis	N controls	Model hazard ratio (95% CI)	Attributable risk for 10-year incidence of MACE
Primary analysis	**14330**	**3603**	**1.53 (1.26-1.85)**	**6.2%**
Inclusion of patients with at least 1 GP visit per year on average	13643	3563	1.50 (1.23-1.81)	-
Primary model with exclusion of methotrexate	13289	1358	1.86 (1.44-2.41)	-
Primary model with exclusion of oral retinoids or ciclosporine	13253	2653	1.42 (1.14-1.77)	-

Primary model restricted to patients who received oral retinoids	13253	303	1.56 (1.05-2.32)	-
Primary model with exclusion of psoriatic arthritis	13289	1156	1.44 (1.16-1.78)	-
Inclusion of patients with at least 6 months of person time	11832	2963	1.60 (1.32-1.95)	-
Primary model with BMI included	9870	2433	1.71 (1.32-2.18)	-
Primary model without BMI included in those who had BMI measured[1]	9870	2433	1.70 (1.32-2.17)	-

[1] BMI is included in n=12303 or 69% of patients.

Author's conclusion:

- Severe psoriasis confers an additional 6.2% absolute risk of a 10-year rate of major adverse cardiac events compared with the general population.
- This potentially has important therapeutic implications for cardiovascular risk stratification and prevention in patients with severe psoriasis.

H.5.13 CARDIOVASCULAR DISEASE

Reference	Study type	Number of patients	Patient characteristics	Prognostic factors	Length of follow-up	Outcome measures	Source of funding
Mehta (2010) Patients with severe psoriasis	**Observational:** cohort study from 1987-2002. **Representative**	N: severe psoriasis group n=3603; control group	**Inclusion criteria:** 18 years or older at index date and had at least 1 day of observation time; severe psoriasis patients their index date was first	General Practice Research Database. Severe psoriasis was defined as those with a diagnostic	Mean 3.4 +/- 2.8 years for non-psoriasis and 3.4 +/- 2.7 years for psoriasis group.	Cardiovascular death defined as diagnoses consistent with MI,	Grant to the Trustees of the University of

are at increased risk of cardiovascular mortality: cohort study using the General Practice Research Database Ref ID: METHA2010	**population sample:** yes GPRD used. **Prognostic factor adequately measured:** yes **Confounders adjusted for:** cardiovascular risk factors including age, sex, hypertension, diabetes, hyperlipidaemia, and smoking (current, former, never). BMI calculated from the data available in medical record. **Attrition bias:** not reported **Outcomes adequately measured:** yes **Appropriate statistical analysis:** yes	n=14330)	date on or after the first diagnosis of psoriasis in which they received a code for treatment consistent with severe disease. Patients without psoriasis the index date was date of medical record entry within 60 days of the psoriasis index date. Up to 4 unexposed subjects were randomly selected, matched on practice, date of registration in practice and psoriasis index date. **Exclusion criteria:** not reported.	code of psoriasis and history of systemic therapy consistent with severe psoriasis.		stroke, peripheral vascular disease, arrhythmia or left ventricular thrombus on or very close to the entry of death.	Pennsylvania from Centocor the Psoriasis Research Foundation in honour of Herman Beerman and grant K23AR0511125 from the National Institute of Arthritis, Musculoskeletal, and Skin Diseases and grant RO1HL089744 from the Heart Lung Blood Institute.

	Blinding: For every death the cause was determined by review of medical codes on or very near date of death by 2 physician reviewers blinded to exposure statues.						

Patient characteristics:

Characteristics	Unexposed group(n=14330)	Psoriasis group (n=3603)	P values
Sex (male)	5783 (40.4%)	1750 (48.6%)	P<0.001
Age (year)[1]		P<0.001	
Mean (SD)	49.7 (19.3)	52.2(16.7)	
Median (IQR)	48 (33-65)	52 (39-66)	
Diabetes mellitus	737 (5.1%)	270 (7.5%)	P<0.001
History of MI	375 (2.6%)	116 (3.2%)	P=0.052
History of stroke	268 (1.9%)	89 (2.5%)	P=0.023
History of TIA	243 (1.7%)	68 (1.9%)	P=0.432
Hyperlipidaemia	842 (5.9%)	250 (6.9%)	P=0.019
Hypertension	3049 (21.3%)	858 (23.8%)	P=0.001

Smoking			
Never	**10465 (73%)**	**2488 (69.1%)**	
Current	**755 (5.3%)**	**241 (6.7%)**	
Former	**3110 (21.7%)**	**874 (24.3%)**	**P<0.001**
BMI[2]			
<25	**5057 (51.2%)**	**1025 (42.1%)**	
>/=25 and <30	**3291 (33.3%)**	**860 (35.4%)**	
>/=30	**1522 (15.4%)**	**548 (22.5%)**	**P<0.001**
Reason for end of study			
Death	**790 (5.5%)**	**297 (8.2%)**	
End of UTS	**11247 (78.5%)**	**2860 (79.4%)**	
Transfer out	**2293 (16%)**	**446 (12.4%)**	**P<0.001**

MI, myocardial infarction; TIA, transient ischaemic attach; BMI, body mass index; SD, standard deviation; IQR, interquartile range.

[1] Wilcoxon test.

[2] Data for BMI were available for 69% of the patients.

Effect size:

Variable	**Unexposed**	**Psoriasis**
Follow-up time (year)		

Mean (SD)	3.4 (2.8)	3.4 (2.7)
Median (IQR)	2.6 (1.2-5.0)	2.7 (1.2-5.1)
Number of person years	48661.8	12346.3
Number of CBD mortality cases	301 (2.1%)*	108 (3%)*
Incidence per 1000 person-years (95% CI)	6.19 (5.51, 6.92)	8.75 (7.18, 10.56)

*p=0.002

Unadjusted and adjusted Cox proportional hazard regression models of the risk of cardiovascular disease mortality in severe psoriasis compared with unexposed patients

Covariate	**Model hazard ratio (95% CI)**
	Severe psoriasis
Unadjusted analysis – psoriasis	1.42 (1.14, 1.76)
Adjusted for age and sex	
Psoriasis	1.57 (1.26, 1.96)
Age per year	1.10 (1.09, 1.11)
Sex (male)	1.61 (1.32, 1.95)

Primary model (adjusted for major cardiovascular risk factors)*	
Psoriasis	1.57 (1.26, 1.96)
Age per year	1.10 (1.09, 1.11)
Sex (male)	1.54 (1.27, 1.88)
Hypertension	1.25 (1.01, 1.53)
Hyperlipidaemia	0.75 (0.42, 1.34)
HX of diabetes	2.25 (1.68, 3.02)
Smoking (current vs never)	1.33 (0.95, 1.86)
Smoking (former vs never)	1.31 (0.98, 1.74)

Interaction term for sex was not statistically significant (p=0.99), but was for age (p=0.07).

*Hypertension, hyperlipidaemia, diabetes, and smoking status.

Sensitivity analysis hazard ratio point estimates

Covariate	**N Psoriasis**	**N controls**	**Model hazard ratio (95% CI)**
Primary analysis	3603	14330	1.57 (1.26, 1.96)
Inclusion of patients with at least 1 GP visit per year on average	3563	13643	1.54 (1.23, 1.93)
Primary model excluding patients with history of myocardial infarction, stroke, and/or TIA or	3310	13335	1.56 (1.20, 2.04)

atherosclerotic disease			
Primary model with exclusion of methotrexate	1489	14330	2.04 (1.51, 2.74)
Primary model with exclusion of oral retinoids or ciclosporine	2914	14330	1.51 (1.18, 1.94)
Primary model restricted to patients who received oral retinoids	333	14663	1.59 (0.97, 2.60)
Primary model with exclusion of psoriatic arthritis	2375	14330	1.52 (1.19, 1.94)
Primary model with BMI included	2433	9870	1.66 (1.19, 2.30)
Primary model without BMI included in those who had BMI measured[1]	2433	9870	1.64 (1.18, 2.27)
Inclusion of patients with at least 6 months of person time	3246	12766	1.66 (1.30, 2.11)
Primary model after matching cases to controls by age (+/-5 years) and sex[2]	3603	7205	1.59 (1.23, 2.04)

[1] BMI is included in n=12303 or 69% of patients.

[2] Two-to-one matching using original controls.

Author's conclusion: patients with severe psoriasis have an increased risk of CV mortality that is independent of traditional CV risk factors. Additional studies are needed to determine the mechanism of this association and the impact that control of psoriasis has on CV risk.

H.5.14 CARDIOVASCULAR DISEASE

Reference	Study type	Number of patients	Patient characteristics	Prognostic factors	Length of follow-up	Outcome measures	Source of funding
Mallbris (2004) Increased risk for cardiovascular mortality in psoriasis inpatients but not outpatients Ref ID: MALLBRIS 2004	**Observational:** retrospective cohort study 1964-1995. **Representative population sample:** yes- used the Swedish inpatient registry. **Prognostic factor adequately measured:** yes **Confounders adjusted for:** yes **Attrition bias:** not reported **Outcomes adequately**	N: 8991 in-patients; 19,757 out-patients.	**Inclusion criteria:** all Swedish residents recorded in the Inpatient Registry with a discharge diagnosis of psoriasis (ICD-7 codes 70600 and 70609; ICD-8 codes 69600 and 69610; code ICD-9 codes 696A and 696B), during January 1964 to December 1995; Only in-patients treated at dermatological wards with psoriasis as the main diagnosis. **Exclusion criteria:** diagnosis of cardiovascular disease prior to index time. Notes: did not exclude members who had a history of hospitalisation. Date of entry into cohort.	Swedish inpatient registry used with ICD codes. Date of entry in cohort was set to 1st January 1987, the year the register was established. Inpatient cohort was followed up through the death registry and registry of population and population changes	**15 years+** **Note**: followed-up to the date of death, emigration or December 31st 1995, whichever occurred first. The outpatient cohort was followed with censoring at death, emigration or December 31st 1998.	Risk of mortality from ISH, cerebrovascular disease and pulmonary embolism	Swedish Heart Lung Foundation, the Swedish Psoriasis Association, the Swedish Medical Research Council, the Welander-Finsen Foundation and Karolinska Institutet.

	measured: not multivariable/regression **Appropriate statistical analysis:** yes comparisons within the cohort were performed with a Cox regression.						

Patient characteristics of the cohort of patients

hospitalised with psoriasis as main diagnosis:

Variables	**Number (%)**
Total	**8991 (100%)**
Sex – male	**4708 (52%)**
Age at first hospital admission	
0-19	**927 (10.3%)**
20-39	**2362 (26.3%)**
40-59	**3069 (34.1%)**
60+	**2633 (29.3%)**
Years of follow-up	
0-1	**216 (2.4%)**

1-5	**1398 (15.6%)**
5-10	**1981 (22%)**
10-15	**1927 (21.4%)**
15+	**3469 (38.6%)**
Calendar year	
64-74	**3145 (35%)**
75-84	**3398 (37.8%)**
85-95	**2448 (27.2%)**

Effect size:

SMRs and 95%CIs for the association between at least one hospitalisation for psoriasis and cardiovascular death

Variables	**Observed number of deaths**	**Expected number of deaths**	**SMR***	**95% CI**	**p-value trend**
Total	1529	1007	1.52	1.44-1.60	
Age at first hospital admission					
0-19	0	0.99	0.00	0.00-3.74	
20-39	46	18	2.62	1.91-3.49	
40-59	453	237	1.91	1.74-2.09	

60+	1030	750	1.37	1.29-1.46	<0.001
Years of follow up					
0-1	90	66	1.36	1.09-1.67	
1-5	349	260	1.34	1.21-1.49	
5-10	431	281	1.53	1.39-1.68	
10-15	304	192	1.58	1.41-1.77	
15+	355	207	1.71	1.54-1.90	<0.001
No. of hospital admissions					
One time	1529	1007	1.52	1.44-1.60	
Two times	851	501	1.70	1.58-1.81	
Three times or more	610	334	1.82	1.68-1.98	<0.001
Calendar year					
64-74	733	471	1.56	1.45-1.67	
75-84	590	403	1.46	1.35-1.59	
85-95	206	132	1.56	1.35-1.79	0.67

***The relative risk was calculated by SMRs and 95% CIs.**

SMRs and 95% CIs for the association between at least one hospitalisation for psoriasis and risk for death from different cardiovascular diseases

	Ischemic heart disease		**Cerbrovascular disease**		**Pulmonary embolism**	
Variable	**SMR**	**95% CI**	**SMR**	**95% CI**	**SMR**	**95% CI**

Total	1.86	1.76-1.96	1.63	1.47-1.80	1.64	1.12-2.31
Sex – male	1.89	1.76-2.03	1.74	1.49-2.01	1.43	0.76-2.45
Sex – female	1.80	1.65-1.97	1.54	1.33-1.77	1.82	1.10-2.84
Age at first hospitalisation						
20-39	2.91	1.98-4.14	1.85	0.68-4.02	5.18	0.63-18.7
40-59	2.22	2.00-2.46	1.92	1.52-2.40	2.24	1.07-4.12
60+	1.71	1.60-1.83	1.56	1.38-1.75	1.36	0.83-2.11

Stratified analysis of the joint effect of number of admissions and age at first admission

	Number of admissions				
	1	**2**		**3 or more**	
Variables	**Reference**	**HR**	**95% CI**	**HR**	**95% CI**
Age at first hospital admission					
0-39	1.00	2.71	1.15-6.41	3.13	1.55-6.32
40-59	1.00	1.11	0.84-1.47	1.43	1.16-1.77
60+	1.00	1.18	0.99-1.42	1.35	1.17-1.57

Observed and expected numbers of deaths from cardiovascular disease in a cohort representing outpatients treated for psoriasis with SMRs and 95% CIs

Variables	Number (%)	Obs	Exp	SMR	95% CI
Total	19,757	1302	1390	0.94	0.89-0.99
Age at start of follow-up					
0-19	758 (3.8%)	0	0.18	0.00	0.00-20.3
20-39	5298 (26.8%)	7	11	0.65	0.26-1.34
40-59	7732 (39.1%)	161	161	1.00	0.85-1.16
60+	5969 (30.2%)	1134	1218	0.93	0.88-0.99
Years of follow-up					
0-1	199	98	108	0.91	0.74-1.11
1-5	923	447	465	0.96	0.87-1.05
5-10	1307	616	667	0.92	0.85-1.00
10-15	17,328	141	150	0.94	0.79-1.11

Author's conclusion: A diagnosis of psoriasis per se does not appear to increase the risk for cardiovascular mortality. Severe psoriasis (repeated admissions, and early age at first admission) is associated with increased risk for cardiovascular risk.

H.5.15 CARDIOVASCULAR DISEASE – systemic therapy vs phototherapy for psoriasis

Reference	Study type	Number of patients	Patient characteristics	Prognostic factors	Length of follow-up	Outcome measures	Source of funding
H. Maradit-Kremers, M. Icen, F. C. Ernste, R. A. Dierkhising, and M. T. McEvoy. Disease severity and therapy as predictors of cardiovascular risk in psoriasis: a population-based cohort study. J.Eur.Acad. Dermatol.Venereol. 26 (3):336-343, 2012. Ref ID: MARADIT-KREMERS 2012	**Observational:** population-based cohort study from 1998-2007 Residents of Olmsted County – data from Rochester Epidemiology Project. **Representative population sample:** no – small sample from one US state only **Prognostic factor adequately measured:** yes – adequate record review **Confounders adjusted for:** Age and sex plus cardiovascular risk factors (obesity,	N 1905 with psoriasis (660 incident psoriasis and 1245 prevalent psoriasis)	**Inclusion criteria:** open cohort of all patients with psoriasis under observation between 1998 and 2007 **Exclusion criteria:** none reported. Baseline characteristics: Mean age: 48.8 ± 17.5 Male (%): 48% PsA: 96 (5%) – an additional 95 were diagnosed over the follow-up (191 with PsA in total)	Data from Rochester Epidemiology Project Psoriasis and PsA diagnoses validated through medical record review (confirmatory dermatologist diagnosis, lesion description or skin biopsy; CASPAR for PsA)	Mean: 6.3 ± 3.5 years	Composite score of cardiovascular events (MI, revascularisation, cerebrocascular events, heart failure and cardiovascular death)	National Institute of Aging and Amgen

	dyslipidaemia, hypertension, diabetes, total cholesterol, HDL cholesterol, LDL cholesterol, blood pressure) **Attrition bias:** not reported, but half did not have measurements of lipid data at baseline **Outcomes adequately measured:** yes **Appropriate statistical analysis:** Cox adjusted models						

Patient characteristics:

	Prevalence cohort (n=1905)
History of CVD (heart failure, stroke or MI/revascularisation)	12%

Hypertension	34%
Diabetes	13%
Dyslipidaemia	33%
Obesity	25%
History of treatment before baseline	
Phototherapy*	21 (1%)
Any systemic treatment*	82 (4%)

*Note: 157 additional patients received phototherapy (total 178) and 191 systemic therapy (total 273; 86 MTX; 73 biologics) during follow-up.

Effect size: excluding those with a history of CVD prior to entry (n=221)

Adjusted hazard ratio (prognostic factors vs not having the prognostic factor in the psoriasis cohort)

Prognostic factor	**Cox model HR (95% CI)**	
	Age and gender adjusted	**Multivariate adjusted**
Phototherapy	3.76 (2.45-5.77)	1.28 (0.55-2.98)
Systemic therapy	2.17 (1.50-3.13)	0.93 (0.49-1.75)

Author's conclusion: Strong associations with phototherapy and systemic therapy suggest that the cardiovascular risk in psoriasis is confined to patients with severe disease. However, the small numbers treated with systemic therapy make it difficult to draw conclusions about the impact of this intervention on CVD risk

H.5.16 DIABETES (type 2)

Reference	Study type	Number of patients	Patient characteristics	Prognostic factors	Length of follow-up	Outcome measures	Source of funding
Wenqing Li, Jiali Han, Frank B. Hu, Gary C. Curhan, and Abrar A. Qureshi. Psoriasis and Risk of Type 2 Diabetes among Women and Men in the United States: A Population-Based Cohort Study. J.Invest.Dermatol., 2011. Ref ID: LI2011	**Observational:** retrospective-prospective cohort study **Representative population sample:** no – predominantly women and all HCPs **Prognostic factor adequately measured:** yes – questionnaire report but conformed by validated tool **Confounders adjusted for:** time-varying covariates updated during follow-up: age, smoking status (never, current, past), body mass index, race, family history of diabetes,	Total n: 184395; n=3074 reporting psoriasis.	**Inclusion criteria:** participants from Nurses Health Study (NHS), NHSII and Health Professionals Follow-up Study (HPFS) **Exclusion criteria:** not stated	Psoriasis determined by self-report of diagnosis and conformed by further self-completed questionnaire (Psoriasis Screening Tool Questionnaire – 99% sensitivity; 94% specificity)	Unclear	T2 diabetes - Identified by self-report of physician diagnosed T2D and confirmed in those reporting diabetes by a further questionnaire (had to meet at least one of the criteria of the National Diabetes Data Group)	None stated

	hypertension, hypercholesterolemia, current aspirin use, multivitamin use, menopausal status, post-menopausal hormone use alcohol intake and physical activity **Attrition bias:** not reported **Outcomes adequately measured:** yes – questionnaire report but conformed by validated tool **Appropriate statistical analysis:** yes, Cox proportional hazards modelling stratified by age and 2-yr follow-up interval to estimate the age-adjusted and multivariate RRs of incident diabetes						

Baseline characteristics						
	NHS		**NHS II**		**HPFS**	
	No psoriasis (n=62,738)	**Psoriasis (n=1189)**	**No psoriasis (n=94,437)**	**Psoriasis (n=1342)**	**No psoriasis (n=24,146)**	**Psoriasis (n=543)**
Mean age, years (SD)	60.9 (6.8)	61.2 (6.8)	36.2 (4.6)	39.7 (4.6)	50.5 (8.0)	50.8 (8.1)
Race, white (%)	95.7	96.6	95.3	96.7	96.0	95.8
BMI, kg/m^2 (SD)	26.2 (4.9)	27.1 (5.4)	24.5 (5.0)	25.4 (5.6)	24.8 (4.4)	25.2 (4.3)
Alcohol intake, g/day	4.6 (8.6)	5.0 (9.9)	2.9 (5.7)	2.9 (5.4)	11.1 (14.5)	11.9 (16.1)
Physical activity, metabolic equivalent hours per week	18.6 (22.4)	16.4 (19.1)	18.8 (26.2)	17.8 (26.2)	22.2 (29.4)	24.4 (34.7)
Current smoking (%)	10.6	14.5	11.5	15.2	6.9	9.2
Family history of diabetes (%)	26.5	28.0	16.3	18.9	14.0	14.7
Postmenopausal hormone (%)	59.0	60.9	2.6	3.7	NA	NA
Hypertension (%)	26.5	29.2	3.1	4.6	15.6	17.9
Hypercholesterolemia (%)	34.6	36.3	8.9	13.1	10.7	11.8
Aspirin use (%)	51.2	51.3	11.1	12.9	26.2	25.4

Multivitamin use (%)	49.2	46.7	38.7	40.2	40.8	41.4

Note that people with psoriasis were more likely to have higher BMI and be smokers

Effect size:

Multivariate relative risks (RRs) for the development of diabetes among people with psoriasis

Study	**Diabetes cases**	**Person-years**	**Multivariate RR[1]**	**Multivariate RR[2]**
NHS	4280	735664		
No psoriasis	4171	720650	1.00	1.00
Psoriasis	109	15014	1.14 (0.95-1.38)	1.01 (0.83-1.22)
NHSII	3968	1496867		
No psoriasis	3835	1470709	1.00	1.00
Psoriasis	133	26159	1.50 (1.26-1.78)	1.25 (1.05-1.49)
HPFS	1690	468427		
No psoriasis	1638	455263	1.00	1.00
Psoriasis	52	13163	0.94 (0.71-1.25)	0.91 (0.69-1.20)
NHS/NHSII/HPFS (pooled – no heterogeneity) – age <60 years during follow-up				
No psoriasis	5190	1881861	-	1.00
Psoriasis	179	35751	-	1.26 (1.08-1.46)

[1]Simultaneously adjusted for age, smoking status (never, current [1-14, 15-24 or ≥25 per day], past), alcohol intake (no, <4.9, 5.0-14.9 or ≥15 g/day) and physical activity in quintiles of metabolic equivalent hours per week, race (Caucasian, Asian, Hispanic or African American, family history of diabetes, hypercholesterolemia, current aspirin use, multivitamin use and post-menopausal hormone use (women only: pre-menopause, never, current or past users).

[2]Simultaneously adjusted for all variables above plus body mass index.

Sensitivity analysis: Multivariate relative risks (RRs) for the development of diabetes among people with *confirmed cases* of psoriasis

Study	Diabetes cases	Person-years	Multivariate RR[1]
NHS			
No psoriasis	4198	725208	1.00
Psoriasis	82	10456	1.14 (0.92-1.42)
NHSII			
No psoriasis	3891	1483100	1.00
Psoriasis	77	13768	1.46 (1.16-1.83)

[1]Simultaneously adjusted for age, BMI, smoking status (never, current [1-14, 15-24 or ≥25 per day], past), alcohol intake (no, <4.9, 5.0-14.9 or ≥15 g/day) and physical activity in quintiles of metabolic equivalent hours per week, race (Caucasian, Asian, Hispanic or African American, family history of diabetes, hypercholesterolemia, current aspirin use, multivitamin use and post-menopausal hormone use (women only: pre-menopause, never, current or past users).

Author's conclusion: Individuals developing psoriasis at a younger age are at significantly elevated risk of T2D

H.5.17 DIABETES AND HYPERTENSION

Reference	Study type	Number of patients	Patient characteristics	Prognostic factors	Length of follow-up	Outcome measures	Source of funding
Quereshi (2009) Psoriasis and the risk of diabetes and hypertension: a prospective study of US female nurses Ref ID: QURESHI2009	**Observational:** prospective cohort study from 1991 to 2005. **Representative population sample:** yes **Prognostic factor adequately measured:** yes **Confounders adjusted for:** Simultaneously adjusted for age, smoking status (never, current, past), body mass index, alcohol intake and physical activity in quintiles of metabolic equivalent hours per week.	Total n: 78061; n=1813 reporting psoriasis.	**Inclusion criteria:** registered nurses from 15 states in the US between ages of 25 and 42 when they completed and returned baseline questionnaire in 1989. **Exclusion criteria:** women with diabetes or hypertension at baseline.	The nurses health study (NHS) II longitudinal study. Longitudinal study of female registered nurses in 15 states in the US.	14 years. Baseline questionnaire in 1989. Followed up from 1991 to 2005 (biennial questionnaires). **Note**: started in 1991 as this was first year that they had corresponding information on smoking and alcohol status.	Diabetes and hypertension.	Partly supported by grants K07CA10897/NCI and CA050385/NCI from the National Cancer institute. One author has been a consultant and speaker for Abbott, Amgen and Genentech.

	Attrition bias: not reported **Outcomes adequately measured:** yes **Appropriate statistical analysis:** yes, Cox proportion hazards modelling to estimate the age-adjusted and multivariate RRs of incident diabetes and hypertension.						

Baseline characteristics of women who self-reported a diagnosis of psoriasis between 1991 and 2005

Characteristic	**Psoriasis no (n=76248)**	**Psoriasis yes (n=1813)**
Mean age, years	36.2	36.4
Mean BMI	23.6	24.4
Smoking status (%)		
Never	66	56
Current	22	26

Past	11	18
Mean alcohol intake, g/wk	3.2	3.7
Mean physical activity, METS/wk	21	20

BMI, body mass index; METS, metabolic equivalent hours

Effect size:

Age-adjusted and multivariate relative risks (RRs) for the development of diabetes and hypertension among women with psoriasis

	Psoriasis no	**Psoriasis yes (95% CI)**
Diabetes		
No. of cases[1]	1500	60
Person-years, millions	1.0	1.0
Age-adjusted RR	1.00	2.08 (1.60-2.69)
Multivariate RR[2]	1.00	1.63 (1.25-2.12)
Hypertension		
No. of cases[1]	15338	386
Person-years, millions	0.99	0.99

Age-adjusted RR	1.00	1.32 (1.19-1.45)
Multivariate RR[2]	1.00	1.17 (1.06-1.30)

[1]Excluding any individuals with concomitant diabetes and hypertension.

[2]Simultaneously adjusted for age, smoking status (never, current, past), body mass index, alcohol intake and physical activity in quintiles of metabolic equivalent hours per week.

To assess for any possible effect from age, BMI and smoking status multivariate models found the association between psoriasis and risk was not modified by BMI for diabetes (p=0.65) or hypertension (p=0.07). There was also no effect modification by smoking status for diabetes of hypertension (p>/=0.50). Additional analyses to limit population to those women who had at least 1 physical exam during follow-up to control for confounder that women with psoriasis may be more likely to see a physician and therefore diagnosed with diabetes or hypertension. There was no material change in the results.

Author's conclusion: Psoriasis was independently associated with an increased risk of diabetes and hypertension.

H.5.18 ALCOHOL-RELATED DISEASES

Reference	Study type	Number of patients	Patient characteristics	Prognostic factors	Length of follow-up	Outcome measures	Source of funding
Poikolainen (1999) Excess	**Observational: cohort study from 1973 to 1984.**	N: 3132 men and 2555 women.	**Inclusion criteria:** Identified all records of patients with psoriasis as	Used the Hospital discharge register which was then	**Mean length follow-up was almost 14 years.**	Date and underlying cause of death	Not reported.

mortality related to alcohol and smoking among hospital-treated patients with psoriasis Ref ID: POIKOLAINAN1999	**Representative population sample:** yes **Prognostic factor adequately measured:** yes **Confounders adjusted for:**. **Attrition bias:** not reported **Outcomes adequately measured:** yes **Appropriate statistical analysis:** not multivariable/regression **Notes:** Patients were hospitalised at least once so most were		main diagnosis in Hospital Discharge Register from January 1st 1973 to December 31st 1984 in Finland **Exclusion criteria:** not reported.	linked with the Population Central Register using personal identification codes. Underlying causes of death were based on official death certificates, coded to the Finnish modification of the International Classification of Diseases, Eighth and Ninth Revision. The causes selected related to alcohol only, smoking only and alcohol and smoking.	**Length of study period was 22 years.** **Note**: follow-up started from month following earliest hospital discharge and follow-up ended on the date of emigration or death or December 31st 1995, whichever was first.	(standard mortality ratios).	

	likely to have severe psoriasis than outpatients.						

Effect size: 1918 observed deaths, whereas 1211 deaths were expected based on the national mortality rates.

Major causes of death among patients with psoriasis*

	Men		Women	
Cause of death	No. of observed deaths	SMR (95% CI)	No. of observed deaths	SMR (95% CI)
Alcohol-related	202	2.14 (1.84-2.44)	89	1.47 (1.16-1.77)
Directly**	94	4.46 (3.60-5.45)	13	5.60 (2.98-8.65)
Indirectly	108	1.47 (1.20-1.75)	76	1.31 (1.03-1.63)
Smoking-related	594	1.44 (1.33-1.56)	400	1.61 (1.45-1.77)
Both	13	1.92 (1.02-3.29)	8	2.52 (1.09-4.96)
Other	330	1.72 (1.54-1.91)	282	1.45 (1.28-1.62)
All	1139	1.62 (1.52-1.71)	779	1.54 (1.43-1.64)

*SMR indicates standardised mortality ratio; CI, confidence interval.

** Includes underlying causes with direct reference to alcohol in the diagnosis, ie alcohol-related psychosis, alcoholism, alcoholic polyneuropathy, alcoholic cardiomyopathy, alcoholic gastritis, alcoholic fatty liver, acute alcoholic hepatitis, alcoholic cirrhosis of the liver, unspecified alcoholic liver damage, alcoholic epilepsy, alcoholic pancreatitis, fetal alcohol syndrome, alcoholic withdrawal syndrome of the newborn, alcohol poisoning, and pregnancy, childbirth, or puerperium complicated by alcoholism.

Alcohol-and Tobacco-related causes of death among patients with psoriasis*

	Men		Women	
Cause of death	**No. of observed deaths**	**SMR (95%CI)**	**No. of observed deaths**	**SMR (95% CI)**
Alcohol-related				
Liver cancer	9	2.86 (1.31-5.42)	1	0.50 (0.01-2.79)
Female breast cancer	0	-	16	1.14 (0.65-1.85)
Alcohol psychosis	5	8.91 (2.89-20.70)	0	0 (0.00-71.70)
Alcohol dependence	9	3.79 (1.73-7.19)	1	5.23 (0.13-29.20)
Hypertension	10	2.23 (1.07-4.09)	10	1.33 (0.64-2.45)
Hemorrhagic stroke	24	1.35 (0.87-2.01)	16	1.01 (0.57-1.63)
Liver disease	61	6.98 (5.34-8.96)	13	5.06 (2.70-8.65)
Alcoholic liver cirrhosis	20	2.88 (1.76-4.44)	6	5.77 (2.12-12.50)
Acute pancreatitis	0	0	0	0 (0.00-5.86)
Chronic pancreatitis	0	0	0	0 (0.00-40.70)
Motor traffic injuries	12	1.40 (0.73-2.45)	4	1.27 (0.35-3.24)
Alcohol poisoning	14	1.86 (1.02-3.12)	1	1.37 (0.03-7.61)
Accidental falls	15	1.57 (0.88-2.58)	14	1.75 (0.96-2.93)

Drowning	1	0.33 (0.01-1.86)	1	2.98 (0.08-16.60)
Machine injuries	1	0.90 (0.02-5.00)	0	0 (0.00-38.40)
Suicide	37	1.56 (1.10-2.15)	9	1.87 (0.86-3.55)
Assault	5	2.15 (0.70-5.01)	3	4.54 (0.94-13.30)
Smoking-related				
Pancreatic cancer	10	1.13 (0.54-2.08)	15	2.03 (1.14-3.34)
Lung cancer	79	1.48 (1.17-1.83)	12	1.86 (0.96-3.24)
Bladder cancer	11	2.56 (1.28-4.58)	2	1.42 (0.17-5.12)
Stomach cancer	19	1.27 (0.77-1.98)	9	0.94 (0.43-1.77)
Coronary heart disease	354	1.49 (1.33-1.65)	235	1.70 (1.48-1.92)
Thromboembolic stroke	56	1.20 (0.91-1.55)	98	1.56 (1.27-1.90)
Atheroslerosis	12	0.70 (0.36-1.22)	15	1.03 (0.58-1.70)
Chronic obstructive pulmonary diseases	44	1.81 (1.31-2.42)	8	1.57 (0.68-3.09)
Peptic ulcer	9	2.31 (1.06-4.38)	6	1.96 (0.72-4.26)
Alcohol- and smoking-related				
Oropharyngeal cancer	1	2.69 (0.07-14.9)	1	2.45 (0.06-13.60)
Esophageal cancer	3	1.01 (0.21-2.94)	5	2.30 (0.75-5.35)

Laryngeal cancer	6	3.80 (1.40-8.27)	1	10.6 (0.27-59.20)
Fire injuries	3	1.64 (0.34-4.78)	1	2.28 (0.06-12.70)

*SMR indicates standardised mortality ratio; CI, confidence interval; and ellipses, not calculated.

Author's conclusion: patients with moderate to severe psoriasis are at increased risk for death. Alcohol is a major cause for this excess mortality**.**

H.5.19 CAUSE-SPECIFIC MORTALITY

Reference	Study type	Number of patients	Patient characteristics	Prognostic factors	Length of follow-up	Outcome measures	Source of funding
Abuabara (2010) Cause-specific mortality in patients with severe psoriasis Ref ID: ABUABARA2010	**Observational:** population-based cohort study from 1987 to 2002. **Representative population sample:** yes – used the general practice research database. **Prognostic factor adequately measured:**	N: severe psoriasis group n=3603; no psoriasis group (n=14330)	**Inclusion criteria:** all patients with severe psoriasis aged 18 years and above at their index date and had at least 1day of follow-up from 1987 and 2002. Severe psoriasis was defined if had a diagnostic code for psoriasis and a prescription consistent with severe disease on or after the first diagnosis date for psoriasis. Prescriptions included phototherapy, psoralen plus ultraviolet A, methotrexate,	GPRD database used investigators performing cause of death coding were blinded to the study group. Cause of death assigned separately by two physicians. Each patient assigned a cause of death based on data in medical record.	3.4 (+/-2.8) for non-psoriasis and 3.4 (+/-2.7) **Note**: follow-up ended at the earliest: date of death, date of transfer out of practice or end of up-to standard designation.	Risk of death from CVDs.	Grant K23AR051125 and RC1AR058204 from the NIAMS. Grant R01HL089777 from the NHLBI. Grant F32AR056799 from the NIAMS, the Doris

	yes **Confounders adjusted for:** Age and sex. **Attrition bias:** not reported **Outcomes adequately measured:** yes **Appropriate statistical analysis:** cox adjusted models		azathioprine, ciclosporin, oral retinnoids (etretinate, acitretin), hydorxyurea, and mycophenolate mofetil. For each patient they included four unexposed patients with no history of psoriasis diagnosis code at any time. They were matched on practice, date of registration in the practice (within 90 days if registration occurred after 1980 or within 5 years if registration before 1980), and index date. Index date for psoriasis patients was first date received a prescription for severe psoriasis on or after their first psoriasis diagnosis date. Non-psoriasis patients the index date was the date of any medical record within 60 days of the psoriasis index date. **Exclusion criteria:** none reported.				Duke Clinical Research Fellowship and the Psoriasis Research Foundation in honour of Herman Berman.

Patient characteristics:

	Control group	Severe psoriasis group	p-value

N	**14330**	**3603**	
Age, years			
Mean (SD)	49.73 (19.33)	52.19 (16.71)	<0.001[1]
Median (IQR)	48 (33-65)	52 (39-66)	
Sex, male (%)	5783 (40.36)	1750 (48.57)	<0.001[2]
Person time, years			
Mean (SD)	3.40 (2.76)	3.43 (2.73)	0.548[2]
Median (IQR)	2.63 (1.18-5.02)	2.69 (1.24-5.05)	
Cumulative	48662	12346	
No. of causes of death listed, mean (SD)	1.20 (0.47)	1.22 (0.47)	0.504[1]
No. of deaths (%)	862 (6.02)	321 (8.92)	
Death rate per 1000 patient-years (95% CI)	17.71 (16.55-18.94)	26.00 (23.23-29.01)	

[1] Student's t-test. [2] X^2 test. IQR, interquartile range; CI, confidence interval.

Effect size:

Cause and relative risk of death by treatment group

	Control group (%)	**Psoriasis group (%)[1]**	**P value[2]**	**Cox model HR (95% CI)[3]**
Accidents	7 (1%)	2 (1%)	1.000	1.03 (0.21-4.96)

Cardiovascular disease	301 (35%)	108 (34%)	0.002	**1.57 (1.26-1.96)**
Chronic lower respiratory disease	44 (5%)	22 (7%)	0.013	**2.08 (1.24-3.48)**
Dementia	10 (1%)	7 (2%)	0.060	**3.64 (1.36-9.72)**
Diabetes	10 (1%)	7 (2%)	0.060	**2.86 (1.08-7.59)**
Infection	195 (23%)	71(22%)	0.009	**1.65 (1.26-2.18)**
Kidney disease	17 (2%)	18 (6%)	0.000	**4.37 (2.24-8.53)**
Liver disease	4 (0%)	2 (1%)	0.347	2.03 (0.37-11.12)
Malignant neoplasms	190 (22%)	67 (21%)	0.019	**1.41 (1.07-1.86)**
Other	33 (4%)	17(5%)	0.02	**2.12 (1.19-3.88)**
Suicide	1 (0%)	1 (0%)	0.361	3.35 (0.21-53.77)
Unknown/missing	218 (25%)	70 (22%)	0.075	**1.43 (1.09-1.89)**
Total deaths	862	321		

[1]Percentages may not sum to 100 because each subject may have had more than one cause of death. [2]Two sided Fisher's exact test.

[3]Adjusted for age and sex.

HR, hazard ratio; CI, confidence interval. Significant HRs are shown in bold face.

Absolute and excess risk of death

Cause of death	**Absolute risk[1]**	**Excess risk[1]**
Cardiovascular disease	**61.9**	**3.5**

Infection	**40.1**	**2.6**
Unknown/missing	**44.8**	**1.9**
Malignant neoplasms	**39.0**	**1.6**
Kidney disease	**3.5**	**1.2**
Chronic lower respiratory disease	**9.0**	**1.0**
Other	**6.8**	**0.8**
Dementia	**2.1**	**0.5**
Diabetes	**2.1**	**0.4**
Liver disease	**0.8**	**0.1**
Suicide	**0.2**	**0.0**
Accidents	**1.4**	**0.0**

[1]Deaths per 1000 patient-years

Median age at death (years) by sex and cause

	Women			**Men**		
	Controls	**Psoriasis**	**p-value[1]**	**Controls**	**Psoriasis**	**p-value[1]**
Overall	82.85	75.49	**<0.001**	78.41	73.49	**<0.001**
Cardiovascular disease	83.71	76.94	**<0.001**	77.98	73.80	**0.018**
Malignant	76.15	71.52	0.518	74.13	69.21	**0.034**

neoplasms						
Chronic lower respiratory disease	72.38	72.74	0.507	80.98	73.23	0.107
Infection	82.22	76.56	**0.001**	83.11	75.10	**0.003**
Kidney disease	83.65	65.59	**0.003**	79.10	66.09	**0.026**
Other	79.91	72.43	0.393	80.86	64.13	**0.011**
Unknown/missing	85.40	80.20	**0.004**	80.27	74.38	**0.010**

[1]Wilcoxon rank-sum test. Significant p-values are shown in bold face.

Author's conclusion: Severe psoriasis is associated with an increased risk of death from a variety of cases, with cardiovascular death being the most common aetiology. These patients were also at increased risk of death from causes not previously reported such as infection, kidney disease and dementia.

H.5.20 LYMPHOMA

Reference	Study type	Number of patients	Patient characteristics	Prognostic factors	Length of follow-up	Outcome measures	Source of funding
Gelfand (2003) Lymphoma rates are low but increased	**Observational:** retrospective population-based cohort study from 1988 to 1996	N: 1718 with psoriasis; n=105203 without psoriasis.	**Inclusion criteria:** a random sample of 10% of the entire GPRD population who were 65 years or older because the incidence of cancer increases with age.	OXMIS code used to define if patients had psoriasis or if they had no history of psoriasis consistent	Median, months (25^{th}, 75^{th} percentile): 39.75 (19.1, 65.1) in psoriasis group	Incidence of lymphoma and internal malignancy.	Grants F32-AR48100, R01-AR44695 and KK24-

in patients with psoriasis Ref ID: GELFAND 2003	**Representative population sample:** yes GPRD used. **Prognostic factor adequately measured:** yes **Confounders adjusted for:** Age and sex. **Attrition bias:** not reported **Outcomes adequately measured:** yes **Appropriate statistical analysis:** yes, unadjusted Cox proportional hazards model. Then adjusted for age and sex for confounding. **Notes:** GPs unaware of the hypotheses to be tested.		**Exclusion criteria:** history of one of the outcome diseases prior to study entry or developed within 6 months of study entry.	with OXMIS code. Any OXMIS code for lymphoproliferative disease (eg Hodgkin or non-Hodgkin lymphoma) occurring after the patient qualified for the study. Secondary analyses for incidence of interest.	and 46 (20.8, 73.1 in the non-psoriasis group. **Note**: for non-psoriasis patients follow-up time counted from patient's registration with a GP and approval of GPs data as 'up to standard'. End of follow-up when patient experienced the outcome of interest, died or left the GPRD. For psoriasis patients follow-up was counted from the patient's diagnosis with psoriasis, registration with the GP and approval of GPs data as up to standard (whichever last) until outcome of interest, died or left the GPRD.		AR02212 from the National Institutes of Health, Bethesda, MD and from an unrestricted grant fro the Herzog Foundation to the Trustees of the University of Pennsylvania.

Patient characteristics:

Variable	With psoriasis	Without psoriasis
Patients	2718 (2.5)	105203 (97.5)
Median age, years (25th, 75th percentile)	60.63 (66.0, 76.6)	71.08 (65.5, 78.4)
Women	1540 (56.7)	61412 (58.4)
Men	1178 (43.3)	43791 (41.6)
Patients treated with methotrexate	42 (1.6)	185 (0.2)

Effect size:

Summary of follow-up time and incidence rate of lymphoma for patients with and without psoriasis

Variable	With psoriasis	Without psoriasis
Follow-up time, median, mo (25th, 75th percentile)	39.75 (19.1, 65.1)	46 (20.8, 73.1)
Person-years	9839	420008
Lymphoma, no.	18	258
Incidence rate of	18.3	6.1

lymphoma per 10000 person-years		
Attributable risk (excess no. of lymphoma cases related to psoriasis	122 per 100000 per year	-

Rates of lymphoma or internal malignancy in patients with psoriasis relative to rates for patients without psoriasis

	Relative risk (95% Confidence interval)	
Analysed malignancy	**Unadjusted**	**Adjusted for age and sex**
Lymphoma	2.95 (1.83-4.76)	2.94 (1.82-4.74)
Lymphoma, previous history of lymphoma excluded	3.39 (2.04-5.64)	3.38 (2.03-5.62)
Lymphoma, excluding patients diagnosed within 6 months of follow-up	3.04 (1.85-4.97)	3.02 (1.85-4.95)
Lymphoma, excluding patients treated with methotrexate	2.84 (1.74-4.64)	2.83 (1.73-4.64)
Lymphoma, excluding mycosis fungoides	2.26 (1.29-3.95)	2.26 (1.29-3.94)
Internal malignancy	1.08 (0.93-1.24)	1.09 (0.94-1.26)
Internal malignancy, previous history of malignancy excluded	1.04 (0.88-1.23)	1.05 (0.89-1.24)

Author's conclusion: patients with psoriasis are at increased risk of developing lymphoma.

H.5.21 CANCER

Reference	Study type	Number of patients	Patient characteristics	Prognostic factors	Length of follow-up	Outcome measures	Source of funding
Y. J. Chen, C. Y. Wu, T. J. Chen, J. L. Shen, S. Y. Chu, C. B. Wang, and Y. T.	**Observational:** retrospective population based cohort study in Taiwan; 1996-2000 to 2007	N: 203,686	**Inclusion criteria:** all patients with a first time diagnosis of psoriasis (ICD-9 code 696.0, 696.1) made in a department of dermatology or rheumatology and a	Data from National Health Insurance Database Note: ICD-9 codes used to define diseases in this study	From 1996/2000 to first-time diagnosis of cancer (except malignancy in situ, metastasis or	Incidence of cancer Note: included cancers coded 140 to 208.91 in	Taichung Veterans General Hospital

Chang. The risk of cancer in patients with psoriasis: A population-based cohort study in Taiwan. J.Am.Acad. Dermatol. 65 (1):84-91, 2011. Ref ID: CHEN2011	**Representative population sample:** unsure – not UK population (Longitudinal Health Insurance Database 2000 [LHID 2000]– a randomly sampled subset of the National Health Insurance Database, which records 99% of the Taiwanese population) **Prognostic factor adequately measured:** yes **Confounders adjusted for:** age and gender, plus sub analysis for treatment modalities **Attrition bias:** not reported **Outcomes adequately measured:** yes – from Registry of Catastrophic Illness Patient Database (subpart of NHIRD)		comparison group of people without psoriasis or a history of malignancies. **Exclusion criteria:** unclear baseline data e.g., conflicting gender or uncertain birth date; history of cancer before diagnosis of psoriasis or before first-time inclusion in this cohort		secondary cancer), death, end of follow-up in medical records, end of observation period or end of 2007 Min 1.5 and max 10 years	ICD-9 CM except metastatic cancers in lymph nodes and secondary cancers	

	Appropriate statistical analysis: yes – hazard ratios using Cox proportional hazards model						

Patient characteristics:

Characteristic	**Control (%)**	**Psoriasis (%)**
Total	200000	3686
Gender – men	51.6%	60.8%
Duration of follow-up, mean±SD	6.68±1.23	4.58±1.68
Mean age±SD	32.93±20.56	44.00±19.62
Prior treatments for psoriasis		
PUVA	-	5.18%
UVB	-	15.2%
Systemics	-	14.4%
Phototherapy or systemics	-	24.4%

Effect size:

HR for specific cancer types adjusted for age and gender

Cancer types	**N**	**HR (95% CI)**
Any	116	1.66 (1.38-2.00)

Skin cancer	5	3.10 (1.24-7.71)
Lymphomatopoietic malignancies	6	2.21 (0.97-5.02)
Oropharynx and larynx	11	2.16 (1.17-3.96)
Digestive tract/liver/gall bladder	23	2.02 (1.33-3.07)
Colorectum	15	1.70 (1.01-2.86)
Stomach	4	0.95 (0.35-2.56)
Lung/mediastinum	14	1.46 (0.85-2.49)
Urinary bladder	8	3.18 (1.54-6.57)
Prostate	6	1.77 (0.78-4.00)
Other	9	1.55 (0.80-3.01)

Subgroup analyses

AGE: HR adjusted for gender only for risk of any cancer

Age (years)	**HR (95% CI)**	**p-value**
0-19	-	
20-39	2.16 (1.15-4.05)	0.0162
40-59	1.84 (1.36-2.50)	<0.0001
60-79	1.50 (1.16-1.95)	0.0022

>80	0.91 (0.34-2.46)	0.8538

TREATMENT MODALITIES: HR adjusted for age and gender and stratified by treatment modalities compared with control subjects for risk of any cancer

Treatment modalities	Adjusted HR (95% CI)	p-value
PUVA		
Yes	2.03 (1.06-3.91)	0.033
No	1.64 (1.35-1.99)	<0.0001
UVB		
Yes	1.01 (0.58-1.78)	0.98
No	1.80 (1.48-2.19)	<0.0001
Systemics		
Yes	2.08 (1.40-3.12)	0.0003
No	1.58 (1.28-1.94)	<0.0001
Phototherapy or systemics		
Yes (moderate-severe pso)	1.85 (1.33-2.57)	0.0002
No (mild psoriasis)	1.59 (1.27-1.98)	<0.0001

TREATMENT MODALITIES: HR adjusted for age and gender for comparisons within the psoriasis group for risk of any cancer

Comparison	Adjusted HR (95% CI)	p-value

PUVA vs no PUVA	1.15 (0.58-2.28)	0.6906
UVB vs no UVB	0.52 (0.29-0.95)	0.0324
Drugs vs no drugs	1.24 (0.79-1.95)	0.3511
Severe vs mild psoriasis	1.09 (0.74-1.63)	0.6583

Note: severe psoriasis = received phototherapy or systemics; mild = received neither

Author's conclusion:

- Psoriasis carries an elevated risk of malignancies, especially in younger and in male patients.
- This effect is independent of systemic treatment for psoriasis.
- Phototherapy with UVB did not increase, but rather reduced, the risk of cancer in psoriasis

H.5.22 CANCER

Reference	Study type	Number of patients	Patient characteristics	Prognostic factors	Length of follow-up	Outcome measures	Source of funding
A. E. Prizment, A. Alonso, A. R. Folsom, R. L. Ahmed, B. A. Virnig, E. M. Warshaw, and K. E.	**Observational:** prospective population based cohort study in Iowa, USA with **retrospective** baseline data sources; 1991 to 2006 Linkage of data from 3	N: 33,266 (2.2% psoriasis)	**Inclusion criteria:** all cancer free women registered on IWHS **Exclusion criteria:** not in Iowa at start of follow-up; cancer at baseline or before start of follow-up	Data from Medicare claims data – psoriasis diagnoses identified using ICD-9 diagnosis code 696.1	Prospective follow-up from 1991/2004 to disenrollment from Medicare; emigration from Iowa; cancer diagnosis; death or end of follow-up	Incidence of cancer	National Cancer Institute grant

Anderson. Association between psoriasis and incident cancer: The Iowa's Women's Health Study. Cancer Causes Control 22 (7):1003-1010, 2011. Ref ID: PRIZMENT 2011	sources: Iowa Women's Health Study (IWHS), Medicare and the Iowa SEER cancer registry **Representative population sample:** no – women over 65 only and limited to those who since 1991 were enrolled in at least 1 month of fee-for-service coverage after reaching 65 years. Derived from cohort of women aged 55-69 recruited by baseline questionnaire in 1986 (used only those over 65 because Medicare pays for health benefits for this group) **Prognostic factor adequately measured:** yes – Medicare claims **Confounders adjusted for:** age at start of follow-up, smoking status and pack use, body mass index, education, physical activity, and hormone			Psoriasis was defined as: 2+ psoriasis claims from any Medicare file during 1991-2004 or 1+ psoriasis claim from a dermatologist (n = 719). Severe psoriasis was defined as 4+ psoriasis claims from a dermatologist in any year (n=121). 4 visits were selected as a cut-off because patients receiving systemics or phototherapy are usually seen every 3 months by dermatologists	on 31 Dec 2006		

	therapy use (and number of live births for breast cancer) Note: alcohol intake, WHR, history of diabetes, oral contraceptive use and start of follow-up did not materially change associations so these variables were not included in the final model **Attrition bias:** not reported (but 99% success in linkage) **Outcomes adequately measured:** yes – from SEER database using ICD-O codes (3rd edition) **Appropriate statistical analysis:** yes – hazard ratios using Cox proportional hazards model and psoriasis as a time-dependent variable						

Patient characteristics:

Characteristic	Control (%)	Psoriasis (%)
Total	32191	719
Mean age at start of follow-up, mean±SD	68.1±3.2	67.8±3.0
BMI (kg/m^2)		
<24.9	39.5	41.3
25-30	37.3	33.4
≥30	23.2	25.3
Education		
Less than high school	19.6	17.9
High school	42.2	38.2
More than high school	38.1	43.9
Smoking		
Never	67.6	53.1
Former	18.6	25.0
Current	13.8	22.0
Alcohol intake		
Never	56.9	52.8

<4g/day	23.6	22.4
≥4g/day	19.5	24.8

Effect size:

Adjusted HR for specific cancer types

	No psoriasis		**All psoriasis**		**Mild psoriasis**		**Severe psoriasis**	
Cancer types	**N**	**HR (95% CI)**	**N**	**HR (95% CI)**	**N**	**HR (95% CI)**	**N**	**HR (95% CI)**
Any	6381	1	107	1.1 (0.9-1.4)	85	1.1 (0.9-1.4)	22	1.2 (0.8-1.8)
Breast	2037	1	29	1.0 (0.7-1.5)	24	1.4 (0.8-2.2)	5	1.0 (0.4-2.7)
Lung	722	1	20	1.3 (0.8-2.0)	16	1.1 (0.7-1.6)	4	1.0 (0.4-2.3)
Colon	925	1	22	1.6 (1.0-2.4)	17	1.5 (0.9-2.4)	5	1.9 (0.8-4.7)

Trend across psoriasis group was tested by including psoriasis severity as a continuous variable (0-no psoriasis; 1-mild; 2-severe); p-value for total = 0.3; breast cancer = 0.4; lung cancer = 0.9 and colon cancer = 0.03

Note: after adjustment for confounders observed associations were attenuated and this was largely due to smoking

Author's conclusion:

- Psoriasis carries an elevated risk of colon cancer, particularly if severe.

H.5.23 CANCER

Reference	Study type	Number of patients	Patient characteristics	Prognostic factors	Length of follow-up	Outcome measures	Source of funding
X. Shu, J. Ji, J. Sundquist, K. Sundquist, and K. Hemminki. Survival in cancer patients hospitalized for psoriasis: A population-based cohort study in Sweden. Br.J.Dermatol. 165 (1):129-136, 2011. Ref ID: SHU2011	**Observational:** retrospective cohort study in Sweden; 1964 to 2006 Linkage of anonymous data **Representative population sample:** yes but indirect (all known to have cancer – survival rate) and also severe because all diagnosed following hospitalisation for psoriasis **Prognostic factor adequately measured:** yes – ICD codes **Confounders adjusted for:** gender, age at diagnosis of primary neoplasm and calendar year at diagnosis of	N: 1,011,757 control; 1746 psoriasis (0.2% psoriasis)	**Inclusion criteria:** psoriasis cohort: all patient diagnosed with psoriasis 1964-2006 in the Swedish Hospital Discharge Registry according to 7-10th edition of ICD Controls: cancer patients without psoriasis **Exclusion criteria:** not stated	Data from Swedish Hospital Discharge Registry – psoriasis diagnoses identified using ICD	Follow-up from cancer diagnosis to emigration; death or end of follow-up on 31 Dec 2006	Incidence of cancer mortality (primary neoplasms only)	Swedish Cancer Society, Swedish Council for Working Life and Social Research and the Deutsche Krebshilfe

	primary neoplasm Also explored in sensitivity analyses: COPD (surrogate for smoking), alcohol-related diseases (surrogate for alcohol intake) and obesity **Attrition bias:** not reported **Outcomes adequately measured:** yes –linkage to Swedish cancer registry (tumours ascertained with 4-digit ICD-7 code; records all new cases and most are cytologically or histologically confirmed; full national coverage) **Appropriate statistical analysis:** yes – hazard ratios using proportional hazards model						

Effect size:

Adjusted HR for mortality from specific cancer types in people diagnosed with cancer with psoriasis compared to people without psoriasis

		Cancer specific mortality		Overall mortality	
Cancer types	**Cases**	**N deaths**	**HR (95% CI)**	**N deaths**	**HR (95% CI)**
Upper aero-digestive tract	57	32	2.38 (1.68-3.37)	46	2.16 (1.62-2.89)
Oesophagus	33	29	1.78 (1.23-2.57)	32	1.69 (1.19-2.39)
Stomach	58	41	1.27 (0.94-1.73)	52	1.38 (1.05-1.81)
Colon	109	48	1.12 (0.85-1.49)	74	1.23 (0.98-1.54)
Rectum	67	31	1.16 (0.81-1.65)	45	0.97 (0.73-1.30)
Anus	11	1	0.48 (0.07-3.42)	3	0.68 (0.22-2.11)
Liver	70	52	1.43 (1.09-1.88)	68	1.50 (1.18-1.90)
Pancreas	56	51	1.23 (0.93-1.62)	56	1.24 (0.95-1.61)
Lung	190	147	1.11 (0.94-1.30)	170	1.11 (0.96-1.29)
Breast	199	31	0.71 (0.50-0.98)	86	1.09 (0.88-1.35)
Cervix	22	9	1.27 (0.66-2.45)	111	0.88 (0.49-1.58)
Endometrium	33	3	1.44 (0.46-4.45)	16	2.21 (1.35-3.61)
Ovary	25	16	1.11 (0.68-1.81)	21	1.10 (0.72-1.68)

Prostate	222	76	1.02 (0.81-1.27)	133	1.11 (0.94-1.32)
Kidney	50	31	1.58 (1.11-2.24)	41	1.44 (1.06-1.96)
Urinary bladder	89	28	1.22 (0.84-1.76)	51	1.10 (0.84-1.45)
Melanoma	46	10	1.85 (1.00-3.44)	20	1.63 (1.05-2.53)
Skin SCC	117	6	3.16 (1.41-7.07)	62	1.37 (1.07-1.76)
nervous system	51	21	1.12 (0.73-1.72)	32	0.95 (0.67-1.34)
Thyroid	11	2	0.54 (0.14-2.17)	5	0.67 (0.28-1.60)
Endocrine glands	30	0	-	15	1.27 (0.76-2.10)
Non-Hodgkin's lymphoma	72	35	1.10 (0.79-1.54)	49	1.03 (0.78-1.36)
myeloma	20	13	0.83 (0.48-1.43)	18	0.98 (0.62-1.56)
Leukaemia	49	28	1.48 (1.02-2.14)	39	1.49 (1.09-2.04)
Acute	16	13	1.15 (0.67-1.98)	14	1.13 (0.67-1.91)
Chronic	15	7	1.53 (0.73-3.21)	10	1.60 (0.86-2.97)
All	1746	754	1.26 (1.18-1.35)	1177	1.27 (1.20-1.35)

Adjusted HR for mortality from specific cancer types in people diagnosed with cancer with psoriasis compared to people without psoriasis, stratified by number of hospitalisations in the psoriasis group (as a surrogate for disease severity)

Cancer types	**One hospitalisation**		**Two or more hospitalisations**	
	N deaths	**HR (95% CI)**	**N deaths**	**HR (95% CI)**

Upper aero-digestive tract	24	2.86 (1.92-4.27)	8	1.73 (0.87-3.46)
Oesophagus	6	1.53 (0.69-3.40)	23	1.86 (1.23-2.80)
Stomach	25	1.17 (0.79-1.73)	16	1.50 (0.92-2.45)
Colon	31	1.06 (0.75-1.51)	17	1.28 (0.80-2.06)
Rectum	18	0.97 (0.61-1.53)	13	1.55 (0.90-2.67)
Anus	1	0.85 (0.12-6.06)	0	-
Liver	26	1.27 (0.86-1.86)	26	1.64 (1.12-2.42)
Pancreas	23	0.92 (0.61-1.39)	28	1.72 (1.19-2.50)
Lung	85	1.06 (0.85-1.31)	62	1.17 (0.91-1.50)
Breast	21	0.71 (0.47-1.10)	10	0.70 (0.38-1.30)
Cervix	4	0.91 (0.34-2.42)	5	1.86 (0.78-4.48)
Endometrium	2	1.33 (0.33-5.35)	1	1.56 (022-11.07)
Ovary	8	0.87 (0.44-1.74)	8	1.50 (0.75-3.01)
Prostate	42	0.85 (0.63-1.16)	34	1.34 (0.95-1.87)
Kidney	15	1.11 (0.67-1.84)	16	2.59 (1.59-4.22)
Urinary bladder	15	0.92 (0.55-1.52)	13	1.90 (1.11-3.28)
Melanoma	5	1.29 (0.54-3.11)	5	2.85 (1.19-6.82)
Skin SCC	2	2.14 (0.53-8.56)	4	3.96 (1.48-10.61)
nervous system	14	1.17 (0.69-1.97)	7	1.06 (0.51-2.23)

Thyroid	2	0.54 (0.14-2.18)	0	-
Endocrine glands	0	-	0	-
Non-Hodgkin's lymphoma	18	0.93 (0.58-1.47)	17	1.32 (0.82-2.13)
myeloma	7	0.71 (0.34-1.48)	6	1.00 (0.45-2.24)
Leukaemia	18	1.33 (0.84-2.11)	10	1.61 (0.87-2.99)
All	419	1.13 (1.03-1.23)	335	1.47 (1.33-1.63)

Adjusted HR for mortality from all cancer in people diagnosed with cancer with psoriasis compared to people without psoriasis, stratified by previously hospitalised for alcohol related diseases or non-alcohol related diseases

Cancer type	**Alcohol-related**		**Non alcohol-related**	
	N deaths	**HR (95% CI)**	**N deaths**	**HR (95% CI)**
All	**53**	**1.74 (1.35-2.24)**	**701**	**1.23 (1.15-1.32)**

Adjusted HR for mortality from specific cancer types in people diagnosed with cancer with psoriasis compared to people without psoriasis, stratified by age at diagnosis of cancer in the psoriasis group

Cancer types	**≤65 years**		**>65 years**	
	N deaths	**HR (95% CI)**	**N deaths**	**HR (95% CI)**

Upper aero-digestive tract	20	3.04 (1.96-4.71)	12	1.83 (1.04-3.22)
Oesophagus	16	1.88 (1.15-3.07)	13	1.78 (1.03-3.07)
Stomach	14	1.49 (0.88-2.51)	27	1.17 (0.80-)1.70
Colon	19	1.37 (0.87-2.14)	29	1.01 (0.70-1.46)
Rectum	11	1.35 (0.75-2.44)	20	1.09 (0.71-1.70)
Anus	1	0.76 (0.11-5.42)	0	-
Liver	17	2.45 (1.52-3.95)	35	1.22 (0.87-1.70)
Pancreas	18	1.42 (0.89-2.25)	33	1.15 (0.82-1.62)
Lung	51	1.04 (0.79-1.36)	96	1.16 (0.95-1.42)
Breast	16	0.78 (0.48-1.27)	15	0.65 (0.39-1.08)
Cervix	3	0.85 (0.27-2.64)	6	1.56 (0.70-3.49)
Endometrium	1	0.83 (0.12-5.91)	2	2.37 (0.59-9.51)
Ovary	4	2.28 (0.85-6.15)	12	1.01 (0.58-1.79)
Prostate	16	1.31 (0.80-2.14)	60	0.94 (0.73-1.21)
Kidney	15	1.61 (0.97-2.68)	16	1.58 (0.97-2.58)
Urinary bladder	3	0.63 (0.20-1.94)	25	1.39 (0.94-2.06)
Melanoma	6	1.77 (0.79-3.94)	4	1.85 (0.69-4.94)
Skin SCC	3	4.78 (1.52-15.02)	3	2.34 (0.75-7.30)
nervous system	15	1.60 (0.96-2.65)	6	0.66 (0.30-1.48)

Thyroid	1	2.01 (0.28-14.29)	1	0.35 (0.05-2.51)
Endocrine glands	0	-	0	-
Non-Hodgkin's lymphoma	22	1.44 (0.94-2.18)	13	0.79 (0.42-1.36)
myeloma	4	1.07 (0.40-2.87)	9	0.75 (0.39-1.45)
Leukaemia	9	1.21 (0.63-2.33)	19	1.62 (1.03-2.54)
All	288	1.39 (1.28-1.52)	466	1.18 (1.08-1.29)

Author's conclusion:

- A previous diagnosis of psoriasis worsens the prognosis of many cancers.
- A worse prognosis was more pronounced in psoriatic cancer patients diagnosed at an earlier age, previously hospitalized for alcohol-related diseases, or with severe symptoms

H.5.24 CANCER

Reference	Study type	Number of patients	Patient characteristics	Prognostic factors	Length of follow-up	Outcome measures	Source of funding
Boffetta (2001) Cancer risk in a population-based cohort of patients hospitalised for psoriasis in Sweden Ref ID: BOFFETTA 2001	**Observational:** population based cohort study 1965-1989 **Representative population sample:** yes. **Prognostic factor adequately measured:** yes **Confounders adjusted for:** Matched for age and sex. **Attrition bias:** not reported **Outcomes adequately**	N: 9773	**Inclusion criteria:** all records in the in-patient register with a hospital discharge diagnosis of psoriasis (ICD-7 code 706; ICD-8 code 696) between 1965-83. **Exclusion criteria:** excluded the first year of observation following the index admission to reduce selection bias, which may occur if psoriasis patients who developed a cancer or died within 1 year are more likely hospitalised than other psoriasis patients and detection bias, if cancer was to be diagnosed during the diagnostic and therapeutic procedures involved in the management of	Swedish National Board of Health and Welfare in-patient register. Linked cohort to the cohort to the nationwide Registers of Total Population, Cause of Death, and Population Migration to identify all patients who lived in Sweden during the study period. Further linked to the Swedish cancer register.	15 years +, no mean given.	Incidence of cancer Standard mortality ratios	Not reported.

	measured: yes **Appropriate statistical analysis:** not multivariable/regression		psoriasis.				

Patient characteristics:

Characteristic	Patients	Person-years
Total	**9,773**	**93,775.6**
Gender – men	**5,306**	**49,138.3**
Duration of follow-up	**4,467**	**44,637.2**
1-4 years	**1,234**	**27,351.4**
5-9 years	**2,926**	**36,475.9**
10-14 years	**2,839**	**20,646.3**
15+years	**2,774**	**9,302.0**
Presence of other diagnoses		
Psoriasis as only diagnosis	**5,164**	**55,512.7**
Other diagnoses, psoriasis as primary	**1,652**	**14,755.0**
Other diagnoses, psoriasis as secondary	**2,957**	**23,,507.9**

Effect size:

Standardised incidence ratio of selected neoplasms among patients hospitalised for psoriasis[1]

Outcome	Men			Women			Both genders		
	N	SIR	95% CI	N	SIR	95% CI	N	SIR	95% CI
All cancers	444	1.34	1.22, 1.47	345	1.41	1.27, 1.57	789	1.37	1.28-1.47
Oral cavity, pharynx	25	2.60	1.68, 3.84	11	3.37	1.68, 6.04	36	2.80	1.96,3.87
Oesophagus	13	3.00	1.59, 5.13	4	3.03	0.82, 7.76	17	3.01	1.75, 4.81
Stomach	22	1.07	0.67, 1.62	10	0.99	0.47, 1.82	32	1.04	0.71, 1.47
Colon	26	1.08	0.71, 1.59	26	1.25	0.81, 1.83	52	1.16	0.87, 1.52
Rectum	19	1.10	0.66, 1.71	17	1.62	0.94, 2.60	36	1.29	0.91, 1.79
Liver	18	2.52	1.49, 3.98	11	1.36	0.68, 2.44	29	1.91	1.28, 2.74
Pancreas	14	1.34	0.73, 2.24	14	1.82	0.99, 3.05	28	1.56	1.02, 2.23
Larynx	6	1.55	0.57, 3.37	0	[0.32]	0,11.5	6	1.43	0.52, 3.12
Lung	65	1.91	1.48, 2.44	25	3.00	1.94, 4.43	90	2.13	1.71, 2.61
Connective tissue	1	0.47	0.01, 2.59	3	1.99	0.40, 5.81	4	1.09	0.29, 2.80
Melanoma	3	0.34	0.07, 1.00	2	0.29	0.03, 1.05	5	0.32	0.10, 0.74
SCC of the skin	35	2.75	1.92, 3.83	13	1.92	1.02, 3.28	48	2.46	1.82, 3.27

Breast	1	1.89	0.02, 10.5	78	1.27	1.00, 1.58	79	1.27	1.01, 1.58
Cervix	-	-	-	11	1.44	0.72, 2.57	11	1.44	0.72, 2.57
Endometrium	-	-	-	15	1.11	0.62, 1.84	15	1.11	0.62, 1.84
Ovary	-	-	-	19	1.38	0.83, 2.16	19	1.38	0.83, 2.16
Female genital organs	-	-	-	6	2.47	0.90, 5.37	6	2.47	0.90, 5.37
Prostate	77	0.96	0.76, 1.21	-	-	-	77	0.96	0.76, 1.21
Male genital organs	8	2.69	1.16, 5.30	-	-	-	8	2.69	1.16, 5.30
Bladder	33	1.37	0.95, 1.93	10		0.78, 2.98	43	1.43	1.03, 1.92
Kidney, pelvis	13	1.10	0.58, 1.88	15	1.62	1.37, 4.04	28	1.56	1.04, 2.25
Brain	4	0.49	0.13, 1.25	6	2.45	0.34, 2.00	10	0.68	0.33, 1.25
Thyroid	4	2.62	0.71, 6.71	3	0.92	020, 2.92	7	1.55	0.62, 3.19
Hodgkin's disease	1	0.58	0.01, 3.24	0	1.00	0,353	1	0.36	0.01, 2.02
Non-Hodgkin's lymphoma[2]	15	1.56	0.87, 2.57	7	[1.04]	0.48, 2.45	22	1.42	0.89, 2.15
Mycosis fungoides	5	26.7	8.60, 62.3	0	1.19	0, 51.3	5	19.3	6.22, 45.1
Multiple myeloma	5	0.92	0.30, 2.14	6	[0.07]	0.62, 3.69	11	1.22	0.61, 2.19
Lymphocytic leukaemia	2	0.44	0.05, 1.58	4	1.70	0.51, 4.84	6	0.90	0.33, 1.96

Non-lymphocytic leukaemia	6	1.74	0.64, 3.79	5	1.89	0.70, 5.09	11	1.92	0.96, 3.43

[1]N, number of observed cases; SIR, standardised incidence ratio; CI, confidence interval; SCC, squamous cell carcinoma. When no cases were observed, expected cases are reported in square brackets.

[2]Excluding mycosis fungoides.

Standardised mortality ratios for selected non-neoplastic causes among patients hospitalised for psoriasis[1]

	Whole cohort			Psoriasis as only diagnosis		
	N	SMR	95% CI	N	SMR	95% CI
All causes	3813	1.94	1.88,2.00	1392	1.56	1.48, 1.64
Infective diseases	28	2.25	1.49, 3.25	9	1.41	0.61, 2.77
Malignant neoplasms	611	1.48	1.36, 1.60	252	1.30	1.15, 1.47
Respiratory diseases	290	2.16	1.91, 2.42	94	1.58	1.27, 1.93
Pneumonia	169	2.02	1.73. 2.35	61	1.66	1.27, 2.14
Bronchitis	35	2.06	1.43, 2l86	8	1.05	0.46, 2.09
Emphysema	29	3.13	2.09, 4.49	6	1.44	0.53, 3.13
Asthma	24	2.46	1.58, 3.67	6	1.31	0.48, 2.85
Cardiovascular disease	2066	1.87	1.79, 1.95	715	1.45	1.35, 1.56

Isch. Heart disease	1357	1.97	1.87, 2.08	479	1.55	1.42, 1.70
Cerebrovasc. Disease	334	1.60	1.43, 1.78	123	1.33	1.11, 1.59
Arterial disease	134	1.83	1.54 2.17	43	1.34	0.97, 1.80
Diabetes mellitus	99	3.14	2.52, 3.87	24	1.88	1.20, 2.79
Neurological disease	33	1.77	1.22, 2.49	12	1.35	0.69, 2.35
Mental disorders	66	2.91	2.25, 3.70	33	3.03	2.08, 4.25
Alcoholism	51	7.19	5.35, 9.44	25	6.37	4.12, 9.39
Digestive diseases	246	3.86	3.39, 4.37	98	3.31	2.69, 4.03
Liver cirrhosis	133	8.13	6.81, 9.64	50	6.05	4.49, 7.97
Genito-urinary disease	74	2.54	2.00, 3.19	20	1.56	0.96, 2.42
Skin/subcutaneouse disease	20	17.7	10.8, 27.3	4	7.87	2.11, 20.1
Muscoloskeletal disease	27	3.34	2.20, 4.85	3	0.81	0.16, 2.35
External causes	213	2.29	2.00, 2.62	101	2.08	1.69, 2.53
Trauma to organs	21	7.13	4.42, 10.9	12	7.26	3.75, 12.7
Open wounds	66	2.19	1.69, 2.78	27	1.99	1.31, 2.89
Trauma of CNS	53	2.04	1.53, 2.67	28	1.91	1.27, 2.76
Adverse toxic	39	3.81	2.71, 5.21	15	2.53	1.42, 4.18

effect						

Author's conclusion: despite some limitations, they provide no evidence for an increased risk of melanoma among patients hospitalised for psoriasis. Indirect evidence that consumption of alcohol and tobacco is increased among patients with severe psoriasis**.**

H.5.25 LYMPHOMA

Reference	Study type	Number of patients	Patient characteristics	Prognostic factors	Length of follow-up	Outcome measures	Source of funding
Gelfand (2006) The risk of lymphoma in patients with psoriasis Ref ID: GELFAND 2006	**Observational: population based** cohort study **Representative population sample:** yes, used GPRD **Prognostic factor adequately measured:** yes **Confounders adjusted for:** Age, gender and person time	N: 153,197 patients with psoriasis (149,203 mild psoriasis and 3994 severe psoriasis) and 765,950 without psoriasis.	**Inclusion criteria:** All psoriasis patients who had at least 1 day of observation time. They were matched to up to five control subjects on matched criteria who did not have psoriasis, who were seen in the same practice and had a date of observation in the practice within 60 days. **Exclusion criteria:** not stated	OXCMIS and Read codes were used to classify diseases. Those receiving systemic therapies were classified (according to treatment codes) as severe psoriasis and those who did not classified as mild psoriasis Classification of having a new	Mean time around 5 years. **Note**: follow-up time ended when they developed a lymphoma, died, transferred out of practice or practice no longer UTS.	Incidence of lymphoma, non-Hodgkin's' lymphoma, Hodgkin's lymphoma and T-cell lymphoma.	Funded by NIH/NIAMS K23AR051125-01 and an unrestricted grant to the Trustees of the University of Pennsylvania from Biogenide c.

	Attrition bias: not reported **Outcomes adequately measured:** yes **Appropriate statistical analysis:** yes, cox proportional hazards model **Notes:** psoriasis patients were older than control patients and mild psoriasis patients were slightly more likely to be females .			lymphoma was determined if they received a medical code after the start date and on or before the end date.			

Patient characteristics:

	Control	**Mild psoriasis**	**Severe psoriasis**
N (%)	**765, 950**	**149,203**	**3.944**
Gender – male	366,238 (48%)	70,742 (47.4%)	1,937 (48.5%)
Gender – female	399,712 (52%0	78,461 (52.6%)	2,057 (51.5%)
Odds ratio (95% CI)	-	0.98 (0.97, 1.00) P=0.0045	1.03 (0.97, 1.09) P=0.3912
Age – mean (median, 25th, 75th percentile)	35.76 (33, 18, 53)	41.51 (40, 26, 57) p=0.0045	48.51 (48, 35, 62) p=0.3912

History of lymphoma			
Yes	538 (0.07%)	179 (0.12%)	11 (0.28%)
No	765,412 (99.93%)	149, 024 (99.88%)	3,983 (99.72%)
Odds ratio (95% CI)	-	1.71 (1.44, 2.03) p<0.0001	3.93 (1.95, 7.09) p=0.0002
Systemic therapies (n%)			
Methotrexate	-	-	2,314 (57.94%)
Psoralen/phototherapy	-	-	681 (17.05%)
Azathioprine	-	-	659 (16.50%)
Ciclosporine	-	-	414 (10.37%)
Etretinate or acitretin	-	-	351 (8.79%)
Hydroxyurea	-	-	224 (5.61%)
Mycophenoalte mofetil	-	-	12 (0.30%)

Odds ratios and p-values refer to the comparison of the mild and severe psoriasis groups with the control group. Percentages for systemic therapies do not add to 100 because patients could have received more than one systemic therapy.

Effect size:

Incidence and relative risk (hazard) of lymphoma in psoriasis patients compared to controls

Variable	**Control**	**Mild psoriasis**	**Severe psoriasis**	**All psoriasis**
Mean follow-up time (media, 25^{th}, 75^{th}	5.61 (5.25, 2.18, 9.13)	4.50 (3.80, 1.64, 7.09)	5.77 (5.53, 2.70, 8.96)	4.54 (3.84, 1.67, 7.16)

percentile)				
Person years (n)	4,297,296	671,914	23,048	694,962
New lymphoma (n)	970	237	11	248
Incidence per 10,000 person years (95% CI)	2.26 (2.12, 2.40)	3.53 (3.09, 4.01)	4.77 (2.38, 8.54	3.57 (3.14 4.04)
Primary analysis				
Unadjusted hazard ratio	-	1.54 (1.33, 1.77) p<0.001	2.12 (1.17, 3.85) p=0.013	1.56 (1.35, 1.79) p<0.001
Adjusted hazard ratio	-	1.34 (1.16, 1.54) p<0.001	1.59 (0.88, 2.89) p=0.124	1.35 (1.17, 1.55) p<0.001
Attributable risk (excess number of lymphoma cases related to psoriasis)	-	-	-	7.9/100,000 per year
Sensitivity analysis				
New lymphoma	711	183	9	192
Unadjusted hazard ratio	-	1.71 (1.45, 2.01) p<0.001	2.37 (1.23, 4.57) p=0.010	1.73 (1.48, 2.03) p<0.001
Adjusted hazard ratio	-	1.48 (1.25, 1.74) p<0.001	1.78 (0.92, 3.44) p=0.085	1.49 (1.27, 1.75) p<0.001

[1]Adjusted for gender, age.

[2] Restricted to subjects with at least 6 months of follow-up time who did not have a history of lymphoma or a lymphoma in the first six months.

Incidence and relative risk (hazard) of NHL in psoriasis patients compared to controls

Variable	Control	Mild psoriasis	Severe psoriasis	All psoriasis
Mean follow-up time (median, 25th, 75th percentile)	5.61 (5.25, 2.18, 9.13)	4.51 (3.81, 1.65, 7.09)	5.77 (5.53, 2.70, 8.96)	4.54 (3.84, 1.67, 7.16)
Person years (n)	4,298,107	672,168	23,061	695,230
New NHL (n)	759	159	4	163
Incidence per 10,000 person years (95% CI)	1.77 (1.64, 1.90)	2.37 (2.01, 2.76)	1.73 (0.47, 4.44)	2.35 (2.00, 2.73)
Primary analysis				
Unadjusted hazard ratio	-	1.33 (1.12, 1.58) p=0.001	0.99 (0.37, 2.63) p=0.980	1.32 (1.11, 1.56) p=0.001
Adjusted hazard ratio	-	1.15 (0.97, 1.37) p=0.103	0.73 (0.28, 1.96) p=0.539	1.14 (0.96, 1.35) p=0.134
Sensitivity analysis				
New NHL (n)	581	128	4	132
Unadjusted hazard ratio	-	1.47 (1.21, 1.78) p<0.001	1.29 (0.48, 3.45) p=0.612	1.47 (1.21, 1.77) p<0.001
Adjusted hazard ratio	-	1.27 (1.05, 1.54) p=0.015	0.96 (0.36, 2.57) p=0.939	1.26 (1.04, 1.52) p=0.018

CI, confidence interval; NHL, non-Hodgkin's lymphoma.

[1] Adjusted for gender, age.

[2] Restricted to subjects with at least 6 months of follow-up time who did not have a history of lymphoma or a lymphoma in the first six months.

Incidence and relative risk (hazard) of HL in psoriasis patients compared to controls

Variable	Control	Mild psoriasis	Severe psoriasis	All psoriasis
Mean follow-up time (median, 25th, 75th percentile)	5.61 (5.25, 2.19, 9.13	4.51 (3.81, 1.65, 7.10)	5.77 (5.52, 2.70, 8.96)	4.54 (3.85, 1.67, 7.16)
Person years (n)	4,299,128	672,418	23,063	695,482
New Hodgkin's lymphoma (n)	160	39	3	42
Incidence per 10,000 person years (95% CI)	0.37 (0.32, 0.44)	0.58 (0.41, 0.79)	1.30 (0.27, 3.80)	0.60 (0.44, 0.82)
Primary analysis				
Unadjusted hazard ratio	-	1.48 (1.04, 2.10) p=0.029	3.50 (1.12, 10.96) p=0.032	1.54 (1.10, 2.17) p=0.012
Adjusted hazard ratio[1]	-	1.42 (1.00, 2.02) p=0.052	3.18 (1.01, 9.97) p=0.048	1.48 (1.05, 2.08) p=0.025
Attributable risk (excess number of lymphoma cases related to psoriasis)				1.8/100,000 per year
Sensitivity analysis[2]				
New HL (n)	98	24	1	25
Unadjusted hazard ratio	-	1.58 (1.01, 2.47) p0.045	1.91 (0.27, 13.68) P=0.521	1.59 (1.03, 2.47) P=0.038

Adjusted hazard ratio[1]	-	1.53 (0.98, 2.40) P=0.063	1.79 (0.25, 12.90) P=0.561	1.54 (0.99, 2.40) P=0.055

Hl, Hodgkin's lymphoma; CTCL cutaneous T-cell lymphoma.

[1]Adjusted for gender, age.

[2]Restricted to subjects with at least 6 months of follow-up time who did not have a history of lymphoma or a lymphoma in the first 6 months.

Incidence and relative risk (hazard) of cutaneous T-cell lymphoma in psoriasis patients compared to controls

Variable	**Control**	**Mild psoriasis**	**Severe psoriasis**	**All psoriasis**
Mean follow-up time (median, 25th, 75th percentile	5.61 (5.25, 2.19, 9.13)	4.51 (3.81, 1.65, 7.10)	5.77 (5.53, 2.70, 8.96)	4.54 (3.85, 1.67, 7.16)
Person years (n)	4,299,563	672, 383	23,054	695,437
New CTCL (n)	51	39	4	43
Incidence per 10,000 person years (95% CI)	0.12 (0.09, 0.16	0.58 (0.41, 0.79)	1.74 (0.47, 4.44)	0.62 (0.45, 0.83)
Primary analysis				
Unadjusted hazard ratio	-	4.78 (3.15, 7.27) p<0.001	14.60 (5.28, 4.40 p<0.001	5.08 (3.38, 7.64) p<0.001
Adjusted hazard ratio	-	4.10 (2.70, 6.23) p<0.001	10.75 (3.89, 29.76) p<0.001	4.34 (2.89, 6.52) p<0.001
Attributable risk (excess number of lymphoma cases related to psoriasis)				4.0/100,000 per year

Sensitivity analysis				
New CTCL (n)	32	31	4	35
Unadjusted hazard ratio	-	6.37 (3.88, 10.46) p<0.001	23.21 (8.21, 65.62) p<0.001	6.89 (4.26, 11.15) p<0.001
Adjusted hazard ratio	-	5.42 (3.30, 8.89) p<0.001	17.18 (6.17, 48.58) p<0.001	5.84 (3.61, 9.44) p<0.001

Author's conclusion: psoriasis is associated with an increased risk of lymphoma. The strongest association is for Hodgkin's lymphoma and cutaneous T-cell lymphoma. Although patients with psoriasis have an increased relative risk of lymphoma, the absolute risk attributable to psoriasis is low as lymphoma is a rare disease and the magnitude of association is modest.

H.5.26 CANCER

Reference	Study type	Number of patients	Patient characteristics	Prognostic factors	Length of follow-up	Outcome measures	Source of funding
Olsen (1992) Malignant tumours in patients with psoriasis Ref ID: OLSEN199	**Observational:** population-based cohort discharged from hospital in Denmark between 1977 to 1987 **Representative population sample:** yes	N: 6910 patients with psoriasis.	**Inclusion criteria:** all discharge records for 1977 through 1987 that included a diagnosis of psoriasis and similar conditions (ICD-8: 696) **Exclusion criteria:** not reported.	National Hospital Discharge Register for discharged psoriasis patients were linked to the Danish Central Population Register which has information on all	On average 5.1 years. Maximum follow-up was 11 years.	Incidence of cancers.	Not reported

2	**Prognostic factor adequately measured:** yes **Confounders adjusted for:** Stratified by age and matched on sex and calendar time **Attrition bias:** not reported **Outcomes adequately measured:** yes **Appropriate statistical analysis:** not multivariable/regression			Danish resident and information on date of emigration or death was obtained. The study cohort was linked to the Danish Cancer Registry. Matched on sex and year of birth at random from the cancer registry files.			
Effect size: **Observed (Obs) and expected (Exp) incidence of cancers among 6917 patients with a diagnosis of psoriasis included in their hospital discharge record, 1977-1987**							

Site	Obs	Exp	RR*	95% CI
All malignant neoplasms	401	296.4	1.35	1.22-1.49
Buccal cavity and pharynx	9	5.8	1.5	0.8-2.8
Oesophagus	1	2.6	0.4	0.0-1.92
Stomach	14	11.6	1.2	0.7-2.0
Colon	34	25.1	1.4	1.0-1.9
Rectum	12	14.4	0.8	0.4-1.5
Liver (primary)	4	3.0	1.3	0.4-3.2
Biliary tract	4	3.1	1.3	0.4-3.1
Pancreas	14	9.5	1.5	0.8-2.5
Larynx	7	3.0	2.4	1.0-4.6
Lung	58	40.6	1.4	1.1-1.8
Breast	24	28.3	0.9	0.5-1.3
Cervix uteri	2	5.6	0.4	0.1-1.2
Corpus uteri	7	7.4	1.0	0.4-1.9
Ovary	7	6.8	1.0	0.5-2.0
Prostate	24	18.4	1.3	0.8-1.9
Testis	1	1.6	0.6	0.0-3.1
Kidney	14	8.2	1.7	1.0-2.8
Bladder	17	16.8	1.0	0.6-1.6

Melanoma of skin	7	5.7	1.2	0.5-2.4
Other skin cancers	04	37.9	2.5	2.0-3.0
Brain and nervous system	5	6.2	0.8	0.3-1.8
Thyroid	1	1.2	0.9	0.0-4.1
Non-Hodgkin's lymphoma	8	5.6	1.4	0.7-2.7
Hodgkin's disease	1	1.0	1.0	0.1-4.9
Multiple myeloma	1	3.0	0.3	0.0-1.6
Leukaemia	8	6.8	1.2	0.5-2.2
Other specified sites	10	9.4	1.4	0.8-2.3
Secondary and unspecified sites	13	7.8	1.3	0.7-2.3

Sex-specific relative risks (RR) for cancers at selected sites among patients with psoriasis

Site	**Men**				**Women**			
	Obs	**Exp**	**RR**	**95% CI**	**Obs**	**Exp**	**RR**	**95% CI**
All malignant neoplasms	226	156.2	1.45	1.26-1.65	175	140.0	1.25	1.07-1.45
Melanoma of skin	0	2.5	-		7	3.2	2.2	1.0-4.3
Other skin cancers	55	20.8	2.6	2.0-3.4	39	17.0	2.3	1.6-3.1
Lung	42	30.3	1.4	1.0-1.9	16	10.3	1.6	0.9-2.5

Larynx	7	2.5	2.8	1.2-5.5	0	0.5	-	
Pharynx	4	1.0	3.9	1.2-9.3	0	0.4	-	
Pancreas	7	4.9	1.4	0.6-2.8	7	4.6	1.5	0.7-3.0
Colon	13	11.6	1.1	0.6-1.9	21	13.4	1.6	1.0-2.4
Kidney	6	4.7	1.3	0.5-2.7	8	3.5	2.3	1.1-4.4

Age-specific relative risks (RR) for nonmelanoma skin, lung and urinary bladder cancer among 7603 patients with psoriasis, 1977-1987

Age group (year)	**Nonmelanoma skin cancer**		**Lung cancer**		**Bladder cancer**	
	No.	**RR**	**No.**	**RR**	**No.**	**RR**
All ages	94	2.5	58	1.4	17	1.0
Up to 29	0	-	0	-	0	-
30-39	8	11.9	1	7.4	0	-
40-49	11	6.0	1	1.0	0	-
50-59	18	3.9	7	1.2	1	0.5
60-69	10	1.0	22	1.5	3	0.6
70-79	32	2.6	24	1.6	9	1.4
>/=80	15	1.9	4	0.9	4	1.4

Author's conclusion: the effect of cigarette smoking on the risk for noncutaneous cancer could not be assessed. Antipsoriatic treatment such as ionizing radiation and oral arsenicals must be considered as a possible cause of colon cancer**.**

H.5.27 CANCER

Reference	Study type	Number of patients	Patient characteristics	Prognostic factors	Length of follow-up	Outcome measures	Source of funding
Ji (2009) Cancer risk in hospitalised psoriasis patients: a follow-up study in Sweden Ref ID: JI2009	**Observational:** cohort study **Representative population sample:** yes **Prognostic factor adequately measured:** yes **Confounders adjusted for:** Rates standardised by age, gender, period, socioeconomic status and residential area. **Attrition bias:** not reported	N: 15858	**Inclusion criteria:** hospitalised one or more times for psoriasis. **Exclusion criteria:** not reported.	Using the Swedish Hospital Discharge Register and linking with the cancer registry. Psoriasis patients were retrieved from the registry according to ICD codes. The cancer registry used a four digit code according to ICD-7 to identify tumours. Additional linking to national census to obtain individual occupational status,	Median follow-up 10 years, range 0 to 40 years. **Note**: follow-up ended after diagnosis of cancer, death, emigration or closing date (31st December 2004), whichever came first.	Incidence of cancer	Supported by Deutsche Krebshilfe, the Swedish cancer society, the Eu, LSHC-CT-2004-503465 and the Swedish council for working life and social research

	Outcomes adequately measured: yes **Appropriate statistical analysis:** not multivariable/regression			national registry of causes of death to identify date of death, and emigration Registry to get date of emigration.			

Effect size:

Standardised incidence ratios (SIRs) for subsequent cancer in patients with hospitalised psoriasis by follow-up time

	Follow-up interval (years)															
	1-4				**5-9**				**>/=10**				**All 1+**			
Cancer site	**O**	**SIR**	**95% CI**		**O**	**SIR**	**95% CI**		**O**	**SIR**	**95% CI**		**O**	**SIR**	**95% CI**	
Upper aerodigestive tract	15	**2.38**	1.33	3.93	12	1.91	0.98	3.35	21	**1.79**	1.11	2.74	48	**1.97**	1.46	2.62
Oesophagus	10	**4.30**	2.05	7.94	6	2.52	0.91	5.52	12	**2.54**	1.31	4.45	28	**2.97**	1.97	4.30
Stomach	16	1.62	0.92	2.64	10	1.07	0.51	1.98	26	**1.57**	1.02	2.30	58	**1.45**	1.08	1.91
Colon	22	1.11	0.69	1.68	27	1.34	0.88	1.95	33	0.83	0.57	1.16	22	1.03	0.82	1.27
Rectum	13	1.16	0.61	1.98	17	1.49	0.87	2.40	24	1.05	0.67	1.56	54	1.18	0.89	1.55

Liver	15	**1.94**	1.08	3.21	13	1.71	0.91	2.93	29	**2.08**	1.39	2.99	57	**1.95**	1.47	2.52
Pancreas	15	**2.00**	1.12	3.31	6	0.82	0.29	1.80	20	1.49	0.91	2.30	41	**1.45**	1.04	1.97
Lung	42	**1.99**	1.43	2.69	37	**1.73**	1.22	2.38	71	**1.71**	1.33	2.15	150	**1.78**	1.51	2.09
Breast	35	1.02	0.71	1.42	42	1.22	0.88	1.65	85	1.15	0.91	1.42	162	1.13	0.97	1.32
Cervix	4	1.11	0.29	2.87	4	1.15	0.30	2.97	11	1.63	0.81	2.93	19	1.38	0.83	2.15
Endometrium	12	1.56	0.80	2.73	10	1.30	0.62	2.41	8	0.53	0.23	1.05	30	0.98	0.66	1.41
Ovary	8	1.27	0.54	2.52	5	0.82	0.26	1.93	8	0.68	0.29	1.35	21	0.87	0.54	1.33
Prostate	44	1.12	0.82	1.51	38	0.92	0.65	1.27	96	1.03	0.84	1.26	178	1.03	0.88	1.19
Kidney	18	**2.27**	1.34	3.59	9	1.16	0.53	2.21	18	1.25	0.74	1.99	45	**1.50**	1.09	2.00
Urinary bladder	20	1.52	0.93	2.36	18	1.35	0.80	2.13	43	**1.58**	1.14	2.13	81	**1.51**	1.20	1.88
Melanoma	9	1.05	0.47	2.00	5	0.56	0.18	1.32	21	1.09	0.67	1.67	35	0.95	0.66	1.32
Skin, squamous cell	26	**2.56**	1.67	3.76	25	**2.35**	1.52	3.47	40	**1.74**	1.24	2.37	91	**2.08**	1.67	2.55
Nervous system	7	0.89	0.35	1.84	8	1.03	0.44	2.03	29	**1.90**	1.27	2.73	44	**1.42**	1.03	1.91
Endocrine glands	4	0.83	0.22	2.16	7	1.46	0.58	3.02	16	1.71	0.98	2.78	27	1.42	0.94	2.08
Non-Hodgkin lymphoma	27	**2.44**	1.61	3.55	9	0.79	0.36	1.51	24	1.03	0.66	1.54	60	**1.31**	1.00	1.69
Leukemia	9	1.91	0.86	3.63	10	**2.15**	1.02	3.96	8	0.89	0.38	1.77	27	1.47	0.97	2.14

All	401	**1.54**	1.39	1.70	333	**1.26**	1.13	1.41	674	**1.26**	1.17	1.36	1408	**1.33**	1.26	1.40

Bold type, 95% confidence interval (CI) does not include 1.00; underline type, 99% CI does not include 1.00

Standardised incidence ratios (SIRs) for subsequent cancer in psoriasis patients by number of hospitalisations

	Number of hospitalisations						
	1		**2-3**		**>/=4**		
Cancer site	**O**	**SIR**	**O**	**SIRs**	**O**	**SIRs**	**Trend test p-value**
Upper aerodigestive tract	33	**2.18**	9	1.51	6	1.85	0.49
Oesophagus	6	1.03	13	**5.59**	9	**6.97**	**0.01**
Stomach	33	**1.48**	13	1.50	6	1.23	0.75
Colon	54	1.08	18	0.92	10	0.96	0.53
Rectum	35	1.23	12	1.08	7	1.18	0.88
Liver	33	**1.81**	17	**2.38**	7	1.81	0.72
Pancreas	21	1.19	7	1.02	13	**3.52**	0.06
Lung	92	**1.75**	37	**1.79**	21	**1.89**	0.78
Breast	104	1.10	41	1.23	17	1.13	0.66
Cervix	11	1.18	6	1.89	2	1.50	0.52
Endometrium	21	1.05	7	0.98	2	0.59	0.50

Ovary	11	0.69	6	1.07	4	1.59	0.12
Prostate	105	1.00	49	1.14	24	0.97	0.85
Kidney	28	1.48	10	1.38	7	1.81	0.76
Urinary bladder	51	**1.54**	16	1.21	14	**1.93**	0.74
Melanoma	24	1.00	8	0.92	3	0.73	0.62
Skin, squamous cell	34	1.26	29	**2.67**	18	**4.76**	**0.01**
Nervous system	29	1.44	8	1.10	7	2.01	0.68
Endocrine glands	16	1.30	6	1.35	5	2.31	0.31
Non-Hodgkin lymphoma	35	1.22	15	1.36	10	1.72	0.31
Leukaemia	15	1.29	9	2.04	3	1.32	0.60
All	835	**1.25**	358	**1.4**	215	**1.61**	**0.01**

Bold type, 95% CI does not include 1.00; underline type, 99% CI does not include 1.00.

Author's conclusion: a significant excess was noted for squamous cell skin cancer and for cancers of the upper aerodigestive tract, oesophagus, stomach, liver, pancreas, lung, kidney, and bladder as well as non-Hodgkin lymphoma. Many of these reflect the effects of alcohol drinking and tobacco smoking. Patients with multiple hospitalisations showed high risk, particularly for oesophageal and skin cancers.

H.5.28 CANCER

Reference	Study type	Number	Patient characteristics	Prognostic factors	Length of follow-	Outcome	Source

		of patients			up	measures	of funding
Hannuksela-Svahn (2000) Psoriasis, its treatment, and cancer in a cohort of Finnish patients Ref ID: HANNUKSELA-SVAHN2000	**Observational:** retrospective cohort study with nested case-control discharged patients in Finland 1973-1984 **Representative population sample:** yes **Prognostic factor adequately measured:** yes **Confounders adjusted for:**. Stratified by sex and age. **Attrition bias:** not reported. **Outcomes adequately measured:** yes	N: 5687	**Inclusion criteria:** all those hospitalised with a diagnosis of psoriasis in the Finnish Hospital Discharge register between 1973 and 1987. **Exclusion criteria:** those not found in the population central register due to an error in the personal identification code in the hospital discharge register;	Hospital patients from the Finnish hospital discharge register which was linked to the Population central register using personal identification codes. linked to the Finnish Cancer Registry. Dates of death and emigration obtained from the population central register .	Mean length of follow-up 14 years.	Incidence of cancers.	supported by the Finnish Psoriasis Association and the University of Oulu.

	Appropriate statistical analysis: not multivariable/regression						

Effect size:

Number of patients with psoriasis under follow-up and number of person-years at risk in 1973-95, by sex and age

	Men		**Women**	
Age	**No ***	**Person years**	**No***	**Person years**
0-14	94	407	198	836
15-29	600	4591	629	7374
30-44	918	12559	419	8767
45-59	860	13165	534	6836
60-74	544	3919	573	8159
>/=76	116	3044	202	3921
Total	3132	41685	2555	35893

***age at the beginning of follow-up**

Observed and expected numbers of cancer and standardised incidence ratios (SIR) with 95% CI among 5687 Finnish patients with psoriasis in 1997-95, by site

Primary site	**Obs**	**Exp**	**SIR**	**95% CI**

All sites	533	425.8	1.3	1.2-1.4
Mouth	1	1.6	0.7	0.0-3.6
Pharynx	3	2.2	1.3	0.3-3.9
Oesophagus	7	5.7	1.2	0.5-2.5
Stomach	34	30.8	1.1	0.8-1.5
Colon	20	23.5	0.9	0.5-1.3
Liver	11	5.9	1.9	0.9-3.3
Pancreas	26	17.2	1.5	1.0-2.2
Larynx	12	4.2	2.9	1.5-5.0
Lung, bronchus	101	68.0	1.5	1.2-1.8
Breast	37	43.4	0.9	0.6-1.2
Kidney and renal pelvis	12	15.1	0.8	0.4-1.4
Bladder, urethra, and urethra	25	17.8	1.4	0.9-2.1
Skin melanoma	8	10.3	0.8	0.3-1.6
Non-melanoma skin ca*	40	12.4	3.2	2.3-4.4
Nervous system	14	12.7	1.1	0.6-1.9
Non-Hodgkin’s lymphoma	21	9.6	2.2	1.4-3.4

Hodgkin's disease	8	2.5	3.3	1.4-6.4

*Excludes basal cell carcinoma: obs. 98; exp 81.1; SIR, 1.2; 95%CI 1.0-1.5.

Author's conclusion: an increased total incidence of cancer was found among the psoriasis patients, mainly attributable to squamous cell skin carcinoma, non-Hodgkin's lymphoma, and Hodgkin's lymphomas well as laryngeal cancer. The patients in the study were likely to have more severe psoriasis than in general because they needed dermatological consultation, which may result in potent therapies. The results are not necessarily applicable to all patients with psoriasis.

H.5.29 CANCER

Reference	Study type	Number of patients	Patient characteristics	Prognostic factors	Length of follow-up	Outcome measures	Source of funding
Brauchli (2009) Psoriasis and risk of incident cancer: an inception cohort study with a nested case-control analysis Ref ID:	**Observational:** population-based inception cohort study with a nested case-control analysis **Representative population sample:** yes used the GPRD **Prognostic factor adequately measured:**	N: 67,761 patients (33,760 with psoriasis and 34,001 psoriasis-free patients.	**Inclusion criteria: all patients with a first-time diagnosis of psoriasis between 1st January 1994 and 31st December 2005. A comparison group of the same number without psoriasis.** **Exclusion criteria:** history of cancer (except nonmelanoma skin cancer) or HIV. Patients	Patients in the GPRD were matched with non-psoriasis patients. The non-psoriasis patients were matched by calendar time, age (same year of birth), sex, general practice, and years of history in the GPRD.	Mean follow-up 4.6 years. Maximum 11 years. **Note**: followed up until a first-time diagnosis of cancer (malignant or in situ, other than nonmelanoma skin cancer); death; end of follow-up in	Incidence of cancer	Funded by an unrestricted grant from Merck Serono International. The first author was supported by a grant from the Senglet

BRAUCHLI 2009	yes **Confounders adjusted for:** Patients were stratified by type of cancer, duration of psoriasis, and treatment. Treatment further classified into amount of topical prescriptions and oral prescriptions. **Attrition bias:** not reported **Outcomes adequately measured:** yes **Appropriate statistical analysis:** not multivariable/regression		with <3 years of history In the database before first-time psoriasis diagnosis (or the corresponding date in the comparison group)	All patients had a recorded code using on a computer-based algorithm and a computer profile review.	the medical record; or end of the follow-up period.		Foundation, Switzerland.
Effect size: **Cancer incidence rates stratified by cancer type in patients with or without psoriasis**							

	Non-psoriasis			Psoriasis		
	Cases	**IR/1,000 py**	**95% CI**	**Cases**	**IR/1,000 py**	**95% CI**
All cancer	776	5.18	4.83-5.55	927	5.83	5.47-6.22
Lymphohematopoietic malignancies	62	0.41	0.32-0.53	119	0.75	0.63-0.90
Lymphohematopoietic malignancies (excluding CTCL)	62	0.41	0.34-0.53	111	0.70	0.58-0.84
CTCL	0	NA	NA	8	0.05	0.03-0.10
Lymphoma overall	36	0.24	0.17-0.33	67	0.42	0.33-0.54
Lymphoma (excluding CTCL)	36	0.24	0.17-0.33	59	0.37	0.29-0.48
Leukemia/MD	26	0.17	0.12-0.25	52	0.33	0.25-0.43
Lung	101	0.67	0.55-0.82	85	0.53	0.43-0.66
Melanoma	33	0.22	0.16-0.31	29	0.18	0.13-0.26
Breast	130	1.71	1.45-2.02	153	1.79	1.53-2.10
Prostate	95	1.38	1.13-1.69	85	1.16	0.93-1.43
Digestive organs	107	0.71	0.59-0.86	159	1.00	0.86-1.17
Pancreas	12	0.08	0.05-0.14	28	0.18	0.12-0.25
Oesophagus	16	0.11	0.07-0.17	23	0.14	0.10-0.22
Colorectal	55	0.37	0.28-0.48	79	0.50	0.40-0.62

Others	24	0.16	0.11-0.24	29	0.18	0.13-0.26
Female genital organs	35	0.43	0.31-0.60	51	0.60	0.45-0.79
Bladder/kidney	43	0.29	0.21-0.39	57	0.36	0.28-0.46
Brain	16	0.11	0.07-0.17	22	0.14	0.09-0.21
Other cancers	97	0.65	0.53-0.79	126	0.79	0.67-0.94
Metastasis	48	0.32	0.24-0.42	41	0.26	0.19-0.35

Incidence rate ratios (IRRs) of cancer, stratified by type, sex, and age (reference group: patients without psoriasis)

Type	**Overall IRR (95% CI)**	**Men IRR (95% CI)**	**Women IRR (95% CI)**	**<60 years IRR (95% CI)**	**>/=60 years IRR (95% CI)**
All cancer	1.13 (1.02-1.24)	1.11 (0.97-1.28)	1.14 (1.00-1.30)	1.19 (0.99-1.43)	1.13 (1.02-1.27)
Lympho-hematopoietic malignancies	1.81 (1.35-2.42)	2.45 (1.67-3.59)	1.24 (0.79-1.94)	2.17 (1.25-3.78)	1.74 (1.24-2.45)
Excluding CTCL	1.69 (1.25-2.27)	2.23 (1.50-3.31)	1.21 (0.77-1.9)	1.98 (1.12-3.52)	1.64 (1.16-2.32)
Lymphoma overall	1.76 (1.19-2.58)	2.15 (1.27-3.63)	1.40 (0.79-2.48)	2.38 (1.19-4.75)	1.59 (1.00-2.53)
Lymphoma (excluding CTCL)	1.55 (1.03-2.31)	1.76 (1.01-3.08)	1.35 (0.76-2.41)	2.07 (1.00-4.28)	1.41 (0.87-2.28)
Leukemia/MD	1.89 (1.21-2.94)	2.88 (1.65-5.05)	1.02 (0.49-2.11)	1.86 (0.74-4.69)	1.95 (1.18-3.23)
Lung	0.79 (0.60-1.06)	0.80 (0.56-1.13)	0.78 (0.48-1.29)	0.74 (0.35-1.58)	0.83 (0.61-1.13)
Melanoma	0.83 (0.50-1.36)	0.73 (0.36-1.46)	0.95 (0.46-1.94)	0.83 (0.43-1.60)	0.84 (0.39-1.80)

Breast	1.04 (0.83-1.31)	NA	1.04 (0.83-1.31)	0.98 (0.68-1.40)	1.11 (0.82-1.49)
Prostate	0.84 (0.63-1.12)	0.84 (0.63-1.12)	NA	0.76 (0.32-1.83)	0.88 (0.65-1.20)
Digestive organs	1.40 (1.10-1.78)	1.25 (0.91-1.71)	1.64 (1.14-2.38)	1.80 (1.00-3.25)	1.38 (1.06-1.79)
Pancreas	2.20 (1.18-4.09)	2.43 (0.97-6.13)	2.03 (0.88-4.69)	NA	2.11 (1.12-3.99)
Oesophagus	1.36 (0.72-2.54)	1.40 (0.64-3.08)	1.27 (0.44-3.61)	2.48 (0.76-8.09)	1.13 (0.54-2.36)
Colorectal	1.35 (0.97-1.90)	1.30 (0.82-2.05)	1.42 (0.86-2.36)	1.21 (0.53-2.74)	1.43 (0.99-2.07)
Others	1.14 (0.67-1.95)	0.80 (0.42-1.52)	2.85 (1.07-7.59)	2.79 (0.70-11.17)	1.02 (0.57-1.83)
Female genital organs	1.38 (0.91-2.11)	NA	1.38 (0.91-2.11)	1.93 (1.04-3.59)	1.06 (0.60-1.90)
Bladder/kidney	1.25 (0.84-1.85)	1.11 (0.70-1.76)	1.71 (0.81-3.59)	0.78 (0.24-2.53)	1.37 (0.90-2.08)
Brain	1.30 (0.69-2.45)	1.74 (0.72-4.18)	0.95 (0.38-2.39)	1.70 (0.66-4.41)	1.07 (0.46-2.52)
Other cancers	1.23 (0.94-1.59)	1.14 (0.77-1.67)	1.31 (0.91-1.88)	1.06 (0.68-1.67)	1.35 (0.98-1.87)
Metastasis	0.81 (0.53-1.22)	1.25 (0.64-2.42)	0.60 (0.35-1.03	1.49 (0.50-4.42)	0.75 (0.48-1.17)

Author's conclusion: the findings suggest that patients with psoriasis seem to be at an increased risk of developing certain cancers, especially those with a long psoriasis duration and possibly severe disease.

H.5.30 CANCER

Reference	Study type	Number of patients	Patient characteristics	Prognostic factors	Length of follow-up	Outcome measures	Source of

							funding
Frentz (1999) Malignant tumours and psoriasis: a follow-up study Ref ID: FRENTZ1999	**Observational:** prospective cohort study of patients discharged from Danish hospital between 1977 and 1993. **Representative population sample:** yes **Prognostic factor adequately measured:** yes **Confounders adjusted for:** Stratified for age and sex **Attrition bias:** not reported **Outcomes adequately measured:** yes **Appropriate statistical analysis:** not	N: 6905 patients	**Inclusion criteria:** patients discharged from a Danish hospital during 1977-87 with a diagnosis of psoriasis. **Exclusion criteria:** those whose identity was questionable.	Psoriasis patients followed up in the Danish Cancer registry which has notified cases of NMSC and other cancers according to ICD-0.. Cohort matched against the central population register for updating information on vital status and migration.	9.3 years (range 0-17 years) **Note**: follow-up ended at date of emigration, date of death or 31st December 1993, whichever occurred first.	Incidence of cancers.	Grants from the Danish Psoriasis Association, Leo pharmaceuticals and the Aage Bang Foundation.

	multivariable/regression Notes: only 62% of the patients had psoriasis as the primary diagnosis (admitted to hospital for treatment of psoriasis)						

Effect size:

Standardised incidence ratios (SIRs) for cancer in 6905 patients with psoriasis discharged from hospital, 1977-87 and followed up for cancer through 1993

	Men		**Women**		**Both sexes**			
Site	**Obs**	**SIR**	**Obs**	**SIR**	**Obs**	**Exp**	**SIR**	**95% CI**
All malignant neoplasms	**421**	**1.44**	**374**	**1.36**	**795**	**566.1**	**1.40**	**1.21-1.51**
Melanoma of skin	**4**	**0.8**	**12**	**1.8**	**16**	**12.1**	**1.3**	**0.8-2.1**
Non-melanoma skin cancer (190)	**101**	**2.36**	**95**	**2.58**	**196**	**79.6**	**2.46**	**2.13-2.83**
Sites other than skin	**316**	**1.30**	**267**	**1.16**	**583**	**474.4**	**1.23**	
Oral cavity	**18**	**2.3**	**1**	**0.3**	**19**	**11.0**	**1.7**	**1.0-2.7**

Pharynx	**8**	**4.1**	**0**	**0.0**	**8**	**2.7**	**2.9**	**1.3-5.8**
Stomach	**13**	**1.2**	**9**	**1.3**	**22**	**18/0**	**1.2**	**0.8-1.8**
Colon	**25**	**1.2**	**35**	**1.4**	**60**	**46.8**	**1.3**	**1.0-1.6**
Rectum	**18**	**1.2**	**6**	**0.6**	**24**	**25.8**	**0.9**	**0.6-1.4**
Larynx	**11**	**2.4**	**0**	**0.0**	**11**	**5.5**	**2.0**	**1.0-3.6**
Lung	**78**	**1.5**	**35**	**1.6**	**113**	**73.4**	**1.5**	**1.3-1.9**
Breast	**1**	**2.2**	**53**	**0.9**	**54**	**46.8**	**1.0**	**0.7-1.2**
Kidney	**10**	**1.1**	**8**	**1.2**	**18**	**15.3**	**1.2**	**0.7-1.9**
Bladder	**29**	**1.1**	**5**	**0.6**	**34**	**34.1**	**1.0**	**0.7-1.4**
Connective tissue	**2**	**2.2**	**3**	**4.4**	**5**	**1.6**	**3.2**	**1.0-7.4**
Non-Hodgkin's lymphoma	**10**	**1.6**	**6**	**1.1**	**16**	**11.7**	**1.4**	**0.8-2.2**
Leukaemia	**7**	**0.9**	**5**	**0.9**	**12**	**13.0**	**0.9**	**0.5-1.6**
Mycosis fungoides	**2**	**10.8**	**2**	**25.4**	**4**	**0.3**	**15.1**	**4.1-38**
Other specified sites **Secondary and unspecified sites**	**14**	**1.3**	**29**	**2.5**	**43**	**23.0**	**1.9**	

Standardised incidence ratios (SIRs) for selected cancer sites by time since first known discharge from hospital with a diagnosis of psoriasis

	Time since first known discharge (years							
	<1		1.4		5-9		>/=10	
Sex: cancer site	Obs	SIR	Obs	SIR	Obs	SIR	Obs	SIR
Both sexes								
Non-melanoma skin cancer	18	2.6	48	1.8	74	2.6	56	2.6
Lung	12	1.6	34	1.3	47	1.8	20	1.5
Bladder	3	0.9	11	0.9	16	1.3	4	0.6
Colon	4	0.8	19	1.1	24	1.5	13	1.5
Mycosis fungoides	2	75.2	2	21.0	0	0	0	0.0
Men								
Larynx	2	4.1	2	1.2	5	3.2	2	2.5
Pharynx	0	0.0	4	5.7	2	2.8	2	5.4
Oral cavity	1	1.2	9	3.2	3	1.1	5	3.5

Standardised incidence ratios (SIRs) for subtypes of skin cancer by gender and by age during follow-up, 1978-93.

	Basal cell carcinoma	Squamous cell carcinoma

	Men		Women		Men		women	
	Obs	SIR	Obs	SIR	Obs	SIR	Obs	SIR
20-29	0	0.0	2	15.9	0	0.0	0	0.0
30-39	2	3.7	8	10.6	1	51.6	0	0.0
40-49	7	3.3	12	5.7	4	29.3	1	11.6
50-59	15	3.2	11	2.7	7	13.9	2	10.4
60-69	15	1.5	14	1.7	3	2.0	3	4.8
70-79	24	2.2	19	2.0	8	2.8	6	5.3
80	9	1.8	8	1.2	5	2.3	5	3.2
All age groups	72	2.16	74	2.33	28	3.86	17	4.7

Standardised incidence ratios (SIRs) for basal cell carcinoma in patients discharged from hospital with a diagnosis of psoriasis

	Total				Men		Women	
Body site	Obs (%)	Exp (%)	SIR	95% CI	Obs	SIR	Obs	SIR
Lip	1 (<1)	0.9 (1)	1.1	0.0-6.0	0	-	1	1.9
Eyelid	2 (1)	2.5 (4)	0.8	0.1-2.9	1	0.8	1	0.8
External ear	5 (3)	1.6 (2)	3.2	1.0-7.4	3	2.3	2	6.8
Face	41 (28)	19.9 (31)	2.1	1.5-2.8	20	2.0	21	2.1
Scalp/neck	8 (5)	3.0 (5)	2.7	1.1-6.2	3	2.1	5	3.2
Trunk	22 (15)	5.6 (7)	4.0	2.5-6.0	8	3.9	14	5.1

Arm/shoulder	**2 (1)**	**1.1 (2)**	**1.8**	**0.2-6.5**	**1**	**1.7**	**1**	**1.9**
Leg/hip	**3 (2)**	**1.2 (2)**	**2.4**	**0.5-7.1**	**3**	**6.8**	**0**	**-**
Multiple	**58 (40)**	**9.8 (15)**	**5.9**	**4.5-7.7**	**30**	**5.7**	**28**	**6.1**
Not otherwise specified	**4 (3)**	**0.7 (1)**	**5.4**	**1.4-13.7**	**3**	**8.1**	**1**	**2.7**
total	**146 (100)**	**65.1 (100)**	**2.24**	**1.9-2.6**	**72**	**2.16**	**74**	**2.33**

Standardised incidence ratios (SIRs) for squamous cell carcinoma in patients discharged from hospital with a diagnosis of psoriasis

	Total				**Men**		**Women**	
Body site	**Obs (%)**	**Exp (%)**	**SIR**	**95% CI**	**Obs**	**SIR**	**Obs**	**SIR**
Lip	**1 (2)**	**0.4 (4)**	**2.6**	**0.0-14.5**	**1**	**3.15**	**0**	**-**
Eyelid	**0 (0)**	**0.3 (3)**	**-**	**-**	**0**	**-**	**0**	**-**
External ear	**4 (9)**	**1.7 (16)**	**2.4**	**0.6-6.1**	**4**	**2.7**	**0**	**-**
Face	**5 (11)**	**2.9 (27)**	**1.8**	**0.6-4.1**	**3**	**2.0**	**2**	**1.5**
Scalp/neck	**3 (7)**	**0.7 (6)**	**4.4**	**0.9-12.8**	**0**	**-**	**3**	**14.7**
Trunk	**3 (7)**	**0.5 (5)**	**5.6**	**1.1-16.4**	**2**	**7.6**	**1**	**3.7**
Arm/shoulder	**7 (16)**	**1.2 (11)**	**5.7**	**2.3-11.8**	**5**	**6.6**	**2**	**4.3**
Leg/hip	**10 (22)**	**0.6 (6)**	**18.0**	**8.6-33.1**	**5**	**19.4**	**5**	**16.8**
Multiple	**11 (24)**	**0.9 (8)**	**11.7**	**5.8-21.0**	**8**	**12.4**	**3**	**10.3**
Not otherwise	**1 (2)**	**0.2 (2)**	**4.0**	**0.1-22.3**	**0**	**-**	**1**	**8.2**

specified								
total	**45 (100)**	**10.9 (100)**	**4.14**	**3.0-5.5**	**28**	**3.86**	**17**	**4.69**

Author's conclusion: There is a significantly increased risk of cancer in psoriasis patients. When monitoring patients extensively treated for psoriasis, the pattern of cancer should be taken in to account.

H.5.31 DIABETES

Reference	Study type	Number of patients	Patient characteristics	Prognostic factors	Length of follow-up	Outcome measures	Source of funding
Brauchli (2008) Psoriasis and the risk of incident diabetes Ref ID: BRAUCHLI 2008	**Observational:** cohort study with nested case-control. **Representative population sample:** yes, used the GPRD **Prognostic factor adequately measured:**	N: 73404; psoriasis patients: 36702; psoriasis-free patients: 36702. After excluding those with prevalent DM, cancer or HIV populatio	**Inclusion criteria:** All patients with a first time diagnosis of psoriasis between 1st January 1994 and 31st December 2005; or matched comparison group. Cases with diabetes mellitus were included in the analyses if had a first-time diabetes mellitus code recorded plus at least one prescription for an antidiabetic drugs such as insulin, sulphonylureas, biguanides,	Matched comparison group on calendar time, age, sex, general practice and years of history in the GPRD.	Followed all patients until they developed a first time diagnosis of diabetes mellitus, died or follow-up in the medical record ended, whichever was first.	Incidence rate and incidence rate ratio.	Unconditional grant from Merck Serono International SA, Switzerland. One author was supported by a grant from the Senglet foundatio

	Confounders adjusted for:. Matched on calendar time (date of the psoriasis diagnosis), age (same year of birth), sex, general practice and years of history in the GPRD. Stratified by age and sex in the cohort study the nested case-control was adjusted for smoking status, BMI, hypertension, hyperlipidaemia, infections and use of systemic steroids. **Attrition bias:** not reported **Outcomes adequately measured:** yes **Appropriate statistical analysis:** No statistical analysis of confounders in the cohort study.	n was 65449 (32593 psoriasis patients and 32856 controls).	thiazolidinediones, acarbose, glinides or guar gum within 30 days prior to or at any time after the first diagnosis of diabetes. Also patients with a recorded diagnosis of diabetes who did not receive any drug treatment but who started on a diet were included. **Exclusion criteria:** prevalent diagnosis of diabetes mellitus as well as cancer or HIV prior to the psoriasis diagnosis (or the corresponding date in the comparison group). Also those who received antidiabetic drugs more than 30 days prior to the first recorded diagnosis of diabetes mellitus.				n, Switzerland.

Effect size:

	Person-years	Cases	IR per 1000 person-years (95%)	IRR (95% CI)
Psoriasis	154316.1	626	4.06 (3.75-4.39)	1.36 (1.20-1.53)
No psoriasis	145783.8	435	2.98 (2.92-3.28)	
Sex				
Male with psoriasis	71084.7	332	4.67 (4.20-5.20)	1.23 (1.04-1.44)
Male no psoriasis	66270.5	252	3.80 (3.36-4.30)	
Female with psoriasis	83231.3	294	3.53 (3.15-3.96)	1.53 (1.28-1.83)
Female no psoriasis	79513.4	183	2.30 (1.99-2.66)	
Age (years)				
0-29 psoriasis	40246.0	18	0.45 (0.28-0.71)	2.75 (1.24-6.13)
0-29 no psoriasis	36928.7	6	0.16 (0.07-0.35)	
30-59 psoriasis	70072.0	237	3.38 (2.98-3.84)	1.33 (1.09-1.61)
30-59 no psoriasis	65861.4	168	2.55 (2.19-2.97)	
60-79 psoriasis	37008.4	330	8.92 (8.01-9.93)	1.43 (1.21-1.69)
60-79 no psoriasis	36312.4	226	6.22 (5.47-7.09)	
80+ psoriasis	6989.7	41	5.87 (4.33-7.95)	1.12 (0.71-1.75)
80+ no psoriasis	6681.5	35	5.24 (3.77-7.28)	

Author's conclusion: The risk of incident diabetes mellitus was increased in the psoriasis patients compared to the psoriasis-free patients. The risk increased with psoriasis duration and severity and was not driven by BMI alone.

H.5.32 DEPRESSION

Reference	Study type	Number of patients	Patient characteristics	Prognostic factors	Length of follow-up	Outcome measures	Source of funding
Kurd (2010) The risk of depression, anxiety and suicidality in patients with psoriasis Ref ID: KURD2010	**Observational:** population-based cohort study from 1987 to 2002. **Representative population sample:** yes GPRD used **Prognostic factor adequately measured:** yes **Confounders adjusted**	N: 146042 with mild psoriasis; 3956 with severe psoriasis and 766950 non-psoriasis patients.	**Inclusion criteria:** all patients with a diagnostic code for psoriasis and 5 random controls with at least one day of observation time. Controls were seen in the same practice and had a date of observation within 60 days of the psoriasis patient's entry. **Exclusion criteria:** Fixed sample size of 150000 psoriasis and	Patient received a diagnostic code for psoriasis . Patients were defined as having incident depression, anxiety or suicidality by a corresponding diagnostic code occurring after the start of follow-up time. Created an algorithm. Severe psoriasis was defined by diagnosis	Not reported. **Note**: follow-up ended when both patients and controls when developed outcome of interest, transferred out of practice, or died or practice was not longer UTS.	Incidence of depression	Funded in part by a grant from the National Research Service Award from the National Institutes of Health, the Doris Duke Foundation, University of Pennsylvania Center for

	for: Adjusted for age, sex. Sensitivity analyses for treatment, diabetes, hypertension, hyperlipidaemia, cancer and BMI **Attrition bias:** not reported **Outcomes adequately measured:** yes **Appropriate statistical analysis:** yes cox proportional regression used.		765000 controls would have greater than 0.95 power to detect an effect size as small as 1.1, assuming baseline rates of 20, 15,and 5 per 1000 person-years for depression, anxiety and suicidality.	code for psoriasis and a code for systemic treatment modality.			Clinical Epidemiology and Biostatistics pharmacoepidemiology training grant and grant K23AR051125 from the National institute of arthritis and musculoskeletal and skin diseases. One author received grant support and is a consultant for Amgen, Centocor, Abbott, Genentech, Novartis and Pfizer.

Summary of baseline variables, follow-up time and incident outcomes by psoriasis severity

	Mild psoriasis			Severe psoriasis		
Variable	**Controls (n=746930; 81.44%)**	**Patients with mild psoriasis (n-146042; 15.94%)**	**P value**	**Controls (n=20020; 2.19%)**	**Patients with severe psoriasis (n=3956; 0.43%)**	**P value**
Male, sex. No. (%)	356669 (47.82)	69231 (47.40)	0.004	9569 (47.80)	1920 (48.53)	0.40
Age, median (IQR), year	33 (18-53)	40 (26-57)	0.001	34 (18-54)	48 (35-62)	0.001
History of depression, no. (%)	31984 (4.29)	14327 (9.81)	0.001	938 (4.69)	493 (12.46)	0.001
History of anxiety, no (%)	24152 (3.24)	10890 (7.46)		651 (3.25)	291 (7.36)	0.001
History of suicidality, no. (%)	2946 (0.39)	1041 (0.71)	0.001	76 (0.38)	40 (1.01)	0.001
Person-years, median (IQR)	5.24 (2.18-9.12)	6.18 (2.97-9.55)	0.001	5.62 (2.45-9.49)	7.59 (3.86-9.90)	0.001
Reason for censorship, no. (%)						
Death	39206 (5.26)	7334 (4.02)	0.001	1095 (5.47)	309 (7.81)	0.001
Practice no longer UTS	493810 (66.20)	108377 (74.21)	0.001	13143 (65.65)	3179 (80.36)	0.001
Transfer	212914 (28.54)	30331 (20.77)	0.001	5782 (28.88)	468 (11.83)	0.001
Unadjusted incidence rate per						

1000 person-years (95% CI)						
Depression	17.4 (17.3-17.6)	25.7 (25.3-26.1)	NA	17.0 (16.2-17.7)	31.8 (29.5-34.3)	NA
Anxiety	14.7 (14.6-14.9)	20.9 (20.6-21.3)	NA	14.5 (13.8-15.2)	20.8 (18.9-22.8)	NA
suicidality	0.66 (0.63-0.68)	0.93 (0.85-1.00)	NA	0.66 (0.52-0.82)	0.92 (0.57-1.41)	NA

Systemic psoriasis therapy

Systemic psoriasis therapy	**Patients with severe psoriasis, no. (%)**
Methotrexate	2284 (57.74)
Psoralen or phototherapy	680 (17.19)
Azathioprine	625 (16.48)
Ciclosporine	412 (10.14)
Etretinate or acitretin	351 (8.87)
Hydroxyurea	222 (5.61)
Mycophonlate mofetil	12 (0.30)

Effect size:

Hazard ratios (HRs) for depression, anxiety and suicidality by psoriasis severity

	Mild psoriasis		**Severe psoriasis**		**All psoriasis**	
Variable	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value
Depression						
Adjusted for age and sex	1.38 (1.35-1.40)	0.001	1.72 (1.5-1.88)	0.001	1.39 (1.37-1.41)	0.001
Sex interaction term	NS	0.81	1.21 (1.00-1.46)	0.05	NS	0.51
Age interaction term	0.99 (0.99-0.99)	0.001	0.98 (0.98-0.99)	0.001	0.99 (0.99-0.99)	0.001
Age, years		NA		NA		NA
20	1.81 (1.59-1.65)		F: 2.51 (2.11-2.98); M: 2.91 (2.39-3.54)		1.83 (1.78-1.87)	
40	1.45 (1.42-1.47)		F: 1.85 (1.65-2.08); M: 2.15 (1.84-2.51)		1.46 1.44-1.49)	
60	1.16 (1.13-1.19)		F; 1.37 (1.21-1.55); M: 1.59 (1.34-1.88)		1.17 (1.14-1.20)	
Anxiety						
Adjusted for age and sex	1.31 (1.29-1.34)	0.001	1.29 (1.15-1.43)	0.001	1.31 (1.29-1.34)	0.001
Sex interaction term	NS	0.91	NS	0.16	NS	0.73
Age interaction term	0.99 (0.99-0.99)	0.001	0.98 (0.98-0.99)	0.001	0.99 (0.99-0.99)	0.001
Age, years		NA		NA		NA

20	1.61 (1.56-1.65)		2.11 (1.75-2.55)		1.61 (1.57-1.66)	
40	1.37 (1.34-1.40)		1.49 (1.33-1.67)		1.37 (1.34-1.40)	
60	1.17 (1.14-1.19)		1.06 (0.93-1.20)		1.16 (1.13-1.19)	
Suicidality						
Adjusted for age and sex	1.44 (1.32-1.57)	0.001	1.51 (0.92-2.49)	0.10	1.44 (1.32-1.57)	0.001
Sex interaction term	NS	0.96	NS	0.77	NS	0.91
Age interaction term	0.99 (0.9-0.99)	0.001	NS	0.43	0.99 (0.98-0.99)	0.001
Age, years		NA		NA		NA
20	1.83 (1.64-2.05)				1.83 (1.64-2.05)	
40	1.38 (1.26-1.51)				1.38 (1.27-1.51)	
60	1.04 (0.90-1.19)				1.04 (0.91-1.20)	

Attributable risk of diagnosis of depression, anxiety and suicidality attributable to psoriasis

Variable	**Mild psoriasis**	**Severe psoriasis**	**All psoriasis**
Depression			
Attributable risk per 1000 person years	11.5	25.5	11.8
Anxiety			
Attributable risk per 1000 person	8.0	8.1	8.1

years			
Suicidality			
Attributable risk per 1000 person years	0.4	0.4	0.4

Author's conclusion: patients with psoriasis have an increased risk of depression, anxiety and suicidality.

H.5.33 Risk of mortality – mild versus severe psoriasis

Reference	Study type	Number of patients	Patient characteristics	Intervention	Length of follow-up	Outcome measures	Source of funding
Gelfand et al. (2007) The risk of mortality in patients with psoriasis Ref ID: GELFAND 2007	**Observational:** population-based cohort from 1987-2002 **Representative population sample:** yes used the GPRD. **Prognostic factor adequately measured:** yes **Confounders adjusted for:** age and sex Smoking, BMI, myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease, rheumatologic	N:133,568 mild psoriasis patients; 2951 with severe psoriasis and 560,358 and 15,075 controls	**Inclusion criteria:** all patients defined as having mild or severe psoriasis (according to the author's definitions) who were 18 years or older at the study start date and who had at least 1 day of observation time. Up to 5 controls were included who were 18 years or older at start date, matched on practice and start date in the practice. **Exclusion criteria:** None stated.	GPRD used. They either received a medical code consistent with the diagnosis or not. Severe psoriasis was based on history of having had systemic therapies.	Mean 4-5 years **Note**: study ended due to: death, end of up to standard or transfer out.	Risk of mortality.	Supported by an unrestricted grant to the trustees of the university of pennsylvania from Centocor and grant from the national institute of arthritis and musculoskeletal and skin diseases

	disease, peptic ulcer disease, mild liver disease, moderate or severe liver disease, diabetes mellitus, diabetes with chronic complications, hemiplegia or paraplegia, renal disease, malignant neoplasm, metastatic solid tumour, and AIDS were all recorded and used in one analysis only **Attrition bias:** **Outcomes adequately measured:** Yes **Appropriate statistical analysis:** yes						

Patient characteristics:

Characteristics	Mild psoriasis		Severe psoriasis	
	Controls	Patients	Controls	Patients
Sex, no (%)	261710 (46.7)	64004 (47.9)	7023 (46.6)	1921 (48.6)

Male	298648 (53.3)	69564 (52.1)	8052 (53.4)	2031(51.4)	
Female	45.3 (42.0; 29.2-59.5)	46.9 (44.8; 31.4-61.3)	45.9 (42.8; 29.8-60.3)	52.4 (52.3;38.7-65.8)	
Age, mean (media, IQR), year	NA	NA	NA		
Systemic therapies, no. (%)					
Methotrexate				2302 (58.3)	
Psoralen or phototherapy				662 (16.8)	
Azathioprine				651 (16.5)	
Ciclosporine				408 (10.3)	
Etretinate or acitretin				350 (8.9)	
Hydroexyurea				224 (5.7)	
Mycophenolate mofetil				11 (0.3)	
Follow-up, mean (median, IQR), y)	5.6 (5.2; 2.2-9.2)	4.5 (3.8; 1.6-7.1)	5.9 (5.6; 2.4-9.5)	3.6 (2.8; 1.3-5.3)	
Cumulative person-years	3147693	600902	88391	14203	
Deaths, no.	38258	7198	1064	303	
Incidence rate of mortality per 1000	12.2 (12.0-12.3)	12.0 (11.7-12.3)	12.0 (11.3-12.8)	21.3 (19.0-23.9)	

person-years (95% CI)				

Effect size:

Hazard ratio of mortality in patients with psoriasis HR (95% CI)

Age, years	All patients with psoriasis	Patients with mild psoriasis	Patients with severe psoriasis
All ages >/=18	1.0 (0.99-1.04)	1.0 (0.97-1.02)	1.5 (1.3-1.7)
35			2.5 (1.7-3.7)
45			2.2 (1.6-2.9)
55			1.9 (1.5-2.3)
65			1.6 (1.4-1.9)
75			1.4 (1.3-1.6)
85			1.3 (1.0-1.5)
95			1.1 (0.8-1.5)

*data adjusted for age and sex.

Attributable risk (AR) and excess risk of death in patients with severe psoriasis

Age group, years	Mortality rate per 1000 patient-years in severe psoriasis	AR, no. of deaths per 1000 patients-years	Excess risk, no. of exposed deaths

	control group		
All ages >/=18	12.0	6.0	1/166 patients per year
30-39	0.8	1.8	1/856 patients per year
40-49	2.0	2.3	1/440 patients per year
50-59	6.4	5.6	1/179 patients per year
60-69	20.1	12.9	1/78 patients per year
70-79	48.5	20.9	1/48 patients per year
80-89	106.7	26.7	1/38 patients per year

*data adjusted for age and sex.

Sensitivity analyses

Analysis	Mortality in severe psoriasis patients HR (95% CI)
Patients with psoriatic arthritis excluded from severe psoriasis group	1.5 (1.3-1.8)
Patients with rheumatologic diseases excluded from psoriasis group	1.5 (1.3-1.8)

Person-time starts with first diagnosis of psoriasis during UTS time	1.1 (1.0-1.3)
Start date for severe psoriasis control group matched to start date for severe psoriasis group	1.7 (1.5-2.0)
Severe psoriasis group restricted to patients who received methotrexate sodium	1.3 (1.1-1.5)
Severe psoriasis group excluding patients treated with methotrexate	1.9 (1.6-2.2)
Severe psoriasis group restricted to patients who had been prescribed an oral retinoid	1.8 (1.3-2.3)

Author's conclusion: Severe but not mild psoriasis is associated with an increased risk of death.