Appendix Q: Additional data

Q.1 Disease severity and impact assessment tools: summary of non-comparative data

Study	Population	Setting	N	Tool	Data/method of analysis				Conclusion/summary
					Internal consistency (Cronbach's α)	Intra-rater reliability	Inter-rater reliability	Sensitivity to change	
Severity									
Dommasch et al (2010)	Psoriasis	Secondary/tertiary care (USA)	140	BSA (PREPI method)	×	✓	✓	✓	• Adequate test-retest reliability (ICC = 0.99/0.98 for number of palms and categorised score) • Inter-rater reliability (self-estimated vs physician estimated): o Visit 1: number of palms (ICC = 0.82) / categorized score (ICC = 0.80) o Visit 2: number of palms (ICC=0.68) / categorized score (ICC = 0.71) • Adequate sensitivity to change: patient measure (AUC = 0.7-0.73); physician measure (AUC = 0.76-0.81) • Practicability: 2-3 mins to administer
Ramsay et al (1991)	Chronic plaque psoriasis	In-patients – Secondary/tertiary care	10	BSA (rule of nines)	×	✓	✓	×	• Acceptable intra-rater reliability (differences of 1-2%; p>0.05 ANOVA) • Poor inter-rater reliability (significantly different p<0.001

Study	Population	Setting	N	Tool	Data/method of analysis				Conclusion/summary
									ANOVA)
Yune et al (2003)	Psoriasis	Secondary/tertiary care (Korea)	30	BSA (visual grading)	×	×	✓	×	• Poor inter-rater reliability (statistically significantly different: p<0.05, Kruskal-Wallis test)
Berth-Jones et al (2008)	Chronic plaque psoriasis	Unclear	16	CoPSI	×	✓	✓	×	• Adequate test-retest reliability (ICC=0.95) • Adequate inter-rater reliability (ICC=0.83)
Kacar et al (2008)	Nail psoriasis	Secondary/tertiary care	45	NAPSI	×	×	✓	×	• Acceptable inter-rater reliability (r = 0.768)
Aktan et al (2007)	Nail psoriasis	Outpatient clinic – Secondary/tertiary care	25	NAPSI	×	×	✓	×	• Poor inter-rater reliability (ICC = 0.781)
Faria et al (2010)	Psoriasis	Ambulatory clinic	20	PASI	×	×	✓	×	• Adequate to acceptable inter-rater reliability (r = 0.729-0.817)
Feldman et al (1996)	Psoriasis	Hospital (USA)– Secondary/tertiary/ care	19	PASI	×	✓	×	×	• Adequate test-retest reliability (r = 0.91)
Berth-Jones et al (2008)	Chronic plaque psoriasis	Unclear	16	PASI	×	✓	✓	×	• Adequate test-retest reliability (ICC=0.96) • Adequate inter-rater reliability (ICC=0.91)
Kirby et al (2000)	Psoriasis	Secondary/tertiary care	20	PASI	×	×	✓	✓	• Acceptable inter-rater reliability (r = 0.71) • Adequate responsiveness (significant decrease in extent and psychosocial impact scores; p<0.0001)
Chandran et al	Psoriatic arthritis	Secondary/tertiary care	20	PASI, LS-PGA, PGA,	×	×	✓	×	• Inter-rater variation (rheumatologists vs

Study	Population	Setting	N	Tool	Data/method of analysis				Conclusion/summary
(2009)		(Canada)		BSA					dermatologists) poor for PASI, LS-PGA, PGA, BSA (0.2-0.8)
Langley et al (2004)	Psoriasis out-patients	Secondary/tertiary care (USA)	35	PASI, PGA, LS-PGA	✓	✓	✓	×	• Adequate internal consistency ($\alpha \geq 0.9$ for each) • Reliability: PGA and LS-PGA better than PASI • Intra-rater variation by ANOVA: PASI $\sigma = 2.5$; PGA $\sigma = 0.2$; LS-PGA $\sigma = 0.5$ • Inter-rater variation by ANOVA: PASI $\sigma = 8.8$; PGA $\sigma = 1.2$; LS-PGA $\sigma = 1.7$
Berth-Jones et al (2006)	Chronic plaque psoriasis	Secondary/tertiary care (UK)	16	PASI, PGA, LS-PGA	×	✓	✓	×	• Adequate intra-rater reliability for PASI (ICC = 0.94) and LS-PGA (ICC = 0.91); acceptable for PGA (ICC = 0.88) • Adequate inter-rater reliability for PASI (ICC = 0.90) and LS-PGA (ICC =0.84); acceptable for PGA (ICC = 0.75)
Berth-Jones et al (2008)	Chronic plaque psoriasis	Unclear	16	PGA	×	✓	✓	×	• Acceptable test-retest reliability (ICC=0.81) • Acceptable inter-rater reliability (ICC=0.61)
Farhi et al (2008)	Plaque psoriasis	Out-patient and phototherapy unit – Secondary/tertiary care	30	PGA (photographs)	×	✓	✓	×	• Acceptable intra-rater reliability (ICC = 0.84) • Acceptable inter-rater reliability (ICC = 0.80)
Fleischer et al (1996)	Psoriasis	Secondary/tertiary care	30	SAPASI	×	×	✓	×	• Adequate inter-rater reliability (97% agreement)

Study	Population	Setting	N	Tool	Data/method of analysis				Conclusion/summary
Feldman et al (1996)	Psoriasis	Hospital (USA)– Secondary/tertiary/ care	19	SAPASI	×	✓	✓ (40 body silhouettes)	×	• Adequate test-retest reliability (r = 0.82) • Adequate inter-rater reliability for BSA (ICC = 0.953)
Kirby et al (2000)	Psoriasis	Secondary/tertiary care	20	SPI	×	×	✓	×	• Adequate- adequate -acceptable inter-rater reliability (r = 0.997, 0.86 and 0.70 for the psychological impact, historical disease severity and extent scores)
Impact									
Shikiar et al (2006)	Moderate-to-severe plaque psoriasis	Clinical trial (multicentre – North America)	147	DLQI	✓	×	×	×	• Adequate internal consistency (α= 0.89 at baseline, 0.92 at end point)
Shikiar et al (2003)	Moderate-to-severe psoriasis	Secondary/tertiary care (North America)	1095	DLQI	✓	×	×	×	• Adequate internal consistency (α= 0.87 at baseline, 0.92 at end point)
McKenna et al (2003)	Psoriasis	Postal survey from hospital database	148	DLQI	✓	×	×	×	• Adequate internal consistency (α=0.88)
McKenna et al (2005)	Psoriasis	Hospital – Secondary/tertiary	72	DLQI	✓	✓	×	×	• Adequate internal consistency ($\alpha \geq 0.88$) • Acceptable test-retest reliability (r=0.80)
Morgan et al (1997)	Psoriasis (attending phototherapy unit)	Out-patients – Secondary/tertiary	41	DQOLS	×	✓	×	×	• Acceptable test-retest reliability (ICC = 0.84)
Nijsten et al (2006)	Psoriasis (first treated with PUVA)	University centres (USA)	792	IPSO	✓	×	×	×	• Adequate internal consistency for physical and psychological scales (0.85 and 0.73); acceptable for social scale (0.63)

Study	Population	Setting	N	Tool	Data/method of analysis				Conclusion/summary
Nijsten et al (2005)	Cutaneous psoriasis	Survey of US patients	1196	PDI	✓	×	×	✓	• Adequate internal consistency for subscales ($\alpha \geq 0.77$-0.81) • Large floor effects and sub-optimal response distributions
Gupta and Gupta (1995)	Psoriasis in-patients and out-patients	Secondary/tertiary care	217	PLSI	✓	×	×	×	• Adequate internal consistency (α= 0.90)
McKenna et al (2003)	Psoriasis	Postal survey from hospital database	148	PSORIQoL	✓	✓	×	×	• Acceptable test-retest reliability (ICC = 0.89) • Adequate internal consistency (α=0.94)
McKenna et al (2005)	Psoriasis	Hospital – Secondary/tertiary	72	PSORIQoL (US version)	✓	✓	×	×	• Adequate internal consistency ($\alpha \geq 0.88$) • Adequate test-retest reliability (Spearman's r = 0.90)

Q.2 Disease severity and impact assessment tools: summary of comparative data

Study	Population	Setting	N	Tool	Comparison	Data/method of analysis		Conclusion/summary
						Construct validity (correlation coefficient)	Sensitivity to change	
Severity compared with impact								
Shikiar et al (2006)	Moderate-to-severe plaque psoriasis	Clinical trial (multicentre – North America)	147	DLQI	PASI, PGA	×	✓	• Acceptable sensitivity to clinically meaningful change (r = 0.69 vs PASI and 0.71 vs PGA) • Significant difference in improvement on DLQI between responders (PASI75) and non-responders (<PASI50)
Shikiar et al (2003)	Moderate-to-severe psoriasis	Secondary/tertiary care (North America) Includes data from 2 separate studies	1095	DLQI	PASI, PGA	✓	✓	• Adequate divergent construct validity vs PASI (r = 0.20 and 0.25 at baseline; 0.51 and 0.59 at end point) • Poor sensitivity to change (r = 0.47 and 0.54 compared with PASI; 0.46 and 0.53 compared with PGA) • Significant difference in improvement on DLQI between responders (PASI75 or PASI50) and non-responders (<PASI50)
Sampogna et al (2004)	Psoriasis in-patients	Secondary/tertiary care (Italy)	786	DLQI, Skindex, IPSO, PDI, PLSI	PASI, Skindex symptoms scale	✓	×	• Poor correlation (adequate divergent construct validity) between: PASI and PLSI, PDI, DLQI, IPSO and Skindex; Skindex symptoms scale and PLSI, PDI, DLQI, IPSO.
Kirby et al (2001)	Psoriasis in-patients and out-patients	Hospital (UK)– Secondary/tertiary/ care	101	PDI	SAPASI, PASI, SPI	✓	×	• Adequate divergent construct validity (r = 0.50-0.52)
Kirby et al (2000)	Psoriasis	Secondary/tertiary care	100	PDI	PASI, SAPASI	✓	×	• Adequate divergent construct validity (r = 0.45 and 0.27 vs PASI and SAPASI, respectively)

Study	Population	Setting	N	Tool	Comparison	Data/method of analysis		Conclusion/summary
Finlay et al (1990)	Psoriasis in-patients and out-patients	Secondary/tertiary care	32	PDI	PASI	✓	×	• Adequate divergent construct validity (r = 0.40)
Kotrulja et al (2010)	50% psoriasis	Hospital – Secondary/tertiary care	140	PLSI	PASI	✓	×	• Adequate divergent construct validity (r = 0.30)
Dommasch et al (2010)	Psoriasis	Secondary/tertiary care (USA)	140	Skindex-29	BSA (PREPI method)	✓	×	• Adequate divergent construct validity (r = 0.59)
Shanker et al (2011)	Psoriasis	Secondary/tertiary care	34	PQOL-12	PASI	✓	×	• Adequate divergent construct validity (r = 0.422)
Kirby et al (2000)	Psoriasis	Secondary/tertiary care	100	SPI subscales	PASI, SAPASI, PDI	✓	×	• Adequate divergent construct validity (r = 0.59 and 0.28 psychological impact score vs PDI and PASI, respectively)
Severity								
Henseler and Schmitt-Rau (2008)	Moderate-to-severe chronic plaque psoriasis	Secondary/tertiary care (clinical trial)	33	BSA, PASI, SAPASI	BSA, PASI, SAPASI	✓	✓	• Adequate construct validity for all comparisons (r > 0.7) SAPASI vs PASI: r = 0.91 (p<0.0001) SAPASI vs BSA; r = 0.73 (p<0.0001) PASI vs BSA; r = 0.81 (p<0.0001) • Sensitivity to change: relative change SAPASI>PASI>BSA SAPASI = 70.6%; PASI = 67.3%; BSA = 48.6%
Berth-Jones et al (2008)	Chronic plaque psoriasis	Unclear	16	CoPSI	PASI, PGA	✓	×	• Adequate construct validity (r = 0.89 vs PASI and r = 0.75 vs PGA)
Shikiar et al (2006)	Moderate-to-severe plaque psoriasis	Clinical trial (multicentre – North America)	147	PASI	PGA	✓	✓	• Adequate construct validity (r = 0.83 at trial end point), but poor construct validity (r = 0.59) at baseline • Acceptable sensitivity to clinically

Study	Population	Setting	N	Tool	Comparison	Data/method of analysis		Conclusion/summary
								meaningful change (r = 0.75) Note: mean score reduction for PASI was 56.5% and for PGA was 39.1%
Kirby et al (2001)	Psoriasis in-patients and out-patients	Hospital (UK)– Secondary/tertiary/ care	101	PASI	SAPASI	✓	×	• Acceptable construct validity (r = 0.65)
Berth-Jones et al (2008)	Chronic plaque psoriasis	Unclear	16	PASI	PGA	✓	×	• Adequate construct validity (r = 0.75)
Robinson et al (2011)	Moderate to severe psoriasis	Secondary/tertiary care – receiving biologics	?	PASI	PGA	✓	×	• Adequate construct validity for correlation of PASI75 and PGA 0 or 1
Kirby et al (2000)	Psoriasis	Secondary/tertiary care	100	PASI	SAPASI	✓	×	• Poor construct validity (r = 0.54)
Sampogna et al (2004)	Psoriasis in-patients	Secondary/tertiary care (Italy)	786	PASI	SAPASI	✓	×	• Acceptable correlation between: SAPASI and PASI
Krenzer et al (2011)	Moderate to severe plaque psoriasis receiving efalizumab	Out-patient departments and dermatological practices	1787	PASI	BSA	✓	✓	• Poor to adequate construct validity (r = 0.450 at baseline; 0.694 at 3 months and 0.832 at 6 months) • Acceptable sensitivity to change (r= 0.771 after 3 months and 0.792 after 6 months)
Langley et al (2004)	Psoriasis out-patients	Secondary/tertiary care (USA)	35	PASI, PGA, LS-PGA	PASI, PGA, LS-PGA	✓	×	• Adequate construct validity for all comparisons (r > 0.8)
Berth-Jones et al (2006)	Chronic plaque psoriasis	Secondary/tertiary care (UK)	16	PASI, PGA, LS-PGA	PASI, PGA, LS-PGA	✓	×	• Adequate construct validity for all comparisons (r > 0.7): LS-PGA vs PASI: r = 0.92 LS-PGA vs PGA; r = 0.73 PGA vs PASI; r = 0.79
Farhi et al (2008)	Plaque psoriasis	Out-patient and phototherapy unit	30	PGA (photographs)	Clinical PGA	✓	×	• Acceptable construct validity (ICC = 0.64) • Adequate construct validity for mean

Study	Population	Setting	N	Tool	Comparison	Data/method of analysis		Conclusion/summary
		– Secondary/tertiary care						panel score (ICC = 0.87)
Iyatomi et al (2009)	Mild psoriasis vulgaris	Secondary/tertiary care	5	Photographs (computer quantification)	PASI	✓	×	• Adequate construct validity (r = 0.922) • Sensitivity = 72.1%; specificity = 97.4% (vs clinical assessment)
Sampogna et al (2003)	Psoriasis in-patients	Hospital (Italy)– Secondary/tertiary care	351	SAPASI	PASI	✓	×	• Acceptable construct validity (r = 0.69)
Fleischer et al (1999)	Psoriasis	Clinical trial – Secondary/tertiary care	182	SAPASI	PASI-equivalent	✓	✓	• Poor construct validity (r = 0.54 at baseline; r = 0.33 at endpoint) • SAPASI less sensitive to change (r=0.16): Decrease in severity 39% vs 62% for SAPASI and PASI respectively
Feldman et al (1996)	Psoriasis	Hospital (USA)– Secondary/tertiary/ care	80	SAPASI	PASI	✓	×	• Poor construct validity on first day: r = 0.58 • Adequate construct validity on second day: r = 0.70 • BSA determinations: Head: r = 0.62 (acceptable) Upper extremities r = 0.75 (adequate) Trunk: r = 0.73 (adequate) Lower extremities: r = 0.69 (acceptable) • Erythema, induration and scale scores: Erythema: r = 0.39 (poor) Induration: r = 0.24 (poor) Scale: r = 0.38 (poor)
Feldman et al (1996)	Psoriasis	Hospital (USA)– Secondary/tertiary/ care	30	SAPASI	PASI	×	✓	• Acceptable sensitivity to change (change in SAPASI vs change in PASI score (r = 0.63)

Study	Population	Setting	N	Tool	Comparison	Data/method of analysis		Conclusion/summary
Szepietowski et al (2001)	Psoriatic (40 psoriasis vulgaris, 11 PsA)	Unclear	51	SAPASI	PASI	✓	×	• Acceptable construct validity (r = 0.62)
Szepietowski et al (2001)	Psoriatic (40 psoriasis vulgaris, 11 PsA)	Unclear	51	SAPASI	SPI extent score	✓	×	• Acceptable construct validity (r = 0.62)
Fleischer et al (1994)	Psoriasis vulgaris	Secondary/tertiary care (USA)	42	SAPASI	PASI	×	✓	• Mean decrease in score: PASI = 7.3±5.7; SAPASI = 5.9±4.7 • Both showed significant improvements: PASI p<0.0003; SAPASI p<0.05
Impact								
Nichol et al (1996)	Psoriasis (upto 20% BSA)	Clinical trial (US multicentre)	644	DLQI	PDI	✓	×	• Adequate construct validity (r = 0.82)
McKenna et al (2003)	Psoriasis	Postal survey from hospital database	148	PSORIQoL	DLQI	✓	×	• Adequate construct validity (r = 0.70)
McKenna et al (2005)	Psoriasis	Hospital	72	PSORIQoL (US version)	DLQI	✓	×	• Adequate construct validity (r = 0.81)
Sampogna et al (2004)	Psoriasis in-patients	Secondary/tertiary care (Italy)	786	Skindex, IPSO, DLQI, PDI, PLSI	Skindex, IPSO, DLQI, PDI, PLSI	✓	×	• Acceptable correlation between: Skindex social function scale and PLSI; Skindex emotions scale and PLSI, PDI, DLQI; DLQI and PLSI; PDI and PLSI • Adequate correlation between: IPSO and PLSI, PDI and DLQI; DLQI and PDI; Skindex social functioning scale and PDI, DLQI, IPSO; Skindex emotions scale and IPSO
Kirby et al	Psoriasis	Secondary/tertiary	100	SPI subscales	PDI	✓	×	• Poor construct validity (r = 0.59 for

Study	Population	Setting	N	Tool	Comparison	Data/method of analysis		Conclusion/summary
(2000)		care						psychological impact score vs PDI)

Q.3 Quality assessment for disease severity and impact tool validity and reliability studies

Q.3.1 Internal consistency reliability – single measurement, multiple people

Study	Same measurement procedure	Same measuring instrument	Same environmental conditions: (e.g. lighting) and same location	Appropriate statistical analysis	Applicability – analysis method (dichotomised/categorised appropriately/continuous? Who is testing/setting/experience)	Quality
Gupta and Gupta (1995)	✓ - patient self-rating	✓	?	✓	✓	High
Langley et al (2004)	✓	✓	✓	✓	Range of severities No medications used during the study Raters given 30 minute training sessions	High
McKenna et al (2003)	✓ - patient self-rating	✓	×	✓	✓	High
McKenna et al (2005)	✓ - patient self-rating	✓	×	✓	✓	High
Nijsten et al (2005)	✓ - patient self-rating	✓	×	✓	Psoriasis survey (any severity but n PsA) Categorical rating scale Excluded patients with missing items	High

Study	Same measurement procedure	Same measuring instrument	Same environmental conditions: (e.g. lighting) and same location	Appropriate statistical analysis	Applicability – analysis method (dichotomised/categorised appropriately/continuous? Who is testing/setting/experience)	Quality
Nijsten et al (2006)	✓ - patient self-rating	✓	×	✓	PUVA cohort Ordinal rating scale Excluded patients with missing items	High
Shikiar et al (2003)	✓	✓	×	✓	Trial of efalizumab vs placebo	High
Shikiar et al (2006)	✓	✓	×	✓	Trial of adalimumab vs placebo	High

Q.3.2 Intra-rater reliability

Study	Same measurement procedure	Same observer and same measuring instrument	Same environmental conditions: (e.g. Lighting) and the same location	Time between measurements not too long (<1 week)	Appropriate statistics – not correlation	Applicability – analysis method Rater/setting/experience)	Quality
Berth-Jones et al (2006)	✓	✓	✓	✓	✓	✓	High
Berth-Jones et al (2008)	✓	✓	✓	✓	✓	✓	High
Dommasch et al (2010)	✓	✓	× - home and clinic	✓	✓	✓ Self-administered (categorised and continuous assessed)	Moderate
Farhi et al (2008)	✓	✓	?	NA - 1 month but same set of photographs	✓	✓	Moderate
Feldman et al (1996)	✓	✓	?	✓	×	✓	Low

Study	Same measurement procedure	Same observer and same measuring instrument	Same environmental conditions: (e.g. Lighting) and the same location	Time between measurements not too long (<1 week)	Appropriate statistics – not correlation	Applicability – analysis method Rater/setting/experience)	Quality
Kirby et al (2000)	✓	✓	✓	✓	×	?	Moderate
Langley et al (2004)	✓	✓	✓	✓	× ANOVA	Range of severities No medications used during the study Raters given 30 minute training sessions Spearman's coefficient	Moderate
McKenna et al (2003)	✓	✓	? completed by postal survey	× 2 weeks	×	✓	Very low
McKenna et al (2005)	✓	✓	? completed by postal survey	× 2 weeks	✓	✓	Very low
Morgan et al. (1997)	✓	✓	?	× 7-10 days	✓	Out-patients attending for phototherapy	Very low
Ramsay et al (1991)	✓	✓	? – likely because in-patients	✓ - recall bias minimised by randomising order of assessment of body areas	× - simple agreement	In-patients Assessed by 3 dermatologists and 1 dermatology specialist nurse Continuous	Low

Q.3.3 Inter-rater reliability

Study	Number of raters	Randomisation of raters to patients (including order of raters)	Blinding of raters results to results of other raters	Time between measurements not too long (<1 week)	Appropriate statistics – not correlation	Applicability – analysis method Rater/setting/experience)	Quality
Aktan et al (2007)	3	?	✓	✓ - also same conditions and well illuminated	✓	Dermatology out-pt clinic Dermatologists – reviewed NAPSI paper Continuous	Moderate
Berth-Jones et al (2006)	14	✓	✓	✓	✓	14 physicians chosen to represent a range of experience – all received detailed training Ordinal scores treated as continuous variables	High
Berth-Jones et al (2008)	14	✓	✓	✓	✓	14 physicians chosen to represent a range of experience – all received detailed training Ordinal scores treated as continuous variables	High
Farhi et al (2008)	5	×	✓	✓	✓	Experienced raters Unclear if continuous	Moderate
Faria et al (2010)	3	×	✓	✓	✓ but only pairwise ICC (not for all 3 raters combined)	Post-graduate dermatology students Psoriasis ambulatory clinic	Moderate
Feldman et al (1996)	5	NA	✓	NA	✓	Dermatologists and psychologists	High
Fleischer et al (1996)	2	NA	?	NA	× - simple agreement	A priori categorisation	Low
Kacar et al (2008)	2	× - same order	?	✓ - same day and same conditions	× - Pearson's correlation coefficient	?	Very low

Study	Number of raters	Randomisation of raters to patients (including order of raters)	Blinding of raters results to results of other raters	Time between measurements not too long (<1 week)	Appropriate statistics – not correlation	Applicability – analysis method Rater/setting/experience)	Quality
Kirby et al (2000)	6	?	?	✓	×	6 trained raters	Low
Langley et al (2004)	17	✓	✓	✓	× ANOVA	Range of severities No medications used during the study Raters given 30 minute training sessions	Moderate

Q.3.4 Construct validity/sensitivity to change

Study	Time between measurements not too long (<1 week)	Test order randomised	Both tests conducted in each patient	Tests conducted by the same raters (or raters randomised to tests and blinded to other raters results)	Applicability – analysis method and rater/setting/experience)	Quality
Berth-Jones et al (2006)	✓	✓	✓	✓	✓ - categorising defined a priori 14 dermatologists with a range of experience (all trained) Ordinal scores treated as continuous variables	High
Berth-Jones et al (2008)	✓	✓	✓	✓	✓ - categorising defined a priori 14 dermatologists with range of experience (all trained) Ordinal scores treated as continuous variables	High

Study	Time between measurements not too long (<1 week)	Test order randomised	Both tests conducted in each patient	Tests conducted by the same raters (or raters randomised to tests and blinded to other raters results)	Applicability – analysis method and rater/setting/experience)	Quality
Dommasch et al (2010)	✓	NA for physician vs self-administered tests	✓	✓ - patient and physician blinded	Dermatology department	High
Farhi et al (2008)	✓	×	✓	× photos by 5 raters and clinical PGA by one	Photo – 5 senior dermatologists with experience	Low
Feldman et al (1996)	✓	NA for physician vs self-administered tests	✓	✓ Physician blind to patient rating	Experienced raters Continuous	High
Finlay et al (1990)	✓	NA for physician vs self-administered tests	✓	× - patient and physician not blinded	Dermatology in and out-patients Continuous	Low
Fleischer et al (1994)	✓	NA for physician vs self-administered tests	✓	✓ Physician blind to patient rating	Dermatology in and out-patients Continuous	High
Fleischer et al (1999)	✓	NA for physician vs self-administered tests	✓	✓ Physician blind to patient rating	Dermatology in and out-patients Continuous	High
Henseler and Schmitt-Rau (2008)	✓	NA for physician vs self-administered tests	✓	× - patient and physician not blinded	Treated group – efalizumab Outpatient Transformation of continuous scales to map onto each other stated	Low
Iyatomi et al (2009)	?	×	✓	×	3 treated with CSA and 2 with UVB	Very low
Kirby et al	✓	? NA for physician vs	✓ - SAPASI in only 72%	✓	Spearman's correlation coefficient Method unclear	High (PASI vs SAPASI; SPI vs

Study	Time between measurements not too long (<1 week)	Test order randomised	Both tests conducted in each patient	Tests conducted by the same raters (or raters randomised to tests and blinded to other raters results)	Applicability – analysis method and rater/setting/experience)	Quality
(2000)		self-administered test comparisons			Experienced clinicians	SAPASI; PDI vs PASI) Moderate (PASI vs SPI; PDI vs SAPASI)
Kirby et al (2001)	? probably same day	? NA for physician vs self-administered test comparisons	✓	× One of 3 raters – not randomised	Spearman's coefficient Method unclear Experienced clinicians	High (PASI vs SAPASI; SPI vs SAPASI; PDI vs PASI) Moderate (PASI vs SPI; PDI vs SAPASI) Moderate (PASI vs SPI; PDI vs SAPASI)
Kotrulja et al (2010)	✓	NA for physician vs self-administered tests	✓	? unclear if patients and investigators blinded to results of other test	PASI and PLSI categorised a priori	Moderate
Krenzer et al (2011)	✓	×	✓	?	Continuous Pearson's correlations Experience unclear	Moderate
Langley et al (2004)	✓	×	✓	✓	Range of severities No medications used during the study Raters given 30 minute training sessions Spearman's coefficient	Moderate
McKenna et al (2003)	? completed at home so could vary	×	?	✓	Method unclear Self-administered	Low
Nichol et al	✓	?	✓	✓	Pearson coefficients	Moderate

Study	Time between measurements not too long (<1 week)	Test order randomised	Both tests conducted in each patient	Tests conducted by the same raters (or raters randomised to tests and blinded to other raters results)	Applicability – analysis method and rater/setting/experience)	Quality
(1996)					Scales expressed as a percentage of maximum disability	
Robinson et al (2012)	✓	?	✓	?	Pearson coefficients Dichotomised outcomes	Moderate
Sampogna et al (2003)	✓	NA for physician vs self-administered tests	✓	? unclear if patients and investigators blinded to results of other test (one self-administered and one physician administered)	Baseline data from in-patient wards of dermatology hospital Pearson coefficient Continuous	Moderate
Sampogna et al (2004)	✓	NA for physician vs self-administered tests	✓	? unclear if patients and investigators blinded to results of other test (one self-administered and one physician administered)	Baseline data from in-patient wards of dermatology hospital Pearson coefficient Continuous	Moderate
Shankar et al (2011)	✓	NA for physician vs self-administered tests	✓	?	Continuous	Moderate
Shikiar et al (2003)	✓	NA for physician vs self-administered tests	✓	✓	Continuous and dichotomised (pre-specified) Data from trial of efalizumab vs placebo	High
Shikiar et al (2006)	✓	NA for physician vs self-administered tests	✓	✓	Continuous and dichotomised (pre-specified) Data from trial of adalimumab vs placebo	High
Szepietowski et al (2001)	?	NA for physician vs self-administered tests	✓	? unclear if patients blinded to initial PASI score	Spearman rank correlation	Low

Q.4 Interpreting post-test probabilities by considering prevalence/pre-test probability

Predictive values or post-test probabilities address the chances of a person having a particular diagnosis given the known test result. However, the values are only accurate for a population with similar prevalence to the population tested because the prevalence of disease in the population can have a large effect on the calculated predictive value. Therefore, the predictive values are not independent of prevalence and are not intrinsic to the test itself.

Consequently, it is necessary to consider the prevalence when interpreting the positive and negative predictive values. In this report, the modified positive and negative predictive values have been calculated, which represent the value-added predictive figures:

Value-added PPV = PPV – prevalence

Value-added NPV = NPV – (1 – prevalence)

These figures convey the additional certainty of the diagnosis that is contributed by a positive or negative test result over the starting probability of a diagnosis (the prevalence in the sample). However, it is important to bear in mind that if there is only a small amount of uncertainty in the diagnosis before the test a small absolute increase in certainty may be important for diagnostic decisions.

Below is a summary matrix to aid interpretation of these values when the post-test probability is high, which superficially suggests a high diagnostic accuracy. Note that if the PPV or NPV is low then the test is unlikely to be useful as it will be unable to accurately discriminate a positive from a negative diagnosis in the majority of cases.

Table 1: Interpreting high post-test probabilities

Prevalence (pre-test probability)	Post-test probability (predictive values)	
	PPV high	NPV high
High	Little value added: limited additional certainty in the diagnosis and so uncertain in the discriminative ability of the test (accurately detected those with disease but there was a large proportion of positives in the sample)	Large value added: considerable additional certainty in the negative diagnosis and so high value of the test (accurately detected those without disease from a small total number of negatives)
Low	Large value added: considerable additional certainty in the positive diagnosis and so high value of the test (accurately detected those with disease from a small total number of positives)	Little value added: limited additional certainty in the diagnosis and so limited value of the test (accurately detected those with disease but there was a large proportion of negatives in the sample)

Q.5 Skin cancer – PUVA dose classification

Stern 1984A

Time to tumour (months)	Time to follow-up interview (months)	PUVA exposure (number of treatments)*		
		Low	Medium	High
22-27	24	<80	80-99	>99
28-39	35	<100	100-119	>119
40-57	47	<100	100-139	>139
58-69	60	<120	120-159	>159
>69	70	<120	120-159	>159

**Average dose of UVA to body is 11 joules/cm^2 per treatment*

Stern 1994

Time to tumour (months)	Time to follow-up interview (years)	PUVA exposure (number of treatments)*		
		Low	Medium	High
0-27	2	<80	80-99	>99
28-39	3	<100	100-119	>119
40-57	4	<100	100-139	>139
58-69	5	<120	120-159	>159
70-96	6	<120	120-159	>159
94-136	10	<140	140-239	>239
>136	13	<160	160-299	>299

**Average dose of UVA to body is 11 joules/cm^2 per treatment*

Stern 1990 and 2002

Time to tumour (months)	Time to follow-up interview (months)	PUVA exposure (number of treatments)*		
		Low	Medium	High
0-27	24	<80	80-99	>99
28-39	35	<100	100-119	>119
40-57	47	<100	100-139	>139
58-69	60	<120	120-159	>159
70-96	70	<120	120-159	>159
>96	121	<140	140-239	>239

**Average dose of UVA to body is 11 joules/cm^2 per treatment*

Q.6 Skin cancer – absolute risk estimates

Study	N with psoriasis	Follow-up time	Outcome	Relative risk estimate	Absolute risk estimate
PUVA					
STERN 1979	1380	2.1 years (1976-1979)	BCC SCC	IRR: 2.63 (1.91-3.90)	30 patients had one or more cutaneous carcinomas (11.4 expected) Total observed: 29 SCC in 18 patients; 19 BCC in 15 patients **NOTE: 39 patients had a history of cutaneous carcinoma before PUVA (17% SCC and 83% BCC)**
STERN 1984A	1380	5.7 years	BCC SCC	**Population rates** BCC 2.2 (1.6-2.9) SCC 16.2 (13.0-19.9) **Person counts** BCC 1.7 (1.2-2.3) SCC 9.3 (6.9-12.2)	Numbers observed (at least 22 months after exposure and only counting one tumour of a given type each year): 89 SCC and 43 BCC (51 patients compared with 5.1 expected) Total observed: 169 SCC in 54 patients; 74 BCC in 50 patients
STERN 1988A	1380	Mean >10 years	SCC	**PUVA dose** / **All pts with *first* tumour ≥58 months after first treatment** **RR** / **95% CI** <160: 4.2 / 2.6-6.4 160-199: 22.2 / 10.6-40.9 200-259: 32.1 / 18.7-51.4 260+: 50.1 / 24.9-89.5 **Total: *9.5* / *7.2-12.3***	**Treatments** / **All pts with *first* tumour ≥58 months after first treatment (number of tumours)** <160: 21 (49) 160-199: 10 (29) 200-259: 17 (52) 260+: 11 (28) **Total: 59 (158)** ⇒ **3.8% increased 10 year risk of SCC** ⇒ **1 excess SCC per 261 people per year**
			BCC	**PUVA** / **All pts with first tumour ≥58 dose months after first treatment (number of tumours)** **RR** / **95% CI** <160: 1.3 / 0.8-1.9	**Treatments** / **All pts with first tumour ≥58 months after first treatment (number of tumours)** <160: 26 (45) 160-199: 7 (11) 200-259: 13 (22)

Study	N with psoriasis	Follow-up time	Outcome	Relative risk estimate	Absolute risk estimate
				160-199 3.0 1.2-6.3 200-259 4.8 3.5-6.5 260+ 6.9 3.2-13.1 **Total *2.1* *1.6-2.7***	260+ 9 (19) **Total 55 (97)**
STERN 1990	1380	12.3 years	Genital SCC	**SMR (95% CI)** **Invasive SCC of penis and scrotum** *95.7 (43.8-181.8)* **Invasive and in situ penile tumours** *58.8 (26.9-111.7)* **Invasive SCC of scrotum** *131.6* (42.7-307.1)	Numbers observed: 30 genital tumours in 14 patients *21 in 10 patients* *19 in 8 patients* 9 in 5 patients
STERN 2002	1380	>20 years	Invasive genital SCC	**Population counts** *SMR: 134.6 (89.5-194.6)* **Person counts** *SMR: 81.7 (52.1-122.6)*	Numbers observed: 28 incident events 17 person counts
STERN 1994	1380	13.2 years	BCC	**PUVA dose** **N** **SMR (95% CI)** **Population counts (one or more tumour/year = an incident event)** Low 114 3.6 (3.0-4.3) Medium 28 2.9 (2.0-4.2) High 75 6.0 (4.8-7.5) *Total 217 4.1 (3.5-4.7)* **Person counts (only the first tumour of a given type is counted)** Low 66 2.1 (1.6-2.7) Medium 19 1.9 (1.2-3.0) High 45 3.8 (2.8-5.1)	Numbers observed: 341 BCCs in 130 patients Population counts: 217 incidence cases of BCC

Study	N with psoriasis	Follow-up time	Outcome	Relative risk estimate			Absolute risk estimate
				Total	*130*	*2.5 (2.1-3.0)*	
			SCC	**PUVA dose**	**N**	**SMR (95% CI)**	Numbers observed: 618 SCCs in 144 patients; Population counts: 326 incident cases of SCC ⇨ 12 expected (314 excess in 1380 people over 13.2 years) ⇨ 1723.8 excess per 100000 person years (1 excess per 58 people per year)
				Population counts (occurrence of one or more tumours of a given type in a given year = an incident event)			
				Low	80	10.6 (8.5-13.2)	
				Medium	51	23.6 (18.0-31.1)	
				High	195	83.0 (72.1-95.5)	
				Total	*326*	*27.0 (24.2-30.1)*	
				Person counts (only the first tumour of a given type is counted)			
				Low	38	5.0 (3.6-6.9)	
				Medium	29	13.4 (9.3-19.3)	
				High	77	32.8 (26.2-41.0)	
				Total	*144*	*11.9 (10.1-14.0)*	

Study	N with psoriasis	Follow-up time	Outcome	Relative risk estimate	Absolute risk estimate
STERN 1998A			SCC BCC	**Total PUVA treatments to 1986** / SCC / **RR** / **95% CI** <100 / 5.1 / 3.5-7.2 100-159 / 8.4 / 5.6-12.1 160-336 / 26.5 / 22.2-31.4 ≥337 / 68.5 / 54.9-84.5 *All dosages* / *17.6* / *15.6-19.8* **Total PUVA treatments to 1986** / BCC / **RR** / **95% CI** <100 / 1.7 / 1.2-2.3 100-159 / 3.9 / 3.0-5.0 160-336 / 4.5 / 3.5-5.7 ≥337 / 11.7 / 9.3-14.5 *All dosages* / *4.1* / *3.7-4.6*	**Exposure** / **Number of patients with cancers developing after 1985 (% in each dose strata)** **Total** / **SCC** / **BCC** **PUVA treatments up to 1986** <100 / 435 (37%) / 18 (13%) / 29 (19%) 100-159 / 243 (21%) / 15 (11%) / 30 (20%) 160-336 / 373 (32%) / 68 (50%) / 58 (38%) ≥337 / 132 (11%) / 34 (25%) / 34 (23%) Total / 1183 / 135 / 151 **Increase in 10-year risk of SCC** <100 / **1.7%** 100-159 / **2.7%** 160-336 / **8.8 %** ≥337 / **12.7%**
NIJSTEN 2003A	1380	>20 years	SCC and BCC	At 25 years post-PUVA vs age matched Arizona population: SCC = 25-times the risk (250-times risk if more than 400 treatments) BCC = 50-times risk if more than 500 treatments	**SCC** 2147 invasive SCC in 303 patients Incidence of SCC (age-adjusted) has increased over the 25 years of the study: **Average incidence rate = 77 per 1000 person years** **Incidence rate at 25 years follow-up = approximately 200 per 1000 person years** **BCC** 1363 BCC in 294 persons Average incidence has increased substantially over the last 10 y of the

Study	N with psoriasis	Follow-up time	Outcome	Relative risk estimate	Absolute risk estimate
					study : **Average incidence rate = 44 per 1000 person years** **Incidence rate at 25 years follow-up = approximately 125 per 1000 person years** *Among patients with 200 or more PUVA exposures approximately half will develop at least one SCC and approximately one third at least one BCC within 25 years of reaching this dose level*
LIM2005	1380	28 years	SCC	**IRR (95% CI)** No. UVB treatments <300[e] 1 ≥300 1.37 1.03–1.83 No. treatments <100[e] 1 100–199 2.36 1.51–3.68 200–299 4.14 2.64–6.50 300–399 5.54 3.38–9.09 400–499 11.05 6.88–17.76 ≥500 10.81 6.76–17.29	

	Person years (%)	Number of tumours (%)	Tumour incidence per 100,000 person years	Number of incident tumours (%)	Incident tumour incidence per 100,000 person years
UVB					
Low (<300)	20,921 (74.9)	1538 (60.8)	7351	696 (63.0)	3327
High (≥300)	7007 (25.1)	990 (39.2)	14,129	408 (37.0)	5823
PUVA					
Low (<100)	11,922 (42.7)	197 (7.8)	1652	118 (10.7)	990
Not low (≥100)	16,006 (57.3)	2331 (92.2)	14,563	986 (89.3)	6160

Study	N with psoriasis	Follow-up time	Outcome	Relative risk estimate	Absolute risk estimate
			BCC	**IRR (95% CI)** No. UVB treatments <300[e] 1 ≥300 1.45 1.07–1.96 No. treatments <100[e] 1 100–199 1.80 1.21–2.70 200–299 2.00 1.32–3.03 300–399 2.81 1.75–4.51 400–499 2.93 1.73–4.98 ≥500 3.65 2.21–6.03	**Variable** / **Person years (%)** / **Number of tumours (%)** / **Tumour incidence per 100,000 person years** / **Number of incident tumours (%)** / **Incident tumour incidence per 100,000 person years** UVB Low (<300) 20,921 (74.9) 880 (56.2) 4206 511 (61.8) 2443 High (≥300) 7007 (25.1) 686 (43.8) 9790 316 (38.2) 4510 PUVA Low (<100) 11,922 (42.7) 256 (16.3) 2147 148 (17.9) 1241 Not low (≥100) 16,006 (57.3) 1310 (83.7) 8184 679 (82.1) 4242
STERN 2001	1380	Mean 22.4 years	Melanoma		**Study period** **All melanoma** **Observed** **Incidence (per 1000 pers. years)** 1975 to 1990 4 0.22 1991 to 29/2/96 10 2.47 29/2/96 to end 11 6.00 All years 25 1.04
Stern 1997	1380	20 years	Invasive melanoma	**RR (95% CI)** <250 treatments 1.3 (0.4-3.1) ≥250 treatments 5.5 (2.0-12.0) **All patients 2.3 (1.1-4.1)**	**Number of invasive melanomas** **Observed** **Expected** <250 treatments 5 3.7 ≥250 treatments 6 1.1 **All patients 11 4.8**

Study	N with psoriasis	Follow-up time	Outcome	Relative risk estimate	Absolute risk estimate
PUVA + retinoids					
NIJSTEN2003	135	>1 years for retinoids	SCC BCC	IRR for retinoid use SCC: 0.79 (0.65-0.95) BCC: 0.94 (0.67-1.32)	**SCC** Retnoid use: 196 SCC per 1000 person years No retinoid use: 302 SCC per 1000 person years Incidence reduction during years of use = 106 SCCs/1000 person-years (95%CI 173, 22) **BCC** Retnoid use: 118 BCC per 1000 person years No retinoid use: 146 BCC per 1000 person years Incidence reduction during years of use = 28 BCCs/1000 person-years (95%CI 79, -22)
PUVA + CSA					
MARCIL 2001	844	6 months for CSA	SCC	**Treatment** **Multivariate IRR** **Time** 5 years before CSA 1.0 After first CSA 2.1 (2.0-2.5) **CSA use** No 1.0 Yes 3.1 (2.6-3.7) **PUVA treatments to 1992** <200 1.0 ≥200 2.8 (2.6-3.2) **MTX use** <36 months 1.0 ≥36 months 1.7 (1.5-1.9)	**Treatment** **Pts** **SCC** **Patient years** **Time** 5 yr before CSA 844 417 4220 **= 99 per 1000 person years** After first CSA 844 1178 4853 **= 243 per 1000 person years** **CSA use** No 816 1426 8901 **= 160 per 1000 person years** Yes 28 169 172 **= 983 per 1000 person years** **PUVA treatments to 1992** <200 525 514 5571 **= 92 per 1000 person years** ≥200 319 1081 3502 **= 309 per 1000 person years** **MTX use** <36 months 710 1107 7653 **= 145 per 1000 person years** ≥36 months 134 488 1419 **= 344 per 1000 person years**
CSA					

Study	N with psoriasis	Follow-up time	Outcome	Relative risk estimate				Absolute risk estimate					
PAUL 2003	1252	5 years	Skin cancers		Person-years	SIR	95% CI	Cancer	Patients N	(%)	Person-Years	Incidence rate	95% CI
				Any skin malignancy	4330	6.1	3.8–9.1	All skin malignancies	23	1.8	4377	5.3	3.3–7.9
				BCC	4379	1.8	0.6–4.1	BCC	5	0.4	4426	1.1	0.4–2.6
				SCC	4354	24.6	13.8–40.7	SCC	15	1.2	4401	3.4	1.9–5.6
				Malignant melanoma	4384	4.7	0.6–17.0	Melanoma	2	0.2	4431	0.5	0.1–1.6
NBUVB													
HEARN 2008	3867 (2130 [55%] with psoriasis)	Median: 5.5 (3.0-9.0) years	BCC SCC MM	**Cancer**	**Treatments**	**SIR (95% CI)**		Observed in total population (55% psoriasis): 27 first BCC; 7 first SCC; 6 first MM 15 BCC vs 7.9 expected among those with psoriasis treated with both NBUVB and PUVA					
				BCC	TL-01 only	156 (57-339)							
					TL-01 + PUVA	190 (106-313)							
				SCC	TL-01 only	0 (0-465)							
					TL-01 + PUVA	126 (15-454)							
				MM	TL-01 only	105 (3-586)							
					TL-01 + PUVA	157 (32-460)							

Q.7 Comorbidities – absolute risk estimates

Q.7.1 Cardiovascular disease

Study	Outcome	Relative risk estimate	Absolute risk estimate
Ahlehoff 2011E	AF	**IRR** **Mild psoriasis** 1.22 (1.14-1.30) **Severe psoriasis** 1.53 (1.23-1.91)	**Event rates per 1000 observational years** Control / Mild / Severe / Absolute risk difference - mild / Absolute risk difference - severe Overall: 3.03 / 4.67 / 5.96 / 1.64 / 2.93 <50: 0.26 / 0.36 / 0.59 / 0.1 / 0.33 ≥50: 6.10 / 7.21 / 9.10 / 1.11 / 3 **Excess events overall = 1 in 610 patients per year for mild/ 1 in 341 patients per year for severe** **Attributable risk %** Mild: 18.0% Severe: 34.6%
Ahlehoff 2011B	Composite	**HR (95% CI)** 1.26 (1.06-1.54)	**Incidence rate per 1000 person years (95% CI)** Psoriasis: 185.6 (155.8-221.0) Control: 149.7 (147.1-152.4) **ARD/1000 person years** 35.9
Abuabara	CVD mortality	Cox model HR (95% CI) 1.57 (1.26-1.96)	**Absolute risk/1000 person years** 61.9 **Attributable risk/1000 person years** 3.5 **Excess risk** 1 death per 286 pts/year
Mehta 2010	CVD death	HR 1.57 (1.26, 1.96)	**Incidence per 1000 person-years (95% CI)** Control: 6.19 (5.51, 6.92) Psoriasis: 8.75 (7.18, 10.56) **Based on HR model** Excess risk of CV death attributable to psoriasis of 1 in 283 patients per year (=3.5 excess deaths per 1000 person years)
Mallbris 2004	CVD mortality - inpatients	**Variables** / **SMR** / **95% CI** Total / 1.52 / 1.44-1.60 Age at first hospitalisation	Incidence during follow-up (0-15+ years; mean not given) **Observed deaths** / **Expected deaths** / **Difference** Total: 1529 / 1007 / 522

Study	Outcome	Relative risk estimate	Absolute risk estimate
		0-19 0.00 0.00-3.74 20-39 2.62 1.91-3.49 40-59 1.91 1.74-2.09 60+ 1.37 1.29-1.46	**Age at first hospitalisation** 0-19 0 0.99 -0.99 20-39 46 18 28 40-59 453 237 216 60+ 1030 750 280 Note: for those with at least 15 years follow-up observed = 355, expected = 207; so 148 excess deaths over 15+ years (9.9/yr) in 3469 patients followed up for 15+ yr (42.7/1000 patients)
Mallbris 2004	CVD mortality - outpatients	**Variables SMR 95% CI** Total 0.94 0.89-0.99 Age at start of follow-up 0-19 0.00 0.00-20.3 20-39 0.65 0.26-1.34 40-59 1.00 0.85-1.16 60+ 0.93 0.88-0.99	Incidence during follow-up (0-15+ years; mean not given) **Variables Obs Exp Difference** Total 1302 1390 -88 Age at start of follow-up 0-19 0 0.18 -0.18 20-39 7 11 -4 40-59 161 161 0 60+ 1134 1218 -84 Note: for those with 10-15 years follow-up observed = 141, expected = 150; so 9 fewer deaths over 10-15 years in 17,328 patients
Wakkee	IHD	HR 1.05 (0.95, 1.17)	**Outcome** **Incidence rate**/100,000 person years **Excess risk**/100,000 person years Ref cohort 559 (522-598) - Psoriasis cohort 611 (562-663) 52 *=1 case per 1923 pt/year*
Mehta 2011	MACE	HR 1.53 (1.26-1.85)	**Incidence per 1000 person-years (95% CI)** Control: 11.6 (10.7-12.6) Psoriasis: 16.4 (14.3-18.9) **Based on HR model:**

Study	Outcome	Relative risk estimate	Absolute risk estimate
			Attributable risk for 10-year incidence of MACE = 6.2% (6.2 excess MACE per 1000 person years) =1 excess event per 161 patients per year
Wakkee	Acute MI	HR 0.94 (0.80, 1.11)	**Outcome** / **Incidence rate**/100,000 person years / **Excess risk**/100,000 person years Ref cohort: 235 (211-260) / - Psoriasis cohort: 234 (201-262) / -1 = 1 fewer case per 100,000 pt/year
Gelfand 2006A	MI	**Age** / **HR Mild** / **Severe** 30: 1.29 (1.14 -1.46) / 3.10 (1.98-4.86) 60: 1.08 (1.03-1.13) / 1.36 (1.13-1.64)	**Incidence per 1000 person years** Control: 3.58 (3.52-3.65) Mild psoriasis: 4.04 (3.88-4.21) Severe psoriasis: 5.13 (4.22-6.17) **Age** / **Attributable risk/ 10,000 person years** (Mild, Severe) / **Excess risk** (Mild, Severe) 30-40: 1.068, 7.222 / 1 MI per 9365 pt/year pt/year, 1 MI per 1385 40-50: 2.743, 16.060 / 1 MI per 3646 pt/year, 1 MI per 623 pt/year 50-60: 4.658, 23.250 / 1 MI per 2147 pt/year, 1 MI per 430 pt/year

Study	Outcome	Relative risk estimate	Absolute risk estimate
Brauchli 2009A	**MI**	IRR All 1.07 (0.89-1.29) 0-29 years NA 30-59 years 1.99 (1.37-2.88) 60-80+ years 0.92 (0.75-1.14)	**IR per 1000 person-years (95% CI)** **ARD/1000 person years** **Excess risk** Psoriasis Control All pts/year 1.58 (1.39-1.79) 1.47 (1.29-1.69) 0.11 1 MI per 9091 Age 0-29 NA 0.03 (0.00-0.15) - - Age 30-59 pts/year 1.08 (0.86-1.35) 0.54 (0.39-0.75) 0.54 1 MI per 1852 Age 60-80+ pts/year 4.01 (3.44-4.68) 4.35 (3.75-5.05) -0.34 -1 MI per 2941
Kaye2008	Myocardial infarction	1.21 (1.10-1.32)	Incident MI cases in the psoriasis and comparison cohorts **Incidence/1000 after 10 y follow-up** **Excess risk from psoriasis/1000** Psoriasis n=44164 Comparison n=219784 27.7 22.6 5.1 = 1 case per 1961 patients per year
Gelfand 2009	Stroke	**HR** **Mild:** 1.06 (1.01, 1.11) **Severe:** 1.43 (1.10, 1.87)	**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)** 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) **Excess risk attributable to psoriasis 1 in 4115 per year and 1 in 530 per year for mild and**

Study	Outcome	Relative risk estimate	Absolute risk estimate
			severe disease (based on adjusted analysis)
Ahlehoff 2011E	Stroke	**Mild psoriasis** 1.25 (1.17-1.34) **Severe psoriasis** 1.65 (1.33-2.05)	**Event rates per 1000 observational years** **Control / Mild / Severe / Absolute risk difference - mild / Absolute risk difference - severe** Overall: 3.06 / 4.54 / 6.82 / 1.48 / 3.76 <50: 0.23 / 0.61 / 1.56 / 0.38 / 1.33 ≥50: 5.94 / 6.74 / 8.88 / 0.8 / 2.94 **Excess events overall = 1 in 676 patients per year for mild/ 1 in 266 patients per year for severe** **Attributable risk %:** Mild: 20.0% Severe: 39.4%
Brauchli 2009A	Stroke	IRR All 0.92 (0.77-1.09) 0-29 years NA 30-59 years 0.75 (0.49-1.16) 60-80+ years 0.98 (0.81-1.18)	**Age / IR per 1000 person-years (95% CI) / ARD/1000 person years / Excess risk** Psoriasis / Control All: 1.69 (1.50-1.90) / 1.84 (1.63-2.07) / 0.15 / 1 stroke per 6667 pts/year 0-29: 0.02 (0.00-0.14) / NA / - 30-59: 0.52 (0.37-0.71) / 0.69 (0.51-0.91) / -0.17 / -1 stroke per 5882 pts/year 60-80+: 5.10 (4.48-5.81) / 5.22 (4.58-5.94) / -0.12 / -1 stroke per 8333 pts/year
Brauchli 2009A	TIA	IRR All 0.98 (0.81-1.19) 0-29 years NA 30-59 years 1.14 (0.66-1.97) 60-80+ years 0.99 (0.80-1.22)	**Age (years)** / IR per 1000 person-years (95% CI) / ARD /1000 person years / Excess risk Psoriasis / Control All: 1.31 (1.14-1.50) / 1.34 (1.16-1.54) / -0.03 / -1 TIA per 33,333 pts/year 0-29: NA / NA / - / - 30-59: 0.39 (0.27-0.56) / 0.34 (0.23-0.51) / 0.05 / 1 TIA per 20,000

Study	Outcome	Relative risk estimate	Absolute risk estimate
			pts/years 60-80+ 4.00 (3.45-4.63) 4.04 (3.48-4.68) -0.04 -1 TIA per 25,000 pts/years
Ahlehoff 2011	VTE	**Adjusted IRR (95% CI)** **< 50 years** **≥ 50 years** Mild 1.24 (0.97-1.58) 1.26 (1.13-1.42) Severe 3.14 (1.98-4.97) 1.74 (1.32-2.28)	**Incidence rate per 1000 person years (95% CI)** **< 50 years** **≥ 50 years** Controls 0.58 (0.57-0.59) 2.03 (2.01-2.05) Mild 0.73 (0.56-0.95) 2.74 (2.4-3.06) Severe 2.10 (1.32-3.33) 3.93 (3.01-5.13) **Absolute risk difference vs control per 1000 person years** **< 50 years** **≥ 50 years** 0.15 (1 VTE per 6667 pts/yr) 0.71 (1 VTE per 1408 pts/yr) 1.52 (1 VTE per 658 pts/yr) 1.9 (1 VTE per 526 pts/yr)
CVD 'risk factors'			
Kaye2008	Diabetes	HR: 1.33 (1.25-1.42)	**Incident diabetes cases in the psoriasis and comparison cohorts** **Incidence/1000 after 10 y follow-up** **Excess risk from psoriasis/1000** **Psoriasis n=44164** **Comparison n=219784** 57.3 43.9 13.4 = 1 case per 746 patients per year
Brauchli 2008	Diabetes	**IRR (95% CI)** **All** **1.36 (1.20-1.53)** 0-29 years 2.75 (1.24-6.13) 30-59 years 1.33 (1.09-1.61) 60-79 years 1.43 (1.21-1.69) 80+ years 1.12 (0.71-1.75)	**Age, years** **IR per 1000 person-years (95% CI)** **ARD/1000 person years** **Excess risk** **Psoriasis** **Control** Overall 4.06 (3.75-4.39) 2.98 (2.92-3.28) 1.08 1 case per 926 pts/year 0-29 0.45 (0.28-0.71) 0.16 (0.07-0.35) 0.29 1 case per 3448 pts/year 30-59 3.38 (2.98-3.84) 2.55 (2.19-2.97) 0.83 1 case per 1205 pts/year 60-79 8.92 (8.01-9.93) 6.22 (5.47-7.09) 2.7 1 case per 370 pts/year 80+ 5.87 (4.33-7.95) 5.24 (3.77-7.28) 0.63 1 case per 1587 pts/year
Kaye2008	Hyperlipidaemia	1.17 (1.11-1.23)	**Incident hyperlipidaemia cases in the psoriasis and comparison cohorts** **Incidence/1000 after 10 y follow-up** **Excess risk from psoriasis/1000** **Psoriasis n=44164** **Comparison n=219784**

Study	Outcome	Relative risk estimate	Absolute risk estimate
			91.1 77.7 13.4 = 1 case per 746 patients per year
Kaye2008	Obesity	1.18 (1.14-1.23)	**Incident obesity cases in the psoriasis and comparison cohorts** *Obesity is defined as body mass index>/=30kgm^{-2} **Incidence/1000 after 10 y follow-up** **Excess risk from psoriasis/1000** **Psoriasis n=44164** **Comparison n=219784** 139.0 118.0 21 = 1 case per 476 patients per year
Kaye2008	Hypertension	1.09 (1.05-1.14)	**Incident hypertension cases in the psoriasis and comparison cohorts** **Incidence/1000 after 10 y follow-up** **Excess risk from psoriasis/1000** **Psoriasis n=44164** **Comparison n=219784** 138.5 129.4 9.1 = 1 case per 1099 patients per year

Q.7.2 Cancer

Study	Outcome	Relative risk estimate	Absolute risk estimate
Gelfand 2003	Lymphoma – based on adjusted figures	IRR (adjusted) 2.94 (1.82-4.74)	**Variable** **Psoriasis** **No psoriasis** Incidence rate of lymphoma per 10000 person-years 18.3 6.1 Attributable risk (excess no. of lymphoma cases related to psoriasis) 122 /100000 per year *1 more per 820 pts/year* -
Gelfand 2006	Lymphoma – based on adjusted figures	HR 1.35 (1.17, 1.55) 1.48 (1.05, 2.08) 4.34 (2.89, 6.52)	**Attributable risk (excess no. of cases related to psoriasis)** **Lymphoma** 7.9/100,000 per year (1 more per 12,658 pts/year) **HL** 1.8/100,000 per year (1 more per 55,556 pts/year) **TCL** 4.0/100,000 per year (1 more per 25,000 pts/year)
Prizment	Cancer	HR (95% CI) Any 1.1 (0.9-1.4)	**Age-adjusted incidence rate per 1000** **Psoriasis** **Control** **Difference** Total 20.8 16.5 4.3

Study	Outcome	Relative risk estimate			Absolute risk estimate				
		Breast	1.0 (0.7-1.5)		Breast	5.3	5.1	0.2	
		Lung	1.3 (0.8-2.0)		Lung	3.5	1.7	1.8	
		Colon	1.6 (1.0-2.4)		Colon	3.9	2.2	1.7	
					Note: follow-up was 2-15 years				
Hannuksela-Svahn 2000	Cancer	**Primary site**	**SIR**	**95% CI**	**Primary site per 1000 pts**	**Obs**	**Exp**	**Difference**	**Attributable risk**
		All sites	1.3	1.2-1.4	All sites	533	425.8	107.2	18.9
		Mouth	0.7	0.0-3.6	Mouth	1	1.6	-0.6	-0.1
		Pharynx	1.3	0.3-3.9	Pharynx	3	2.2	0.8	0.1
		Oesophagus	1.2	0.5-2.5	Oesophagus	7	5.7	1.3	0.2
		Stomach	1.1	0.8-1.5	Stomach	34	30.8	3.2	0.6
		Colon	0.9	0.5-1.3	Colon	20	23.5	-3.5	-0.6
		Liver	1.9	0.9-3.3	Liver	11	5.9	5.1	0.9
		Pancreas	1.5	1.0-2.2	Pancreas	26	17.2	8.8	1.5
		Larynx	2.9	1.5-5.0	Larynx	12	4.2	7.8	1.4
		Lung, bronchus	1.5	1.2-1.8	Lung, bronchus	101	68.0	33	5.8
		Breast	0.9	0.6-1.2	Breast	37	43.4	-6.4	-1.1
		Kidney and renal pelvis	0.8	0.4-1.4	Kidney and renal pelvis	12	15.1	-3.1	-0.5
		Bladder, urethra, and urethra	1.4	0.9-2.1	Bladder, urethra, and urethra	25	17.8	7.2	1.3
		Skin melanoma	0.8	0.3-1.6	Skin melanoma	8	10.3	-2.3	-0.4
		Non-melanoma skin cancer	3.2	2.3-4.4	Non-melanoma skin cancer	40	12.4	27.6	4.9
		Nervous system	1.1	0.6-1.9	Nervous system	14	12.7	1.3	0.2
		Non-Hodgkin's lymphoma	2.2	1.4-3.4	Non-Hodgkin's lymphoma	21	9.6	11.4	2.0
		Hodgkin's disease	3.3	1.4-6.4	Hodgkin's disease	8	2.5	5.5	1.0
					Note: mean follow-up 14 years; 5687 people with psoriasis				
Brauchli 2009	Cancer	**Type**	**Overall IRR (95% CI)**		**IR/1,000 person years**			**Difference in IR**	**Excess risk**
					Control	Psoriasis			
		All cancer	1.13 (1.02-1.24)						

Study	Outcome	Relative risk estimate		Absolute risk estimate						
		Lympho-hematopoietic malignancies	1.81 (1.35-2.42)	All cancer	5.18	4.83-5.55	5.83	5.47-6.22	0.65	1 event per 1538 pts/year
		Excluding CTCL	1.69 (1.25-2.27)	Lymphohematopoietic malignancies	0.41	0.32-0.53	0.75	0.63-0.90	0.34	1 event per 2941 pts/year
		Lymphoma overall	1.76 (1.19-2.58)	Lymphohematopoietic malignancies (excluding CTCL)	0.41	0.34-0.53	0.70	0.58-0.84	0.29	1 event per 3448 pts/year
		Lymphoma (excluding CTCL)	1.55 (1.03-2.31)	CTCL	NA	NA	0.05	0.03-0.10	0.05	1 event per 20000 pts/year
		Leukaemia/MD	1.89 (1.21-2.94)	Lymphoma overall	0.24	0.17-0.33	0.42	0.33-0.54	0.18	1 event per 5556 pts/year
		Lung	0.79 (0.60-1.06)	Lymphoma (excluding CTCL)	0.24	0.17-0.33	0.37	0.29-0.48	0.13	1 event per 7692 pts/year
		Melanoma	0.83 (0.50-1.36)	Leukaemia/ MD	0.17	0.12-0.25	0.33	0.25-0.43	0.16	1 event per 6250 pts/year
		Breast	1.04 (0.83-1.31)	Lung	0.67	0.55-0.82	0.53	0.43-0.66	-0.14	-1 event per 7143 pts/year
		Prostate	0.84 (0.63-1.12)	Melanoma	0.22	0.16-0.31	0.18	0.13-0.26	-0.04	-1 event per 25000 pts/year
		Digestive organs	1.40 (1.10-1.78)	Breast	1.71	1.45-2.02	1.79	1.53-2.10	0.08	1 event per 12500 pts/year
		Pancreas	2.20 (1.18-4.09)	Prostate	1.38	1.13-1.69	1.16	0.93-1.43	-0.22	-1 event per 4545 pts/year
		Oesophagus	1.36 (0.72-2.54)	Digestive organs	0.71	0.59-0.86	1.00	0.86-1.17	0.29	1 event per 3448 pts/year
		Colorectal	1.35 (0.97-1.90)	Pancreas	0.08	0.05-0.14	0.18	0.12-0.25	0.1	1 event per 10000 pts/year
		Others	1.14 (0.67-1.95)							
		Female genital organs	1.38 (0.91-2.11)							
		Bladder/kidney	1.25 (0.84-1.85)							
		Brain	1.30 (0.69-2.45)							
		Other cancers	1.23 (0.94-1.59)							
		Metastasis	0.81 (0.53-1.22)							

Study	Outcome	Relative risk estimate			Absolute risk estimate						
					Oesophagus	0.11	0.07-0.17	0.14	0.10-0.22	0.03	1 event per 33333 pts/year
					Colorectal	0.37	0.28-0.48	0.50	0.40-0.62	0.13	1 event per 7692 pts/year
					Others	0.16	0.11-0.24	0.18	0.13-0.26	0.02	1 event per 50000 pts/year
					Female genital organs	0.43	0.31-0.60	0.60	0.45-0.79	0.17	1 event per 5882 pts/year
					Bladder/kidney	0.29	0.21-0.39	0.36	0.28-0.46	0.07	1 event per 14286 pts/year
					Brain	0.11	0.07-0.17	0.14	0.09-0.21	0.03	1 event per 33333 pts/year
					Other cancers	0.65	0.53-0.79	0.79	0.67-0.94	0.14	1 event per 7143 pts/year
					Metastasis	0.32	0.24-0.42	0.26	0.19-0.35	-0.06	-1 event per 16667 pts/year
Frentz 1999	Cancer	**Site**	**SIR**	**95% CI**	**Site**	**Obs**	**Exp**	**Difference**	**Excess risk per 1000 pts**		
		All malignant neoplasms	1.40	1.21-1.51							
		Melanoma of skin	1.3	0.8-2.1	All malignant neoplasms	795	566.1	228.9	33.1		
		Non-melanoma skin cancer	2.46	2.13-2.83	Melanoma of skin	16	12.1	3.9	0.6		
		Oral cavity	1.7	1.0-2.7	Non-melanoma skin cancer	196	79.6	116.4	16.9		
		Pharynx	2.9	1.3-5.8	Oral cavity	19	11.0	8	1.2		
		Stomach	1.2	0.8-1.8	Pharynx	8	2.7	5.3	0.8		
		Colon	1.3	1.0-1.6	Stomach	22	18.0	4	0.6		
		Rectum	0.9	0.6-1.4	Colon	60	46.8	13.2	1.9		
		Larynx	2.0	1.0-3.6	Rectum	24	25.8	-1.8	-0.3		
		Lung	1.5	1.3-1.9	Larynx	11	5.5	5.5	0.8		
		Breast	1.0	0.7-1.2	Lung	113	73.4	39.6	5.7		
		Kidney	1.2	0.7-1.9	Breast	54	46.8	7.2	1.0		

Study	Outcome	Relative risk estimate			Absolute risk estimate				
		Bladder	1.0	0.7-1.4	Kidney	18	15.3	2.7	0.4
		Connective tissue	3.2	1.0-7.4	Bladder	34	34.1	-0.1	0.0
		Non-Hodgkin's lymphoma	1.4	0.8-2.2	Connective tissue	5	1.6	3.4	0.5
		Leukaemia	0.9	0.5-1.6	Non-Hodgkin's lymphoma	16	11.7	4.3	0.6
					Leukaemia	12	13.0	-1	33.1

Q.7.3 Mortality

Study	Outcome	Relative risk estimate		Absolute risk estimate			
Abuabara	Mortality – various causes		**HR (95% CI)**	**Cause of death**	**Absolute risk/1000 person years**	**Excess risk/ person years**	**Excess risk**
		Diabetes	2.86 (1.08-7.59)	Diabetes	2.1	0.4	1 more death per 2500 pts/year
		Kidney disease	4.37 (2.24-8.53)	Kidney disease	3.5	1.2	1 more death per 833 pts/year
		Liver disease	2.03 (0.37-11.12)	Liver disease	0.8	0.1	1 more death per 10,000 pts/year
		Malignant neoplasms	1.41 (1.07-1.86)	Malignant neoplasms	39.0	1.6	1 more death per 625 pts/year
Ahlehoff 2011B	All cause mortality	HR (95% CI) 1.18 (0.97-1.43)		**Incidence rate per 1000 person years (95% CI)**	**ARD/1000 person years**	**Excess risk in psoriasis**	
				Psoriasis: 138.3 (114.1-167.7) Control: 119.4 (117.2-138.8)	18.9	1 death per 53 pts/year	
Gelfand 2007	All cause mortality	HR (95% CI) All psoriasis: 1.0 (0.99-1.04)		Incidence rate of mortality per 1000 person-years (95% CI) Control: 12.2 (12.0-12.3)			

Study	Outcome	Relative risk estimate	Absolute risk estimate
		mild psoriasis: 1.0 (0.97-1.02) severe psoriasis: 1.5 (1.3-1.7)	Mild psoriasis: 12.0 (11.7-12.3) Difference = -0.2 (1 fewer deaths per 5000 pts per year) **Severe psoriasis (age and sex adjusted)**

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

Q.7.4 Depression

Study	Outcome	Relative risk estimate	Absolute risk estimate		
Kurd2010	**Depression**	**HR** **Mild:** 1.38 (1.35-1.40) **Severe**: 1.72 (1.5-1.88) **All**: 1.39 (1.37-1.41)	**Attributable risk of diagnosis of depression attributable to psoriasis adjusted for age and sex per 1000 person years**		
			Mild psoriasis	**Severe psoriasis**	**All psoriasis**
			11.5 =1 case for every 87 patients with psoriasis per year	25.5 =1 case for every 39 patients with psoriasis per year	11.8 =1 case for every 85 patients with psoriasis per year

Q.8 Biologics

Q.8.1 Sensitivity analysis: ustekinumab

One study for the comparison of ustekinumab in those with and without prior biologic exposure (section 3.1B) included patients who had received overlap therapy with non-biologic systemic agents in the primary analysis. However, in the call for evidence data the numbers who had received overlap therapy were available and a sensitivity analysis was performed excluding these patients.

Of 80 who achieved PASI75 at week 16, 10 received overlap therapy during induction; 4 of these were still on an additional systemic therapy at 16 weeks. Additional therapies included: ciclosporin (n=5), methotrexate (n=4) and acitretin (n=1). Of these 10, 7 had previous biologic exposure and 3 were biologic naïve. Of the 47 patients who failed to achieve PASI75, 19 patients had additional systemic therapy (18 received treatment as overlap and 1 as rescue). Of the 19 patients 3 were biologic naïve, including the patient who received rescue therapy, and 16 had previous biologic exposure.

Please see evidence profile below.

Q.8.1.1 Evidence profile

Quality assessment							No of patients		Effect		Quality
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Ustekinumab in those with previous biologic	No previous biologic	Relative (95% CI)	Absolute	
PASI75 (week 16) - any biologic exposure vs none											
1 Laws 2011	observational studies	very serious[a]	no serious inconsistency	serious[b]	serious[c]	none	64/106 (60.4%)	16/21 (76.2%)	RR 0.79 (0.6 to 1.05)	160 fewer per 1000 (from 305 fewer to 38 more)	⊕OOO VERY LOW
PASI75 (week 16) - any biologic exposure vs none (overlap therapy responders removed)											
1 Laws 2011	observational studies	very serious[a]	no serious inconsistency	no serious indirectness[d]	serious[c]	none	57/83 (68.7%)	13/15 (86.7%)	RR 0.79 (0.62 to 1.01)	182 fewer per 1000 (from 329 fewer to 9 more)	⊕OOO VERY LOW

(a) Failure to adequately control for confounding (no matching for prognostic factors or adjustment in statistical analyses)
(b) Note: prior biologics included efalizumab (proportion unclear)
(c) 10/80 who achieved PASI75 at week 16 received overlap therapy (CSA, MTX or acitretin) during induction; 4 of these were still on an additional systemic therapy at 16 weeks. Of these 10, 7 had had previous biologic exposure and 3 were biologic naive. Also, prior biologics included efalizumab (proportion unclear).

(d) Confidence interval ranges from clinically important effect to no effect

Q.8.1.2 Evidence statement

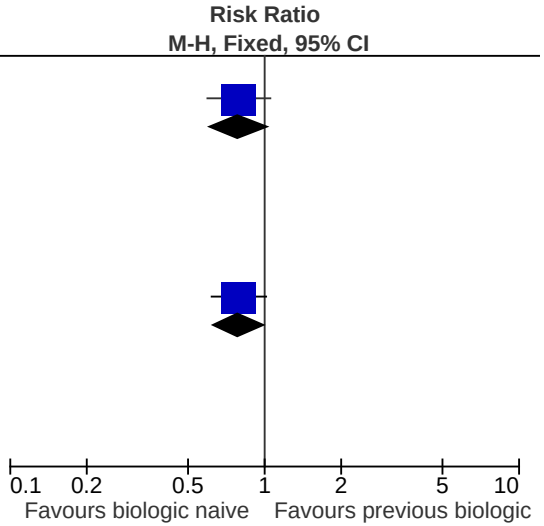
In people with psoriasis being treated with ustkeinumab, there was no statistically significant difference between those with and without prior exposure to biologic therapy for:

- PASI75 (week 16) [1 study; 98 participants; very low quality evidence][6;11]

Q.8.1.3 Forest plot

Figure 1: PASI75 (week 16)

Study or Subgroup	Previous biologic Events	Previous biologic Total	Biologic naive Events	Biologic naive Total	Weight	Risk Ratio M-H, Fixed, 95% CI
4.27.1 Any biologic exposure vs none						
Laws 2011 - CFE	64	106	16	21	100.0%	0.79 [0.60, 1.05]
Subtotal (95% CI)		**106**		**21**	**100.0%**	**0.79 [0.60, 1.05]**
Total events	64		16			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.60 (P = 0.11)						
4.27.2 Any biologic exposure vs none (overlap therapy removed)						
Laws 2011 - CFE	57	83	13	15	100.0%	0.79 [0.62, 1.01]
Subtotal (95% CI)		**83**		**15**	**100.0%**	**0.79 [0.62, 1.01]**
Total events	57		13			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.85 (P = 0.06)						



Test for subgroup differences: Chi² = 0.00, df = 1 (P = 1.00), I² = 0%

There was no notable difference between the effect estimate for the full sample and for the sample including only those receiving no concomitant therapy, although the response rates in both groups were higher when those requiring additional therapy were removed from the sample.

Q.10.1 Ustekinumab vs ustekinumab following failure of etanercept

These data were included in the original review presented to the GDG but were superseded by the evidence made available in the call for evidence, which are presented in sections 3.1A, 3.1D, 3.6 and 3.7 and provide more direct evidence to address the review question. Note that in the data summarised below those who received ustekinumab in the first trial phase included 10.4% in whom this was not the first biologic.

Q.10.1.1 Evidence profile

Quality assessment							No of patients		Effect		Quality
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Ustekinumab in those who failed etanercept	Ustekinumab	Relative (95% CI)	Absolute	
Clear/nearly clear (PASI90; 12 weeks)											
1 Griffiths 2010	randomised trials	serious[a]	no serious inconsistency	serious[b]	no serious imprecision	none	12/50 (24%)	155/347 (44.7%)	RR 0.54 (0.32 to 0.89)	205 fewer per 1000 (from 49 fewer to 304 fewer)	⊕⊕OO LOW
Clear/nearly clear (PGA; 12 weeks)											
1 Griffiths 2010	randomised trials	serious[a]	no serious inconsistency	serious[b]	no serious imprecision	none	20/50 (40%)	245/347 (70.6%)	RR 0.57 (0.4 to 0.8)	304 fewer per 1000 (from 141 fewer to 424 fewer)	⊕⊕OO LOW
PASI75 (12 weeks)											
1 Griffiths 2010	randomised trials	serious[a]	no serious inconsistency	serious[b]	no serious imprecision	none	24/50 (48%)	256/347 (73.8%)	RR 0.65 (0.48 to 0.87)	258 fewer per 1000 (from 96 fewer to 384 fewer)	⊕⊕OO LOW
Withdrawal due to toxicity											
1 Griffiths 2010	randomised trials	serious[a]	no serious inconsistency	serious[b]	very serious[c]	none	2/295 (0.68%)	4/347 (1.2%)	RR 0.59 (0.11 to 3.19)	5 fewer per 1000 (from 10 fewer to 25 more)	⊕OOO VERY LOW
Serious adverse events											
1 Griffiths	randomised trials	serious[a]	no serious inconsistency	serious[b]	serious[d]	none	10/295 (3.4%)	4/347 (1.2%)	RR 2.94 (0.93 to 9.28)	22 more per 1000 (from 1 fewer to 95	⊕OOO VERY LOW

2010										more)	

(a) Unclear allocation concealment
(b) Not a direct comparison: data available for initial response in ustekinumab group and response among etanercept non-responders who crossover to ustekinumab during later phase of trial; selective outcome reporting: response rates following failure of initial therapy not given for all groups; 11.8% of those receiving etanercept initially and 10.4% of those receiving ustekinumab initially had previously received another biologic agent. Also, high dose of etanercept (50 mg twice weekly).
(c) Confidence interval crosses the boundary for clinical significance in favour of both groups, as well as line of no effect
(d) Confidence interval ranges from clinically important effect to no effect

Q.10.1.2 Evidence statements

In people with psoriasis, ustekinumab 90 mg in the first trial phase was statistically significantly better than ustekinumab 90 mg following failure of etanercept for:

- Clear or nearly clear (PASI90 or PGA; 12 weeks) [1 study; 397 participants; low quality evidence][2]
- PASI75 (12 weeks) [1 study; 397 participants; low quality evidence][2]

Note: even in these cases where those using ustekinumab in the first trial phase had a statistically significantly better result, those who had previously failed etanercept still had substantial response rates (24% PASI90; 40% clear/nearly clear PGA; 48% PASI75).

In people with psoriasis, there was no statistically significant difference between ustekinumab 90 mg following failure of etanercept and ustekinumab 90 mg in the first trial phase for:

- Withdrawal due to toxicity (12 weeks) [1 study; 642 participants; very low quality evidence][2]
- Serious adverse events (12 weeks) [1 study; 642 participants; very low quality evidence][2]

Q.10.1.3 Forest plots

Figure 2: Clear/nearly clear (PASI90; week 12)

Study or Subgroup	Etanercept crossover Events	Total	Ustekinumab Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Griffiths 2010	12	50	155	347	100.0%	0.54 [0.32, 0.89]
Total (95% CI)		**50**		**347**	**100.0%**	**0.54 [0.32, 0.89]**
Total events	12		155			

Heterogeneity: Not applicable
Test for overall effect: Z = 2.40 (P = 0.02)

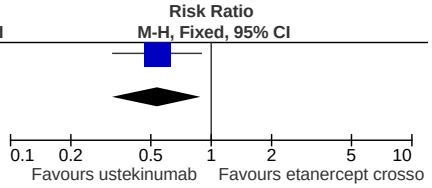


Figure 3: Clear/nearly clear (PGA; week 12)

Study or Subgroup	Etanercept crossover Events	Total	Ustekinumab Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Griffiths 2010	20	50	245	347	100.0%	0.57 [0.40, 0.80]
Total (95% CI)		**50**		**347**	**100.0%**	**0.57 [0.40, 0.80]**
Total events	20		245			

Heterogeneity: Not applicable
Test for overall effect: Z = 3.22 (P = 0.001)

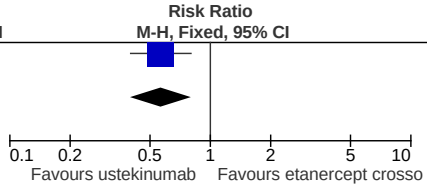


Figure 4: PASI75 (week 12)

Study or Subgroup	Etanercept crossover Events	Total	Ustekinumab Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Griffiths 2010	24	50	256	347	100.0%	0.65 [0.48, 0.87]
Total (95% CI)		**50**		**347**	**100.0%**	**0.65 [0.48, 0.87]**
Total events	24		256			

Heterogeneity: Not applicable
Test for overall effect: Z = 2.85 (P = 0.004)

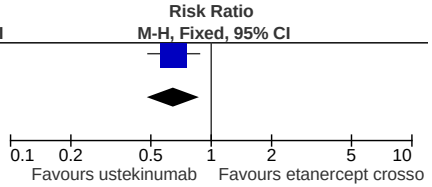


Figure 5: Withdrawal due to toxicity

Study or Subgroup	Etanercept crossover Events	Total	Ustekinumab Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Griffiths 2010	2	295	4	347	100.0%	0.59 [0.11, 3.19]
Total (95% CI)		**295**		**347**	**100.0%**	**0.59 [0.11, 3.19]**
Total events	2		4			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.62 (P = 0.54)

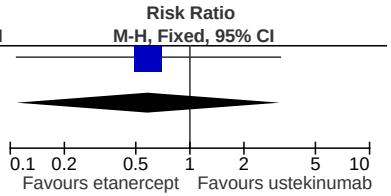
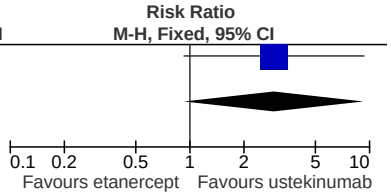


Figure 6: Serious adverse events

Study or Subgroup	Etanercept crossover Events	Total	Ustekinumab Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Griffiths 2010	10	295	4	347	100.0%	2.94 [0.93, 9.28]
Total (95% CI)		**295**		**347**	**100.0%**	**2.94 [0.93, 9.28]**
Total events	10		4			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.84 (P = 0.07)