Further details of questions identified and prioritised by the JLA PSP in Psoriasis

ID	Indicative question [uncertainty]	Example of original uncertainty submitted	Number of uncertainties submitted to survey around this question	Rank of uncertainty at priority setting workshop on 17 September 2018	Evidence in last 5 years	Hyperlinks
A	**Is a person with psoriasis more likely to develop other health conditions? If so, which ones?**	What makes someone with psoriasis likely to develop PsA?	147	9		
					Abbott, 2015 Evidence that TNF-α inhibitor therapy reduces depression in people who have chronic diseases (including those with psoriasis) though the effects are small. Limited data available. Further studies investigating a more detailed timeline of changes in depression, inflammatory biomarkers and disease activity status in patients with psoriasis (and other chronic diseases) are required.	https://www.ncbi.nlm.nih.gov/pubmed/25935351
					Alinaghi, 2019 This study found that 1 in 5 patients with psoriasis have PsA. There were high levels of heterogeneity between the studies which were included in the analysis and very few studies from certain geographical regions – eg Africa and Australia. Studies were excluded if they were not written in English which may have introduced publication bias. Further studies required.	https://www.ncbi.nlm.nih.gov/pubmed/29928910
					Armstrong 2013a Some evidence that mild and severe psoriasis is associated with an increased risk of myocardial infarction and stroke. Severe psoriasis is also associated with an increased risk of cardiovascular mortality. Some limitations documented. Future studies needed - these should include more complete covariate adjustment and characterisation of psoriasis severity.	https://www.ncbi.nlm.nih.gov/pubmed/23557749
					Armstrong 2013b Evidence that psoriasis and psoriatic arthritis are associated with greater prevalence of hypertension. Patients with severe psoriasis have greater odds of hypertension than those with mild psoriasis. Some limitations with study. Further studies are needed – specifically to elucidate the basic mechanisms underlying the association between psoriasis and hypertension, to explore the relationship between psoriasis and hypertension severity, and to examine the effects of systemic treatments for psoriasis on hypertension control.	https://www.ncbi.nlm.nih.gov/pubmed/23249828
					Armstrong 2013c Compared with the general population, psoriasis patients have higher prevalence of metabolic syndrome, and patients with more severe psoriasis have greater odds of metabolic syndrome than those with milder psoriasis. Some limitations with study. More studies needed to determine the mechanisms underlying the association between these two conditions and to determine the effect of psoriasis systemic therapies on metabolic syndrome.	https://www.ncbi.nlm.nih.gov/pubmed/23360868
					Armstrong 2013d Evidence that psoriasis is associated with an increased prevalence and incidence of diabetes. The association of psoriasis with diabetes may be strongest among patients with severe psoriasis. Some limitations with the study. Future studies should more closely assess the relationship between psoriasis severity, age at disease onset, and diabetes.	https://www.ncbi.nlm.nih.gov/pubmed/23407990
					Bhatia, 2014 Epidemiologic and clinical studies suggest there is an association among psoriasis, coeliac disease, and coeliac disease markers. Further studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/24780176
					Candia, 2015 Case - control studies support an association between psoriasis and non-alcoholic fatty liver disease (NAFLD). Screening of NAFLD in patients with psoriasis may be warranted. More studies are needed.	https://www.ncbi.nlm.nih.gov/pubmed/25418531
					Cullen, 2019 Evidence for a positive overall association between non-neurological autoimmune (NNAI) disorders and psychosis, which was not consistent across all NNAI disorders. Separate meta-analyses were conducted for individual autoimmune disorders. A significant positive association was observed for psoriasis. Future work recommended: 1) studies should be designed to better disentangle the temporal nature of the association between NNAI disorders and psychosis, as such studies have demonstrated that both psychosis and depression show bidirectional associations with autoimmune disorders; 2) larger studies should be undertaken to examine the presence of neuronal surface autoantibodies among individuals with psychosis; 3) greater efforts should be made in large cohort studies to include information on potential confounders, such as socioeconomic status, adversity, and tobacco use; and 4) studies should be undertaken to evaluate the effect of corticosteroid treatment on the relationship between NNAI disorders and psychosis.	https://www.ncbi.nlm.nih.gov/pubmed/30122288

					Coto-Segura, 2013 Evidence to support an association between psoriasis, PsA and type 2 diabetes mellitus. Heterogeneity between studies. Further work to understand the relations more completely needed.	https://www.ncbi.nlm.nih.gov/pubmed/23772556
					De Vecchis, 2016 Evidence that methotrexate at low doses, such those used for maintenance therapy of rheumatoid arthritis, predicts a decreased risk of cardiovascular events. Randomised controlled trials to establish causality recommended.	https://www.ncbi.nlm.nih.gov/pubmed/26467356
					Dowlatshahi, 2014 Evidence that psoriasis patients are at least one and a half times more likely to manifest signs of clinical depression compared with their healthy peers. More than one-quarter of psoriasis patients show symptoms of depression and approximately one-tenth have signs of clinical depression. High heterogeneity between studies. Further work to clarify this relationship needed.	https://www.ncbi.nlm.nih.gov/pubmed/24284419
					Fang, 2016 Evidence that patients with psoriasis have excessive risk of subclinical atherosclerosis compared with the healthy controls. Further studies are needed particularly on whether treatment of psoriasis will reverse subclinical atherosclerosis.	https://www.ncbi.nlm.nih.gov/pubmed/27196459
					Ferreira, 2016 Evidence that many mental disorders are associated with psoriasis although the aetiopathogenesis of that connection is wide. Some psychiatric comorbidities may result from the psychosocial impact of having a chronic skin condition. However, psoriasis can be maintained and exacerbated by an underlying psychiatric condition. Further studies to explore these relationships in more detail and establish aetiology are needed.	https://www.ncbi.nlm.nih.gov/pubmed/27386050
					Ferreira 2017 Evidence that the prevalence of psychiatric conditions in psoriasis may range from 24% to 90%. The link between psoriasis and associated mental disorders is frequently forgotten or not considered in clinical practice and psychiatric disorders in patients with psoriasis may be underdiagnosed. Limited data available – further study required.	https://www.ncbi.nlm.nih.gov/pubmed/29197196
					Fleming 2015 Evidence that treatment with adalimumab, etanercept and ustekinumab are associated with statistically significant reductions in depressive symptom scores using various scales in patients with moderate-to-severe psoriasis. A robust RCT including standardised criteria is required to better determine the clinical significance of these findings. In the interim, it is suggested that patients with psoriasis should be screened for depression when appropriate and refered accordingly.	https://www.ncbi.nlm.nih.gov/pubmed/25490866
					Fleming, 2017 Evidence for a high prevalence of anxiety of adult patients with psoriasis suggesting that patients would benefit from systematic screening. Although the data suggest that anxiety may be improved through various psoriasis treatments, larger prospective randomized trials are needed to confirm this effect. Chi This systemic review and meta-analysis concluded that the available limited, very low-quality evidence does not support an association between psoriasis and suicidal thought and behaviour. Further studies that provide data for different age and sex groups are needed to clarify whether a subgroup of patients with psoriasis has an elevated risk of suicidality.	https://www.ncbi.nlm.nih.gov/pubmed/27620704
					Gaeta, 2013 Evidence that patients with psoriasis carry an about 25% increased relative risk of cardiovascular disease. This risk appears to be independent of smoking, obesity and hyperlipidemia. Further work needed to confirm this and to assess the impact of psoriasis in risk stratification, and the benefit of its effective treatment in the prevention of associated cardiovascular events.	https://www.ncbi.nlm.nih.gov/pubmed/23490084
					González-Álvarez, 2018 This systematic review concluded that diagnosis of geographic tongue (GT) is mainly clinical and that GT is an asymptomatic disorder that usually requires no treatment. GT can be associated with psoriasis. Further studies are needed.	https://www.ncbi.nlm.nih.gov/pubmed/29903400
					Gupta, 2016 This systematic review evidences a link between psoriasis and PsA with obstructive sleep apnoea and restless legs syndrome. In this study there was no conclusive evidence that psoriasis and PsA are associated with an elevated prevalence of insomnia, periodic limb movement disorder, narcolepsy, or shift work disorder. The relationship between psoriatic conditions and other sleep disorders was not examined.Future research recommended including: 1. It is important that epidemiological studies in psoriasis evaluate sleep disorders following the standard ICSD-3 criteria, in order to accurately measure the prevalence and incidence of sleep disorders in this population. 2. It will be critical to establish if biologics targeting immune mechanisms in psoriasis are effective in decreasing immune markers linked to additional systemic diseases that mediate the risk for sleep-disordered breathing. 3. The incidence of acute vs. chronic insomnia should be measured in patients with psoriasis to determine if the sleep disturbance is acute and stems directly from pruritus and pain, or if it represents ICSD-3 chronic insomnia.	https://www.ncbi.nlm.nih.gov/pubmed/26624228

					Henry 2016 Evidence that in psoriasis, reported sleep rates of sleep disturbance varied substantially. Most studies examined lacked a hypothesis driven research question and/or failed to use validated measures of sleep. This study was unable to draw firm conclusions about the precise prevalence and nature of sleep disturbance within the psoriasis population. Need to systematically and consistently examine sleep in psoriasis populations, employing comprehensive and validated measures of sleep in specifically designed studies.	https://www.ncbi.nlm.nih.gov/pubmed/27327082
					Horreau, 2013 Evidence that there may be a small, but significant increased risk of CVE, but not of CV mortality in psoriasis and PsA patients. The psoriasis attributable risk was difficult to assess due to confounding factors. Heterogeneity in study design, outcome definition and assessment were major limitations. Further studies recommended - (especially those designed to evaluate the true causal relationship between psoriasis and CVD and the relationship between psoriasis severity, age at onset and CVD).	https://www.ncbi.nlm.nih.gov/pubmed/23845149
					Khan, 2017 This meta-analysis suggested that thyroid peroxidase antibody positivity, hypothyroidism and hyperthyroidism may be associated with prevalent psoriatic disease. However, there were only few studies with large heterogeneity regarding psoriatic disease definition and indication of publication bias. Additional prospective data are needed to assess the association of autoimmune thyroid disease with incident psoriatic disease.	https://www.ncbi.nlm.nih.gov/pubmed/28747386
					Kyriakou, 2017 Evidence that leptin and resistin concentrations are higher and adiponectin concentrations are lower in patients with psoriasis compared to controls. High heterogeneity among studies. Although there is evidence that systemic inflammation drives the increased cardiovascular risk and metabolic dysregulation in psoriasis, it is unclear whether psoriatic inflammation leads to the development of cardio-metabolic comorbidities or whether the pre-existing metabolic dysfunction results in immunologic dysregulation and onset of psoriasis. Further studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/29232663
					Li, 2015 Evidence that psoriasis patients have a greater risk of developing chronic obstructive pulmonary disease (COPD) than the general population (odds ratio, 1.90; 95% confidence interval, 1.36–2.65) and that the association between psoriasis and COPD is stronger among patients with severe psoriasis (odds ratio, 2.15; 95% confidence interval, 1.26–3.67). Future research is needed including prospective follow-up studies to explore the mechanisms underlying the observed association and to investigate the role of systemic therapies for psoriasis in the prevention of COPD.	https://www.ncbi.nlm.nih.gov/pubmed/26700640
					Li, 2016 This meta-analysis evidenced a correlation between psoriasis and hyperuricaemia which was ethnicity- or region-dependent; patients with psoriasis in Western Europe were more likely to have hyperuricaemia. Further research needed.	https://www.ncbi.nlm.nih.gov/pubmed/27175702
					Ma, 2013 This systematic review found that psoriasis was significantly associated with greater odds and incidence of dyslipidaemia. Greater psoriasis severity appeared to be associated with higher prevalence of dyslipidaemia. Further studies needed (important to consider directly measure dyslipidaemia via laboratory workup and control for medication use in order to clarify the relationship between psoriasis and dyslipidaemia. Whether well-controlled dyslipidaemia contributes to amelioration of psoriasis symptoms was considered an important and clinically relevant question to be addressed by future study.	https://www.ncbi.nlm.nih.gov/pubmed/23106411
					Miller 2013a Some evidence that psoriasis is associated with ischemic heart disease and cardiovascular risk factors. The association was only significant for hospital-based studies, except for dyslipidemia, which was also significant in population-based studies. Heterogeneity of included studies. Further studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/24238156
					Miller 2013b Evidence that quantifying cardiovascular disease (CVD) risk factors as continuous variables has clinical utility attributing CVD risk for patients with psoriasis. Heterogeneity of included studies. Further studies needed – particularly case control studies reporting continuous data, i.e. mean values and differences instead of odds ratios only (including standardised physical examinations and blood samples).	https://www.ncbi.nlm.nih.gov/pubmed/23815240
					Molina-Leyva, 2015 Evidence that psoriasis patients have a higher risk of sexual dysfunction as compared to the general population. Prospective longitudinal studies are needed to explore the causal factors involved in sexual dysfunction among psoriasis patients.	https://www.ncbi.nlm.nih.gov/pubmed/25424331
					Mosca 2015 Some evidence that psoriatic patients are at increased CV risk, related to raised prevalence and incidence of CV risk factor and to inflammatory status. Further studies needed to establish appropriate targets for CV risk factors, assess the clinical value of screening for subclinical organ damage and determine the impact of disease-modifying therapies on CV risk profile in psoriatic patients.	https://www.ncbi.nlm.nih.gov/pubmed/25464252

					Papp, 2013 Evidence that the prevalence of hypertension, hyperlipidemia, diabetes, obesity, smoking, and metabolic syndrome in the psoriasis population is greater than that in the general population. Future prospective studies with long-term follow-up recommended - including more thorough collection of data on lifestyle factors to determine the following: whether there is a causal relationship between psoriasis and individual CV risk factors or the association is through multiple shared factors; the true magnitude and directionality of the association between psoriasis and CV risk factors; the role of psoriasis in CV risk and the effect of psoriasis duration on CV risk; the impact of therapy on reduction of CV risk and mortality; and whether early intervention with an effective systemic therapy reduces the risk of subsequently developing comorbidities.	https://www.ncbi.nlm.nih.gov/pubmed/23582163
					Phan, 2018 Evidence from this pooled meta-analysis demonstrates a significant association between bullous pemphigoid and psoriasis. This association is stronger in males, in contrast with many other auto-immune conditions. The study is constrained by several limitations. Further studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/30141189
					Pietrzak, 2013 The meta-analysis performed in this study indicated elevated risk of cardiovascular events in psoriatic patients in relation to non-psoriatic controls. Future prospective, longitudinal studies, which incorporate methods of assessing inflammation and psoriasis activity, are needed to fully determine the pathogenic links between psoriasis and CVD.	https://www.ncbi.nlm.nih.gov/pubmed/23347301
					Pouplard, 2013 This systematic literature review shows a small increased risk of some solid cancers in psoriasis, especially those linked to alcohol drinking and cigarette smoking. A higher risk of non-melanoma skin cancers, especially squamous cell carcinoma, is also shown. There is a need for further studies to obtain data from ongoing psoriasis registries including robust assessment of comorbidities and pharmacological treatments to better characterise the risk of cancer in psoriasis.	https://www.ncbi.nlm.nih.gov/pubmed/23845151
					Puig, 2014 Evidence collated regarding a large number of small controlled or cross-sectional studies which report increased prevalence of cardiometabolic and psychological co-morbidities in patients with psoriasis. Evidence from a number of large cohort studies presented to describe the incidence of various cardiometabolic co-morbidities in patients with psoriasis. Evidence for association of severe psoriasis with increased mortality (most common cause of death is cardiovascular disease). Comment that studies on the management of co-morbidities and their impact on psoriasis treatment are scarce and that many questions on the co-morbidities of psoriasis remain to be answered. Further studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/24752135
					Raaby, 2017 This meta-analysis confirmed that patients with psoriasis have an increased risk of CVD, especially those with severe psoriasis. Further studies to investigate whether increased control followed by treatment of cardiovascular risk factors improves the prognosis of psoriatic patients are needed.	https://www.ncbi.nlm.nih.gov/pubmed/28213804
					Rodríguez-Zúñiga 2017a Evidence that the risk for metabolic syndrome is increased by 40% in patients with psoriasis compared with in the general population. Systemic review limited by missing data, high heterogeneity among studies examined, high risk selection bias in studies included in analysis and high probability of selection bias. Further studies recommended.	https://www.ncbi.nlm.nih.gov/pubmed/28917453
					Rodríguez-Zúñiga 2017b Evidence that psoriasis is highly associated with the metabolic syndrome in Latin America. The association is stronger for severe psoriasis and when the adult treatment panel guidelines (ATP-III criteria) are used to identify cardiovascular disease risk. Limited data available – further study required.	https://www.ncbi.nlm.nih.gov/pubmed/28117050
					Roubille 2015 This meta-analysis provided evidence that TNF inhibitors and methotrexate decrease the risk of cardiovascular events (CVEs) in patients with rheumatoid arthritis (RA) whereas NSAIDs and corticosteroids increase the risk of CVEs. In patients with psoriasis and psoriatic arthritis (PsA/Pso) limited evidence suggested that treatment with systemic therapies is associated with a decrease in the risk of all CVEs. Large, prospective, adequately controlled and powered studies are needed to explore the effects of systemic/biologic therapies on cardiovascular morbidity and mortality in both the RA and PsA/Pso populations.	https://www.ncbi.nlm.nih.gov/pubmed/25561362
					Rouzaud, 2014 More work needed to define which psoriasis clinical features indicate an increased risk of PsA. The presence of scalp, nail and intergluteal involvement appear to be important warning signs for dermatologists that their psoriasis patients may be at increased risk of PsA. Severity and extent of psoriasis may also be significant risk factors for PsA.	https://www.ncbi.nlm.nih.gov/pubmed/24985559

					Rungapiromnan, 2017 Biologic therapies including TNFi, an anti-IL-12/23 agent (ustekinumab) and anti-IL-17A agents (secukinumab and ixekizumab) have no significant impact on the risk of major adverse cardiovascular events (MACEs) in adult patients with plaque psoriasis over the short term. However, follow-up was limited and patient characteristics were those of patients participating in RCTs. Recommendation – need for well-designed observational studies that involve larger numbers of patients and longer durations of treatment exposure reflecting routine clinical practice required to determine the impact of biologic therapies on the risk of MACEs in patients with psoriasis.	https://www.ncbi.nlm.nih.gov/pubmed/27518205
					Saleem, 2017 Database studies might not fully account for confounders, resulting in overestimates of the risk impact of comorbidities. Knowing the baseline risk, relative risk, and attributed risk, together, provides a better overall understanding of the impact an exposure has on any given disease in a defined population. Further work to understand whether screening and intervention (for co-morbid disease) should be done requires more than just knowing there is a greater relative risk and more than knowing that a treatment that can reduce that risk. Studies to consider costs and benefits, including how big a problem the comorbidity is on an absolute basis not just on a relative basis, need to be carried out.	https://www.ncbi.nlm.nih.gov/pubmed/27986396
					Samarasekera, 2013 Evidence that severe psoriasis is associated with an increased risk of CVD. Uncertainty remains about whether CVD risk is directly attributable to psoriasis, as the majority of studies failed to adequately adjust for key traditional risk factors. Further research is required to better understand the complex relationship between psoriasis, traditional risk factors, and CVD. Long-term, large-scale cohort studies that adequately control for confounding factors and detection bias are required to address the question of whether aggressive treatment of severe psoriasis has an impact on clinically relevant CVD end points.	https://www.ncbi.nlm.nih.gov/pubmed/23528816
					Shaharyar, 2014 Evidence that patients with psoriasis have an increased burden of subclinical atherosclerosis and endothelial dysfunction. Further clinical trials to identify appropriate screening strategies for subclinical cardiovascular disease (CVD), and whether non-pharmacological and pharmacological approaches result in slower progression of subclinical CVD / reduction in clinical events among patients with psoriasis are needed.	https://www.ncbi.nlm.nih.gov/pubmed/24401219
					Singh, 2016 Evidence that patients with psoriasis have a greater prevalence of metabolic syndrome as well as its individual components when compared to the general population. The odds of metabolic syndrome and its components are higher with increased psoriasis disease severity. Prospective studies are needed to better understand the contribution of psoriasis in the development of metabolic syndrome.	https://www.ncbi.nlm.nih.gov/pubmed/27589483
					Singh 2017a Evidence that patients with psoriasis have higher odds of having metabolic syndrome when compared with the general population. The pathologic mechanisms shared by these two disease processes, as well as the directionality of the relationship, are not well understood and need to be elucidated through further translational research.	https://www.ncbi.nlm.nih.gov/pubmed/28719618
					Singh, 2017b Evidence that patients with psoriasis have a significantly higher likelihood of suicidal ideation, suicide attempts, and completed suicides. In patients with psoriasis, those who are younger and whose psoriasis is more severe are at particular risk for suicidality. Potential sources of bias and study heterogeneity. Further investigation to understand this association more fully needed. Jin Patients with psoriasis have a higher prevalence of metabolic syndrome and hypertension compared with controls. More prospective, controlled and randomised studies need to be performed in the future.	https://www.ncbi.nlm.nih.gov/pubmed/28807109
					Thrastardottir, 2018 The data from this study were inconsistent and further studies are needed to verify or refute the purported association between infection and the risk of developing PsA – in particular laryngeal infections and infections caused by streptococci.	https://www.ncbi.nlm.nih.gov/pubmed/29124396
					Tsai, 2018 Some evidence that patients with psoriasis might have higher serum homocysteine and lower folate levels than control patients who do not have psoriasis. However, due to significant heterogeneity between studies reviewed and other limitations, further research needed.	https://www.ncbi.nlm.nih.gov/pubmed/30074615
					Tzellos, 2013 Some evidence that, there is a significant difference in the rate of major adverse cardiovascular events (MACEs) observed in patients receiving anti-IL-12/23 biological agents compared to those treated with placebo. Further studies recommended including post-marketing surveillance and meta-analysis of observational studies and RCTs.	https://www.ncbi.nlm.nih.gov/pubmed/22404103
					Ungprasert 2016a This meta-analysis provided evidence for a significant association between psoriasis and COPD, an under-recognised co-morbidity, with an overall 1.45-fold increased risk. Further studies are required.	https://www.ncbi.nlm.nih.gov/pubmed/26458363
					Ungprasert 2016b Some evidence for increased risk of incident atrial fibrillation among patients with psoriasis. Limitations in study design acknowledged. Further studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/27451924

					Ungprasert, 2016c Some evidence for increased risk of Parkinson's disease among patients with psoriasis. Limitations in study design acknowledged. Further studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/27057013
					Ungprasert, 2017 This meta-analysis demonstrated an approximately 3-fold increased risk of coeliac disease among patients with psoriasis. The pathophysiologic mechanisms behind this increased risk are not known, and further investigations are required.	https://www.ncbi.nlm.nih.gov/pubmed/28216724
					Ungprasert 2018a Evidence that risk of psoriasis among patients with schizophrenia was significantly higher than non-schizophrenia subjects (83% excess risk). Future work needed to determine this nature and mechanism of this observation.	https://www.ncbi.nlm.nih.gov/pubmed/29128620
					Ungprasert 2018b Evidence for a significantly increased risk of incident chronic kidney disease and end-stage renal disease among patients with psoriasis compared with individuals without psoriasis. How this risk should be addressed in clinical practice requires more study with emphasis on prevention and surveillance programmes.	https://www.ncbi.nlm.nih.gov/pubmed/29644523
					Upala, 2017 This meta-analysis of prospective studies demonstrated that patients with psoriasis have increased risk of new-onset atrial fibrillation. Future interventional studies addressing the impact of psoriasis treatment and prevention of atrial fibrillation are required.	https://www.ncbi.nlm.nih.gov/pubmed/27794626
					Villani, 2015 The prevalence of undiagnosed PsA was 15.5% when all studies were considered and 10.1% when only epidemiological studies were considered. Data were obtained from studies not designed to determine the prevalence of undiagnosed PsA among those with psoriasis. Heterogeneity between studies was high. Need for dermatologists and rheumatologists to work closely together but further studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/26054432
					Wang, 2016 This meta-analysis demonstrated no significant difference in total cholesterol, LDL, HDL or triglycerides between patients with psoriasis and controls. Patients with psoriasis had higher epicardial fat tissue (EFT) compared to controls which may suggest that EFT is an independent risk factor of psoriasis. Further studies needed to elucidate these relationships.	https://www.ncbi.nlm.nih.gov/pubmed/27245937
					Wang, 2017 Some evidence that there are associations between psoriasis and cardiovascular risk, homocysteine, and aberrant DNA methylation. However, more work is needed, specifically new and efficient studies to evaluate whether homocysteine acts as a bridge between cardiovascular risk and aberrant DNA methylation.	https://www.ncbi.nlm.nih.gov/pubmed/28776552
					Wang 2018 This meta-analysis indicated that patients with psoriasis had an increased risk of asthma which was higher in older patients with psoriasis than in younger patients. Further studies are needed to confirm this observation and overcome the limitations of this analysis (particularly with respect to diagnostic accuracy of both complex conditions).	https://www.ncbi.nlm.nih.gov/pubmed/29490768
					Whitlock, 2018 There are no known clinical trials of treatment specifically for concurrent psoriasis and inflammatory bowel disease. Evidence that infliximab and adalimumab have efficacy in psoriasis, psoriatic arthritis, ulcerative colitis, and Crohn's disease; other agents have demonstrated efficacy for some, but not all, of these indications. Further studies including rigorous examination of long-term data is needed.	https://www.ncbi.nlm.nih.gov/pubmed/29332708
					Wu, 2015 Evidence for an overall increased risk of autism in children with family history of autoimmune disease (including psoriasis) was identified. More mechanistic studies are needed to further explain the association between family history of autoimmune disease and increased risk of autism in children.	https://www.ncbi.nlm.nih.gov/pubmed/25981892
					Wu, 2018 This meta-analysis examined the relationship between psoriasis and risk of erectile dysfunction. The studies included were mostly cross-sectional or small sample cohorts, which could introduce bias and heterogeneity into the analysis. Some evidence that psoriasis is associated with an increased risk of erectile dysfunction. Prospective cohort studies are needed to elucidate these relationships and to advance knowledge in this field.	https://www.ncbi.nlm.nih.gov/pubmed/29735408
					Yang, 2016 Evidence for TNF inhibitors having clinical benefit with regard to adverse cardiovascular events in psoriasis and/or PsA. Rigorous randomised controlled trials needed to evaluate whether TNF inhibitors truly result in reduction of cardiovascular diseases.	https://www.ncbi.nlm.nih.gov/pubmed/27300248
					Zhang, 2017 Evidence that there is a correlation between psoriasis and erectile dysfunction. Patients with psoriasis may have a higher incidence of erectile dysfunction though this observation needs to be further confirmed by further high quality studies. Ungprasert 2014 Evidence for a statistically significant increased risk of venous thromboembolism among patients with psoriasis. Limited data available – further study required.	https://www.ncbi.nlm.nih.gov/pubmed/29706048

B	**To what extent is psoriasis caused by a person's genes or other factors, such as stress, gut health, water quality, change in the weather or temperature?**	Does stress aggravate psoriasis and if so to what degree?	252	8		
					Albert 2014 Evidence that an exacerbation of psoriasis is frequently associated with lithium treatment. More studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/24572579
					Brenaut, 2013 Evidence that alcohol consumption is greater in psoriasis patients than in the general population. However, there is not enough evidence to establish whether alcohol consumption is a risk factor for psoriasis. More research needed.	https://www.ncbi.nlm.nih.gov/pubmed/23845150
					Al-Dhubaibi, 2018 Evidence that there is a correlation between psoriasis and Vitamin D deficiency. There is a need for larger scale case-control studies to assess the role of vitamin D deficiency in psoriasis.	https://www.ncbi.nlm.nih.gov/pubmed/29623015
					Armstrong, 2014 Evidence of an association between smoking and incidence of psoriasis, with a possible dose-effect of smoking intensity and duration on psoriasis incidence. This review suggested that smoking is an independent risk factor for the development of psoriasis, and that patients with established psoriasis continue to smoke more than patients without psoriasis. More studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/24117435
					Aune, 2018 Evidence that adiposity as measured by BMI, waist circumference, waist-to-hip ratio, and weight gain is associated with increased risk of psoriasis. Further research needed.	https://www.ncbi.nlm.nih.gov/pubmed/29680995
					Dobson, 2013 Evidence for a significant increase in the risk of psoriasis in people with multiple sclerosis (MS). Evidence for no increased risk of psoriasis in first-degree relatives of people with MS. Limited data available. More studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/23315260
					Fleming 2015 Increased severity of psoriasis appears to be associated with increased BMI. Most studies were cross-sectional or case-control, making it difficult to determine temporality. Further studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/26271963
					Han Evidence that apolipoprotein E (ApoE) polymorphisms are associated with the risk of psoriasis, especially ε2 and ε3 alleles. Further studies are needed.	https://www.ncbi.nlm.nih.gov/pubmed/23142524
					Jia 2013 This meta-analysis evidenced that the TNF-a –238 and –308 promoter polymorphisms may play different roles in conferring susceptibility to psoriasis. Further functional and well-designed studies should be conducted to confirm these results.	https://www.ncbi.nlm.nih.gov/pubmed/24252077
					Lee 2013 This meta-analysis evidenced that the IL-23R (rs11209026 and rs7530511) polymorphisms are associated with psoriasis risk in Europeans and that the IL-12B (rs6887695 and rs3212227) polymorphisms are associated with susceptibility to psoriasis in Europeans. Further studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/23844553
					Lee 2015 This meta-analysis provided evidence for the vascular endothelial growth factor VEGF +405 C/G polymorphism conferring susceptibility to psoriasis in Asians, with the -460 C/T and -1154 A/G polymorphisms conferring susceptibility to psoriasis in Europeans. Further investigation of the associations between VEGF polymorphisms and psoriasis susceptibility needed. Liang Evidence that the cytotoxic T-lymphocyte antigen-4 (CTLA-4) +49A/G polymorphism may not contribute to psoriasis and vitiligo susceptibility. Further well-designed studies with large sample size are needed to confirm this.	https://www.ncbi.nlm.nih.gov/pubmed/26600499
					Liu 2012 This meta-analysis showed that ApaI, TaqI polymorphisms in the vitamin D receptor gene are associated with psoriasis in Caucasians. Further studies are needed.	https://www.ncbi.nlm.nih.gov/pubmed/22540341
					Liu 2013 Evidence that the angiotensis-converting enzyme (ACE) polymorphism is associated with the risk of psoriasis in Asians, especially the I/I genotype and I allele. Further studies are needed.	https://www.ncbi.nlm.nih.gov/pubmed/23621089
					Marrie, 2015 Evidence that there is a lack of data/studies to provide a good estimate of the incidence or prevalence of autoimmune comorbidity (including psoriasis) in multiple sclerosis. Further studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/25533299
					Nie 2016 Evidence that the IL-6 -174G/C polymorphism contributes to psoriasis risk. Further studies needed to validate these results.	https://www.ncbi.nlm.nih.gov/pubmed/27421005
					Pollock 2017 Evidence for the involvement of epigenetic mechanisms in the aetiology of psoriatic disease. Further studies needed. Several recommendations made regards to research questions and study design.	https://www.ncbi.nlm.nih.gov/pubmed/27965059

					Phan, 2018 Evidence from this pooled meta-analysis demonstrates a significant association between bullous pemphigoid and psoriasis. This association is stronger in males, in contrast with many other auto-immune conditions. The study is constrained by several limitations. Further studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/30141189
					Qi 2014 Evidence from this meta-analysis support the hypothesis that single-nucleotide polymorphism markers at + 405C > G, - 460C > T, and - 1154G >A of the VEGF gene may serve as biological markers of psoriasis. Future studies should investigate interactions among multiple genotypes and environmental exposures to identify the role of proangiogenic markers in psoriasis and to delineate the underlying mechanisms of psoriasis.	https://www.ncbi.nlm.nih.gov/pubmed/24678886
					Qi 2015 This meta-analysis indicated that the methylenetetrahydrofolate reductase (MTHFR) 677C/T polymorphism may not be associated with psoriasis risk. Further studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/25966157
					Qiu, 2013 This meta-analysis provided evidence that CD226 Gly307Ser (rs763361) is significantly associated with the risk of multiple autoimmune diseases. Further studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/23073294
					Richer, 2016 Evidence for a positive association between the prevalence of smoking and psoriasis as well as an association between smoking and severity of psoriasis. Further research required.	https://www.ncbi.nlm.nih.gov/pubmed/26553732
					Romiti, 2016 Evidence that psoriasis (and guttate psoriasis) may be a drug-induced phenomenon with anti-TNFα therapies. More studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/27001339
					Shi 2016 Evidence for a significant association between the CARD14 rs11652075 polymorphism and psoriasis. Due to the current lack of data concerning clinical subtypes and genotype frequencies, more careful stratification and interaction analyses, taking into account disease subgroups, are needed. The pathogenicity of the association with rs11652075 needs to be validated further in independent cohorts and subsequent pathophysiologic and therapeutic studies.	https://www.ncbi.nlm.nih.gov/pubmed/27706581
					Song 2014 This meta-analysis showed that the major histocompatibility complex class I chain-related gene A transmembrane (MICA-TM) A9 allele is associated with psoriasis susceptibility in Asian populations and that the MICA-TM A9 allele is associated with a PsA risk in Europeans. Further studies are required.	https://www.ncbi.nlm.nih.gov/pubmed/23974432
					Song 2015 Evidence that the angiotensin converting enzyme (ACE) insertion / deletion (I/D) polymorphism is associated with susceptibility to rheumatoid arthritis, especially in Arab populations. Association with psoriasis was also investigated. Further studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/23413281
					Shen 2015 Evidence that the genetic variant(s) within the late cornified envelop (LCE)3 genes may influence the development of psoriasis and PsA possibly by interrupting the terminal differentiation of keratinocytes. Further studies are recommended to explore the precise role of LCE3 genes in the pathogenesis of psoriasis and PsA.	https://www.ncbi.nlm.nih.gov/pubmed/25697099
					Stefanic, 2013 Evidence that no genetic variant in the vitamin D receptor (VDR) gene has a robust and reproducible association with risk for psoriasis. Any association that may exist is likely to be weak and potentially restricted to specific populations. Further studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/23488577
					Stewart, 2018 This systematic review demonstrates a probable temporal association between different measures of psychological stress and onset, recurrence, and severity of psoriasis. Future research needed.	https://www.ncbi.nlm.nih.gov/pubmed/29516474
					Snast, 2018 Evidence that the association between preceding stress and exacerbation/onset of psoriasis is based primarily on retrospective studies with many limitations. No convincing evidence exists that preceding stress is strongly associated with exacerbation/onset of psoriasis. Future research needed.	https://www.ncbi.nlm.nih.gov/pubmed/29124739
					Ungprasert 2017 Evidence that patients with periodontitis have a significantly elevated risk of psoriasis. Further research is needed to determine whether the association between periodontitis and psoriasis is causal.	https://www.ncbi.nlm.nih.gov/pubmed/28216724
					Ungprasert 2018a Evidence that risk of psoriasis among patients with schizophrenia was significantly higher than non-schizophrenia subjects (83% excess risk). future work needed to determine this nature and mechanism of this observation.	https://www.ncbi.nlm.nih.gov/pubmed/29128620
					van Vugt 2018 Evidence that pharmacogenetic studies in psoriasis have generated divergent results. HLA-Cw6 may be promising as a predictor for ustekinumab efficacy. Replication of findings in larger cohorts is required. Large-scale hypothesis-free searches for genetic biomarkers are needed to uncover the complete genetic background of outcomes for treatment with biologics.	https://www.ncbi.nlm.nih.gov/pubmed/28646581

					Versini 2014 Evidence that obesity worsens the course of, and impairs the treatment response of psoriasis, PsA (and other autoimmune diseases). Extensive clinical data and experimental models demonstrate the involvement of adipokines in the pathogenesis of these autoimmune diseases. Obesity appears to be a major environmental factor contributing to the onset and progression of autoimmune diseases. More studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/25092612
					Wu 2016 Evidence that the methylenetetrahydrofolate reductase (MTHFR) C677T polymorphism, , is not a genetic factor for the pathogenesis of psoriasis (qualitatively) but could influence the severity of psoriasis (quantitatively). Further research required.	https://www.ncbi.nlm.nih.gov/pubmed/26212228
					Wei 2015 Evidence that the vascular endothelial growth factor VEGF +405G-C polymorphism may be associated with chronic immune-mediated inflammatory diseases, and vary between ethnic groups. Further studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/26007152
					Xiao 2016 Evidence that the IL-12B 3′-untranslated region (UTR) and rs6887695 single nucleotide polymorphisms (SNPs) are associated with susceptibility to autoimmune diseases (including psoriasis). More research needed including large sample studies, different ethnic groups with careful matching between cases and controls. Also, further evaluation of the effect of gene–gene and gene–environment interactions on the IL-12B 30-UTR and rs6887695 SNP and autoimmune disease risk is recommended.	https://www.ncbi.nlm.nih.gov/pubmed/27068848
					Xia 2014 Evidence from this meta-analysis that the presence of the CD143 ID polymorphism may modify the risk of psoriasis in individuals with East Asian ancestry. Further large-scale studies to evaluate the impact of CD143ID polymorphism on psoriasis are needed.	https://www.ncbi.nlm.nih.gov/pubmed/24997622
					Zhao 2013 Evidence for a significant association between psoriasis and 50 HLAB alleles. The association varied in terms of race, and clinical type and onset age of psoriasis. Future studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/23600465
					Zhao 2014 Evidence that psoriasis is associated with a number of HLA-A alleles, some are confer susceptibility, some are protective. The association of some alleles is different in terms of different races, clinical types and onset age. Further studies are needed.	https://www.ncbi.nlm.nih.gov/pubmed/23981037
					Zhao 2016 This meta-analysis demonstrated that IL-12 p40 gene (IL-12B rs3212227) was associated with the risk of psoriasis in European and Asian populations. More studies are required for the exploration of the pathogenesis of psoriasis.	https://www.sciencedirect.com/science/article/pii/S1027811716000021
					Zhuang 2013 This meta-analysis evidenced that the TNF-α 308 G/A polymorphism is associated with decreased risk of psoriasis, while TNF-α 238 G/A is associated with increased risk of psoriasis. Further studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/24324571
					Zhu 2013a Evidence for a significant association between IL12B gene polymorphisms and psoriasis and PsA. Further studies needed. Zhu 2013b Single nucleotide polymorphisms (SNPs) in the TNFα gene promoter region alter the risk of psoriasis and/or PsA. Further studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/23717605
					Zheng, 2018 Evidence that intense physical activity may lower the prevalence of psoriasis. Further research needed.	https://www.ncbi.nlm.nih.gov/pubmed/29979432
C	**Do lifestyle factors such as diet, dietary supplements, alcohol, smoking, weight loss and exercise play a part in treating psoriasis?**	What lifestyle changes if any are proven to help psoriasis	159	1		
					Notay, 2017 Some evidence presented for probiotics for symptomatic and clinical improvement in atopic dermatitis and acne. No clinical psoriasis data presented (inflammatory markers only). More research required.	https://www.ncbi.nlm.nih.gov/pubmed/28681230
					Upala, 2017 Some evidence for nonsurgical weight loss intervention presented. More RCTs required to provide greater quality data.	https://www.ncbi.nlm.nih.gov/pubmed/27794626
D	**What is the best way to treat the symptoms of psoriasis: itching, burning, redness, scaling and flaking?**	How can itching be controlled properly?	54	4		
					Shahwan Evidence of no significant difference in mean baseline itch scores in patients with psoriasis or atopic dermatitis who need treatment with systemic therapies. Evidence that pruritus is a more significant component of psoriasis than previously recognised. Pruritus in psoriasis has been associated with occupational impairment, anxiety, depression, and has a negative impact on overall quality of life, mood, concentration, sleep, sexual desire, and appetite. Further research is needed.	https://www.ncbi.nlm.nih.gov/pubmed/28522048

					van Laarhoven Evidence that placebo can have a substantial effect in the treatment of itch in dermatological patients with chronic itch due to a variety of skin diseases including psoriasis. Further research needed.	https://www.ncbi.nlm.nih.gov/pubmed/25609025
E	**How does psoriasis affect a person psychologically?**	Does living with psoriasis make you more likely to want to commit suicide?	8	16		
					Abbott, 2015 Evidence that TNF-α inhibitor therapy reduces depression in people who have chronic diseases (including those with psoriasis) though the effects are small. Limited data available. Further studies investigating a more detailed timeline of changes in depression, inflammatory biomarkers and disease activity status in patients with psoriasis (and other chronic diseases) are required.	https://www.ncbi.nlm.nih.gov/pubmed/25935351
					Cullen, 2019 Evidence for a positive overall association between non-neurological autoimmune (NNAI) disorders and psychosis, which was not consistent across all NNAI disorders. Separate meta-analyses were conducted for individual autoimmune disorders. A significant positive association was observed for psoriasis. Future work recommended: 1) studies should be designed to better disentangle the temporal nature of the association between NNAI disorders and psychosis, as such studies have demonstrated that both psychosis and depression show bidirectional associations with autoimmune disorders; 2) larger studies should be undertaken to examine the presence of neuronal surface autoantibodies among individuals with psychosis; 3) greater efforts should be made in large cohort studies to include information on potential confounders, such as socioeconomic status, adversity, and tobacco use; and 4) studies should be undertaken to evaluate the effect of corticosteroid treatment on the relationship between NNAI disorders and psychosis.	https://www.ncbi.nlm.nih.gov/pubmed/30122288
					Chi, 2017 This systemic review and meta-analysis concluded that the available limited, very low-quality evidence does not support an association between psoriasis and suicidal thought and behaviour. Further studies that provide data for different age and sex groups are needed to clarify whether a subgroup of patients with psoriasis has an elevated risk of suicidality.	https://www.ncbi.nlm.nih.gov/pubmed/28409490
					Chen 2014 Evidence that psychological and/or educational interventions improve psychological and quality of life (QOL) outcomes in psoriasis. The review concluded that further research is needed to examine the effectiveness of psychological and/or educational interventions for individuals with psoriasis, including a greater number of RCTs in order to increase the methodological validity of intervention studies. Also, future research needs to be conducted to establish which interventions are most effective for specific sub-populations who may best profit from psycho-educational interventions.	https://www.ncbi.nlm.nih.gov/pubmed/25109476
					Dowlatshahi, 2014 Evidence that psoriasis patients are at least one and a half times more likely to manifest signs of clinical depression compared with their healthy peers. More than one-quarter of psoriasis patients show symptoms of depression and approximately one-tenth have signs of clinical depression. High heterogeneity between studies. Further work to clarify this relationship needed.	https://www.ncbi.nlm.nih.gov/pubmed/24284419
					Ferreira 2016 Evidence that many mental disorders are associated with psoriasis although the aetiopathogenesis of that connection is wide. Some psychiatric comorbidities may result from the psychosocial impact of having a chronic skin condition. However, psoriasis can be maintained and exacerbated by an underlying psychiatric condition. Further studies to explore these relationships in more detail and establish aetiology are needed.	https://www.ncbi.nlm.nih.gov/pubmed/27386050
					Ferreira 2017 Evidence that the prevalence of psychiatric conditions in psoriasis may range from 24% to 90%. The link between psoriasis and associated mental disorders is frequently forgotten or not considered in clinical practice and psychiatric disorders in patients with psoriasis may be underdiagnosed. Limited data available – further study required.	https://www.ncbi.nlm.nih.gov/pubmed/29197196
					Fleming 2015 Evidence that treatment with adalimumab, etanercept and ustekinumab are associated with statistically significant reductions in depressive symptom scores using various scales in patients with moderate-to-severe psoriasis. A robust RCT including standardised criteria is required to better determine the clinical significance of these findings. In the interim, it is suggested that patients with psoriasis should be screened for depression when appropriate and refered accordingly.	https://www.ncbi.nlm.nih.gov/pubmed/25490866
					Fleming 2017 Evidence for a high prevalence of anxiety of adult patients with psoriasis suggesting that patients would benefit from systematic screening. Although the data suggest that anxiety may be improved through various psoriasis treatments, larger prospective randomized trials are needed to confirm this effect.	https://www.ncbi.nlm.nih.gov/pubmed/27620704

					Fordham 2013 Due to low quality evidence it is currently insufficient to judge stress reduction interventions as either effective or ineffective. The authors make nine recommendations for future research in this multidisciplinary field.	https://www.ncbi.nlm.nih.gov/pubmed/23116223
					Gupta, 2016 This systematic review evidences a link between psoriasis and PsA with obstructive sleep apnoea and restless legs syndrome. In this study there was no conclusive evidence that psoriasis and PsA are associated with an elevated prevalence of insomnia, periodic limb movement disorder, narcolepsy, or shift work disorder. The relationship between psoriatic conditions and other sleep disorders was not examined. Future research recommended including: 1. It is important that epidemiological studies in psoriasis evaluate sleep disorders following the standard ICSD-3 criteria, in order to accurately measure the prevalence and incidence of sleep disorders in this population. 2. It will be critical to establish if biologics targeting immune mechanisms in psoriasis are effective in decreasing immune markers linked to additional systemic diseases that mediate the risk for sleep-disordered breathing. 3. The incidence of acute vs. chronic insomnia should be measured in patients with psoriasis to determine if the sleep disturbance is acute and stems directly from pruritus and pain, or if it represents ICSD-3 chronic insomnia.	https://www.ncbi.nlm.nih.gov/pubmed/26624228
					Henry, 2016 Evidence that in psoriasis, reported sleep rates of sleep disturbance varied substantially. Most studies examined lacked a hypothesis driven research question and/or failed to use validated measures of sleep. This study was unable to draw firm conclusions about the precise prevalence and nature of sleep disturbance within the psoriasis population. Need to systematically and consistently examine sleep in psoriasis populations, employing comprehensive and validated measures of sleep in specifically designed studies.	https://www.ncbi.nlm.nih.gov/pubmed/27327082
					Mattei 2014 Evidence that mean PASI and DLQI correlate predictably in patients with chronic moderate-to-severe plaque psoriasis undergoing treatment with biological agents. A reduction in PASI of at least 75% can translate to significant quality-oflife improvement in patients treated with these therapies. Further research important to quantify benefit following greater degrees of skin clearance.	https://www.ncbi.nlm.nih.gov/pubmed/23425140
					Puig, 2014 Evidence collated regarding a large number of small controlled or cross-sectional studies which report increased prevalence of cardiometabolic and psychological co-morbidities in patients with psoriasis. Evidence from a number of large cohort studies presented to describe the incidence of various cardiometabolic co-morbidities in patients with psoriasis. Evidence for association of severe psoriasis with increased mortality (most common cause of death is cardiovascular disease). Comment that studies on the management of co-morbidities and their impact on psoriasis treatment are scarce and that many questions on the co-morbidities of psoriasis remain to be answered. Further studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/24752135
					Stewart, 2018 This systematic review demonstrates a probable temporal association between different measures of psychological stress and onset, recurrence, and severity of psoriasis. Future research needed.	https://www.ncbi.nlm.nih.gov/pubmed/29516474
					Snast, 2018 Evidence that the association between preceding stress and exacerbation/onset of psoriasis is based primarily on retrospective studies with many limitations. No convincing evidence exists that preceding stress is strongly associated with exacerbation/onset of psoriasis. Future research needed.	https://www.ncbi.nlm.nih.gov/pubmed/29124739
					Singh, 2017b Evidence that patients with psoriasis have a significantly higher likelihood of suicidal ideation, suicide attempts, and completed suicides. In patients with psoriasis, those who are younger and whose psoriasis is more severe are at particular risk for suicidality. Potential sources of bias and study heterogeneity. Further investigation to understand this association more fully needed.	https://www.ncbi.nlm.nih.gov/pubmed/28807109
					Ungprasert 2018a Evidence that risk of psoriasis among patients with schizophrenia was significantly higher than non-schizophrenia subjects (83% excess risk). Future work needed to determine this nature and mechanism of this observation.	https://www.ncbi.nlm.nih.gov/pubmed/29128620
					Ungprasert 2018b Evidence that risk of psoriasis among patients with schizophrenia was significantly higher than non-schizophrenia subjects (83% excess risk). Future work needed to determine this nature and mechanism of this observation.	https://www.ncbi.nlm.nih.gov/pubmed/29644523
F	**What's the best way to treat sudden flare ups of psoriasis?**	How do you stop psoriasis flare ups?	7	10		
					No systematic reviews identified	**No systematic reviews identified**

G	**How do changes in female hormones, such as during puberty, pregnancy, miscarriage, menopause and contraceptive use, affect psoriasis and its treatment?**	Do hormonal changes at puberty, pregnancy, menopause etc have any effect on the severity of psoriasis symptoms?	20	18		
					Bobotsis, 2016 No clear evidence of increased adverse (pregnancy) outcomes in pregnant women with psoriasis. Future research needed.	https://www.ncbi.nlm.nih.gov/pubmed/26991866
					Paziana 2013 Evidence that ciclosporin use during pregnancy may be a safe alternative for patients with autoimmune disease (including psoriasis) refractory to conventional treatment. Further studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/23516008
					Pottinger, 2018 This systematic review concluded that the potential effect of biologics on pregnancy outcomes specifically in women with psoriasis has not been adequately studied to quantify accurately. Data on use in other indications is limited. Women of child-bearing potential should be advised routinely to use regular contraception; however, when planning conception the risks and benefits of continuing vs. stopping therapy should be discussed on a case-by-case basis. To address the clinical uncertainty, large disease-matched cohort studies are required, taking into account potential confounders such as disease activity, concomitant therapies and maternal demographics. Psoriasis-specific pharmacovigilance registries, for example the British Association of Dermatologist Biologics Intervention Register (BADBIR) in collaboration with others via the European Psoriasis Registry Network (PSONET), provide opportunity to collate such data.	https://www.ncbi.nlm.nih.gov/pubmed/28718898
H	**Are lifestyle factors such as diet, alcohol intake, weight change and smoking involved in causing psoriasis?**	What is the connection between nicotine and psoriasis?	91	13		
					Armstrong, 2014 Evidence of an association between smoking and incidence of psoriasis, with a possible dose-effect of smoking intensity and duration on psoriasis incidence. This review suggested that smoking is an independent risk factor for the development of psoriasis, and that patients with established psoriasis continue to smoke more than patients without psoriasis. More studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/24117435
					Aune, 2018 Evidence that adiposity as measured by BMI, waist circumference, waist-to-hip ratio, and weight gain is associated with increased risk of psoriasis. Further research needed.	https://www.ncbi.nlm.nih.gov/pubmed/29680995
					Brenaut Evidence that alcohol consumption is greater in psoriasis patients than in the general population. However, there is not enough evidence to establish whether alcohol consumption is a risk factor for psoriasis. More research needed.	https://www.ncbi.nlm.nih.gov/pubmed/23845150
					Richer, 2016 Evidence for a positive association between the prevalence of smoking and psoriasis as well as an association between smoking and severity of psoriasis. Further research required. Fleming Increased severity of psoriasis appears to be associated with increased BMI. Most studies were cross-sectional or case-control, making it difficult to determine temporality. Further studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/26553732
					Versini 2014 Evidence that obesity worsens the course of, and impairs the treatment response of psoriasis, PsA (and other autoimmune diseases). Extensive clinical data and experimental models demonstrate the involvement of adipokines in the pathogenesis of these autoimmune diseases. Obesity appears to be a major environmental factor contributing to the onset and progression of autoimmune diseases. More studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/25092612
					Zheng, 2018 Evidence that intense physical activity may lower the prevalence of psoriasis. Further research needed.	https://www.ncbi.nlm.nih.gov/pubmed/29979432
I	**Could gene therapy help to treat psoriasis?**	What gene therapy is being developed to help Psoriasis sufferers?	5	15		
					Han Evidence that apolipoprotein E (ApoE) polymorphisms are associated with the risk of psoriasis, especially ε2 and ε3 alleles. Further studies are needed.	https://www.ncbi.nlm.nih.gov/pubmed/23142524
					Jia 2013 This meta-analysis evidenced that the TNF-a –238 and –308 promoter polymorphisms may play different roles in conferring susceptibility to psoriasis. Further functional and well-designed studies should be conducted to confirm these results.	https://www.ncbi.nlm.nih.gov/pubmed/24252077
					Lee 2013 This meta-analysis evidenced that the IL-23R (rs11209026 and rs7530511) polymorphisms are associated with psoriasis risk in Europeans and that the IL-12B (rs6887695 and rs3212227) polymorphisms are associated with susceptibility to psoriasis in Europeans. Further studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/23844553

					Lee 2015 This meta-analysis provided evidence for the vascular endothelial growth factor VEGF +405 C/G polymorphism conferring susceptibility to psoriasis in Asians, with the -460 C/T and -1154 A/G polymorphisms conferring susceptibility to psoriasis in Europeans. Further investigation of the associations between VEGF polymorphisms and psoriasis susceptibility needed.	https://www.ncbi.nlm.nih.gov/pubmed/26600499
					Liang 2015 Evidence that the cytotoxic T-lymphocyte antigen-4 (CTLA-4) +49A/G polymorphism may not contribute to psoriasis and vitiligo susceptibility. Further well-designed studies with large sample size are needed to confirm this.	https://www.ncbi.nlm.nih.gov/pubmed/26013045
					Liu 2012 This meta-analysis showed that ApaI, TaqI polymorphisms in the vitamin D receptor gene are associated with psoriasis in Caucasians. Further studies are needed.	https://www.ncbi.nlm.nih.gov/pubmed/22540341
					Liu 2013 Evidence that the angiotensis-converting enzyme (ACE) polymorphism is associated with the risk of psoriasis in Asians, especially the I/I genotype and I allele. Further studies are needed.	https://www.ncbi.nlm.nih.gov/pubmed/23621089
					Nie 2016 Evidence that the IL-6 -174G/C polymorphism contributes to psoriasis risk. Further studies needed to validate these results.	https://www.ncbi.nlm.nih.gov/pubmed/27421005
					Pollock 2017 Evidence for the involvement of epigenetic mechanisms in the aetiology of psoriatic disease. Further studies needed. Several recommendations made regards to research questions and study design.	https://www.ncbi.nlm.nih.gov/pubmed/27965059
					Qi 2014 Evidence from this meta-analysis support the hypothesis that single-nucleotide polymorphism markers at + 405C > G, - 460C > T, and - 1154G >A of the VEGF gene may serve as biological markers of psoriasis. Future studies should investigate interactions among multiple genotypes and environmental exposures to identify the role of proangiogenic markers in psoriasis and to delineate the underlying mechanisms of psoriasis.	https://www.ncbi.nlm.nih.gov/pubmed/24678886
					Qi 2015 This meta-analysis indicated that the methylenetetrahydrofolate reductase (MTHFR) 677C/T polymorphism may not be associated with psoriasis risk. Further studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/25966157
					Qiu, 2013 This meta-analysis provided evidence that CD226 Gly307Ser (rs763361) is significantly associated with the risk of multiple autoimmune diseases. Further studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/23073294
					Shen 2015 Evidence that the genetic variant(s) within the late cornified envelop (LCE)3 genes may influence the development of psoriasis and PsA possibly by interrupting the terminal differentiation of keratinocytes. Further studies are recommended to explore the precise role of LCE3 genes in the pathogenesis of psoriasis and PsA.	https://www.ncbi.nlm.nih.gov/pubmed/25697099
					Shi 2016 Evidence for a significant association between the CARD14 rs11652075 polymorphism and psoriasis. Due to the current lack of data concerning clinical subtypes and genotype frequencies, more careful stratification and interaction analyses, taking into account disease subgroups, are needed. The pathogenicity of the association with rs11652075 needs to be validated further in independent cohorts and subsequent pathophysiologic and therapeutic studies.	https://www.ncbi.nlm.nih.gov/pubmed/27706581
					Song 2014 This meta-analysis showed that the major histocompatibility complex class I chain-related gene A transmembrane (MICA-TM) A9 allele is associated with psoriasis susceptibility in Asian populations and that the MICA-TM A9 allele is associated with a PsA risk in Europeans. Further studies are required.	https://www.ncbi.nlm.nih.gov/pubmed/23974432
					Song 2015 Evidence that the angiotensin converting enzyme (ACE) insertion / deletion (I/D) polymorphism is associated with susceptibility to rheumatoid arthritis, especially in Arab populations. Association with psoriasis was also investigated. Further studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/23413281
					Stefanic, 2013 Evidence that no genetic variant in the vitamin D receptor (VDR) gene has a robust and reproducible association with risk for psoriasis. Any association that may exist is likely to be weak and potentially restricted to specific populations. Further studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/23488577
					van Vugt 2018 Evidence th at pharmacogenetic studies in psoriasis have generated divergent results. HLA-Cw6 may be promising as a predictor for ustekinumab efficacy. Replication of findings in larger cohorts is required. Large-scale hypothesis-free searches for genetic biomarkers are needed to uncover the complete genetic background of outcomes for treatment with biologics.	https://www.ncbi.nlm.nih.gov/pubmed/28646581
					Wei 2015 Evidence that the vascular endothelial growth factor VEGF +405G-C polymorphism may be associated with chronic immune-mediated inflammatory diseases, and vary between ethnic groups. Further studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/26007152
					Wu 2016 Evidence that the methylenetetrahydrofolate reductase (MTHFR) C677T polymorphism, , is not a genetic factor for the pathogenesis of psoriasis (qualitatively) but could influence the severity of psoriasis (quantitatively). Further research required.	https://www.ncbi.nlm.nih.gov/pubmed/26212228

					Xia 2014 Evidence from this meta-analysis that the presence of the CD143 ID polymorphism may modify the risk of psoriasis in individuals with East Asian ancestry. Further large-scale studies to evaluate the impact of CD143ID polymorphism on psoriasis are needed.	https://www.ncbi.nlm.nih.gov/pubmed/24997622
					Xiao 2016 Evidence that the IL-12B 3'-untranslated region (UTR) and rs6887695 single nucleotide polymorphisms (SNPs) are associated with susceptibility to autoimmune diseases (including psoriasis). More research needed including large sample studies, different ethnic groups with careful matching between cases and controls. Also, further evaluation of the effect of gene–gene and gene–environment interactions on the IL-12B 30-UTR and rs6887695 SNP and autoimmune disease risk is recommended.	https://www.ncbi.nlm.nih.gov/pubmed/27068848
					Zhao 2013 Evidence for a significant association between psoriasis and 50 HLAB alleles. The association varied in terms of race, and clinical type and onset age of psoriasis. Future studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/23600465
					Zhao 2014 Evidence that psoriasis is associated with a number of HLA-A alleles, some are confer susceptibility, some are protective. The association of some alleles is different in terms of different races, clinical types and onset age. Further studies are needed.	https://www.ncbi.nlm.nih.gov/pubmed/23981037
					Zhao 2016 This meta-analysis demonstrated that IL-12 p40 gene (IL-12B rs3212227) was associated with the risk of psoriasis in European and Asian populations. More studies are required for the exploration of the pathogenesis of psoriasis.	https://www.sciencedirect.com/science/article/pii/S1027811716000021
					Zhu 2013a Evidence for a significant association between IL12B gene polymorphisms and psoriasis and PsA. Further studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/23717605
					Zhuang 2013 This meta-analysis evidenced that the TNF-α 308 G/A polymorphism is associated with decreased risk of psoriasis, while TNF-α 238 G/A is associated with increased risk of psoriasis. Further studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/24324571
J	**What triggers a sudden flare up of psoriasis and how long do these usually last?**	Are there specific things that induce a Psoriasis flare up?	8	20		
					No systematic reviews identified	**No systematic reviews identified**
K	**Does treating psoriasis early (or proactively) reduce the severity of the disease, make it more likely to go into remission, or stop other health conditions developing?**	Does early/aggressive treatment reduce severity or duration of disease overall?	16	2		
					No systematic reviews identified	**No systematic reviews identified**
L	**What factors predict how well psoriasis will respond to a treatment?**	Why is it that one treatment works for one and not the other?	34	3		
					No systematic reviews identified	**No systematic reviews identified**
M	**Does treating psoriasis help improve other health conditions, such as psoriatic arthritis, cardiovascular disease, metabolic syndrome and stress?**	Does the use of biologics for psoriasis interfere with control or treatment of Diabetes?	24	6		

					Abbott, 2015 Evidence that TNF-α inhibitor therapy reduces depression in people who have chronic diseases (including those with psoriasis) though the effects are small. Limited data available. Further studies investigating a more detailed timeline of changes in depression, inflammatory biomarkers and disease activity status in patients with psoriasis (and other chronic diseases) are required.	https://www.ncbi.nlm.nih.gov/pubmed/25935351
					Armstrong 2013a Some evidence that mild and severe psoriasis is associated with an increased risk of myocardial infarction and stroke. Severe psoriasis is also associated with an increased risk of cardiovascular mortality. Some limitations. Future studies needed - these should include more complete covariate adjustment and characterisation of psoriasis severity.	https://www.ncbi.nlm.nih.gov/pubmed/23557749
					Armstrong 2013b Evidence that psoriasis and psoriatic arthritis are associated with greater prevalence of hypertension. Patients with severe psoriasis have greater odds of hypertension than those with mild psoriasis. Some limitations with study. Further studies are needed – specifically to elucidate the basic mechanisms underlying the association between psoriasis and hypertension, to explore the relationship between psoriasis and hypertension severity, and to examine the effects of systemic treatments for psoriasis on hypertension control.	https://www.ncbi.nlm.nih.gov/pubmed/23249828
					Armstrong 2013c Compared with the general population, psoriasis patients have higher prevalence of metabolic syndrome, and patients with more severe psoriasis have greater odds of metabolic syndrome than those with milder psoriasis. Some limitations with study. More studies needed to determine the mechanisms underlying the association between these two conditions and to determine the effect of psoriasis systemic therapies on metabolic syndrome.	https://www.ncbi.nlm.nih.gov/pubmed/23360868
					Armstrong 2013d Evidence that psoriasis is associated with an increased prevalence and incidence of diabetes. The association of psoriasis with diabetes may be strongest among patients with severe psoriasis. Some limitations with the study. Future studies should more closely assess the relationship between psoriasis severity, age at disease onset, and diabetes.	https://www.ncbi.nlm.nih.gov/pubmed/23407990
					Armstrong 2014 This review concluded that epidemiologic data is insufficient to reach definitive conclusions with regards to the effects of biologics and other disease modifying anti rheumatic drugs (DMARDs) on cardiovascular outcomes in psoriasis and psoriatic arthritis patients. Adequately powered, long-term, controlled studies are necessary to determine the cardioprotective effects of TNF inhibitors observed in preliminary studies on psoriasis and psoriatic arthritis populations.	https://www.ncbi.nlm.nih.gov/pubmed/23565631
					Bhatia, 2014 Epidemiologic and clinical studies suggest there is an association among psoriasis, coeliac disease, and coeliac disease markers. Further studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/24780176
					Candia, 2015 Case - control studies support an association between psoriasis and non-alcoholic fatty liver disease (NAFLD). Screening of NAFLD in patients with psoriasis may be warranted. More studies are needed.	https://www.ncbi.nlm.nih.gov/pubmed/25418531
					Chi 2017 This systemic review and meta-analysis concluded that the available limited, very low-quality evidence does not support an association between psoriasis and suicidal thought and behaviour. Further studies that provide data for different age and sex groups are needed to clarify whether a subgroup of patients with psoriasis has an elevated risk of suicidality.	https://www.ncbi.nlm.nih.gov/pubmed/28409490
					Coto-Segura, 2013 Evidence to support an association between psoriasis, PsA and type 2 diabetes mellitus. Heterogeneity between studies. Further work to understand the relations more completely needed.	https://www.ncbi.nlm.nih.gov/pubmed/23772556
					Cullen, 2019 Evidence for a positive overall association between non-neurological autoimmune (NNAI) disorders and psychosis, which was not consistent across all NNAI disorders. Separate meta-analyses were conducted for individual autoimmune disorders. A significant positive association was observed for psoriasis. Future work recommended: 1) studies should be designed to better disentangle the temporal nature of the association between NNAI disorders and psychosis, as such studies have demonstrated that both psychosis and depression show bidirectional associations with autoimmune disorders; 2) larger studies should be undertaken to examine the presence of neuronal surface autoantibodies among individuals with psychosis; 3) greater efforts should be made in large cohort studies to include information on potential confounders, such as socioeconomic status, adversity, and tobacco use; and 4) studies should be undertaken to evaluate the effect of corticosteroid treatment on the relationship between NNAI disorders and psychosis.	https://www.ncbi.nlm.nih.gov/pubmed/30122288

					De Vecchis, 2016 Evidence that methotrexate at low doses, such those used for maintenance therapy of rheumatoid arthritis, predicts a decreased risk of cardiovascular events. Randomised controlled trials to establish causality recommended. Ungprasert 2014 Evidence for a statistically significant increased risk of venous thromboembolism among patients with psoriasis. Limited data available – further study required.	https://www.ncbi.nlm.nih.gov/pubmed/26467356
					Dowlatshahi, 2014 Evidence that psoriasis patients are at least one and a half times more likely to manifest signs of clinical depression compared with their healthy peers. More than one-quarter of psoriasis patients show symptoms of depression and approximately one-tenth have signs of clinical depression. High heterogeneity between studies. Further work to clarify this relationship needed. Phan Evidence from this pooled meta-analysis demonstrates a significant association between bullous pemphigoid and psoriasis. This association is stronger in males, in contrast with many other auto-immune conditions. The study is constrained by several limitations. Further studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/24284419
					Fang, 2016 Evidence that patients with psoriasis have excessive risk of subclinical atherosclerosis compared with the healthy controls. Further studies are needed particularly on whether treatment of psoriasis will reverse subclinical atherosclerosis.	https://www.ncbi.nlm.nih.gov/pubmed/27196459
					Ferreira 2016 Evidence that many mental disorders are associated with psoriasis although the aetiopathogenesis of that connection is wide. Some psychiatric comorbidities may result from the psychosocial impact of having a chronic skin condition. However, psoriasis can be maintained and exacerbated by an underlying psychiatric condition. Further studies to explore these relationships in more detail and establish aetiology are needed.	https://www.ncbi.nlm.nih.gov/pubmed/27386050
					Ferreira 2017 Evidence that the prevalence of psychiatric conditions in psoriasis may range from 24% to 90%. The link between psoriasis and associated mental disorders is frequently forgotten or not considered in clinical practice and psychiatric disorders in patients with psoriasis may be underdiagnosed. Limited data available – further study required.	https://www.ncbi.nlm.nih.gov/pubmed/29197196
					Fleming 2015 Evidence that treatment with adalimumab, etanercept and ustekinumab are associated with statistically significant reductions in depressive symptom scores using various scales in patients with moderate-to-severe psoriasis. A robust RCT including standardised criteria is required to better determine the clinical significance of these findings. In the interim, it is suggested that patients with psoriasis should be screened for depression when appropriate and refered accordingly.	https://www.ncbi.nlm.nih.gov/pubmed/25490866
					Fleming 2017 Evidence for a high prevalence of anxiety of adult patients with psoriasis suggesting that patients would benefit from systematic screening. Although the data suggest that anxiety may be improved through various psoriasis treatments, larger prospective randomized trials are needed to confirm this effect.	https://www.ncbi.nlm.nih.gov/pubmed/27620704
					Gaeta, 2013 Evidence that patients with psoriasis carry an about 25% increased relative risk of cardiovascular disease. This risk appears to be independent of smoking, obesity and hyperlipidemia. Further work needed to confirm this and to assess the impact of psoriasis in risk stratification, and the benefit of its effective treatment in the prevention of associated cardiovascular events.	https://www.ncbi.nlm.nih.gov/pubmed/23490084
					González-Álvarez, 2018 This systematic review concluded that diagnosis of geographic tongue (GT) is mainly clinical and that GT is an asymptomatic disorder that usually requires no treatment. GT can be associated with psoriasis. Further studies are needed.	https://www.ncbi.nlm.nih.gov/pubmed/29903400
					Gupta, 2016 This systematic review evidences a link between psoriasis and PsA with obstructive sleep apnoea and restless legs syndrome. In this study there was no conclusive evidence that psoriasis and PsA are associated with an elevated prevalence of insomnia, periodic limb movement disorder, narcolepsy, or shift work disorder. The relationship between psoriatic conditions and other sleep disorders was not examined. Future research recommended including: 1. It is important that epidemiological studies in psoriasis evaluate sleep disorders following the standard ICSD-3 criteria, in order to accurately measure the prevalence and incidence of sleep disorders in this population. 2. It will be critical to establish if biologics targeting immune mechanisms in psoriasis are effective in decreasing immune markers linked to additional systemic diseases that mediate the risk for sleep-disordered breathing. 3. The incidence of acute vs. chronic insomnia should be measured in patients with psoriasis to determine if the sleep disturbance is acute and stems directly from pruritus and pain, or if it represents ICSD-3 chronic insomnia.	https://www.ncbi.nlm.nih.gov/pubmed/26624228
					Henry, 2016 Evidence that in psoriasis, reported sleep rates of sleep disturbance varied substantially. Most studies examined lacked a hypothesis driven research question and/or failed to use validated measures of sleep. This study was unable to draw firm conclusions about the precise prevalence and nature of sleep disturbance within the psoriasis population. Need to systematically and consistently examine sleep in psoriasis populations, employing comprehensive and validated measures of sleep in specifically designed studies.	https://www.ncbi.nlm.nih.gov/pubmed/27327082

					Horreau, 2013 Evidence that there may be a small, but significant increased risk of CVE, but not of CV mortality in psoriasis and PsA patients. The psoriasis attributable risk was difficult to assess due to confounding factors. Heterogeneity in study design, outcome definition and assessment were major limitations. Further studies recommended - (especially those designed to evaluate the true causal relationship between psoriasis and CVD and the relationship between psoriasis severity, age at onset and CVD).	https://www.ncbi.nlm.nih.gov/pubmed/23845149
					Khan, 2017 This meta-analysis suggested that thyroid peroxidase antibody positivity, hypothyroidism and hyperthyroidism may be associated with prevalent psoriatic disease. However, there were only few studies with large heterogeneity regarding psoriatic disease definition and indication of publication bias. Additional prospective data are needed to assess the association of autoimmune thyroid disease with incident psoriatic disease.	https://www.ncbi.nlm.nih.gov/pubmed/28747386
					Kyriakou, 2017 Evidence that leptin and resistin concentrations are higher and adiponectin concentrations are lower in patients with psoriasis compared to controls. High heterogeneity among studies. Although there is evidence that systemic inflammation drives the increased cardiovascular risk and metabolic dysregulation in psoriasis, it is unclear whether psoriatic inflammation leads to the development of cardio-metabolic comorbidities or whether the pre-existing metabolic dysfunction results in immunologic dysregulation and onset of psoriasis. Further studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/29232663
					Li 2015 Evidence that psoriasis patients have a greater risk of developing chronic obstructive pulmonary disease (COPD) than the general population (odds ratio, 1.90; 95% confidence interval, 1.36–2.65) and that the association between psoriasis and COPD is stronger among patients with severe psoriasis (odds ratio, 2.15; 95% confidence interval, 1.26–3.67). Future research is needed including prospective follow-up studies to explore the mechanisms underlying the observed association and to investigate the role of systemic therapies for psoriasis in the prevention of COPD.	https://www.ncbi.nlm.nih.gov/pubmed/26700640
					Ma 2013 This systematic review found that psoriasis was significantly associated with greater odds and incidence of dyslipidaemia. Greater psoriasis severity appeared to be associated with higher prevalence of dyslipidaemia. Further studies needed (important to consider directly measure dyslipidaemia via laboratory workup and control for medication use in order to clarify the relationship between psoriasis and dyslipidaemia. Whether well-controlled dyslipidaemia contributes to amelioration of psoriasis symptoms was considered an important and clinically relevant question to be addressed by future study.	https://www.ncbi.nlm.nih.gov/pubmed/23106411
					Miller 2013a Some evidence that psoriasis is associated with ischemic heart disease and cardiovascular risk factors. The association was only significant for hospital-based studies, except for dyslipidemia, which was also significant in population-based studies. Heterogeneity of included studies. Further studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/24238156
					Miller 2013b Evidence that quantifying cardiovascular disease (CVD) risk factors as continuous variables has clinical utility attributing CVD risk for patients with psoriasis. Heterogeneity of included studies. Further studies needed – particularly case control studies reporting continuous data, i.e. mean values and differences instead of odds ratios only (including standardised physical examinations and blood samples).	https://www.ncbi.nlm.nih.gov/pubmed/23815240
					Molina-Leyva, 2015 Evidence that psoriasis patients have a higher risk of sexual dysfunction as compared to the general population. Prospective longitudinal studies are needed to explore the causal factors involved in sexual dysfunction among psoriasis patients.	https://www.ncbi.nlm.nih.gov/pubmed/25424331
					Mosca 2015 Some evidence that psoriatic patients are at increased CV risk, related to raised prevalence and incidence of CV risk factor and to inflammatory status. Further studies needed to establish appropriate targets for CV risk factors, assess the clinical value of screening for subclinical organ damage and determine the impact of disease-modifying therapies on CV risk profile in psoriatic patients.	https://www.ncbi.nlm.nih.gov/pubmed/25464252
					Pouplard, 2013 This systematic literature review shows a small increased risk of some solid cancers in psoriasis, especially those linked to alcohol drinking and cigarette smoking. A higher risk of non-melanoma skin cancers, especially squamous cell carcinoma, is also shown. There is a need for further studies to obtain data from ongoing psoriasis registries including robust assessment of comorbidities and pharmacological treatments to better characterise the risk of cancer in psoriasis.	https://www.ncbi.nlm.nih.gov/pubmed/23845151

					Puig, 2014 Evidence collated regarding a large number of small controlled or cross-sectional studies which report increased prevalence of cardiometabolic and psychological co-morbidities in patients with psoriasis. Evidence from a number of large cohort studies presented to describe the incidence of various cardiometabolic co-morbidities in patients with psoriasis. Evidence for association of severe psoriasis with increased mortality (most common cause of death is cardiovascular disease). Comment that studies on the management of co-morbidities and their impact on psoriasis treatment are scarce and that many questions on the co-morbidities of psoriasis remain to be answered. Further studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/24752135
					Raaby, 2017 This meta-analysis confirmed that patients with psoriasis have an increased risk of CVD, especially those with severe psoriasis. Further studies to investigate whether increased control followed by treatment of cardiovascular risk factors improves the prognosis of psoriatic patients are needed.	https://www.ncbi.nlm.nih.gov/pubmed/28213804
					Richard 2014 This systematic literature research and meta-analysis was designed to marshall the evidence base for selected clinically relevant questions to help dermatologists i) identify patients at risk of PsA, ii) to diagnose PsA in collaboration with rheumatologists and iii) manage PsA. There was no high-quality evidence to support the "expert" recommendations regarding PsA screening. However, treatment options for PsA were supported by strong evidence. Further studies are required to provide an adequate evidence base for risk profiling, screening and management of PsA (by dermatologists in partnership with rheumatologists).	https://www.ncbi.nlm.nih.gov/pubmed/24985557
					Roubille 2015 This meta-analysis provided evidence that TNF inhibitors and methotrexate decrease the risk of cardiovascular events (CVEs) in patients with rheumatoid arthritis (RA) whereas NSAIDs and corticosteroids increase the risk of CVEs. In patients with psoriasis and psoriatic arthritis (PsA/Pso) limited evidence suggested that treatment with systemic therapies is associated with a decrease in the risk of all CVEs. Large, prospective, adequately controlled and powered studies are needed to explore the effects of systemic/biologic therapies on cardiovascular morbidity and mortality in both the RA and PsA/Pso populations.	https://www.ncbi.nlm.nih.gov/pubmed/25561362
					Rodríguez-Zúñiga 2017a Evidence that the risk for MS is increased by 40% in patients with psoriasis compared with in the general population. Systemic review limited by missing data, high heterogeneity among studies examined, high risk selection bias in studies included in analysis and high probability of selection bias. Further studies recommended.	https://www.ncbi.nlm.nih.gov/pubmed/28917453
					Rodríguez-Zúñiga 2017b Evidence that psoriasis is highly associated with the metabolic syndrome in Latin America. The association is stronger for severe psoriasis and when the adult treatment panel guidelines (ATP-III criteria) are used to identify cardiovascular disease risk. Limited data available – further study required.	https://www.ncbi.nlm.nih.gov/pubmed/28117050
					Rungapiromnan, 2017 Biologic therapies including TNFi, an anti-IL-12/23 agent (ustekiumab) and anti-IL-17A agents (secukinumab and ixekizumab) have no significant impact on the risk of major adverse cardiovascular events (MACEs) in adult patients with plaque psoriasis over the short term. However, follow-up was limited and patient characteristics were those of patients participating in RCTs. Recommendation – need for well-designed observational studies that involve larger numbers of patients and longer durations of treatment exposure reflecting routine clinical practice required to determine the impact of biologic therapies on the risk of MACEs in patients with psoriasis.	https://www.ncbi.nlm.nih.gov/pubmed/27518205
					Saleem, 2017 Database studies might not fully account for confounders, resulting in overestimates of the risk impact of comorbidities. Knowing the baseline risk, relative risk, and attributed risk, together, provides a better overall understanding of the impact an exposure has on any given disease in a defined population. Further work to understand whether screening and intervention (for co-morbid disease) should be done requires more than just knowing there is a greater relative risk and more than knowing that a treatment that can reduce that risk. Studies to consider costs and benefits, including how big a problem the comorbidity is on an absolute basis not just on a relative basis, need to be carried out.	https://www.ncbi.nlm.nih.gov/pubmed/27986396
					Samarasekera, 2013 Evidence that severe psoriasis is associated with an increased risk of CVD. Uncertainty remains about whether CVD risk is directly attributable to psoriasis, as the majority of studies failed to adequately adjust for key traditional risk factors. Further research is required to better understand the complex relationship between psoriasis, traditional risk factors, and CVD. Long-term, large-scale cohort studies that adequately control for confounding factors and detection bias are required to address the question of whether aggressive treatment of severe psoriasis has an impact on clinically relevant CVD end points.	https://www.ncbi.nlm.nih.gov/pubmed/23528816

					Shaharyar, 2014 Evidence that patients with psoriasis have an increased burden of subclinical atherosclerosis and endothelial dysfunction. Further clinical trials to identify appropriate screening strategies for subclinical cardiovascular disease (CVD), and whether non-pharmacological and pharmacological approaches result in slower progression of subclinical CVD / reduction in clinical events among patients with psoriasis are needed.	https://www.ncbi.nlm.nih.gov/pubmed/24401219
					Singh 2016 Evidence that patients with psoriasis have a greater prevalence of metabolic syndrome as well as its individual components when compared to the general population. The odds of metabolic syndrome and its components are higher with increased psoriasis disease severity. Prospective studies are needed to better understand the contribution of psoriasis in the development of metabolic syndrome.	https://www.ncbi.nlm.nih.gov/pubmed/27589483
					Singh 2017a Evidence that patients with psoriasis have higher odds of having metabolic syndrome when compared with the general population. The pathologic mechanisms shared by these two disease processes, as well as the directionality of the relationship, are not well understood and need to be elucidated through further translational research.	https://www.ncbi.nlm.nih.gov/pubmed/28719618
					Singh 2017b Evidence that patients with psoriasis have a significantly higher likelihood of suicidal ideation, suicide attempts, and completed suicides. In patients with psoriasis, those who are younger and whose psoriasis is more severe are at particular risk for suicidality. Potential sources of bias and study heterogeneity. Further investigation to understand this association more fully needed. Jin Patients with psoriasis have a higher prevalence of metabolic syndrome and hypertension compared with controls. More prospective, controlled and randomised studies need to be performed in the future.	https://www.ncbi.nlm.nih.gov/pubmed/28807109
					Tsai, 2018 Some evidence that patients with psoriasis might have higher serum homocysteine and lower folate levels than control patients who do not have psoriasis. However, due to significant heterogeneity between studies reviewed and other limitations, further research needed.	https://www.ncbi.nlm.nih.gov/pubmed/30074615
					Tzellos, 2013 Some evidence that, there is a significant difference in the rate of major adverse cardiovascular events (MACEs) observed in patients receiving anti-IL-12／23 biological agents compared to those treated with placebo. Further studies recommended including post-marketing surveillance and meta-analysis of observational studies and RCTs.	https://www.ncbi.nlm.nih.gov/pubmed/22404103
					Ungprasert 2016a This meta-analysis provided evidence for a significant association between psoriasis and COPD, an under-recognised co-morbidity, with an overall 1.45-fold increased risk. Further studies are required.	https://www.ncbi.nlm.nih.gov/pubmed/26458363
					Ungprasert 2016b Some evidence for increased risk of Parkinson's disease among patients with psoriasis. Limitations in study design acknowledged. Further studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/27451924
					Ungprasert 2016c Some evidence for increased risk of incident atrial fibrillation among patients with psoriasis. Limitations in study design acknowledged. Further studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/27057013
					Ungprasert 2017 This meta-analysis demonstrated an approximately 3-fold increased risk of coeliac disease among patients with psoriasis. The pathophysiologic mechanisms behind this increased risk are not known, and further investigations are required.	https://www.ncbi.nlm.nih.gov/pubmed/28216724
					Ungprasert 2018a Evidence that risk of psoriasis among patients with schizophrenia was significantly higher than non-schizophrenia subjects (83% excess risk). Future work needed to determine this nature and mechanism of this observation.	https://www.ncbi.nlm.nih.gov/pubmed/29128620
					Ungprasert 2018b Evidence for a significantly increased risk of incident chronic kidney disease and end-stage renal disease among patients with psoriasis compared with individuals without psoriasis. How this risk should be addressed in clinical practice requires more study with emphasis on prevention and surveillance programmes.	https://www.ncbi.nlm.nih.gov/pubmed/29644523
					Upala, 2017 This meta-analysis of prospective studies demonstrated that patients with psoriasis have increased risk of new-onset atrial fibrillation. Future interventional studies addressing the impact of psoriasis treatment and prevention of atrial fibrillation are required.	https://www.ncbi.nlm.nih.gov/pubmed/27794626
					Wang 2016 This meta-analysis demonstrated no significant difference in total cholesterol, LDL, HDL or triglycerides between patients with psoriasis and controls. Patients with psoriasis had higher epicardial fat tissue (EFT) compared to controls which may suggest that EFT is an independent risk factor of psoriasis. Further studies needed to elucidate these relationships.	https://www.ncbi.nlm.nih.gov/pubmed/27245937
					Wang 2018 This meta-analysis indicated that patients with psoriasis had an increased risk of asthma which was higher in older patients with psoriasis than in younger patients. Further studies are needed to confirm this observation and overcome the limitations of this analysis (particularly with respect to diagnostic accuracy of both complex conditions).	https://www.ncbi.nlm.nih.gov/pubmed/29490768

					Whitlock, 2018 There are no known clinical trials of treatment specifically for concurrent psoriasis and inflammatory bowel disease. Evidence that infliximab and adalimumab have efficacy in psoriasis, psoriatic arthritis, ulcerative colitis, and Crohn's disease; other agents have demonstrated efficacy for some, but not all, of these indications. Further studies including rigorous examination of long-term data is needed.	https://www.ncbi.nlm.nih.gov/pubmed/29332708
					Wu 2015 Evidence for an overall increased risk of autism in children with family history of autoimmune disease (including psoriasis) was identified. More mechanistic studies are needed to further explain the association between family history of autoimmune disease and increased risk of autism in children.	https://www.ncbi.nlm.nih.gov/pubmed/25981892
					Wu 2018 This meta-analysis examined the relationship between psoriasis and risk of erectile dysfunction. The studies included were mostly cross-sectional or small sample cohorts, which could introduce bias and heterogeneity into the analysis. Some evidence that psoriasis is associated with an increased risk of erectile dysfunction. Prospective cohort studies are needed to elucidate these relationships and to advance knowledge in this field.	https://www.ncbi.nlm.nih.gov/pubmed/29735408
					Yang, 2016 Evidence for TNF inhibitors having clinical benefit with regard to adverse cardiovascular events in psoriasis and/or PsA. Rigorous randomized controlled trials needed to evaluate whether TNF inhibitors truly result in reduction of cardiovascular diseases.	https://www.ncbi.nlm.nih.gov/pubmed/27300248
					Zhang, 2017 Evidence that there is a correlation between psoriasis and erectile dysfunction. Patients with psoriasis may have a higher incidence of erectile dysfunction though this observation needs to be further confirmed by further high quality studies.	https://www.ncbi.nlm.nih.gov/pubmed/29706048
N	**What are the long-term risks and benefits of oral and biological psoriasis treatments?**	Are biologic's safe in the long term?	63			
					Ahn, 2015 Evidence for TB testing as part of the pre-biologics screening. Study limited by lack of standardised CTs evaluating utility of screening / monitoring. Clinicians advised to use their judgement. Further evidence / investigation required.	https://www.ncbi.nlm.nih.gov/pubmed/26184440
					Farahnik, 2017 Review of oral BOTANICAL therapy – not standard therapy. Minimal literature (quality and quantity). More evidence required.	https://www.ncbi.nlm.nih.gov/pubmed/28157393
					Marra, 2016 Some data on risk of herpes zoster in patients on biologics, DMARDs and corticosteroids. Multiple indications – not limited to psoriasis. Post-marketing surveillance (especially of newer agents) is required.	https://www.ncbi.nlm.nih.gov/pubmed/27942537
					No, 2018 Drug survival data presented. Limited data. Heterogeneity of included studies. New treatments now available (sine paper published). Evidence for long-term efficacy, utility and tolerability of (some) commonly prescribed biologics. Further evidence required.	https://www.ncbi.nlm.nih.gov/pubmed/29076754
					Peleva, 2018 8 studies met the inclusion criteria – investigating the risk of cancer in patients on biological therapy. Analysis limited due to differences in studies identified. Recommendation made for further enquiry / collection of pharmacovigilance data to determine risk specifically attributable to biological therapy.	https://www.ncbi.nlm.nih.gov/pubmed/28722163
					Snast, 2017 Retrospective cohort study. Some evidence for low risk of Hep C reactivation but considerable risk for chronic Hep B (needing antiviral prophylaxis). Heterogeneous studies evaluated. Further evaluation and studies (especially large-scale prospective trials) needed.	https://www.ncbi.nlm.nih.gov/pubmed/28495497
					Yiu, 2016 No association between biologic therapies and serious infections detected. Further observational studies are needed to inform the uncertainty about this risk in the real world. No paper download.	https://www.ncbi.nlm.nih.gov/pubmed/27085754
O	**Why do psoriasis treatments stop working well against psoriasis and when they stop working well, what's the best way to regain control of the disease?**	Why do psoriasis treatments only last for a short amount of time?	15	7		
					No systematic reviews identified	**No systematic reviews identified**

P	**Are oral and biological treatments for psoriasis safe to use for people with psoriasis or their partner if they are trying to have a baby, and are they safe to use during pregnancy?**	What is the best treatment for pregnant women with psoriasis?	6	11		
					Pottinger, 2018 This systematic review concluded that the potential effect of biologics on pregnancy outcomes specifically in women with psoriasis has not been adequately studied to quantify accurately. Data on use in other indications is limited. Women of child-bearing potential should be advised routinely to use regular contraception; however, when planning conception the risks and benefits of continuing vs. stopping therapy should be discussed on a case-by-case basis. To address the clinical uncertainty, large disease-matched cohort studies are required, taking into account potential confounders such as disease activity, concomitant therapies and maternal demographics. Psoriasis-specific pharmacovigilance registries, for example the British Association of Dermatologist Biologics Intervention Register (BADBIR) in collaboration with others via the European Psoriasis Registry Network (PSONET), provide opportunity to collate such data.	https://www.ncbi.nlm.nih.gov/pubmed/28718898
Q	**What is the best and most cost-effective way of monitoring an oral or biological therapy for psoriasis e.g. clinical review, blood tests and measurement of medicine/antibodies levels?**	What is the safe/optimal monitoring strategy for patients established on biologic therapy?	6	19		
					Kromer, 2018 Some evidence for cost-effectiveness of biological therapy (ie high-cost treatment / high efficacy) presented. Several studies reviewed were sponsored by pharma. Some comparative data presented but future research recommended.	https://www.ncbi.nlm.nih.gov/pubmed/29298315
R	**How well do psychological and educational interventions work for adults and children with psoriasis?**	Why does stress and anxiety have such an impact on Psoriasis flares? Would tailored CBT or similar therapy help?	12	5		
					Randa, 2017 Some evidence for impairment of health related QOL in children and adolescents. Further studies recommended.	https://www.ncbi.nlm.nih.gov/pubmed/27983745
S	**Can oral and biological treatments for psoriasis be combined safely and does combining them work well?**	Combination therapy in an era with increasing choice of therapeutics	3	14		
					Armstrong, 2015 Some evidence presented to support use of combination therapy (biological with systemic therapies) in selected patients to increase efficacy while minimising toxicity. Rigorously conducted trials and observational studies evaluating efficacy and safety of combination therapy needed.	https://www.ncbi.nlm.nih.gov/pubmed/25517130
					Van Bezooijen – Letter. Review of methotrexate in combination with biological therapy. Significant limitations documented. Recommendation made for adequately powered RCTs to compare biologic monotherapy with biologic / MTX combination therapy. Short and long term follow up needed to assess clinical outcomes, safety and drug survival.	https://www.ncbi.nlm.nih.gov/pubmed/26537336
					Zweegers, 2016 Summary of real-world evidence, including 32 studies, on effectiveness of biologics and systemics presented. Limited data on combination (biologic and systemic) therapy. Limited comparative data. Recommendation made to improve quality of reporting and where further work to investigate treatments is needed.	https://www.ncbi.nlm.nih.gov/pubmed/25470815

T	**What factors affect how psoriasis will progress, or whether it will go into remission?**	Which patients will have disease (that will) get worse over time?	24	17		
					No systematic reviews identified	**No systematic reviews identified**
U	**Does treating other health conditions, such as psoriatic arthritis, cardiovascular disease, metabolic syndrome and stress, help psoriasis to get better, or does it make psoriasis harder to treat?**	How does Blood Pressure medication start psioriasis or exacerbate it if a person already has it?	13	n/a		
					Abbott, 2015 Evidence that TNF-α inhibitor therapy reduces depression in people who have chronic diseases (including those with psoriasis) though the effects are small. Limited data available. Further studies investigating a more detailed timeline of changes in depression, inflammatory biomarkers and disease activity status in patients with psoriasis (and other chronic diseases) are required.	https://www.ncbi.nlm.nih.gov/pubmed/25935351
					Armstrong 2013a Some evidence that mild and severe psoriasis is associated with an increased risk of myocardial infarction and stroke. Severe psoriasis is also associated with an increased risk of cardiovascular mortality. Some limitations. Future studies needed - these should include more complete covariate adjustment and characterisation of psoriasis severity.	https://www.ncbi.nlm.nih.gov/pubmed/23557749
					Armstrong 2013b Evidence that psoriasis and psoriatic arthritis are associated with greater prevalence of hypertension. Patients with severe psoriasis have greater odds of hypertension than those with mild psoriasis. Some limitations with study. Further studies are needed – specifically to elucidate the basic mechanisms underlying the association between psoriasis and hypertension, to explore the relationship between psoriasis and hypertension severity, and to examine the effects of systemic treatments for psoriasis on hypertension control.	https://www.ncbi.nlm.nih.gov/pubmed/23249828
					Armstrong 2013c Compared with the general population, psoriasis patients have higher prevalence of metabolic syndrome, and patients with more severe psoriasis have greater odds of metabolic syndrome than those with milder psoriasis. Some limitations with study. More studies needed to determine the mechanisms underlying the association between these two conditions and to determine the effect of psoriasis systemic therapies on metabolic syndrome.	https://www.ncbi.nlm.nih.gov/pubmed/23360868
					Armstrong 2013d Evidence that psoriasis is associated with an increased prevalence and incidence of diabetes. The association of psoriasis with diabetes may be strongest among patients with severe psoriasis. Some limitations with the study. Future studies should more closely assess the relationship between psoriasis severity, age at disease onset, and diabetes.	https://www.ncbi.nlm.nih.gov/pubmed/23407990
					Armstrong 2014 This review concluded that epidemiologic data is insufficient to reach definitive conclusions with regards to the effects of biologics and other disease modifying anti rheumatic drugs (DMARDs) on cardiovascular outcomes in psoriasis and psoriatic arthritis patients. Adequately powered, long-term, controlled studies are necessary to determine the cardioprotective effects of TNF inhibitors observed in preliminary studies on psoriasis and psoriatic arthritis populations.	https://www.ncbi.nlm.nih.gov/pubmed/23565631
					Bhatia, 2014 Epidemiologic and clinical studies suggest there is an association among psoriasis, coeliac disease, and coeliac disease markers. Further studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/24780176
					Candia, 2015 Case - control studies support an association between psoriasis and non-alcoholic fatty liver disease (NAFLD). Screening of NAFLD in patients with psoriasis may be warranted. More studies are needed.	https://www.ncbi.nlm.nih.gov/pubmed/25418531

					Chi, 2017 This systemic review and meta-analysis concluded that the available limited, very low-quality evidence does not support an association between psoriasis and suicidal thought and behaviour. Further studies that provide data for different age and sex groups are needed to clarify whether a subgroup of patients with psoriasis has an elevated risk of suicidality.	https://www.ncbi.nlm.nih.gov/pubmed/28409490
					Coto-Segura, 2013 Evidence to support an association between psoriasis, PsA and type 2 diabetes mellitus. Heterogeneity between studies. Further work to understand the relations more completely needed.	https://www.ncbi.nlm.nih.gov/pubmed/23772556
					Cullen, 2019 Evidence for a positive overall association between non-neurological autoimmune (NNAI) disorders and psychosis, which was not consistent across all NNAI disorders. Separate meta-analyses were conducted for individual autoimmune disorders. A significant positive association was observed for psoriasis. Future work recommended: 1) studies should be designed to better disentangle the temporal nature of the association between NNAI disorders and psychosis, as such studies have demonstrated that both psychosis and depression show bidirectional associations with autoimmune disorders; 2) larger studies should be undertaken to examine the presence of neuronal surface autoantibodies among individuals with psychosis; 3) greater efforts should be made in large cohort studies to include information on potential confounders, such as socioeconomic status, adversity, and tobacco use; and 4) studies should be undertaken to evaluate the effect of corticosteroid treatment on the relationship between NNAI disorders and psychosis.	https://www.ncbi.nlm.nih.gov/pubmed/30122288
					De Vecchis, 2016 Evidence that methotrexate at low doses, such those used for maintenance therapy of rheumatoid arthritis, predicts a decreased risk of cardiovascular events. Randomised controlled trials to establish causality recommended. Ungprasert 2014 Evidence for a statistically significant increased risk of venous thromboembolism among patients with psoriasis. Limited data available – further study required.	https://www.ncbi.nlm.nih.gov/pubmed/26467356
					Dowlatshahi, 2014 Evidence that psoriasis patients are at least one and a half times more likely to manifest signs of clinical depression compared with their healthy peers. More than one-quarter of psoriasis patients show symptoms of depression and approximately one-tenth have signs of clinical depression. High heterogeneity between studies. Further work to clarify this relationship needed. Phan Evidence from this pooled meta-analysis demonstrates a significant association between bullous pemphigoid and psoriasis. This association is stronger in males, in contrast with many other auto-immune conditions. The study is constrained by several limitations. Further studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/24284419
					Fang, 2016 Evidence that patients with psoriasis have excessive risk of subclinical atherosclerosis compared with the healthy controls. Further studies are needed particularly on whether treatment of psoriasis will reverse subclinical atherosclerosis.	https://www.ncbi.nlm.nih.gov/pubmed/27196459
					Ferreira 2016 Evidence that many mental disorders are associated with psoriasis although the aetiopathogenesis of that connection is wide. Some psychiatric comorbidities may result from the psychosocial impact of having a chronic skin condition. However, psoriasis can be maintained and exacerbated by an underlying psychiatric condition. Further studies to explore these relationships in more detail and establish aetiology are needed.	https://www.ncbi.nlm.nih.gov/pubmed/27386050
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					Fleming 2017 Evidence for a high prevalence of anxiety of adult patients with psoriasis suggesting that patients would benefit from systematic screening. Although the data suggest that anxiety may be improved through various psoriasis treatments, larger prospective randomized trials are needed to confirm this effect.	https://www.ncbi.nlm.nih.gov/pubmed/27620704
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					González-Álvarez, 2018 This systematic review concluded that diagnosis of geographic tongue (GT) is mainly clinical and that GT is an asymptomatic disorder that usually requires no treatment. GT can be associated with psoriasis. Further studies are needed.	https://www.ncbi.nlm.nih.gov/pubmed/29903400
					Gupta, 2016 This systematic review evidences a link between psoriasis and PsA with obstructive sleep apnoea and restless legs syndrome. In this study there was no conclusive evidence that psoriasis and PsA are associated with an elevated prevalence of insomnia, periodic limb movement disorder, narcolepsy, or shift work disorder. The relationship between psoriatic conditions and other sleep disorders was not examined. Future research recommended including: 1. It is important that epidemiological studies in psoriasis evaluate sleep disorders following the standard ICSD-3 criteria, in order to accurately measure the prevalence and incidence of sleep disorders in this population. 2. It will be critical to establish if biologics targeting immune mechanisms in psoriasis are effective in decreasing immune markers linked to additional systemic diseases that mediate the risk for sleep-disordered breathing. 3. The incidence of acute vs. chronic insomnia should be measured in patients with psoriasis to determine if the sleep disturbance is acute and stems directly from pruritus and pain, or if it represents ICSD-3 chronic insomnia.	https://www.ncbi.nlm.nih.gov/pubmed/26624228
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					Ma, 2013 This systematic review found that psoriasis was significantly associated with greater odds and incidence of dyslipidaemia. Greater psoriasis severity appeared to be associated with higher prevalence of dyslipidaemia. Further studies needed (important to consider directly measure dyslipidaemia via laboratory workup and control for medication use in order to clarify the relationship between psoriasis and dyslipidaemia. Whether well-controlled dyslipidaemia contributes to amelioration of psoriasis symptoms was considered an important and clinically relevant question to be addressed by future study.	https://www.ncbi.nlm.nih.gov/pubmed/23106411
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					Puig, 2014 Evidence collated regarding a large number of small controlled or cross-sectional studies which report increased prevalence of cardiometabolic and psychological co-morbidities in patients with psoriasis. Evidence from a number of large cohort studies presented to describe the incidence of various cardiometabolic co-morbidities in patients with psoriasis. Evidence for association of severe psoriasis with increased mortality (most common cause of death is cardiovascular disease). Comment that studies on the management of co-morbidities and their impact on psoriasis treatment are scarce and that many questions on the co-morbidities of psoriasis remain to be answered. Further studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/24752135
					Raaby, 2017 This meta-analysis confirmed that patients with psoriasis have an increased risk of CVD, especially those with severe psoriasis. Further studies to investigate whether increased control followed by treatment of cardiovascular risk factors improves the prognosis of psoriatic patients are needed.	https://www.ncbi.nlm.nih.gov/pubmed/28213804
					Richard 2014 This systematic literature research and meta-analysis was designed to marshall the evidence base for selected clinically relevant questions to help dermatologists i) identify patients at risk of PsA, ii) to diagnose PsA in collaboration with rheumatologists and iii) manage PsA. There was no high-quality evidence to support the "expert" recommendations regarding PsA screening. However, treatment options for PsA were supported by strong evidence. Further studies are required to provide an adequate evidence base for risk profiling, screening and management of PsA (by dermatologists in partnership with rheumatologists).	https://www.ncbi.nlm.nih.gov/pubmed/24985557
					Roubille 2015 This meta-analysis provided evidence that TNF inhibitors and methotrexate decrease the risk of cardiovascular events (CVEs) in patients with rheumatoid arthritis (RA) whereas NSAIDs and corticosteroids increase the risk of CVEs. In patients with psoriasis and psoriatic arthritis (PsA/Pso) limited evidence suggested that treatment with systemic therapies is associated with a decrease in the risk of all CVEs. Large, prospective, adequately controlled and powered studies are needed to explore the effects of systemic/biologic therapies on cardiovascular morbidity and mortality in both the RA and PsA/Pso populations.	https://www.ncbi.nlm.nih.gov/pubmed/25561362
					Rodríguez-Zúñiga 2017a Evidence that the risk for MS is increased by 40% in patients with psoriasis compared with in the general population. Systemic review limited by missing data, high heterogeneity among studies examined, high risk selection bias in studies included in analysis and high probability of selection bias. Further studies recommended.	https://www.ncbi.nlm.nih.gov/pubmed/28917453
					Rodríguez-Zúñiga 2017b Evidence that psoriasis is highly associated with the metabolic syndrome in Latin America. The association is stronger for severe psoriasis and when the adult treatment panel guidelines (ATP-III criteria) are used to identify cardiovascular disease risk. Limited data available – further study required.	https://www.ncbi.nlm.nih.gov/pubmed/28117050

					Rungapiromnan, 2017 Biologic therapies including TNFi, an anti-IL-12/23 agent (ustekiumab) and anti-IL-17A agents (secukinumab and ixekizumab) have no significant impact on the risk of major adverse cardiovascular events (MACEs) in adult patients with plaque psoriasis over the short term. However, follow-up was limited and patient characteristics were those of patients participating in RCTs. Recommendation – need for well-designed observational studies that involve larger numbers of patients and longer durations of treatment exposure reflecting routine clinical practice required to determine the impact of biologic therapies on the risk of MACEs in patients with psoriasis.	https://www.ncbi.nlm.nih.gov/pubmed/27518205
					Saleem, 2017 Database studies might not fully account for confounders, resulting in overestimates of the risk impact of comorbidities. Knowing the baseline risk, relative risk, and attributed risk, together, provides a better overall understanding of the impact an exposure has on any given disease in a defined population. Further work to understand whether screening and intervention (for co-morbid disease) should be done requires more than just knowing there is a greater relative risk and more than knowing that a treatment that can reduce that risk. Studies to consider costs and benefits, including how big a problem the comorbidity is on an absolute basis not just on a relative basis, need to be carried out.	https://www.ncbi.nlm.nih.gov/pubmed/27986396
					Samarasekera, 2013 Evidence that severe psoriasis is associated with an increased risk of CVD. Uncertainty remains about whether CVD risk is directly attributable to psoriasis, as the majority of studies failed to adequately adjust for key traditional risk factors. Further research is required to better understand the complex relationship between psoriasis, traditional risk factors, and CVD. Long-term, large-scale cohort studies that adequately control for confounding factors and detection bias are required to address the question of whether aggressive treatment of severe psoriasis has an impact on clinically relevant CVD end points.	https://www.ncbi.nlm.nih.gov/pubmed/23528816
					Shaharyar, 2014 Evidence that patients with psoriasis have an increased burden of subclinical atherosclerosis and endothelial dysfunction. Further clinical trials to identify appropriate screening strategies for subclinical cardiovascular disease (CVD), and whether non-pharmacological and pharmacological approaches result in slower progression of subclinical CVD / reduction in clinical events among patients with psoriasis are needed.	https://www.ncbi.nlm.nih.gov/pubmed/24401219
					Singh 2016 Evidence that patients with psoriasis have a greater prevalence of metabolic syndrome as well as its individual components when compared to the general population. The odds of metabolic syndrome and its components are higher with increased psoriasis disease severity. Prospective studies are needed to better understand the contribution of psoriasis in the development of metabolic syndrome.	https://www.ncbi.nlm.nih.gov/pubmed/27589483
					Singh 2017a Evidence that patients with psoriasis have higher odds of having metabolic syndrome when compared with the general population. The pathologic mechanisms shared by these two disease processes, as well as the directionality of the relationship, are not well understood and need to be elucidated through further translational research.	https://www.ncbi.nlm.nih.gov/pubmed/28719618
					Singh 2017b Evidence that patients with psoriasis have a significantly higher likelihood of suicidal ideation, suicide attempts, and completed suicides. In patients with psoriasis, those who are younger and whose psoriasis is more severe are at particular risk for suicidality. Potential sources of bias and study heterogeneity. Further investigation to understand this association more fully needed. Jin Patients with psoriasis have a higher prevalence of metabolic syndrome and hypertension compared with controls. More prospective, controlled and randomised studies need to be performed in the future.	https://www.ncbi.nlm.nih.gov/pubmed/28807109
					Tsai, 2018 Some evidence that patients with psoriasis might have higher serum homocysteine and lower folate levels than control patients who do not have psoriasis. However, due to significant heterogeneity between studies reviewed and other limitations, further research needed.	https://www.ncbi.nlm.nih.gov/pubmed/30074615
					Tzellos, 2013 Some evidence that, there is a significant difference in the rate of major adverse cardiovascular events (MACEs) observed in patients receiving anti-IL-12／23 biological agents compared to those treated with placebo. Further studies recommended including post-marketing surveillance and meta-analysis of observational studies and RCTs.	https://www.ncbi.nlm.nih.gov/pubmed/22404103
					Ungprasert 2016a This meta-analysis provided evidence for a significant association between psoriasis and COPD, an under-recognised co-morbidity, with an overall 1.45-fold increased risk. Further studies are required.	https://www.ncbi.nlm.nih.gov/pubmed/26458363
					Ungprasert 2016b Some evidence for increased risk of Parkinson's disease among patients with psoriasis. Limitations in study design acknowledged. Further studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/27451924
					Ungprasert 2016c Some evidence for increased risk of incident atrial fibrillation among patients with psoriasis. Limitations in study design acknowledged. Further studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/27057013

					Ungprasert 2017 This meta-analysis demonstrated an approximately 3-fold increased risk of coeliac disease among patients with psoriasis. The pathophysiologic mechanisms behind this increased risk are not known, and further investigations are required.	https://www.ncbi.nlm.nih.gov/pubmed/28216724
					Ungprasert 2018a Evidence that risk of psoriasis among patients with schizophrenia was significantly higher than non-schizophrenia subjects (83% excess risk). Future work needed to determine this nature and mechanism of this observation.	https://www.ncbi.nlm.nih.gov/pubmed/29128620
					Ungprasert 2018b Evidence for a significantly increased risk of incident chronic kidney disease and end-stage renal disease among patients with psoriasis compared with individuals without psoriasis. How this risk should be addressed in clinical practice requires more study with emphasis on prevention and surveillance programmes.	https://www.ncbi.nlm.nih.gov/pubmed/29644523
					Upala, 2017 This meta-analysis of prospective studies demonstrated that patients with psoriasis have increased risk of new-onset atrial fibrillation. Future interventional studies addressing the impact of psoriasis treatment and prevention of atrial fibrillation are required.	https://www.ncbi.nlm.nih.gov/pubmed/27794626
					Wang 2016 This meta-analysis demonstrated no significant difference in total cholesterol, LDL, HDL or triglycerides between patients with psoriasis and controls. Patients with psoriasis had higher epicardial fat tissue (EFT) compared to controls which may suggest that EFT is an independent risk factor of psoriasis. Further studies needed to elucidate these relationships.	https://www.ncbi.nlm.nih.gov/pubmed/27245937
					Wang 2018 This meta-analysis indicated that patients with psoriasis had an increased risk of asthma which was higher in older patients with psoriasis than in younger patients. Further studies are needed to confirm this observation and overcome the limitations of this analysis (particularly with respect to diagnostic accuracy of both complex conditions).	https://www.ncbi.nlm.nih.gov/pubmed/29490768
					Whitlock, 2018 There are no known clinical trials of treatment specifically for concurrent psoriasis and inflammatory bowel disease. Evidence that infliximab and adalimumab have efficacy in psoriasis, psoriatic arthritis, ulcerative colitis, and Crohn's disease; other agents have demonstrated efficacy for some, but not all, of these indications. Further studies including rigorous examination of long-term data is needed.	https://www.ncbi.nlm.nih.gov/pubmed/29332708
					Wu 2015 Evidence for an overall increased risk of autism in children with family history of autoimmune disease (including psoriasis) was identified. More mechanistic studies are needed to further explain the association between family history of autoimmune disease and increased risk of autism in children.	https://www.ncbi.nlm.nih.gov/pubmed/25981892
					Wu 2018 This meta-analysis examined the relationship between psoriasis and risk of erectile dysfunction. The studies included were mostly cross-sectional or small sample cohorts, which could introduce bias and heterogeneity into the analysis. Some evidence that psoriasis is associated with an increased risk of erectile dysfunction. Prospective cohort studies are needed to elucidate these relationships and to advance knowledge in this field.	https://www.ncbi.nlm.nih.gov/pubmed/29735408
					Yang, 2016 Evidence for TNF inhibitors having clinical benefit with regard to adverse cardiovascular events in psoriasis and/or PsA. Rigorous randomized controlled trials needed to evaluate whether TNF inhibitors truly result in reduction of cardiovascular diseases.	https://www.ncbi.nlm.nih.gov/pubmed/27300248
					Zhang, 2017 Evidence that there is a correlation between psoriasis and erectile dysfunction. Patients with psoriasis may have a higher incidence of erectile dysfunction though this observation needs to be further confirmed by further high quality studies.	https://www.ncbi.nlm.nih.gov/pubmed/29706048
V	**What treatments work best for health conditions related to psoriasis, such as psoriatic arthritis, cardiovascular disease, metabolic syndrome, and stress?**	How best to treat psoriatic arthritis?	26	n/a		
					Abbott, 2015 Evidence that TNF-α inhibitor therapy reduces depression in people who have chronic diseases (including those with psoriasis) though the effects are small. Limited data available. Further studies investigating a more detailed timeline of changes in depression, inflammatory biomarkers and disease activity status in patients with psoriasis (and other chronic diseases) are required.	https://www.ncbi.nlm.nih.gov/pubmed/25935351

					Armstrong, 2013a Some evidence that mild and severe psoriasis is associated with an increased risk of myocardial infarction and stroke. Severe psoriasis is also associated with an increased risk of cardiovascular mortality. Some limitations. Future studies needed - these should include more complete covariate adjustment and characterisation of psoriasis severity.	https://www.ncbi.nlm.nih.gov/pubmed/23557749
					Armstrong 2013b Evidence that psoriasis and psoriatic arthritis are associated with greater prevalence of hypertension. Patients with severe psoriasis have greater odds of hypertension than those with mild psoriasis. Some limitations with study. Further studies are needed – specifically to elucidate the basic mechanisms underlying the association between psoriasis and hypertension, to explore the relationship between psoriasis and hypertension severity, and to examine the effects of systemic treatments for psoriasis on hypertension control.	https://www.ncbi.nlm.nih.gov/pubmed/23249828
					Armstrong 2013c Compared with the general population, psoriasis patients have higher prevalence of metabolic syndrome, and patients with more severe psoriasis have greater odds of metabolic syndrome than those with milder psoriasis. Some limitations with study. More studies needed to determine the mechanisms underlying the association between these two conditions and to determine the effect of psoriasis systemic therapies on metabolic syndrome.	https://www.ncbi.nlm.nih.gov/pubmed/23360868
					Armstrong 2013d Evidence that psoriasis is associated with an increased prevalence and incidence of diabetes. The association of psoriasis with diabetes may be strongest among patients with severe psoriasis. Some limitations with the study. Future studies should more closely assess the relationship between psoriasis severity, age at disease onset, and diabetes.	https://www.ncbi.nlm.nih.gov/pubmed/23407990
					Armstrong 2014 This review concluded that epidemiologic data is insufficient to reach definitive conclusions with regards to the effects of biologics and other disease modifying anti rheumatic drugs (DMARDs) on cardiovascular outcomes in psoriasis and psoriatic arthritis patients. Adequately powered, long-term, controlled studies are necessary to determine the cardioprotective effects of TNF inhibitors observed in preliminary studies on psoriasis and psoriatic arthritis populations.	https://www.ncbi.nlm.nih.gov/pubmed/23565631
					Bhatia, 2014 Epidemiologic and clinical studies suggest there is an association among psoriasis, coeliac disease, and coeliac disease markers. Further studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/24780176
					Candia, 2015 Case - control studies support an association between psoriasis and non-alcoholic fatty liver disease (NAFLD). Screening of NAFLD in patients with psoriasis may be warranted. More studies are needed.	https://www.ncbi.nlm.nih.gov/pubmed/25418531
					Chi, 2017 This systemic review and meta-analysis concluded that the available limited, very low-quality evidence does not support an association between psoriasis and suicidal thought and behaviour. Further studies that provide data for different age and sex groups are needed to clarify whether a subgroup of patients with psoriasis has an elevated risk of suicidality.	https://www.ncbi.nlm.nih.gov/pubmed/28409490
					Coto-Segura, 2013 Evidence to support an association between psoriasis, PsA and type 2 diabetes mellitus. Heterogeneity between studies. Further work to understand the relations more completely needed.	https://www.ncbi.nlm.nih.gov/pubmed/23772556
					Cullen, 2019 Evidence for a positive overall association between non-neurological autoimmune (NNAI) disorders and psychosis, which was not consistent across all NNAI disorders. Separate meta-analyses were conducted for individual autoimmune disorders. A significant positive association was observed for psoriasis. Future work recommended: 1) studies should be designed to better disentangle the temporal nature of the association between NNAI disorders and psychosis, as such studies have demonstrated that both psychosis and depression show bidirectional associations with autoimmune disorders; 2) larger studies should be undertaken to examine the presence of neuronal surface autoantibodies among individuals with psychosis; 3) greater efforts should be made in large cohort studies to include information on potential confounders, such as socioeconomic status, adversity, and tobacco use; and 4) studies should be undertaken to evaluate the effect of corticosteroid treatment on the relationship between NNAI disorders and psychosis.	https://www.ncbi.nlm.nih.gov/pubmed/30122288
					De Vecchis, 2016 Evidence that methotrexate at low doses, such those used for maintenance therapy of rheumatoid arthritis, predicts a decreased risk of cardiovascular events. Randomised controlled trials to establish causality recommended. Ungprasert 2014 Evidence for a statistically significant increased risk of venous thromboembolism among patients with psoriasis. Limited data available – further study required.	https://www.ncbi.nlm.nih.gov/pubmed/26467356

					Dowlatshahi, 2014 Evidence that psoriasis patients are at least one and a half times more likely to manifest signs of clinical depression compared with their healthy peers. More than one-quarter of psoriasis patients show symptoms of depression and approximately one-tenth have signs of clinical depression. High heterogeneity between studies. Further work to clarify this relationship needed. Phan Evidence from this pooled meta-analysis demonstrates a significant association between bullous pemphigoid and psoriasis. This association is stronger in males, in contrast with many other auto-immune conditions. The study is constrained by several limitations. Further studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/24284419
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					Mosca 2015 Some evidence that psoriatic patients are at increased CV risk, related to raised prevalence and incidence of CV risk factor and to inflammatory status. Further studies needed to establish appropriate targets for CV risk factors, assess the clinical value of screening for subclinical organ damage and determine the impact of disease-modifying therapies on CV risk profile in psoriatic patients.	https://www.ncbi.nlm.nih.gov/pubmed/25464252
					Pouplard, 2013 This systematic literature review shows a small increased risk of some solid cancers in psoriasis, especially those linked to alcohol drinking and cigarette smoking. A higher risk of non-melanoma skin cancers, especially squamous cell carcinoma, is also shown. There is a need for further studies to obtain data from ongoing psoriasis registries including robust assessment of comorbidities and pharmacological treatments to better characterise the risk of cancer in psoriasis.	https://www.ncbi.nlm.nih.gov/pubmed/23845151

					Puig, 2014 Evidence collated regarding a large number of small controlled or cross-sectional studies which report increased prevalence of cardiometabolic and psychological co-morbidities in patients with psoriasis. Evidence from a number of large cohort studies presented to describe the incidence of various cardiometabolic co-morbidities in patients with psoriasis. Evidence for association of severe psoriasis with increased mortality (most common cause of death is cardiovascular disease). Comment that studies on the management of co-morbidities and their impact on psoriasis treatment are scarce and that many questions on the co-morbidities of psoriasis remain to be answered. Further studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/24752135
					Raaby, 2017 This meta-analysis confirmed that patients with psoriasis have an increased risk of CVD, especially those with severe psoriasis. Further studies to investigate whether increased control followed by treatment of cardiovascular risk factors improves the prognosis of psoriatic patients are needed.	https://www.ncbi.nlm.nih.gov/pubmed/28213804
					Richard 2014 This systematic literature research and meta-analysis was designed to marshall the evidence base for selected clinically relevant questions to help dermatologists i) identify patients at risk of PsA, ii) to diagnose PsA in collaboration with rheumatologists and iii) manage PsA. There was no high-quality evidence to support the "expert" recommendations regarding PsA screening. However, treatment options for PsA were supported by strong evidence. Further studies are required to provide an adequate evidence base for risk profiling, screening and management of PsA (by dermatologists in partnership with rheumatologists).	https://www.ncbi.nlm.nih.gov/pubmed/24985557
					Roubille 2015 This meta-analysis provided evidence that TNF inhibitors and methotrexate decrease the risk of cardiovascular events (CVEs) in patients with rheumatoid arthritis (RA) whereas NSAIDs and corticosteroids increase the risk of CVEs. In patients with psoriasis and psoriatic arthritis (PsA/Pso) limited evidence suggested that treatment with systemic therapies is associated with a decrease in the risk of all CVEs. Large, prospective, adequately controlled and powered studies are needed to explore the effects of systemic/biologic therapies on cardiovascular morbidity and mortality in both the RA and PsA/Pso populations.	https://www.ncbi.nlm.nih.gov/pubmed/25561362
					Rodríguez-Zúñiga 2017a Evidence that the risk for MS is increased by 40% in patients with psoriasis compared with in the general population. Systemic review limited by missing data, high heterogeneity among studies examined, high risk selection bias in studies included in analysis and high probability of selection bias. Further studies recommended.	https://www.ncbi.nlm.nih.gov/pubmed/28917453
					Rodríguez-Zúñiga 2017b Evidence that psoriasis is highly associated with the metabolic syndrome in Latin America. The association is stronger for severe psoriasis and when the adult treatment panel guidelines (ATP-III criteria) are used to identify cardiovascular disease risk. Limited data available – further study required.	https://www.ncbi.nlm.nih.gov/pubmed/28117050
					Rungapiromnan, 2017 Biologic therapies including TNFi, an anti-IL-12/23 agent (ustekiumab) and anti-IL-17A agents (secukinumab and ixekizumab) have no significant impact on the risk of major adverse cardiovascular events (MACEs) in adult patients with plaque psoriasis over the short term. However, follow-up was limited and patient characteristics were those of patients participating in RCTs. Recommendation – need for well-designed observational studies that involve larger numbers of patients and longer durations of treatment exposure reflecting routine clinical practice required to determine the impact of biologic therapies on the risk of MACEs in patients with psoriasis.	https://www.ncbi.nlm.nih.gov/pubmed/27518205
					Saleem, 2017 Database studies might not fully account for confounders, resulting in overestimates of the risk impact of comorbidities. Knowing the baseline risk, relative risk, and attributed risk, together, provides a better overall understanding of the impact an exposure has on any given disease in a defined population. Further work to understand whether screening and intervention (for co-morbid disease) should be done requires more than just knowing there is a greater relative risk and more than knowing that a treatment that can reduce that risk. Studies to consider costs and benefits, including how big a problem the comorbidity is on an absolute basis not just on a relative basis, need to be carried out.	https://www.ncbi.nlm.nih.gov/pubmed/27986396
					Samarasekera, 2013 Evidence that severe psoriasis is associated with an increased risk of CVD. Uncertainty remains about whether CVD risk is directly attributable to psoriasis, as the majority of studies failed to adequately adjust for key traditional risk factors. Further research is required to better understand the complex relationship between psoriasis, traditional risk factors, and CVD. Long-term, large-scale cohort studies that adequately control for confounding factors and detection bias are required to address the question of whether aggressive treatment of severe psoriasis has an impact on clinically relevant CVD end points.	https://www.ncbi.nlm.nih.gov/pubmed/23528816

					Shaharyar, 2014 Evidence that patients with psoriasis have an increased burden of subclinical atherosclerosis and endothelial dysfunction. Further clinical trials to identify appropriate screening strategies for subclinical cardiovascular disease (CVD), and whether non-pharmacological and pharmacological approaches result in slower progression of subclinical CVD / reduction in clinical events among patients with psoriasis are needed.	https://www.ncbi.nlm.nih.gov/pubmed/24401219
					Singh 2016 Evidence that patients with psoriasis have a greater prevalence of metabolic syndrome as well as its individual components when compared to the general population. The odds of metabolic syndrome and its components are higher with increased psoriasis disease severity. Prospective studies are needed to better understand the contribution of psoriasis in the development of metabolic syndrome.	https://www.ncbi.nlm.nih.gov/pubmed/27589483
					Singh 2017a Evidence that patients with psoriasis have higher odds of having metabolic syndrome when compared with the general population. The pathologic mechanisms shared by these two disease processes, as well as the directionality of the relationship, are not well understood and need to be elucidated through further translational research.	https://www.ncbi.nlm.nih.gov/pubmed/28719618
					Singh 2017b Evidence that patients with psoriasis have a significantly higher likelihood of suicidal ideation, suicide attempts, and completed suicides. In patients with psoriasis, those who are younger and whose psoriasis is more severe are at particular risk for suicidality. Potential sources of bias and study heterogeneity. Further investigation to understand this association more fully needed. Jin Patients with psoriasis have a higher prevalence of metabolic syndrome and hypertension compared with controls. More prospective, controlled and randomised studies need to be performed in the future.	https://www.ncbi.nlm.nih.gov/pubmed/28807109
					Tsai, 2018 Some evidence that patients with psoriasis might have higher serum homocysteine and lower folate levels than control patients who do not have psoriasis. However, due to significant heterogeneity between studies reviewed and other limitations, further research needed.	https://www.ncbi.nlm.nih.gov/pubmed/30074615
					Tzellos, 2013 Some evidence that, there is a significant difference in the rate of major adverse cardiovascular events (MACEs) observed in patients receiving anti-IL-12／23 biological agents compared to those treated with placebo. Further studies recommended including post-marketing surveillance and meta-analysis of observational studies and RCTs.	https://www.ncbi.nlm.nih.gov/pubmed/22404103
					Ungprasert 2016a This meta-analysis provided evidence for a significant association between psoriasis and COPD, an under-recognised co-morbidity, with an overall 1.45-fold increased risk. Further studies are required.	https://www.ncbi.nlm.nih.gov/pubmed/26458363
					Ungprasert 2016b Some evidence for increased risk of Parkinson's disease among patients with psoriasis. Limitations in study design acknowledged. Further studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/27451924
					Ungprasert 2016c Some evidence for increased risk of incident atrial fibrillation among patients with psoriasis. Limitations in study design acknowledged. Further studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/27057013
					Ungprasert 2017 This meta-analysis demonstrated an approximately 3-fold increased risk of coeliac disease among patients with psoriasis. The pathophysiologic mechanisms behind this increased risk are not known, and further investigations are required.	https://www.ncbi.nlm.nih.gov/pubmed/28216724
					Ungprasert 2018a Evidence that risk of psoriasis among patients with schizophrenia was significantly higher than non-schizophrenia subjects (83% excess risk). Future work needed to determine this nature and mechanism of this observation.	https://www.ncbi.nlm.nih.gov/pubmed/29128620
					Ungprasert 2018b Evidence for a significantly increased risk of incident chronic kidney disease and end-stage renal disease among patients with psoriasis compared with individuals without psoriasis. How this risk should be addressed in clinical practice requires more study with emphasis on prevention and surveillance programmes.	https://www.ncbi.nlm.nih.gov/pubmed/29644523
					Upala, 2017 This meta-analysis of prospective studies demonstrated that patients with psoriasis have increased risk of new-onset atrial fibrillation. Future interventional studies addressing the impact of psoriasis treatment and prevention of atrial fibrillation are required.	https://www.ncbi.nlm.nih.gov/pubmed/27794626
					Wang 2016 This meta-analysis demonstrated no significant difference in total cholesterol, LDL, HDL or triglycerides between patients with psoriasis and controls. Patients with psoriasis had higher epicardial fat tissue (EFT) compared to controls which may suggest that EFT is an independent risk factor of psoriasis. Further studies needed to elucidate these relationships.	https://www.ncbi.nlm.nih.gov/pubmed/27245937
					Wang 2018 This meta-analysis indicated that patients with psoriasis had an increased risk of asthma which was higher in older patients with psoriasis than in younger patients. Further studies are needed to confirm this observation and overcome the limitations of this analysis (particularly with respect to diagnostic accuracy of both complex conditions).	https://www.ncbi.nlm.nih.gov/pubmed/29490768

					Whitlock, 2018 There are no known clinical trials of treatment specifically for concurrent psoriasis and inflammatory bowel disease. Evidence that infliximab and adalimumab have efficacy in psoriasis, psoriatic arthritis, ulcerative colitis, and Crohn's disease; other agents have demonstrated efficacy for some, but not all, of these indications. Further studies including rigorous examination of long-term data is needed.	https://www.ncbi.nlm.nih.gov/pubmed/29332708
					Wu 2015 Evidence for an overall increased risk of autism in children with family history of autoimmune disease (including psoriasis) was identified. More mechanistic studies are needed to further explain the association between family history of autoimmune disease and increased risk of autism in children.	https://www.ncbi.nlm.nih.gov/pubmed/25981892
					Wu 2018 This meta-analysis examined the relationship between psoriasis and risk of erectile dysfunction. The studies included were mostly cross-sectional or small sample cohorts, which could introduce bias and heterogeneity into the analysis. Some evidence that psoriasis is associated with an increased risk of erectile dysfunction. Prospective cohort studies are needed to elucidate these relationships and to advance knowledge in this field.	https://www.ncbi.nlm.nih.gov/pubmed/29735408
					Yang, 2016 Evidence for TNF inhibitors having clinical benefit with regard to adverse cardiovascular events in psoriasis and/or PsA. Rigorous randomized controlled trials needed to evaluate whether TNF inhibitors truly result in reduction of cardiovascular diseases.	https://www.ncbi.nlm.nih.gov/pubmed/27300248
					Zhang, 2017 Evidence that there is a correlation between psoriasis and erectile dysfunction. Patients with psoriasis may have a higher incidence of erectile dysfunction though this observation needs to be further confirmed by further high quality studies.	https://www.ncbi.nlm.nih.gov/pubmed/29706048
W	**People with psoriatic arthritis may have symptoms such as: pain, fatigue, eye problems and fibromyalgia. What is the best way to treat these symptoms?**	How to best manage fatigue in PA?	14	n/a		
					Boehncke Evidence that of the numerous disease-modifying antirheumatic drugs available for treating PsA — both nonbiologic and biologic, with different modes of action —all of them also exhibit at least some efficacy as therapy for psoriasis. However, although a wealth of literature exists for treating psoriasis and a substantial body of evidence exists for treating PsA, few studies assess the efficacy of a systemic therapy initiated with the intention of simultaneously controlling PsA and psoriasis. Further studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/25362715
					Richard 2014 This systematic literature research and meta-analysis was designed to marshall the evidence base for selected clinically relevant questions to help dermatologists i) identify patients at risk of PsA, ii) to diagnose PsA in collaboration with rheumatologists and iii) manage PsA. There was no high-quality evidence to support the "expert" recommendations regarding PsA screening. However, treatment options for PsA were supported by strong evidence. Further studies are required to provide an adequate evidence base for risk profiling, screening and management of PsA (by dermatologists in partnership with rheumatologists).	https://www.ncbi.nlm.nih.gov/pubmed/24985557
X	**How common is psoriasis? Is psoriasis equally common in all parts of the world or are there certain populations who are more likely to develop psoriasis?**	How many other people have psoriasis?	10	n/a		
					Burden, 2016 The Evidence that the prevalence of childhood psoriasis is higher in European countries, older children and girls. Up to 48.8% of children have a family history of psoriasis in a first-degree relative. Well designed epidemiological studies are needed to provide precise and consistent information about the frequency and clinical presentation, risk factors, associated diseases and long-term outcomes in childhood psoriasis.	https://www.ncbi.nlm.nih.gov/pubmed/26928555

					Hay, 2014 Evidence that collectively, skin conditions (including psoriasis) range from the 2nd to the 11th leading cause of years lived with disability at a country level. At the global level, skin conditions are the 4th leading cause of nonfatal disease burden. The burden due to skin diseases is enormous in both high- and low-income countries. More studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/24166134
					Hernández-Vásquez, 2017 Evidence there is an important lack of information from Latin America and Caribbean concerning the burden of psoriasis. Further studies investigating the burden of psoriasis in representative Latin America and Caribbean populations are needed.	https://www.ncbi.nlm.nih.gov/pubmed/28608530
					Michalek, 2017 Evidence that psoriasis is a common disease, occurring more frequently with advancing age. Limited data on the epidemiology of psoriasis are available. The available prevalence data come from only 20 countries, meaning there are huge geographic gaps in knowledge, especially from low- and middle-income settings. More studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/27573025
					Parisi, 2013 Evidence that the occurrence of psoriasis varies according to age and geographic region, being more frequent in countries more distant from the equator. Prevalence estimates also vary in relation to demographic characteristics; studies confined to adults report higher estimates of psoriasis compared with those involving all age groups. Studies on the prevalence and incidence of psoriasis have contributed to a better understanding of the burden of the disease. Further research is required to fill existing gaps in understanding the epidemiology of psoriasis and trends in incidence over time.	https://www.ncbi.nlm.nih.gov/pubmed/23014338
					Prignano, 2018 Evidence that psoriasis and PsA affect a substantial number of people and will likely have an important impact on the Italian healthcare system. Prevalence in Italy of psoriasis (1.8–3.1%) and PsA (4.7–47.1%). More research needed	https://www.ncbi.nlm.nih.gov/pubmed/29846817
Y	**What is the best way to assess the severity of psoriasis?**	How we can we simplify disease assessment beyond the clunky and time consuming PASI And DLQI?	7	n/a		
					Ahn, 2015 Evidence that baseline tuberculosis testing remains the only screening test with strong evidence to support its practice. Other screening and monitoring tests commonly performed in patients who are taking biologic agents are supported only in certain clinical settings or lack evidence to support or recommend against their practice. More research needed.	https://www.ncbi.nlm.nih.gov/pubmed/26184440
					NICE Clinical guideline [CG153] - Psoriasis: assessment and management The recommendations for further research from this guideline have been incorporated into the indicative questions for the PsPSP.	https://www.nice.org.uk/guidance/cg153/evidence
					Yang, 2015 Evidence that the validity and responsiveness of one of the three widely used generic preference-based measures of health-related quality of life - EQ-5D - was good in people with skin diseases, especially psoriasis / psoriatic arthritis. No evidence on the other two measures - SF-6D and Health Utility Index 3 (HUI3) - was available. More studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/25358263
Z	**Why does psoriasis affect particular areas of the body and why are these often the same areas on both sides of the body?**	Why does psoriasis project a mirror image on the body ie right and left leg?	19	n/a		
					No systematic reviews identified	**No systematic reviews identified**
AA	**Can tests be developed to predict whether a person will develop psoriasis in the future or to diagnose psoriasis in the early stages of the disease?**	A definitive test for Psoriasis so that it is not misdiagnosed and mistreated?	21	n/a		

					No systematic reviews identified	**No systematic reviews identified**
AB	**Can we predict potential side effects related to psoriasis treatments?**	Identification and validation of biomarkers of psoriasis, including those predicting response to therapy and potential drug-related toxicity	1	n/a		
					No systematic reviews identified	**No systematic reviews identified**
AC	**How do psoriasis and other health conditions related to it affect the quality of life of a person with psoriasis and that of their family and carers?**	How psoriasis affect the quality of life?	17	n/a		
					Ali, 2017 Evidence that quality of life (QoL) measurement is increasingly being reported in randomized controlled trials (RCTs) of psoriasis. Formal guidelines are needed for assessment and publishing of QoL data. Researchers should consider whether minimal clinically important difference (MCID) information is available, and development of MCID data should be encouraged. Further studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/27273146
					Amin, 2018 Evidence that individuals with psoriasis are less likely to participate in vigorous physical activity compared to individuals without psoriasis. Further research is necessary to clarify this relationship.	https://www.ncbi.nlm.nih.gov/pubmed/29718018
					Cardona-Arias, 2014 Evidence that psoriasis has a negative impact on health related quality of life (HRQOL). Women report the most unfavorable scores, and this highlights the need to consider gender in the multidisciplinary care of these patients. More studies needed.	www.scielo.org.ar/scielo.php?script=sci_arttext&pid=S1851-300X2014000200002
					Gisondi, 2013 Evidence that Dermatology Life Quality Index (DLQI) is the most common used tool for investigating health related quality of life (HRQoL) in patients with skin disease including psoriasis. For the majority of patients with skin diseases, the most important negative impacts on QoL are appearance related. Generally, the burden on QoL correlates with the severity of skin disease and the improvement in QoL achieved by TNF-α blockers is proportional to the degree of disease remission. Achieving the highest clearing of skin disease with anti-TNF-α agents is required for optimal improvement in QoL. Further research needed.	https://www.ncbi.nlm.nih.gov/pubmed/23670060
					Gonzalez, 2016 Evidence that both dermatologists and primary care physicians should treat the visible cutaneous lesions and disease comorbidities and address the psychosocial impact of psoriasis in their adolescent patients. Use of both a general and dermatology- specific health related quality of life (HRQL) questionnaire may allow physicians to better identify the impact of the disease and recognise improvement or impairment over time. More studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/27811471
					Hay, 2014 Evidence that collectively, skin conditions (including psoriasis) range from the 2nd to the 11th leading cause of years lived with disability at a country level. At the global level, skin conditions are the 4th leading cause of nonfatal disease burden. The burden due to skin diseases is enormous in both high- and low-income countries. More studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/24166134
					Hernández-Vásquez, 2017 Evidence there is an important lack of information from Latin America and Caribbean concerning the burden of psoriasis. Further studies investigating the burden of psoriasis in representative Latin America and Caribbean populations are needed.	https://www.ncbi.nlm.nih.gov/pubmed/29846817
					Karimkhani, 2017 Evidence that skin and subcutaneous diseases were the 18th leading cause of global disability-adjusted life years (DALYs) in Global Burden of Disease 2013. Excluding mortality, skin diseases were the fourth leading cause of disability worldwide. Further research needed.	https://www.ncbi.nlm.nih.gov/pubmed/28249066

					Mattei, 2014 Evidence that mean PASI and DLQI correlate predictably in patients with chronic moderate-to-severe plaque psoriasis undergoing treatment with biological agents. A reduction in PASI of at least 75% can translate to significant quality-oflife improvement in patients treated with these therapies. Further research important to quantify benefit following greater degrees of skin clearance.	https://www.ncbi.nlm.nih.gov/pubmed/23425140
					Møller, 2015 Evidence that the ranges of disutility among psoriasis patients are within the ranges of other chronic diseases (cardiovascular diseases, diabetes, end-stage renal diseases, liver diseases, cancer, and visual disorders). Further research needed.	https://www.ncbi.nlm.nih.gov/pubmed/26185476
					Obradors, 2016 Evidence that several disease- and patient-related factors contribute to the deterioration in health-related quality fo life (HRQoL) in patients with psoriasis in Europe. Therapeutic measures with proven effectiveness in controlling disease symptoms and reducing PASI should be considered in patients with a severe disease who have a poorer HRQoL. More research needed.	https://www.ncbi.nlm.nih.gov/pubmed/27259580
					Olsen, 2016 Evidence that most skin conditions in children have a 'small' mean effect on quality of life (QoL). However, the range is large and a significant proportion of children with many common skin conditions (including psoriasis) will experience a very large effect on quality of life. Future studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/26686685
					Puig, 2017 Evidence that substantial improvement in clinical efficacy is associated with improved quality of life (QoL) in patients with moderate-to-severe psoriasis suggesting that PASI 90 responders (clear or almost clear skin) could achieve a superior QoL compared to PASI 75–89 responders. Further studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/27739123
					Randa 2017 Evidence that children and adolescents with psoriasis experience moderate impairment of health related quality of life (HRQOL). Certain demographic characteristics (e.g. sex) and clinical characteristics (e.g. age at onset) appear to moderate this impact. Further research needed.	https://www.ncbi.nlm.nih.gov/pubmed/27983745
					Sampogna, 2017 Evidence that there are nine instruments that are designed to measure the impact on the lives of family members, partners and carers of having someone in the family with a skin disease. Further studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/28426906
					Shahwan, 2017 Evidence of no significant difference in mean baseline itch scores in patients with psoriasis or atopic dermatitis who need treatment with systemic therapies. Evidence that pruritus is a more significant component of psoriasis than previously recognised. Pruritus in psoriasis has been associated with occupational impairment, anxiety, depression, and has a negative impact on overall quality of life, mood, concentration, sleep, sexual desire, and appetite. Further research is needed.	https://www.ncbi.nlm.nih.gov/pubmed/28522048
					Théréné, 2018 Evidence that anti-IL-17, JAK inhibitors, adalimumab and apremilast are effective in reducing pruritus in psoriasis with variable effect size; systemic treatments, including UVB phototherapy, improve pruritus in psoriasis. More studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/28887107
					Wu 2018 This meta-analysis examined the relationship between psoriasis and risk of erectile dysfunction. The studies included were mostly cross-sectional or small sample cohorts, which could introduce bias and heterogeneity into the analysis. Some evidence that psoriasis is associated with an increased risk of erectile dysfunction. Prospective cohort studies are needed to elucidate these relationships and to advance knowledge in this field.	https://www.ncbi.nlm.nih.gov/pubmed/29735408
					Yang, 2015 Evidence that the validity and responsiveness of one of the three widely used generic preference-based measures of health-related quality of life - EQ-5D - was good in people with skin diseases, especially psoriasis / psoriatic arthritis. No evidence on the other two measures - SF-6D and Health Utility Index 3 (HUI3) - was available. More studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/25358263
					Zhang, 2017 Evidence that there is a correlation between psoriasis and erectile dysfunction. Patients with psoriasis may have a higher incidence of erectile dysfunction though this observation needs to be further confirmed by further high quality studies.	https://www.ncbi.nlm.nih.gov/pubmed/29706048
					Zheng, 2018 Evidence that intense physical activity may lower the prevalence of psoriasis. Further research needed.	https://www.ncbi.nlm.nih.gov/pubmed/29979432
AD	**What are the financial costs of psoriasis to society?**	What effect does severe psoriasis have on work and relationships?	7	n/a		
					Burgos-Pol, 2016 Evidence that due to the economic burden of psoriasis and psoriatic arthritis costs increase with the treatment and management of more severe disease and the use of biologics. More research needed.	https://www.ncbi.nlm.nih.gov/pubmed/27316590
					Brezinski, 2015 Evidence that the economic burden of psoriasis is substantial and significant in the United States. Research gap; more studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/25565304

					Feldman, 2014 Evidence that costs associated with psoriasis are high in many countries, indicating a continued need for treatments that offer good value for money. More research needed.	https://www.ncbi.nlm.nih.gov/pubmed/25052261
					Vanderpuye-Orgle, 2015 The economic burden of psoriasis in the US is significant, with a majority of it coming from indirect costs, such as productivity and health related quality of life (HRQoL) losses. More research needed.	https://www.ncbi.nlm.nih.gov/pubmed/25882886
AE	**What is the most cost-effective way to treat psoriasis?**	How cost effective are specialist services for psoriasis?	3	n/a		
					Armstrong, 2018 Evidence that the number needed to treat (NNT) and incremental cost per responder are meaningful ways to assess comparative effectiveness and cost effectiveness among psoriasis treatments. More research needed.	https://www.ncbi.nlm.nih.gov/pubmed/29619856
					Wang 2014 Evidence that infliximab and ustekinumab 90mg had the highest efficacy. Adalimumab had the best cost-efficacy, followed by ustekinumab 45mg and infliximab. More studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/24738910
					Gupta, 2014 Evidence that although infliximab had the highest efficacy relative to other systemic treatments for psoriasis, adverse effects, cost, and patient preferences should also be considered when deciding on treatment. More studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/25348757
					Gutknecht, 2016 Evidence for lack of standard on methods and outcome measures for management of psoriasis which leads to limited comparability of health economic studies and presents no basis with which to examine a meta-analysis of health economic results. Further studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/27435415
					Hamilton, 2015 Evidence that the economic literature is dominated by comparisons of interventions to placebo, with implicit comparisons of different therapies. There is a lack of evaluations of service model innovations to deliver complex packages of care for psoriasis. Primary and secondary integrated clinical and economic research is needed to address the limitations and to identify patient preferences and barriers/ facilitators to treatment.	https://www.ncbi.nlm.nih.gov/pubmed/25324036
					Kromer, 2018 This systematic review provides an actual overview on economic evaluations of biologicals including pairwise comparisons, but also highlights limitations and gaps in health economic evidence and the need to address these with future research.	https://www.ncbi.nlm.nih.gov/pubmed/29298315
					Mauskopf, 2014 Evidence that cost-effectiveness models of first-line biologics for moderate to severe plaque psoriasis either do not include subsequent treatment regimens or include only some of the regimens recommended in current treatment guidelines. Results may be sensitive to assumptions about treatment sequencing and the choice and efficacy of subsequent treatment regimens. More studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/24469676
					Wang, 2014 Evidence that in a Taiwanese setting, adalimumab and ustekinumab had lower 1-year costs per PASI 75 responder than etanercept. Ustekinumab had the lowest 2-year cost per PASI 75 responder. More studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/24738910
					Zhang, 2015 Evidence that the main key drivers of cost effectiveness are the costs related to the treatment, values and choice of efficacy, utility values, hospitalisation for non-responders, time horizon, model structure, and utility mapping method. Recommendation that high-quality cost-effectiveness studies are required to facilitate resource allocation decision-making. To improve study quality, future research should provide evidence on the long-term experience with psoriasis treatments, and resolve the uncertainty associated with key drivers of cost effectiveness.	https://www.ncbi.nlm.nih.gov/pubmed/25475964
AF	**In children with psoriasis, what are the risk factors for developing psoriasis, the most common symptoms seen, and the long-term outcomes?**	What is the natural history of child-onset psoriasis and can we predict who will have severe and persistent disease?	8	n/a		
					Burden-The Evidence that the prevalence of childhood psoriasis is higher in European countries, older children and girls. Up to 48.8% of children have a family history of psoriasis in a first-degree relative. Well designed epidemiological studies are needed to provide precise and consistent information about the frequency and clinical presentation, risk factors, associated diseases and long-term outcomes in childhood psoriasis.	https://www.ncbi.nlm.nih.gov/pubmed/26928555

					Gonzalez, 2016 Evidence that both dermatologists and primary care physicians should treat the visible cutaneous lesions and disease comorbidities and address the psychosocial impact of psoriasis in their adolescent patients. Use of both a general and dermatology- specific health related quality of life (HRQL) questionnaire may allow physicians to better identify the impact of the disease and recognise improvement or impairment over time. More studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/27811471
					Olsen, 2016 Evidence that most skin conditions in children have a 'small' mean effect on quality of life (QoL). However, the range is large and a significant proportion of children with many common skin conditions (including psoriasis) will experience a very large effect on quality of life. Future studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/26686685
					Pourchot, 2018 Evidence that the prevalence of tongue involvement is 7.7% in children with psoriasis. No clinical or epidemiological association was shown. Tongue involvement does not modify the management of psoriasis. It was not possible to evaluate either the prevalence of tongue involvement in psoriasis or its positive predictive value. More research needed.	https://www.ncbi.nlm.nih.gov/pubmed/29773283
AG	**How well do psoriasis treatments work in children and how safe are they?**	Which are the best/ most effective treatments for psoriasis in children?	15	n/a		
					Kravvas, 2018 Some evidence for topical therapies but further randomised controlled trials needed	https://www.ncbi.nlm.nih.gov/pubmed/29493005
					Napolitano, 2016 Evidence for systemic, photo and biologic therapies reviewed but further prospective studies / registries needed	https://www.ncbi.nlm.nih.gov/pubmed/27085539
					Sanclemente, 2015 Assessment of efficacy and safety of anti-TNF therapies. Cochrane. One RCT identified, risk pf publication bias high. Further studies required.	https://www.ncbi.nlm.nih.gov/pubmed/26598969
					Van Geel, 2015 Some evidence on systemic therapy but limited. Compelling need for prospective, multicentre, international registry to investigate further.	https://www.ncbi.nlm.nih.gov/pubmed/25346019
					Posso-De Los Rios, 2014 Some evidence for systemic treatment of pustular psoriasis in children presented. Included palmo-plantar ps psoriasis which is excluded from the PSP. No RCTs available. More studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/24890463
AH	**What treatments work best and are safe and cosmetically acceptable to use on psoriasis on certain parts of the body, including: scalp, genitals, face, ears, skin creases, nails, hands and feet?**	What is the most effective treatment for nail psoriasis?	116	n/a		
					Crowley, 2015 Limited evidence found and inconsistent results reporting. Comparison between treatment options virtually impossible based on the current literature. More studies needed together with uniform reporting and QOL measures specific for nail disease.	https://www.ncbi.nlm.nih.gov/pubmed/25471223
					De Vries, 2013 Cochrane. Some evidence presented but quality of trials considered relatively poor. Recommendation made for future trials to be conducted – rigorous in design with adequate reporting, using validated nail scores.	https://www.ncbi.nlm.nih.gov/pubmed/23440816
					Jales, 2015 Topical treatments for scalp disease compared with placebo. Some evidence presented. Recommendation for further work to explore maintenance of the outcomes reported and recurrence rates, also to investigate the most effective vehicle.	http://file.scirp.org/pdf/JCDSA_2015062913403448.pdf
					Schlager, 2016 Some evidence for topical treatments for scalp psoriasis presented. Future studies recommended (RCTs) to investigate how treatment impacts QOL and long-term outcomes.	https://www.ncbi.nlm.nih.gov/pubmed/26915340
AI	**What's the best way to treat guttate psoriasis?**	How do you best help guttate psoriasis?	20	n/a		
					No systematic reviews identified	**No systematic reviews identified**

AJ	**What are the long-term consequences of guttate psoriasis e.g. risk of developing chronic plaque psoriasis in later life?**	What is protecting the unaffected skin in plaque psoriasis?	12	n/a		
					No systematic reviews identified	**No systematic reviews identified**
AK	**What are the best over-the-counter skincare and hair care products that people with psoriasis can use?**	I have been advised I have Psoriasis on my scalp, all creams, lotions, gels have not worked, what else can I do.	16	n/a		
					No systematic reviews identified	**No systematic reviews identified**
AL	**What are the most comfortable fabrics to wear for people with psoriasis?**	Do particular fabrics cause more irritation?	4	n/a		
					No systematic reviews identified	**No systematic reviews identified**
AM	**What's the best way to change from one psoriasis treatment to another, such as from an oral therapy to a biological therapy, or from one biological therapy to another?**	When a treatment is stopped through lack of results, should there not be a maximum wait time before starting new treatment to prevent distressing return of psoriasis?	4	n/a		
					No systematic reviews identified	**No systematic reviews identified**
AN	**What medicines make psoriasis worse, or stop psoriasis treatments from working well?**	I was told Hydroxy is bad for Psoriasis	5	n/a		
					No systematic reviews identified	**No systematic reviews identified**
AO	**How do different oral or biological treatments for psoriasis compare in terms of how well they work and how safe they are in people of different ages and gender, and people who have different types and severities of psoriasis?**	What is the best treatment for psoriasis	141	n/a		
					de Carvalho, 2017 Evidence presented for the comparative efficacy of immunobiologic and small molecule inhibitor drugs. Only RCTs (double-blind) included. Limited data. Further work required to compare treatments, analyse data for newer treatments and assess long-term outcomes.	https://www.ncbi.nlm.nih.gov/pubmed/27838901

					Fink, 2017 Efficacy and safety of biological therapies (for a number of indications including psoriasis) in HIV-infected individuals. Firm conclusions not possible. Some evidence to suggest that individuals with well-controlled HIV should be included in future trials.	https://www.ncbi.nlm.nih.gov/pubmed/27733707
					Fleming, 2015 Limited data available (3 RCTS). Adalimumab, etanercept, ustekinumab treatments were associated with significant reductions in depressive symptoms. More evidence (RCTs) required including standardised psychiatric enquiry.	https://www.ncbi.nlm.nih.gov/pubmed/25490866
					Gomez-Garcia 2017 Short-term effectiveness of Il-23 treatments (biologic) considered. Direct and indirect comparison among biological treatment options. Data presented but further work required – especially with respect to long-term outcomes and direct / indirect comparison.	https://www.ncbi.nlm.nih.gov/pubmed/28893571
					Jabbar-Lopez, 2017 Some evidence presented on the relative efficacy and tolerability of biologic therapy. Lack of head-to-head RCTs. Lack of longer-term outcome data. Need to compare trail data with real-world (registry) safety and effectiveness data. Further work reqiored so that it is possible to discriminate between biologics in a manner which will inform clinical practice and decision making.	https://www.ncbi.nlm.nih.gov/pubmed/28457908
					Messori, 2015 Network meta-analysis to rank relative profile (effectiveness and safety) of the subcut biologic therapies. Evidence presented – but now data relatively old. Further work needed to aid selection between drug choices eg speed of onset of action, dosing and cost.	https://www.ncbi.nlm.nih.gov/pubmed/27747609
					Napolitano, 2016 Evidence for systemic, photo and biologic therapies reviewed but further prospective studies / registries needed	https://www.ncbi.nlm.nih.gov/pubmed/27085539
					Rungapiromnan, 2017 Limited evidence presented suggesting that licensed biologic therapies are not associated with MACEs during the short duration of randomised controlled periods in clinical trials. Well-designed observational studies involving large numbers of patients and longer durations of treatment exposure recommended.	https://www.ncbi.nlm.nih.gov/pubmed/27518205
					Sanchez 2017 Palmoplantar pustulosis excluded from PSP. Some evidence presented for treatment of palmoplantar psoriasis with biologics. Further work recommended particularly with respect to comparison of biologics with systemic therapy and phototherapy.	https://www.ncbi.nlm.nih.gov/pubmed/29143230
					Sanchez-Regana 2014 Spanish guidelines for the treatment of psoriasis with biological therapy in "difficult-to-treat" sites. Limited data available. Further evidence required. Newer agent now available. No paper download available.	https://www.ncbi.nlm.nih.gov/pubmed/24852726
					Signorovitch, 2015 Comparative efficacy data presented for (some) of the currently available biological therapies. Limited analysis was possible because there was only one head-to-head trial available. Further work required as newer agents now available and direct (rather than indirect) comparison should be made.	https://www.ncbi.nlm.nih.gov/pubmed/25288183
					Sorenson 2015 Evidence presented for safety of adalimumab, etanercept and ustekinumab (biological therapies). Further research recommended including long-term studies.	https://www.ncbi.nlm.nih.gov/pubmed/25886082
					Strand 2017 Review to explore the immunogenicity of biologic therapies (across multiple indications) and its impact on efficacy / safety. Highest rates of immunogenicity observed with infliximab and adalimumab. Further work needed – especially with respect to assay standardisation and cross-lab validation so that data outputs are directly comparable. Newer agents need evaluation. Real-world data needed.	https://www.ncbi.nlm.nih.gov/pubmed/28612180
					Van Vugt 2018 Evidence from pharmacogenetics studies on response to biologic therapy. Replication of findings in larger cohorts required. Large-scale hypothesis free searches for genetic biomarkers recommended.	https://www.ncbi.nlm.nih.gov/pubmed/28646581
AP	**Can treating psoriasis induce disease remission?**	Can we stop biologic treatment in those patients who have maintained clear skin for several years?	6	n/a		
					No systematic reviews identified	**No systematic reviews identified**
AQ	**When can treatments for psoriasis be stopped without losing disease control?**	If I stop taking methotrexate will the psoriasis come back even worse?	8	n/a		
					No systematic reviews identified	**No systematic reviews identified**

AR	**Which topical treatments for psoriasis work best and are the safest to use for all types and severities of psoriasis?**	Which topical tar therapy is most cost effective	78	n/a		
					Jales, 2015 Topical treatments for scalp disease compared with placebo. Some evidence presented. Recommendation for further work to explore maintenance of the outcomes reported and recurrence rates, also to investigate the most effective vehicle.	http://file.scirp.org/pdf/JCDSA_2015062913403448.pdf
					Kravvas, 2018 Some evidence for topical therapies but further randomised controlled trials needed	https://www.ncbi.nlm.nih.gov/pubmed/29493005
					Koo, 2017 Strategies for improved efficacy from topical therapy. More research needed to investigate this field and verify findings already reported. Large cohorts needed – multicentre, adherence factors, anatomical considerations.	https://www.ncbi.nlm.nih.gov/pubmed/28481664
					Maruani 2015 Multiple indications considered (including but not limited to psoriasis). Comparative effectiveness of topical treatments considered. More direct head-to head trials to compare clinical effectiveness of topical therapy for psoriasis are needed. Yan – Limited to review of combination topical Vit D / steroid for psoriasis. Further study needed – especially RCTs – especially with respect to standardised: treatment protocols, outcome measures, treatment duration and long-term follow up data.	https://www.ncbi.nlm.nih.gov/pubmed/25046338
					Schlager, 2016 Some evidence for topical treatments for scalp psoriasis presented. Future studies recommended (RCTs) to investigate how treatment impacts QOL and long-term outcomes.	https://www.ncbi.nlm.nih.gov/pubmed/26915340
					Svendsen 2017 Global use of topical agents. Lack of data and noncomparable studies made analysis challenging. Call for further studies (world-wide perspective) to provide evidence about use of topicals by psoriasis population.	https://www.ncbi.nlm.nih.gov/pubmed/27151546
AS	**How do topical treatments for psoriasis induce remission and what molecular pathways do they target?**	What makes coal tar so effective in psoriasis treatment?	3	n/a		
					No systematic reviews identified	**No systematic reviews identified**
AT	**How acceptable are topical treatments for patients with psoriasis? What formulation of topical treatments and moisturisers works best e.g. cream, foam, ointment, gel?**	What are the most patient friendly coal tar products to use?	5	n/a		
					Svendsen 2017 Global use of topical agents. Lack of data and noncomparable studies made analysis challenging. Call for further studies (world-wide perspective) to provide evidence about use of topicals by psoriasis population.	https://www.ncbi.nlm.nih.gov/pubmed/27151546
AU	**Do topical treatments for psoriasis made by different manufacturers work as well as each other?**	Is there proven bioequivalency between topical formulations from various manfucaturers?	13	n/a		
					Iversen 2017 Reformulations of topical treatments. Innovative reformulation can result in therapies which have improved clinical outcomes and patient reported outcomes. Changing the vehicle may result in significant patient and clinical benefit. Pharma sponsored work (Leo). More research required in this field.	https://www.ncbi.nlm.nih.gov/pubmed/28419600

AV	**What is the best way to apply topical treatments and emollients e.g. best sequence and timing?**	Which order should I put emollient and steroid on?	21	n/a		
					No systematic reviews identified	**No systematic reviews identified**
AW	**What light-based treatments work best and are safest to treat psoriasis? What is the best way to avoid side effects (including risk of skin cancer) associated with light treatment?**	Have many people developed skin cancer following UVB or PUVA treatment?	38	n/a		
					Almutawa 2013 Evidence that as a monotherapy, PUVA was more effective than narrow-band UVB (NB-UVB), and NB-UVB was more effective than broad-band UVB (BB-UVB) and bath PUVA in the treatment of adults with moderate to severe plaque-type psoriasis, based on clearance as an end point. Based on PASI-75, the results were similar except for BB-UVB, which showed a high mean PASI-75 (73 %) that was similar to PUVA, but with a wide confidence interval (CI; 18–98). The short-term adverse effects were mild as shown by the low rate of withdrawal due to adverse effects. Further studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/23572293
					Almutawa 2015 Evidence that topical PUVA and targeted UVB phototherapy are very effective in the treatment of localized psoriasis. Topical PUVA seems more effective than non-laser targeted UVB phototherapy. However, photodynamic therapy (PDT) has low efficacy and a high percentage of side effects in treating localized psoriasis. More studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/24283358
					Armstrong 2015 Among appropriately selected patients with psoriasis, carefully chosen treatment combinations (systemic and biologic) result in greater efficacy, while minimizing toxicity. More research needed.	https://www.ncbi.nlm.nih.gov/pubmed/25517130
					Chen 2013 Evidence that narrow-band UVB (NB-UVB) therapy significantly decreases the serum levels of VEGF and IL-8 in patients with psoriasis. VEGF and IL-8 levels correlated with disease status, indicating that they are sensitive biomarkers for evaluating the effectiveness of psoriasis therapy. More studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/24151011
					Choi, 2015 Evidence that the variability in clinical response and painful side effects have made topical ALA-PDT an unsuitable treatment option for chronic plaque psoriasis. Early clinical studies of other modalities such as topical hypericin and methylene blue, as well as systemic ALA and verteporfin, have shown that these photosensitizers are efficacious and much better tolerated than topical ALA. More research needed.	https://www.ncbi.nlm.nih.gov/pubmed/24881473
					Chen, 2016 Current evidence is heterogeneous and needs to be interpreted with caution. The clearance rate between oral PUVA and narrow band UVB (NB-UVB) is inconsistent among the included studies. Evidence regarding NB-UVB versus bath PUVA is also inconsistent. Retinoid (re)-NB-UVB and re-PUVA are similarly effective for treating people with chronic plaque psoriasis or guttate psoriasis. In practice, NB-UVB may be more convenient to use since exogenous photosensitiser is not required before phototherapy. NB-UVB is considered ineffective for palmoplantar psoriasis in clinical practice, and a small RCT did not detect a statistically significant difference between NB-UVB and topical PUVA for clearing PPP. NB-UVB seemed to be similar to selective BB-UVB for clearing chronic plaque psoriasis. Larger prospective studies are needed to confirm the long-term safety of NB-UVB.	https://www.ncbi.nlm.nih.gov/pubmed/26308328

					Fortina 2017 This article provides comprehensive recommendations for the systemic treatment of severe pediatric psoriasis based on evidence obtained from a systematic review of the literature and the consensus opinion of expert dermatologists and pediatricians. For each systemic treatment, the grade of recommendation (A, B, C) based on the treatment's approval by the European Medicines Agency for childhood psoriasis and the experts' opinions is discussed. The grade of recommendation for narrow-band-ultraviolet B phototherapy, cyclosporine, and retinoids is C, while that for methotrexate is C/B. The use of adalimumab, etanercept, and ustekinumab has a grade A recommendation. No conventional systemic treatments are approved for pediatric psoriasis. Adalimumab is approved by the European Medicines Agency as a first-line treatment for severe chronic plaque psoriasis in children (≥ 4 years old) and adolescents. Etanercept and ustekinumab are approved as second-line therapy in children ≥6 and ≥ 12 years, respectively. More studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/28836064
					Franken, 2016 Evidence that home-based phototherapy is as effective and safe as phototherapy in an outpatient setting. Patients are more satisfied with home-based phototherapy. More studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/29387594
					Ho 2017 This systematic review concluded that further characterisation of the effects of LED phototherapy to treat psoriasis in patients may increase adoption of LED-based modalities and provide clinicians and patients with new therapeutic options that balance safety, efficacy, and cost. More studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/28628685
					Koo, 2017 This article reviews five types of strategies for improved efficacy from topical agents beyond monotherapy. These strategies include proactive use, rotational therapy, sequential therapy, using topical agents to shorten the onset of therapeutic action for slower internal agents or phototherapy, and combination use for added efficacy. More research needed.	https://www.ncbi.nlm.nih.gov/pubmed/28481664
					Mysore 2016 Evidence that phototherapy is useful in psoriasis, either alone or in combination with drugs, even in resistant forms such as palmoplantar psoriasis. In view of expense and practical application, phototherapy use is limited to resistant lesions and localized disease - Level of evidence 2+, Grade of recommendation B). More studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/26728802
					Napolitano, 2016 This review concluded that more prospective studies and multicenter, international registries are needed to evaluate systemic therapies in pediatric psoriasis to develop international guidelines on paediatric psoriasis treatment.	https://www.ncbi.nlm.nih.gov/pubmed/27085539
					Pai, 2015 Evidence that both bath PUVA and bathing suit PUVA are very effective and safe treatments for generalized stable plaque psoriasis (strength of recommendation, A). Soak PUVA is very effective in the treatment of palmoplantar psoriasis (strength of recommendation, A). More studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/26515832
					Thérénè, 2018 Evidence that anti-IL-17, JAK inhibitors, adalimumab and apremilast are effective in reducing pruritus in psoriasis with variable effect size; systemic treatments, including UVB phototherapy, improve pruritus in psoriasis. More studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/28887107
AX	**What causes psoriatic arthritis and what are the risk factors for developing it?**	Why is so little known about the reasons for psoriatic arthritis?	10	n/a		
					NICE Clinical guideline [CG153] The recommendations for further research from this guideline have been incorporated into the indicative questions for the PsPSP.	https://www.nice.org.uk/guidance/cg153/evidence
					Rouzaud, 2014 More work needed to define which psoriasis clinical features indicate an increased risk of PsA. The presence of scalp, nail and intergluteal involvement appear to be important warning signs for dermatologists that their psoriasis patients may be at increased risk of PsA. Severity and extent of psoriasis may also be significant risk factors for PsA.	https://www.ncbi.nlm.nih.gov/pubmed/24985559
					Thrastardottir, 2018 The data from this study were inconsistent and further studies are needed to verify or refute the purported association between infection and the risk of developing PsA – in particular laryngeal infections and infections caused by streptococci.	https://www.ncbi.nlm.nih.gov/pubmed/29124396

AY	**What is the best way to diagnose psoriatic arthritis? Can we identify which patients with psoriatic arthritis are at risk of having severe destructive disease?**	How to get a quick, definitive diagnosis of psoriatic arthritis when eventually getting through to seeing a specialist?	15	n/a		
					Richard 2014 This systematic literature research and meta-analysis was designed to marshall the evidence base for selected clinically relevant questions to help dermatologists i) identify patients at risk of PsA, ii) to diagnose PsA in collaboration with rheumatologists and iii) manage PsA. There was no high-quality evidence to support the "expert" recommendations regarding PsA screening. However, treatment options for PsA were supported by strong evidence. Further studies are required to provide an adequate evidence base for risk profiling, screening and management of PsA (by dermatologists in partnership with rheumatologists).	https://www.ncbi.nlm.nih.gov/pubmed/24985557
AZ	**What is the best way to measure treatment success in psoriatic arthritis?**	what should treat to target look like in PsA?	7	n/a		
					Boehncke Evidence that of the numerous disease-modifying antirheumatic drugs available for treating PsA — both nonbiologic and biologic, with different modes of action —all of them also exhibit at least some efficacy as therapy for psoriasis. However, although a wealth of literature exists for treating psoriasis and a substantial body of evidence exists for treating PsA, few studies assess the efficacy of a systemic therapy initiated with the intention of simultaneously controlling PsA and psoriasis. Further studies needed.	https://www.ncbi.nlm.nih.gov/pubmed/25362715
					Richard 2014 This systematic literature research and meta-analysis was designed to marshall the evidence base for selected clinically relevant questions to help dermatologists i) identify patients at risk of PsA, ii) to diagnose PsA in collaboration with rheumatologists and iii) manage PsA. There was no high-quality evidence to support the "expert" recommendations regarding PsA screening. However, treatment options for PsA were supported by strong evidence. Further studies are required to provide an adequate evidence base for risk profiling, screening and management of PsA (by dermatologists in partnership with rheumatologists).	https://www.ncbi.nlm.nih.gov/pubmed/24985557
BA	**In people with psoriasis, what are the differences between affected and unaffected skin?**	Is the rest of my skin normal?	3	n/a		
					No systematic reviews identified	**No systematic reviews identified**
BB	**Does having psoriasis (or active psoriasis, with visible plaques) hamper recovery from, or outcome of, surgery, or increase the risk of an infection after surgery?**	To what degree do infections arise through broken skin? Perhaps septicaemia?	1	n/a		
					No systematic reviews identified	**No systematic reviews identified**
BC	**Should people with psoriasis stop their psoriasis treatment (oral or biological therapy) before they have surgery?**	What is the evidence for stopping (or not) biologic therapy for major surgery?	1	n/a		
					No systematic reviews identified	**No systematic reviews identified**