Appendix R: High-priority research recommendations

The Guideline Development Group has made the following recommendations for research, based on its review of evidence, to improve NICE guidance and patient care in the future.

R.1 Assessment of disease severity and impact

What validated tools can be used in people (including children and young people) to assess disease severity and impact in non-specialist and specialist healthcare settings to facilitate assessment, appropriate referral, treatment planning and measurement of outcomes?

Why this is important:

Assessment of disease severity and impact is fundamental to delivering high-quality health care and measuring outcomes. The evidence review indicates that the existing tools have important limitations, and have not been validated in relevant healthcare settings or in children. Future research should ensure that tools are developed that capture information on site of involvement as well as extent, and the impact of previous treatments. Tools that can be used by patients (as well as healthcare professionals) to assess disease severity and that encompass new technologies should be evaluated to facilitate, when appropriate, modern healthcare delivery models (for example, remote monitoring of disease activity).

Criteria for selecting high-priority research recommendations:

Criterion	Explanation
Importance to patients or the population	Assessment of disease severity and impact is fundamental to delivering high-quality health care and measuring outcomes
Relevance to NICE guidance	Results would inform recommendations for assessment methods in future updates of the guideline
Relevance to the NHS	Highly relevant to the NHS to ensure appropriate referral, treatment planning and effective targeting of resources
Study design	The study should include a sufficient sample size. Tools that capture information on site of involvement as well as extent, and the impact of previous treatments are of particular interest. In addition, tools that can be used by patients (as well as healthcare professionals) to assess disease severity and that encompass new technologies should be evaluated to facilitate, when appropriate, modern healthcare delivery models (for example, remote monitoring of disease activity).
National priorities	No
Current evidence base	No evidence was found for the use of the tools in children, in primary care settings or specifically for different psoriasis phenotypes. The evidence review indicates that the existing tools have important limitations, and have not been validated in relevant healthcare settings

Equality	Research should include children, young people and older people
Feasibility	No known feasibility issues
Other comments	None

1.1 Identification of comorbidities

Does treating psoriasis modify the risk of cardiovascular disease and are there any clinical (for example demographic or phenotypic) or laboratory (for example genetic or immune) biomarkers that identify those most likely to benefit?

Why this is important:

Psoriasis is a common disease, and the evidence review indicates that in all people affected there is a clinically relevant increase in cardiovascular disease incidence. If treatment of the psoriasis also improved cardiovascular morbidity or mortality, this would be of major importance to patients, and also justify early and/or more aggressive treatment of psoriasis.

Criteria for selecting high-priority research recommendations:

Criterion	Explanation
Importance to patients or the population	If treatment of the psoriasis also improved cardiovascular morbidity or mortality, this would be of major importance to patients, and also justify early and/or more aggressive treatment of psoriasis.
Relevance to NICE guidance	A positive impact of psoriasis treatment on cardiovascular morbidity or mortality may influence future recommendations concerning the timing of initiation and escalation of treatment options.
Relevance to the NHS	If earlier or more aggressive treatment of psoriasis reduced the incidence of cardiovascular disease in this population this would be important for reducing NHS expenditure by reducing the number of people with psoriasis developing serious comorbidities.
Study design	A large, long-term prospective cohort study comparing people with psoriasis not receiving any treatment with those treated with topical therapy, phototherapy, systemic non-biological and/or biological interventions. Multivariable regression analysis accounting for time and controlling for all relevant confounders should be performed. It would be important to a priori specify subgroup analysis for those with mild and severe psoriasis, if possible using psoriasis severity assessment tools rather than surrogate markers of severity.
National priorities	No
Current evidence base	The GDG were not aware of any suitable studies addressing this question.
Equality	This research question has no particular equality issues.
Feasibility	This study is likely to require multi-centre co-operation across different health

	care settings.
Other comments	None

1.2 Methotrexate and risk of hepatotoxicity

What is the impact of methotrexate compared with other approaches to care (for example other systemic non-biological or biological treatments) on risk of significant liver disease in people with psoriasis and do risk factors such as obesity, alcohol use or diabetes alter this risk?

Why this is important:

The evidence review indicates that people with psoriasis may be at risk of liver disease, and there is great uncertainty about the contributing role of methotrexate. Clinician and patient concerns about this side effect are a common cause of treatment discontinuation. However, existing studies are poorly controlled for important confounders and many are very old. Methotrexate is a low cost intervention that is effective in an important proportion of patients. Research in this area will properly delineate the size of risk and how to minimise it. Future research should be adequately powered to detect clinically relevant liver disease, use relevant tools to do so, and properly control for relevant confounders.

Criteria for selecting high-priority research recommendations:

Criterion	Explanation
Importance to patients or the population	Methotrexate is a commonly prescribed drug in psoriasis and psoriatic arthritis. It is also used as co-therapy with TNF-antagonists to improve efficacy. People with psoriasis may be at risk of liver disease, and there is great uncertainty about the contributing role of methotrexate.
Relevance to NICE guidance	Outcomes will inform future NICE guidance. At present there may be a reluctance in clinical practice to use methotrexate in people with psoriasis who have risk factors and/or reluctance to continue methotrexate with high cumulative doses (>3g). However, there is not robust evidence to underpin this view.
Relevance to the NHS	The insidious development of liver fibrosis and ultimately cirrhosis is of great clinical concern given this may be irreversible, and of very significant impact. Research in this area will properly delineate the size of risk and how to minimise it.
Study design	Large, prospective cohort study of people with psoriasis receiving methotrexate compared with those receiving other interventions in a sample group matched for disease severity. Research in this area would need to involve large numbers of patients given that the absolute risk of liver fibrosis may be low, control properly for confounders (obesity, diabetes, alcohol), and use relevant tools (including standardised histology grading scales) and validated outcomes. Follow up should be long term. Details should include whether liver pathology was present prior to MTX administration.
National priorities	Nil

Current evidence base	Existing studies are small, inadequately controlled for important confounders, report insufficient data and many are very old.
Equality	This research recommendation will include all relevant groups
Feasibility	Long term follow up may be difficult
Other comments	Nil

1.3 Biological therapy

In people with psoriasis, does early intervention to achieve and maintain complete disease remission alter the long-term prognosis in terms of psoriasis severity, comorbidities (including psoriatic arthritis), or treatment-related adverse effects, and are there any clinical (for example demographic or phenotypic) or laboratory (for example genetic or immune) biomarkers that can be used to identify those most likely to benefit from this treatment approach?

Why this is important:

At present the treatment pathway for people with psoriasis follows clinical need as no studies have been conducted to evaluate whether early intervention alters prognosis. Consequently, patients with more severe disease sequence through all therapies in the treatment pathway, with a proportion requiring high-cost biological interventions to maintain disease control. The evidence indicates that there are very few treatment options for people with chronic disease, all of them are associated with side effects, many are co-dependent (for example escalated risk of skin cancer in people treated with the phototherapy and ciclosporin sequence), and loss of response to biological therapies is a significant clinical issue. If early intervention was shown to alter the prognosis, particularly if there were markers that could stratify those likely to benefit, this would be of major importance to patients, and likely to deliver much more cost-effective treatment strategies.

Criteria for selecting high-priority research recommendations:

Criterion	Explanation
Importance to patients or the population	The current treatment pathway for people with psoriasis requires those with more severe disease to sequence through all therapies in the treatment pathway. The findings of this study could mean that people with more severe disease are able to receive more appropriate interventions, and so achieve satisfactory disease control, sooner with exposure to fewer interventions. This could improve prognosis, quality of life and adverse event risk.
Relevance to NICE guidance	Future NICE guidance may recommend more intensive and earlier up stream treatment for those people with psoriasis.
Relevance to the NHS	Potential for delivering more cost effective treatment strategies.
Study design	Prospective cohort study with long-term follow-up comparing early intervention with current standard care. Multivariable regression analysis accounting for time and controlling for all relevant confounders should be performed. It would be important to a priori specify subgroup analysis for those with mild and severe psoriasis, if possible using psoriasis severity assessment tools rather than surrogate markers of severity.

National priorities	Improved quality of life for those living with psoriasis which may reduce work loss. Potentially this may reduce both chronic worklessness due to psoriasis and also short term work absence due to flares.
Current evidence base	Extremely limited
Equality	This research question has no particular equality issues.
Feasibility	This research should probably take place in a specialist environment (secondary care)
Other comments	None

1.4 Self-management

Do structured psoriasis-focussed educational programmes improve patient confidence, wellbeing and disease control compared with standard care?

Why this is important:

Virtually all patients self-manage their condition to a greater or lesser extent and this involves complex topical applications as well as systemic therapies to be used over many years in response to fluctuating disease severity. The evidence indicates that in contrast to many chronic disorders, there are no validated programmes to help patients achieve effective self-management. Establishing a focussed educational programme that effectively improves outcomes for patients would be of clinical benefit and likely deliver healthcare savings.

Criteria for selecting high-priority research recommendations:

Criterion	Explanation
Importance to patients or the population	Results would inform national recommendations regarding specific factors that are important for self management. All patients living with a long-term condition self-manage to a greater or lesser degree. Simply telling the person why or showing them how may not be enough to ensure it happens, information provision alone does not change behaviour. A well-designed programme will allow those living with psoriasis to make the most appropriate use of treatment options and fully engage with their treatment plan.
Relevance to NICE guidance	Future NICE guidance would be able to address self management recommendations for psoriasis.
Relevance to the NHS	Access to self-management support may reduce the need for service use. Clinically the degree of effective self-management in order to optimise clinical outcomes is of interest.
Study design	Adequately powered, cluster randomised study with moderate to long term follow up
National priorities	Self care and self management are central to UK health policy on managing long-term conditions
Current evidence base	There is a paucity of evidence, only four RCTs were found all of which had methodological limitations. There was no direct evidence for concordance with treatment, distress, anxiety, depression or stress. No studies were available that

	assessed self-management exclusively in children with psoriasis.
Equality	Children, younger people and older people should be included in future research on self management
Feasibility	Teasing out the specific factors that are important for self management may be difficult. Education, information provision and self management concepts all impact upon behaviour changes. Distilling out those factors that successfully contribute to helping people self manage their condition would need careful planning.
Other comments	Self-management education programmes are distinct from patient education or skills training, in that they are designed to encourage people with long-term conditions to take a more active part in the management of their own condition.