Executive summary

Background
It is estimated that between 2 and 4% of the population have psoriasis. Psoriasis primarily affects the skin, but can also be associated with metabolic syndrome and an increased risk of excess weight, diabetes and cardiovascular disease. Joint problems (psoriatic arthritis) are a common complication. Psoriasis is a chronic condition, and people with psoriasis may need treatment over extended periods of their lives.

Objective
The purpose of this review is to evaluate effects of treatments for moderate to severe psoriasis, and to highlight health economic and ethical issues related to treatment.

Method
The report systematically reviews randomised controlled trials (RCT) which investigate the effects of phototherapies, photochemotherapies and systemic treatments on psoriatic symptoms and health related quality of life in people with moderate to severe psoriasis. In addition, we present cost analyses of phototherapies, photochemotherapies and conventional, synthetic systemic, treatments, and discuss ethical issues related to the treatment of psoriasis.

Results
The review is based on 77 RCTs. One of the included studies investigated effects of phototherapy, 17 of conventional synthetic drugs and 47 of biological drugs.

The results show that biological drugs approved for psoriasis are effective and that a high proportion of those treated achieve a clinically important improvement. Health related quality of life also improves, but for some substances, the evidence of a clinically relevant effect is weaker. Two conventional synthetic drugs, methotrexate and apremilast, are effective, but fewer of those treated reach a clinically important improvement.

Few studies compared active treatments, but available comparisons between etanercept (the biological substance first approved for psoriasis) and adalimumab, ixekizumab, sekukinumab or ustekinumab show more persons improve after treatment with the latter substances. A comparison between sekukinumab and ustekinumab shows more persons improve with sekukinumab. Comparisons of effects on quality of life show more improvement with ixekizumab than etanercept, but are uncertain for other comparisons.

Due to a lack of studies of adequate design and quality we were unable to evaluate the effects of phototherapy, photochemotherapy and the synthetic drugs acitretin, cyclosporine and fumaric acids on psoriasis.

Health economic and ethical issues
Analyses show that the yearly cost of treating one person differs significantly between different phototherapies and different conventional, synthetic drugs. Due to non-disclosure agreements, which affect the real, and to us unknown, prices healthcare providers...
pay, we chose not to evaluate the costs of biological substances. These comparatively costly drugs are currently only subsidized for persons who do not improve adequately when treated with other drugs.

A person with moderate to severe psoriasis needs access to effective treatment. Left untreated the condition can cause suffering and contribute to a higher risk for other long-term health issues. The challenge for health care providers is to offer effective treatment to all persons with psoriasis, while limiting access to more expensive treatment options to those who do not adequately respond to lower cost therapies.

**Knowledge gaps**

Most of the included studies compared different treatments with placebo. For some treatments we were unable to find any head-to-head trials comparing active treatments. More head-to-head trials are needed to determine whether one treatment performs better than another. There is also a need for long-term studies with a controlled design, as they may mirror clinical praxis better.

Results describing health related quality of life, the outcome that best describes experiences of treatment from the patient’s perspective, were often less reliable than outcomes describing the effect on psoriasis. A greater focus on quality of life in efficacy studies in future could increase their clinical value.

In addition, there is a need of more studies of effects and risks regarding the treatment of children with moderate to severe psoriasis.