

**JLA uncertainty:****How effective is UVB light when combined with creams / ointments?****JLA uncertainty:****How effective is UVB light when combined with creams / ointments? (Ranked 4<sup>th</sup>)*****What is the research question or clinical uncertainty that you think needs more research?***

Is narrow band ultra-violet light therapy (NB-UVB) combined with topical corticosteroid better than topical corticosteroid alone for the treatment of vitiligo?

***What is the health care intervention or technology\* for which the research is needed?***

\*The definition of "health care intervention or technology" is very broad and can range from interventions to promote health and prevent disease, the use of a diagnostic test or questionnaire, drug treatments, devices, non-drug interventions such as physical or talking therapies, surgical techniques, settings of care and screening.

**Intervention 1:**

NB-UVB combined with topical corticosteroid (either hospital-based UVB or hand held NB-UVB for home-use), although our recommendation would be for hand-held NB-UVB.

Narrowband UVB is now the most common form of phototherapy used to treat skin diseases. Narrow-band refers to a specific wavelength of ultraviolet (UV) radiation, 311 to 312 nm. Patients attend the hospital usually 3 times weekly. The patient is placed in a specially designed cabinet containing fluorescent light tubes. The patient stands in the centre of the cabinet, undressed except for underwear, and wears protective goggles. Usually the whole body is exposed to the UVB for a short time (seconds to minutes). NB-UVB is also used in the treatment of many other skin conditions including psoriasis and eczema. Hospital NB-UVB is suitable for extensive, generalised vitiligo i.e. large lesions.

The hand held NB-UVB unit is a portable and light weight NB-UVB device that is slightly larger than a usual hairbrush. Some of these devices also have an integrated timer for easy monitoring of the phototherapy session time. The hand held device can be held above any small area of the skin and spacers are provided in order to standardise the distance from the skin. Hand held NB-UVB units are suitable for small lesions making phototherapy available for patients with limited disease, and for patients who find it difficult to attend a phototherapy clinic several times a week. Some dermatology departments in the UK now supply home UVB units for use by patients with eczema and psoriasis (personal communication). Early reports suggest that these are well tolerated and effective<sup>1,2</sup>.

**Intervention 2:**

Topical corticosteroid (moderate or potent)

Corticosteroid medicines are mainly used for their effect in controlling inflammation, and topical corticosteroids are applied to the skin for the localised treatment of various inflammatory skin disorders.

Topical corticosteroids are easily applicable for self administration at home.

Like all topical treatments, corticosteroids are usually applicable to limited rather than generalised disease i.e. small size lesions or small number of lesions.

Although the exact pathophysiology of the disease is not clear, histological reports of early stages of vitiligo showed increased inflammatory infiltrates in the vitiliginous skin, which are possibly responsible for the disappearance of melanocytes (pigment cells). Therefore by reducing the inflammation in the affected areas could possibly stop the spreading of the disease and repigment the vitiliginous skin.<sup>3</sup>

We would recommend a trial design that compares topical corticosteroids with hand-held NB-UVB on the grounds that both interventions are appropriate for the treatment of localised

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disease at high impact sites (such as the hands and face), and can be used at home. Blinding of the trial would also be easier as it would be possible to provide placebo hand-held units (something that would be difficult to achieve in multiple hospital settings), and treatment could be targeted at specific sites (and so blinding would not be compromised by tanning of the unaffected sites).

We would recommend a factorial trial as follows:

- Group A: Topical corticosteroid + placebo UVB
- Group B: NB-UVB (hand-held) + placebo topical
- Group C: Topical corticosteroid + NB-UVB
- Group D: Placebo topical corticosteroid + placebo NB-UVB

### ***Please describe the patient group or people that are likely to be offered this health care intervention.***

Patients with localised vitiligo (both segmental and non segmental), who are suitable for NB-UVB therapy.

### ***Briefly explain why the evidence produced by this research will be important to patients, clinicians or the wider NHS.***

Vitiligo is an autoimmune disease that results in white patches on the skin. This can be particularly distressing for people with darker skin types, especially if the vitiligo occurs on highly visible sites such as the face and hands.

Vitiligo affects around 1% of the world's population. The cosmetic disfigurement of this seemingly inconsequential skin disease has a major impact on the quality of life of patients and negatively affects sexual relationships<sup>4</sup>. Many people are frightened and embarrassed by vitiligo. They experience discrimination from others and believe that they do not receive adequate support from their doctors<sup>5,6</sup>. Patients with vitiligo receive limited or ambivalent support from friends and family, and experience a number of psychological problems such as shame, depression and anxiety, which leads to low self-esteem and social isolation<sup>7</sup>. Self image of vitiligo patients is also considerably decreased<sup>8</sup>.

Current clinical guidelines for the diagnosis and management of vitiligo recommend NB-UVB, tacrolimus and topical steroids<sup>9</sup>. However, the only product that is currently licensed for use in the treatment of vitiligo is cosmetic camouflage, and the evidence base for this and other treatments is currently poor<sup>10</sup>. This makes it difficult to reach firm recommendations regarding clinical practice.

Vitiligo patients are treated in both primary and secondary care. This is a chronic condition that requires long-term treatment. Patients can experience periods of rapid spread, and periods when the vitiligo is relatively stable. In order to induce remission, treatment is often given over periods of several months. In the UK, NB-UVB is almost exclusively available in secondary care, suitable for widespread vitiligo only and requires regular visits to the hospital (typically 3-4 times per week for up to six months).

Should a hand-held device that can be used at home prove to be effective for the treatment of localised vitiligo, this could be an important addition to the treatment options available to patients with localised disease such as on the face, hands. Also, it could potentially improve treatment adherence and the quality of life of vitiligo patients by offering them an effective treatment option in the comfort of their own homes. Home NB-UVB devices (sun beds, hand held units) are now being used for the treatment of other skin conditions (e.g. psoriasis) with good effect<sup>2,11</sup> and initial efforts have been made to evaluate the effectiveness of home NB-

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UVB in vitiligo patients<sup>1</sup>. Feedback from patients (via the Vitiligo Society) and healthcare professionals from other European countries also suggests that patients with vitiligo are currently buying these hand held NB-UVB units for home use, and are using them in an unsupervised way.

The topic of vitiligo was identified as a priority topic as part of an NIHR programme grant award looking at “Setting Priorities and Reducing Uncertainties for people with Skin Disease”. One aspect of this work has been to conduct a formal Priority Setting Partnership in collaboration with the James Lind Alliance and the Vitiligo Society. The top 10 treatment uncertainties identified through this process have all been submitted to DUETs and form the basis of this trial suggestion. This particular topic suggestion was ranked 4<sup>th</sup> in the list of treatment uncertainties, and was considered to be important by both healthcare professionals and patients.

***Please provide any information you can on the existing evidence for this health care intervention or technology and include here any other comments you would like to make.***

A Cochrane systematic review looking at interventions for the treatment of vitiligo has recently been updated<sup>10</sup>. This review identified 57 trials covering 68 different treatment options. However, the quality of the trials included in the review was generally poor, which makes it difficult to make clinical recommendations based in the current evidence base.

NB-UVB is considered to be more effective light therapy for the treatment of vitiligo compared to PUVA.<sup>12</sup>

Twelve trials compared NB-UVB as monotherapy to combination of NB-UVB with other agents<sup>10</sup>. The Cochrane systematic review concluded that the light combination interventions were superior to monotherapies. Some form of light therapy is probably needed in order to induce the development and proliferation of the pigment cells, hence repigment the skin. However larger studies are needed in order to provide stronger evidence for the many combination interventions that have shown promise in treating vitiligo.<sup>10</sup>

No RCTs to date have looked at hand held home NB-UVB devices for vitiligo.

In total 10 studies were evaluated on the effectiveness of topical corticosteroids as monotherapy as well as in combination with other interventions. There is moderate evidence for the use of topical corticosteroids in the short term, but side effects (such as thinning of the skin) are a concern when used long-term. Only one study has assessed the effects of topical steroids in combination with NB-UVB<sup>13</sup>. This trial reported no difference in the effectiveness of clobetasol monotherapy compared to combination of clobetasol and NB-UVB therapy; however, with only 20 participants, the trial was under powered to show an effect. The dropout rate for this study was 20% (inconvenience of the hospital visits was cited as the main reason for this)<sup>13</sup>. Another study on combination of excimer laser (UVB) therapy and topical hydrocortisone, in 84 patients, showed that the combination therapy was twice as likely to repigment vitiliginous skin compared to laser monotherapy alone.<sup>14</sup>

***What would be the important outcomes of this intervention for the patient or NHS? Where known, please state normal clinical practice in this field.***

The updated Cochrane systematic review reported wide variety in the outcome measures used. No two studies used exactly the same method of scoring repigmentation, and only a few studies assessed cessation of spread or improvement of quality of life.

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International consensus over the most appropriate outcome measures to use in vitiligo clinical trials is lacking. We are currently conducting feasibility work to establish the outcomes that are most important to patients in order to guide the choice of outcomes to be used. Results of this work should be available in early 2011.

Finally, there is a need for trials to look at “establishment of remission” and “maintenance of remission / long-term control”<sup>10</sup> and therefore we would recommend that these outcomes to be considered alongside repigmentation, cessation of spreading and quality of life.

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