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[Intervention Review]

Interventions for vitiligo

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ABSTRACT

Background

Vitiligo is a chronic skin disorder characterised by patchy loss of skin colour. Some people experience itching before the appearance of a new patch. It affects people of any age or ethnicity, more than half of whom develop it before the age of 20 years. There are two main types: generalised vitiligo, the common symmetrical form, and segmental, affecting only one side of the body. Around 1% of the world's population has vitiligo, a disease causing white patches on the skin. Several treatments are available. Some can restore pigment but none can cure the disease.

Objectives

To assess the effects of all therapeutic interventions used in the management of vitiligo.

Search methods

We updated our searches of the following databases to October 2013: the Cochrane Skin Group Specialised Register, CENTRAL in *The Cochrane Library* (2013, Issue 10), MEDLINE, Embase, AMED, PsycINFO, CINAHL and LILACS. We also searched five trials databases, and checked the reference lists of included studies for further references to relevant randomised controlled trials (RCTs).

Selection criteria

Randomised controlled trials (RCTs) assessing the effects of treatments for vitiligo.

Data collection and analysis

At least two review authors independently assessed study eligibility and methodological quality, and extracted data.

Main results

This update of the 2010 review includes 96 studies, 57 from the previous update and 39 new studies, totalling 4512 participants. Most of the studies, covering a wide range of interventions, had fewer than 50 participants. All of the studies assessed repigmentation, however only five reported on all of our three primary outcomes which were quality of life, > 75% repigmentation and adverse effects. Of our secondary outcomes, six studies measured cessation of spread but none assessed long-term permanence of repigmentation resulting from treatment at two years follow-up.

Most of the studies assessed combination therapies which generally reported better results. New interventions include seven new surgical interventions.

We analysed the data from 25 studies which assessed our primary outcomes. We used the effect measures risk ratio (RR), and odds ratio (OR) with their 95% confidence intervals (CI) and where N is the number of participants in the study.

We were only able to analyse one of nine studies assessing quality of life and this showed no statistically significant improvement between the comparators.

Nine analyses from eight studies reported >75% repigmentation. In the following studies the repigmentation was better in the combination therapy group: calcipotriol plus PUVA (psoralen with UVA light) versus PUVA (paired OR 4.25, 95% CI 1.43 to 12.64, one study, N = 27); hydrocortisone-17-butyrate plus excimer laser versus excimer laser alone (RR 2.57, 95% CI 1.20 to 5.50, one study, N = 84); oral minipulse of prednisolone (OMP) plus NB-UVB (narrowband UVB) versus OMP alone (RR 7.41, 95% CI 1.03 to 53.26, one study, N = 47); azathioprine with PUVA versus PUVA alone (RR 17.77, 95% CI 1.08 to 291.82, one study, N = 58) and 8-Methoxypsoralen (8-MOP) plus sunlight versus psoralen (RR 2.50, 95% CI 1.06 to 5.91, one study, N = 168). In these three studies *ginkgo biloba* was better than placebo (RR 4.40, 95% CI 1.08 to 17.95, one study, N = 47); clobetasol propionate was better than PUVAsol (PUVA with sunlight) (RR 4.70, 95% CI 1.14 to 19.39, one study, N = 45); split skin grafts with PUVAsol was better than minipunch grafts with PUVAsol (RR 1.89, 95% CI 1.25 to 2.85, one study, N = 64).

We performed one meta-analysis of three studies, in which we found a non-significant 60% increase in the proportion of participants achieving >75% repigmentation in favour of NB-UVB compared to PUVA (RR 1.60, 95% CI 0.74 to 3.45; I^2 = 0%).

Studies assessing topical preparations, in particular topical corticosteroids, reported most adverse effects. However, in combination studies it was difficult to ascertain which treatment caused these effects. We performed two analyses from a pooled analysis of three studies on adverse effects. Where NB-UVB was compared to PUVA, the NB-UVB group reported less observations of nausea in three studies (RR 0.13, 95% CI 0.02 to 0.69; I^2 = 0% three studies, N = 156) and erythema in two studies (RR 0.73, 95% CI 0.55 to 0.98; I^2 = 0%, two studies, N = 106), but not itching in two studies (RR 0.57, 95% CI 0.20 to 1.60; I^2 = 0%, two studies, N = 106).

Very few studies only assessed children or included segmental vitiligo. We found one study of psychological interventions but we could not include the outcomes in our statistical analyses. We found no studies evaluating micropigmentation, depigmentation, or cosmetic camouflage.

Authors' conclusions

This review has found some evidence from individual studies to support existing therapies for vitiligo, but the usefulness of the findings is limited by the different designs and outcome measurements and lack of quality of life measures. There is a need for follow-up studies to assess permanence of repigmentation as well as high-quality randomised trials using standardised measures and which also address quality of life.

PLAIN LANGUAGE SUMMARY

Treatments for vitiligo

Background

Vitiligo is a chronic skin disorder characterised by patchy loss of skin colour. Some people experience itching before the appearance of a new patch. It affects people of any age or ethnicity, more than half of whom develop it before the age of 20 years. There are two main types: generalised vitiligo, the common symmetrical form, and segmental, affecting only one side of the body. Recent genetic research suggests that generalised vitiligo is, at least in part, an autoimmune condition which destroys melanocytes (pigment cells). Although our understanding of vitiligo has increased, its causes are still poorly understood. Several treatments are available. Some can restore pigment but none can cure it or prevent its spread or recurrence. Vitiligo patches can have a major psychosocial impact, especially for people with dark or tanned skin or when the face or hands are affected. People with vitiligo can be stigmatised, often experiencing low self-esteem and a lack of self-confidence. Children with vitiligo may be teased and bullied at school. Despite this, we found only one study assessing psychological therapy for vitiligo.

Review question

What treatments work best to help manage vitiligo?

Study characteristics

In this update search we found 39 new randomised controlled trials which, added to the 57 studies included previously, makes a total of 96 studies with 4512 participants.

Key results

Twenty-one (21/39, 54%) of the new studies assessed new treatments, most of which involved the use of light. Narrowband UVB (NB-UVB) light was used in 35/96 (36% of all included studies), either alone or in combination with other therapies and achieved the best results. There were 18 surgical studies and 31 studies compared active treatment versus placebo.

Half of the studies lasted longer than six months. Most of them 69/96 (72%) had fewer than 50 participants. Only seven studies assessed children and one study only recruited men.

The majority of studies (53/96, 55%), most of which were of combination treatments with light, assessed more than 75% repigmentation. Eight studies reported a statistically significant result for this outcome, including the following four results: topical corticosteroids were better than PUVAsol (psoralen with sunlight), hydrocortisone plus laser light was better than laser light alone, *ginkgo biloba* was better than placebo and oral minipulse of prednisolone (OMP) plus NB-UVB was better than OMP alone. None of the studies reported the long-term benefit of the treatment i.e. two years' sustained repigmentation. The maximum follow-up time, reported in only one study, was one year post-treatment.

Only 9/96 (9%) reported the quality of life of participants, but the majority of all studies (65/96, 68%) reported adverse effects, mainly for topical treatments, some of which caused itching, redness, skin thinning, telangiectasia and atrophy. Neither mometasone furoate nor hydrocortisone produced adverse effects. Some NB-UVB studies reported phototoxic reaction and Koebnerisation whereas some PUVA (psoralen with artificial light UVA as a light source) studies caused dizziness and nausea.

Six studies reported cessation of spread of vitiligo, one of which showed that *ginkgo biloba* was more than twice as likely to stop vitiligo spreading than placebo.

This review has highlighted the recent surge in vitiligo research providing insights into its causes. The majority of the studies reporting successful repigmentation were combinations of various interventions with light, indicating this is an effective, though not necessarily permanent, treatment for generalised vitiligo.

In view of the fact that vitiligo has no cure, providing ways of coping with it could be of benefit to patients and should be part of standard care. Better designed studies, consensus on how to measure treatment success, more studies involving children and studies assessing psychological interventions, are needed.

Quality of the evidence

Since the last update (2010), the design and reporting of vitiligo trials have not greatly improved. Only five studies met the criteria for a well-designed trial. Poor design, the number and complexity of the treatments and the fact that many of the studies assessed individual vitiligo patches in the same participant, made comparison of the studies difficult. Consequently, we could only perform one meta-analysis of three studies comparing NB-UVB with PUVA which showed that NB-UVB has fewer side effects and is marginally better than PUVA.

BACKGROUND

Unfamiliar terms are listed in the glossary in Table 1.

Description of the condition

Definition

Vitiligo results in a loss of functional melanocytes (pigment producing cells) and has been shown in genetic studies to be associated with other autoimmune diseases. It is characterised by the appearance of white patches on the skin sometimes accompanied by whitening of the hair. It can also have a major psychosocial impact due to the unsightly appearance, especially on dark or tanned skin and on exposed areas of the body, such as the face and hands. Although vitiligo may develop at any age, it is rarely present at birth when it may be confused with piebaldism or nevus depigmentosus (inherited localised skin pigment loss). Most people develop the disease before the age of 20 years (Lerner 1971; Picardo 2010)

Vitiligo is normally asymptomatic, although around 20% of patients report itching at the onset of a new lesion (Ezzedine 2011a). Recent findings suggest that various local triggers alert the skin's innate immune system creating a silent micro-inflammatory process, still poorly understood (Taïeb 2012). Vitiligo can appear anywhere on the skin but is commonly seen on areas around the orifices, the genitals, face and hands. Friction may also trigger vitiligo on areas such as the neck, elbows and ankles. This is known as the Koebner phenomenon (Gauthier 2003). A recent study proposes the hypothesis that the Koebner phenomenon could be used to assess and predict the clinical profile and course of vitiligo in some cases (Van Geel 2012). The most common form of vitiligo, non-segmental vitiligo or vitiligo vulgaris, is symmetrical and may be localised to certain areas. It may also spread to involve the entire body surface. In contrast, segmental vitiligo only affects one side of the body and usually has limited progression. The two types of vitiligo may co-exist, in which case response to treatment in the segmented areas is usually poor (Ezzedine 2011b; Picardo 2010).

Flare-ups of vitiligo may be separated by stable periods sometimes followed by rapid spreading. The disease can also stop spreading spontaneously without any treatment and may even improve, at least partially, for a short time. However, loss of pigmentation normally recurs, even after successful treatment in some areas. From the clinical perspective, if the disease is stable, it is likely to respond better to surgical treatment. Paradoxically, there are many anecdotal accounts of people with vitiligo whose lesions improve while new patches are appearing at the same time. Most of the reported cases of spontaneous repigmentation are seen on sun-exposed sites.

Prevalence

It is difficult to get a true picture of the prevalence of vitiligo. The largest epidemiological study of the prevalence of vitiligo is based on 47,033 inhabitants of the island of Bornholm in Denmark (Howitz 1977) where vitiligo affected 0.38% of the population. Although many papers quote an estimate of 0.5% to 1% prevalence worldwide this estimate may vary according to cultural and social differences.This is confirmed in a recent review on vitiligo prevalence which found a worldwide prevalence of 0.5% to 2% (Krüger 2012). When vitiligo is more visible, such as on dark skin or when there is more stigma attached to the disease, people with vitiligo are more likely to consult a doctor, thus reported estimates of prevalence may be higher. Figures as high as 8.8% have been reported in India where considerable stigma is attached to the disease (Behl 1972).

Impact

Vitiligo occurs worldwide, affecting all skin types. Vitiligo, classified as a disease by the WHO (L80), results in a loss of functional melanocytes and is often associated with other autoimmune diseases. It can be a cosmetically and psychologically devastating disease (Lerner 1978) resulting in low self-esteem (Papadopoulos 1999), poor body image (Porter 1979), and difficulties in sexual relationships (Porter 1990). Some people with vitiligo may experience high levels of anxiety because of the unpredictability of the disease. Its visibility often makes it difficult for those affected to cope with it from day to day (Schmid-Ott 2007). The use of cosmetic camouflage can be helpful (Levy 2012), especially for people with dark complexions where vitiligo is much more noticeable, but this is not always available (Talsania 2010). A recent study (Pahwa 2013) describes the psychosocial impact on people with vitiligo in India and a review of their quality of life confirmed their experience of social isolation and stigmatisation (Parsad 2003a). People with vitiligo sometimes encounter discrimination in employment, particularly in jobs where they have to deal with the public (Ongenae 2005a; Porter 1987). The impact of vitiligo on children and adolescents should not be underestimated. It can be the cause of bullying and teasing, often restricting sports activities or attendance at school (Silverberg 2014). Adults who had negative experiences linked with their vitiligo in childhood report significantly more problems in social development (Lindhorst Homan 2008).

Despite the fact that vitiligo can significantly affect quality of life, there are still very few studies addressing this important aspect of the disease or the efficacy of psychological interventions. There has been an increase in published studies in recent years, but more research in this area is needed.

Causes

The exact origin of vitiligo is still under investigation. Several mechanisms including autoimmunity, genetic, and environmental factors probably interact in combination in its pathogenesis (Ezzedine 2014 (in press); Richmond 2013; Schallreuter 2008; Spritz 2007; Westerhof 2007). Almost one third of people with vitiligo have a positive family history of the disease (Ezzedine 2012a). Moreover, there is increasing genetic evidence underlining the link between vitiligo and other autoimmune diseases (Jin 2007; Spritz 2013). Indeed, NALP-1 polymorphism has been associated with generation of inflammation and other genes for the induction of autoimmunity. The gene NLRP1 is genetically associated with the risk of several autoimmune diseases including generalised vitiligo, Addison's disease, type 1 diabetes, rheumatoid arthritis, and others (Levandowski 2013). It also seems that triggers such as trauma to the skin, hormonal changes in some women after pregnancy and psychological stress may affect the course of the disease. Some studies support the theory that psychological stress is implicated in the onset and exacerbation of some skin diseases, including vitiligo, in some individuals (Ezzedine 2012b). In one particular study, people with vitiligo experienced a significantly higher number of stressful life events than controls, suggesting that stress may be an

important factor in the cause of the disease (Papadopoulos 1998). However, more evidence is needed to support this theory.

Association with other diseases

Vitiligo is sometimes associated with autoimmune or auto-inflammatory diseases such as thyroid disorders (Van Geel 2012), psoriasis, atopic dermatitis (Ezzedine 2012a), diabetes mellitus, pernicious anaemia and Addison's disease (Rezaei 2007). People with vitiligo have been found to have antibodies directed against melanocytes and some develop antibodies to other tissues and either suffer from the above mentioned autoimmune diseases themselves or have close relatives that do (Bystryn 1988; Cui 1995; Klaus 1984). These observations have been strengthened by recent genome research (Jin 2012) strongly pointing to the conclusion that vitiligo is an autoimmune disease as it shares genes with other autoimmune diseases. Furthermore, it has also been shown that vitiligo has an inverse relationship with melanoma which means that people with vitiligo are less likely to develop melanoma (Spritz 2010). A survey carried out in the Netherlands suggests that vitiligo patients are also at lower risk of non-melanoma skin cancer as well as melanoma (Teulings 2013). A recent genome-wide association study has also found a susceptibility variant for non-segmental vitiligo in the tyrosinase gene (TYR) in the European white population, rarely found in melanoma patients (Jin 2010) suggesting a genetic disregulation of immunosurveillance against the melanocytic system. However, the precise links between these diseases have not yet been fully elucidated.

Description of the intervention

It is important to stress that as yet there is no cure or any effective method of stopping the spread of this disease. Several interventions, based mainly on new findings on the possible causes of this disease, have been used to treat vitiligo (Borderé 2009; Forschner 2007; Njoo 1998). These include pharmacological interventions (e.g. topical corticosteroids and immunomodulators); various forms of phototherapy (i.e. ultraviolet A (UVA), narrow- and broadband ultraviolet B (NB-UVB, BB-UVB), psoralen and UVA (PUVA), excimer laser, and monochromatic excimer light (MEL)); surgical procedures (grafting, melanocyte transplantation, dermabrasion, micropigmentation); cosmetic measures (depigmentation, cosmetic camouflage, fake tan); complementary therapies, and psychotherapy. Although we found no randomised trials of cosmetic camouflage or fake tanning products they are often recommended or prescribed for the face and other exposed areas. When vitiligo is extensive, depigmentation of the skin using topical products such as MBEH (monobenzyl ether of hydroquinone) is sometimes used. Many published studies describe combination therapies, usually combining a light source with another form of treatment in order to enhance repigmentation.

In the previous review, published in 2010, we described the interventions in more detail. However, in view of the large number of included studies and the length of this review update, we have put some of this information in Table 2 with references to direct the reader to more information on the various interventions.

Why it is important to do this review

When this systematic review was originally published in 2006 (Whitton 2006), there were few randomised controlled trials (RCTs) and no systematic review covering all available interventions for vitiligo. An update published in 2010 (Whitton 2010) found 38 new studies, giving a total of 57 RCTs.

This update is important to assess new interventions, to highlight the gaps in research and the need for better designed and powered studies, thus informing clinical decisions and future research priorities.

OBJECTIVES

To assess the effects of all therapeutic interventions used in the management of vitiligo.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled trials (RCTs).

Types of participants

People of all age groups who have any type of vitiligo.

Types of interventions

All types of interventions used in the management of vitiligo including topical and oral preparations, various forms of light therapy, surgical techniques, psychological therapy, and unconventional or complementary therapies.

Types of outcome measures

Primary outcomes

- Quality of life measured using a validated tool e.g. DLQI (Dermatology Quality of Life Index), CDLQI (Children's Dermatology Quality of Life Index), Skindex-29
- Percentage of repigmentation (restoration of normal skin colour) of vitiliginous skin: success rate in terms of more than 75% repigmentation of individual patches or of total body surface area, measured by objective means (e.g. photographs, planimetry, rule of nines). This could be reported as: 75%, >75%, ≥75%, 75% to 90%/100% or 76% to 90%/100%
- Adverse effects

Secondary outcomes

- Cessation of spread of vitiligo or stabilisation of the disease defined as:
  - No increase in the size of individual vitiligo patches measured objectively with Wood's light, photography, or other objective means within a period of a) less than one year or b) one year or more
  - No new lesions appearing, despite no improvement in existing patches resulting from treatment, within a period of a) less than one year or b) one year or more
- Long-term permanence of repigmentation resulting from treatment (at least two years' follow-up)

Search methods for identification of studies

We aimed to identify all relevant randomised controlled trials (RCTs) regardless of language or publication status (published, unpublished, in press, or in progress).

Electronic searches

For this update, we re-ran our existing search strategy for the Skin Group's Specialised Register. We slightly revised our search strategies for CENTRAL, MEDLINE, Embase, AMED, PsycINFO, LILACS and CINAHL (see Appendices). We searched the following databases up to 15 October 2013:

- the Cochrane Skin Group Specialised Register using the search terms: vitiligo OR leucoderma OR leukoderma;
- the Cochrane Central Register of Controlled Trials (CENTRAL) 2013, Issue 10, in *The Cochrane Library* using the search strategy in Appendix 1;
- MEDLINE via Ovid (from 1946) using the strategy in Appendix 2;
- Embase via Ovid (from 1974) using the strategy in Appendix 3;
- PsycINFO via Ovid (from 1806) using the strategy in Appendix 4;
- AMED via Ovid (Allied and Complementary Medicine, from 1985) using the strategy in Appendix 5;
- LILACS (Latin American and Caribbean Health Science Information database, from 1982) using the strategy in Appendix 6; and
- CINAHL via EBSCO (Cumulative Index to Nursing and Allied Health Literature, from 1981) using the strategy in Appendix 7.

We identified a number of recent relevant RCTs using a PubMed alert received by the lead author. These studies are listed in the 'Characteristics of studies awaiting classification' tables.

A final prepublication search for this review was undertaken on 16 October 2014. Although it has not been possible to incorporate RCTs identified through this search within this review, relevant references are listed under Studies awaiting classification. They will be incorporated into the next update of the review.

Trials registers

We searched the following trials registers to October 2013 using the terms 'vitiligo' or 'leucoderma' or 'leukoderma'.

- The metaRegister of Controlled Trials www.controlled-trials.com.
- The U.S. National Institutes of Health ongoing trials register www.clinicaltrials.gov.
- The Australian and New Zealand Clinical Trials Registry www.anzctr.org.au.
- The World Health Organization International Clinical Trials Registry platform www.who.int/trialsearch.
- The EU Clinical Trials Register (https://www.clinicaltrialsregister.eu/).

Searching other resources

References from published studies and reviews

We checked the bibliographies of included studies and relevant reviews to identify further reports of relevant trials.

Unpublished literature

We found some studies which are completed but not yet published in our searches of the trials registers. These studies are listed in the 'Characteristics of ongoing studies' section.

Conference proceedings

For the previous update we searched ISI Web of Knowledge from 2004 to February 2009 using search terms 'vitiligo', 'leucoderma', or 'leukoderma'. Published studies from this search are included in this review. For this update we searched PubMed using search terms described above, and we also identified conference proceedings from the main search results.

Data collection and analysis

Some parts of the methods section of this review use text that was originally published in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011), as well as text that was originally published in other Cochrane reviews co-authored by JLB (predominantly, *Interventions for infantile haemangiomas (strawberry birthmarks) of the skin* (Leonardi-Bee 2011). One review author (JLB) checked the extracted statistical data, entered the data into Review Manager, and conducted the statistical analyses. She also gave expert advice on statistical issues arising in the review.

Selection of studies

Two of the review authors (MW, JB) checked the titles and abstracts identified in the search and independently assessed the full text of all studies of possible relevance. At least two of the review authors (MW, JB, MP,KE) decided which trials met the inclusion criteria. We resolved any disagreements by discussion and made final decisions by consensus.

Data extraction and management

One review author (MP) extracted data from all the new studies, which we also allocated randomly to two of the other authors (ZJ, VE), who independently extracted data. Three of the review authors checked the data extraction forms for discrepancies (MW, JB, UG). Where discrepancies could not be resolved by reference to the text of the studies, we resolved differences by consensus.

Assessment of risk of bias in included studies

At least two review authors (MW, JB, MP) independently assessed risk of bias for the new studies identified in the updated search and we resolved differences by consensus.

We made an assessment of the risk of bias which includes an evaluation of the following components for each included study, using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

(a) The method of generation of the randomisation sequence.
(b) The method of allocation concealment - it was considered 'adequate' if the assignment could not be foreseen.
(c) Who was blinded or not blinded (participants, clinicians, outcome assessors).
(d) How many participants dropped out of the study overall, and whether participants were analysed in the groups to which they were originally randomised (intention-to-treat).

In addition, the following quality assessment also included.
(e) Baseline assessment of the participants for age, sex, duration and severity of vitiligo.
(f) Aims, interventions (including drug doses and duration of treatment) and outcome measures clearly and objectively defined.

(g) Whether or not the assessment of compliance was reported.

Measures of treatment effect

For the primary outcomes, we expressed the results as risk ratio (RR) with 95% confidence intervals (CI) for dichotomous outcomes, and difference in means (MD) with 95% CI for continuous outcomes. Dichotomous outcomes are presented as more than 75% of repigmentation on the body surface since these levels are regarded as clinically important levels of repigmentation. Where data are presented as other dichotomous categories (that is, not as 75%), we calculated RRs but data were not presented in figures. Where small numbers of events were seen in the intervention groups, we have reported P values using Fisher's Exact test to assess statistical significance.

Unit of analysis issues

Where there were multiple intervention groups within a trial, we made pair-wise comparisons of similar active interventions versus no treatment, placebo, or another active intervention. We did not include cross-over trials in the review. We analysed internally controlled trials using appropriate techniques for paired designs (for example, for continuous outcomes using Wilcoxon Signed Ranks test or paired t-test; or for dichotomous data using McNemars test), where available, and we did not pool them with studies of other designs. Where dichotomous data permitted, we estimated paired odds ratios (OR) with 95% CI. Where paired data could not be extracted from the papers, we presented the data.

Dealing with missing data

If participant dropout led to missing data we conducted an intention-to-treat analysis, as reported in the publications of the trials. We contacted trial authors to provide missing statistics, such as standard deviations, where appropriate.

Assessment of heterogeneity

We assessed statistical heterogeneity using the I^2 statistic. We synthesised data using meta-analysis techniques if the I^2 statistic was less than 80%.

Assessment of reporting biases

We did not test publication bias, since too few studies were available for similar types of interventions.

Data synthesis

For studies with a similar type of active intervention, we performed a meta-analysis, to calculate a weighted treatment effect across trials, using a random-effects (DerSimonian and Laird) model. Where it was not possible to perform a meta-analysis, we summarised the data for each trial and have only presented forest plots for primary outcome measures. We have presented the corresponding results as P values. If raw data could not be extracted, we extracted the results from appropriate statistical analyses presented in the paper and reported these in the review. We considered a P value < 0.05 as statistically significant. Excluded studies and reasons for exclusion are described in the 'Characteristics of excluded studies' tables but not discussed further.

Subgroup analysis and investigation of heterogeneity

We did not conduct subgroup analyses, since no substantial heterogeneity (I^2 statistic > 50%) existed between studies for the primary outcomes.

Sensitivity analysis

We planned to conduct sensitivity analyses to examine the effects of excluding poor quality studies, defined as those with a moderate or high risk of bias as described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011), but insufficient numbers of studies were included in the meta-analysis to make this necessary.

RESULTS

Description of studies

This review assessed all published randomised controlled trials (RCTs) of interventions for vitiligo, which are described in more detail in Table 2. Please note in the table some interventions may be found in more than one category: e.g. tetrahydrocurcuminoid cream in Topical and Complementary; *Ginkgo biloba* in Oral and Complementary. Similarly, some references may appear in more than one category.

Results of the search

In this updated version of the review we retrieved 430 references from our electronic searches, detailed above. The Cochrane search strategy is wide and designed to minimise the possibility of missing published trials which are randomised but which may have been wrongly indexed. Of the 430 studies retrieved, 378 were rejected because randomisation was not mentioned in the titles or abstracts. Of the remaining 52, we excluded 13 studies which, though stating they were RCTs, were deemed to be not randomised either by correspondence with study authors,or where review authors concluded that the method of randomisation was not adequate. These studies are presented in the 'Characteristics of excluded studies' tables. There were therefore 39 eligible new RCTs from the updated electronic searches which, when added to the 57 RCTs included in the 2010 review makes a total of 96 studies assessed for this review. There were 4512 participants overall.

Searches of the trials registers retrieved details of 41 ongoing RCTs. They are listed in the 'Characteristics of ongoing studies' section.

There are 32 studies awaiting assessment. These are studies we could not include in the review as they were published after the date of our final search, or for which we have insufficient evidence of randomisation. They are listed in the 'Characteristics of studies awaiting classification' section.

Included studies

Ninety-six studies met the inclusion criteria for this review. Details of these studies are provided in the 'Characteristics of included studies' tables. Summary details are provided below.

Designs

Of the 96 included RCTs, 40 were within-participant studies and the rest were parallel group studies. Ozdemir 2002 used an inter-technique comparison using randomised grafts on non-symmetrical vitiliginous areas. Asawanonda 2008, Hofer 2005, and

Sharquie 2005 randomly assigned lesions, in the same body area, to receive different treatments or treatment regimens. All included studies allocated either participants or bilaterally symmetrical lesions to treatment groups in a random manner. Thirty-one studies were placebo-controlled (Agarwal 2005; Bakis-Petsoglou 2009; Dawid 2006; Ermis 2001;Esfandiarpour 2009; Farajzadeh 2009; Galarza 2009; Ho 2011; Kandil 1974; Kawalek 2004; Lim-Ong 2005; Lu-Yan 2006; Mehrabi 2006; Middelkamp-Hup 2007; Navarro 2002; Nordal 2011; Parsad 1998; Parsad 2003b; Pathak 1984; Procaccini 1995; Reyes 2006; Rodriguez-Martin 2009; Rojas-Urdaneta 2007; Ruiz-Maldonado 1975; Schallreuter 2002; Sharquie 2005; Siddiqui 1994; Souto 1997; Van Geel 2004; Vasistha 1979; Verhaeghe 2011).

Size

The number of participants evaluated in the studies varied from six to 596. The majority of studies (69) consisted of a small sample size (less than 50 participants). Twenty-six studies contained a medium sample size (between 51 to 150 participants) and only one study (Pathak 1984) involved a large sample size (more than 150 participants).

Population

The type of vitiligo and the extent, distribution, and duration of lesions varied between studies and within studies. The majority of studies included participants with non-segmental vitiligo, authors frequently referred to this as 'symmetrical' or 'generalised' vitiligo. One study included participants with segmental vitiligo only. Two studies specified the type of vitiligo included as localised or generalised. One study included only participants with localised vitiligo. Sixteen studies assessed any type of vitiligo, including segmental vitiligo. The remaining studies did not specify the type of vitiligo. Only half of the studies reported the skin phototype of the participants. All these studies included participants with high skin phototypes, where III and IV were predominant. Only eight studies (16.7%) also included participants with both skin phototypes I and II (Bakis-Petsoglou 2009; Kawalek 2004; Linthorst Homan 2012; Nistico 2012; Sassi 2008; Siddiqui 1994; Souto 1997; Yones 2007) and 23 (47.9%) included participants with skin phototype II (Akhyani 2005; Bayoumi 2012; Casacci 2007; Cestari 2001; Dell'Anna 2007; Elgoweini 2009; Ermis 2001; Goldinger 2007; Hamzavi 2004; Hofer 2005; Hui-Lan 2009; Le Duff 2010; Leone 2006; Middelkamp-Hup 2007; Nordal 2011; Passeron 2004; Reyes 2006; Stinco 2009; Tjioe 2002; Van Geel 2004; Verhaeghe 2011; Wazir 2010; Westerhof 1999).

The majority of studies included male and female participants but there was one study, Arca 2006, which included only male participants. Participants were of any age except in seven studies that only recruited children (Farajzadeh 2009; Ho 2011; Hui-Lan 2009; Khalid 1995; Köse 2010; Lepe 2003; Ruiz-Maldonado 1975) and 29 studies that recruited adults only (Asawanonda 2010; Bakis-Petsoglou 2009; Bayoumi 2012; Dawid 2006; Dell'Anna 2007; Elgoweini 2009; El-Zawahry 2012; Goldinger 2007; Hamzavi 2004; Kawalek 2004; Klahan 2009; Le Duff 2010; Leone 2006; Linthorst Homan 2012; Mehrabi 2006; Middelkamp-Hup 2007; Nordal 2011; Papadopoulos 2004; Sassi 2008; Schallreuter 2002; Sheth 2012; Shin 2012; Siddiqui 1994; Stinco 2009; Tjioe 2002; Verhaeghe 2011; Westerhof 1999; Wind 2011; Yones 2007). Seven studies did not report the age of the participants (Farah 1967; Navarro 2002; Radakovic 2009; Radmanesh 2006; Rojas-Urdaneta 2007; Vasistha 1979; Wazir 2010).

Setting

The 96 included studies were undertaken on various continents. The studies were most commonly carried out in Asia or Australasia (49) followed by Europe (27), with only a small number undertaken in the Americas (14) and Africa (6). India conducted the largest number of studies (17) compared to any other country. Two studies were conducted across two countries (Casacci 2007; Dell'Anna 2007).

Interventions

The studies evaluated a wide range of interventions including topical treatments, light therapies, oral treatments, surgical methods, and psychological therapies. In the 39 new studies retrieved from the literature search for this update we found that 54% (21/39) of the studies assessed new interventions. We also found that 33% (13/39) of the studies assessed single interventions, whereas the rest assessed combination interventions, mainly with some form of light therapy.

The new light therapies consisted of oral psoralen plus narrowband ultraviolet B light (NB-UVB) (Bansal 2013), Helium Neon laser (de Macedo 2012), broadband ultraviolet A light (BB-UVA) (El Mofty 2013a), broadband ultraviolet B light (BB-UVB) (El Mofty 2013b), and needling plus NB-UVB (Mohaghegh 2012).

The new combination topical treatments included tetrahydrocurcuminoid cream plus targeted NB-UVB (Asawanonda 2010), pseudocatalase cream in combination with NB-UVB (Bakis-Petsoglou 2009), topical anti-oxidant gel containing pseudocatalase, superoxide, glutathione, coenzyme Q10, carotenoids, vitamins A, E, C, and selenium, antioxidant plus mitochondrial stimulating cream (Galarza 2009), pimecrolimus in combination with 308-nm excimer laser (Hui-Lan 2009), tacrolimus cream in combination with NB-UVB light (Nordal 2011), topical clobetasol propionate cream in combination with oral zinc sulphate (Yaghoobi 2011), superoxide dismutase combined with catalase (Paracha 2010), 308-nm MEL combined with 0.1% tacrolimus and oral vitamin E (Nistico 2012), topical tacalcitol combined with 308-nm xenon chloride excimer laser (Oh 2011),

The new combination oral treatments included oral psoralen plus NB-UVB (Bansal 2013), oral vitamin E plus 308-nm MEL and 0.1% tacrolimus (Nistico 2012), and oral zinc sulphate and topical clobetasol propionate cream (Yaghoobi 2011).

Finally, seven new studies assessed the efficacy of surgical methods including dermabrasion combined with UVB light and topical hydrocortisone-17-butyrate (Bayoumi 2012), autologous non-cultured epidermal cell suspension (NCES) combined with sunlight versus suction blister epidermal grafting (SBEG) combined with sunlight (Budania 2012), epidermal abrasion by using microdermabrasion and topical pimecrolimus (Farajzadeh 2009), autologous non-cultured melanocytes suspended in the participant's own serum (Sahni 2011), ablative fractional CO_2 laser plus NB-UVB (Shin 2012), autologous non-cultured epidermal cell suspension (NCES) versus autologous non-cultured extracted hair follicle outer root sheath cell suspension (NCORSHFS) (Singh 2013), and punch grafts plus Helium-Neon (HeNe) laser (Wind 2011).

No new studies assessed either psychological or cosmetic therapies.

See Table 3 for further details.

Outcomes

Primary outcomes

Quality of Life

Despite the fact that the main impact of vitiligo is psychosocial, only nine studies investigated our primary outcome: improvement in quality of life (Agarwal 2005; Akdeniz 2013; Budania 2012; Middelkamp-Hup 2007; Papadopoulos 2004; Sahni 2011; Sassi 2008; Singh 2013; Yones 2007). Middelkamp-Hup 2007 and Sassi 2008 assessed quality of life using Skindex-29, whereas Agarwal 2005, Akdeniz 2013, Budania 2012, Papadopoulos 2004, Sahni 2011, Singh 2013 and Yones 2007 used the Dermatology Life Quality Index (DLQI). Agarwal 2005 and Papadopoulos 2004 also used measurements such as the Children's Dermatology Life Quality Index (CDLQI) (Agarwal 2005) and the Rosenburg Self-Esteem Scale, the Body Image Automatic Thoughts Questionnaire, the Situational Inventory of Body Image Dysphoria, and the General Health Questionnaire. (Papadopoulos 2004).

Percentage repigmentation >75%

Most studies assessed the presence of repigmentation with the exception of four (Agarwal 2005; Barman 2004; Dawid 2006; Papadopoulos 2004). No two studies used exactly the same method of scoring in relation to repigmentation; however, the majority scored the percentage repigmentation and placed participants into categories (e.g. 1% to 25%, 26% to 50%, 51% to 75%, > 75%). Fifty-three of the 96 included studies (55%) addressed our primary outcome of 'percentage of repigmentation of vitiliginous skin: success rate reported as more than 75% repigmentation of individual patches or of total body surface area'. This outcome was expressed in various ways: 75%, >75%, more than 75%, ≥75%, 76 -100% (76% to 100%) in the text of the study. A larger proportion of the new studies 26/39 (67%) compared to 28/57 (49%) of the studies from the previous update, assessed this outcome. Many authors made an attempt to clarify the amount of repigmentation that was deemed successful as 'marked', 'complete' or 'excellent', but opinions varied considerably. For example, authors from nine studies perceived more than 50% repigmentation to be 'excellent', whereas others believed it should be higher (e.g. more than 60% (two studies); more than 70% (two studies), more than 80% (three studies) or more than 90% (two studies). Other studies used the terms poor, fair, good, very good and excellent to report levels of repigmentation (Budania 2012; Khandpur 2005; Sahni 2011; Singh 2013; Vasistha 1979). Ruiz-Maldonado 1975 expressed repigmentation rates as 'slight', 'marked', and 'clinically cured', and Souto 1997 used 'improvement', 'deterioration', and 'no change' to describe differences in repigmentation. Finally, three studies presented repigmentation in millimetres (Navarro 2002; Rojas-Urdaneta 2007; Wind 2011).

Assessment was commonly made visually by a clinician using photographs of lesions. However, some studies used planimetry (i.e. drawing lesions on transparent papers) to determine repigmentation and a small number took photographs of lesions and subjected them to morphometry analysis using Corel Draw, version 9.0. Seven studies (Akdeniz 2013; Bayoumi 2012; El Mofty 2013a; Nordal 2011; Rodriguez-Martin 2009; Sassi 2008; Yones 2007) used a visual analogue scale (VAS),

Adverse Effects

Sixty-five (68%) of the 96 included studies assessed adverse effects. Interestingly, most of the studies included in this update assessed adverse effects (84.6% (33/39), whereas only 56.1% (32/57) of the studies included in the previous two versions of this systematic review addressed this outcome.

Secondary outcomes

Cessation of spread

Only six studies measured cessation of spread of vitiligo (Agarwal 2005; Barman 2004; Dawid 2006; Lim-Ong 2005; Parsad 2003b; Siddiqui 1994), all of which were old studies from the previous review.

Permanence of repigmentation

None of the studies assessed long-term permanence of repigmentation resulting from treatment at two years follow-up.

The duration of the studies varied widely (three weeks to three years) and was partly related to the outcomes being observed, such as initiation of repigmentation or extent of repigmentation. Forty-eight studies (50%) lasted less than six months, and the other 48 (50%) lasted more than six months, of which 17% (8/48) lasted between one and three years. Within these periods, some studies continued treatment until an optimal response was achieved. It is also worth noting that some surgical methods are likely to show an improvement quicker than other interventions. The longest study was Pathak 1984, which lasted up to three years, although the placebo group was not followed up beyond 12 months.

See Table 4 for details of which of our primary and secondary outcomes were assessed in the 96 included studies. We have also included details about the percentage level of repigmentation.

Excluded studies

Overall we excluded 13 studies, of which two RCTs (Babu 2008; Ghosh 1994) were excluded because the authors recruited consecutive participants with vitiligo, although they claimed that all these participants were randomly selected. Moreover, they did not mention whether the participants were randomly distributed into the study groups or how. One study (El Mofty 2006b) reported that participants were randomly allocated to each study but treatment allocation was not randomised within each study. One RCT (Rondon Lugo 1987), although randomised, had insufficient published data to assess the study. Six Chinese studies (Du 1996; Sun 1996; Shi 1995;Suo 2010; Xu 1992; Zhang 2008) were identified as RCTs in the MEDLINE search but after translation were excluded as they proved to be non-randomised clinical trials. Two other RCTs (El Zawahry 1997; Godse 2008) stated that they were randomised but the methodology revealed that they were not. One study (Bahmani 2011) was excluded because the randomisation method was not confirmed in correspondence with the author.

Details of these studies are listed in the 'Characteristics of excluded studies' tables.

Studies awaiting classification

We found 32 RCTs that are awaiting assessment (see the 'Characteristics of studies awaiting classification' tables for more details).

Six studies assessed surgical methods (Awasthi 2011; Budania 2014; Daniel 2011; Gimenez-Azcarate 2013; Martin 2007; Verma 2014), and a further study assessed a combination of surgery and light therapy (Zhang 2014).

Six studies assessed light therapies in combination with topical treatments (Al Rubaie 2002; Baldo 2014; Kalafi 2014; Passeron 2011; Ramaiah 2011; Suo 2010), two in combination with oral treatment (De Leeuw 2011; Pacifico 2009) and one in combination with acupuncture (Zhang 2013).

Three studies assessed light therapies alone (Eleftheriadou 2014; Li 2010; Yan 2013), eight studies assessed topical treatments alone (De la Fuente-Garcia 2014; Fatemi-Naeini 2014; Ghorbanibirgani 2014; Naini 2012; Nitayavardhana 2014; Phiske 2011; Seckin 2007; Syed 2006), one study assessed oral versus topical treatments (Singh 2014), one study assessed a combination of topical treatment and psychotherapy (Caballero 2011), one examined psychotherapies alone (Shah 2014), and one assessed a combination of surgical and light therapy plus topical treatment (De Leeuw 2011).

One study Ediriweera 2009 assessed the effect of traditional Sri Lankan oil 'the kakodumbaradi taila' with selected ayurvedic preparations for vitiligo.

Ongoing studies

We found 41 registered ongoing RCTs which indicates a rise in interest in vitiligo.

See the 'Characteristics of ongoing studies' tables for details.

Risk of bias in included studies

In respect of risk of bias in the included studies, we looked at the following four possible sources of bias: generation of the randomisation sequence; allocation concealment; blinding and Incomplete outcome data (losses to follow-up). We did not look for evidence of selective reporting. We did not formally assess publication bias as there were too few studies for each comparison.

Figure 1 and Figure 2 give a graphical summary of the 'Risk of bias' components.

Figure 1. Methodological quality graph: review authors' judgements about each methodological quality item presented as percentages across all included studies.

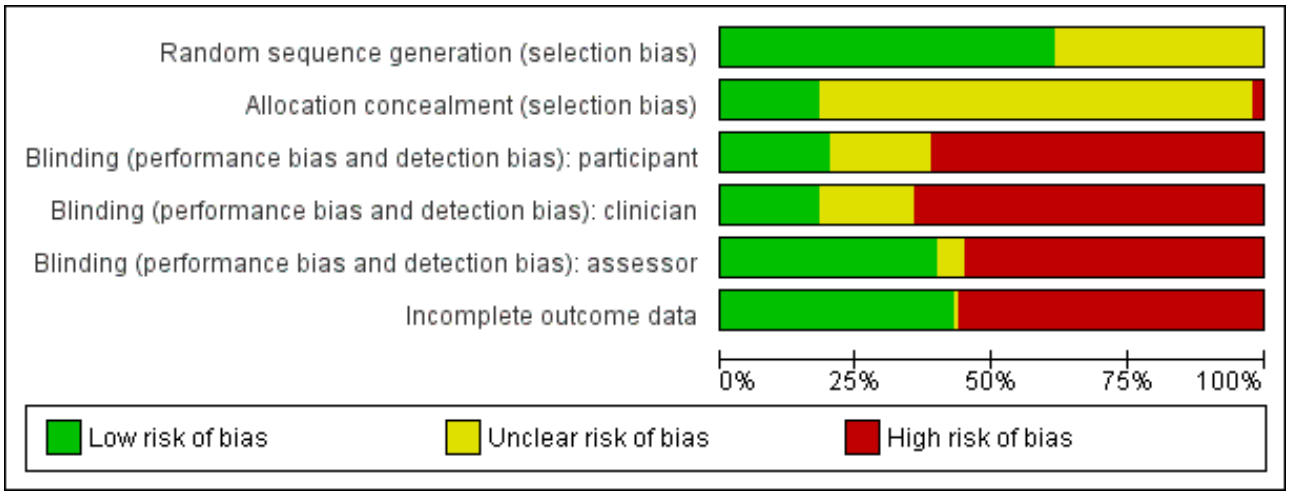


Figure 2. Methodological quality summary: review authors' judgements about each methodological quality item for each included study.

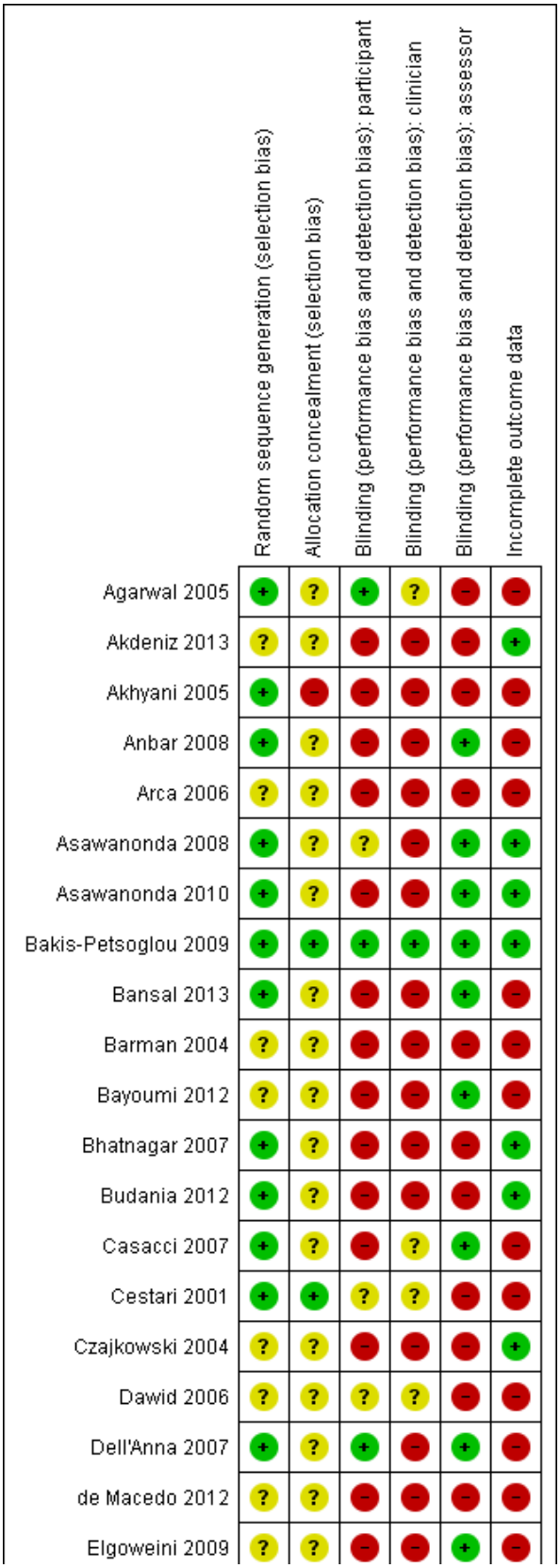


Figure 2. (Continued)

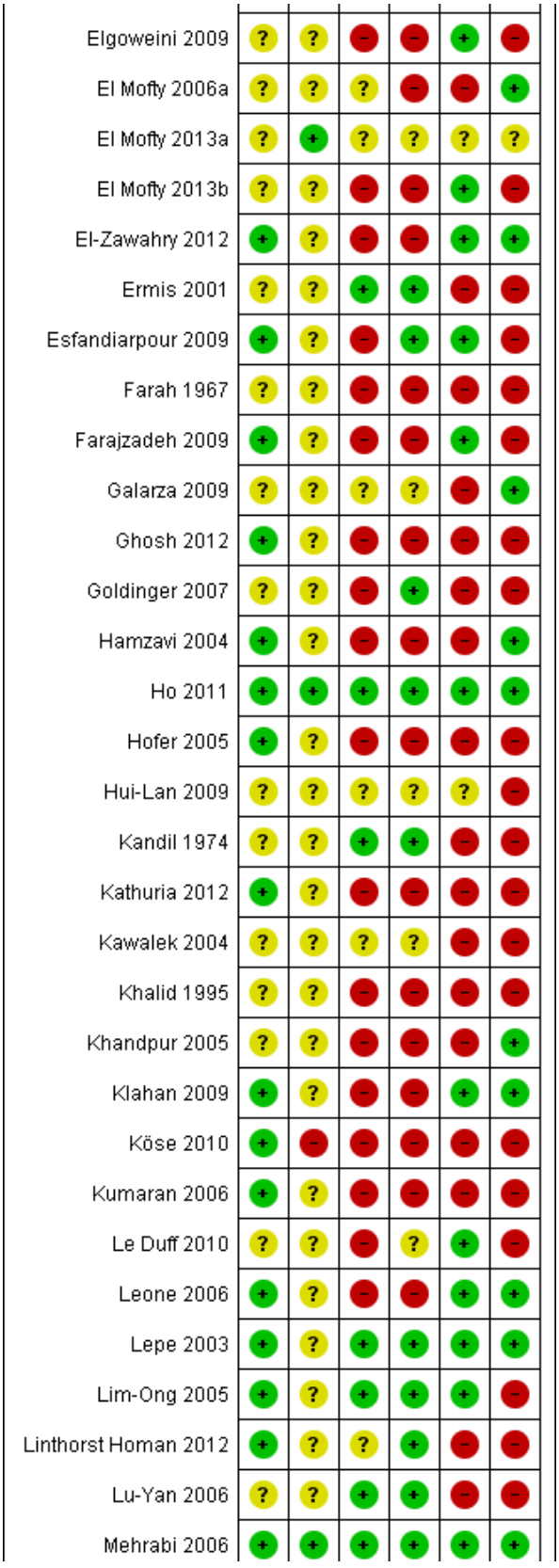


Figure 2. (Continued)

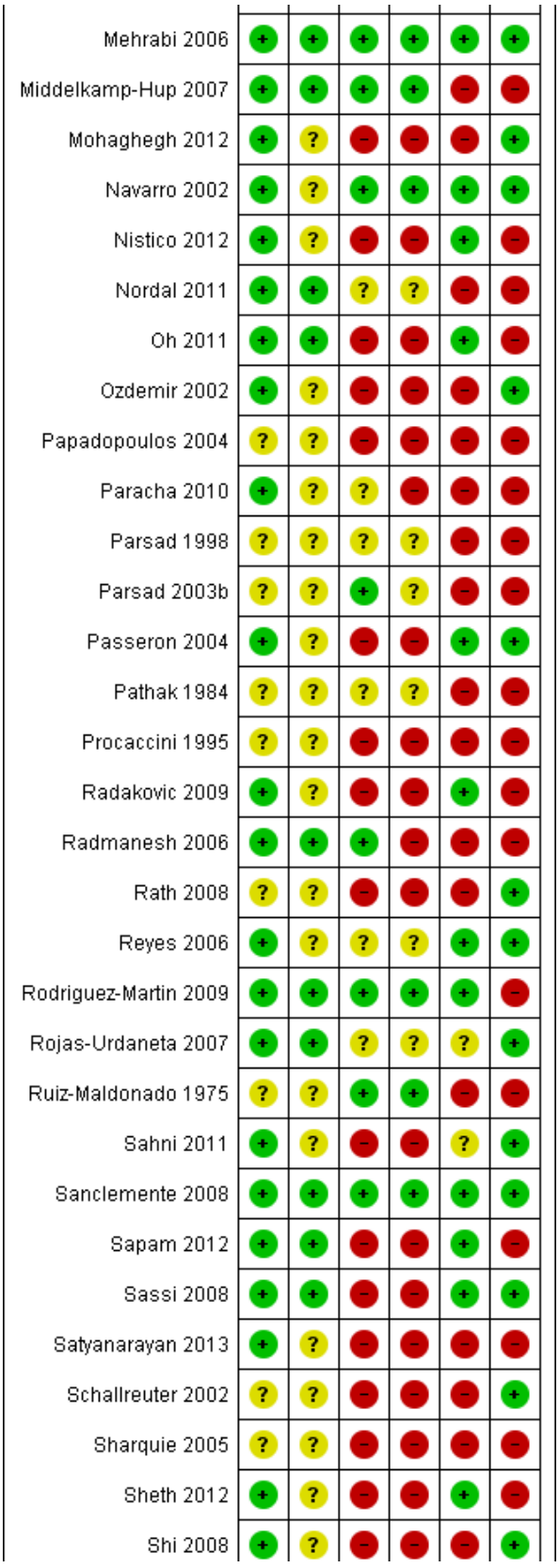
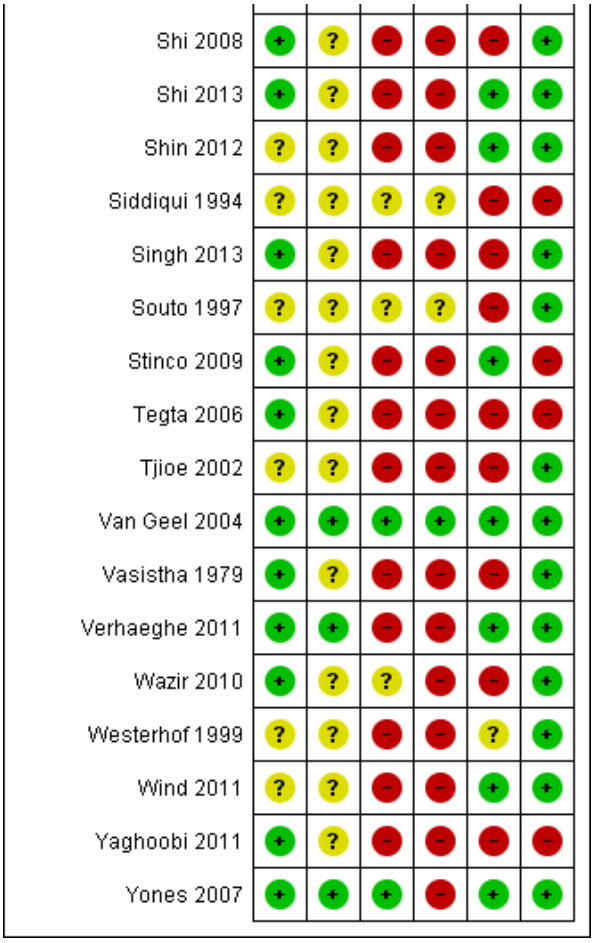


Figure 2. (Continued)



There were only five studies (Bakis-Petsoglou 2009; Ho 2011; Mehrabi 2006; Sanclemente 2008; Van Geel 2004) with all 'Risk of bias' components classified as low, and two with only one component classified as unclear, namely: allocation concealment (Lepe 2003; Navarro 2002), and two with one component classified as high; incomplete outcome data (Rodriguez-Martin 2009) and blinding of clinicians (Yones 2007). Only two studies were found with all Risk of bias' components classified as high except for the random sequence generation component which was classified as low (Akhyani 2005; Köse 2010). See the 'Characteristics of included studies' tables and the 'Risk of bias' tables for each study.

Allocation

Sequence generation and allocation concealment

The method of generation of the randomisation sequence was deemed adequate in 59/96 (61%) of the studies. Adequate sequence generation by computer-generated random list or random number sequence was described in 34 studies (Agarwal 2005; Akhyani 2005; Anbar 2008; Bansal 2013; Bhatnagar 2007; Budania 2012; Cestari 2001; Dell'Anna 2007; Köse 2010; Kumaran 2006; Leone 2006; Lim-Ong 2005; Linthorst Homan 2012; Middelkamp-Hup 2007; Nistico 2012; Nordal 2011; Oh 2011; Ozdemir 2002; Paracha 2010; Radakovic 2009; Reyes 2006; Sahni 2011; Sanclemente 2008; Sapam 2012; Satyanarayan 2013; Sheth 2012; Shi 2008; Shi 2013; Singh 2013; Stinco 2009; Tegta 2006; Vasistha 1979; Wazir 2010; Yaghoobi 2011). The old study by Vasistha 1979 was judged in the first review to have adequate sequence generation following correspondence with the author and this has not been changed, despite the very unequal numbers of participants in each group.

Block randomisation was used in eight studies (Bakis-Petsoglou 2009; Farajzadeh 2009; Ghosh 2012; Ho 2011; Kathuria 2012; Lepe 2003; Rodriguez-Martin 2009; Sassi 2008) of which two studies (Bakis-Petsoglou 2009; Ho 2011) used blocks of six, Kathuria 2012 used blocks of 10, three used permuted blocks (Ghosh 2012; Lepe 2003; Rodriguez-Martin 2009), while Sassi 2008 used stratified blocks, and one study (Farajzadeh 2009) did not specify block randomisation.These were all judged at low risk of bias.

Esfandiarpour 2009 and Mohaghegh 2012 used simple randomisation, Asawanonda 2008, Klahan 2009 and Radmanesh 2006 used cards, Hamzavi 2004 and Mehrabi 2006 used coin toss, Navarro 2002 used chips, Asawanonda 2010, Casacci 2007, Passeron 2004 and Verhaeghe 2011 randomised by drawing lots, El-Zawahry 2012 and Hofer 2005 used envelope concealed method, Van Geel 2004 used a type of lottery, and Yones 2007 used a sequentially numbered list. For the Ermis 2001 study, although in the first review we judged it to be low risk of bias for generation of the randomisation sequence, we have now judged it as unclear

as the randomisation sequence was not described. Rojas-Urdaneta 2007 used a list created using a random number generator (calculator).

Of the 59 aforementioned studies, the treatment allocation of each participant was kept concealed in 16 studies so were judged at low risk of bias for this domain. In addition, El Mofty 2013a was also judged at low risk of bias for this domain. Overall, allocation was kept concealed in 17/96 studies, whereas in 77/96 studies allocation concealment was not clear whether or not the treatment allocation was kept concealed, and we were unable to obtain further information regarding allocation concealment from some of the study authors. In the remaining two studies (Akhyani 2005; Köse 2010) allocation concealment was not kept concealed and judged as high risk of bias.

Methods of allocation concealment included: using centralised telephone randomisation (Sassi 2008); using opaque, sealed envelopes containing cards with treatment allocations written on them (El Mofty 2013a; Radmanesh 2006; Rodriguez-Martin 2009); using the same opaque container where the generation of the randomisation sequence was carried out which contained identical cards with the treatment code (Verhaeghe 2011); sealed, individual code-break envelopes (Bakis-Petsoglou 2009; Oh 2011); sequentially numbered list with the treatment group written on a sealed brown envelope provided by an independent dermatologist (Sapam 2012); generation of the allocation sequence by a third party not associated with the study (Mehrabi 2006; Middelkamp-Hup 2007; Rojas-Urdaneta 2007; Sanclemente 2008; Van Geel 2004); or having a trial pharmacist responsible for preparing treatments and who was the only person to know which active agent they had dispensed, revealing this information only at the end of the study (Cestari 2001; Ho 2011; Nordal 2011; Yones 2007).

Of note, some studies did not randomise participants but instead randomised vitiligo lesions within the same participant to different interventions (otherwise known as a within-participant comparison).·

Blinding

Although some studies were described as 'double-blind' or implied double-blinding, not all of them provided details as to how blinding was maintained. Many studies were within-participant comparisons of different interventions so it was not possible for the participants (and sometimes the clinicians) to be blinded in these studies. Blinding of participants was also not possible in some other studies because two different modalities of intervention were being assessed (e.g. oral versus topical interventions). Furthermore, it was not possible for participants (and sometimes clinicians or outcome assessors) to be blinded in some studies, due to the use of certain interventions (e.g. surgical interventions).

Five of the 14 studies which were described as 'double-blind' (or implied double-blinding) did not have separate blinded outcome assessors. In 22 studies it was stated that the outcome assessor was blinded but neither the participants nor the clinicians were blinded. Fourteen of these studies were within-participant and eight were parallel groups. In 32 studies blinding of participants, clinicians or outcome assessors was not performed or not stated. However in only nine studies (Bakis-Petsoglou 2009; Ho 2011; Lepe 2003; Lim-Ong 2005; Mehrabi 2006; Navarro 2002; Rodriguez-Martin 2009; Sanclemente 2008; Van Geel 2004) were participants, clinicians and assessors all blinded and authors provided information on how blinding was maintained.Thus these were all graded as having a low risk of bias for these three domains.

Incomplete outcome data

The overall number of participants lost to follow-up was 685/4512 i.e.15.2% of the total number of study participants included in the review. In 41 of the included studies (44%), data were analysed on an intention-to-treat basis and these were judged at low risk of bias. This was either because there were no losses to follow-up (31 studies) or because data from dropouts were included in an explicit intention-to-treat analysis (e.g. Hamzavi 2004; Souto 1997).

There is one study (El Mofty 2013a) that mentioned in the text the clinical response was graded according to intention-to-treat analysis; however, losses to follow-up were considered as poor responders but as the text was not entirely clear we judged this as unclear risk of bias. Another study from the same author (El Mofty 2013b) mentioned in the text that intention-to-treat analysis had been used but as losses to follow-up were excluded from the analysis we judged this to be at high risk of bias

Only 19 of the 41 studies that we assessed at low risk of bias for this domain addressed our primary outcome of more than 75% repigmentation.

Further details are provided in the 'Risk of bias' tables (see the 'Characteristics of included studies' tables) where we have summarised the adequacy of blinding with particular attention to those studies, (54 in total), that addressed > 75% repigmentation, a primary outcome of this review.

Effects of interventions

In this section, mainly because of the large number of studies, we present the results for the effects of interventions only for studies that examined the primary and secondary outcomes of interest in this review. Of the 39 new studies, 17 (44%) assessed monotherapies and the other 22 (56%) assessed combinations of interventions. Nearly all of the studies examined insufficiently similar interventions to allow data pooling, with the exception of one meta-analysis. A large number of studies (40) used an intra-participant design. This design can have implications for the applicability of findings, especially for topical interventions, as it is not always possible to exclude systemic effects of different interventions used within the same participant.

Therefore, as not all 96 studies reported the outcomes of interest and almost half of them used a within-participant design, forest plots are only presented for 25 of the 55 parallel studies. Many of the trials had control arms in which none of the participants improved. This resulted in large risk ratios (RRs) with very large associated 95% confidence intervals (CIs), exacerbated by the relatively small participant numbers in many of the trials. Thus the magnitude of the RRs quoted should be considered with caution, but some conclusions may be drawn on statistical significance (or lack of it) over control from using the Fisher's Exact test.

We have addressed the effects of interventions under the following headings

1. Topical therapies: 1.1 Topical corticosteroids; 1.2 Intralesional corticosteroids; 1.3 Topical vitamin D analogues - (calcipotriol

and tacalcitol); 1.4 Topical calcineurin inhibitors (tacrolimus and pimecrolimus); 1.5 Khellin; 1.6 Pseudocatalase and catalase / dismutase superoxide; 1.7 Melagenina (human placental extract); 1.8 Tetrahydrocurcuminoid cream; 1.9 Topical anti-oxidant gel.

2. Oral therapies
3. Light therapies: 3.1 Oral PUVA; 3.2 Oral PUVAsol; 3.3 Topical PUVA; 3.4 Topical PUVAsol; 3.5 UVA; 3.6 UVB (including BB-UVB, NB-UVB and P-NB-UVB); 3.7 Laser light devices; 3.8 Other forms of light therapy.
4. Surgical interventions: 4.1 Suction blister grafts; 4.2 Punch grafts, minigrafts, and split thickness skin grafts; 4.3 Micropigmentation; 4.4 Melanocyte transplantation; 4.5 Dermabrasion; 4.6 Needling; 4.7 Fractional CO2 laser.
5. Psychological therapy
6. Complementary therapies

We have grouped the studies according to intervention types. Where combinations of interventions were used (e.g. topical and light therapy together), we have included the studies under the heading of what we consider to be the 'main' intervention.

Due to the number and complexity of the interventions in this review, we have not repeated our results for those studies with combination interventions under each of the relevant headings. Instead where studies examined two or more different types of intervention, we have mentioned the study under each intervention heading, for example in 'Section 3.1, Oral PUVA' we did not include details of the primary outcome, more than 75% of repigmentation, for Ermis 2001 because the main intervention was calcipotriol, not PUVA so this was reported in 'Section 1.3 Topical vitamin D analogues'.

In these instances please refer to the Characteristics of included studies for the main comparator for that study and the outcomes that were addressed.

For the explanation of technical or medical terms found mainly in 'Adverse Effects', please refer to the Glossary Table 1. NB-UVB studies are listed in Table 5.

(1) Topical therapies

1.1 Topical corticosteroids

A total of 17 studies examined the effect of topical steroids, either as monotherapy or in combination with other interventions. Fifteen of these studies examined one or more outcomes of interest, and two did not examine any outcomes of interest other than adverse effects.

Primary outcomes

a) Quality of life

Two studies assessing topical corticosteroids assessed patient-rated quality of life measures (Akdeniz 2013; Sassi 2008).

Sassi 2008 compared the effects of topical hydrocortisone-17-butyrate plus laser versus laser alone. One outcome measure in this study was patient-rated quality of life, as measured by Skindex-29 (higher score indicates higher quality of life); however no statistically significant difference was seen between the intervention groups (mean difference (MD) 4.75, 95% confidence interval (CI) -1.56 to 11.06, Analysis 1.1).

Akdeniz 2013, which compared the effects of NB-UVB, NB-UVB and calcipotriol and NB-UVB and betamethasone plus calcipotriol, assessed quality of life using the Dermatology Life Quality Index (DLQI). A reduction in DLQI scores, indicating an improvement in quality of life, was demonstrated in all groups (suggesting improvement in quality of life). However, the data provided were only end of trial scores, rather than change scores from baseline, and the baseline scores were not comparable between groups, therefore, we did not perform any analyses.

b) Percentage of repigmentation > 75%

Twelve studies examining the effect of topical corticosteroids addressed this outcome, although repigmentation was measured in various different ways. Eight of these studies examined the effect of topical steroids as monotherapy against other monotherapies or combinations of therapies, and the other four examined the effect of topical corticosteroids in combination with other therapies.

Of the studies which only examined the effect of topical corticosteroids in combination with other therapies, Akdeniz 2013 compared the effects of NB-UVB, NB-UVB and calcipotriol and NB-UVB and betamethasone plus calcipotriol. Although the authors stated a statistically significant difference in favour of NB-UVB plus betamethasone plus calcipotriol compared to NB-UVB alone, results were presented as mean percentages of repigmentation within the treatment groups, therefore, we were unable to assess how many individuals had achieved > 75% repigmentation. Sassi 2008 compared topical hydrocortisone 17-butyrate plus laser versus laser. There was a statistically significant difference in favour of the combination treatment; these participants were more than twice as likely to achieve 75% repigmentation than those receiving laser treatment alone (risk ratio (RR) 2.57, 95% CI 1.20 to 5.50, Analysis 1.2).

In one RCT of children with vitiligo, Khalid 1995 compared topical clobetasol propionate with topical PUVAsol in children with vitiligo. Participants receiving clobetasol propionate were significantly more likely than those receiving PUVAsol to achieve greater than 75% repigmentation (RR 4.70, 95% CI 1.14 to 19.39, Analysis 2.1).

Kathuria 2012 compared 0.05% fluticasone propionate cream 0.1% once daily with 0.1% tacrolimus ointment twice daily for six months. Participants had segmental vitiligo, with or without focal vitiligo. Only one participant in the fluticasone group achieved greater than 75% repigmentation, compared to none in the tacrolimus group. No analysis was performed as the effect size was not estimable.

Köse 2010 compared 0.1% mometasone furoate cream once daily with 1% pimecrolimus cream twice daily, for three months. Although there was a trend towards superior repigmentation in the mometasone group, this was not statistically significant (RR 7.00, 95% CI 0.38 to 127.32, Analysis 3.1; Fisher's Exact test, P = 0.231).

Kumaran 2006 compared topical betamethasone dipropionate with either calcipotriol or betamethasone dipropionate plus calcipotriol. None of the participants achieved greater than 75% repigmentation. Yaghoobi 2011 compared topical 0.05% clobetasol propionate (or 0.1% triamcinolone acetonide for flexures), as

monotherapy and in combination with oral zinc sulphate. Again, none of the participants achieved >75% repigmentation.

Wazir 2010 compared topical 0.01% mometasone furoate, both as monotherapy and in combination with topical 0.03% tacrolimus. Although a greater proportion of participants treated with combination therapy were reported to achieve >75% repigmentation, the data could not be compared to the data from other studies because the repigmentation categories were classified as 51% to 75% and 76% to 95%.

The following studies assessing topical corticosteroids used an intra-participant design; however, data were not sufficient to allow for appropriate analyses to be conducted: Lim-Ong 2005 (which compared topical clobetasol propionate plus NB-UVB versus placebo plus NB-UVB); Lepe 2003 (which compared topical clobetasol propionate and 0.1% tacrolimus); Westerhof 1999 (which compared topical fluticasone propionate (FP) versus FP plus UVA or versus UVA alone); and Bayoumi 2012 (which compared hydrocortisone butyrate and NB-UVB with the same combination after laser dermabrasion).

c) Adverse effects

Sixteen of the 17 studies examining the effect of topical corticosteroids reported adverse effects in some of the participants receiving them. For combination therapies it was not always possible to ascertain which of these adverse effects were attributable to the topical steroids.

Of the studies that examined the effects of topical corticosteroids as monotherapy, Ho 2011 reported folliculitis in one participant treated with clobetasol propionate. No specific details were given regarding other adverse effects. Khalid 1995 reported mild atrophy (four cases), telangiectasia (two), hypertrichosis (one), or acneiform papules (two) in participants treated with clobetasol propionate. Kathuria 2012 reported burning (one case), mild pruritus (two cases), dryness (one case), mild erythema (two cases), atrophy (two cases), telangiectasia (two cases) and acneiform lesions (three cases) in participants treated with 0.05% fluticasone propionate. Köse 2010 reported atrophy (two cases), telangiectasia (two cases) and erythema (one case) in participants treated with 0.1% mometasone furoate. Lepe 2003 also reported atrophy (three cases) and telangiectasia (two) in participants after treatment with clobetasol. Kumaran 2006 reported side effects in seven participants treated with betamethasone, including lesional atrophy, soreness, and hypertrichosis. One participant treated with a combination of betamethasone plus calcipotriol had hypertrichosis and another had dry skin in the lesions. Wazir 2010 reported that there were no adverse events in participants treated with topical 0.01% mometasone furoate, either as monotherapy or in combination with topical 0.03% tacrolimus. Westerhof 1999 detected no evidence of dermal or epidermal atrophy on skin biopsy in participants treated with fluticasone propionate. Yaghoobi 2011 reported only data for adverse events related to oral zinc but not to the topical steroid used by participants.

Of the studies examining effects of combination therapies, Barman 2004 compared the effect of applying a topical corticosteroid (0.1% fluocinolone acetonide) after punch grafting with the use of PUVA therapy after punch grafting. Cobblestoning, depigmentation of the grafts, infection, and graft displacement were seen in some participants in both of the groups. Bayoumi 2012 compared hydrocortisone butyrate and NB-UVB with the same combination after laser dermabrasion. The only adverse events seen were attributable to dermabrasion (oedema and hypertrophic scarring). Lim-Ong 2005 reported adverse effects of vesicles, acneiform eruptions, hypertrichosis, and striae in some participants treated with betamethasone plus NB-UVB. Agarwal 2005 (see Section 2: Oral therapies) reported local atrophy and telangiectasia in participants from both intervention groups and acneiform lesions in one participant in the mometasone plus levamisole group. (These adverse effects were attributable to topical mometasone, not levamisole, so we have listed them here, rather than in Section 2: Oral therapies.) Sassi 2008 reported hyperpigmentation in some participants receiving combination treatment with hydrocortisone-17-butyrate plus laser, although this was also seen in participants receiving only laser treatment.

Two studies assessing the effect of topical corticosteroids mentioned adverse events but did not address any other outcomes of interest in this review. Kandil 1974 compared betamethasone valerate in 50% isopropyl alcohol versus the alcohol base alone. Adverse effects attributed to betamethasone valerate included hypertrichosis in two participants and a localised acneiform eruption in three participants. Sanclemente 2008 compared twice daily application of betamethasone with a topical catalase/dismutase superoxide. No adverse events were reported in participants receiving betamethasone.

Secondary outcomes

a) Cessation of spread of vitiligo

Lim-Ong 2005 was the only study to assess the ability of interventions to halt the spread of vitiligo. It assessed the effect of topical clobetasol propionate plus NB-UVB versus placebo plus NB-UVB on vitiligo disease activity by comparing pre- and post-treatment vitiligo disease activity (VIDA) scores and permanence of repigmentation and development of new lesions within one year post-treatment, as documented by photographs. We did not perform analyses as the study used a within-participant design. Repigmentation in the majority of participants (15/20, 75%) was maintained in both treatment arms within one year post-treatment but eight of the participants developed new lesions on both sides within that time.

b) Long-term repigmentation

None of the studies assessed this outcome.

1.2 Intralesional corticosteroids

One study (Vasistha 1979) assessed the effect of intralesional corticosteroids, but it did not examine any outcomes of interest other than adverse effects. This study compared intralesional triamcinolone acetonide injections with placebo injections. Adverse effects in the intralesional steroid group included atrophy in eight participants, telangiectasia in two, infection in one, and intradermal haemorrhage in one.

1.3 Topical vitamin D analogues - (calcipotriol and tacalcitol)

A total of 11 studies assessed the effect of vitamin D analogues as monotherapy or in combination with other interventions.

Primary outcomes

a) Quality of life

Akdeniz 2013, which compared the effects of NB-UVB and calcipotriol, NB-UVB and betamethasone plus calcipotriol and NB-UVB alone, assessed quality of life using the Dermatology Life Quality Index (DLQI). (See Section 1.1, Topical Corticosteroids)

b) Percentage of repigmentation > 75%

Kumaran 2006 was the only study to include a vitamin D analogue as monotherapy and which assessed this outcome (see Section 1.1, Topical Corticosteroids).

Five studies examining the effect of vitamin D analogues in combination with other interventions assessed the percentage of repigmentation greater than 75%. Rodriguez-Martin 2009 compared tacalcitol plus sunlight versus placebo plus sunlight, but found no difference between the groups (RR 0.33, 95% CI 0.01 to 7.89, Analysis 4.1; Fisher's Exact test P = 1.00). Arca 2006 compared calcipotriol plus NB-UVB with NB-UVB alone; there was no statistically significant difference between groups (RR 1.11, 95% CI 0.52 to 2.35, Analysis 5.1).

The following three studies used an intra-participant design (Parsad 1998 (which compared calcipotriol plus PUVAsol with placebo plus PUVAsol); Ermis 2001 (which compared calcipotriol plus PUVA with placebo plus PUVA); and Lu-Yan 2006 (which compared tacalcitol plus 308-nm monochromatic excimer light (MEL) with placebo plus MEL), but only one of these studies reported sufficient data to allow for analysis (Ermis 2001). This study found the side of participants treated with the calcipotriol plus PUVA group had a significant four-fold increase in the likelihood of achieving greater than 75% repigmentation sooner than the side treated with placebo plus PUVA (paired odds ratio (OR) 4.25, 95% CI 1.43 to 12.64, Analysis 6.1) (Ermis 2001).

c) Adverse effects

Parsad 1998 reported mild skin irritation in three participants treated with calcipotriol. Ermis 2001 reported mild to moderate erythema, xerosis (dryness), and itching in two participants treated with calcipotriol. In the Kumaran 2006 study, one participant using calcipotriol had perilesional hyperpigmentation and one had an irritant reaction. Lu-Yan 2006 reported that a total of six participants had mild to moderate erythema xerosis and itching after combination treatment with tacalcitol and MEL. In the Rodriguez-Martin 2009 study, a number of participants experienced itching or contact dermatitis at the site of application of tacalcitol and a larger number noted transient erythema of the treated skin.

Three studies did not assess any outcomes of interest other than adverse effects. Oh 2011 compared high strength (20 µg/g) tacalcitol ointment monotherapy with 308-nm excimer laser monotherapy and also with combination treatment, and one participant in the tacalcitol monotherapy group reported itching after application of the ointment. Leone 2006 compared tacalcitol plus NB-UVB with NB-UVB alone. In the tacalcitol plus NB-UVB group, they reported erythema and itching (all participants), mild irritation (12 cases), and desquamation (12). Arca 2006 compared calcipotriol plus NB-UVB with NB-UVB alone, itching and erythema were mentioned but it was not clear in which group they occurred.

Two studies did not report adverse effects or any other predetermined outcomes of interest (Goldinger 2007; (see Section 3.7, Laser light devices), Akhyani 2005).

Secondary outcomes

a) Cessation of spread of vitiligo

b) Long-term repigmentation

None of the studies assessed these outcomes.

1.4 Topical calcineurin inhibitors (tacrolimus and pimecrolimus)

A total of 19 studies assessed the effect of calcineurin inhibitors as monotherapy or in combination with other interventions (13 more studies compared to the previous update).

Primary outcomes

a) Quality of life

None of the studies assessed this outcome.

b) Percentage of repigmentation > 75%

Five studies that included calcineurin inhibitors as monotherapy assessed this outcome.

Kathuria 2012 compared 0.05% fluticasone propionate cream 0.1% once daily with 0.1% tacrolimus ointment twice daily for six months; Köse 2010 compared 0.1% mometasone furoate cream once daily with 1% pimecrolimus cream twice daily, for three months; Wazir 2010 compared topical 0.01% mometasone furoate, both as monotherapy and in combination with topical 0.03% tacrolimus (For all studies: see Section 1.1, Topical corticosteroids).

Paracha 2010 compared topical 0.03% tacrolimus ointment with superoxide dismutase and catalase creams. More participants in the tacrolimus group achieved greater than 75% repigmentation, but this was not statistically significant (RR 0.20, 95%CI 0.02 to 1.61, Analysis 7.1; Fisher's Exact test P = 0.195). Stinco 2009 compared 0.1% tacrolimus ointment twice daily with 1% pimecrolimus cream twice daily and with NB-UVB in a three-armed study. After 24 weeks of treatment, some participants in both the pimecrolimus and tacrolimus groups achieved greater than 75% repigmentation, but only in certain anatomical sites (especially the face). However, there was no statistically significant difference in favour of either intervention for lesions based on the face (RR 2.15, 95% CI 0.72 to 6.48, Analysis 8.1; Fisher's Exact test P = 0.226).

The other studies assessing this outcome examined the effect of topical calcineurin inhibitors in combination with other interventions.

Esfandiarpour 2009 compared topical pimecrolimus plus NB-UVB versus placebo plus NB-UVB, but found no statistically significant difference in rates of repigmentation between the groups (RR 3.38, 95% CI 0.93 to 12.29, Analysis 9.1). Nistico 2012 compared 308-nm monochromatic excimer light (MEL) plus 0.1% tacrolimus plus oral vitamin E with 308-nm MEL monotherapy plus oral vitamin E with oral vitamin E alone. The addition of tacrolimus did not confer any additional benefit over MEL plus oral vitamin E, in terms of participants achieving greater than 75% repigmentation (RR 1.20, 95% CI 0.44 to 3.30, Analysis 10.1).

The following studies used an intra-participant design, but sufficient data were not reported to allow for appropriate analyses to be conducted:

Lepe 2003 (which compared topical 0.1% tacrolimus with topical clobetasol propionate); Kawalek 2004 and Passeron 2004 (both of which compared topical 0.1% tacrolimus plus 308-nm xenon chloride excimer laser with placebo plus laser); Farajzadeh 2009 (which compared once daily 1% pimecrolimus cream, both as monotherapy and after microdermabrasion, with placebo); Hui-Lan 2009 (which compared a combination of 1% pimecrolimus cream and 308-nm excimer laser with excimer laser monotherapy); Klahan 2009 (which compared a combination of 0.1% tacrolimus ointment and targeted NB-UVB with targeted NB-UVB alone); Radakovic 2009 (which compared twice-daily application of 0.1% tacrolimus ointment with once-daily application and with no treatment); and Satyanarayan 2013 (which compared a combination of 0.1% tacrolimus ointment plus NB-UVB with NB-UVB alone).

c) Adverse effects

Fourteen out of the 19 studies reported adverse effects.

Dawid 2006 reported no adverse effects in response to topical 1% pimecrolimus. Esfandiarpour 2009 reported only self-limiting erythema and pruritus with pimecrolimus plus NB-UVB.

Kathuria 2012 reported the following adverse effects in participants treated with 0.1% tacrolimus ointment: burning sensation (three cases); mild pruritus (four cases); mild erythema (seven cases); atrophy (one case) and pyoderma localised to lesion (one case).

Köse 2010 reported a burning sensation in two participants and pruritus in one participant treated with 1% pimecrolimus cream. Lepe 2003 reported burning sensations in the skin of two participants during the first two weeks of treatment with 0.1% tacrolimus.

Paracha 2010 reported skin-coloured papules in one participant and erythema or burning in a further participant treated with 0.03% tacrolimus. Stinco 2009 reported the following adverse effects in participants treated with 1% pimecrolimus: soreness and erythema (two cases); mild erythema (one case); intense erythema (one case); burning sensation (four cases); intense lachrymation (one case). Two participants reported facial flushing after alcohol intake. In participants treated with 0.1% tacrolimus, the following adverse effects were reported: burning sensation (nine cases); soreness (one case); pruritus (one case); and conjunctival erythema (one case). Five participants reported refacial flushing after alcohol intake.

Wazir 2010 reported that there were no adverse events in participants treated with a combination of 0.03% tacrolimus and 0.01% mometasone furoate. Kawalek 2004 reported mild to moderate erythema in all vitiligo patches treated with 0.1% tacrolimus plus laser, with blistering occurring at one site. Eighty per cent of participants treated with this combination experienced a tingling and burning sensation and erythema at the treatment site, compared to 30% treated with placebo plus laser.

Passeron 2004 observed moderate to severe erythema at least one time in all participants from both groups; localised bullous eruptions were observed in two lesions in both groups. However, stinging was only observed in five participants treated with laser and topical 0.1% tacrolimus. Klahan 2009 compared a combination of 0.1% tacrolimus ointment and targeted NB-UVB with targeted NB-UVB alone, and reported 'only minor and well-known adverse effects', but it was not clear in which group these occurred.

Satyanarayan 2013 compared a combination of 0.1% tacrolimus ointment plus NB-UVB with NB-UVB alone. Twelve participants experienced side effects, with no adverse effects exclusive to the side on which tacrolimus was applied. No serious adverse reactions were noted and permanent discontinuation due to adverse events never occurred.

Mehrabi 2006 compared topical tacrolimus plus NB-UVB with placebo plus NB-UVB, and Nordal 2011 compared 0.1% tacrolimus ointment combined with NB-UVB, but the only outcome of interest assessed in these studies was adverse effects. Mehrabi 2006 reported erythema, pruritus, blistering, or a burning sensation, but it was not clear which treatment combination led to these effects. Nordal 2011 reported perioral dermatitis in one participant using tacrolimus.

Secondary outcomes

a) Cessation of spread of vitiligo

Dawid 2006 compared topical pimecrolimus with vehicle. Cessation of spread was assessed using the VIDA (Vitiligo Index of Disease Activity) score, and found no significant difference between the two groups (topical pimecrolimus: median difference 90, range -2046 to +509; vehicle: median difference 114, range -1230 to +615; P value 0.5, (Wilcoxon signed rank test).

b) Long-term repigmentation

None of the studies assessed this outcome.

1.5 Khellin

Two studies examined the effect of khellin in combination with UVA. Only one of them, Procaccini 1995, which compared the application of khellin in two different vehicles (5% khellin in O/W (oil in water) cream or 3% khellin in methyl-2-pyrrolidine, PYR) plus UVA, with the vehicles alone plus UVA, is discussed in this section. The other study, Cestari 2001, compared topical 2% khellin plus UVA with PUVA (see Section 3.1, Oral PUVA).

Primary outcomes

a) Quality of life

Procaccini 1995 did not assess this outcome.

b) Percentage of repigmentation > 75%

Procaccini 1995 assessed this outcome, but it used an intra-participant design and did not report the data sufficiently to allow for appropriate analyses to be conducted.

c) Adverse effects

Secondary outcomes

a) Cessation of spread of vitiligo

b) Long-term repigmentation

Procaccini 1995 did not assess these outcomes.

1.6 Pseudocatalase and catalase/dismutase superoxide

Five studies examined the effect of pseudocatalase or similar compounds.

Primary outcomes

a) Quality of life

None of the studies assessed this outcome.

b) Percentage of repigmentation > 75%

Only one study assessed this outcome: Paracha 2010 compared superoxide dismutase and catalase creams with topical 0.03% tacrolimus ointment (see Section 1.4, Topical calcineurin inhibitors).

Bakis-Petsoglou 2009, which compared NB-UVB both in combination with pseudocatalase and with placebo, collected data on the proportion of participants achieving greater than 90% repigmentation but these data were not reported in a way that enabled an analysis of the percentage of repigmentation >75%. Galarza 2009 compared a gel (containing pseudocatalase, superoxide, glutathione, coenzyme Q10, carotenoids, vitamins A, E, C, and selenium) with placebo. Repigmentation was only reported as 'partial' or 'complete'. No definition was given for 'partial' repigmentation and no participants achieved complete repigmentation.

c) Adverse effects

Bakis-Petsoglou 2009 reported pruritus, erythema and sweating in some participants, but it was not clear in which group these effects occurred. Paracha 2010 reported no adverse effects in participants treated with superoxide dismutase and catalase creams. Galarza 2009 reported no adverse effects in participants treated with a gel containing pseudocatalase, superoxide, glutathione, coenzyme Q10, carotenoids, vitamins A, E, C, and selenium.

Sanclemente 2008 (see Section 1.1, Topical Corticosteroids) reported a self-limiting erythematous papular rash in one participant treated with a topical catalase/dismutase superoxide, but did not examine any other outcomes of interest.

Schallreuter 2002 compared Dead Sea climatotherapy plus pseudocatalase cream (PC-KUS) with Dead Sea climatotherapy plus placebo cream and Dead Sea climatotherapy alone. However, this study did not examine any outcomes of interest and there was no mention of adverse effects in the paper.

Secondary outcomes

a) Cessation of spread of vitiligo

b) Long-term repigmentation

None of the studies assessed these outcomes.

1.7 Melagenina (human placental extract)

Souto 1997 was the only study to examine the effects of melagenina, which it compared with placebo. However, the study examined no outcomes of interest and reported two cases of burning with infra-red light but the group was not specified.

1.8 Tetrahydrocurcuminoid cream

Asawanonda 2010 compared a combination of tetrahydrocurcuminoid cream and targeted NB-UVB, with NB-UVB alone. Data were presented as mean repigmentation scores, but no participants achieved greater than 75% repigmentation and there was minimal difference between the groups. The only other outcome of interest assessed by this study was adverse effects: asymptomatic erythema, itching, burning sensation and hyperpigmentation at sites of treatment were observed at equal frequencies in both groups.

1.9 Topical anti-oxidant gel

Galarza 2009 compared a gel (containing pseudocatalase, superoxide, glutathione, coenzyme Q10, carotenoids, vitamins A, E, C and selenium) with placebo. (See Section 1.6 Pseudocatalase and catalase / dismutase superoxide).

(2) Oral therapies

In this section we present the results of studies that used oral therapies, either as monotherapy or combined with other interventions. The majority of these studies examined the effect of oral therapies in combination with other interventions. Studies examining oral PUVA as monotherapy are discussed in Section 3.1, Oral PUVA, although some of the studies in this section used oral PUVA in combination with other oral therapies. In total, 13 studies examined the effect of oral therapies.

Primary outcomes

a) Quality of life

Two studies assessed patient-rated quality of life. In Middelkamp-Hup 2007, participants received either *Polypodium leucotomos* capsules plus NB-UVB or placebo plus NB-UVB. Patient-rated quality of life was assessed using Skindex 29 and no significant differences were reported in the paper for change in quality of life.

Agarwal 2005 compared oral levamisole plus topical mometasone furoate with oral placebo plus topical mometasone. Quality of life was assessed using three measures: Dermatology Life Quality Index (DLQI), Children's Dermatology Life Quality Index (CDLQI), and the WHO Quality of Life Brief Questionnaire (WHO QOL-BREF). No significant differences were seen between the intervention groups at six months' follow-up: DLQI (oral levamisole: median 1, range 0 to 7; placebo: median 1, range 0 to 14); CDLQI (oral levamisole: median 1, range 0 to 6; placebo: median 1, range 0 to 2). Data were not reported for WHO QOL-BREF.

b) Percentage of repigmentation > 75%

Six studies assessed this outcome. One study (Elgoweini 2009) compared NB-UVB combined with oral vitamin E supplementation with NB-UVB alone. There was no difference between the two treatment groups and the results were not statistically significant (RR 1.36, 95% CI 0.44 to 4.21, Analysis 11.1; Fisher's Exact Test, P = 0.67).

Nistico 2012 also examined the effects of oral vitamin E supplementation with two different combination interventions (see Section 1.4 Topical calcineurin inhibitors (tacrolimus and pimecrolimus)). None of the participants taking oral vitamin E alone achieved >75% pigmentation.

Parsad 2003b examined the effect of an oral intervention as monotherapy, namely oral *Ginkgo biloba*, compared with placebo. Overall, *Ginkgo biloba* showed a significant improvement over placebo (RR 4.40, 95% CI 1.08 to 17.95, Analysis 12.1).

Rath 2008 compared the effect of oral minipulses of betamethasone (OMP) alone and with three different combination interventions, namely: OMP plus PUVA; OMP plus NB-UVB, and OMP plus BB-UVB. There was a statistically significant difference in favour of OMP plus NB-UVB compared to OMP alone (RR 7.41, 95% CI 1.03 to 53.26, Analysis 13.1; Fisher's Exact test P=0.014), but not for OMP plus PUVA versus OMP alone (RR 3.70, 95% CI 0.47 to 29.28, Analysis 14.1; Fisher's Exact test P = 0.221) or for OMP plus BB-UVB versus OMP alone (RR 1.67, 95% CI 0.11 to 24.26, Analysis 15.1; Fisher's Exact test P = 1.00).

Radmanesh 2006 compared oral azathioprine plus 8-MOP plus UVA versus 8-MOP plus UVA. Those in the group receiving azathioprine were statistically significantly more likely to achieve greater than 75% repigmentation four months after treatment (RR 17.77, 95% CI 1.08 to 291.82, Analysis 16.1; Fisher's Exact test P = 0.002).

Dell'Anna 2007 compared an oral antioxidant pool plus NB-UVB with NB-UVB alone. No statistically significant difference was found between the two groups (RR 2.59, 95% CI 0.67 to 10.00, Analysis 17.1; Fisher's Exact test P = 0.226).

c) Adverse effects

Of the studies mentioned above, Siddiqui 1994 reported only mild nausea in participants treated with L-phenylalanine. Agarwal 2005 reported no adverse effects that were likely to be due to oral levamisole. Parsad 2003b reported nausea in two participants receiving *Ginkgo biloba*. Radmanesh 2006 reported two cases of gastrointestinal upset in participants receiving azathioprine plus PUVA. Middelkamp-Hup 2007 observed mild and transient itching (10 cases), dryness of the skin due to NB-UVB (five cases), and mild gastrointestinal complaints due to capsule intake (four cases) in the NB-UVB plus P*olypodium leucotomos* group. In the NB-UVB alone group they observed the same adverse effects in five participants (mild and transient itching), three (dryness) and five (mild gastrointestinal complaints due to capsule intake).

Rath 2008 reported nausea and weight gain in 11 participants receiving OMP plus PUVA and excessive erythema and blistering of the skin in five. Weight gain was reported in 10 participants receiving OMP plus NB-UVB. Excessive erythema occurred in six participants receiving OMP plus BB-UVB and weight gain in five. Ten participants receiving OMP alone experienced weight gain.

Elgoweini 2009 reported erythema in both groups, with 70% of participants experiencing this in the vitamin E supplementation group, compared with 85% in the NB-UVB alone group. Nistico 2012 reported symptomatic erythema, burning pain, stinging, and perilesional hyperpigmentation in six participants in the MEL and vitamin E group. Five participants experienced similar side effects in the MEL/tacrolimus/vitamin E group.

The following three studies did not assess any of the predetermined outcomes of interest other than adverse effects:

Tjioe 2002 compared oral vitamin B12 and folic acid plus NB-UVB with NB-UVB alone. The only adverse effects were prickling sensations on depigmented areas and an occasional phototherapy-induced erythema. Rojas-Urdaneta 2007 compared an antioxidant and mitochondrial stimulating cream plus oral antioxidants and phenylalanine with a placebo cream plus oral antioxidants and phenylalanine and also with the active cream alone and placebo treatment alone. The only adverse effect reported was mild acne and pruritus in one participant receiving the active topical treatment. Shi 2008 compared Zengse pill (ZSP), with or without oral cobamamide plus topical psoralea tincture. There were five or six reports of skin redness and itching in both groups, and one participant receiving ZSP experienced constipation.

Three studies did not observe adverse effects (Agarwal 2005; Dell'Anna 2007; Reyes 2006). The latter reported no adverse effects that were likely to be due to oral levamisole.

Secondary outcomes

a) Cessation of spread of vitiligo

Three studies assessed this outcome. Parsad 2003b assessed cessation of spread of vitiligo as defined by the 'arrest of progression of vitiligo in participants with unstable disease', presumably at the end of the study period (six months). The study reported a statistically significant difference in favour of the group receiving oral *Ginkgo biloba* (RR 2.20, 95% CI 1.22 to 3.95).

Siddiqui 1994 examined the effectiveness of oral L-phenylalanine, either with or without UVA. Participants received either L-phenylalanine or placebo and were divided into two groups, one of which received UVA and the other did not. The study reported no statistically significant difference between the L-phenylalanine plus UVA group and the no active treatment group (RR 1.36, 95% CI 0.86 to 2.13) or between the L-phenylalanine alone group versus the no active treatment group (RR 1.31, 95% CI 0.74 to 2.32).

Agarwal 2005 compared oral levamisole plus topical mometasone furoate with oral placebo plus topical mometasone, and assessed cessation of spread by means of counting the number of any new vitiligo lesions at each monthly visit. The study reported no statistically significant difference between the groups (RR 1.38, 95% CI 0.92 to 2.06).

b) Long-term repigmentation

None of the studies assessed this outcome.

(3) Light therapies

We found 65 (65/96, 68%) studies assessing light therapies, 50 in combination with other therapies and 15 as monotherapy. Twenty-seven of these were new and 38 were from the previous update. In this section we have treated PUVA and PUVAsol as light therapies although psoralen is used either topically or orally to enhance the effect of the light.

3.1 Oral PUVA

Of a total of 12 RCTs evaluating oral PUVA, four studies assessed oral PUVA alone (Bhatnagar 2007; El Mofty 2013b; Sapam 2012; Yones 2007). Eight studies assessed oral PUVA in combination with other therapies such as calcipotriol (Akhyani 2005; Ermis 2001), azathioprine (Radmanesh 2006), *Polypodium leucotomos* (Reyes 2006), topical dimethoxyamoidina (khellin) (Cestari 2001), and surgical therapies e.g. punch grafting plus PUVA (Barman 2004), transplantation of cultured autologous melanocytes plus PUVA (CMP), suction blister transplantation plus PUVA (SBP) or

cryotherapy plus PUVA (CP) (Czajkowski 2004). The psoralen employed in most studies was 8-MOP (8 methoxypsoralen), although Bhatnagar 2007 used trimethylpsoralen (TMP).

We have not included the study by (Van Geel 2004) in this section as data were not presented clearly for the PUVA/NB-UVB arm of the study (see Section 4.4; Melanocyte transplantation).

Primary outcomes

a) Quality of life

One study (Yones 2007) measured patient-rated quality of life: Differences between the groups for the Dermatology Life Quality Index and Visual Analogue Scale at one year post-treatment were not statistically significant (reduction in DLQI P = 0.8; reduction in VAS P = 0.5).

b) Percentage of repigmentation > 75%

In a meta-analysis of three studies (Bhatnagar 2007; Sapam 2012; Yones 2007), we found a non-significant 60% increase in the proportion of participants achieving >75% repigmentation which was in favour of NB-UVB compared to PUVA (RR 1.60, 95% CI 0.74 to 3.45; I^2 = 0%; Analysis 18.1).

El Mofty 2013b did not measure > 75% repigmentation and none of the participants achieved the outcome of > 80% repigmentation stated in the study.

Ermis 2001; (see Section 1.3, Topical vitamin D analogues). Radmanesh 2006; (see Section 2, Oral therapies).

c) Adverse effects

Adverse effects were reported in eight studies.
In the study by Barman 2004, cobblestoning, depigmentation of the grafts, infection, and graft displacement were the important side effects seen in some participants in both the groups.

The only adverse effect reported in the study by Radmanesh 2006, was gastric upset in two participants from the PUVA plus azathioprine group. This adverse effect could be attributable to either psoralen or azathioprine.

In the study by Bhatnagar 2007, herpes labialis was found in four participants from the NB-UVB group; mild to moderate itching was found in three from the NB-UVB group and four from the PUVA group; acute urticaria and symptomatic dermographism was found in one participant from the NB-UVB group. Sedation, xerosis, exacerbation of acne lesions, and nausea were only observed in the PUVA group, three participants experienced each of these side effects, except for nausea which was observed in two participants.

Yones 2007 reported erythema in 24 participants from the psoralen plus UVA (PUVA) group. Nausea was observed in eight participants treated with PUVA and who switched from 8-MOP to 5-MOP during the study because of nausea.

Van Geel 2004, erythema was observed in all test lesions during the first two weeks, changing to a pink colour that persisted for a maximum of one month. However, data may relate to either PUVA or NB-UVB; (see Section 4.4, Melanocyte transplantation).

In Cestari 2001, a burning sensation was reported in three out of 14 participants from the khellin 2% group and in six out of 13 participants from the khellin 0.1% group. There were signs of phototoxicity in one participant from the khellin 2% group and in two participants from the khellin 0.1% group, vesiculation in one participant from the khellin 2% group and in six participants from the khellin 0.1% group, pruritus in five participants from the khellin 2% group and in eight participants from the khellin 0.1% group, and perilesional hyperpigmentation in two participants from the khellin 2% group and in six participants from the khellin 0.1% group.

Sapam 2012 reported that adverse effects were more common in the PUVA group (57.2%) than the NB-UVB group (7.4%). Of the 28 participants who received oral PUVA, two participants discontinued therapy due to severe dizziness and 15/26 remaining other participants reported pruritus (five); hyperpigmentation (two); erythema (two); thickening (four), and nausea (two), whereas only two participants complained of pruritus in the NB-UVB group.

In the study by El Mofty 2013b, compared with PUVA, there was a significantly lower incidence of adverse effects in the higher-dose UVA group, but not in the lower-dose UVA group. These adverse effects were reported as phototoxicity in 8/13 participants with oral PUVA (itching, burning sensation or erythema) or thickening of the skin in 3/13 participants.

Czajkowski 2004 reported no adverse effects and also no predetermined outcomes of interest.

In a meta-analysis of three studies (Bhatnagar 2007; Sapam 2012; Yones 2007) there was some evidence of a significant reduction in nausea (RR 0.13, 95%CI 0.02 to 0.69) and erythema (RR 0.73, 95%CI 0.55 to 0.98) seen in those who received NB-UVB compared to PUVA, but no significant effect was seen for itching (RR 0.57, 95%CI 0.20 to 1.60, Analysis 18.2).

Secondary outcomes

a) Cessation of spread of vitiligo

b) Long-term repigmentation

None of the studies assessed these outcomes.

3.2 Oral PUVAsol

Five studies assessed oral PUVAsol. Pathak 1984 compared different psoralen compounds, doses and combinations, combined with exposure to sunlight. Ruiz-Maldonado 1975 compared oral trimethylpsoralen (TMP) plus sunlight or sun lamp with placebo and the same light exposure in children. Farah 1967 compared oral PUVAsol versus topical PUVAsol versus oral triamcinolone combined with PUVAsol, although neither the precise treatment regimens nor the exact length of treatment were described. Parsad 1998 compared topical calcipotriol plus PUVAsol with placebo combined with PUVAsol (outcomes reported in Section 1.3 Topical vitamin D analogues); Khandpur 2005 assessed mini punch grafting plus PUVAsol versus split skin grafting plus PUVAsol.

Primary outcomes

a) Quality of life

None of the studies assessed this outcome.

b) Percentage of repigmentation > 75%

There were several comparisons of different psoralen compounds combined with exposure to sunlight which were all based in data

from one study (Pathak 1984). There was no difference between 8-MOP plus TMP versus placebo RR 12.05, 95% CI 0.75 to 194.88 Analysis 19.1; or between any doses of TMP and either placebo or other treatments Analysis 20.1. When PUVAsol was compared to other treatments or placebo, only the comparisons in favour of 8-MOP at any dose (RR 0.40, 95% CI 0.17 to 0.94) and compared to 8-MOP plus TMP at any dose (RR 0.35, 95% CI 0.14 to 0.87) were statistically significant Analysis 21.1. Comparison of 8-MOP at any dose versus other treatments or placebo was only statistically significant for 8-MOP versus psoralen (RR 2.50, 95% CI 1.06 to 5.91) Analysis 22.1 (please note that this comparison is the same as shown in RR 0.40, 95% CI 0.17 to 0.94, Analysis 21.1 where the intervention groups have been reversed, but repigmentation is better in the 8-MOP group. These results are based on numbers followed up as there is no indication in the trial data of the number randomised to each group. There was considerable regional variation in response; the face best, followed by head and neck, chest, abdomen and back, then arms and legs, and finally lips, hands, feet, palms, and soles.

There were no statistical differences in participants treated with oral minipulses of betamethasone (OMP) plus PUVAsol (8-MOP plus UVA) compared to participants treated with OMP alone six months after treatment Rath 2008; see Section 2, Oral therapies).

Khandpur 2005; (see Section 4.2, Punch grafts, minigrafts and split skin grafts).

Ruiz-Maldonado 1975 compared oral trimethylpsoralen (TMP) plus sunlight or sun lamp with placebo and the same light exposure in children but no differences were observed (RR 0.44, 95% CI 0.04 to 4.53, Analysis 23.1; Fisher's Exact test P = 0.593).

c) Adverse effects

Adverse effects were reported in five studies. In one study (Pathak 1984) 49% of participants overall reported side effects including nausea, pruritus, dizziness, headaches, eye discomfort, and vague gastrointestinal symptoms. The incidence was lowest in the placebo group followed by the TMP group, and was highest in the group which used a combination of TMP and 8-MOP.

In another study (Ruiz-Maldonado 1975), there were no side effects in the placebo group. However, in the TMP group one participant had severe pruritus, one had hyperpigmentation of the uninvolved skin, and two of those who used the sun lamp had blisters due to overexposure by the parents. There was no evidence of liver or blood toxicity in either group.

In the study by (Parsad 1998), three participants complained of mild irritation on applying calcipotriol. In one study (Rath 2008), nausea (11 cases), blistering (20 cases), and perilesional hyperpigmentation (27 cases) was only observed in participants treated with OMP plus PUVA; excessive erythema was reported only in the OMP plus PUVA group (five cases) and in the OMP plus BB-UVB group (six cases). Weight gain was reported in all groups, 11 in the OMP plus PUVA group, 10 in the OMP alone and OMP combined with NB-UVB groups, and five in the OMP plus BB-UVB group.

Secondary outcomes

a) Cessation of spread of vitiligo

b) Long-term repigmentation

None of the studies assessed these outcomes.

3.3 Topical PUVA

No studies found.

3.4 Topical PUVAsol

Two studies assessed PUVAsol administered topically. One study compared topical PUVAsol with a topical corticosteroid one year after treatment (Khalid 1995). The other study compared topical PUVAsol with oral PUVAsol alone and combined with an oral corticosteroid (Farah 1967).

Primary outcomes

a) Quality of life

Neither of the two studies assessed this outcome.

b) Percentage of repigmentation > 75%

Khalid 1995; (see Section 1.1, Topical corticosteroids).

c) Adverse effects

Blistering occurred in two participants on topical PUVAsol, requiring cessation of treatment for one month (Khalid 1995).

Secondary outcomes

a) Cessation of spread of vitiligo

b) Long-term repigmentation

Neither of the two studies assessed these outcomes.

3.5 UVA

Nine studies are included in this section.

Three studies assessed BB-UVA: El Mofty 2013a compared BB-UVA and NB-UVB, El Mofty 2013b BB-UVA and PUVA, Wind 2011 assessed BB-UVA with punch grafts versus NB-UVB with punch grafts versus punch grafts alone.

Six studies assessed UVA: El Mofty 2006a compared two doses of UVA, 15J/cm^2 to UVA 5J/cm^2, Siddiqui 1994 examined the effectiveness of a combination of oral phenylalanine and UVA compared with placebo plus UVA, Westerhof 1999 compared FP (fluticasone propionate) alone on one side of the body and FP plus UVA on the other; with another group that used UVA alone on one side and FP plus UVA on the other side. Procaccini 1995 compared khellin in two different vehicles followed by UVA exposure with application of the vehicles alone followed by UVA exposure. Sharquie 2005 compared topical 15% lactic acid and UVA alone, the combination of both or tap water as the control group. One study El-Zawahry 2012 assessed UVA-1 in two doses versus NB-UVB (see Section 3.6 NB-UVB).

We did not perform statistical analysis in two studies (El Mofty 2006a; Sharquie 2005) as they did not report outcomes of interest for this review. El Mofty 2006a assessed > 60% repigmentation and did not report adverse effects or quality of life and Sharquie 2005 expressed improvement as more than half of the patch showing repigmentation and did not report adverse effects or quality of life.

For Wind 2011 (see Section 4.2 Punch grafts) and Siddiqui 1994 (see Section 2 Oral Therapies).

Primary outcomes

a) Quality of life

None of the studies assessed this outcome.

b) Percentage of repigmentation > 75%

Fluticasone propionate (FP) plus UVA was no better than FP alone (see Section 1.1, Topical corticosteroids).

In the El Mofty 2013a study, a very good response (> 75% to 100%) was reported in 8/20 participants of the BB-UVA group as compared with 3/20 in the NB-UVB group although not statistically significant (RR 2.67, 95% CI 0.82 to 8.62, Analysis 24.1).

For Procaccini 1995 (see Section 1.5, Khellin).

c) Adverse effects

Five studies reported adverse effects. Westerhof 1999, (see Section 1.1, Topical corticosteroids) reported adverse effects where a mild atrophy was detected in the lesion treated with UVA alone and also in the symmetrical lesion treated with a combination of UVA and fluticasone propionate. No evidence of dermal or epidermal atrophy was detected by skin biopsy in the FP monotherapy group. El Mofty 2006a did not report adverse effects and El Mofty 2013a reported no side effects in the BB-UVA group.

In the study by El Mofty 2013b, the incidence of side effects was similar between the higher-dose BB-UVA group (3/14 and the lower-dose BB-UVA group (5/14). These side effects were reported as phototoxicity (itching, burning sensation or erythema) or thickening of the skin. El-Zawahry 2012 reported no side effects in the UVA-1 group.

Siddiqui 1994; (see Section 2, Oral Therapies)

Secondary outcomes

a) Cessation of spread of vitiligo

There were no statistical differences in repigmentation between L-Phenylalanine plus UVA and no treatment and between L-Phenylalanine and no treatment six months after treatment (Siddiqui 1994; see Section 2, Oral therapies).

b) Long-term repigmentation

None of the studies assessed this outcome.

3.6 UVB (including BB-UVB, NB-UVB and P-NB-UVB)

BB-UVB

Two studies assessed BB-UVB: Asawanonda 2008 compared BB-UVB with NB-UVB, whilst Rath 2008 evaluated the effects of oral minipulses of betamethasone (OMP) combined with BB-UVB versus OMP alone or in combination with PUVA or NB-UVB.

Primary outcomes

a) Quality of life

Neither of the studies assessed this outcome.

b) Percentage of repigmentation > 75%

In the study by Rath 2008, the clinical evaluation method for measuring this outcome was not described so we do not know how investigators arrived at these results. The study reported improvement after three and six months in grades as follows: marked >75%; moderate 50% to 75%, mild 25% to 50% and poor < 25%. After three months none of the participants in the group combining BB-UVB with OMP achieved > 75% repigmentation. After six months one participant (1/12) in this group achieved >75%. In the study by Asawanonda 2008, none of the participants in either the NB-UVB or BB-UVB groups achieved >75% repigmentation

c) Adverse effects

Asawanonda 2008 reported some perilesional pigmentation and mild to moderate erythema, not necessitating cessation of treatment, which occurred in all participants.

Rath 2008 assessed outcomes at three and six months. After three months, no adverse effects were reported. After six months nausea and weight gain (Cushingoid habitus) was reported in five (5/12) participants, excessive erythema in six (6/12) participants.

Secondary outcomes

a) Cessation of spread of vitiligo

b) Long-term repigmentation

Neither of the studies assessed these outcomes.

NB-UVB

For this update there has been an increase (from 17 to 35, i.e. 18 new studies) in the number of studies assessing NB-UVB, 11 as monotherapy and the rest in combination with other therapies. In order to make this section more readable, we have put the basic information including study interventions and whether outcomes have been assessed in these studies in Table 5. As none of the studies assessed long-term repigmentation this outcome has been omitted from this table. Although Van Geel 2004 is included in the table, the number of participants allocated to NB-UVB or PUVA was not clearly reported in the study. We are therefore unable to report on the outcomes for NB-UVB and PUVA respectively (see Section 4.4, Melanocyte transplantation, for further details on this study). One study, Bansal 2013 assessed psoralen combined with NB-UVB versus NB-UVB alone; (see also Section 3.8, Other forms of light therapy). Details of outcomes assessed in all the studies are given below.

Primary outcomes

a) Quality of life

Four studies assessed quality of life. Akdeniz 2013 (see Section 1.1, Topical corticosteroids), Tjioe 2002 and Yones 2007 assessed quality of life using DLQI whereas Middelkamp-Hup 2007 used Skindex-29 (see Section 2, Oral therapies).

b) Percentage of repigmentation > 75%

We have reported this outcome for the following studies in the sections listed: Dell'Anna 2007; Lim-Ong 2005; Rath 2008 in Section 1.1, Topical corticosteroids; Satyanarayan 2013 and Esfandiarpour 2009 (in Section 1.4, Topical calcineurin inhibitors); Bayoumi 2012 (in Section 1.1, Topical corticosteroids) and (4.5 Laser dermabrasion); Bhatnagar 2007 (in Section 3.1, Oral PUVA); Elgoweini 2009 (in Section 2, Oral therapies); El Mofty 2013a (in Section 3.5, UVA); Yones 2007 (in Section 3.1 Oral PUVA).

One study (Anbar 2008), compared combined therapy (5-fluorouracil plus Er-YAG laser plus NB-UVB) and NB-

UVB phototherapy alone and observed greater than 75% repigmentation in the former group, but no analyses were performed as data from the study were not reported in a suitable way to enable appropriate analysis of this intra-participant designed study.

El-Zawahry 2012 compared NB-UVB and UVA-1, and reported the number of participants who experienced 60% to 80% repigmentation and those experiencing 'excellent' repigmentation (over 80%). We did not perform a statistical analysis as these categories do not fit our outcome criteria of >75% repigmentation. The report of the study states that only one participant had excellent repigmentation i.e. > 80% and there is no way of knowing which of the five participants who achieved 60% to 80% had more than 75% repigmentation.

One study (Casacci 2007), compared monochromatic excimer light (MEL) and NB-UVB alone and repigmentation greater than 75% was observed in both groups, but no analyses were performed as data for the study were not reported in a suitable way to enable appropriate analyses to be conducted for this intra-participant designed study. Hamzavi 2004 compared NB-UVB to no treatment. Our outcome of interest was not measured but a structured monthly estimation of body surface area of vitiligo involvement using the VASI (vitiligo area scoring index) was done. Linthorst Homan 2012 compared punch grafts followed by excimer laser with punch grafts followed by NB-UVB and reported that 10 participants in the NB-UVB group achieved >75% repigmentation compared to two in the excimer laser group, (see Section 4.2, Punch grafts). In one study comparing BB-UVB with NB-UVB, none of the participants in either treatment group achieved at least 75% repigmentation (Asawanonda 2008).

c) Adverse effects

We have reported this outcome for the following studies in the sections listed: Dell'Anna 2007; Middelkamp-Hup 2007; Rath 2008; Tjioe 2002 (in Section 2, Oral therapies), Lim-Ong 2005 (in Section 1.1, Topical corticosteroids); Esfandiarpour 2009 (in Section 1.4, Topical calcineurin inhibitors); Bakis-Petsoglou 2009 (in Section 1.6 Pseudocatalase and catalase/dismutase superoxide); Leone 2006 (in Section 1.3, Topical vitamin D analogues); Mohaghegh 2012 (in Section 4.6, Needling); Nordal 2011 (in Section 1.4, Topical calcineurin inhibitors); Sapam 2012 (in Section 3.1, Oral PUVA).

In one study (Arca 2006), itching and erythema were observed although it was not clear whether this occurred in participants treated with NB-UVB alone. In the study by Bansal 2013, one participant in the NB-UVB group had a phototoxic reaction, three had depigmented macules and one had hyperpigmented macules. One study (Casacci 2007), observed symptomatic erythema in nine participants (group unknown) during the first 12 treatments. El-Zawahry 2012 compared UVA-1 and NB-UVB and reported that in the NB-UVB group, one participant (5%) had a phototoxic reaction and one participant (5%) showed Koebnerization with no statistically significant difference (P = 0.349). In another study (Hamzavi 2004), they observed hyperpigmentation and mild phototoxic effects. Mehrabi 2006 compared NB-UVB combined with tacrolimus to NB-UVB with placebo. Adverse effects were reported by all participants, but data were not presented separately for intervention groups. These were as follows: redness 7/9 (78%); pruritus 8/9 (89%); blistering 4/9 (44%); burning sensation 4/9 (44%); vesicle formation 2/9 (22%); mild to moderate burning 3/9 (33%). Stinco 2009 reported that in the NB-UVB arm of the study two participants had slight erythema and pruritus within five hours after the phototherapy but this was managed by keeping the irradiation dose steady for the subsequent session. Yones 2007 reported erythema in 17 participants in the NB-UVB plus placebo group.

Secondary outcomes

a) Cessation of spread of vitiligo

Lim-Ong 2005; (see Section 1.1, Topical corticosteroids).

Wind 2011; (see Section 4.2, Punch grafts)

b) Long-term repigmentation

None of the studies assessed this outcome therefore this outcome was omitted from Table 2.

3.7 Laser light devices

Twelve studies assessed laser light therapies, six of them in combination with topical therapies, namely: pimecrolimus (Hui-Lan 2009), and tacrolimus (Kawalek 2004; Passeron 2004; see Section 1.4, Topical calcineurin inhibitors); high concentration tacalcitol (Oh 2011) and calcipotriol (Goldinger 2007) (see Section 1.3, Topical vitamin D analogues); and hydrocortisone 17-butyrate (Sassi 2008; see Section 1.1, Topical corticosteroids).

Three studies assessed laser light devices as monotherapy: Hofer 2005 evaluated three different regimens of laser monotherapy whereas two studies (Le Duff 2010 and Shi 2013) compared excimer lamp and excimer laser. Two studies assessed lasers combined with surgical therapies; Linthorst Homan 2012 compared punch grafts and excimer laser (post graft) with punch grafts and NB-UVB (post graft); in a four arm study, Wind 2011 compared punch grafts alone or combined with UVB, NB-UVB or Helium Neon (HeNe) laser (see Section 4.2 Punch grafts).

One study de Macedo 2012 compared HeNe laser with 290-320 nm UVB fluorescent lamp.

Primary outcomes

a) Quality of life

Sassi 2008; (see Section 1.1, Topical corticosteroids).

b) Percentage of repigmentation > 75%

Hui-Lan 2009; Kawalek 2004; Passeron 2004 (see Section 1.4, Topical calcineurin Inhibitors). Sassi 2008; (see Section 1.1, Topical corticosteroids).

Shi 2013 compared 308-nm excimer laser and excimer lamp and observed greater than 75% repigmentation in both groups, but no analyses were performed as this intra-participant designed study did not report the data in a suitable way to enable appropriate analyses to be conducted.

Linthorst Homan 2012 observed greater than 75% repigmentation after punch grafting and excimer laser and also after punch grafting and NB-UVB, but again no appropriate analyses could be performed due to inadequate reporting of the data related to the intra-participant design of the study (see Section 4.2, Punch grafts).

c) Adverse effects

Passeron 2004; (see Section 1.4, Topical calcineurin Inhibitors). Sassi 2008; (see Section 1.1, Topical corticosteroids).

One study (Hofer 2005) observed burning, stinging, moderate to severe erythema, and oedema in participants treated with laser once a week (two participants), laser twice a week (four participants), and laser three times a week (nine participants). They also observed blisters in one participant treated with laser once a week, laser twice a week (two participants), and laser three times a week (four participants). Hui-Lan 2009 reported adverse effects in both arms of the study. In the excimer laser combined with pimecrolimus group 8/48 experienced slight burning which worsened after application of pimecrolimus, 3/48 had blisters and 7/48 had itching. In the excimer laser group 6/48 had slight burning and 3/48 had blisters. In the study by Le Duff 2010 both treatments were well-tolerated. Only one blister reported with the lamp and three with the laser. The majority of participants had persistent erythema but this did not affect tolerance of the treatment. In Oh 2011 only one participant reported itching after application of high concentration tacalcitol.

Secondary outcomes

a) Cessation of spread of vitiligo

b) Long-term repigmentation

None of the studies assessed these outcomes.

3.8 Other forms of light therapy

Eight studies assessed other forms of light therapies.

One study (Schallreuter 2002) compared Dead Sea climatotherapy combined with pseudocatalase cream *versus* Dead Sea climatotherapy plus placebo cream *versus* Dead Sea climatotherapy alone (see Section 1.6, Pseudocatalase and catalase/dismutase superoxide). In another study Rodriguez-Martin 2009 compared tacalcitol combined with sunlight with vehicle and sunlight (see Section 1.3, Topical vitamin D analogues).

Four studies assessed monochromatic excimer light (MEL): (Lu-Yan 2006) compared tacalcitol plus 308-nm monochromatic excimer light (MEL) with placebo plus MEL (see Section 1.3, Topical vitamin D analogues); (Casacci 2007) compared NB-UVB monotherapy with MEL (see Section 3.6, UVB); Verhaeghe 2011 compared NB-UVB with MEL and placebo MEL (see Section 3.6 UVB) and Nistico 2012 compared 308-nm MEL plus oral Vitamin E versus MEL plus tacrolimus plus oral vitamin E versus vitamin E alone (see Section 2, Oral therapies).

Bansal 2013 assessed psoralen combined with NB-UVB (P-NB-UVB) versus NB-UVB alone (see Section 3.6 UVB);

One study de Macedo 2012 compared HeNe laser with 290-320 nm fluorescent lamp (see also Section 3.7 Laser light devices). This study did not report any outcomes of interest.

Primary outcomes

a) Quality of life

Rodriguez-Martin 2009; (see Section 1.3, Topical vitamin D analogues).

b) Percentage of repigmentation > 75%

Rodriguez-Martin 2009; (see Section 1.3, Topical vitamin D analogues). Anbar 2008; (see Section 3.6, UVB). Lu-Yan 2006; (see Section 1.3, Topical Vitamin D analogues).

c) Adverse effects

Anbar 2008; (see Section 3.6, UVB).

In the study by Bansal 2013, nine participants experienced nausea in the P-NB-UVB group, one had a phototoxic reaction, two had depigmented macules and five had hyperpigmented macules.

One study (Lu-Yan 2006; see also Section 1.3, Topical vitamin D analogues) reported that a total of six participants had mild to moderate erythema xerosis and itching after combination treatment with tacalcitol and MEL.

One study (Rodriguez-Martin 2009 (see also Section 1.3, Topical vitamin D analogues), observed itching in 12 participants treated with tacalcitol plus sunlight and in 15 participants treated with vehicle plus sunlight; mild contact dermatitis in seven participants treated with tacalcitol plus sunlight and in four participants treated with vehicle plus sunlight. They also observed mild to moderate transient erythema confined to the lesion during the study period in 26 participants treated with tacalcitol plus sunlight and in 14 participants treated with vehicle plus sunlight; and photosensitivity with persistent erythema lasting > 24 hours was found in one participant treated with vehicle plus sunlight.

Secondary outcomes

a) Cessation of spread of vitiligo

b) Long-term repigmentation

None of the studies assessed these outcomes.

(4) Surgical interventions

A total of 18 studies assessed surgical interventions, either alone or in combination with other interventions.

4.1 Suction blister grafts

Three studies assessed suction blister grafting. Ozdemir 2002 compared suction blister grafts with thin split thickness grafts. In Czajkowski 2004, participants either underwent transplantation of cultured autologous melanocytes plus PUVA therapy (CMP) on one limb and PUVA only (PO) on another or suction blister transplantation plus PUVA (SBP) on one limb and cryotherapy plus PUVA (CP) on another (see Section 3.1, Oral PUVA). Budania 2012 compared autologous non-cultured epidermal cell suspension (NCES) with suction blister epidermal grafting (SBEG).

Primary outcomes

a) Quality of life

None of the studies assessed this outcome.

b) Percentage of repigmentation > 75%

Budania 2012 did assess percentage of repigmentation greater than 75%, although they used an intra-participant design and did not report the data suitably to allow for an appropriate analysis to be conducted.

c) Adverse effects

Ozdemir 2002 reported the Koebner phenomenon (19 cases), hypopigmentation (14), hyperpigmentation (three), scarring (seven) and infection (three) at the donor sites and milia (four), pigment loss (eight), papules (19), peripheral hypopigmentation (two), scarring (one), and infection (six) at the recipient sites. Budania 2012 reported postoperative discomfort and pain, which was relieved by oral analgesics. However, adverse effects were not reported by group and the number of cases was described vaguely.

Secondary outcomes

a) Cessation of spread of vitiligo

b) Long-term repigmentation

None of the studies assessed these outcomes.

4.2 Punch grafts, minigrafts, and split thickness skin grafts

Seven studies assessed grafts alone or combined with light therapies. One study (Khandpur 2005) assessed mini punch grafting plus 8-MOP plus sunlight (PUVAsol) versus split skin grafting plus PUVAsol. Navarro 2002 made a five-way comparison between autologous skin minigraft plus 8-MOP, minigraft plus placebo, minigraft alone, 8-MOP alone, and placebo alone. It did not assess any outcomes of interest. Barman 2004 compared pigmentation spread resulting from the use of a topical corticosteroid (0.1% fluocinolone acetonide) after punch grafting with PUVA therapy after punch grafting (see Section 1.1, Topical corticosteroids). Wind 2011 compared four treatment arms between punch grafts alone, with punch grafts combined with light therapies (UVA, NB-UVB and Helium-Neon (HeNe) laser). Linthorst Homan 2012 also compared two treatments with punch grafts with light therapies (308-nm xenon chloride excimer laser (EL) versus NB-UVB). Sheth 2012 compared 1.5 mm minigrafts and MEL device with 1.5 mm minigrafts and a hand-foot NB-UVB device. Singh 2013 made a two-way comparison between autologous non-cultured epidermal cell suspension (NCES), which is a surgical procedure using non-cultured epidermal cell suspension and autologous non-cultured extracted hair follicle outer root sheath cell suspension (NCORSHFS), which is a surgical procedure using non-cultured extracted hair follicle outer root sheath suspension. In both treatment groups participants were asked to expose the area to sunlight.

Two studies, Navarro 2002 and Wind 2011, although they reported repigmentation, did not assess this outcome as a percentage but used methods that did not fit the criteria for this review.

Primary outcomes

a) Quality of life

One parallel study measured quality of life using the Dermatology Life Quality Index (DLQI). A significant reduction in DLQI scores was observed in both groups ranging from a mean value of 10.73 before NCES to 2.13 after surgery and from a mean value of 10.47 before NCORSHFS to 3.27 afterwards (P < 0.001). However, this decline in DLQI was not significantly different between the two groups (P = 0.244) (Singh 2013).

b) Percentage of repigmentation > 75%

Those treated with split skin grafting plus PUVAsol were found to be statistically significantly more likely to achieve greater than 75% repigmentation (RR 1.89, 95% CI 1.25 to 2.85, Analysis 25.1) than those receiving mini punch grafts three months after treatment (Khandpur 2005).

Singh 2013 examined the effectiveness of NCES and NCORSHFS 16 weeks after the transplantation procedure, although no statistically significant difference was found between the two groups (RR 1.17, 95% CI 0.92 to 1.50, Analysis 26.1)

c) Adverse effects

Barman 2004 reported cobblestoning, depigmentation of the grafts, infection, and graft displacement. In the Khandpur 2005 study, cobblestoning (13), superficial scarring (all participants), and variegated appearance (seven) were observed in the mini punch grafting group. In the split skin grafting group, superficial scarring was observed in all cases, hypertrophic scarring in three participants, depigmentation of the graphs in two participants, tyre-pattern appearance in two participants, milia formation in four participants, rejection of seven grafts was reported in one participant, graft contracture in four grafts was reported in three participants, and achromic fissuring in four participants. In the Sheth 2012 study there were no adverse events. In the Singh 2013 study adverse effects were minimal although not reported.

Secondary outcomes

a) Cessation of spread of vitiligo

Only one of the studies assessed this outcome. Barman 2004 reported in group I, the average pigment spread was 6.38 mm, whereas in group II, it was 6.94 mm, showing a slightly higher pigment spread in group II, which was statistically not significant (P = 0.301). There was no difference in response to therapy in patients having segmental vitiligo as compared with non-segmental vitiligo.

b) Long-term repigmentation

None of the studies assessed this outcome.

4.3 Micropigmentation

No studies found.

4.4 Melanocyte transplantation

Five studies assessed this intervention (Czajkowski 2004; Ghosh 2012; Sahni 2011; Tegta 2006; Van Geel 2004).

Tegta 2006 assessed a technique involving transplantation of epidermal cell suspension obtained from a skin graft approximately one-third or one-fifth the size of the recipient area. In Czajkowski 2004, participants either underwent transplantation of cultured autologous melanocytes plus PUVA therapy (CMP) on one limb and PUVA only (PO) on another, or suction blister transplantation plus PUVA (SBP) on one limb and cryotherapy plus PUVA (CP) on another. Van Geel 2004 compared a cellular suspension (melanocytes plus hyaluronic acid plus epidermal cells) and either NB-UVB or PUVA three weeks after transplantation, with a 'placebo suspension' of (melanocytes medium plus hyaluronic acid without epidermal cells) and either NB-UVB or PUVA three weeks after transplantation. Sahni 2011 compared two ways of suspending melanocytes uniformly spread onto the dermabraded area: autologous non-cultured melanocytes suspended in normal saline versus those suspended in the participant's own serum. Ghosh 2012 made a two way comparison between cultured

graft placed on the dermabraded area and the use of a similar polyurethane film dressing covering the dermabraded area.

Primary outcomes

a) Quality of life

One study measured DLQI by comparing the mean change in DLQI from before, to 16 weeks after surgery (Sahni 2011). The study investigators observed a significant reduction (P = 0.002) in DLQI in both groups, being significantly greater when the melanocytes were suspended in the participant's own serum (P = 0.005). However, the investigators did not report their data in such a way that allowed for it to be included in a forest plot, therefore we can only report results as P values taken directly from the text.

b) Percentage of repigmentation > 75%

In the Tegta 2006 study, using the Fisher's Exact test, the proportion of participants achieving more than 75% repigmentation was significantly greater in those who had skin grafts a third of the size of the recipient area compared to participants who had skin grafts only a fifth of the size of the recipient (P = 0.03, Fisher's Exact test). Please note, caution must be used in interpreting the risk ratio and its 95% CI presented in the forest plot due to the small number of events in the intervention groups (RR 11.00, 95% CI 0.69 to 175.86, Analysis 27.1).

Sahni 2011, examining the effectiveness of two ways of suspending melanocytes, either in normal saline or in the participant's own serum, found a borderline effect favouring the latter (RR 0.71, 95% CI 0.50 to 1.00, Analysis 28.1) although it did not reach statistical significance.

c) Adverse effects

The only adverse effect reported in Tegta 2006 was one case of bacterial infection at the recipient site in a participant treated with a suspension derived from the smaller-sized donor site (one-fifth of recipient site area). In the Sahni 2011 study, halo phenomenon, infection at the recipient site and hyperpigmentation were observed in both treatment groups as follows: halo phenomenon and infection at the recipient site (one case in the suspension with normal saline group and two in the suspension with participant's own serum), and hyperpigmentation (five cases in the suspension with normal saline group and three in the suspension with participant's own serum). However, scarring at the donor site was only observed in those participants whose melanocytes were suspended in normal saline (two cases). Erythema (Van Geel 2004) was observed in all test lesions during the first two weeks, changing to a pink colour that persisted for a maximum of one month. In the Ghosh 2012 study a total of four adverse effects (pyrexia, nasopharyngitis, foot fracture and heat rash) were reported in one participant in each group. None of the adverse effects were related to the cultured graft.

Secondary outcomes

a) Cessation of spread of vitiligo

b) Long-term repigmentation

None of the studies assessed these outcomes.

4.5 Dermabrasion

Bayoumi 2012 compared two treatment arms: dermabrasion with NB-UVB and topical steroids versus NB-UVB and topical steroids. Farajzadeh 2009 compared three treatment arms: topical 1% pimecrolimus cream versus 1% pimecrolimus cream applied to a dermabraded area versus placebo as the control group. Sahni 2011 study compared two ways of suspending melanocytes uniformly spread onto the dermabraded area: autologous non-cultured melanocytes suspended in normal saline versus those suspended in the participant's own serum.

Ghosh 2012; (see Section 4.4, Melanocyte transplantation).

Primary outcomes

a) Quality of life

Bayoumi 2012; (see Section 1.1, Topical corticosteroids).

b) Percentage of repigmentation > 75%

Bayoumi 2012; (see Section 1.1, Topical corticosteroids).

Farajzadeh 2009 (see section 1.4 Topical calcineurin inhibitors) reported that dermabrasion was favoured, however statistical analyses could not be performed due to the lack of sufficient data to allow for an appropriate analysis, owing to the intra-participant study design.

c) Adverse effects

In the Bayoumi 2012 study, adverse effects were only observed in the lesions treated with dermabrasion. The adverse effects reported were the following: delayed healing (up to three weeks; one case), oedema lasting for two to 15 days when extremities were treated (one case), and hypertrophic scars (two cases). In the Farajzadeh 2009 study a mild burning sensation during microdermabrasion was reported in 18 participants.

Secondary outcomes

a) Cessation of spread of vitiligo

b) Long-term repigmentation

None of the studies assessed these outcomes.

4.6 Needling

Only one study (Mohaghegh 2012) assessed the needling technique. The authors compared NB-UVB used with needling with NB-UVB alone.

Primary outcomes

a) Quality of life

b) Percentage of repigmentation > 75%

This study did not assess these outcomes

c) Adverse effects

The only adverse effect reported was five cases of purpura in the injection side, which cleared rapidly, and generalised darkening of the irradiated peripheral border, although which group this was associated with is unknown.

Secondary outcomes

a) Cessation of spread of vitiligo

b) Long-term repigmentation

This study did not assess these outcomes

4.7 Fractional CO2 laser

Only one study, Shin 2012, compared fractional CO2 laser followed by NB-UVB therapy with NB-UVB therapy alone.

Primary outcomes

a) Quality of life

This study did not assess this outcome

b) Percentage of repigmentation > 75%

Although this intra-participant study assessed this outcome two months after cessation of treatment, none of the participants achieved greater than 75% repigmentation.

c) Adverse effects

Adverse effects were observed in all participants from the fractional CO2 laser treatment group. All participants reported pain during laser treatment although symptoms were relieved within a day and post-treatment crusting disappeared within a week, burning sensation during laser treatment, and erythema or oedema after laser treatment. No noticeable adverse effects such as infection, scarring, Koebner phenomenon and aggravation of vitiligo were observed.

Secondary outcomes

a) Cessation of spread of vitiligo

b) Long-term repigmentation

This study did not assess these outcomes

(5) Psychological therapy

None of the newly included studies in this update assessed psychological therapies. Papadopoulos 2004 is the only study assessing psychological interventions by comparing cognitive-behavioural therapy (CBT) with person-centred therapy (PCT) and also with controls receiving no psychological therapy. A total of 45 participants were enrolled.The study did not assess any other outcomes of interest. This trial reported changes within each of the three treatment groups, not between them.

Primary outcomes

a) Quality of life

Patient-rated quality of life was assessed using a battery of validated and reliable questionnaires, including the Rosenberg Self-Esteem Questionnaire, the Body Image Automatic Thoughts Questionnaire, the Situational Inventory of Body Image Dysphoria, The General Health Questionnaire, the Perceived Stress Scale, and the Dermatology Life Quality Index (DLQI). Participants receiving CBT and PCT showed significant improvements in their responses to the General Health Questionnaire up to 12 months after therapy, but there was no improvement in their responses to any of the other questionnaires.

b) Percentage of repigmentation > 75%

c) Adverse effects

This study did not assess these outcomes

Secondary outcomes

a) Cessation of spread of vitiligo

b) Long-term repigmentation

This study did not assess these outcomes

(6) Complementary therapies

A total of seven studies examined the effects of complementary therapies alone (Middelkamp-Hup 2007; Souto 1997) or combined with either NB-UVB (Asawanonda 2010; Bakis-Petsoglou 2009; Dell'Anna 2007; Elgoweini 2009) or PUVA (Siddiqui 1994). All of them have been reported in the above sections. For further details see Section 1.6, Pseudocatalase and catalase/dismutase superoxide (Bakis-Petsoglou 2009); see Section 1.7, Melagenina (human placental extract) (Souto 1997); see Section 1.8, Tetrahydrocurcuminoid cream (Asawanonda 2010); and see Section 2, Oral therapies for the following studies (Siddiqui 1994; Dell'Anna 2007; Middelkamp-Hup 2007; Elgoweini 2009).

We found no published randomised controlled trials of depigmentation or cosmetic camouflage.

DISCUSSION

Summary of main results

In this update, 39 new studies were retrieved from the literature search, giving a total of 96 studies. Over half of the new studies assessed new interventions, most of which were new combination therapies. New topical interventions included topical anti-oxidant gel containing pseudocatalase, superoxide, glutathione, coenzyme Q10, carotenoids, vitamins A, E, C, and selenium, antioxidant plus mitochondrial stimulating cream (Galarza 2009) and tetrahydrocurcuminoid cream (Asawanonda 2010). In terms of oral interventions, two new studies (Elgoweini 2009; Nistico 2012) examined the use of oral vitamin E. New light therapies consisted of oral psoralen plus narrowband ultraviolet B light (P-NB-UVB) (Bansal 2013), Helium Neon laser (de Macedo 2012), broadband ultraviolet A light (BB-UVA) (El Mofty 2013a) and broadband ultraviolet B light (BB-UVB) (El Mofty 2013b).

New combination treatments included topical treatments such as pseudocatalase cream in combination with NB-UVB (Bakis-Petsoglou 2009), pimecrolimus in combination with 308-nm excimer laser (Hui-Lan 2009), tacrolimus cream in combination with NB-UVB light (Nordal 2011), topical clobetasol propionate cream in combination with oral zinc sulphate (Yaghoobi 2011), superoxide dismutase combined with catalase (Paracha 2010) and topical tacalcitol combined with 308-nm xenon chloride excimer laser (Oh 2011). In terms of new combination light therapies, Mohaghegh 2012 used needling plus NB-UVB. New surgical interventions included dermabrasion (Bayoumi 2012; Farajzadeh 2009) and ablative fractional CO2 laser (Shin 2012).

Light therapy remains the most common intervention assessed in this update, either as monotherapy or in combination with other treatments. Sixty-five studies of various types of light therapies were assessed in total. Twenty-seven were new studies and 38 were from the previous two versions of the review. This update has shown a considerable increase in the number of studies assessing NB-UVB either as monotherapy or in combination with

other therapies (35 in total, 18 from this update, 17 from previous versions). Two studies assessed Helium Neon (HeNe) laser. One in combination with surgical techniques (Wind 2011) compared punch grafts alone or combined with UVB, NB-UVB or HeNe laser, and the other as monotherapy (de Macedo 2012) compared HeNe laser with 290-320nm UVB fluorescent lamp.

There was also a notable increase in the number of studies assessing surgical interventions for stable vitiligo as well as topical calcineurin inhibitors (tacrolimus and pimecrolimus) in this update, perhaps reflecting a tendency to use these agents in place of topical corticosteroids, for which the concern about adverse effects may be greater.

We found no studies on camouflage, depigmentation, or psychological interventions in the updated search.

We have not produced a 'Summary of findings' table due to the large number of studies, the complexity of the interventions and the predominance of the intra-participant design.

Primary Outcomes

Quality of life

Despite the fact that vitiligo causes no major physical symptoms other than depigmentation, and its impact is mainly psychosocial, only nine studies (9/96) assessed our primary outcome of quality of life (Agarwal 2005; Akdeniz 2013; Budania 2012; Middelkamp-Hup 2007; Papadopoulos 2004; Sahni 2011; Sassi 2008; Singh 2013; Yones 2007).

Middelkamp-Hup 2007 and Sassi 2008 assessed quality of life using Skindex-29, whereas Agarwal 2005, Akdeniz 2013, Budania 2012, Papadopoulos 2004, Sahni 2011, Singh 2013 and Yones 2007 used the Dermatology Life Quality Index. Agarwal 2005 and Papadopoulos 2004 also used other instruments such as the Children's Dermatology Life Quality Index (Agarwal 2005) and the Rosenburg Self-Esteem Scale, the Body Image Automatic Thoughts Questionnaire, the Situational Inventory of Body Image Dysphoria, and the General Health Questionnaire (Papadopoulos 2004). Only one of the studies (Papadopoulos 2004), which assessed psychological interventions, reported quality of life as their primary outcome measure. The only study where investigators found a statistically significant result for this outcome was Sahni 2011, which showed a result in favour of melanocyte suspension suspended in the patient's own serum, compared to suspension in normal saline. However, there is no forest plot for this study as there were insufficient data to enable us to perform an analysis.

Percentage of repigmentation > 75%

Twenty-five of the new studies in this update assessed the primary outcome of >75% repigmentation. However, not all of the studies used objective methods of scoring repigmentation and thus we were unable to analyse the data on many occasions.

In the previous version of this review, analyses of 15 studies showed statistically significant differences in the proportion of participants achieving >75% repigmentation and these were predominately combination interventions that included some form of light treatment and also included intra-participant studies.

In this update we found only eight studies achieving statistically significant increased risks of repigmentation as we were more specific about >75% repigmentation. The results for these eight studies are summarised below, with the figures in parentheses showing the risk ratio (RR) and 95% confidence interval (CI) for the result.

Khalid 1995 showed a result in favour of clobetasol propionate versus PUVAsol (RR 4.70, 95% CI 1.14 to 19.39); Sassi 2008 showed a result in favour of hydrocortisone-17-butyrate plus excimer laser versus excimer laser alone (RR 2.57, 95% CI 1.20 to 5.50); Parsad 2003b showed a result in favour of *Ginkgo biloba* versus placebo (RR 4.40, 95% CI 1.08 to 17.95); Rath 2008 showed a result in favour of oral minipulse of prednisolone (OMP) plus NB-UVB versus OMP alone (RR 7.41, 95% CI 1.03 to 53.26); Radmanesh 2006 showed a result in favour of azathioprine plus PUVA versus PUVA alone (RR 17.77, 95% CI 1.08 to 291.82); Pathak 1984 showed results in favour of 8-MOP plus TMP versus psoralen plus sunlight (comparison of psoralen plus sunlight versus 8-MOP plus TMP**:** RR 0.35, 95% CI 0.14 to 0.87) and also 8-MOP plus sunlight versus psoralen (RR 2.50, 95% CI 1.06 to 5.91); Ermis 2001 found calcipotriol plus PUVA group resulted in a higher likelihood of achieving greater than 75% repigmentation sooner than placebo plus PUVA (paired OR 4.25, 95% CI 1.43 to 12.64); and finally Khandpur 2005 showed a result in favour of split skin grafts plus PUVAsol versus mini punch grafts plus PUVAsol (RR 1.89, 95% CI 1.25 to 2.85).

We were only able to carry out one meta-analysis of three studies (Bhatnagar 2007, Yones 2007, Sapam 2012) for this outcome, in which 60% more participants achieved >75% repigmentation in favour of NB-UVB compared to Psoralen plus UVA. This was not statistically significant (RR 1.60, 95% CI 0.74 to 3.45; $I^2 = 0\%$).

Adverse effects

Most of the studies included in the updated search assessed adverse effects (33/39 new studies; 84%). Most studies examining topical corticosteroids reported adverse effects including folliculitis, burning, mild pruritus, dryness, mild erythema, atrophy, telangiectasia and acneiform lesions. Wazir 2010, however, reported no adverse effects in participants treated with 0.01% mometasone furoate. Similarly, Bayoumi 2012 reported no adverse effects with hydrocortisone butyrate.

Adverse effects of topical tacalcitol included itching, transient erythema, desquamation and contact dermatitis at the site of application. Most studies that examined the use of topical calcineurin inhibitors used 0.1% tacrolimus ointment and the main adverse effects reported were a burning sensation, pruritus, erythema, atrophy and facial flushing after alcohol intake. Köse 2010 and Stinco 2009 used 1% pimecrolimus and similar adverse effects were reported. No adverse effects were reported in the studies that looked at pseudocatalase, except for Bakis-Petsoglou 2009 who reported some adverse effects although it is not clear if this was in the placebo or pseudocatalase group. Asawanonda 2010 reported similar rates of adverse effects in participants treated with tetrahydrocurcuminoid cream and NB-UVB to those treated with NB-UVB alone.

With regard to oral therapies, both studies which looked at vitamin E supplementation in combination with other therapies reported lower frequencies of side effects in the vitamin E supplementation group.

In terms of light therapy, new PUVA studies reported adverse effects similar to those previously reported such as erythema, pruritus, nausea, dizziness and thickening of the skin. Sapam 2012 reported that adverse effects were more common in the PUVA group in comparison to the NB-UVB group and two participants in this study discontinued oral PUVA therapy due to severe dizziness. Similar adverse effects were reported with BB-UVA, particularly with low-dose BB-UVA, which included itching, burning, erythema and thickening of the skin. With regard to NB-UVB, phototoxic reaction and Koebnerisation have been reported as well as transient itching and dryness of the skin in several older studies. Bansal 2013 assessed oral psoralen with NB-UVB (P-NB-UVB) versus NB-UVB alone. Nausea was reported in the P-NB-UVB group, and a phototoxic reaction, depigmentation and hyperpigmentation in both groups. Curiously, a meta-analysis of adverse events showed a significantly greater risk of nausea for NB-UVB than for PUVA (RR 0.13, 95% CI 0.02 to 0.69). This is unexpected, as the addition of psoralen is expected to cause nausea in some people but NB-UVB does not characteristically produce nausea.

Surgical interventions such as punch grafts or minigrafts sometimes led to adverse effects such as cobblestoning, scarring, graft depigmentation, and graft displacement. Suction blister grafts or split skin grafts led mainly to the Koebner phenomenon, which, because it triggers new vitiligo lesions as a result of damage to the skin, is of major clinical importance. It can also cause hypopigmentation, or, to a lesser extent, hyperpigmentation, scarring, and infection at both donor and recipient sites. In the Sahni 2011 study, a halo phenomenon, infection at the recipient site and hyperpigmentation were observed in both treatment groups. Scarring at the donor site was only observed where melanocytes were suspended in normal saline, although the scarring is unlikely to be related to the suspension process and this difference between groups was probably due to the small numbers of participants.

With regard to dermabrasion, delayed healing, oedema and hypertrophic scars have been reported as well as a mild burning sensation reported with microdermabrasion. Purpura was reported as an adverse effect of needling, although this cleared rapidly. All participants undergoing fractional CO2 laser reported pain and burning sensation during laser treatment, and erythema or oedema after laser treatment.

Secondary outcomes

Cessation of spread of vitiligo

Six studies assessed the secondary outcome of cessation of spread of vitiligo or stabilisation of the disease. This is defined as no increase in the size of individual vitiligo patches measured objectively within a period of a) less than one year or b) one year or more. These studies were: (Agarwal 2005; Barman 2004; Dawid 2006; Lim-Ong 2005; Parsad 2003b; Siddiqui 1994), all of which were included in the last update of the review.The only study to show the superiority of active intervention over placebo was by Parsad 2003b, in which participants receiving oral *Ginkgo biloba* were more than twice as likely to achieve cessation of spread than those receiving placebo.

Long-term permanence of repigmentation

None of the studies was able to demonstrate long-term repigmentation as specified in our secondary outcomes (i.e. at two years' follow-up).

Overall completeness and applicability of evidence

Most of the studies in this review update have small numbers of participants, due mainly to the large numbers of intra-participant studies (40/96, 42%), of which 14 (35%) are surgical studies. The smallest number of participants in any study was six (Wind 2011) and the largest was 596 (Pathak 1984). As with the original review, the majority of studies differ greatly in the ways in which vitiligo is measured and in the myriad combination interventions assessed. As a result, with the exception of one meta-analysis, it was not possible to pool data and so we have had to report the data from individual studies. As well as these data being harder to digest, it is difficult to make any firm inferences from them in respect of recommendations for clinical practice. With regard to the studies with an intra-participant design, it was not possible to calculate the appropriate test statistic for many of these studies because of inadequate data, so we made the decision that to describe them narratively was not going to be of value in such a huge review as these studies are unlikely to be pivotal

In the last review update, we suggested that, given the impact vitiligo has on quality of life (Ongenae 2005a), patient-centred outcomes should be incorporated into the study design. More studies in this review update addressed the primary outcome of patient-rated quality of life. However, such studies are still in a minority; just over 9% (9/96) studies (Akdeniz 2013; Agarwal 2005; Budania 2012; Middelkamp-Hup 2007; Papadopoulos 2004; Sahni 2011; Sassi 2008; Singh 2013; Yones 2007) addressed this and in only one study (Papadopoulos 2004) was this a primary outcome. Successful treatment as measured by more than 75% repigmentation in affected areas of skin, which was another primary outcome, was assessed in 56% (54/96) of the studies. Five further studies (Bakis-Petsoglou 2009; El Mofty 2013b; El-Zawahry 2012; Kandil 1974; Leone 2006) reported numbers of participants achieving higher percentages of repigmentation than 75%, but it was not possible to determine the number of participants achieving 75% repigmentation, so data from these studies were not included in our analyses. More than 67% (65/96) of the studies assessed our final primary outcome (adverse effects).

Some studies did not specify greater than 75% repigmentation as an outcome measure, but instead assessed higher levels of repigmentation, whilst others considered greater than 50% repigmentation to be a good response. It is difficult to know precisely what constitutes a 'good' or 'successful' response, especially from the patient's perspective. Arbitrary cut-offs such as 75% have traditionally been used, but it is questionable as to whether this is really meaningful for people with vitiligo. Work to develop patient-rated outcome measures is a priority for ongoing vitiligo research.

Of our secondary outcomes, cessation of spread of vitiligo or stabilisation of the disease, was only reported in 6% (6/96) of the studies (Agarwal 2005; Barman 2004; Dawid 2006; Lim-Ong 2005; Parsad 2003b; Siddiqui 1994), all of which were in the last update, so no new studies addressed this outcome. Only one study (Wind 2011) assessed permanence of repigmentation after treatment, but

only after one year follow-up and the data were presented in a manner such that they could not be interpreted.

In the case of natural phototherapy or sun exposure, variable factors including the compliance of the participant, the degree of exposure, and the country where the trial is conducted, can limit the interpretation and applicability of results. On the other hand, more reliable forms of light therapy such as UV devices are not always accessible or feasible, especially in developing countries.

The majority of studies included participants with symmetrical vitiligo but only one (Kathuria 2012) included participants with only segmental vitiligo. Sixteen studies included participants with any type of vitiligo. Only seven studies were carried out specifically on children (Farajzadeh 2009; Ho 2011; Hui-Lan 2009; Khalid 1995; Köse 2010; Lepe 2003 Ruiz-Maldonado 1975), despite the fact that the onset of vitiligo before the age of 20 has been observed in a large proportion of the population (Lindhorst Homan 2008).

A large number of studies (40) used an intra-participant design, 14 (35%) of them were surgical studies. This design can have implications for the applicability of findings, especially for topical interventions, as it is not always possible to exclude systemic effects of different interventions used within the same participant.

Quality of the evidence

Overall, the quality of the studies included in this review was very mixed. Since the last update of the review published in 2010, there has been a further increase in the number of randomised controlled trials (RCTs) assessing interventions for vitiligo. There has also been a small but noticeable improvement in the quality of the design of some of the more recent studies, although the methodological quality of studies is still highly variable. Awareness of the importance of good reporting of trials, such as that proposed in the CONSORT statement (Begg 1996), is increasing, and this is reflected in the quality of reporting in a few, but by no means all, of the studies in this updated review.

Regarding the quality of methodology and reporting, adequate randomisation was reported in 61% (59/96) of the included studies, which is slightly better than for the last update (56%). Nearly 18% (17/96) reported allocation concealment adequately (fewer than for the last update; 21%). Participants were blinded in nearly 20% (19/96) of the studies; clinicians were blinded in nearly 18% (17/96) of the studies and independent assessors were blinded in 39% (38/96) of the studies. In some studies, blinding was not always possible due to the nature of some of the interventions (e.g. surgical interventions) and the intra-participant design of many of the studies could make blinding difficult. However, other aspects of study quality were very good.

The majority of trials reported dropouts of less than 10%, and only two studies (Pathak 1984; Sharquie 2005) reported more than 50% dropouts. Intention-to-treat analysis was performed in 43% (41/96) of the studies. However, only 10 of these studies reported dropouts, and the other 31 were intention-to-treat 'by default'.

We found five trials (Bakis-Petsoglou 2009; Ho 2011; Mehrabi 2006; Sanclemente 2008; Van Geel 2004) of high quality that described randomisation, allocation concealment, blinding, and ITT adequately and were judged at low risk of bias for all these domains.

Potential biases in the review process

For the new studies in this review update, if the method of randomisation was unclear we tried to seek clarification from the study authors. In the original review, all studies that were described as randomised were accepted as such. If the methods of randomisation were unclear, this was simply recorded but no further clarification was sought. This could potentially introduce some bias into the review process.

This review aimed to provide comprehensive evidence on all interventions, including non-conventional medicines such as Traditional Chinese Medicine (TCM), for treating vitiligo. However, we did not specifically search Chinese bibliographic databases to identify such studies. As a result, we may have missed relevant studies assessing interventions such as TCM.

There are some other limitations of this review: We were not able to assess for publication bias, due to the small number of studies assessing similar interventions. We also did not assess sources of funding for individual studies, which can have implications for the risk of bias in the studies that we have included.

Agreements and disagreements with other studies or reviews

A systematic review (Wu 2009) which looked at the safety and efficacy of topical calcineurin inhibitors (pimecrolimus and tacrolimus) in the treatment of vitiligo, concluded that a combination of tacrolimus and monochromatic excimer light (MEL) could improve the efficacy of vitiligo treatment. It also reported that the combination of pimecrolimus and MEL shortens the number of treatments needed to initiate repigmentation and works better on the face. We are unable to support these findings, as our Cochrane review, which identified studies assessing these interventions, and many more studies and types of interventions, had limited evidence of effect for any intervention.

Szczurko 2008 assessed natural health products such as vitamins, herbs, and other supplements for the treatment of vitiligo, and included 15 randomised or non-randomised controlled studies. In common with our review, the studies were of poor methodological quality and the authors did not pool data for meta-analysis due to the number of different outcome measurements and quality of reporting, although L-phenylalanine combined with phototherapy and oral *Ginkgo biloba* monotherapy were potentially promising interventions. Our review update found evidence of benefit from G*ingko biloba* but we would be cautious about making any firm inferences from this single study (Parsad 2003b).

Another systematic review of studies retrieved from searches of nine databases between 1990 and 2010, (Chan 2012) reported the effectiveness of therapeutic interventions on the quality of life of vitiligo patients. All treatments that improved physical appearance by repigmentation or directly addressed psychological distress improved the quality of life of patients to some degree. However, the authors concluded that current interventions alone were not successful in addressing all the quality of life challenges faced by people with vitiligo. We can concur with this finding as the majority of studies do not really assess this important outcome adequately, if at all.

A systematic review (Eleftheriadou 2012) of the outcome measures used in RCTs was compared with outcomes suggested by patients

and clinicians used in vitiligo trials. Repigmentation was assessed in 96% of the studies but 48 different scales were used to measure it. The most important outcome for patients and clinicians was cosmetically acceptable repigmentation (rather than percentage of repigmentation) (68%), followed by cessation of spread of vitiligo (15%), quality of life (8%) and maintenance of repigmentation (4%). There is a lack of consensus on core outcome measures and Vrijman 2012 in a systematic review, recommended an e-Delphi approach to agree on terminology, and to define core outcome domains which should enable easier comparisons between studies.

Mulekar 2013 conducted a systematic review of surgical therapies for vitiligo and included searches of PubMed, MEDLINE and Cochrane databases. Split thickness skin grafts had the highest repigmentation success rate but more RCTs of surgical interventions for vitiligo as well as a standardised objective method of assessing repigmentation are needed.

A more recent systematic review (Xiao 2014) assessed seven studies of combinations of NB-UVB with other treatments in the intervention groups and the control groups. The authors concluded that "NB-UVB showed equivalent efficacies to UVA, PUVA or 308-nm EL control in the treatment of vitiligo. Side effects of NB-UVB were acceptable. More RCTs were needed to validate the results." Although we cannot support these findings, the evidence from our review suggests that combination therapies, particularly those involving some form of light, are superior to monotherapies.

The other reviews and studies we found are broadly in agreement with our findings, particularly those statements concerning the effectiveness of any intervention for vitiligo, the need for better quality of study design and reporting, and in particular, the use of patient-important standardised outcome measures.

AUTHORS' CONCLUSIONS

Implications for practice

Although some consensus exists among researchers as to the causes of vitiligo, there is still a wide variety of theories and so the trials performed in recent years examine a wide range of interventions. It is important to stress that, at present, there is neither a cure for vitiligo nor an effective method of limiting the spread of the disease. Current treatment practices tend to centre on whatever theory is believed to be the most important while newer, more controversial ideas take time to become established. The small numbers of participants and heterogeneity of design of the studies in this review makes it difficult to make firm statements regarding recommendations for clinical practice.

The ever-expanding range of interventions being assessed in vitiligo randomised controlled trials (RCTs) is perhaps a reflection of the fact that there are still no interventions which are obviously superior to others. Of the interventions intended to induce repigmentation, we found low-quality RCT evidence for a number of different interventions that produce a varying degree of repigmentation of unknown long-term permanence.

There is moderate evidence for the use of topical corticosteroids, although long-term use is likely to lead to adverse effects. When used as monotherapy, it may be preferable to use superpotent preparations to give a better chance of therapeutic response, but close monitoring for adverse effects will be necessary. The topical immunomodulator, tacrolimus, seems to be a reasonable alternative to topical corticosteroids, particularly on anatomical sites where there may be a higher risk of adverse effects with topical corticosteroids. Although clinical advice has usually been to exercise caution when combining topical immunomodulators with light therapies, due to the theoretical long-term risk of skin cancer, these combinations may have benefit if used under close medical supervision.

In general, combination interventions were superior to monotherapies; the majority of analyses giving significant results were in favour of various combination treatments. Most of the studies that assessed combination interventions employed light therapies (UVA, PUVA, or UVB, particularly NB-UVB) and laser light therapies. Our search uncovered limited to moderate evidence for various types and regimens of light therapy (UVA and UVB) used alone or in combination with psoralens, topical corticosteroids, vitamin D analogues, 5-fluorouracil, azathioprine, and oral prednisolone, although adverse effects were common with the latter. There is some evidence that excimer laser is more effective in combination with topical interventions such as hydrocortisone 17-butyrate, tacrolimus, or tacalcitol. There is also limited evidence for the benefit of oral *Ginkgo biloba*, and split thickness skin grafts plus PUVAsol. Surgical therapies can be effective for small areas in people with stable disease. Clinicians should bear in mind that suction blister grafts may result in adverse effects, the most significant of which is precipitation of new areas of vitiligo at donor sites, due to the Koebner phenomenon. Autologous transplantation of melanocytes is a promising novel therapy, giving superior cosmetic results compared to more conventional surgical therapies, but access to this treatment may be limited.

Although there is empirical evidence in the literature to support the use of cosmetic camouflage to improve the quality of life of people with vitiligo, we found no trials of this intervention. Depigmentation is sometimes used in severe cases of vitiligo but we found no RCTs of this intervention either. There may also be some people who require more in-depth psychological support. As with the previous update, we found only one RCT comparing the use of cognitive-behavioural therapy and person-centred approaches and this study found little support for any particular psychological intervention; we could not perform statistical analysis of the study data. As things stand, although there is limited evidence for this kind of intervention anecdotal evidence strongly suggests that a form of psychological intervention or support could be of benefit to some individuals.

Although vitiligo commonly presents before the age of 20 years, only seven of the 96 included studies looked specifically at interventions for vitiligo in children. The remainder of the studies either included adults alone or had no specified age. Treatment in children is limited by compliance, tolerance of treatment and concerns regarding long-term side effects. None of the studies had long-term follow-up beyond two years. These seven studies looked at a range of interventions including topical treatments such as tacrolimus and corticosteroids, NB-UVB, PUVA, 308-nm excimer laser and dermabrasion. Stigmatisation can be a particular problem in children with vitiligo and treatment options beyond topical therapies should be explored after a discussion regarding side effects, effectiveness and impact on quality of life. Although further evidence is required, psychological and cosmetic

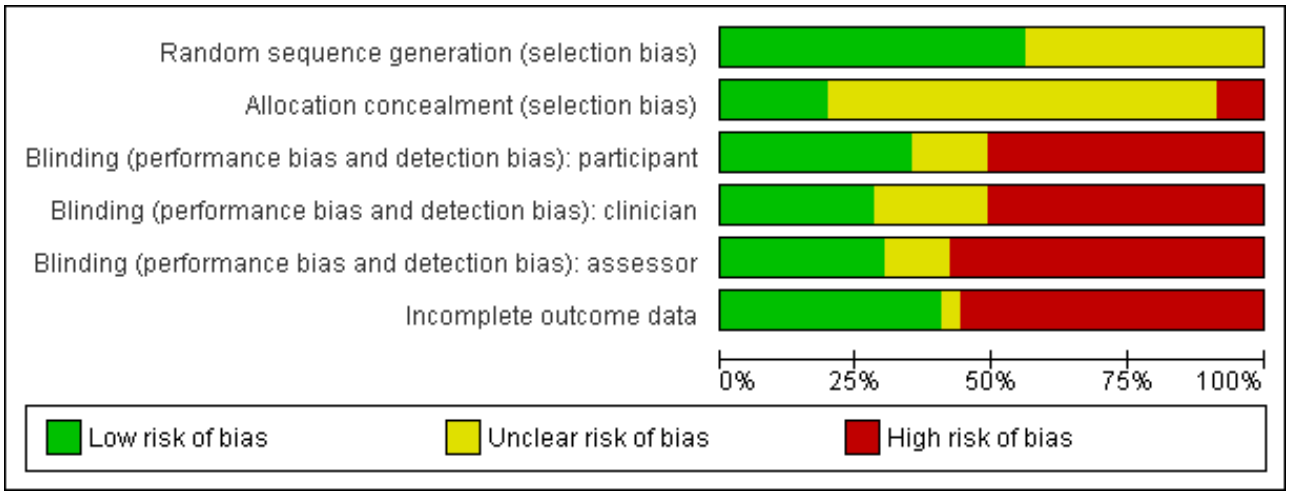
interventions may be of particular benefit in this population of patients.

Implications for research

Since the original review was carried out in 2006, there has been a rapid increase in the number of clinical trials, particularly randomised controlled trials, assessing interventions for vitiligo. However, it is still not clear which are the best interventions for this condition. Until the causes of vitiligo are better understood, treatments will continue to be based on the many theories that exist for this disease. Although there has been a noticeable increase in basic scientific research, more investment is needed so that new discoveries in experimental models can be systematically advanced to preclinical and clinical stages.

- Standardised methodologies for describing and classifying vitiligo and for assessing the effect of interventions need to be developed and used by trial investigators. The establishment of a Vitiligo European Task Force (VETF; Taïeb 2007) is an important step in this direction and the work of this group should hopefully lead to studies measuring repigmentation in a more standardised way. However, many studies still use their own measures, so the work of the VETF group needs to be disseminated as widely as possible.
- There is also a general need for better quality RCTs of treatments for vitiligo. Overall, it seems that there has been only a slight improvement in the quality of the methodology of RCTs since the last update of this review (Figure 3), and since the publication of the "Guidelines for Designing and Reporting Clinical Trials in Vitiligo" (González 2011), which were based on the last update.

Figure 3. Methodological quality graph (review authors' judgements about each methodological quality item presented as percentages across all included studies) of the last version of the review (Whitton 2010)



- Specific recommendations from the "Guidelines for Designing and Reporting Clinical Trials in Vitiligo" (González 2011), which should be followed in order to ensure the best design and reporting of any future vitiligo trials, include the following.

1. Participants: Clear description of inclusion and exclusion criteria; clear description of baseline characteristics of participants; clear description of study setting.
2. Interventions: Adequate description of intervention(s); adequate choice and description of control group; adherence to treatment should be measurable and reported.
3. Outcomes: Adequate follow-up (at least one year) and frequency of data recording; standardised definition of treatment effect and measurement scales; clear definition of primary, patient-centred outcomes, including quality of life measured using a validated tool and percentage repigmentation; clear definition of secondary outcomes, including cessation of spread or stabilisation of the disease and long-term permanence of repigmentation. (There is currently an international group developing an agreed set of core outcomes for vitiligo trials, as part of the COMET initiative.)
4. Study design: Adequate generation of randomisation sequence and concealment; detailed description of methodology of blinding of assessors and participants; calculation of sample size; clear reporting of losses to follow-up and analysis of the total number of randomised participants.
5. Data reporting: should follow CONSORT reporting guidelines.

- Study design should take into account variations in participant features, including skin colour, age or duration of the disease, extent and type of vitiligo, as well as the site of affected areas. These factors may determine the applicability of results in particular clinical settings and may cause the response to treatment to vary. There should also be larger, multi-centre studies and fewer intra-participant studies to allow comparison and meta-analysis.
- Melanocytes are slow to grow and develop, so in order to properly assess the efficacy of an intervention, interventions should ideally be continued for long enough to allow complete repigmentation; this may need to be at least six months and possibly up to a year.
- Cessation of spread of vitiligo and long-term permanence of repigmentation are very important outcome measures for people with vitiligo. Future studies should include these outcomes and should ideally include at least two-years' follow-up of participants.
- Patient-rated outcome measures (especially measures of treatment success) should be incorporated into the design of future studies. Further work is needed to develop and validate

suitable outcome measures that are meaningful to patients (Eleftheriadou 2012).

- The inclusion of health-related quality of life measures such as the VitiQOL scale and the Dermatology Life Quality Index would not only improve the relevance of trials but could allow comparison between trials using different interventions.
- More studies are needed to establish the dosage, safety, and long-term efficacy of NB-UVB monotherapy in treating vitiligo. In particular, the possibility of long-term skin damage and possible skin cancer following prolonged UV treatment for vitiligo needs to be researched.
- Topical tacrolimus appears to have a similar effect to topical corticosteroids, but with a better safety profile (Ho 2011). More studies are needed to establish it as a viable, cost-effective alternative, particularly in combination with other interventions (e.g. light therapies).
- Larger studies are needed in order to provide stronger evidence for the many combination interventions that have shown promise in treating vitiligo. Because vitiligo is a disease affecting pigment cells, the use of some form of phototherapy may be necessary in order for these cells to proliferate and develop, thus giving faster repigmentation. Combination therapy may therefore be more desirable from both a clinician and participant point of view.
- Although there are some studies of complementary or psychological interventions at present, a greater number of well-conducted RCTs in these areas would provide more useful evidence for their efficacy. Psychological interventions are particularly important in view of the fact that the main symptoms of vitiligo are not physical but psychosocial.
- Studies are needed on the use of cosmetic camouflage, which is often recommended with no other treatment. Although it helps to disguise the condition and can give some degree of self-confidence, it cannot be used on large affected areas of skin and has to be reapplied frequently. It can also create anxiety in those whose vitiligo is actively spreading. There is no good evidence to show that cosmetic camouflage improves the quality of life of people with vitiligo in the long term.

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Whitton ME, Batchelor J, Lushey C, Leonardi-Bee J, González U. Interventions for vitiligo. *Cochrane Database of Systematic Reviews* 2010, Issue 1. [DOI: 10.1002/14651858.CD003263.pub4]

* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Agarwal 2005

Methods	A randomised, placebo-controlled, double-blind, parallel study lasting 6 months.
Participants	**Inclusion criteria of the trial** • Vitiligo of any type • < 2% involvement and slow spreading (5 new lesions in previous month or 6 to 15 in previous 3 months) **Exclusion criteria of the trial** • Segmental vitiligo • Leucopenia • Preganant women • Those who had received systemic steroids or other immune suppressants in 2 months before trial or PUVA I or topical therapy in previous month

Agarwal 2005 *(Continued)*

	60 participants (32 intervention, 28 control) with slow spreading symmetrical vitiligo affecting less than 2% of their body surface area. Slow spreading was defined as 5 new lesions in the previous month or 6 to 15 in the previous 3 months. The age of the adult participants was not reported, however the children were aged between 6 and 12 years old, and 18 were male and 15 were female. 17 participants were lost at follow-up (9/32 = 28% in the intervention group; 8/28 in the control group = 29%), resulting in 43 participants evaluated (23 intervention and 20 control). This study was conducted in India.
Interventions	**Intervention** **A:** oral levamisole (150 mg for adults and 100 mg for children) on 2 consecutive days in a week plus mometasone furoate cream (0.1%) once a day. **Control Intervention** **B:** oral placebo plus mometasone furoate cream once a day.
Outcomes	**Pimary outcomes of the trial** 1) Cessation of spread of vitiligo. 2) Quality of life measured using the Dermatology Life Quality Index (DLQI), the Children's Dermatology Life Quality Index (CDLQI), and the World Health Organization Quality of Life Brief Questionnaire. 3) Adverse effects. Measured pre- and post-treatment (6 months).
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 164): "A colleague not associated with the study generated the allocation sequence for blocks of 10 patients using a random number table. A separate sequence was generated for children."
Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	Low risk	Participants were blinded. Quote (page 164): "Participants were given numbered containers with levamisole or placebo tablets. One group received oral levamisole 150 mg...The other group received placebo tablets of the same size and shape as levamisole."
Blinding (performance bias and detection bias) clinician	Unclear risk	Investigator probably blinded but not clearly stated in the text.
Blinding (performance bias and detection bias) assessor	High risk	No separate outcome assessor mentioned.
Incomplete outcome data	High risk	Intention-to-treat analysis was not used. Intervention- A: 9 dropouts (reasons: unknown reasons (5), discontinued intervention (rapid progression of vitiligo) (3), and side effects (1))

Agarwal 2005 *(Continued)*

	Control- B: 8 dropouts (reasons: unknown reasons (5), discontinued intervention (rapid progression of vitiligo) (1), and did not complete 6 months of therapy (2))

Akdeniz 2013

Methods	Randomised parallel group study lasting 6 months.
Participants	**Inclusion criteria** • Patients with NSV • With involvement of lesion larger than 10% of the body area • Who had received no treatment except moisturising cream and sun cream **Exclusion criteria** • Patients with cataracts • Liver and/or kidney dysfunction • Pregnancy • Hypercalcaemia • Hypercalciuria and kidney stones • Patients with malignancy • Patients with a history of photosensitivity or photosensitive disorders 45 patients were included in this study, 20 males and 25 females. Participants were aged between 13 and 55. 15 participants were assigned to each group.
Interventions	**A:** combination of topical calcipotriol, NB-UVB, and betamethasone therapies. **B:** combination of NB-UVB and topical calcipotriol. **C:** NB-UVB alone.
Outcomes	**Primary outcomes of the trial** 1) Percentage improvement in repigmentation. Repigmentation improvement was evaluated as follows: poor ≤ 25%, moderate = 26% to 50%, good = 51% to 75% and excellent ≥ 75%. 2) The quality of life was evaluated on pre-treatment and post-treatment by the Dermatology Life Quality Index (DLQI). 3) Visual Analogue Scale (VAS) (0 to 10, 0 = absent, 10 = worst vitiligo) was used to measure the patients' subjective view of the impact of living with vitiligo. The repigmenting effects of the therapies were also measured with VAS by the patients with vitiligo.
Notes	No mention of the adverse effects. No explanation of how successful therapy was evaluated

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 4): "The participants were randomized over the three treatment regimes." Comment: Insufficient detail was reported about the method used to generate the allocation sequence.

Akdeniz 2013 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	High risk	Participants were not blinded.
Blinding (performance bias and detection bias) clinician	High risk	Clinicians were not blinded.
Blinding (performance bias and detection bias) assessor	High risk	Outcome assessors were not blinded.
Incomplete outcome data	Low risk	Intention-to-treat analysis was used. No dropouts.

Akhyani 2005

Methods	Randomised parallel group study lasting 9 months.
Participants	**Inclusion criteria of the trial** • Generalised vitiligo with BSA of more than 15% and less than 40% involvement **Exclusion criteria of the trial** • Pregnant or nursing • Segmental vitiligo • Treatment received in the previous three months • Unusual response to PUVA • Under treatment with calcium or vitamin K • History of allergy to calcipotriol. 55 participants with generalised vitiligo and more than 15% of their body surface area affected by vitiligo, but less than 40%. Participants were aged over 15 years of age. The intervention group consisted of 25 participants and the control group included 30 participants. Those in the intervention group had a mean age of 28.9 years (SD 3.9) and 8 were male and 13 female. Those in the control group had a mean age of 31.2 years (SD 3.1) and 12 were male and 14 female. 8 participants were lost at follow-up (4/25 = 16% in the intervention group; 4/30 = 13% in control group), which resulted in 47 evaluable participants. This study was conducted in Iran.
Interventions	**Intervention** **A:** topical calcipotriol (0.005%) plus PUVA. Participants took 0.5 mg/kg methoxsalen orally 2 hours before UVA, which was administered 3 times a week. The calcipotriol cream was applied half an hour after UVA. The initial UVA dose was 2 J/cm^2 and this increased by 0.5 J every third session. A maximum of 200 PUVA sessions were delivered. **Control Intervention**

Akhyani 2005 *(Continued)*

	B: PUVA only. Participants took 0.5 mg/kg methoxsalen orally 2 hours before UVA, which was administered 3 times a week. The initial UVA dose was 2 J/cm^2 and this increased by 0.5 J every third session. A maximum of 200 PUVA sessions were delivered.
Outcomes	**Primary outcomes of the trial** 1) Mean repigmentation. Measured pre-and post-intervention (6 months).
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (Abstract): " 47 patients with generalized vitiligo were randomly assigned to 2 treatment groups." Comment: Insufficient detail was reported about the method used to generate the allocation sequence. We e-mailed the author on 03/03/09 and they reported that they used a randomisation table.
Allocation concealment (selection bias)	High risk	This was not stated in the abstract. Comment: We e-mailed the author on 03/03/09 and they reported that they did not perform allocation concealment.
Blinding (performance bias and detection bias) participant	High risk	Participants were not blinded. Comment: We e-mailed the author on 03/03/09 and they reported that the study was open.
Blinding (performance bias and detection bias) clinician	High risk	Clinicians were not blinded. Comment: We e-mailed the author on 03/03/09 and they reported that the study was open.
Blinding (performance bias and detection bias) assessor	High risk	Outcome assessors were not blinded. Comment: We e-mailed the author on 03/03/09 and they reported that the study was open.
Incomplete outcome data	High risk	Intention-to-treat analysis was not used. Intervention- A: 4 dropouts (reasons: moved from Tehran (2) and intolerance to oral methoxsalen (2).) Control- B: 4 dropouts (reasons: moved from Tehran (4).)

Anbar 2008

Methods	Randomised, double-blind, within-participant, left/right comparison study lasting 4 months.
Participants	**Inclusion criteria of the trial** • Patients with non-segmental vitiligo who had more or less symmetrical lesions **Exclusion criteria of the trial**

Anbar 2008 *(Continued)*

	• Face lesions that are known to have good and rapid response to conventional treatment modalities • Pregnant or lactating females • Patients with segmental vitiligo 50 participants (24 male, 26 female) with symmetrical vitiligo and with more or less symmetrical lesions, aged between 17 and 54 years old (mean 30.7). 1 person was lost to follow-up. This study was conducted in Egypt.
Interventions	**Intervention** **A:** Er-YAG laser ablation, followed by 5-fluorouracil (5FU) application and NB-UVB therapy twice a week (never on 2 consecutive days). The initial dose was 0.21 J/cm^2 and this increased by 20% every session until mild erythema was reached that disappeared the next day of the session. **Control Intervention** **B:** NB-UVB therapy delivered twice a week (never on 2 consecutive days). The initial dose was 0.21 J/cm^2 and this increased by 20% every session until mild erythema was reached that disappeared the next day of the session.
Outcomes	**Primary outcomes of the trial** 1) Repigmentation: mild (< 25%), moderate (26% to 75%), and marked (> 75%). Measured at baseline, monthly and post-treatment (4 months). 2) Adverse effects
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 323): "Treatment sides were randomly chosen." Comment: Insufficient detail was reported about the method used to generate the allocation sequence. We e-mailed the author who replied the following "The method of randomisation used in our study was the random number allocation of patients and this was designed before the start of the study."
Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	High risk	Participants were not blinded. Comment: Type of intervention and left/right design makes blinding impossible.
Blinding (performance bias and detection bias) clinician	High risk	Clinicians were not blinded. Comment: Type of intervention and left/right design makes blinding impossible.
Blinding (performance bias and detection bias) assessor	Low risk	Outcome assessors were blinded. Quote (page 323): "Estimation of the response was performed by 2 independent dermatologists."
Incomplete outcome data	High risk	Intention-to-treat analysis was not used.

Anbar 2008 *(Continued)*

	Because it is a within-participant study there was 1 dropout in both groups (reason quote (page 324): "1 participant developed inflammatory reactions after she mistakenly applied 5FU cream for 8 days, an incident that necessitated discontinuation of therapy. Therefore this participant was excluded from further analysis")

Arca 2006

Methods	A randomised, parallel group study lasting 10 weeks.
Participants	**Inclusion criteria of the trial** • Patients with stable vitiligo, defined as where symptoms had not changed for one year. • > 10% involvement **Exclusion criteria of the trial** • Hypercalcaemia, hypercalciuria, thyroid or parathyroid disease • Pregnancy • Concomitant use of vitamin D or calcium homeostasis • Less than 10% involvement • Known sensitivity to calcipotriol • Segmental vitiligo 40 participants (15 intervention, 25 control) with stable (defined as 'no change in symptoms for one year') symmetrical vitiligo affecting less than 10% of their body surface area. All participants were male. 3 participants were lost at follow-up (2/15 = 13%; 1/25 = 4%), resulting 37 evaluated (13 intervention, 24 control). The mean age was 21.95 years for the control group and 21.50 for the intervention group. The duration of the condition was 9.70 years for the control group and 5.65 for the intervention group. This study was conducted in Turkey.
Interventions	**Interventon** **A:** NB-UVB plus topical calcipotriol (0.05%). Therapy was administered 3 times a week and the initial dose was 100 mj/cm^2 followed by increments of 50 mj/cm^2 on non-consecutive days. The calcipotriol was applied twice a day **Control Interventon** **B:** NB-UVB alone. Therapy was administered 3 times a week and the initial dose was 100 mj/cm^2 followed by increments of 50 mj/cm^2 on non-consecutive days.
Outcomes	**Primary outcomes of the trial** 1) Repigmentation: minimal (0% to 24%), moderate (25% to 49%), and marked to complete (50% to 100%). 2) Reduction in percentage of body surface area affected. 3) Adverse effects. Measured pre-and post-treatment (10 weeks).
Notes	-
Risk of bias	

Arca 2006 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 339): "The patients were randomised into two NB-UVB treatment groups." Comment: Insufficient detail was reported about the method used to generate the allocation sequence.
Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	High risk	Participants were not blinded.
Blinding (performance bias and detection bias) clinician	High risk	Investigator blinding not specifically mentioned. Comment: Blinding impossible because only 1 group of participants received topical treatment.
Blinding (performance bias and detection bias) assessor	High risk	No separate outcome assessor mentioned.
Incomplete outcome data	High risk	Intention-to-treat analysis was not used. Intervention- A: 2 dropouts due to personal reasons. Control- B: 1 dropout due to personal reasons.

Asawanonda 2008

Methods	This is a randomised, double-blind, within-participants study lasting 12 weeks.
Participants	**Inclusion criteria of the trial** • Age ≥ 16 years • Stable focal or generalised vitiligo ('Stable' defined as no repigmentation, or new depigmentation within 8 weeks of recruitment) • Lesions in sun-protected areas, within the same anatomical area, and on the same side of the body, chosen as preferred study patches.If this was not possible, then lesions symmetrically located in contralateral areas were allowed. **Exclusion criteria of the trial** • History of skin cancer or photosensitive conditions (e.g. xeroderma pigmentosum, solar urticaria, chronic actinic dermatitis or lupus erythematosus) • Pregnant or lactating 10 participants (3 males, 7 females) with stable, focal, or generalised vitiligo aged between 22 and 66 years old (mean 41.8). 5 of the participants had been affected by vitiligo for between 0 and 5 years, 3 for 6 to 10 years, 11 for 11 to 15 years and 1 for 16 to 20 years. 3 participants were lost at follow-up, but all were included in the analysis. This study was conducted in Thailand.
Interventions	**Intervention**

Asawanonda 2008 *(Continued)*

	A: BB-UVB twice weekly on non-consecutive days. Dose was 100 mJ/cm² delivered within approximately 0.7 seconds through a square aperture measuring 1.9 x 1.9 cm. Dose increased by 10% if no erythema, 5% if erythema was mild, and no increment if erythema lasted for more than 24 hours. If erythema was significant treatment was skipped. **Control Intervention** **B:** NB-UVB twice weekly on non-consecutive days. Dose was 100 mJ/cm² delivered within approximately 0.7 seconds through a square aperture measuring 1.9 x 1.9 cm. Dose increased by 10% if no erythema, 5% if erythema was mild, and no increment if erythema lasted for more than 24 hours. If erythema was significant treatment was skipped.
Outcomes	**Primary outcomes of the trial** 1) Repigmentation: grade 0 (no change), grade 1 (1% to 25%), grade 2 (26% to 50%), grade 3 (51% to 75%) and grade 4 (76% to 100%). 2) Depigmentation: grade -1 (1% to 25%), grade -2 (26% to 50%), grade -3 (51% to 75%) and grade -4 (> 75%). Measured pre-and post-treatment (12 weeks).
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 377): "Lesions were then randomized, using randomization cards, to receive either targeted BB-UVB or targeted NB-UVB."
Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	Unclear risk	Participants likely to be blinded. Quote (page 377): "The irradiation used in this study...was a high-pressure mercury lamp capable of emitting either BB-UVB or NB-UVB via a switch on the hand-piece." Comment: Participants would probably not be aware of which type of irradiation they were getting but no details are provided.
Blinding (performance bias and detection bias) clinician	High risk	Clinicians unlikely to be blinded. Quote (page 377): "The irradiation used in this study...was a high-pressure mercury lamp capable of emitting either BB-UVB or NB-UVB via a switch on the hand-piece." Comment: Clinicians would need to know which type of irradiation to switch to.
Blinding (performance bias and detection bias) assessor	Low risk	Outcome assessors were blinded. Quote (page 377): "Three investigators blinded to the treatment assignment (PA, WS and WK) independently graded the lesions through examining the digital images."
Incomplete outcome data	Low risk	Intention-to-treat analysis was used.

Asawanonda 2008 *(Continued)*

	Because it is a within-participant study there were 3 dropouts in both groups due to difficulties in work scheduling but all were included in analysis.

Asawanonda 2010

Methods	This is a randomised, within-participants study lasting 12 weeks
Participants	**Inclusion criteria of the trial** • Stable non-segmental vitiligo – defined as lesions that have not shown either repigmentation or depigmentation within 2 months prior to enrolment. • At least 18 years of age **Exclusion criteria of the trial** • A history of skin cancer or any photosensitive conditions • Known allergy to curcuminoids 10 participants (4 males, 6 females) with stable vitiligo (defined as lesions that had not shown either repigmentation or depigmentation within 2 months prior to enrolment). Age ranged from 29 to 59 (mean 41.8). 6 patients had been affected by vitiligo for 0 to 5 years, 2 patients for 6 to 10 years and 2 patients for >10 years. 4 patients had generalised vitiligo and 6 patients had localised vitiligo. This study was conducted in Thailand.
Interventions	**Intervention** **A:** targeted NB-UVB phototherapy plus topical tetrahydrocurcuminoid cream. Phototherapy took place twice a week. Tetrahydrocurcuminoid was applied topically twice daily and not before UV light treatment. Initial fluencies were 100mJ/cm^2 followed by 50mJ/cm^2 increments at each successive session, until the very first sign of repigmentation of minimal asymptomatic erythema was observed. **Control Intervention** **B:** targeted NB-UVB alone. Phototherapy took place twice a week. Initial fluencies were 100mJ/cm^2 followed by 50mJ/cm^2 increments at each successive session, until the very first sign of repigmentation of minimal asymptomatic erythema was observed.
Outcomes	**Primary outcomes of the trial** 1) Repigmentation: grade 0 (no change), grade 1 (1% to 25%), grade 2 (26% to 50%), grade 3 (51% to 75%) and grade 4 (76% to 100%). If depigmentation occurred this was graded as: grade -1 (1% to 25%), grade -2 (26% to 50%), grade -3 (51% to 75%) and grade -4 (76% to 100%). 2) Adverse effects. For all outcomes assessments were made pre-and post-treatment (12 weeks).
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 680): “One patch was randomly assigned to be treated with combination therapy (group A) and the other with targeted narrowband UVB alone (group B)."

Asawanonda 2010 *(Continued)*

		Comment: Insufficient detail was reported about the method used to generate the allocation sequence. Thus, we e-mailed the authors who responded that "The lesions were randomized by simple drawing of pieces of paper with numbers 1 (THC + NB-UVB) and 2 (NB-UVB alone)."
Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	High risk	Participants were not blinded. Quote (page 680): "No placebos were used." Comment: No placebos were used so it was very difficult to blind participants
Blinding (performance bias and detection bias) clinician	High risk	Clinicians were not blinded. Quote (page 680): "No placebos were used." Comment: No placebos were used so it was very difficult to blind clinicians
Blinding (performance bias and detection bias) assessor	Low risk	Outcome assessor was blinded. Quote (page 680): "The evaluator blinded to the treatment assignments graded the lesions through projections of the digital images."
Incomplete outcome data	Low risk	Intention-to-treat analysis was used. No dropouts.

Bakis-Petsoglou 2009

Methods	Double-blind, placebo-controlled, randomised, single-centre trial.
Participants	**Inclusion criteria of the trial** • Aged > 18 years • Had 'active' (visible) vitiligo on their face and/or dorsum of hands • Did not react to an application of the cream on their anterior forearm after 24 hours **Exclusion criteria of the trial** • Patients who had received any systemic (specifically quinolone or tetracycline antibiotics, beta-blockers, calcium-channel blockers, immunosuppressants,plasma lipoprotein lowering agents) or radiation therapy in the 2 months and/or topical therapies for 2 weeks preceding the screening visit • Female patients who were pregnant, lactating or not using adequate contraception • Patients with any significant systemic, psychiatric or other dermatological conditions that may compromise the results of the study 32 participants were randomised to either the pseudocatalase arm (n = 14) or placebo (n = 18).
Interventions	**Intervention** **A:** Pseudocatalase cream and NB-UVB. Participants with active vitiligo on their face and/or hands applied pseudocatalase cream to their whole body, twice daily for 24 weeks. NB-UVB therapy was administered three times a week for the duration of the trial. **Control Itervention**

Bakis-Petsoglou 2009 *(Continued)*

	B: Placebo and NB-UVB. Participants with active vitiligo on their face and/or hands applied placebo to their whole body, twice daily for 24 weeks. NB-UVB therapy was administered three times a week for the duration of the trial.
Outcomes	**Primary outcomes of the trial** 1) Efficacy was assessed primarily by digital image analysis of photographs. Between-group analysis did not show a statistically significant improvement in percentage area affected in the pseudocatalase cream group when compared with placebo. A statistically significant improvement was found within each group by week 12, which was maintained throughout the study.
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 911): "Consecutive patient allocation was performed using a central predetermined, computer-generated randomization schedule (Epitag Elite software supplied by Episys Ltd, Royston, U.K.). Randomization was carried out in blocks of six."
Allocation concealment (selection bias)	Low risk	Quote (page 911): "The investigator was supplied with sealed, individual code-break envelopes that were to be opened only in an emergency."
Blinding (performance bias and detection bias) participant	Low risk	Participants were blinded. Quote (page 911): "The active and placebo creams were identical in colour, smell, consistency and packaging."
Blinding (performance bias and detection bias) clinician	Low risk	Clinicians were blinded. Quote (page 911): "The active and placebo creams were identical in colour, smell, consistency and packaging."
Blinding (performance bias and detection bias) assessor	Low risk	Outcome assessor was blinded. Quote (page 911): "The active and placebo creams were identical in colour, smell, consistency and packaging."
Incomplete outcome data	Low risk	Intention-to-treat analysis and per-protocol analysis were used. Quote (page 912-3): "Patients were assessed according to the intention-to-treat (ITT) principle defined as all patients randomized to the study who used at least one dose of study medication or had at least one NB-UVB treatment and who had at least one post-treatment efficacy measurement. A per-protocol population (PPP) analysis was also performed. If the violation was at visits 1 or 2, patients were completely excluded from the PPP." 39 participants enrolled in the study, 7 dropped out prior to commencement of treatment and thus were excluded from the ITT analysis. Intervention- A: 8 dropouts (reasons: prior to commencement of treatment (6); refusal to co-operate (1); personal reasons and changes in domestic/social situations (1)) Control- B: 6 dropouts (reasons: prior to commencement of treatment (1); adverse events (1); refusal to co-operate (2); personal reasons and changes in domestic/social situations (2))

Bansal 2013

Methods	This is a randomised, parallel group study lasting 6 months.
Participants	**Inclusion criteria of the trial** • Patients with vitiligo aged 17 to 30 years. • Had > 5% body surface area involvement and had not been on any topical or systemic treatment in the previous 2 months. **Exclusion criteria of the trial** • Participants who had a history of previous skin malignancy • had received phototherapy or photochemotherapy in the preceding 3 months • Had experienced failure of or intolerance to phototherapy or photochemotherapy • Had received more than 100 sessions of phototherapy or photochemotherapy in their lifetime • Were taking photosensitising drugs • Had a history of photosensitivity or lupus erythematosus • Were pregnant or lactating • Had a history of cardiac/hepatic/renal disease • Had cataracts 45 patients, 19 male and 21 female, were randomised in this trial. 5 patients were lost to follow-up, reasons not stated. There was no intention-to-treat analysis. This study was conducted in New Delhi, India.
Interventions	**A:** NB-UVB 3 weekly for 60 sessions or 6 months, whichever came earlier. Initial dose was 0.33J/cm^2, increased by 20% increments at every subsequent visit if tolerated. Total cumulative dose ranged from 59.9 to 257.9J/cm^2 **B:** Psoralen-NBUVB 3 weekly for 60 sessions or 6 months, whichever came earlier. 8-methoxypsoralen: dose of 0.6 mg/kg body weight, rounded off to the nearest 10 mg, 2h prior to each treatment session. Initial dose of NB-UVB was 0.33J/cm^2, increased by 20% increments at every subsequent visit if tolerated Total cumulative dose ranged from 23.2 to 180.6J/cm^2
Outcomes	**Primary outcomes of the trial** 1) Percentage of Repigmentation assessed by VASI score. The extent of the disease was assessed in terms of % BSA (body surface area) involvement, taking the principal investigator's hand unit as 1% BSA to decrease bias in the study. VASI score was graded as follows: grade 1 (10% repigmentation), grade 2 (25% repigmentation), grade 3 (50% repigmentation), grade 4 (75% repigmentation), grade 5 (90% repigmentation), grade 6 (100% repigmentation). 2) Adverse effects Assessments were made before treatment and after every 20 sessions.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 2): "Patients were randomly allocated to receive either NBUVB or P-NBUVB by means of random number tables"

Bansal 2013 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	High risk	Participants were not blinded.
Blinding (performance bias and detection bias) clinician	High risk	Clinicians were not blinded.
Blinding (performance bias and detection bias) assessor	Low risk	Outcome assessors was blinded. Quote (page 2): "All patients were assessed by the principal investigator, who was not blinded in terms of allocation to study group"
Incomplete outcome data	High risk	Intention-to-treat analysis was not used. Quote (page 3): "Patients who were enrolled in the study but lost to follow-up for any reason were excluded from statistical analysis" There were 5 dropouts of 45 participants in total (11%). Dropouts were not reported by group.

Barman 2004

Methods	Randomised parallel group study lasting 6 months.
Participants	**Inclusion criteria of the trial** • Stable vitiligo, which could be segmental, acrofacial or vitiligo vulgaris which had ceased to respond to treatment with no new lesions or spread of old lesions for more than 6 months **Exclusion criteria of the trial** • Pregnant females • Lactating mothers • More than 5% involvement • History of keloid scarring • Children under 12 years of age. 50 participants (22 in group 1 and 28 in group 2) with static lesions and aged between 13 and 60 years old (mean 22.52). 23 were male and 27 were female. The participants had vitiligo for between 1.5 and 26 years (mean 7.33). 6 participants were lost at follow-up and 2 were excluded from the study, resulting in 42 evaluated. This study was conducted in India.
Interventions	**A:** Both groups received punchgrafting to static lesions. 4 weeks after grafting 1 group received PUVA twice weekly. **B:** Both groups received punchgrafting to static lesions. 4 weeks after grafting this group applied 0.1% fluocinolone acetonide cream once daily.
Outcomes	**Primary outcomes of the trial:** 1) Cessation of spread of vitiligo.

Barman 2004 *(Continued)*

	2) Adverse effects. Measured at baseline and then followed up monthly for a minimum of 6 months.
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 50): "In a randomised case study, these patients were divided into two groups." Comment: Insufficient detail was reported about the method used to generate the allocation sequence.
Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	High risk	Participants were not blinded. Comment: Nature of the intervention (surgical) made blinding impossible.
Blinding (performance bias and detection bias) clinician	High risk	Clinicians were not blinded. Comment: Nature of the intervention (surgical) made blinding impossible.
Blinding (performance bias and detection bias) assessor	High risk	This was not stated.
Incomplete outcome data	High risk	Intention-to-treat analysis was not used. Intervention- A: 5 dropouts (reasons: lost to follow-up (3) and because of reactivation of the disease (2)) Control- B: 3 dropouts due to lost to follow-up.

Bayoumi 2012

Methods	This is a randomised, within-participants, left/right comparison study lasting 12 weeks
Participants	**Inclusion criteria of the trial** • Patients between 18 to 85 years • Non-segmental vitiligo with at least two symmetrical patches of > 4 cm^2 located on bony prominences and/or extremities **Exclusion criteria of the trial** • Pregnancy or lactation • Personal history of skin cancer • Personal history of photodermatosis • Personal history of keloid or hypertrophic scar • Concomitant use of treatment potentially effective on vitiligo such as steroids or topical tacrolimus or pimecrolimus

Bayoumi 2012 *(Continued)*

	18 participants (4 male, 12 female) with age range 29 to 72 (mean 49) were included. 7 patients had skin type II, 7 had skin type III and 2 had skin type IV. 2 participants were lost to follow-up and the final number of participants evaluated was 16. This study was conducted in France.
Interventions	**A:** dermabrasion with NB-UVB and topical steroids. Dermabrasion was performed using a 2940-nm erbium laser and daily dressing with hyaluronic acid cream was applied for the first 2 days of treatment. Then, hydrocortisone 17-butyrate cream was applied daily on all lesions for three periods of 3 weeks followed by a 1-week steroid-free interval. Concomitantly NB-UVB was started on all the lesions with twice weekly sessions also for 12 weeks. **B:** NB-UVB and topical steroids. Hydrocortisone 17-butyrate cream was applied daily on all lesions for three periods of 3 weeks followed by a 1-week steroid-free interval. Concomitantly NB-UVB was started on all the lesions with twice weekly sessions also for 12 weeks.
Outcomes	**Primary outcomes of the trial** 1) Repigmentation: Grade 0 (none), Grade 1 (< 25%), Grade 2 (25% to 49%), grade 3 (50% to 74%), grade 4 (≥ 75%). 2) Adverse effects **Secondary outcomes of the trial** 1) Subjective evaluations of the tolerability of treatment. 2) Global satisfaction of the patients. For all outcomes, assessments were made pre-treatment and 1 month after session of treatment (13 weeks).
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 209); "After verification of the inclusion criteria and after patient consent was obtained one side of the body was randomly assigned to receive the laser-assisted dermabrasion." Comment: Insufficient detail was reported about the method used to generate the allocation sequence.
Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	High risk	Participants were not blinded. Comment: "One side of the body received dermabrasion so it was impossible to blind participants."
Blinding (performance bias and detection bias) clinician	High risk	Clinicians were not blinded. Comment: "One side of the body received dermabrasion so it was impossible to blind clinicians."
Blinding (performance bias and detection bias) assessor	Low risk	Outcome assessors were blinded. Quote (page 209): "Evaluation was done by two independent physicians blinded to the type of treatment received on standardized pictures (taken under

Bayoumi 2012 *(Continued)*

		visible light and UV radiation) performed before treatment and 1 month after the end of the treatment."
Incomplete outcome data	High risk	Intention-to-treat analysis was not used. Intervention - A: 2 dropouts due to personal reasons. Control - B: 2 dropouts due to personal reasons.

Bhatnagar 2007

Methods	Randomised parallel group study lasting 12 months.
Participants	**Inclusion criteria of the trial** • Not specified other than 'patients with vitiligo' **Exclusion criteria of the trial** • Age < 12 years or > 50 years • BSA involvement < 5% • Segmental vitiligo • Prior exposure to carcinogenic agents • History of photo-mediated disorders • Pregnancy and lactation • Prior history of phototherapy (topical or systemic PUVA or NB-UVB) 50 participants were split into 2 groups of 25. All in the NB-UVB group had vitiligo vulgaris, whereas in PUVA group 23 had vitiligo vulgaris, 1 had focal, and 1 acrofacial. The mean age of the NB-UVB group was 28.96 years (SD 0.64) and 26.64 (SD 11.13) in the PUVA group. 18 were male and 32 female (8M/17F NB-UVB, 10M/15F PUVA). This study was conducted in India.
Interventions	**A:** NB-UVB was delivered 3 times per week on non-consecutive days. The initial dose was 280 mJ/cm^2. When 75% repigmentation was achieved exposure to NB-UVB was reduced to twice a week. **B:** Trimethylpsoralen (0.6 mg/kg) was taken with food 2 hours before exposure to UVA. The initial dose was 2 J/cm^2 and this increased by 0.5 J/cm^2 each visit.
Outcomes	**Primary outcomes of the trial** 1) Percentage repigmentation: no improvement (0%), minimal (< 25%), mild (25% to 50%), moderate (50% to 75%), and marked to complete (> 75%). 2) Mean repigmentation in individual participants and groups. 3) Colour of repigmentation: somewhat darker, somewhat lighter, and the same as compared with the normally pigmented skin surrounding skin. Measured pre- and post-treatment (12 months).
Notes	None of the participants completed the intended 12-month study period due to difficulties in attending 3 times a week for treatment. All participants had variable courses of treatment making comparison difficult.
Risk of bias	

Bhatnagar 2007 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 638): "Patients were allocated in either of the groups using random number table."
Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	High risk	Participants were not blinded. Comment: This study was open.
Blinding (performance bias and detection bias) clinician	High risk	Clinicians were not blinded. Comment: This study was open.
Blinding (performance bias and detection bias) assessor	High risk	Outcome assessors were not blinded. Comment: This study was open and non-observer blinded.
Incomplete outcome data	Low risk	Intention-to-treat analysis was used. No dropouts.

Budania 2012

Methods	This is a randomised, within-participant study lasting 16 weeks.
Participants	**Inclusion criteria** • Patients with a clinical diagnosis of vitiligo which had been stable for a period of one year • Not responding to medical therapy **Exclusion criteria** • Patients < 10 years, • Actively spreading vitiligo, • History of Köebnerisation, • History of hypertrophic and keloidal scars, bleeding disorder • Vitiligo patch of >100 cm^2 • Pregnant patients 41 patients were recruited and were randomly divided into two groups using randomisation table. Group 1 comprised of 21 patients with 28 stable vitiligo lesions and group 2 comprised of 20 patients with 26 stable vitiligo lesions.
Interventions	**A:** was treated by autologous non cultured epidermal cell suspension (NCES) **B:** was treated by suction blister epidermal grafting (SBEG).
Outcomes	1) Repigmentation assessed subjectively by digital photography as follows: • < 50% Poor repigmentation • 50% to 74% Fair repigmentation • 75% to 89% Good repigmentation

Budania 2012 *(Continued)*

	• 90% to 100% Excellent repigmentation 2) Repigmentation pattern was noted as 'diffuse', 'perifollicular' or 'dotted'. A note was also made of the colour matching of repigmented skin as 'somewhat lighter than', 'same as' or 'somewhat darker than' normal skin. 3) At each visit, patients were also asked about any adverse events and patient were asked to fill a questionnaire about the satisfaction with the procedure results at week 4, 8, 12 and 16 and also DLQI Questionnaire at week 16. Follow-up visits were at week 4, 8, 12 and 16. None of the patients in the two groups developed infection, scarring or milia at any site, donor or recipient.
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 3): "All the patients were randomly divided into two groups using randomization table."
Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	High risk	This was not stated.
Blinding (performance bias and detection bias) clinician	High risk	This was not stated.
Blinding (performance bias and detection bias) assessor	High risk	This was not stated.
Incomplete outcome data	Low risk	Intention-to-treat analysis was used. No dropouts.

Casacci 2007

Methods	Randomised single-blind, within-participant, left/right comparison study lasting 6 months.
Participants	**Inclusion criteria of the trial** • Patients with vitiligo aged 15-65 years who were referred to dermatology clinics in two participating centres **Exclusion criteria of the trial** • Phototherapy or PUVA in last 6 months • Lesions on face • Lesions on extremities • History of skin cancer

Casacci 2007 *(Continued)*

- Photosensitivity disorders
- Immunosuppressive treatment
- Pregnancy or breastfeeding

21 participants with vitiligo. 5 (24%) were lost to follow-up, resulting in 16 evaluated (6 males and 10 females). Participants were aged between 16 and 58 years old (mean 38) and had been affected with vitiligo for between 6 months and 24 years (mean 9.46 years). All had at least 2 symmetrical lesions randomly assigned to treatment.

This study was conducted in Italy and France.

Interventions	**A:** 308 nm monochromatic excimer light (MEL) was delivered twice a week. 50 mW/cm^2 at 15 cm distance. Maximum irradiation area 36 x 16cm = 576 cm^2. 70% minimum erythemal dose, with increments of 40% (treatments 1 to 4), 30% (treatments 4 to 8), and 20% (8 onwards). **B:** NB-UVB was delivered twice a week. The initial dose was 70% minimum erythemal dose, with increments of 40% (treatments 1 to 4), 30% (treatments 4 to 8), and 20% (8 onwards).
Outcomes	**Primary outcomes of the trial** 1) Repigmentation: score 0 (0%), score 1 (< 25%), score 2 (26% to 50%), score 3 (51% to 75%), and score 4 (76% to 100%). 2) Repigmentation pattern: follicular, peripheral, or a combination of both. 3) Adverse effects. Measured pre- and post-treatment (6 months).
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 957): "The lesion to be treated with 308 nm MEL was selected by drawing lots according to a left/right randomization table."
Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	High risk	Participants were not blinded.
Blinding (performance bias and detection bias) clinician	Unclear risk	Clinicians were blinded. Quote (page 958): "This was an investigator blinded study." Details regarding blinding procedure were not provided.
Blinding (performance bias and detection bias) assessor	Low risk	Outcome assessor was blinded. Comment: We emailed the author who responded with the following "The investigator that assessed the pigmentary response was different from the physician that performed the treatment and of course did not know which side was treated with MEL or NB-UVB."
Incomplete outcome data	High risk	Intention-to-treat analysis was not used.

Casacci 2007 *(Continued)*

	Both intervention and control as it is a within-patient study- 5 dropouts (mainly because of non-compliance)

Cestari 2001

Methods	Randomised, single-blind, parallel group study lasting 3 months.
Participants	**Inclusion criteria of the trial** • Over 3 years of age, both sexes, with lesions less than 2% of the corporal surface. **Exclusion criteria of the trial** • Pregnancy • Used specific medication against vitiligo within a month prior to the study. 27 participants with vitiligo. 9 were male and 18 were female, with a mean age of 19.7 years. 8 were lost at follow-up, resulting in 19 evaluated. This study was conducted in Brazil.
Interventions	**A:** 2% 4-dimethoxyamoidina (4-DMA) (khellin) plus UVA. Area to be treated was painted with medication 30 minutes before exposure to UVA, the untreated area was protected with light blocking paste. Treatment was delivered twice weekly for at least 3 months and treatment was adjusted every 15 days. **B:** 0.1% khellin plus 8-methoxypsoralen (8-MOP) plus UVA. Area to be treated was painted with medication 30 minutes before exposure to UVA, the untreated area was protected with light blocking paste. Treatment was delivered twice weekly for at least 3 months and treatment was adjusted every 15 days. Both gel-based and supplied by Sigma Chemical Co.
Outcomes	**Primary outcomes of the trial** 1) Repigmentation: 0 = null (absence of repigmentation), 1 = regular (presence of islands of repigmentation in approximately 25% of the surface lesions or in 25% of these), 2 = good (signs of repigmentation in 25% to 50% of the lesions), and 3 = excellent (repigmentation in over 50% of the lesions). Measured pre-treatment, monthly, and post-treatment (3 months).
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 685): "The patients were instructed to use either substance A or substance B according to a table of random numbers."
Allocation concealment (selection bias)	Low risk	Quote (page 684): "The active agents were designated substance A and B, only the pharmaceutical responsible for their manipulation knew which active agent they combined and this information was only revealed at the end of the study."
Blinding (performance bias and detection bias) participant	Unclear risk	Participants were blinded. Comment: Details were not provided.
Blinding (performance bias and detection bias)	Unclear risk	Clinicians were blinded.

Cestari 2001 *(Continued)*

clinician		Comment: Details were not provided.
Blinding (performance bias and detection bias) assessor	High risk	This was not stated.
Incomplete outcome data	High risk	Intention-to-treat analysis was not used. Intervention- A: 5 dropouts due to lost to follow-up. Control- B: 3 dropouts due to lost to follow-up. Comment: Quote (686) : "Eight patients participated in a pilot project and were only analyzed for side effects, phototherapy doses and anatomical distribution of the vitiligo."

Czajkowski 2004

Methods	Randomised parallel group study lasting 6 months.
Participants	**Inclusion criteria of the trial** • Localised or generalised vitiligo with lesions in the dorsum of the hands or lower limbs. **Exclusion criteria of the trial** • Prior treatment for 12 months before start of the study 20 participants with localised or generalised vitiligo, with lesions in the dorsum of the hands or lower limbs. Participants in intervention 1 group had a mean age of 35.6 years and had been affected by vitiligo for an average of 4.2 years. 7 were female and 3 were male. Participants in intervention group 2 had a mean age of 28.4 years and had been affected by vitiligo for an average of 3.1 years. 6 were female and 4 were male. This study was conducted in Poland.
Interventions	**A:** transplantation of cultured autologous melanocytes plus PUVA therapy (CMP) on 1 limb and PUVA only on another (PO) **B:** suction blister transplantation plus PUVA (SBP) on 1 limb and cryotherapy plus PUVA (CP) on another.
Outcomes	**Primary outcomes of the trial** 1) Repigmentation: success or failure. Measured pre- and post-treatment (6 months).
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 1400): "The patients were randomly split into two groups of ten patients." Comment: Insufficient detail was reported about the method used to generate the allocation sequence.

Czajkowski 2004 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	High risk	Participants were not blinded. Comment: Different surgical interventions used therefore not possible to blind.
Blinding (performance bias and detection bias) clinician	High risk	Clinicians were not blinded. Comment: Different surgical interventions used therefore not possible to blind.
Blinding (performance bias and detection bias) assessor	High risk	No separate outcome assessor mentioned.
Incomplete outcome data	Low risk	Intention-to-treat analysis was used. No dropouts.

Dawid 2006

Methods	Randomised, double-blind, placebo-controlled, within-participants, left/right comparison study lasting 6 months.
Participants	**Inclusion criteria of trial** • Male or female patients, age 12-60 years with generalised (symmetrical vitiligo) **Exclusion criteria of trial** • Known sensitivity to study drug or drugs in same class (i.e. calcineurin inhibitors). • Any other 'investigational agent' (no definition given of what this means) in the last 30 days. • Pregnant or breast-feeding women • Women with childbearing potential not using an adequate contraception method. 20 participants with symmetrical vitiligo. 6 were male and 14 were female with a mean age of 36.9 years. Participants had been affected with vitiligo for under 2 years. 4 participants were lost at follow-up, resulting in 16 evaluated. This study was conducted in Austria.
Interventions	**Intervention** **A:** pimecrolimus cream (1%) twice a day to a lesion on 1 side of their body. **Control Intervention** **B:** vehicle cream twice a day to a lesion on the other side of their body.
Outcomes	**Primary outcomes of the trial** 1) Cessation of spread of vitiligo: -1 (repigmentation in the last year), 0 (stable within the last year), +1 (new lesion within the last year), 2 (new lesion within the last 6 months), 3 (new lesion within the last 3 months), and 4 (new lesion within the last 6 weeks). Measured pre- and post-intervention (6 months) and at 9 months follow-up.

Dawid 2006 *(Continued)*

Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Comment: No mention in paper that participants were randomised. However, as there was no response from emails to authors, further information obtained from published company documents confirmed that the study was randomised.
Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	Unclear risk	Participants were blinded. Comment: Study states that it is double-blind although blinding unlikely because application of pimecrolimus may cause stinging whereas placebo may not.
Blinding (performance bias and detection bias) clinician	Unclear risk	Clinicians were blinded. Comment: Study states that it is double-blind but no details given as to how clinician blinding was ensured.
Blinding (performance bias and detection bias) assessor	High risk	No separate outcome assessor mentioned.
Incomplete outcome data	High risk	Intention-to-treat analysis although planned could not be used for the evaluation of the primary efficacy variable. Because it is a within-participant study there were 4 dropout in both groups (reasons: because of presumed lack of efficacy (2), lost to follow-up (1), and personal reasons (1))

de Macedo 2012

Methods	This is a randomised, parallel study lasting 5 weeks
Participants	**Inclusion criteria of the trial** • Patients diagnosed with vitiligo **Exclusion criteria of the trial** • Partipicpants with associated dermatological diseases • Sun exposure time > 4 hours/day • Use of drugs and/or being currently treated for Vitiligo with phototherapy, homeopathy and other treatments that could alter the results of the study 22 participants with age range 12 to 60 years were included. 10 participants were lost to follow-up and the final number of participants evaluated was 12 (5 male, 7 female). This study was conducted in Brazil.

de Macedo 2012 *(Continued)*

Interventions	**A:** Helium-Neon (He-Ne) Laser with a 632.8 wavelength). He-Ne Laser was applied at a dose of 61 J / cm^2 with a duration of one minute and 15 seconds per lesion. Treatment was done twice a week for 5 weeks. **B:** UVB fluorescent lamp (290-320 nm). Dermabrasion was performed using a 290-320 nm lamp applied perpendicular 10 cm away from the participant's skin twice a week for 5 weeks. Saidman's test was performed to calculate minimum erythematous dose 24 hours later.
Outcomes	**Primary outcomes of the trial** 1) Repigmentation: They calculated the decrease in size of the lesion using the AUTOCAD program, photos were taken at the beginning and at the end of treatment. For all outcomes, assessments were made pre-treatment and immediately after treatment.
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Translated quote (page 483): "Patients were randomly assigned, according to the order of attendance at the service and were divided randomly into two groups." Comment: Insufficient detail was reported about the method used to generate the allocation sequence.
Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	High risk	This was not stated.
Blinding (performance bias and detection bias) clinician	High risk	This was not stated.
Blinding (performance bias and detection bias) assessor	High risk	This was not stated.
Incomplete outcome data	High risk	Intention-to-treat analysis was not used. Intervention - A: 6 dropouts (the reasons for dropouts were not reported.) intervention - B: 4 dropouts (the reasons for dropouts were not reported.)

Dell'Anna 2007

Methods	A randomised, double-blind, parallel group study lasting 8 months.
Participants	**Inclusion criteria of the trial** • Patients with vitiligo referred to dermatology clinics in the three participating centres who were >18 years old

Dell'Anna 2007 *(Continued)*

- > 15% of body surface
- > 1 year duration

Exclusion criteria of the trial

- Treatment with UVB or PUVA in previous 12 months
- Use of antioxidants, topical steroids, vitamin derivatives or systematic immuno-modulators in previous 6 months
- Renal insufficiency
- Pregnancy

35 participants (21 intervention, 14 control) with symmetrical vitiligo, affecting more than 15% of their body surface area (15% to 42% of body surface areas affected in the intervention group and 15% to 38% in the control group), with the condition for more than 1 year (duration of 2 to 10 years in the intervention group and 1 to 8 years in the control group). Participants were aged between 24 and 61 years (mean age 39.9 years) and 14 were male and 21 female. 7 participants were lost at follow-up resulting in 28 participants evaluated (17 intervention, 11 control).

This study was conducted in Italy and the Netherlands.

Interventions	**Intervention** **A:** NB-UVB plus antioxidant pool (AP) containing alpha lipoic acid, vitamin C and E, and polyunsaturated fatty acids. Participants took 2 tablets a day for 8 weeks before starting the phototherapy, which continued for 6 months during the NB-UVB. The NB-UVB started with 70% of the minimal erythemal dose, increasing in increments of 30% (treatments 1 and 4), 20% (treatments 4 and 8), and 10% (treatment 8 and onwards). **Control Intervention** **B:** NB-UVB alone administered as described above.
Outcomes	**Primary outcomes of the trial** 1) Repigmentation: absent (grade 0), moderate < 50% (grade 1), good 50% to 75% (grade 2), and excellent > 75% (grade 3). 2) Biochemical parameters measure. Measured pre- and post-treatment (8 months).
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 632): "Patients were allocated using a randomised-number table in a one-to-one manner."
Allocation concealment (selection bias)	Unclear risk	This was not stated. Comment: study conducted in 3 centres so allocation probably concealed but unclear.
Blinding (performance bias and detection bias) participant	Low risk	Participants were blinded. Comment: 1 group of participants took antioxidants before the treatment and the other group were given a placebo. Quote (page 632): "The trial was a prospective, randomised, double-blind placebo-controlled multi-centre

Dell'Anna 2007 *(Continued)*

		study". Of note, the administration of placebo tablets to 1 group is implied but not explicitly described.
Blinding (performance bias and detection bias) clinician	High risk	This was not stated.
Blinding (performance bias and detection bias) assessor	Low risk	Outcome assessors were blinded. Quote (page 633): "Two independent observers, blinded to the treatment, evaluated the size and number of lesions."
Incomplete outcome data	High risk	Intention-to-treat analysis was not used. Intervention- A: 4 dropouts due to reasons unconnected with the therapy (fever, physical trauma, job changes). Control- B: 3 dropouts due to reasons unconnected with the therapy (fever, physical trauma, job changes).

El Mofty 2006a

Methods	Randomsied parallel group study lasting 16 weeks.
Participants	**Inclusion criteria of the trial** • People with vitiligo affecting more than 30% of their body surface area, with a bilateral/symmetrical (generalised) distribution. **Exclusion criteria of the trial** • None reported. 20 participants with symmetrical vitiligo affecting more than 30% of their body surface area. 3 were male and 17 were female and they had a mean age of 28 years old. The participants were divided equally into 2 treatment groups. This study was conducted in Egypt.
Interventions	**A:** Participants received UVA 15 J/cm^2 3 times a week. **B:** Participants received UVA 5 J/cm^2 3 times a week.
Outcomes	**Primary outcomes of the trial** 1) Repigmentation: poor (0% to 40%), moderate (40% to 60%), good, and very good (> 60%). Measured pre- and post-intervention (i.e.16 weeks).
Notes	Singe intervention, dose-dependent study

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 214): "Patients were randomly divided into two groups each of 10 patients."

El Mofty 2006a *(Continued)*

		Comment: Insufficient detail was reported about the method used to generate the allocation sequence.
Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	Unclear risk	Participants were not blinded. Comments: It seems it is an open study.
Blinding (performance bias and detection bias) clinician	High risk	Clinicians were not blinded. Comments: Clinician would have had to know what dose of UVA they were giving.
Blinding (performance bias and detection bias) assessor	High risk	No separate outcome assessor mentioned.
Incomplete outcome data	Low risk	Intention-to-treat analysis was used. No dropouts.

El Mofty 2013a

Methods	This is a randomised parallel group study lasting 16 weeks.
Participants	**Inclusion criteria of the trial** • Bilateral symmetrical vitiligo • Involving > 305 body surface area • Not received any topical, systemic or photo/photochemotherapy 1 month prior to enrolment **Exclusion criteria of the trial** • Segmental or localised vitiligo patients • History of cutaneous malignancy • Photosensitivity • Children below 10 years • Pregnant females 40 patients were randomised, 10 males and 30 females. 4 patients were lost to follow-up, reasons were not reported. Intention-to-treat analysis was applied. This study was conducted in Cairo, Egypt.
Interventions	**A:** BBUVA 3 times per week for 16 weeks. Fixed dose of 15J/cm^2 and the mean duration of exposure was 25 minutes **B:** NBUVB 3 times per week for 16 weeks. Starting dose was 0.5J7cm^2. Increments of 20% performed on alternate sessions if tolerated. The mean final dose was 2.5J/cm^2 and the mean duration of exposure was 2.54 minutes.
Outcomes	**Primary outcomes of the trial** 1) Percentage of repigmentation. This was graded as poor response: 0% to 40% plus dropouts, moderate response: > 40% to 60%, good response: > 60% to 75% and very good response: >75% to 100%. 2) Patients' satisfaction was evaluated using a visual analogue scale. They were asked to specify level of satisfaction by pointing to a position along a continuous line between two endpoints. Point 0 indicates

El Mofty 2013a *(Continued)*

	0% satisfaction and point 100 indicates 100% or complete satisfaction. On the scale: grade 1: 0 to 30, grade 2: 31 to 60 and grade 3: 60 to 100. 3) Adverse effects.
Notes	**This study has been published with the wrong title. The intervention is not BB-UVB but BB-UVA. Now correct in PubMed**

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 240): "Patients were randomly divided into two equal groups each of 20 patients..." Comment: Insufficient detail was reported about the method used to generate the allocation sequence.
Allocation concealment (selection bias)	Low risk	Quote (page 240): "...allocation concealment was done using opaque sealed envelopes containing odd and even numbers, designated each for a specific modality, prepared and given by a colleague external to the study"
Blinding (performance bias and detection bias) participant	Unclear risk	Comment: Although in the abstract it is mentioned that the study is single-blinded "The study was a prospective, randomized, controlled, and single-blinded clinical trial, conducted on 40 patients with bilateral symmetrical vitiligo", we do not know who is blinded.
Blinding (performance bias and detection bias) clinician	Unclear risk	Comment: Although in the abstract it is mentioned that the study is single-blinded "The study was a prospective, randomized, controlled, and single-blinded clinical trial, conducted on 40 patients with bilateral symmetrical vitiligo", we do not know who is blinded.
Blinding (performance bias and detection bias) assessor	Unclear risk	Comment: Although in the abstract it is mentioned that the study is single-blinded "The study was a prospective, randomized, controlled, and single-blinded clinical trial, conducted on 40 patients with bilateral symmetrical vitiligo", we do not know who is blinded.
Incomplete outcome data	Unclear risk	Intention-to-treat analysis was partially used. Quote (page 241): "Clinical response was graded according to 'intention-to-treat analysis'" Figure 1: "Dropouts were considered as poor responders" Comment: ITT analysis was only performed for the percentage of repigmentation outcome. Intervention- A: 3 dropouts (the reasons for dropouts were not reported). Intervention- B: 1 dropout (the reasons for dropouts were not reported).

El Mofty 2013b

Methods	This is a randomised parallel group study lasting 5 months.
Participants	**Inclusion criteria of the trial** • Generalised vitiligo

El Mofty 2013b *(Continued)*

	• Age >12 years with normal results for liver function and eye fundus examination **Exclusion criteria of the trial** • Presence of focal, segmental and acrofacial vitiligo • Any contraindication to photo(chemo)therapy exposure, such as pregnancy • Presence of malignant or premalignant skin lesions. 45 participants were randomised, 13 males and 32 females. The age range was from 13 to 60 years. 4 patients were lost to follow-up: 3 due to lack of compliance and 1 due to failure of response. There was no intention-to-treat analysis. This study was conducted in Cairo, Egypt.
Interventions	**A:** BB-UVA 15 J/cm^2 3 sessions/week for 5 months (60 sessions in total). Fixed dose of 15J/cm^2 each session: any patients who could not tolerate the full session duration had their session split into two 10-min sessions with a 10-min break between sessions. **B:** BB-UVA 10 J/cm^2 3 sessions/week for 5 months (60 sessions in total). Fixed dose of 10J/cm^2 each session. **C:** PUVA 3 sessions/week for 5 months (60 sessions in total). Took 8-methoxypsoralen 0.5 to 0.7 mg/kg with a meal, 2 hours before exposure to UVA (sessions started at a dose of 1J/cm^2, and the doses were increased by 20% increments according to the patient's response and tolerance).
Outcomes	Primary outcomes of the trial 1) Percentage of repigmentation. Extent of response was scored as: poor (0% to 20%), moderate (20% to 40%), good (40% to 60%), very good (60% to 80%), almost complete response of the lesion (excellent) (> 80%). 2) Adverse effects. All outcomes measured before (session 0), at the mid-point (session 30) and at the end (session 60) of treatment.
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 2): "This was a randomized controlled clinical trial, with randomization using the envelope concealment method." Comment: Insufficient detail was reported about the method used to generate the allocation sequence.
Allocation concealment (selection bias)	Unclear risk	Quote (page 2): "This was a randomized controlled clinical trial, with randomization using the envelope concealment method." Comment: Comment: Insufficient detail was reported about the method used for allocation concealment.
Blinding (performance bias and detection bias) participant	High risk	Participants were not blinded.
Blinding (performance bias and detection bias) clinician	High risk	Clinicians were not blinded.

El Mofty 2013b *(Continued)*

Blinding (performance bias and detection bias) assessor	Low risk	Outcome assessor was blinded. Quote (page 2): "The author responsible for assessing treatment response was blinded to the treatment allocation: the other two authors were not blinded"
Incomplete outcome data	High risk	Intention-to-treat analysis was not used. Comment: According to Figure 1 it is mentioned that 14 patients were analysed on Intention-to-treat analysis in both UVA 15J/cm2 and UVA 10 J/cm2 groups, respectively and 13 patients on Intention-to-treat basis in the PUVA group. However, dropouts were not analysed. In total 3 participants dropped out due to lack of compliance and one participant dropped out due to failure of response. However, dropouts were not reported by group.

El-Zawahry 2012

Methods	This is a randomised, parallel group study lasting 12 weeks
Participants	**Inclusion criteria of the trial** • Adult patients with generalised vitiligo vulgaris affecting more than 10% of body surface area **Exclusion criteria of the trial** • Treatment within 4 weeks 40 participants (15 male, 25 female) with age ranging from 18 to 65 years were included in this study. The duration of condition ranged from 0.5 to 20 years. This study was conducted in Egypt.
Interventions	**A:** UVA1 phototherapy. 10 participants received a moderate dose of UVA1 (40 to 70 J/session) and 10 patients received a low-dose UVA1 with a maximum dose of 20 J/cm^2/session. Phototherapy 3 times per week for 12 weeks. For the UVA1 group, participants started at a dose of 5 J/cm^2/session and increased by 5 J/cm^2 every session. **B:** NB-UVB. Phototherapy 3 times per week for 12 weeks. Participants started at a dose of 0.25 J/cm^2 and increased by 20% increments according to the patient's response and tolerance until reaching minimal erythema dose then this was fixed.
Outcomes	**Primary outcomes of the trial** 1) Degree of repigmentation. This was graded as: poor (0% to 20%), moderate (20% to 40%), good (40% to 60%), very good (60% to 80%) and excellent (> 80%). **Secondary outcomes of the trial** 2) Percentage change in VASI and VETF area scores. 3) Adverse effects. For all outcomes, assessments were made pre- and post-treatment (12 weeks).
Notes	-
Risk of bias	

El-Zawahry 2012 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 85): "Randomization was done using envelope concealed method." Comments: It is not described whether these envelopes were sealed and opaque, but we assume the term 'concealed' accounts for that.
Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	High risk	Participants were not blinded.
Blinding (performance bias and detection bias) clinician	High risk	Clinicians were not blinded.
Blinding (performance bias and detection bias) assessor	Low risk	Outcome assessor was blinded. Quote (page 85): "...the senior researcher who performed the final clinical assessment was blinded."
Incomplete outcome data	Low risk	Intention-to-treat analysis was used. No dropouts.

Elgoweini 2009

Methods	This is a randomised parallel group study lasting months.
Participants	**Inclusion criteria of the trial** • Adult patients with stable vitiligo **Exclusion criteria of the trial** • History of photosensitivity • A known history of skin malignancy • Thyroid dysfunction • Other dermatological, systemic, or autoimmune diseases • Patients who had taken systemic or used topical treatment within 2 months prior to study entry 24 participants with stable vitiligo and age ranging from 19 to 50 years old. The duration of condition varied from 1 year to 5 years with a mean of 3.3 years. Lesions covered 15% to 50% of the body surface area. 4 patients were lost to follow-up due to reasons unrelated to their treatment. There was no intention-to-treat analysis. In the final analysed sample there were 6 females and 14 males. The study was conducted in Egypt.
Interventions	**Intervention** **A:** Narrowband (TL-01) ultraviolet B (NB-UVB) plus oral supplement of alpha-tocopherol (vitamin E). Patients received 400 IU of Vitamin E once/day which started 2 weeks before NB-UVB. NB-UVB therapy was administered 3 times a week on nonconsecutive days. The starting dose was 0.21 J/cm^2 with 20% dose increments at each subsequent treatment for the first 10 treatments, followed by 10% increment

Elgoweini 2009 *(Continued)*

	per treatment for another 10 treatments. The increments stopped when minimal erythema developed in the lesions. **Control Intervention** **B:** Narrowband (TL-01) ultraviolet B (NB-UVB) alone. NB-UVB therapy 3 times a week on nonconsecutive days. The starting dose was 0.21 J/cm^2 with 20% dose increments at each subsequent treatment for the first 10 treatments, followed by 10% increment per treatment for another 10 treatments. The increments stopped when minimal erythema developed in the lesions.
Outcomes	**Primary outcomes of the trial** 1) The extent of repigmentation was recorded as: none (0%), mild (1% to 25%), moderate (26% to 50%), marked (51% to 75%), and excellent (>75%). 2) Adverse effects. All outcomes were measured pre- and post-treatment (6 months).
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 852): "Patients were divided randomly into 2 treatment groups." Comment: Insufficient detail was reported about the method used to generate the allocation sequence.
Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	High risk	Participant were not blinded.
Blinding (performance bias and detection bias) clinician	High risk	Clinicians were not blinded.
Blinding (performance bias and detection bias) assessor	Low risk	Outcome assessors were blinded. Quote (page 853): "Improvement was recorded, by 2 independent observers."
Incomplete outcome data	High risk	Intention-to-treat analysis was not used. Intervention - A: 1 dropout who discontinued because of reasons unrelated to treatment Control - B: 3 dropouts who discontinued because of reasons unrelated to treatment

Ermis 2001

Methods	Randomised, placebo-controlled, double-blind, within-participants, left/right comparison study. Treatment continued until cosmetically acceptable repigmentation had been achieved and stopped when repigmentation ceased.

Ermis 2001 *(Continued)*

Participants	**Inclusion criteria of the trial** • Aged over 16 years • Generalised vitiligo **Exclusion criteria of the trial** • Patients with involvement of less than 10% of the body surface area • Showing any evidence of spontaneous repigmentation • Patients who had known hypersensitivity to calcipotriol or abnormal reactions to UVA radiation • Had received topical or systemic treatment during the last 2 months • Patients with other autoimmune diseases • Those who had segmentary vitiligo 27 participants with symmetrical vitiligo. 9 were female and 18 were male and they had a mean age of 29.8 years. 8 participants failed to complete the study. This study was conducted in Turkey.
Interventions	**Intervention** **A:** calcipotriol cream 0.05 mg/kg plus PUVA on 1 side of their body. The cream was applied 1 hour before PUVA, which was delivered twice a week. **Control Intervention** **B:** placebo cream plus PUVA on the other side. The cream was applied 1 hour before PUVA, which was delivered twice a week.
Outcomes	**Primary outcomes of the trial** 1) Repigmentation: initial repigmentation (< 25%), complete repigmentation (75% to 100%), and initial repigmentation (up to 25%). Measured pre- and post-intervention. Treatment continued until cosmetically acceptable repigmentation had been achieved and stopped when repigmentation ceased.
Notes	This study had a high dropout rate - nearly one third.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 473): "In this randomised left-right comparison study, calcipotriol 0.05 mg/g cream or placebo (kept in boxes labelled 'left' and 'right') were applied to the reference lesions." Comment: Insufficient detail was reported about the method used to generate the allocation sequence.
Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	Low risk	Participants were blinded. Quote (page 473): "The clinical investigator and the patients were unaware of the specific drugs that were applied to each side." "The vehicle base of calcipotriol (identical in appearance to the calcipotriol cream) was used as placebo."

Ermis 2001 *(Continued)*

Blinding (performance bias and detection bias) clinician	Low risk	Clinicians were blinded. Quote (page 473): "The clinical investigator and the patients were unaware of the specific drugs that were applied to each side." "The vehicle base of calcipotriol (identical in appearance to the calcipotriol cream) was used as placebo."
Blinding (performance bias and detection bias) assessor	High risk	No separate outcome assessor mentioned.
Incomplete outcome data	High risk	Intention-to-treat analysis was not used. Because it is a within-patient study there were a total of 8 dropouts in both groups (reasons: non-compliance (4), use of additional medication (3), and insufficient repigmentation (1)).

Esfandiarpour 2009

Methods	A randomised, double-blind, placebo-controlled, parallel group study lasting 12 weeks.
Participants	**Inclusion criteria of the trial** • Stable non segmental vitiligo, wash out period of at least 1 month and a stable period of at least 3 months were required **Exclusion criteria of the trial** • Spontaneous repigmentation 68 participants with stable symmetrical vitiligo (least 3 months). 18 participants were lost at follow-up, resulting in 50 evaluated participants (25 intervention, 25 control). The intervention group consisted of 7 males and 18 females and they were aged between 16 and 56 years old (mean 25.92, SD 10.31). The mean duration of vitiligo for this group was 9.72 years (SD 7.9). The control group consisted of 6 males and 19 females and were aged between 15 and 72 years old (mean 34.6, SD 15.67). The mean duration of vitiligo for this group was 11.44 years (SD 9.32). This study was conducted in Iran.
Interventions	**Intervention** **A:** NB-UVB plus pimecrolimus. The pimecrolimus cream was applied twice a day. The NB-UVB was administered 3 times a week on non-consecutive days for 3 months. The minimal erythema dose was not measured and the standard initial dose of 280 mj/cm^2 was used for all. According to response, a 15% increment in dosage was given for each subsequent treatment until minimal erythema or a maximum of 800 mj/cm^2 was achieved. **Control Intervention** **B:** NB-UVB plus placebo (petrolatum). The placebo cream was applied twice a day. The NB-UVB was administered 3 times a week on non-consecutive days for 3 months. The minimal erythema dose was not measured and the standard initial dose of 280 mj/cm^2 was used for all. According to response, a 15% increment in dosage was given for each subsequent treatment until minimal erythema or a maximum of 800 mj/cm^2 was achieved.
Outcomes	**Primary outcomes of the trial** 1) Repigmentation: minimal (< 25%), moderate (25% to 49%), marked (50% to 75%), and excellent (> 75%).

Esfandiarpour 2009 *(Continued)*

	2) Adverse effects. Measured pre- and post-treatment (12 weeks).
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 2): "Using simple complete randomisation, patients were randomised into two NB-UVB treatment groups."
Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	High risk	Participants were not blinded. Comments: Blinding unlikely because application of pimecrolimus may cause stinging whereas placebo may not.
Blinding (performance bias and detection bias) clinician	Low risk	Clinician was blinded. Comments: "The same dermatologist who was blind to the treatment options measured all the vitiliginous patches in transverse and longitudinal axes and recorded the data."
Blinding (performance bias and detection bias) assessor	Low risk	Outcome assessor was blinded. Comments: "The same dermatologist who was blind to the treatment options measured all the vitiliginous patches in transverse and longitudinal axes and recorded the data."
Incomplete outcome data	High risk	Intention-to-treat analysis was not used. Intervention-A: 9 dropouts (reasons: because of non-compliance due to slow response, particularly on the hands) Control -B: 9 dropouts (reasons: because of non-compliance due to slow response, particularly on the hands)

Farah 1967

Methods	Randomised parallel group study. Duration of study not stated but some participants continued treatment for up to 7 months.
Participants	**Inclusion criteria of the trial** • Not reported **Exclusion criteria of the trial** • Not reported 88 participants randomly allocated to 4 groups: 20 in group 1 (oral psoralens) of whom 9 were followed up, 18 in group 2 (topical psoralen) of whom 10 were followed up, 23 in group 3 (combined psoralen and triamcinolone) of whom 15 were followed up, and 27 in group 4 (no treatment). This study was conducted in Lebanon.

Farah 1967 *(Continued)*

Interventions	**A:** Oral psoralens, topical psoralens (dosage and brand of psoralens not given). Exposure to midday sun 2 hours after taking oral medication and immediately after topical application of psoralen. Exposure time increased according to how participants tolerated the sun. **B:** Methoxypsoralen 20 mg orally and 8 to 12 mg of oral triamcinolone. Exposure to midday sun 2 hours after taking oral medication and immediately after topical application of psoralen. Exposure time increased according to how participants tolerated the sun.
Outcomes	**Primary outcomes of the trial** 1) Repigmentation: none (< 50%) and good (> 50%). Measured post-treatment (up to 7 months).
Notes	Participant evaluation of outcome also taken into account.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 89): "The patients were divided at random into four groups." Comment: Insufficient detail was reported about the method used to generate the allocation sequence.
Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	High risk	This was not stated.
Blinding (performance bias and detection bias) clinician	High risk	This was not stated.
Blinding (performance bias and detection bias) assessor	High risk	This was not stated.
Incomplete outcome data	High risk	Intention-to-treat analysis was not used. Intervention-A: 11 dropouts, B: 8 dropouts, C: 8 dropouts (the reasons for dropouts were not reported.) Control-D: 0 dropouts Comments: Study duration not fixed. Poor table of results.

Farajzadeh 2009

Methods	This is a randomised within-participant placebo controlled study lasting 3 months.
Participants	**Inclusion criteria of the study** • Paedatric patients aged 2 to 18 years with clinically diagnosed vitiligo • Stable vitiligo only, without evidence of spontaneous repigmentation

Farajzadeh 2009 *(Continued)*

	Exclusion criteria of the study • Patients with evidence of spontaneous repigmentation • Unstable vitiligo • Systemic disease and autoimmune disease • Renal and hepatic dysfunction • Sensitivity to macrolide • Segmental vitiligo 65 participants with stable vitiligo and age ranging from 2 to 18 years and mean of 12.5. The mean duration of the condition was 51.3 months. There were 26 males and 34 females. 5 patients were lost to follow-up for reasons unrelated to treatment. There was no intention-to-treat analysis. This study was conducted in Iran.
Interventions	**A:** 1% pimecrolimus cream (Elidel) applied once daily. Treatment was applied for 10 days. **B:** Dermabrasion on the first day followed by 1% pimecrolimus cream applied once daily. Treatment was applied for 10 days. **C:** Placebo cream was applied once daily. Treatment was applied for 10 days.
Outcomes	**Primary outcomes of the trial** 1) The degree of repigmentation was graded as follows: no and minimal repigmentation (< 25%), moderate (25% to 49%), marked (50% to 74%), excellent (75% to 99%), and complete (100%) response. 2) Adverse effects. All outcomes were measured pre-treatment and 10 days post-treatment as well as 1 month, 2 months and 3 months post-treatment.
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 287): "The lesions allocated to treatment groups by block randomization."
Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	High risk	Participants were not blinded. Quote (page 287): "This is a single-blind, randomized placebo-controlled study."
Blinding (performance bias and detection bias) clinician	High risk	Clinicians were not blinded. Quote (page 287): "This is a single-blind, randomized placebo-controlled study."
Blinding (performance bias and detection bias) assessor	Low risk	Outcome assessors was blinded. Quote (page 287): "The measurement of the lesions was performed by an independent observer who was blind to the treatment options."
Incomplete outcome data	High risk	Intention-to-treat analysis was not used.

Farajzadeh 2009 *(Continued)*

	Intervention- A: 5 dropouts due to reasons unrelated to treatment; - B: 0 dropouts Control- C: 0 dropouts

Galarza 2009

Methods	Randomised, parallel group, double-blind, placebo-controlled trial lasting for 10 weeks
Participants	**Inclusion criteria of the trial** • Partícipants with clinically diagnosed generalised vitiligo of recent onset • Duration of condition: 1 to 6 months **Exclusion criteria of the trial** • Concomitant autoimmune diseases 60 participants with generalised vitiligo of recent onset and mean age of 37.9 ±12.4 years. There were 32 males and 28 females. There were no losses to follow-up. This study was conducted in Peru.
Interventions	**Intervention** **A:** Pseudocatalase and other topical antioxidants activated by solar light (topical antioxidant therapy): Gel containing pseudocatalase, superoxide, glutathione, coenzyme Q10, carotenoids, vitamins A, E, C, and selenium that was applied topically to the lesions every 12 hours for 10 weeks. **Control Intervention** **B:** Placebo gel devoid of pharmacological activity that was applied topically to the lesions every 12 hours for 10 weeks. In both groups participants were prescribed 30 mins of sun exposure without the use of sunscreen upon lesions.
Outcomes	**Primary outcomes of the trial** 1) Percentage of repigmentation: partial and total repigmentation. 2) Adverse events Percentage of repigmentation was measured at week 10 and adverse events were assessed 30 days after end of treatment.
Notes	In the abstract it is mentioned that topical antioxidant treatment was applied to the lesions every 12 hours for 30 days. Then in the methods section it says that it was applied to the lesions every 12 hours for 10 weeks. Partial repigmentation was not defined.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 200): "ensayo clínico, aleatorizado, doble ciego, controlado con placebo..."

Galarza 2009 *(Continued)*

		Comments: Insufficient detail was reported about the method used to generate the allocation sequence.
Allocation concealment (selection bias)	Unclear risk	Quote (page 200): "Luego de la aplicación de la terapia tópica antioxidante se tuvo un período de seguimiento de 30 días para evaluar la posiblidad de reacciones adversas tardías. Finalmente se reveló a qué grupo de estudio correspondían los pacientes estudiados" Comments: Insufficient detail was reported about the method used to conceal allocation
Blinding (performance bias and detection bias) participant	Unclear risk	Participants were blinded. Quote (page 200): "ensayo clínico, aleatorizado, doble ciego, controlado con placebo..." Comment: Insufficient details were provided regarding the blinding method.
Blinding (performance bias and detection bias) clinician	Unclear risk	Clinicians were blinded. Quote (page 200): "ensayo clínico, aleatorizado, doble ciego, controlado con placebo..." Comment: Insufficient details were provided regarding the blinding method.
Blinding (performance bias and detection bias) assessor	High risk	This was not stated
Incomplete outcome data	Low risk	Intention-to-treat analysis was used. No dropouts.

Ghosh 2012

Methods	Open-label within-participant randomised controlled study lasting 9 months
Participants	**Inclusion criteria** - Patients with stable vitiligo was defined as no new lesions or expansion of existing lesions for at least 2 years before enrolment into the trial. - Who had not responded earlier to routine therapy. - Who had a minimum of two achromic maculae of similar size at least 10 cm apart with a lesion size between 2 and 12 cm^2. **Exclusion criteria** - Patients with Köebner response in the past; scarring or keloidal tendencies; infection at the recipient site - Patients with infection with human immunodeficiency virus or hepatitis B or C. 22 participants were randomised in this study. The mean age was 28.7 years, range 14 to 50 years.
Interventions	**Intervention** **A:** cultured graft placed on the dermabraded area so that the cells were in apposition to the wound bed. The graft was held in place with a polyurethane film dressing. After 7 to 8 days, participants were advised to expose the control and treated areas daily to sunlight for 15 to 20 minutes until signs of pigmentation were seen.

Ghosh 2012 *(Continued)*

	Control Intervention **B:** no graft but similarly the dermabraded area was covered with similar polyurethane film dressing. After 7 to 8 days, participants were advised to expose the control and treated areas daily to sunlight for 15 to 20 minutes until signs of pigmentation were seen.
Outcomes	**Primary outcome of the trial** 1) Repigmentation of 70% or more of the treated area at the end of the study. The repigmentation was measured using photographs of test and control sites taken on day 0 (before dermabrasion and before application of the test device) and at each subsequent visit. The extent of repigmentation of the test and control sites was clinically and photographically evaluated using NIH-J image software. **Safety measurement** At each study visit, the investigators assessed the study lesions for wound breakdown.
Notes	Although not clearly stated in the inclusion/exclusion criteria, apparently if vitiligo covers more than 30% of BSA they are also excluded. This is mentioned on page1984, results, line 5.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 1983): "On each patient, control and test recipient areas were allocated based on the randomisation schedule that the clinical research group provided using the fixed, permuted block randomisation method.·
Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	High risk	Participants were not blinded. Quote (page 1982): "A prospective, open-label, randomised, multicenter clinical trial..."
Blinding (performance bias and detection bias) clinician	High risk	Clinicians were not blinded. Quote (page 1982): "A prospective, open-label, randomised, multicenter clinical trial..."
Blinding (performance bias and detection bias) assessor	High risk	Outcome assessors were not blinded. Quote (page 1982): "A prospective, open-label, randomized, multicenter clinical trial..."
Incomplete outcome data	High risk	Intention-to-treat analysis was not used. Because it is a within-participant study there was 5 dropouts in both groups (reasons: the melanocytes could not be expanded in culture (2), the cultured graft was not implanted because the participant was found to have vitiliginous patches on more than 30% of the total body surface area (1), reason for dropout not reported in the study (2).)

Goldinger 2007

Methods	Randomised, placebo-controlled, within-participant, left/right comparison study lasting 8 weeks.

Goldinger 2007 *(Continued)*

Participants	**Inclusion criteria of the trial** • Bilateral symmetrical vitiligo lesions **Exclusion criteria of the trial** • Patients who showed evidence of spontaneous repigmentation • Had received topical or systemic treatment or underwent phototherapy during the previous 6 months 10 participants with symmetrical vitiligo aged between 24 and 60 years old (mean 40). 4 were female and 5 male. 1 participant was lost at follow-up, resulting in 9 evaluated participants. This study was conducted in Switzerland.
Interventions	**Intervention** **A:** Xenon-chloride excimer laser (XCEL) plus calcipotriol. Participants were subjected to 308 nm XCEL 3 times a week. The initial dose of UV light was 100 mJ/cm^2 and this was increased by 50 mJ/cm^2 each session unless erythema persisted for more than 48 hours. A thin coat of calcipotriol ointment was applied to the affected area (on 1 side of the body) twice a day (morning and night). The mean cumulative dose used was 10.1 J/cm^2 (4.5 to 17.5 J/cm^2). **Control Intervention** **B:** Xenon-chloride excimer laser plus verum. Participants were subjected to 308 nm XCEL 3 times a week. The initial dose of UV light was 100 mJ/cm^2 and this was increased by 50 mJ/cm^2 each session unless erythema persisted for more than 48 hours. The mean cumulative dose used was 10.1 J/cm^2 (4.5 to 17.5 J/cm^2).
Outcomes	**Primary outcomes of the trial** 1) Mean percentage of repigmentation. Measured pre- and post-treatment (8 weeks).
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 505): "The site to be treated with verum was determined by random selection." Comment: Insufficient detail was reported about the method used to generate the allocation sequence.
Allocation concealment (selection bias)	Unclear risk	Quote (page 505): "The patient kept the paper indicating the treated side in a closed envelope until the end of the study period." Comments: It did not mention whether the envelope was sealed or opaque.
Blinding (performance bias and detection bias) participant	High risk	Participants were not blinded. Quote (page 505): "This is a prospective right/left comparative, single-blinded study."
Blinding (performance bias and detection bias) clinician	Low risk	Clinicians were blinded. Quote (page 505): "The investigator did not know which side was treated with calcipotriol (Daivonex®) and which one received only phototherapy."

Goldinger 2007 *(Continued)*

Blinding (performance bias and detection bias) assessor	High risk	This was not stated.
Incomplete outcome data	High risk	Intention-tot-treat analysis was not used. Because it is a within-participant study there was 1 dropout in both groups (the reason for the dropout was unrelated to the study.)

Hamzavi 2004

Methods	Randomised, placebo-controlled, within-participant, left/right comparison study lasting for either 6 months or 60 treatments, depending on which was achieved first.
Participants	**Inclusion criteria of the trial** • Patients older than 18 years with stable vitiligo involving at least 5% of their total body surface in a symmetric distribution • No significant medical problems • Were not being treated with photosensitisers. • Did not receive topical or systemic treatment for their vitiligo for 2 weeks prior to the initiation of NB–UV-B phototherapy nor for the duration of their participation in the study. **Exclusion criteria of the trial** • Not reported. 22 participants (9 male, 13 female) aged 18 years or older with stable symmetrical vitiligo affecting at least 5% of their body surface area. The participants age ranged from 23 to 77 years old (mean 47). The mean duration of the disease was 24 years (range: 4 to 51 years) and the mean extent of the disease was 15.7% (range: 4.0% to 35.7%). 1 participant was lost at follow-up, resulting in 21 evaluated participants. This study was conducted in Canada.
Interventions	**A:** NB-UVB was delivered to 1 side of the body 3 times a week on non-consecutive days. The average total NB-UVB dose was 7.3 J/cm^2 (range: 5.6 to 30.7 J/cm^2). The initial dose was 70% of minimal erythema and subsequent doses increased in 10% increments until repigmentation was clinically evident. At that point, the dose was kept constant. If persistent erythema lasting more than 24 hours developed, further treatment was delayed until this was resolved. Treatments were then re-introduced using the last previous dose and then either: the dose increased in 5% increments until repigmentation or signs and symptoms of phototoxicity redeveloped, or the dose was decreased by 25% if the participant developed persistent signs of phototoxicity. Dose increased again gradually in 5% increments until repigmentation or mild phototoxic effect was observed.
Outcomes	**Primary outcomes of the trial** 1) Repigmentation: complete improvement (100%), very much improved (76% to 99%), much improved (51% to 75%), improved (18% to 50%), minimal change (1% to 25%), and no change (0%). 2) Adverse effects. Measured pre- and post-treatment (6 months).
Notes	Single intervention dose dependent study
Risk of bias	

Hamzavi 2004 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 678): "For each patient we determined by coin toss which side of the body would receive NB-UVB treatment and the contralateral side received no active treatment."
Allocation concealment (selection bias)	Unclear risk	This was not stated. Comment: Coin toss performed openly and allocation therefore probably not concealed.
Blinding (performance bias and detection bias) participant	High risk	Participants were not blinded Comments: It was not possible to blind this study because of the unilateral tanning induced by NB-UVB.
Blinding (performance bias and detection bias) clinician	High risk	Clinicians were not blinded Comments: It was not possible to blind this study because of the unilateral tanning induced by NB-UVB.
Blinding (performance bias and detection bias) assessor	High risk	It was not stated.
Incomplete outcome data	Low risk	Intention-to-treat analysis was used. Because it is a within-participant study there was 1 dropout in both groups (the reason for the dropout was hyperpigmentation.)

Ho 2011

Methods	This is a randomised parallel group study lasting 6 months.
Participants	**Inclusion criteria of the trial** • Children aged 2-16 7years with vitiligo involving a max of 20% of body surface area **Exclusion criteria of the trial** • Pregnancy or lactation • Recognised adrenal suppression • Any serious chronic condition for which the use of tacrolimus is contraindicated • Active infection at the treatment sites 100 participants were randomised with 10 losses to follow-up/withdrawing for the following reasons: 4 withdrew for family/personal reasons, one due to spontaneous repigmentation before starting the study treatment, and three lost in follow-up and 4 withdrew due to concerns over the black box warning by the US FDA for tacrolimus – two of the latter had used their study medication up to 20 and 21 weeks and their data were included in the final analysis. 50% of patients were female. The age range was 2 to 16 years of age. 84/100 had non-segmental pattern, which was generalised in 50% of these. Mean duration was 2.5 years (range 2 months to 5 years).
Interventions	**A:** Topical clobetasol propionate (CP) 0.05%. Patients received intermittent therapy with CP ointment during first 2 months, an inactive vehicle (Vaseline® petroleum jelly) for next 2 months and 0.05% CP ointment again for the remaining 2 months. Patients instructed to apply the study medication in a thin

Ho 2011 *(Continued)*

	layer twice daily on all lesions of vitiligo; however, only the lesions of the chosen site (facial or non-facial) were evaluated. **B:** Tacrolimus (T) 0.1%. Patients received ointment for 6 months. Patients instructed to apply the study medication in a thin layer twice daily on all lesions of vitiligo; however, only the lesions of the chosen site (facial or non-facial) were evaluated. **C:** Placebo. Patients received an inactive vehicle (Vaseline petroleum jelly) during 6 months of the study. Patients instructed to apply the study medication in a thin layer twice daily on all lesions of vitiligo; however, only the lesions of the chosen site (facial or non-facial) were evaluated.
Outcomes	**Primary outcomes of the trial** 1) Degree of repigmentation. Successful repigmentation was deemed to be that which was > 50%. Patients with no repigmentation were classified as nonresponders. Complete clearance meant total repigmentation. The others were classified as: worsening, no change, < 50% partial clearing, > 50% partial clearing. The pattern of repigmentation was classified as : perifollicular, marginal, diffuse, or mixed. 2) Global score for the overall changes. A global score for the overall changes in the repigmentation of the treated vitiligo lesions was obtained using a visual analogue scale with range from -100 to 100, where -100 was doubling the extent and 100 was complete resolution. 3) Adverse effects. Incidence of adverse events throughout the study were noted either being reported by the parent/guardian (during the interview or in the diary) or observed by the investigators.
Notes	All had a 8-week wash-out period during which topical corticosteroids, phototherapy, or other topical or systemic therapy were prohibited before receiving study medication. 36 were treated with topical medications prior to the study with no substantial response

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 627): "The enrolled subjects were assigned by independent investigators into 'facial' or 'nonfacial' groups, even if both areas were affected. They were then blindly randomized 1 : 1 : 1 to receive one of the three study medications" Comment: We e-mailed the authors to ascertain whether ALL randomised patients were included in the analysis or not to which they responded that "yes, they all participants were randomised." We also e-mailed the authors to know the method of randomisation sequence and they answered that "The study was randomized as block 6 1:1:1 (tacrolimus: clobetasol: placebo) and stratified by site of application (Face, Not Face) and clinic site. The research pharmacist used a random number generator table to obtain the randomization sequences for the 4 strata. The master randomization tables were kept in the pharmacy department and the investigators and subjects/families remained blinded."
Allocation concealment (selection bias)	Low risk	Quotes (page 627): "An identification number was assigned to each patient after registration to a randomization study group by the pharmacy personnel. These numbers were used throughout the study during data collection, later compiled by an independent research assistant, then analysed by an independent statistician." "Only the pharmacy personnel involved in making up the ointments knew the contents of the jars and made sure to supply the patients of each distinct study group with the appropriate trial ointment renewed at every 2-month visit, during the time frame of the study."
Blinding (performance bias and detection bias) participant	Low risk	Participants were blinded.

Ho 2011 *(Continued)*

		Comment: Participants were supplied with an ointment in identical jars, the ointments were similar in texture, colour and smell.
Blinding (performance bias and detection bias) clinician	Low risk	Clinicians were blinded. Quote (page 627): "Only the pharmacy personnel involved in making up the ointments knew the contents of the jars."
Blinding (performance bias and detection bias) assessor	Low risk	Outcome assessors were blinded. Quotes (page 627): "Assessors were blinded regarding the arm to which the patient was assigned." "These numbers were used throughout the study during data collection, later compiled by an independent research assistant, then analysed by an independent statistician."
Incomplete outcome data	Low risk	Intention-to-treat analysis was used. Quote (page 627): "intention to treat analysis adjusted for baseline factors was performed, and patients were further stratified into two groups: facial and non-facial." Intervention - A: 3 dropouts (reasons: withdrew consent (1), due to tacrolimus black box warning (2)) - B: 2 dropouts (two were lost in follow up) Control- B: 7 dropouts (reasons: lost in follow up (2), due to spontaneous repigmentation prior to treatment (1), withdrew from the study (1), due to tacrolimus black box warning (1), withdrew at weeks 20 and 21 due to tacrolimus black box warning but were still included in final analysis (2))

Hofer 2005

Methods	Randomised within-participant study, lasting for between 6 and 12 weeks.
Participants	**Inclusion criteria of the trial** • Vitiligo patients with at least 3 stable lesions in the same area of the body. • Generalised and localised vitiligo. **Exclusion criteria of the trial** • Immunosuppressive agents in the 2 months before study entry. • Used topical steroids in the 4 weeks before the study. • Been exposed extensively to sunlight or phototherapy in the 6 weeks before the study. 14 participants with 3 stable generalised vitiligo lesions in the same area of the body. Participants were aged between 11 and 50 years old (mean 25) and 3 were male and 11 female. The majority of participants had generalised vitiligo (12), whilst the remaining had localised vitiligo (2). 1 participant was lost at follow-up, resulting in 13 evaluated participants. This study was conducted in Austria.
Interventions	**A:** Laser therapy once a week. The lesions were treated with 308 nm radiation emitted by an xenon-chloride excimer laser at a maximal output of 200 nWcm-2 pulse -1, emitted to a 15 x 15 mm spot of the skin. Prior to treatment, the minimal erythema dose (MED) was determined for each participant by irradiating vitiligo patches that had not been selected for treatment or as a control. The initial dose of UV was 50 mJ cm^{-2} less than the erythema dose in vitiligo skin. **B:** Laser therapy as above twice a week.

Hofer 2005 *(Continued)*

	C: Laser therapy as above three times a week. .
Outcomes	**Primary outcomes of the trial** 1) Repigmentation: grade 0 (0%), grade 1 (1% to 5%), grade 2 (6% to 25%), grade 3 (26% to 50%), grade 4 (51% to 75%), and grade 5 (76% to 100%). Measured pre- and post-treatment (12 weeks). 2) Adverse effects. 3) Persistence of repigmentation and participant satisfaction: 0 (low) to 10 (high). Measured at 12 months follow-up.
Notes	Single intervention dose dependent study

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 982): "The three stable lesions in the same body area were randomly assigned to one of three treatment regimens." Comments: Insufficient detail was reported about the method used to generate the allocation sequence. We e-mailed the authors to ascertain which was the randomisation method used if any to which they responded that "For each patient, we had prepared three opaque, sealed envelopes with a carte carrying a treatment frequency of 1, 2, or 3. After mixing the envelopes, we drew envelope after envelope for each of the three lesions and hereby allocated the treatment frequency."
Allocation concealment (selection bias)	Unclear risk	This was not stated. Comments: From the response to the e-mail above described, although using opaque, sealed envelopes these were not sequentially numbered.
Blinding (performance bias and detection bias) participant	High risk	This was not stated.
Blinding (performance bias and detection bias) clinician	High risk	This was not stated.
Blinding (performance bias and detection bias) assessor	High risk	This was not stated.
Incomplete outcome data	High risk	Intention-to-treat analysis was not used. Intervention group not reported: 1 dropout due to noncompliance with the treatment regimen.

Hui-Lan 2009

Methods	This is a randomised left/right within-participant study lasting 15 weeks.
Participants	**Inclusion criteria of the trial**

Hui-Lan 2009 *(Continued)*

- Paediatric vitiligo patients with symmetrical lesions bilaterally distributed on the face, trunk, and hands

Exclusion criteria of the trial

- None reported

49 paediatric participants with symmetrical vitiligo were randomised. The age ranged from 6-14 years with mean age of 10.1 years. The disease duration ranged from 6 months to 3 years with a mean disease duration of 1.31 ± 0.50 years. There were 17 patients with Fitzpatrick skin type II, 27 with type III and 5 with type IV. The study included 29 males and 20 females. 1 participant was lost to follow-up due to worsening of vitiligo.

The study was conducted in China.

Interventions	**Intervention** **A:** 308-nm excimer laser plus topical 1% pimecrolimus cream. The pimecrolimus cream was applied twice daily and the excimer laser was used twice a week for a total of 30 sessions. **Control Intervention** **B:** 308 nm excimer laser alone. The laser was used twice a week for a total of 30 sessions.
Outcomes	Primary outcomes of the trial 1) The degree of repigmentation was graded as: Grade 1: ≤ 25% improvement, Grade 2: 26% to 50% improvement, Grade 3: 51% to 75% improvement, Grade 4 repigmentation: ≥75% improvement. Secondary outcomes of the trial 2) Adverse effects. All outcomes were measured pre- and post-treatment (15 weeks).
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 354): "Forty-nine patients with symmetrical lesions were randomly divided into two groups." Comment: Insufficient detail was reported about the method used to generate the allocation sequence.
Allocation concealment (selection bias)	Unclear risk	This was not stated
Blinding (performance bias and detection bias) participant	Unclear risk	This was not stated. Quote (page 354): "...in this right/left comparative, single-blinded trial." Comment: It is not clear from the text who was blinded.
Blinding (performance bias and detection bias) clinician	Unclear risk	This was not stated. Quote (page 354): "...in this right/left comparative, single-blinded trial." Comment: It is not clear from the text who was blinded.

Hui-Lan 2009 *(Continued)*

Blinding (performance bias and detection bias) assessor	Unclear risk	This was not stated. Quote (page 354): "...in this right/left comparative, single-blinded trial." Comment: It is not clear from the text who was blinded.
Incomplete outcome data	High risk	Intention-to-treat analysis was not used. Because it is a within-participant study there was 1 dropout in both groups. The reason for dropping out was due to the worsening of vitiligo.

Kandil 1974

Methods	Randomised, double-blind, placebo-controlled, within-participant, left/right comparison study lasting 4 months.
Participants	**Inclusion criteria of the trial** • Symmetrically distributed vitiligo lesions **Exclusion criteria of the trial** • Not reported 19 participants with symmetrical vitiligo. Sex and age not mentioned. This study was conducted in Kuwait.
Interventions	**Intervention** **A:** 0.1% betamethasone valerate in 50% isopropyl alcohol. Applied twice daily. **Control Intervention** **B:** Alcohol base, applied to affected areas twice daily.
Outcomes	**Primary outcomes of the trial** 1) Repigmentation: no response, beginning repigmentation, good repigmentation (25% to 90%), and complete cure (90% to 100%). Measure pre- and post-interventions (4 months). 2) Adverse effects included hypertrichosis in 2 participants and acneiform eruptions in 3 in intervention group.
Notes	Improvement not defined. Participants not followed-up.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 457): "The medicated and unmedicated applications were randomly allocated to the right and left patches" Comment: Insufficient detail was reported about the method used to generate the allocation sequence.
Allocation concealment (selection bias)	Unclear risk	This was not stated

Kandil 1974 *(Continued)*

Blinding (performance bias and detection bias) participant	Low risk	Participants were blinded. Quote (page 457): "Neither the investigator nor the patients were aware which of the two applications contained the active principle."
Blinding (performance bias and detection bias) clinician	Low risk	Clinicians were blinded. Quote (page 457): "Neither the investigator nor the patients were aware which of the two applications contained the active principle."
Blinding (performance bias and detection bias) assessor	High risk	This was not stated. Comment: Study described as double-blind. No mention of assessor blinding.
Incomplete outcome data	High risk	Intention-to-treat analysis was not used. Because it is a within-participant study, there were 2 dropouts in both groups (the reason for dropouts were not reported.)

Kathuria 2012

Methods	This is a randomised parallel group study lasting 6 months.
Participants	**Inclusion criteria of the trial** • Patients with segmental vitiligo who were untreated, had not taken any topical treatment in previous 1 month or systemic treatment in previous 2 months **Exclusion criteria of the trial** • Children below 5 years of age • Pregnant and lactating women • Patients with known hypersensitivity to either tacrolimus or fluticasone • patients with segmental vitiligo having multiple lesions of other types of vitiligo 60 participants with segmental vitiligo and age ranging from 5 to 55 years were included (25 females, 35 males). The duration of the condition ranged from 0.08 to 16 years. The percentage of body surface area affected ranged from 0.9% to 6%. 20 patients were lost to follow-up and these were not included in the final analysis. This study was conducted in India.
Interventions	**A:** 0.1% tacrolimus ointment twice daily for 6 months **B:** 0.05% fluticasone propionate cream once daily for 6 months
Outcomes	**Primary outcomes of the trial** 1) Percentage of repigmentation. Repigmentation response was calculated as the percentage of total lesional area of all the macules within the segment showing repigmentation and was graded as follows: 0 - no response or worsening (non-responders), unacceptable (1% to 25%), less than satisfactory (26% to 50%), good (51% to 75%), excellent (76% to 99%), complete (100%). Treatment failure was classified as < 50%. The colour match at 6 months was graded as excellent, good and poor. 2) Adverse effects. All outcomes were measured pre-treatment and at 1, 2, 3, 4, 5, and 6 months.

Kathuria 2012 *(Continued)*

Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 70): "The random allocation sequence was computer generated and consisted of series of group number (either 1 = A or 2 = B) for each consecutive patient. Block randomization method was used and each block was of 10 patients"
Allocation concealment (selection bias)	Unclear risk	Quote (page 70): "The group number was written on a paper and sealed into separate envelopes which bore the number of the corresponding patient, by a departmental colleague not associated with the study. None of the investigators were involved in the generation of random allocation sequence or preparing the envelopes." Comment: Although sealed, it is not clear whether the envelopes were opaque or not.
Blinding (performance bias and detection bias) participant	High risk	Participants were not blinded. Comment: This study was an open-labelled pilot study.
Blinding (performance bias and detection bias) clinician	High risk	Clinicians were not blinded. Comment: This study was an open-labelled pilot study.
Blinding (performance bias and detection bias) assessor	High risk	This was not stated.
Incomplete outcome data	High risk	Intention-to-treat analysis was not used. Intervention - A: 10 dropouts (the reasons for dropouts were not reported.) Control- B: 10 dropouts (the reasons for dropouts were not reported.)

Kawalek 2004

Methods	Randomised, double-blind, placebo-controlled, within-participant, left/right comparison study lasting between 8 and 10 weeks.
Participants	**Inclusion criteria of the trial** • Symmetric vitiliginous patches, present for > 1 year **Exclusion criteria of the trial** • Participants with rapidly progressing disease • Evidence of spontaneous repigmentation • Treatment for their vitiligo within the last 6 months 8 participants with more than 1 stable vitiligo patch, a total of 24 symmetrical patches, were recruited. There were 2 dropouts. 20 patches from 6 participants were evaluated. Non-symmetrical patches were used as controls and received no treatment.

Kawalek 2004 *(Continued)*

	This study was conducted in the US.
Interventions	**Intervention** **A:** 1% tacrolimus ointment was applied to 1 randomised symmetrical patch twice daily. Patches were then exposed to 308 nm xenon-chloride excimer laser up to 3 times per week - maximum number of treatments 24 or 10 weeks whichever was sooner. Initial exposure was for 2 seconds and this was increased by 2 seconds every other visit until erythema (reddening). Erythema and repigmentation were recorded on separate point scales. Repigmentation was scored: 0 = no response, 1 = minimal (25%), 2 = moderate (25% to 75%), 3 = marked (75%), and 4 = complete (100%). Participant skin type noted as per Fitzpatrick. Non-compliance led to discontinuation of the treatment. **Control Intervention** **B:** placebo cream was applied to the other symmetrical patch twice daily. Patches were then exposed to 308 nm xenon-chloride excimer laser up to 3 times per week - maximum number of treatments 24 or 10 weeks whichever was sooner. Irradiation regimen as above.
Outcomes	**Primary outcomes of the trial** 1) Repigmentation: 0 (no response), 1 (minimal, 25%), 2 (moderate, 25% to 75%), 3 (marked, 75%), and 4 (complete, 100%). 2) Rate of repigmentation. 3) Adverse effects. Measured pre- and post-treatment (6 months).
Notes	3 participants who completed the study developed lesional and perilesional hyperpigmentation patches using the combination treatment which subsided within 3 weeks of completing the trial. Adverse effects were not significant, including mild to moderate erythema and blistering on 1 patch. Some participants in both groups (30% placebo, 80% tacrolimus) felt tingling sensation, burning, and erythema. These effects subsided in all participants after several days of treatment.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 131): "Subjects with multiple lesions were instructed to apply tacrolimus 0.1% to one randomised symmetrical patch and placebo cream to the other." Comment: Insufficient detail was reported about the method used to generate the allocation sequence.
Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	Unclear risk	Participants were blinded. Comment: The study described as double-blind. However, no information is provided.
Blinding (performance bias and detection bias) clinician	Unclear risk	Clinicians were blinded. Comment: The study described as double-blind. However, no information is provided.
Blinding (performance bias and detection bias)	High risk	This was not stated.

Kawalek 2004 *(Continued)*

assessor		
Incomplete outcome data	High risk	Intention-to-treat analysis was not used. Because it is a within-participant there were 2 dropouts in both groups due to non-adherence to treatment regimen.

Khalid 1995

Methods	Randomised parallel group study lasting 6 months.
Participants	**Inclusion criteria of the trial** • Clinically diagnosed vitiligo patients under 12 years of age **Exclusion criteria of the trial** • Segmental or mucosal vitiligo • Vitiligo involving more than 20% of the cutaneous surface 50 children under 12 years of age with symmetrical vitiligo. 5 participants were lost at follow-up, resulting in 45 evaluated (23/22). This study was conducted in Pakistan.
Interventions	**A:** -methoxypsoralen (0.1%) ointment, applied 45 minutes prior to exposure to sunlight (topical PUVA-sol). In this group after every 6 weeks treatment was interrupted for 2 weeks. **B:** clobetasol propionate (0.05%) cream applied twice daily. In this group after every 6 weeks treatment was interrupted for 2 weeks.
Outcomes	**Primary outcomes of the trial** 1) Repigmentation: 1% to 25%, 26% to 50%, 51% to 75%, and > 75% . 2) Adverse effects. Measured pre- treatment and 1 year after the treatment had ended.
Notes	1 of 3 studies specifically of children found.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 203): "The patients were randomly assigned to one of the two groups." Comment: Insufficient detail was reported about the method used to generate the allocation sequence.
Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	High risk	This was not stated.

Khalid 1995 *(Continued)*

Blinding (performance bias and detection bias) clinician	High risk	This was not stated.
Blinding (performance bias and detection bias) assessor	High risk	This was not stated.
Incomplete outcome data	High risk	Intention-to-treat analysis was not used. Intervention- A: 2 dropouts (the reasons for dropouts were not reported.) Control- B: 3 dropouts (the reasons for dropouts were not reported.)

Khandpur 2005

Methods	Randomised parallel group study lasting 3 months.
Participants	**Inclusion criteria of the trial** • Vitiligo for 1 to 18 years • Lesions that were resistant to conventional medical treatment, such as topical corticosteroids with or without levamisole and photochemotherapy, • Neither progressed nor regressed for a period of 6 months **Exclusion criteria of the trial** • Patients with bleeding diathesis • Keloidal tendency • Serious uncontrolled systemic illnesses • Pregnant women 64 participants (34 mini punchgrafting (MPG), 30 split skin grafting (SSG)) with stable localised vitiligo whose lesion were resistant to conventional medical treatment and neither progressed nor regressed for a period of 6 months. In the MPG group 10 were male and 24 female, they were aged between 10 and 28 years old (mean 19.91) and had had vitiligo for between 1 and 12 years. In the SSG group 9 were male and 21 were female, they were aged between 12 and 42 years (mean 22.6), and had had vitiligo for between 2 and 18 years. This study was conducted in India.
Interventions	**A:** Mini-punchgrafting using 2.5 mm diameter punches, grafts were obtained from the upper thigh after infiltrating the area with 2% lignocaine without adrenaline. The grafts ranged from approximately 1 (1 X 1 cm) to 18 cm^2 (6 X 3 cm). After 2 weeks, once the grafts were accepted, the participants were advised to undergo PUVAsol therapy (tablet 8-methoxypsoralen, 0.6 mg/kg/d, followed 2 hours later by sun exposure) on alternate days. **B:** Split skin grafts were obtained from the thigh region after scrutiny for scars, striae, or infection. The grafts ranged from approximately 1 (1 X 1 cm) to 18 cm^2 (6 X 3 cm). After 2 weeks, once the grafts were accepted, the participants were advised to undergo PUVAsol therapy (tablet 8-methoxypsoralen, 0.6 mg/kg/d, followed 2 hours later by sun exposure) on alternate days.
Outcomes	**Primary outcomes of the trial** 1) Repigmentation: fair (31% to 50%), good (51% to 75%), very good (76% to 90%), and excellent (91% to 100%). 2) Adverse effects.

Khandpur 2005 *(Continued)*

	Measured pre- and post-treatment (3 months).
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 436): "They were randomized into two groups." Comment: Insufficient detail was reported about the method used to generate the allocation sequence.
Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	High risk	This was not stated.
Blinding (performance bias and detection bias) clinician	High risk	This was not stated.
Blinding (performance bias and detection bias) assessor	High risk	This was not stated.
Incomplete outcome data	Low risk	Intention-to-treat analysis was used. No dropouts.

Klahan 2009

Methods	This is a randomised, within-participant study lasting 12 weeks.
Participants	**Inclusion criteria of the trial** • Patients aged ≥ 18 years with generalised and focal vitiligo • Stable vitiligo, defined as unchanged for at least 8 weeks before enrolment **Exclusion criteria of the trial** • None reported 15 participants with stable vitiligo, defined as unchanged for at least 8 weeks before enrolment, were included in this study. The mean age was 41.67 and the range was 27–65 years. 6 males and 5 females were included. 7 participants had had vitiligo for 0 to 5 years (46.7%), 3 participants for 6 to 10 years (20%) and 5 participants for >10 years (33.3%). This study was conducted in Thailand.
Interventions	**Intervention** **A:** Tacrolimus 0.1% ointment plus NB-UVB. Tacrolimus ointment was applied twice daily and never before phototherapy. Phototherapy was given twice weekly for a maximum of 24 sessions or 12 weeks. **Control Intervention**

Klahan 2009 *(Continued)*

	B: NB-UVB alone. Phototherapy was given twice weekly for a maximum of 24 sessions or 12 weeks.
Outcomes	**Primary outcomes of the trial** 1) Degree of repigmentation was graded using a 9-point score. Depigmentation was graded as -4 = 76% to 100% depigmentation, -3 = 51% to 75% depigmentation, -2 = 26% to 50% depigmentation, and -1 = 1% to 25% depigmentation, 0 = no change. Repigmentation was scored as: 1 = 1% to 25% repigmentation, 2 = 26% to 50% repigmentation; 3 = 51% to 75% repigmentation and 4 = 76% to 100% repigmentation. 2) Adverse effects. All outcomes were measured pre- and post-treatment (12 weeks) and at 4 and 8 weeks.
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page e1029): "Participants were randomized by the assessor (SK, who also performed the treatment) drawing cards with the names of the treatment groups (i.e., combination or monotherapy) for each participant."
Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	High risk	Participants were not blinded.
Blinding (performance bias and detection bias) clinician	High risk	Clinicians were not blinded.
Blinding (performance bias and detection bias) assessor	Low risk	Outcome assessor was blinded. Quote (page e1029): "This was a within-subject, randomized study with assessor blinding."
Incomplete outcome data	Low risk	Intention-to-treat analysis was used. No dropouts.

Kumaran 2006

Methods	Randomised, parallel group study lasting 3 months.
Participants	**Inclusion criteria of the trial** • Vitiligo patients with a body surface area involvement of ≤ 5% **Exclusion criteria of the trial** • Patients with leucoderma secondary to other causes • Segmental vitiligo • Zosteriform vitiligo • Rapidly spreading vitiligo

Kumaran 2006 *(Continued)*

	• Pregnancy • Those with lesions on areas known to be recalcitrant to therapy such as mucosal vitiligo and lesions over dorsa of hands and feet. 49 participants (group 1: 18 participants, group 2: 16 participants, group 3: 15 participants) with symmetrical vitiligo affecting less than 5% of their body surface area and aged between 10 and 60 years old. 4 participants from intervention groups 1 and 2 were lost to follow-up, resulting in 45 evaluated (15 in each group) of which 21 were male and 24 female. This study was conducted in India.
Interventions	**A:** Topical betamethasone dipropionate (0.05%) twice daily. **B:** Topical calcipotriol ointment (0.005%) twice daily. **C:** Topical betamethasone dipropionate (0.05%) in the morning and topical calcipotriol ointment (0.005%) in the evening.
Outcomes	**Primary outcomes of the trial** 1) Repigmentation: minimal/no response (< 25%), moderate (25% to 50%), marked (50% to 75%), and excellent (> 75%). 2) Adverse effects. Measured pre- and post-treatment (3 months) and at 2 months follow-up.
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 270): "The patients were randomised into three treatment groups according to the Tippet random number table."
Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	High risk	Participants were not blinded. Comment: Not possible as some participants used only cream, some only ointment, and some used both so the qualities of the topical applications were different.
Blinding (performance bias and detection bias) clinician	High risk	Clinicians were not blinded. Comment: 3 separate treatments used so blinding of clinician not possible.
Blinding (performance bias and detection bias) assessor	High risk	This was not stated.
Incomplete outcome data	High risk	Intention-to-treat analysis was not used. Intervention A: 3 dropouts, Intervention B: 1 dropout (the reasons for dropouts were not reported.) Intervention C: 0 dropouts

Köse 2010

Methods	This is a randomised parallel group study lasting 12 weeks.
Participants	**Inclusion criteria of the trial** • Paediatric patients with stable localised vitiligo (including vitiligo vulgaris, focal vitiligo, segmental vitiligo and acrofacial vitiligo) • Lesions not exceeding 10% of their body surface **Exclusion criteria of the trial** • Patients who had undergone any treatment for vitiligo within the past 6 months • Thyroid or parathyroid disease • Renal or hepatic dysfunction 50 children with stable vitiligo were randomised. The age range varied from 3.41 to 13.7 years and the mean age of the mometasone furoate group was 9.15 years whilst the mean age of the pimecrolimus group was 8.61 years. Overall, the study included 26 females and 24 males. The mean duration of vitiligo for the mometasone furoate group was 12.4 months (range 1.05 to 36.25) and in the pimecrolimus group this was 13.75 months (range 2.45 to 45.15). 5 patients (20%) were lost to follow-up from the mometasone furoate group - 4 of these discontinued due to side effects. 5 patients (20%) were also lost to follow-up from the pimecrolimus group - 3 of these discontinued due to side effects. There was no intention-to-treat analysis. The study was conducted in Turkey.
Interventions	**A:** 0.1% mometasone furoate cream (M-Furo) once daily for 12 weeks. **B:** 1% pimecrolimus cream (Elidel) twice daily for 12 weeks.
Outcomes	**Primary outcomes of the trial** 1) The degree of repigmentation was graded as follows: minimal response (0% to 25% decrease in lesion size), moderate response (25% to 50% decrease in lesion size), marked response (50% to 75% decrease in lesion size), excellent (> 75% decrease in lesion size) or no change. The total vitiligo score was also calculated from the sum of the surface area of all lesions. 2) Adverse effects. All outcomes were measured pre- and post-treatment (12 weeks) as well as follow-up examinations at the 2nd, 4th, and 6th months after ceasing the medication.
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 134): "A computer-generated random list was used for patient randomization."
Allocation concealment (selection bias)	High risk	This was not stated. Comment: quote (page 134): "Also, the investigator (OK) was aware of the randomization list at the time of actual randomization of each patient."
Blinding (performance bias and detection bias) participant	High risk	Participants were not blinded.

Köse 2010 *(Continued)*

		Quote (page 134): "This study was an open label, single-center, comparative trial."
Blinding (performance bias and detection bias) clinician	High risk	Clinicians were not blinded. Quote (page 134): "This study was an open label, single-center, comparative trial."
Blinding (performance bias and detection bias) assessor	High risk	This was not stated.
Incomplete outcome data	High risk	Intention-to-treat analysis was not used. Intervention - A: 5 dropouts (reasons: lost to follow-up (1); discontinued therapy due to side effects (4)) Intervention - B: 5 dropouts (reasons: lost to follow-up (2); discontinued therapy due to side effects (3))

Le Duff 2010

Methods	This is a randomised within-participant study lasting 12 weeks.
Participants	**Inclusion criteria of the trial** • Adult patients with symmetrical non-segmental vitiligo • Lesions of at least 10 cm^2 • Evolving for at least 3 months **Exclusion criteria of the trial** • Pregnancy • Personal history of skin cancer • Radiotherapy on the area treated • Other contraindications for phototherapy (photodermatosis, photosensitive treatments) • Leucotrichia • Topical or systemic treatment 4 weeks before inclusion, and phototherapy 12 weeks before inclusion 20 participants with symmetrical non-segmental vitiligo were randomised. The mean age was 38 with age range of 21 to 54 years. On average participants had had vitiligo for 17 years (range 3 to 35 years). Five patients (29%) were phototype V, one (6%) was phototype IV, six (36%) were phototype III and five (29%) were phototype II. The sex ratio of females to males was 1.4:1. 3 patients were lost to follow-up for professional reasons. There was no intention-to-treat analysis.
Interventions	**A:** 308-nm excimer laser. The treatment was given twice weekly on nonconsecutive days (every Tuesday and Friday) for a total of 24 sessions. The MED was assessed for both lamp and laser. If the MED obtained with the two devices was different, the lower dose was chosen as reference to determine the initial treatment dose. Doses were then increased by 50mJ cm)2 every two sessions.14 If erythema lasted more than 48 hours or if blisters were observed, the doses were decreased to the highest doses that did not induce such side effects. The fluence was kept exactly identical for lamp and laser for the same pair of symmetrical patches. **B:** 308-nm excimer lamp. The treatment was given twice weekly on nonconsecutive days (every Tuesday and Friday) for a total of 24 sessions. The MED was assessed for both lamp and laser. If the MED obtained with the two devices was different, the lower dose was chosen as reference to determine the initial treatment dose. Doses were then increased by 50mJ cm) 2 every two sessions.14 If erythema lasted more than 48 hours or if blisters were observed, the doses were decreased to the highest doses that did

Le Duff 2010 *(Continued)*

	not induce such side effects. The fluence was kept exactly identical for lamp and laser for the same pair of symmetrical patches.
Outcomes	**Primary outcomes of the trial** 1) The degree of repigmentation was graded as: 0 = 0% change, 1 = 1% to 25% repigmentation, 2 = 26% to 50% repigmentation, 3 = 51% to 75% repigmentation and 4 = 76% to 100% repigmentation. The main criterion used was the rate of repigmentation > 50% (score 3 and 4) at the final visit compared with baseline in each treatment group. 2) Adverse effects. All outcomes were measure pre- and post-treatment (24 sessions) and 1 month after the last session.
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 188): "In a pair, laser treatment was randomly assigned to a patch, lamp treatment was used on the counterpart lesion." Comment: Insufficient detail was reported about the method used to generate the allocation sequence.
Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	High risk	Participants were not blinded.
Blinding (performance bias and detection bias) clinician	Unclear risk	Clinicians were blinded. Comment: However no information was provided.
Blinding (performance bias and detection bias) assessor	Low risk	Outcome assessors were blinded. Quote (page 189): "The evaluation of repigmentation was made by blinded comparison of pictures between the first and final visit by two independent observers."
Incomplete outcome data	High risk	Intention-to-treat analysis was not used. Quote (page 189): "Of the 20 patients included, 17 were analysed..." Because it is a within-participant study there were 3 dropouts in both groups. The reasons for dropouts were professional.

Leone 2006

Methods	Randomised, single-blind, within-participant, left/right comparison study lasting 6 months.
Participants	**Inclusion criteria of the trial** • Adults with vitiligo with symmetrical distribution (generalised). • Lesions stable for at least 6 months before enrolment.

Leone 2006 *(Continued)*

	Exclusion criteria of the trial • Age < 18 years • Treatment with phototherapy, PUVA or sun exposure in the previous 3 months • Presence of spontaneous repigmentation • Segmental vitiligo 64 participants with stable symmetrical vitiligo affecting more than 20% of their body surface area. Participants were aged between 18 and 54 years old (mean 35.8) and 11 were male and 21 female. This study was conducted in Italy.
Interventions	**A:** tacalcitol ointment once a day (in the evening) at a dose of 10 mg/4 cm^2 to one side of their body and they were subjected to NB-UVB twice a week. The initial dose was 70% of the minimal erythema dose on unaffected skin. The doses were increased by 30% for treatments 1 to 4, 20% for treatments 4 to 8, and 10% for treatments 8 and onwards. The dose was held constant if minimal asymptomatic erythema occurred. If symptomatic erythema occurred or blistering developed, treatment was withheld and the last dose was decreased by 20% when treatment resumed. **B:** NB-UVB alone twice a week, administered as described above.
Outcomes	**Primary outcomes of the trial** 1) Repigmentation: none (score 0), moderate (< 50%, score 1), good (50% to 80%, score 2), and excellent (> 80%, score 3). Pre- and post-treatment (6 months).
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 201): "This study was a randomized, prospective, assessor-blinded, bilateral-paired study of tacalcitol in combination with NB-UVB vs. NB-UVB alone for treatment of generalized vitiligo in adults." Comment: Insufficient detail was reported about the method used to generate the allocation sequence. We therefore e-mailed the authors who responded that they used the "Adaptive Randomisation version 3.2."
Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	High risk	Participants were not blinded. Comment: Not possible to blind as some participants received topical treatment and some did not.
Blinding (performance bias and detection bias) clinician	High risk	Clinicians were not blinded. Comment: Not possible to blind as some participants received topical treatment and some did not.
Blinding (performance bias and detection bias) assessor	Low risk	Outcome assessors were blinded. Quote (page 201): "Treated areas were evaluated for repigmentation and were assessed in a blinded manner by a single observer at baseline and at the end of the study."

Leone 2006 *(Continued)*

Incomplete outcome data	Low risk	Intention-to-treat analysis was used. Quote (page 201): "All subjects completed the 6 months of therapy and all were included in the statistical analysis for efficacy."

Lepe 2003

Methods	Randomised, double-blind, within-participants, left/right comparison study lasting 2 months.
Participants	**Inclusion criteria of the trial** • <18 years of age • VIDA score >3 • No vitiligo therapy for 2 months prior to the study **Exclusion criteria of the trial** • Segmental and mucosal vitiligo 20 children aged between 4 and 17 years old with symmetrical vitiligo. This study was conducted in Mexico.
Interventions	**A:** 0.1% tacrolimus twice per day. **B:** 0.05% clobetasol propionate twice per day.
Outcomes	**Primary outcomes of the trial** 1) Repigmentation: none (0%), poor (1% to 25%), moderate (26% to 50%), good (51% to 75%), and excellent (> 75%). 2) Adverse effects. Pre- and post-treatment (2 months).
Notes	1 of 3 studies on children with vitiligo. 3 participants on clobetasol propionate presented atrophy and 2 lesions incurred telangiectasias. Tacrolimus caused a burning sensation in 2 lesions.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 582): "The method of randomisation was the technique of permuted block randomisation for right or left selection."
Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	Low risk	Participants were blinded. Quote (page 582): "Two lesions....were selected....in a double-blind randomised way. The medications were in exactly the same containers packed by a person unaware of the study."
Blinding (performance bias and detection bias) clinician	Low risk	Clinicians were blinded.

Lepe 2003 *(Continued)*

		Quote (page 582): "..in a double-blind randomised way. The medications were in exactly the same containers packed by a person unaware of the study."
Blinding (performance bias and detection bias) assessor	Low risk	Outcome assessors were blinded. Quote (page 582): "Colour slides were taken at the beginning and end of the treatment period. The slides were analysed visually by two clinicians not involved in the study."
Incomplete outcome data	Low risk	Intention-to-treat analysis was used. No dropouts.

Lim-Ong 2005

Methods	Randomised, double-blind, placebo-controlled, within-participants, left/right comparison study lasting 6 months.
Participants	**Inclusion criteria of the trial** • Age 4 years and above • Generalised vitiligo defined as vitiligo with widespread distribution of lesions often in a symmetric array • 5% to 50% BSA involvement • Not limited to hands or feet • At least 2 bilateral comparative vitiligo patches • No treatment for vitiligo in the past 3 months **Exclusion criteria of the trial** • Claustrophobia • History of photosensitivity • Skin cancer • Severe uncontrolled systemic disease • Concomitant radiotherapy or chemotherapy • Use of immunosuppressive of photosensitising drugs • Pregnant or lactating 25 participants with generalised vitiligo that affected between 5% and 25% of their body surface area (mean 13.5). 4 participants were male and 16 were female and they were aged between 10 and 55 years old (mean 38.15). The participants had been affected by vitiligo for between 0.25 and 20 years (mean 6.08). 5 participants were lost at follow-up, resulting in 20 evaluated. This study was conducted in the Phillipines.
Interventions	**Intervention** **A:** clobetasol propionate ointment (at bedtime) to 1 side of their body once a day. The participants then received NB-UVB 3 times a week. The initial dose was 75 mJ/cm^2, which increased by 20% at each subsequent session until an optimal dose was reached (erythema without pain) and maintained. If pain/vesiculation occurred, treatment was withheld and the dose was reduced by 25%. **Control Intervention** **B:** white petrolatum (placebo) to the other side of their body, once a day. The participants then received NB-UVB 3 times a week administered as described above.
Outcomes	**Primary outcomes of the trial**

Lim-Ong 2005 *(Continued)*

	1) Repigmentation: minimal (< 25%), moderate (26% to 75%) and marked (> 75%), which was measured pre- and post-treatment (6 months). 2) Adverse effects. 3) Cessation of spread, which was measured at 1-year follow-up.
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 18): "The left and right halves of the body were randomised...using a computer-generated table of random numbers."
Allocation concealment (selection bias)	Unclear risk	This was not stated. Comment: Although a computer-generated table was used no information was given as to whether it was kept concealed.
Blinding (performance bias and detection bias) participant	Low risk	Participants were blinded. Quote (page 18): "Patients were provided weekly with...medication placed in identical containers."
Blinding (performance bias and detection bias) clinician	Low risk	Clinicians were blinded. Quote (page 18): "Patients were provided weekly with...medication placed in identical containers....which were packed and dispensed by investigator 1."
Blinding (performance bias and detection bias) assessor	Low risk	Outcome assessor was blinded. Quote (page 19): "To avoid inter-investigator variability, a single investigator who was blinded to the treatment groups performed the evaluation. An independent statistician, who was blinded regarding the identities of treatment groups, performed all statistical analyses."
Incomplete outcome data	High risk	Intention-to-treat analysis was not used. Because it is a within-participant study there were 5 dropouts in both groups (the reasons for dropouts were due to Köebner phenomenon secondary to phototherapy (1), gastrointestinal malignancy diagnosis (1), uncontrolled diabetes mellitus (1), schedule inconvenience (2).)

Linthorst Homan 2012

Methods	This is a randomised within-participant study lasting 3 months.
Participants	**Inclusion criteria of the trial** • Adult patients (18 years or older) with stable generalised vitiligo defined as no progression of existing lesions or no appearance of new lesions during the previous 6 months • Absence of the Köebner phenomenon • A positive minigrafting test • The presence of two symmetrical vitiligo patches on the extremities or the trunk **Exclusion criteria of the trial**

Linthorst Homan 2012 *(Continued)*

- A history of hypertrophic scarring and/or keloid
- Allergic/phototoxic reaction (Lidocaine, Tegaderm, Suture strips and sunlight)
- A personal or family history of skin cancer
- Photosensitivity and/or photo toxicity disorders
- Skin type I (according to Fitzpatrick classification I-VI)
- Pregnancy
- Use of medications known to cause photosensitivity and/or photo toxicity
- Other skin diseases that would impair evaluation of repigmentation
- Local immunosuppressive treatment within 6 weeks prior to enrolment.

16 participants with stable generalised vitiligo were randomised. Stable vitiligo was defined as no progression of existing lesions or no appearance of new lesions during the previous 6 months, the absence of the Köebner phenomenon and a positive minigrafting test. The median age was 47.2 with 4 patients having had vitiligo for 1 to 5 years and 10 patients for over 10 years. There were 5 males and 9 females. 2 patients were lost to follow-up for private reasons unrelated to the study. There was no intention-to-treat analysis.

The study was conducted in the Netherlands.

Interventions	**A:** Punch grafting and treatment with 308-nm xenon chloride excimer laser (EL) after grafting. The punch grafting method consists of harvesting small 1.5 mm full thickness punch grafts from normally pigmented donor sites (such as hip, buttocks and outer thigh). These were subsequently transplanted to the two depigmented acceptor sites in which similar punches were taken and removed. The grafts were placed 5 mm apart and were covered with suture strips and a transparent adhesive tape (Tegaderm) during 7 days. 7 days after punch grafting, the grafted areas were irradiated with EL for 3 months. Treatment was given twice a week, on non-consecutive days amounting to 24 treatments. The initial dose of EL was 0.05 J/cm^2 and sequential doses had an increment according to the manufacturer's guidelines, with a range of 0.025–0.10 J/cm^2. Doses were not increased if there was erythema lasting for 24 hours or more. The mean cumulative dose was 7.32 ± 3.50 J/cm^2 **B:** Punch grafting and treatment with narrow-band ultraviolet B (NB-UVB) after grafting. The punch grafting method consists of harvesting small 1.5 mm full thickness punch grafts from normally pigmented donor sites (such as hip, buttocks and outer thigh). These were subsequently transplanted to the two depigmented acceptor sites in which similar punches were taken and removed. The grafts were placed 5 mm apart and were covered with suture strips and a transparent adhesive tape (Tegaderm) during 7 days. 7 days after punch grafting, the grafted areas were irradiated with NB-UVB for 3 months. Treatment was given twice a week, on non-consecutive days amounting to 24 treatments. The initial irradiation dose of NB-UVB was 0.25 J/cm^2. Irradiation dose was increased by 50 mJ/cm^2 with each subsequent treatment when minimal erythema occurred in the lesions, which means an erythema vanishing within 24 hours. If the erythema was lasting for 24 hours or more the dose was held constant for the subsequent treatment. The mean cumulative dose was 25.60 ± 11.62 J/cm^2
Outcomes	**Primary outcomes of the trial** 1) The degree of repigmentation was assessed and the mean degree of repigmentation was calculated. More than 75% repigmentation was obtained in two patients after EL. More than 75% repigmentation was obtained in three patients after NB-UVB 2) Treatment satisfaction was also measured using a study-specific questionnaire. Answers were given on a 7-point scale running from 'very good' to 'very poor', and 'yes, certainly' to 'no, certainly not' respectively. Outcomes were measured pre- and post-treatment (3 months).
Notes	-
Risk of bias	

Linthorst Homan 2012 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 691): "The site of treatment with EL and NB-UVB was randomly assigned with a randomization computer program (Graphpad Software Inc., La Jolla, CA, USA)."
Allocation concealment (selection bias)	Unclear risk	Quote (page 691): "Treatment allocation was blinded for the physicians, not for the patients." Comment: Insufficient detail was reported about the method used to generate the allocation concealment.
Blinding (performance bias and detection bias) participant	Unclear risk	Participants were not blinded. Quote (page 691): "We employed a prospective, single blinded, randomized withinpatient controlled study design." "Treatment allocation was blinded for the physicians, not for the patients."
Blinding (performance bias and detection bias) clinician	Low risk	Clinicians were blinded. Quote (page 691): "We employed a prospective, single blinded, randomized withinpatient controlled study design." "Treatment allocation was blinded for the physicians, not for the patients."
Blinding (performance bias and detection bias) assessor	High risk	This was not stated.
Incomplete outcome data	High risk	Intention-to-treat analysis was not used. Because it is a within-participant study there were 2 dropouts in both groups due to private problems unrelated to the study.

Lu-Yan 2006

Methods	A randomised, single-blind, placebo-controlled, within-participant, left/right comparison study lasting 12 weeks.
Participants	**Inclusion criteria of the trial** • Patients with vitiligo, type not stated. **Exclusion criteria of the trial** • Pregnant or breastfeeding women • History of melanoma or malignant skin tumours • Immunosuppression or taking immunosuppressive medicine • Taking photosensitising drugs • Phototherapy or any other treatment for vitiligo within the last 3 months • History of spontaneous repigmentation during 1-year period • Photosensitivity, • History of thyroid or parathyroid disease and • History of contact allergy to tacalcitol

Lu-Yan 2006 *(Continued)*

	38 participants with vitiligo. 3 participants were lost at follow-up, resulting in 35 evaluated participants. Participants were aged between 6 and 65 years old (mean 34.8, SD 16). 6 participants had segmental vitiligo and 29 had vitiligo vulgaris, which affected between 5% and 30% of their body surface area. This study was conducted in China.
Interventions	**Intervention** **A:** tacalcitol plus 308 nm monochromatic excimer light. The tacalcitol was applied twice a day, 2 hours before monochromatic excimer light. The initial dose of monochromatic excimer light was 0.5 to 0.6 J/mc^2. Subsequent treatments increased by 0.1 J/mc^2 according to erythema and/or repigmentation response. The initial fluence for each participant was 70% of minimal erythema doses. The dose was held constant when minimal asymptomatic erythema occurred in the lesions. If symptomatic erythema or blistering developed, the following treatment was omitted either once or twice. **Control Intervention** **B:** vehicle plus 308 nm monochromatic excimer light. The initial dose of monochromatic excimer light was 0.5 to 0.6 J/mc^2. Subsequent treatments increased by 0.1 J/mc^2 according to erythema and/or repigmentation response. The initial fluence for each participant was 70% of minimal erythema doses. The dose was held constant when minimal asymptomatic erythema occurred in the lesions. If symptomatic erythema or blistering developed, the following treatment was omitted either once or twice.
Outcomes	**Primary outcomes of the trial** 1) Repigmentation: excellent (75% to 100%), good (50% to 74%), moderate (25% to 49%), poor (1% to 24%), and zero (0%). 2) Adverse effects. Measured pre- and post-treatment (3 months).
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 311): "Patients were asked to apply...on the randomly selected side." Comment: Insufficient detail was reported about the method used to generate the allocation sequence.
Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	Low risk	Participants were blinded. Although study is reported as single-blind, the following quote is in the text (page 311): "The clinical investigator and patients were unaware of the specific drugs that were applied to each side during the course of the study."
Blinding (performance bias and detection bias) clinician	Low risk	The clinician was blinded. Although study is reported as single-blind, the following quote is in the text (page 311): "The clinical investigator and patients were unaware of the specific drugs that were applied to each side during the course of the study."
Blinding (performance bias and detection bias)	High risk	No separate outcome assessor mentioned.

Lu-Yan 2006 *(Continued)*

assessor		
Incomplete outcome data	High risk	Intention-to-treat analysis was not used. Because it is a within-participant there were 3 dropouts in both groups (reasons: non-compliance (2), and use of additional medication (1).)

Mehrabi 2006

Methods	Randomised, placebo-controlled, double-blind, within-participant, left/right comparison study lasting 12 weeks.
Participants	**Inclusion criteria of the trial** • Generalised vitiligo (symmetrical). • Stable disease (<10% change in the last 6 months) **Exclusion criteria of the trial** • Segmental, acrofacial, or localised vitiligo • Areas classically resistant to treatment (elbows, hands, knees and feet) • Sun-exposed areas • Immunosupression • History of skin cancer 9 participants (5 female, 4 male) with stable generalised vitiligo affecting between 5% to 50% of their body surface area and 2 vitiligo patches at least 2 x 2 cm in dimension. Participants were aged between 28 and 49 years old (mean 39.8) and had been affected by vitiligo for between 1 and 41 years (mean 19.2). 1 participant was lost at follow-up, resulting in 8 evaluated participants. This study was conducted in the US.
Interventions	**Intervention** **A:** Narrowband UVB plus tacrolimus 3 times a week. The initial dose was 70% of the minimal erythema dose (MED) for each participant or 196 mJ/cm^2. The dose was subsequently increased by 15% each visit. If mild erythema was reached, fluence was held at a constant level; if moderate erythema was experienced, fluence was decreased by 15%; if severe erythema was experienced, or vesicles or bullae, treatment was withheld. Tacrolimus 0.1% was applied topically to 1 side of the body. **Control Intervention** **B:** Narrowband UVB plus placebo 3 times a week. The initial dose was 70% of the minimal erythema dose (MED) for each participant or 196 mJ/cm^2. The dose was subsequently increased by 15% each visit. If mild erythema was reached, fluence was held at a constant level; if moderate erythema was experienced, fluence was decreased by 15%; if severe erythema was experienced, or vesicles or bullae, treatment was withheld. Petrolatum applied topically to the other side of the body.
Outcomes	**Primary outcomes of the trial** 1) Average percentage of repigmentation. 2) Adverse effects. Measured pre- and post-treatment (12 weeks).
Notes	The frequency of the application of tacrolimus and placebo was not reported

Mehrabi 2006 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 927): "Investigators and patients were blinded to the contents of the identical containers, which were labelled A and B, and the side to which the active drug was applied was randomly determined by a third party" Comment: Insufficient detail was reported about the method used to generate the allocation sequence. Information from full manuscript provided by author: "The randomisation list was created by this third party by coin flip."
Allocation concealment (selection bias)	Low risk	This was not stated. Comment: insufficient detail was reported about the method used to generate the allocation concealment. Information from full manuscript provided by author: "The randomisation list was created by this third party by coin flip."
Blinding (performance bias and detection bias) participant	Low risk	Participant were blinded. Quote (page 927): "Investigators and patients were blinded to the contents of the identical containers, which were labelled A and B."
Blinding (performance bias and detection bias) clinician	Low risk	Clinicians were blinded. Quote (page 927): "Investigators and patients were blinded to the contents of the identical containers, which were labelled A and B."
Blinding (performance bias and detection bias) assessor	Low risk	Outcome assessor was blinded. Comment: All Polaroid® photographs and computer analysed measurements were performed by the same person (DM), who had no knowledge of treatment assignments.
Incomplete outcome data	Low risk	Intention-to-treat analysis was used. One patient dropped out because she had missed 9 of the first 20 NB UV-B treatments.

Middelkamp-Hup 2007

Methods	Randomised, double-blind, placebo-controlled, parallel study lasting between 25 and 26 weeks.
Participants	**Inclusion criteria of the trial** • A clinical diagnosis of vitiligo vulgaris and aged 18 years or older **Exclusion criteria of the trial** • A history of skin cancer • Abnormal photosensitivity • Pregnancy or lactation • Segmental vitiligo • Phototherapy or sun exposure 3 months prior to enrolment • Use of topical treatments during the study and starting vitamin intake during the study. Participants with vitiligo vulgaris aged 18 years or over.The intervention group consisted of 25 participants aged between 22 and 58 years old (mean 38.6). 10 were male and 15 were female and had been

Middelkamp-Hup 2007 *(Continued)*

	affected by vitiligo for between two and 51 years (mean 21.7). 68% had vitiligo affecting 0% to 15% of their body surface area, 20% had vitiligo affecting 26% to 50% of their body surface area, and 12% had vitiligo affecting 76% to 100% of their body surface area. The control group comprised of 25 participants aged between 28 and 65 years old (mean 46.3). 7 were male and 18 were female and had been affected by vitiligo for between 1 and 48 years (mean 20.5). 72% of participants had vitiligo affecting 0% to 25% of their body surface area, 20% had vitiligo affecting 26% to 50% of their body surface area and 4% had vitiligo affecting 51% to 75% of their body surface area. 1 participant was lost at follow-up, resulting in 49 evaluated participants. This study was conducted in the Netherlands.
Interventions	**Intervention** **A:** *Polypodium leucotomos* plus NB-UVB. The intervention group took *polypodium leucotomos* capsules (250 mg) 3 times a day. Participants were subjected to NB-UVB twice a week (on non-consecutive days), using light tubes emitting UVB with a spectrum of 310 to 315 nm and a maximal wavelength of 311 nm. The initial dose was between 210 and 360 mJ/cm^2 according to skin type and doses were gradually increased until a mild erythema was reached between 5 and 12 hours after exposure. Lesions requiring more exposure were exposed longer. **Control Intervention** **B:** placebo plus NB-UVB. The control group took placebo capsules 3 times a day. Participants were subjected to NB-UVB twice a week (on non-consecutive days), using light tubes emitting UVB with a spectrum of 310 to 315 nm and a maximal wavelength of 311 nm. The initial dose was between 210 and 360 mJ/cm^2 according to skin type and doses were gradually increased until a mild erythema was reached between 5 and 12 hours after exposure. Lesions requiring more exposure were exposed longer.
Outcomes	**Primary outcomes of the trial** 1) Percentage of repigmentation. 2) Patient-rated quality of life: Skindex-29. 2) The effect of treatment cytokines in serum. 4) Clinician global assessment (severity of vitiligo): very severe, severe, more or less severe, and not so severe. 5) Participant global assessment (severity of vitiligo): grade from 0 to 10. 6) Adverse effects. Measured pre- and post-treatment (26 weeks).
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 2): "Randomisation occurred via an automated computerised method using Clipper, Version 5.2c and the library Nantucket tools II (Software developer: P Duarte Mejías, Madrid, Spain)."
Allocation concealment (selection bias)	Low risk	Quote (page 2): "Medication was dispensed by Dr Middelkamp-Hup, whereas randomization was performed by a third party that possessed the code during the entire study."
Blinding (performance bias and detection bias) participant	Low risk	Participants were blinded.

Middelkamp-Hup 2007 *(Continued)*

		Quote (page 2): "To ensure the reliability of blinding, medication was packaged in identical (numbered) containers holding identical capsules.... The randomisation remained blinded for the study investigators and participants."
Blinding (performance bias and detection bias) clinician	Low risk	Clinicians were blinded. Quote (page 2): "To ensure the reliability of blinding, medication was packaged in identical (numbered) containers holding identical capsules...The randomisation remained blinded for the study investigators and participants."
Blinding (performance bias and detection bias) assessor	High risk	No separate outcome assessor mentioned.
Incomplete outcome data	High risk	Intention-to-treat analysis was not used. Intervention- A: 0 dropouts. Control- B: 1 dropout (the reason for the dropout was unknown. Quote (page 3): "One patient was lost to follow-up by not attending the last visit for unknown reasons, despite repeated contact efforts.")

Mohaghegh 2012

Methods	This was a randomised within-participant study lasting 3 months.
Participants	Inclusion criteria of the trial • 2 different vitiligo patches per patient which did not respond to any type of treatment during the last 6 months. Exclusion criteria of the trial • Those who had disease that could be exacerbated by ultraviolet light (like systemic lupus erythematosus). 21 participants were randomised. The age range was from 14 to 40 years. The duration of vitiligo was from 10 months to 21 years. There were no losses to follow-up.
Interventions	**Interevention** **A:** NB-UVB in adjunction with needling. Initial radiation dose was 0.5-1 J/cm^2 modified due to presence and severity of lesional erythema by 0.1 J/cm^2 to decrease side effects and enhance therapeutic response. One patch per participant was subjected to needling from the peripheral border just before each session of NB-UVB by using a 30G insulin needle. The needle was inserted by a 15 degree angle to reach the dermo-epidermal junction in several points 1 cm apart. Treatment was performed 3 times per week. **Control Intervention** **B:** NB-UVB alone. Initial radiation dose was 0.5-1 J/cm^2 modified due to presence and severity of lesional erythema by 0.1 J/cm^2 to decrease side effects and enhance therapeutic response. This was given 3 times per week.
Outcomes	Primary outcomes of the trial 1) Percentage of repigmentation. This was graded as: grade 0 none, grade 1 up to 25%, grade 3 25% to 50%, grade 3 > 50%. 2) Adverse effects

Mohaghegh 2012 *(Continued)*

	Outcomes were measured at baseline and after completion of treatment (3 months).
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page S132): "...vitiligo patients, who were selected randomly with simple random sampling"
Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	High risk	Participants were not blinded. Comment: Not stated but guess impossible since needles are involved in one treatment.
Blinding (performance bias and detection bias) clinician	High risk	Clinicians were not blinded. Comment: Not stated but guess impossible since needles are involved in one treatment.
Blinding (performance bias and detection bias) assessor	High risk	Outcome assessors were not blinded. Comment: Not stated but guess impossible since needles are involved in one treatment.
Incomplete outcome data	Low risk	Intention-to-treat analysis was used. No dropouts.

Navarro 2002

Methods	Randomised, single-bind, placebo-controlled, parallel group study lasting 4 months.
Participants	**Inclusion criteria of the trial** • Stable vitiligo vulgaris confirmed by a histologic study • No treatment 6 months prior the start of the study. **Exclusion criteria of the trial** • Stable vitiligo vulgaris with a concomitant disease; • Presence of achromic patches in the retroauricular region • Patients with a history of keloidal scar formation. 40 participants with stable vitiligo vulgaris. 17 were male and 23 female. Participants were split equally into 5 different treatment groups (including a control). This study was conducted in Mexico.
Interventions	**A:** Autologous skin minigraft plus 8-MOP. **B:** Minigraft plus placebo. **C:** Skin minigraft alone.

Navarro 2002 *(Continued)*

	D: 8-MOP alone. **E:** Placebo alone.
Outcomes	**Primary outcomes of the trial** 1) Repigmentation: 0 points (absence of repigmentation), 1 point (repigmentation of up to 2 mm of extension), 3 points (2.1 to 4 mm), 5 points (4.1 to 6 mm), 7 points (6.1 to 8 mm), 9 points (8.1 to 10 mm), and 11 points (> 10 mm). 2) Amount of melanocytes.
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Translated quote (page 262): "Patiens were randomly assigned to 5 groups". Comment: Insufficient detail was reported about the method used to generate the allocation sequence. We therefore e-mailed the authors who responded that "Patients given numbers 1 to 40 and allocated by random sample using 40 chips in two urns labelled A and B, corresponding to participants and treatment groups. Chips were drawn at random."
Allocation concealment (selection bias)	Unclear risk	This was not stated. Comment: Although sealed envelopes were used it was unclear whether they were opaque and sequentially numbered.
Blinding (performance bias and detection bias) participant	Low risk	Participants were blinded. Comment: in the text it is quoted (page 261): "We conducted an experimental, randomized, double-blinded clinical trial". We thus e-mailed the author to ascertain some more details and responded that "Neither the unit of investigation nor the investigator knew which the active principle was."
Blinding (performance bias and detection bias) clinician	Low risk	Clinicians were blinded. Translated quote (page 262): "None of the team members knew the identity of the substances until the end of the analysis of clinical and histological results"
Blinding (performance bias and detection bias) assessor	Low risk	Outcome assessors were blinded. "The selection for the monthly biopsy for the measurement of the melanocyte quantity is taken by an independent observer and the microscopic re-count is done by two independent observers."
Incomplete outcome data	Low risk	Intention-to-treat analysis was used. No dropouts.

Nistico 2012

Methods	This is a randomised parallel group study lasting 12 weeks.
Participants	**Inclusion criteria of the trial**

Nistico 2012 *(Continued)*

- Caucasian patients with vitiliginous patches ≥ 2 cm^2 who had been stable over the last 6 months
- Localised and generalised vitiligo

Exclusion criteria of the trial

- Topical or systemic treatments
- Phototherapy during the previous 3 months
- Photosensitivity and photomediated disorders
- Radiotherapy
- Systemic immunosuppressive treatments
- Immunosuppressive diseases
- History of skin cancer
- Pregnant and breast-feeding women
- Age <10 years.

53 Caucasian patients with vitiligo that had been stable for 6 months were randomised. The mean age varied from 26.4 to 31.95. The mean duration of disease ranged from 20 to 30 months. The study included 28 males and 25 females.1 patient discontinued treatment due to lack of efficacy. There was intention-to-treat analysis.

The study was conducted in Italy.

Interventions	**A:** 308-nm excimer light (MEL) monotherapy and oral vitamin E. MEL was given twice weekly. The minimal erythemal dose (MED) was determined at increasing light dosages following the initial dose of MEL, which was calculated according to patient's skin type. An initial dose of 75% of the MED reported for MEL was applied and increased at subsequent treatments by 0.25 J/cm^2 to 0.75 J/cm^2 of the dose used in the previous session, according to the erythematous response. The mean number of sessions for the group was 23. During therapy, when marked erythema occurred, the next dose was reduced by 25% of the previous dose. Oral vitamin E 400iu was given twice a day. **B:** 308-nm MEL combined with 0.1% tacrolimus and oral vitamin E. MEL was given twice weekly. The minimal erythemal dose (MED) was determined at increasing light dosages following the initial dose of MEL, which was calculated according to patient's skin type. An initial dose of 75% of the MED reported for MEL was applied and increased at subsequent treatments by 0.25 J/cm^2 to 0.75 J/cm^2 of the dose used in the previous session, according to the erythematous response. The mean number of sessions for the group was 23. During therapy, when marked erythema occurred, the next dose was reduced by 25% of the previous dose. Oral vitamin E 400iu was given twice a day and topical tacrolimus was given once a day. **C:** oral vitamin E alone. Oral vitamin E 400iu was given twice a day.
Outcomes	**Primary outcomes of the trial** 1) Degree of repigmentation was graded as: no change–poor repigmentation = up to 25% repigmentation, moderate repigmentation = 25% to 50% repigmentation, good repigmentation = 51% to 75% repigmentation, and excellent repigmentation = 76% to 100%. 2) Adverse effects. All outcomes were measured pre- and post-treatment (12 weeks).
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 2): "Patients were randomly divided into three groups."

Nistico 2012 *(Continued)*

		Comment: Insufficient detail was reported about the method used to generate the allocation sequence. We therefore e-mailed the authors who responded that "Our study was a randomized controlled study using a computer generated scheme sequence with a ratio 2:2:1."
Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	High risk	Participants were not blinded. Quote (page 2): "...were enrolled in this open pilot prospective study."
Blinding (performance bias and detection bias) clinician	High risk	Clinicians were not blinded. Quote (page 2): "...were enrolled in this open pilot prospective study."
Blinding (performance bias and detection bias) assessor	Low risk	Outcome assessors were blinded. Quote (page 2): "Assessment of treatment efficacy performed by two independent physicians was based on the percentage of repigmentation in the treated area."
Incomplete outcome data	High risk	Intention-to-treat analysis was not used. Intervention - A: 0 dropouts; - B: 0 dropouts. Control - C: 1 dropout due to lack of efficacy.

Nordal 2011

Methods	This is a randomised within-participant study lasting 6 months.
Participants	**Inlcusion criteria of the trial** • Patients aged above 18 years • Fitzpatrick skin type II–VI • Stable symmetrical vitiligo **Exclusion criteria of the trial** • Pregnant or breast-feeding women 46 participants were randomised with 6 losses to follow-up for unclear reasons. This included 13 males and 27 females. The mean age was 44.8years (range 23 to 69). This study was conducted in Norway.
Interventions	**Intervention** **A:** Whole-body phototherapy was given with NB-UVB and tacrolimus ointment. NB-UVB was applied two or three times a week. Tacrolimus ointment (0.1%) was applied to all vitiliginous skin on one-half of the body every night. 17 to 68UV treatments were given (mean 46). The number of topical treatment ranged from 33 to 221 (mean 148). **Control Intervention** **B:** Whole-body phototherapy was given with NB-UVB and a placebo ointment. The placebo ointment was the base of Protopic® and it was applied on the opposite half in a randomised double-blind set-up.

Nordal 2011 *(Continued)*

	17 to 68UV treatments were given (mean 46). The number of topical treatment ranged from 33 to 221 (mean 148).
Outcomes	**Primary outcomes of the trial** 1) Lesion reduction. The total vitiligo area was assessed using the palm and thumb method on 1% of the skin surface. The area of the target lesions was recorded precisely using VisitrakTM (Smith & Nephew Inc., Largo, FL, USA). 2) The patients' subjective impact of living with vitiligo. This was measured using a visual analogue scale [(VAS) 1 to 10]. 3) Adverse effects.
Notes	All except 3 patients were compliant with overnight applications. At baseline, 23 patients had had one or several prior uncontrolled series of NB-UVB (of which three in combination with tacrolimus ointment), three had had tacrolimus ointment as monotherapy and 14 were previously untreated.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 1441): "The medications were supplied by Astellas Pharma. Tacrolimus ointment (0.1%) was applied to all vitiliginous skin on one-half of the body every night and placebo ointment was applied on the opposite half in a randomized double-blind set-up." Comment: Insufficient detail was reported about the method used to generate the allocation sequence. We therefore e-mailed the authors who responded that "The tubes with active substance or placebo ointment were blinded and randomly marked right or left according to a computer programme, and carried out by the provider of the ointment tubes."
Allocation concealment (selection bias)	Low risk	This was not stated. Comment: However in the e-mail the authors stated that randomisation and allocation concealment was carried out by the provider of the ointment tubes.
Blinding (performance bias and detection bias) participant	Unclear risk	Participants were blinded. Comment: States that the trial was double-blinded but no details given as to how blinding was maintained for participants.
Blinding (performance bias and detection bias) clinician	Unclear risk	Clinicians were blinded. Comment: States that the trial was double-blinded but no details given as to how blinding was maintained for clinicians.
Blinding (performance bias and detection bias) assessor	High risk	This was not stated. Comment: The study stated to be double-blind but it is not clear who is blind.
Incomplete outcome data	High risk	Intention-to-treat analysis was not used. Because it is a within-participant study there were 6 dropouts in both groups. The reasons for dropouts were not reported.

Oh 2011

Methods	This is a randomised within-participant study lasting 16 weeks.
Participants	**Inclusion criteria of the trial** • Non-segmental vitiligo **Exclusion criteria of the trial** • None reported 20 participants with non-segmental vitiligo were randomised. The mean age was 38.5 years (15 to 60 yrs range). The average duration of vitiligo was 4.1 yrs (range 0.5 to 11 yrs). There were 7 males and 9 females after losses to follow-up. 4 patients were lost to follow-up for unknown reasons. There was no intention-to-treat analysis. The study was conducted in Korea.
Interventions	**A:** High concentration tacalcitol (HT) ointment alone. Patients were asked to apply a thin layer of HT (20 µg/g) ointment to the lesions once nightly. **B:** 308-nm xenon chloride excimer laser alone. Excimer laser was administered twice weekly for 16 weeks. The initial starting dose was 100mJ/cm2, hands and feet: 200 mJ/cm^2.This dose was increased by 10% each session. **C:** High concentration tacalcitol (HT) ointment plus 308-nm xenon chloride excimer laser. Patients were asked to apply a thin layer of HT (20 µg/g) ointment to the lesions once nightly. Excimer laser was administered twice weekly for 16 weeks. The initial starting dose was 100mJ/cm^2, hands and feet: 200 mJ/cm^2.This dose was increased by 10% each session. In this group the dose increment of the excimer laser was minimized to avoid masking the effect of excimer laser over HT.
Outcomes	**Primary outcomes of the trial** 1) Degree of repigmentation was assessed based on patient satisfaction using the visual analogue scale (VAS; 0 to 10) and two blinded dermatologists' evaluation based on a quartile grading scale (0 to 4). 2) Adverse effects. All outcomes were measured pre- and post-treatment (16 weeks).
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 428): "This study was a 16-week, open-label, prospective, randomized, single-blinded, paired comparative study." Comment: Insufficient detail was reported about the method used to generate the allocation sequence. We therefore e-mailed the authors who responded that "Before randomization, three lesions, which were assigned to combination, excimer only and tacalcitol only group were selected and randomly numbered…. randomization of each group was done via tables of random numbers."
Allocation concealment (selection bias)	Low risk	This was not stated. Comment: We e-mailed the authors who responded that "The allocation sequence was concealed by a sealed box."

Oh 2011 *(Continued)*

Blinding (performance bias and detection bias) participant	High risk	Participants were not blinded.
Blinding (performance bias and detection bias) clinician	High risk	Clinicians were not blinded.
Blinding (performance bias and detection bias) assessor	Low risk	Outocome assessors were blinded. Quote (page 429): "Repigmentation was assessed by patient satisfaction using the visual analogue scale (VAS; 0-10) and two blinded dermatologists' evaluation based on a quartile grading scale (0-4)."
Incomplete outcome data	High risk	Intention-to-treat analysis was not used. Because it is a within-participant study there were 4 dropouts in both groups. The reasons for dropouts were not reported in the text. However, we e-mailed the authors for ITT analysis and the reasons of dropouts and answered that "Four patients dropped out of this study due to various reasons including spreading of vitiligous lesions and shortage of compliance. The reasons for the withdrawal were not related to adverse effects and these patients were excluded from the analysis."

Ozdemir 2002

Methods	Randomised, single-blind, within-participant study. Results were followed up after 3 months.
Participants	**Inclusion criteria of the trial** • Generalised vitiligo, clinically diagnosed • The lesions had been present for at least 1 year on regions of the body not exposed to sunlight • Patients without any treatment for at least one year into the study **Exclusion criteria of the trial** • Not reported 20 participants aged between 10 and 49 years with generalised vitiligo of at least 1 years duration with patches on sites of the body not exposed to sunlight. This study was conducted in Turkey.
Interventions	**A:** Suction blister technique **B:** Thin-split thickness graft technique.
Outcomes	**Primary outcomes of the trial** 1) Percentage of repigmentation. 2) Adverse effects. Measured at 3-month follow-up.
Notes	This study was 1 of 2 using surgical techniques study for vitiligo found.

Ozdemir 2002 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 136): "The graft used for each recipient area was chosen randomly and the donor and recipient areas were mapped." Comment: Insufficient detail was reported about the method used to generate the allocation sequence. We therefore e-mailed the authors who responded the following "In this study, randomisation was done according to a computer-generated randomizations list."
Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	High risk	Participants were not blinded. Comment: Blinding not possible because of type of intervention.
Blinding (performance bias and detection bias) clinician	High risk	Clinicians were not blinded. Comment: Blinding not possible because of type of intervention.
Blinding (performance bias and detection bias) assessor	High risk	Outcome assessors were blinded with the exception of one outcome assessor who was not blinded. Quote (page 136): "Assessment of the results was conducted by one nonblind and two blind observers bimonthly during the 3-month follow-up period."
Incomplete outcome data	Low risk	Intention-to-treat analysis was used. No dropouts.

Papadopoulos 2004

Methods	Randomised, placebo-controlled, parallel group study lasting 8 weeks.
Participants	**Inclusion criteria of the trial** • Aged >18 years. • Were formally diagnosed by a dermatologist • Had not previously undergone, or were receiving counselling to help them cope with their condition • Had the condition for at least 1 year • Were not taking any form of psychotropic medication. • Type of vitiligo not reported. **Exclusion criteria of the trial** • Not reported 44 participants, aged 18 years or over, who had been affected with vitiligo for at least 1 year and were not taking any form of psychotropic medication or receiving or previously undergone counselling to help them cope with their condition. Intervention group 1 consisted of 15 participants with a mean age of 36.39 (SD 12.05) and 5 were male and 10 female. Intervention group 2 comprised of 14 participants with a mean age of 35.86 (SD 11.72) and 5 were male and 9 female. The control group included 15 participants with a mean age of 37.71 (SD 11.09) and 3 were male and 12 female.

Papadopoulos 2004 *(Continued)*

	This study was conducted in the UK.
Interventions	**A:** group cognitive behavioural therapy (CBT). Both CBT and person centred therapy (PCT) lasted approximately 90 minutes and was delivered weekly. Due to the large number of participants receiving either CBT or person centred counselling, participants were separated into smaller groups. The first CBT group contained 8 participants and the second comprised of 7 participants. **B:** group person centred therapy. Both CBT and person centred therapy (PCT) lasted approximately 90 minutes and was delivered weekly. Due to the large number of participants receiving either CBT or person centred counselling, participants were separated into smaller groups. The first person centred counselling group included 6 participants and the second group consisted of 8 participants. **Control group:** Participants received no counselling.
Outcomes	**Primary outcomes of the trial** 1) Improvements in vitiligo. Battery of validated and reliable questionnaires including the Rosenburg Self-Esteem Scale, the Body Image Automatic Thoughs Questionnaire, the Situational Inventory of Body Image Dysphoria, the General Health Questionnaire and the Dermatology Quality of Life Index. Measured pre- and post-treatment (8 weeks) and at 6 months and 12 months follow-up.
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 172): " Participants were randomly allocated to either the control group, the CBT treatment group or the person-centred treatment group." Comment: Insufficient detail was reported about the method used to generate the allocation sequence.
Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	High risk	Participants were not blinded. Comment: Not possible with these interventions.
Blinding (performance bias and detection bias) clinician	High risk	Clinicians were not blinded. Comment: Not possible with these interventions.
Blinding (performance bias and detection bias) assessor	High risk	No separate outcome assessor mentioned.
Incomplete outcome data	High risk	Intention-to-treat analysis was not used. Intervention- A: 1 dropout (the reason for the dropout was that the participant was unable to arrive at the first session); B: 0 dropouts. Control- B: 0 dropouts

Paracha 2010

Methods	Randomised, parallel group study lasting 6 months
Participants	**Inclusion criteria** • Men and women of more than 5 years of age with stable vitiligo involving head and neck i.e. • No change in size and colour for at least the last six months • No evidence of spontaneous repigmentation • No known hypersensitivity to super oxide dismutase/catalase or tacrolimus **Exclusion criteria** • Unstable vitiligo • Lip tip vitiligo • Systemic or topical treatment over four weeks preceding the study • Vitiligo associated with non melanic- hair • Association with any systemic disease or autoimmune disorder • Pregnant and lactating women 60 participants were enrolled in this study, 34 females and 26 males. There were 30 participants in each group.
Interventions	**A:** Topical application of super oxide dismutase / catalase **B:** Topical tacrolimus
Outcomes	**Primary outcomes of the trial** 1)Area of repigmentation according to grading. 1% to 25% - poor; 26% to 50% -mild; 51% to 75% - moderate; 76% to 95%- marked; 96% to 100% excellent 2) Adverse effects (erythema, burning, pruritus, sore lips, rashes,scaling, papules, headache and muscle pain)
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 116): "They were randomly divided into 2 groups (super oxide dismutase & catalase and tacrolimus) by using random number table."
Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	Unclear risk	Participants were blinded. Comment: Insufficient detail was reported about blinding of participants. We e-mailed the authors who responded on 26/06/2013 that participants were blinded but they did not provide information on how participants were blinded.
Blinding (performance bias and detection bias) clinician	High risk	Clinicians were not blinded.
Blinding (performance bias and detection bias)	High risk	Outcome assessors were not blinded.

Paracha 2010 *(Continued)*

assessor

Incomplete outcome data	High risk	Intention-to-treat analysis was not used. Intervention - A: 0 dropouts. Intervention - B: 2 dropouts (the reasons for dropouts were not reported)

Parsad 1998

Methods	Randomised, double-blind, placebo-controlled, within-participants, left/right comparison study lasting 18 months.
Participants	**Inclusion criteria of the trial** • Bilateral symmetrical vitiligo **Exclusion criteria of the trial** • Spontaneous repigmentation in any of the lesions 19 participants with bilateral symmetrical lesions were enrolled. 2 participants withdrew for reasons unrelated to the study therefore 17 were evaluated, 10 of whom were female and 7 male. Age range 14 to 39 years (mean 24). Participants showing spontaneous repigmentation were excluded from the study. This study was conducted in India.
Interventions	**Intervention** **A:** 0.6 mg/kg 8-MOP given to all participants 2 hours before exposure to sunlight 3 times a week. Calcipotriol 50 µg/g was applied to 1 side of the body twice a day. **Control Intervention** **B:** 0.6 mg/kg 8-MOP given to all participants 2 hours before exposure to sunlight 3 times a week. Placebo ointment applied to one side twice a day.
Outcomes	**Primary outcomes of the trial** 1) Percentage of repigmentation: minimal (25%), moderate (50%), marked (75%), and complete. 2) Adverse effects. Measured pre- and post-treatment (6 months).
Notes	Calcipotriol appears to give a faster repigmentation when used in combination with PUVA than PUVA alone. It reduces the number of treatments and gives better repigmentation on hands and feet. More trials are needed to establish these results.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 168): "The study was designed as a randomised, double-blind, right-left comparative trial." Comment: Insufficient detail was reported about the method used to generate the allocation sequence.

Parsad 1998 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	Unclear risk	Participants were blinded. Comment: States that the trial was double-blinded but no details given as to how blinding was maintained for participants.
Blinding (performance bias and detection bias) clinician	Unclear risk	Clinicians were blinded. Comments: States that the trial was double-blinded but no details given as to how blinding was maintained for participants.
Blinding (performance bias and detection bias) assessor	High risk	No separate outcome assessor mentioned.
Incomplete outcome data	High risk	Intention-to-treat analysis was not used. Because it is a within-participant there were 2 dropouts in both groups (the reason for dropouts were unrelated to the study.)

Parsad 2003b

Methods	Randomised, double-blind, placebo-controlled, parallel group study lasting 6 months.
Participants	**Inclusion criteria of the trial** • Gradually progressive or slow-spreading vitiligo. This was arbitrarily defined as the appearance of not more than three lesions or a surface area of depigmentation of not more than 10 cm2, including lesional spread over the last month. **Exclusion criteria of the trial** • None reported. 52 participants with gradually progressive symmetrical vitiligo. 5 participants were lost at follow-up, resulting in 47 evaluated (25 intervention, 22 control). The participants in the intervention group had a mean age of 28.2 (SD 10.77); 9 had focal vitiligo, 9 vitiligo vulgaris, and 7 acrofacial vitiligo. 7 had been affected by vitiligo for less than 1 year, 10 for 1 to 3 years, and 8 for more than 3 years. Participants in the control group had a mean age of 29.7 (SD 9.65); 10 had focal vitiligo, 6 had vitiligo vulgaris, and 6 had acrofacial vitiligo. 10 had been affected by vitiligo for less than 1 year, 6 for one to 3 years, and 6 for more than 3 years. This study was conducted in India.
Interventions	**Intervention** **A:** The intervention group took 1 Ginkgo biloba (40 mg) tablet 3 times per day. **Control intervention** **B:** The control group took 1 placebo (sugar) tablet 3 times per day.
Outcomes	**Primary outcomes of the trial** 1) Percentage of repigmentation: minimal (25%), moderate (50%), marked (75%), and complete. 2) Adverse effects.

Parsad 2003b *(Continued)*

	Measured pre- and post-treatment (6 months).
Notes	Mild nausea was reported in 2 participants.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 286): "Participants were randomly assigned in a double-blind fashion to two treatment groups." Comment: Insufficient detail was reported about the method used to generate the allocation sequence.
Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	Low risk	Participants were blinded. Quote (page 286): "Participants in group B were given placebo (same coloured capsule containing sugar) in three divided doses orally."
Blinding (performance bias and detection bias) clinician	Unclear risk	Clinicians were blinded. Comment: States that the trial was double-blinded but no details given as to how blinding was maintained for clinicians.
Blinding (performance bias and detection bias) assessor	High risk	No separate outcome assessor mentioned.
Incomplete outcome data	High risk	Intention-to-treat analysis was not used. Intervention- A: 1 dropout due to reasons unrelated to the study. Control- B: 4 dropouts (reasons: unrelated to the study (4).)

Passeron 2004

Methods	Randomised, within-participant, left/right comparison study lasting 12 weeks.
Participants	**Inclusion criteria of the trial** • Older than 12 years • The development of vitiligo before the past 3 months • The presence of at least 2 pairs of symmetrical patches of vitiligo (with surfaces of at least 4 cm^2), **Exclusion criteria of the trial** • Pregnant or breastfeeding women • Personal history of a hypertrophic scar • Melanoma or other skin cancer • Immunosuppression or taking immunosuppressive or photosensitising drugs • Undergoing phototherapy or other vitiligo treatment during the past 3 months 14 participants who had developed vitiligo more than 3 months ago and had at least 2 pairs of symmetrical patches of vitiligo (with surfaces of at least 4 cm^2). Participants were aged between 12 and 63

Passeron 2004 *(Continued)*

	years old (mean 36.6) and 2 were males and 12 females. The duration of vitiligo ranged from between 3 and 33 years (mean 18.1). This study was conducted in France.
Interventions	**Intervention** **A:** 308 nm excimer laser plus 0.1% tacrolimus. **Control Inerventon** **B:** 308 nm excimer laser alone.
Outcomes	**Primary outcomes of the trial** 1) Clinician-rated repigmentation: 0 (no repigmentation), 1 (1% to 24%), 2 (25% to 49%), 3 (50% to 74%), 4 (75% to 99%), and 5 (total repigmentation). 2) Participant treated repigmentation: excellent, good, moderate, and poor. 3) Adverse effects. Measured pre- and post-treatment (12 weeks).
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 1066): "The treatment applied to each target lesion was randomly selected by drawing lots."
Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	High risk	Participants were not blinded. Comment: Unlikely as no placebo given with comparison between laser alone and laser and tacrolimus.
Blinding (performance bias and detection bias) clinician	High risk	This was not stated.
Blinding (performance bias and detection bias) assessor	Low risk	Outcome assessors were blinded. Quote (page 1066): "Efficacy was blindly evaluated by two independent physicians."
Incomplete outcome data	Low risk	Intention-to-treat analysis was used. No dropouts.

Pathak 1984

Methods	Randomised, double-blind, placebo-controlled, parallel group study. Placebo arm abandoned after 9 to 12 months. Study lasted 2 to 3 years.

Pathak 1984 *(Continued)*

Participants	**Inclusion criteria of the trial** • Over 1% vitiligo, regardless of the site • Over 8 years of age • No history of previous photosensitivity **Exclusion criteria of the trial** • Pregnant/lactating women 596 participants of East Indian origin were enrolled and 366 were evaluated. More than 70% of the rest lost to follow-up. Participants had 10% to 70% of body affected and disease duration was 1 to 50 years. Age range between 12 and 70 with roughly the same number of males and females overall. This study was conducted in India.
Interventions	8-MOP, 4,5,8-trimethylpsoralen (TMP), or psoralen, plus exposure to sunlight. Participants were randomly allocated to 8 groups and exposure to sunlight was for 45 to 60 minutes between 11am and 2pm 3 times a week, 2 hours after taking the drug. Dosage was as follows: **A:** 0.3 and 0.6 mg 8-MOP/kg (2 groups); **B:** 0.8,1.8, and 3.6 mg TMP/kg (3 groups); **C:** a combination of 0.3 mg 8-MOP and 0.6 mg TMP/kg (1 group); **D:** 0.6 & 1.2 mg psoralen/kg (2 groups); and **E:** the placebo group which ended after 12 months.
Outcomes	**Primary outcomes of the trial** 1) Rate of repigmentation (percentage)."The two year 75 -95% repigmentation response appeared to be best with the combination group of 8-MOP + TMP" 2) Adverse effects. Measured pre- and post-treatment (either 1 or 2 years).
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 166): "The patients were randomly assigned to 1 of 8 treatment groups." Comment: Insufficient detail was reported about the method used to generate the allocation sequence.
Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	Unclear risk	Participants were blinded. Quote (page 166): "Neither the investigators nor the patients were aware of the psoralen being ingested."
Blinding (performance bias and detection bias) clinician	Unclear risk	Clinicians were blinded. Quote (page 166): "Neither the investigators nor the patients were aware of the psoralen being ingested."

Pathak 1984 *(Continued)*

Blinding (performance bias and detection bias) assessor	High risk	No separate outcome assessor mentioned.
Incomplete outcome data	High risk	Intention-to-treat analysis was not used. There were 230 dropouts not reported by groups. The reasons for dropouts were the following: some moved to other cities, others had job changes that made midday sun exposure impossible.

Procaccini 1995

Methods	Randomised, placebo-controlled, parallel group, left/right comparison study (using bilaterally symmetrical lesions and a placebo control for possible vehicle effects). The study lasted for 9 months.
Participants	**Inclusion criteria of the trial** • Patients with localised or generalised vitiligo **Exclusion criteria of the trial** • History of photosensitivity • Segmental vitiligo 72 participants (24 male, 48 female) aged between 7 and 54 years. Participants with a history of photosensitivity or segmental vitiligo were excluded. This study was conducted in Italy.
Interventions	**Intervention** **A:** 5% or 3% khellin cream plus UVA. 40 participants with bilateral symmetrical lesions received the active ingredient. They were split into 2 groups of 20, 1 group applied 5% khellin cream on 1 side of the body and vehicle alone to the other side prior to UVA exposure every other day. The dose of UVA was 3 J/cm^2 at first with increments of 0.5 J/cm^2 per session up to maximum of 15 J/cm^2 for both groups. The other group of 20 participants applied 3% khellin in 1-methyl-pyrrolidinone on 1 side and the vehicle alone on the other. **Control Intervention** **B:** cream vehicle (o/w or PYR) plus UVA
Outcomes	**Primary outcomes of the trial** 1) Repigmentation: L1 (0% to 25%), L2 (25% to 50%), L3 (50% to 75%), and L4 (75% to 100%). Measure pre- and post-treatment (9 months).
Notes	Treatment was carried out at home by all participants. No adverse effects were reported in this study.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 117): "In group A 40 patients were randomly assigned." Comment: Insufficient detail was reported about the method used to generate the allocation sequence. Moreover, the left-right side of the body was randomised only in group A but not in group B who were asked to apply the ve-

Procaccini 1995 *(Continued)*

		hicle to all vitiligo patches either the vehicle: either the o/w cream (16 participants) or the PYR (16 participants).
Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	High risk	This was not stated.
Blinding (performance bias and detection bias) clinician	High risk	This was not stated.
Blinding (performance bias and detection bias) assessor	High risk	This was not stated.
Incomplete outcome data	High risk	Intention-to-treat analysis was not used. Intervention-A: 10 dropouts (the reason for dropouts were because of not completing treatment or the monthly evaluations.) Control-B: 6 dropouts (the reason for dropouts were because of not completing treatment or the monthly evaluations.)

Radakovic 2009

Methods	Randomised, controlled within-participant, observer-blinded study.
Participants	**Inclusion criteria of the trial** • Generalised vitiligo of limited extent • A washout period of at least 4 weeks was allowed for patients using other vitiligo treatments **Exclusion criteria of the trial** • Not reported 17 participants (age range unknown) with generalised vitiligo. 2 lesions were randomly selected for each participant
Interventions	**A:** 0.1% tacrolimus applied once daily for 6 months **B:** 0.1% tacrolimus applied twice daily for 6 months In 10 participants a third patch was left untreated as a control.
Outcomes	15 participants (40 target lesions) completed the study. Twice daily application resulted in excellent (> 75%) repigmentation in 2 lesions, 4 lesions had moderate repigmentation (> 25% to 50%) and 4 had poor repigmentation (1% to 25%). Once daily treatment resulted in moderate repigmentation in 2 lesions and poor in 5. The other 8 lesions showed no improvement.
Notes	Single intervention dose-dependent study

Risk of bias

Bias	Authors' judgement	Support for judgement

Radakovic 2009 *(Continued)*

Random sequence generation (selection bias)	Low risk	Quote (page 951): "In each patient two lesions similar in size, localization and evolution were selected and allocated by computer-generated randomization list..."
Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	High risk	Participants were not blinded.
Blinding (performance bias and detection bias) clinician	High risk	Clinicians were not blinded
Blinding (performance bias and detection bias) assessor	Low risk	Outcome assessor was blinded. Quote (page 952): "Clinical examinations were performed in monthly intervals by a blinded observer who visually classified the degree of repigmentation...."
Incomplete outcome data	High risk	Intention-to-treat analysis was not used. Because it is a within-participant study there were 2 dropouts in both groups. The reasons for dropouts were not reported.

Radmanesh 2006

Methods	Randomised, single-blind, parallel-group study lasting 4 months.
Participants	**Inclusion criteria of the trial** • Patients with vitiligo, type not specified **Exclusion criteria of the trial** • Children • Pregnant and lactating women • Those who used no contraception • Patients with limited, poorly responsive areas of involvement including lips, palmoplantar areas, distal phalangeals, dorsum of carpophalangeal • Any type of topical or systemic therapy with or without PUVA in last 6 months • > 50% BSA involvement 92 participants (46 PUVA plus azathioprine, 46 PUVA) with vitiligo. 32 participants were lost at follow-up and 4 participants were excluded from the study due to lack of response, resulting in 58 evaluated participants (30 PUVA plus azathioprine, 28 PUVA). This study was conducted in Iran.
Interventions	**Intervention** **A:** PUVA plus azathioprine. The azathioprine dose was 0.6 to 0.75 mg/kg per day and a maximum of 50 mg was given in a single dose. The dose of methoxypsoralen was 0.3 to 0.4 mg/kg with a maximum of up to 20 mg, administered 2 hours before UVA. The dose of PUVA was 4.0 J/cm^2 per session (starting from 1.0 J/cm^2 and increasing gradually by 0.5 J per session to 4 J) twice weekly. **Control Intervention**

Radmanesh 2006 *(Continued)*

	B: PUVA alone, dosage as above.
Outcomes	**Primary outcomes of the trial** 1) Repigmentation: excellent (> 75%), good (25% to 75%), and poor (< 25%). 2) Adverse effects. Measured pre- and post-treatment (4 months).
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 152): "Two series of cards labelled as PUVA and PUVAZ were prepared in equal numbers. The labelled cards were inserted into uniform and opaque pockets and sealed. The eligible patients were asked to pick a pocket from the container."
Allocation concealment (selection bias)	Low risk	Quote (page 152): "Two series of cards labelled as PUVA and PUVAZ were prepared in equal numbers. The labelled cards were inserted into uniform and opaque pockets and sealed. The eligible patients were asked to pick a pocket from the container."
Blinding (performance bias and detection bias) participant	Low risk	Participants were blinded. Quote (page 152): "The eligible patients were asked to pick a pocket from the container."
Blinding (performance bias and detection bias) clinician	High risk	This was not stated.
Blinding (performance bias and detection bias) assessor	High risk	This was not stated.
Incomplete outcome data	High risk	Intention-to-treat analysis was not used. Intervention-A: 16 dropouts (the reason for dropouts were migration, economic problems, a lack of easy access to the centre, and mistrust about the outcome of the therapy.) Control-B: 16 dropouts (the reason for dropouts were migration, economic problems, a lack of easy access to the centre, and mistrust about the outcome of the therapy.)

Rath 2008

Methods	Randomised parallel-group, study lasting 6 months.
Participants	**Inclusion criteria of the trial** • Individuals with progressive vitiligo. • Involving 25% to 50% of BSA.

Rath 2008 *(Continued)*

	Exclusion criteria of the trial • People with diabetes and hypertension. • > 50% BSA involvement. • A history of photosensitivity and photodermatitis. 86 participants with vitiligo, aged between 10 and 50 years old with 25% to 50% of their body surface area affected by vitiligo. 5 participants were lost at follow-up resulting in 27 receiving intervention 1, 27 intervention 2, 9 intervention 3, and 18 intervention 4. This study was conducted in India.
Interventions	**A:** oral minipulses (OMP) of betamethasone plus PUVA. Participants took betamethasone (0.1 mg/kg body weight) twice a week on 2 consecutive days for 3 months followed by tapering of the dose 1 mg every month over the following 3 months. PUVA (8-methoxypsoralen 0.6 mg/kg) was delivered on alternate days. The initial dose was 0.5 J/cm^2, with increments of 0.2 J/cm^2 for every third dose (up to a maximum of 6 J/cm^2) **B:** OMP plus NB-UVB. Participants took betamethasone (0.1 mg/kg body weight) twice a week on 2 consecutive days for 3 months followed by tapering of the dose 1 mg every month over the following 3 months. NB-UVB was delivered 3 times a week on alternate days. The initial dose was 0.3 J/cm^2, with increments of 0.1 J/cm^2 in every dose (up to a maximum of 3 J/cm^2). **C:** OMP plus BB-UVB. Participants took betamethasone (0.1 mg/kg body weight) twice a week on 2 consecutive days for 3 months followed by tapering of the dose 1 mg every month over the following 3 months. BB-UVB was delivered 3 times a week on alternate days. The initial dose was 0.05 J/cm^2, with increments of 0.02 J/cm^2 every third dose. **D:** OMP alone. Participants took betamethasone (0.1 mg/kg body weight) twice a week on 2 consecutive days for 3 months followed by tapering of the dose 1 mg every month over the following 3 months.
Outcomes	**Primary outcomes of the trial** 1) Repigmentation: marked (> 75%), mild (25% to 50%), and poor or no improvement (< 25%). Measured pre-treatment, at 3 months and post-treatment (6 months).
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 358): "Patients were randomly assigned to different study groups according to a continuous selection method over a period of one year." Comment: Insufficient detail was reported about the method used to generate the allocation sequence.
Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	High risk	Participants were not blinded. Comment: Open-labelled study comparing 4 different interventions.
Blinding (performance bias and detection bias) clinician	High risk	Clinicians were not blinded. Comment: Open-labelled study comparing 4 different interventions.

Rath 2008 *(Continued)*

Blinding (performance bias and detection bias) assessor	High risk	Outcome assessors were not blinded. Comment: Open-labelled study comparing 4 different interventions.
Incomplete outcome data	Low risk	Intention-to-treat analysis was used. Intervention- A: 0 dropouts; B: 0 dropouts; C: 3 dropouts (the reasons for dropouts were not reported.) Control- D: 2 dropouts (the reasons for dropouts were not reported.)

Reyes 2006

Methods	Randomised, double-blind, placebo-controlled, parallel group study lasting 12 weeks.
Participants	**Inclusion criteria of the trial** • All patients had generalised vitiligo • All patients had skin phototype II—III. • None of the patients had previously received treatment with PUVA, steroidal drugs, cytokines or other immunomodulators for at least 6 months E**xclusion criteria of the trial** • Acral and/or segmental vitiligo patients • No significant intercurrent disease of the immune system, such as AIDS, congenital immunodeficiencies, lymphoma, leukaemia or myelodysplasic syndrome • Autoimmune diseases • Active infection • History of malignancy • Psychiatric or severe organic diseases 19 participants (10 intervention, 9 control) with generalised vitiligo. The intervention group were aged between 19 and 71 years old (mean 38.6) and the control group were aged between 20 and 59 years old (mean 40.2). In the intervention group there were equal numbers of males and females, however in the control group 4 were male and 5 were female. The intervention group had been affected by vitiligo for an average of 9.12 years (range: 1.24 to 23.55), whereas it was 8.23 years for the control group (range: 3.04 to 13.20). This study was conducted in Spain.
Interventions	**Intervention** **A:** PUVA plus Polypodium leucotomos. 8-methoxpsoralen was given 2 hours before UVA irradiation at a dose of 0.6 mg/kg body weight. UVA irradiation was applied with a solar simulator which emits 90% UVA and 10% UVB irradiation. The initial irradiation dose was 0.5 J/cm^2 with subsequent increases of 0.5 J/cm^2 in order to reach moderate and asymptomatic erythema (mean dose of 8 J/cm^2). PUVA sessions were delivered 3 times a week. The cumulative UVA dose after 12 weeks was 324 J/cm^2. Polypodium leucotomos was given orally at a dose of 720 mg per day and an additional dose of 720 mg was given 1 hour before irradiation. **Control Intervention** **B:** PUVA plus placebo. Details of irradiation dosage as above. Placebo (starch) was given orally.
Outcomes	**Primary outcomes of the trial** 1) Repigmentation: none or minimal (< 25%), mild (25% to 50%), and moderate to excellent (> 50%).

Reyes 2006 *(Continued)*

	2) Peripheral blood mononuclear isolation, immunofluorescence, and proliferative response. Measured pre- and post-intervention (12 weeks).
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 214): "A computer program makes the assignment in placebo and PL arms."
Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	Unclear risk	Participants were blinded. Comment: Study claims to be double-blinded but blinding not mentioned in the text.
Blinding (performance bias and detection bias) clinician	Unclear risk	Clinicians were blinded. Comment: Study claims to be double-blinded but blinding not mentioned in the text.
Blinding (performance bias and detection bias) assessor	Low risk	Outcome assessors were blinded. Quote (page 213): "Repigmentation response was evaluated by three independent dermatologists."
Incomplete outcome data	Low risk	Intention-to-treat analysis was used. No dropouts.

Rodriguez-Martin 2009

Methods	Randomised, double-blind, placebo-controlled, parallel group study lasting 16 weeks.
Participants	**Inclusion criteria of the trial** • Non-segmental vitiligo **Exclusion criteria of the trial** • Age under 18 years old • Pregnant or breastfeeding women • History of melanoma • Immunosuppression • Photosensitising drug intake • Phototherapy or any other topical or systemic treatment for vitiligo within the past month • Photosensitivity • Hypercalcaemia • History of contact allergy to tacalcitol • Other treatments of vitiligo were not allowed during the study.

Rodriguez-Martin 2009 *(Continued)*

	80 participants with symmetrical vitiligo. 40 participants were in the intervention group and 40 in the control group. The intervention group consisted of 21 males and 19 females and were aged between 18 and 71 years old (mean 42.16, SD 16.71). The mean duration of vitiligo in this group was 9.79 years (SD 13.34) and 75% had vitiligo affecting less than 25% of their body surface area, whereas the remaining 25% had vitiligo affecting 25% to 50% of their body surface area. The control group comprised of 16 males and 24 females and were aged between 19 and 71 years old (mean 43.78, SD 14.63). The mean duration of vitiligo is this group was 7.58 years (SD 7.72) and 78.8% had vitiligo affecting less than 25% of their body surface area, 15.1% had vitiligo affecting 25% to 50% of their body surface area, 4.1% had vitiligo affecting 50% to 75% of their body area, and the remaining 1.5% had vitiligo affecting more than 75% of their body surface area. This study was conducted in the Canary Islands.
Interventions	**Intervention** **A:** topical tacalcitol (4 ug/g) once a day at night and daily sunlight exposure for 30 minutes. The sunlight exposure was increased at each treatment according to erythema response. **Control Intervention** **B:** topical vehicle (4 ug/g) once a day at night and daily sunlight exposure for 30 minutes. The sunlight exposure was increased at each treatment according to erythema response.
Outcomes	**Primary outcomes of the trial** 1) Clinician-rated repigmentation: poor response (< 25%), moderate (25% to 49%), good (50% to 74%), and excellent (> 75%). 2) Participant-rated repigmentation using the visual analogue scale (VAS): maximal improvement (+5), no change (0), and maximal deterioration (-5). Measured pre- and post-intervention (16 weeks).
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 2): "Patients were randomized in a 1 : 1 ratio to receive active agent or placebo". Comment: Insufficient detail was reported about the method used to generate the allocation sequence, thus we e-mailed the authors who responded that "The lab that supplied the blinded samples used permuted block randomisation."
Allocation concealment (selection bias)	Low risk	This was not stated. Comment: We e-mailed the authors who responded that "The concealed allocation was opaque envelopes for me and the assessor. The envelopes were custodied by the Pharmacist assessor until the end of the study."
Blinding (performance bias and detection bias) participant	Low risk	Participants were blinded. Quote (page 2): "The investigators and the patients were masked to the treatment received. The clinical investigator and patients were unaware of the specific topical treatment (tacalcitol vs vehicle) that was applied during the course of the study."

Rodriguez-Martin 2009 *(Continued)*

Blinding (performance bias and detection bias) clinician	Low risk	Clinicians were blinded. Quote (page 2): "The investigators and the patients were masked to the treatment received. The clinical investigator and patients were unaware of the specific topical treatment (tacalcitol vs vehicle) that was applied during the course of the study."
Blinding (performance bias and detection bias) assessor	Low risk	Outcome assessor was blinded. Comment: we e-mailed the author who responded that "The concealed allocation was opaque envelopes for me and the assessor."
Incomplete outcome data	High risk	Intention-to-treat analysis was not used. Intervention- A: 8 dropouts (the reasons for dropouts were nonattendance at scheduled visits and noncompliance. The reasons for the withdrawal were not related to adverse effects in any patient.) Control- B: 8 dropouts (the reasons for dropouts were nonattendance at scheduled visits and noncompliance. The reasons for the withdrawal were not related to adverse effects in any patient.)

Rojas-Urdaneta 2007

Methods	Randomised, double-blind, placebo-controlled, parallel group study lasting 5 months.
Participants	**Inclusion criteria of the trial** • Stable vulgar vitiligo confirmed in the Hospital Jose Antonio Vargas of the Instituto Venezolano de los Seguros Sociales (IVSS) • Without prior therapy for the vitiligo in the past 5 months. • Age range from 18 to 50 years. • No history of other concomitant diseases. • Informed consent signed. **Exclusion criteria of the trial** • With prior therapy for the vitiligo in the past 5 months. • Having a history of other concomitant diseases. 100 participants with stable vulgar vitiligo. 50 were male and 50 female. This study was conducted in Venezuela.
Interventions	**A:** antioxidant and mitochondrial stimulating cream plus oral antioxidants and phenylalanine **B:** placebo cream plus oral antioxidants and phenylalanine **C:** oral antioxidants and phenylalanine **D:** placebo cream **E:** antioxidant and mitochondrial stimulating cream
Outcomes	**Primary outcomes of the trial** 1) Repigmentation: 0 (absence of repigmentation), 1 (3 mm), 3 (3.1 to 5 mm), 5 (5.1 to 7 mm), 7 (7.1 to 9 mm), 9 (9.1 to 11 mm), and 11 (> 11 mm).

Rojas-Urdaneta 2007 *(Continued)*

	2) Adverse effects. Measured pre- and post-treatment (5 months).
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Translated quote (page 25): "The participants were randomly distributed in 5 groups; 20 participants in each group by the "randomisation with no replacement" method." Comment: Insufficient detail was reported about the method used to generate the allocation sequence, thus we e-mailed the authors who responded that "The application form of the patients contained randomised numbers, where each number contained three-figure numbers that were obtained by means of a scientific calculator. These were given to the patients as soon as they fulfilled the included criteria established in the protocol of the clinical trial. In case the patient withdrew from the study, "his number" wasn't assigned to another patient, meaning that the patient that had that concrete number wasn't replaced by another one. New patients used another randomised number from the list. A statistician was in charge of the domain of the codification of the numbers and he didn't break the codes until the end of the study (when he analysed statistically the results)." List created using random number generator (calculator).
Allocation concealment (selection bias)	Low risk	Translated quote (page 25): "An independent observer was responsible for the distribution of the participants as well as the distribution of the drugs in labelled tubes."
Blinding (performance bias and detection bias) participant	Unclear risk	Participants were blinded. Translated quote (page 25): "At the beginning of the study, there was an independent observer who was in charge of the distribution of the participants as well as the distribution of the drugs in labelled tubes. None on the members of the study team knew anything about the identity of the creams, until the end of the analysis of the clinical and histological outcomes. " Comment: However, of the 5 different interventions some were topical, some oral, and some combination and thus blinding not possible.
Blinding (performance bias and detection bias) clinician	Unclear risk	Clinicians were blinded. Translated quote (page 25): "At the beginning of the study, there was an independent observer who was in charge of the distribution of the participants as well as the distribution of the drugs in labelled tubes. None on the members of the study team knew anything about the identity of the creams, until the end of the analysis of the clinical and histological outcomes. " Comment: However, of the 5 different interventions some were topical, some oral, and some combination and thus blinding not possible.
Blinding (performance bias and detection bias) assessor	Unclear risk	The text states on page 25 that "none of the investigators involved in the study knew the identity of the creams, till the end of the clinical results and the histological analysis" but it is not clear whether or not 1 of these investigators was an independent outcome assessor.
Incomplete outcome data	Low risk	Intention-to-treat analysis was used.

Rojas-Urdaneta 2007 *(Continued)*

	No dropouts.

Ruiz-Maldonado 1975

Methods	Randomised, placebo-controlled, parallel group study lasting 8 months.
Participants	**Inclusion criteria of the trial** • To live in the city of Mexico. • To have vitiligo lesions affecting at least 5% of the body surface. • Not receiving other treatments. • Good liver function, healthy kidneys and normal haematic biometry tests. • Willing to follow a prolonged treatment and to purchase a sunlight lamp or to be exposed to the sun. **Exclusion criteria of the trial** • None reported. 50 children with a clinical diagnosis of vitiligo with an average age of 9 to 10, minimum of 5% of skin affected. This study was conducted in Mexico.
Interventions	**Intervention** **A:** Oral trimethylpsoralen plus exposure to sunlight or sun lamp. Between 10 and 30 mg (average 15 mg) per day, 3 hours before exposure or in 2 doses after breakfast and lunch for those using sunlight. Exposure time from 3 to 30 minutes daily until erythema appeared in the white patches **Control Intervention** **B:** Oral placebo plus light exposure. Exposure time from 3 to 30 minutes daily until erythema appeared in the white patches.
Outcomes	**Primary outcomes of the trial** 1) Repigmentation: slight, marked, and clinically cured. 2) Adverse effects. Measured pre- and post-treatment (8 months).
Notes	There was no clear definition of improvement. 1 of the few studies on children included in the review.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Translated quote (page 515): "Following the order of arrival at the outpatient department, patients received in a sequential fashion the containers labelled 171 to the first patient, 172 to the next patient and so forth. " Comment: Insufficient detail was reported about the method used to generate the allocation sequence.
Allocation concealment (selection bias)	Unclear risk	This was not stated.

Ruiz-Maldonado 1975 *(Continued)*

Blinding (performance bias and detection bias) participant	Low risk	Participants were blinded. Translated quote (page 515): The Trimethylpsoralen (TMP) and placebo were placed in identical containers, numbered 171 and 172...each contained 28 identical tablets.
Blinding (performance bias and detection bias) clinician	Low risk	Clinicians were blinded. Translated quote (page 515): "Both oral treatments (trimethylpsoralen and placebo) were provided to the investigators in identical containers, identified with the numbers 171 and 172. Each container had 28 identical tablets. The investigators were blinded to the treatments until the study was ended. "
Blinding (performance bias and detection bias) assessor	High risk	No separate outcome assessor mentioned.
Incomplete outcome data	High risk	Intention-to-treat analysis was not used. Intervention- A: 0 dropouts Control- B: 3 dropouts (the reasons for dropouts were unknown.)

Sahni 2011

Methods	This is a randomised, parallel group study lasting 16 weeks.
Participants	**Inclusion criteria of the trial** • Stable vitiligo only • Fitzpatrick skin phototype IV and V **Exclusion criteria of the trial** • Patients with unstable disease • Köebner phenomenon • Keloidal tendency 25 patients were randomised, this included 14 males and 11 females. There were no losses to follow-up. This study was conducted in India.
Interventions	**Intervention** **A:** Autologous Non-cultured Melanocyte Transplantation with melanocytes suspended in normal saline. The pellet containing melanocytes and basal keratinocytes was diluted 1:2 in normal saline. This suspension was loaded in a tuberculin syringe attached to an 18-G needle. On the next day, the recipient vitiliginous area in both groups was anaesthetised by infiltrating 2% lignocaine. It was then manually dermabraded using manual dermabraders until uniform pinpoint bleeding was observed. The melanocyte suspension was uniformly spread onto the dermabraded area (using a tuberculin syringe and 18-G needle) and covered using a multilayered dressing. The first layer was sterile nonadherent chlorhexidine gauze followed by meshed collagen sheet and then a sterile surgical pad soaked in phosphate buffered saline that was kept in place with a sterile transparent occlusive dressing. The area was immobilised by bandaging with Dynaplast, and the patient was advised to restrict movement at the site as much as possible. **Control Intervention**

Sahni 2011 *(Continued)*

	B: Autologous Non-cultured Melanocyte Transplantation with melanocytes suspended in the patient's own serum. The pellet containing melanocytes and basal keratinocytes was diluted 1:2 in patient's own serum. A 5-mL blood sample was taken and centrifuged at 1,000 rpm for 10 minutes, and the serum was decanted into a sterile container. On the next day the recipient vitiliginous area in both groups was anaesthetised by infiltrating 2% lignocaine. It was then manually dermabraded using manual dermabraders until uniform pinpoint bleeding was observed. The melanocyte suspension was uniformly spread onto the dermabraded area (using a tuberculin syringe and 18-G needle) and covered using a multilayered dressing. The first layer was sterile nonadherent chlorhexidine gauze followed by meshed collagen sheet and then a sterile surgical pad soaked in phosphate buffered saline that was kept in place with a sterile transparent occlusive dressing. The area was immobilised by bandaging with Dynaplast, and the patient was advised to restrict movement at the site as much as possible. The dressing was identical in both groups and served to allow proper retention of the suspension at the site and faster healing of the dermabraded area.
Outcomes	**Primary outcomes of the trial** 1) Degreee of repigmentation. Pigmentation was graded as: Excellent (> 90%), Very good (76% to 90%), Good (51% to 75%), Fair (26% to 50%), and Poor (≤ 25%). cf published study "Successful repigmentation classed as any repigmentation of 75% or greater" **Secondary outcomes of the trial** 1) Improvement in DLQI: comparing the mean change in DLQI from before to 16 weeks after surgery. 2) Adverse effects. 3) Patient satisfaction - via questionnaire. 4) Colour match and improvement in leukotrichia - subjective assessment.
Notes	The suspension diluted in patients' serum was more viscous and adhered better to the dermabraded site than the suspension diluted in normal saline.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 177): "Selected patients were randomized using a computer-generated random number table into two groups for autologous noncultured melanocyte transplantation."
Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	High risk	Participants were not blinded. Comment: We e-mailed the authors who responded that "this was not blinded study."
Blinding (performance bias and detection bias) clinician	High risk	Clinicians were not blinded. Comment: The clinicians performing the surgery could not be blinded as they prepared the suspension etc. Moreover as quoted on page 181 "The sample size was small, and the investigators were not blinded." .
Blinding (performance bias and detection bias) assessor	Unclear risk	Outcome assessors were not blinded. Comment: As quoted on page 178 "The primary measure of efficacy of treatment was the percentage of repigmentation at 16 weeks after surgery as assessed by two independent investigators, with the lesser value being used for assessment of results." It looks like they were blinded since they were inde-

Sahni 2011 *(Continued)*

		pendent but we e-mailed the authors who responded that the study was not blinded.
Incomplete outcome data	Low risk	Intention-to-treat analysis was used. No dropouts.

Sanclemente 2008

Methods	Randomised, double-blind, within-participant, left/right comparison study lasting 10 months.
Participants	**Inclusion criteria of the trial** • Patients > 18 years old or between 12 and 18 years with parent's informed consent • With stable or active bilateral vitiligo **Exclusion criteria of the trial** • Patients with acral or periorificial vitiligo • Treatment for vitiligo within the last 6 weeks with phototherapy, systemic therapy, topical therapy with corticosteroids, vitamin D analogues or tacrolimus • Patients with cutaneous atrophy • Pregnancy • Narrow-band UVB or PUVA therapy 25 participants with stable or active bilateral vitiligo. Participants were aged between 12 and 74 years old (mean 40) and consisted of 21 females and 4 males. The participants had been affected by vitiligo for between 0.5 and 46 years (mean 12.75). 2 participants were lost at follow-up (1 male and 1 female). All participants were included in the analysis. This study was conducted in Columbia.
Interventions	**A:** topical 0.05% betamethasone to one side of their face. Sun exposure was between 10.30am and 2.30pm for 15 minutes. **B:** catalase/dismutase superoxide C/DSO to the other side twice a day. Sun exposure was between 10.30am and 2.30pm for 15 minutes.
Outcomes	**Primary outcomes of the trial** Mean percentage of repigmentation. Measured pre- and post-treatment (10 months). Adverse effects
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 2): "Once enrolled, patients were randomized to receive 0.05% betamethasone on one side of the face and C/DSO on the other side using a random number generator (RALLOC program, Stata co. 8.2, College Station, TX, USA)."

Sanclemente 2008 *(Continued)*

Allocation concealment (selection bias)	Low risk	Quote (page 2): "Each patient previously coded with a number by a nurse not involved in study**,** left or right application of each substance only determined by manufacturer."
Blinding (performance bias and detection bias) participant	Low risk	Participants were blinded. Comment: "Identical cream containers were coded by the manufacturer, thus patients and investigators were blinded to both substances."
Blinding (performance bias and detection bias) clinician	Low risk	Clinicians were blinded. Comment: "Identical cream containers were coded by the manufacturer, thus patients and investigators were blinded to both substances."
Blinding (performance bias and detection bias) assessor	Low risk	Outcome assessors were blinded. Quote (page 2): "All assessments were made by two blinded investigators."
Incomplete outcome data	Low risk	Intention-to-treat analysis was used. Because it is a within-participant study there were 2 dropouts in both groups (reasons: difficulties for attending follow-ups (1), and because of pregnancy (1).)

Sapam 2012

Methods	Randomised parallel group study lasting 6 months.
Participants	**Inclusion criteria of the trial** • Patients with vitiligo affecting > 5% body surface area **Exclusion criteria of the trial** • Ages < 13 years or > 70 years • Mucosal involvement only • Segmental vitiligo and unstable vitiligo • Pregnancy and lactation • History of photosensitivity • Usage of photosensitive drugs • Previous intolerance or lack of response to phototherapy • History of skin cancer • Arsenic exposure • Radiographic therapy • Grenz ray exposure 56 patients with vitiligo affecting > 5% of body surface area were randomised. The mean age of the first group was 29.17 years and the second group was 31.25 years. The duration of vitiligo ranged from 1 to 12 years. The study included 19 males and 36 females, post losses to follow-up. 3 patients were lost to follow up - 2 discontinued due to giddiness and 1 for unknown reasons. There was no intention-to-treat analysis. The study took place in Nepal.
Interventions	**A:** oral psoralen + UVA (PUVA). 0.6 mg/kg 8-methoxypsoralen was given orally with some food two hours before the light session. Patients received three sessions/week of UVA light therapy. The initial dose of UVA varied from 0.5 to 2.5 J/cm^2 depending on the Fitzpatrick skin type. Subsequent incre-

Sapam 2012 *(Continued)*

	ments in the dose were by 0.5 J/cm^{2}. Treatment was given until completion of a six-month therapy or complete repigmentation was achieved, whichever was earlier. **B:** NB-UVB. 70% of the Minimal Erythema Dose or 280 mJ/cm2 was given as the initial dose, with subsequent 15% increments from the previous dosage in every session until minimal erythema appeared. The dose was maintained for a total of 30 sessions and was continued until the completion of the sixth month of therapy or complete repigmentation was achieved, whichever occurred first.
Outcomes	**Primary outcomes of the trial** 1) Degree of repigmentation was graded as: Group A (0%) no improvement; Group B (1% to 25% repigmentation) mild; Group C (26% to 50%) moderate; Group D (51% to 75% repigmentation) good; Group E (76% to 100% repigmentation) excellent. When there was no response after 30 sessions of phototherapy the patient was classified as treatment failure. 2) Adverse effects. All outcomes were measured pre-treatment and at each visit during the first three months and then monthly within the next three months until the end of treatment.
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 1107): “Based on a randomization list (1 : 1 patient) generated with the help of computer-generated random numbers”
Allocation concealment (selection bias)	Low risk	Quote (page 1107): "The sequentially numbered list with the treatment group written on a sealed brown envelope was provided by an independent dermatologist."
Blinding (performance bias and detection bias) participant	High risk	Participants were not blinded. Quote (page 1107): "This was an observer-blinded, randomized study of 56 patients with vitiligo..."
Blinding (performance bias and detection bias) clinician	High risk	Clinicans were not blinded. Quote (page 1107): "This was an observer-blinded, randomized study of 56 patients with vitiligo..."
Blinding (performance bias and detection bias) assessor	Low risk	Outcome assessor was blinded. Quote (page 1108): "The percentage of repigmentation over depigmented areas using photographic and graphic presentations as well as any adverse effects were evaluated by a blinded dermatologist at each visit during the first three months and then monthly for the next three months."
Incomplete outcome data	High risk	Intention-to-treat analysis was not used. Intervention - A: 2 dropouts due to giddiness. Intervention - B: 1 dropout (reasons were stated in the text as "unknown")

Sassi 2008

Methods	Randomised parallel group study, lasting 12 weeks.
Participants	**Inclusion criteria of the trial** • Age 18 to 75 years • Focal or generalised vitiligo. • Only face and neck **Exclusion criteria of the trial** • Previous treatment with 308nm excimer laser. • Purely segmental vitiligo. • Pregnant or breast-feeding. • History of diseases associated with excessive reaction to visible or UV radiation (e.g. porphyria cutanea tarda, polymorphic light eruption) or reported photosensitivity. 84 participants with symmetrical vitiligo. Participants were aged between 18 and 75 years old (mean 44) and 44 were female and 40 male. There were equal numbers of participants in both intervention groups, which both consisted of 20 males and 22 females. The amount of body surface area affected with vitiligo varied; with 17 participants from intervention 1 (308 nm laser phototherapy) reporting less than 3% affected, 20 reporting 3% to 15% affected, and 5 reporting more than 15% affected. 15 participants from intervention 2 (308 nm laser phototherapy with hydrocortisone 17-butyrate) reported less than 3% of their body surface area affected, 19 reported 3% to 15% affected, and 8 reported more than 15% affected. 8 participants were lost at follow-up (6 from intervention 1, 2 from intervention 2). All participants were included in the analysis. This study was conducted in Italy.
Interventions	**Intervention** **A:** 308 nm laser phototherapy twice weekly in combination with hydrocortisone 17-butyrate cream twice daily for 3 periods of 3 weeks, followed by a 1 week steroid-free interval. The laser generated monochromatic light at 308 nm, with pulse frequency of 200 Hz, pulse duration of about 30 ns, energy density (fluence) of 3 mJ/cm^2, and spot size of 4.0 cm^2. Initial influences in the vitiligo areas were half the minimal erythema dose (MED) determined on normal non-sun-exposed skin. Fluences were increased by half the MED at every other session. Participants were instructed to apply a thin layer of the hydrocortisone 17-butyrate cream **Control Intervention** **B:** 308 nm laser phototherapy twice weekly alone. The laser generated monochromatic light at 308 nm, with pulse frequency of 200 Hz, pulse duration of about 30 ns, energy density (fluence) of 3 mJ/cm^2, and spot size of 4.0 cm^2. Initial influences in the vitiligo areas were half the minimal erythema dose (MED) determined on normal non-sun-exposed skin. Fluences were increased by half the MED at every other session. Participants were instructed to apply a thin layer of the hydrocortisone 17-butyrate cream.
Outcomes	**Primary outcome of the trial** 1) Percentage repigmentation: at least 75% reduction of lesional areas. 2 Patient-rated quality of life: Skindex-29. 3) Adverse effects. Measured pre- and post-treatment (12 weeks).
Notes	-

Sassi 2008 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 2): "Stratified blocked randomisation was used to balance age and gender."
Allocation concealment (selection bias)	Low risk	Quote (page 2): "Centralised telephone randomisation procedures were adopted and investigators were blinded to the randomisation rule."
Blinding (performance bias and detection bias) participant	High risk	Participants were not blinded. Comment: "In our study only the assessor making the image analysis evaluation was treatment blinded." Verified by email.
Blinding (performance bias and detection bias) clinician	High risk	Clinicians were not blinded. Comment: "In our study only the assessor making the image analysis evaluation was treatment blinded." Verified by email.
Blinding (performance bias and detection bias) assessor	Low risk	Outcome assessor was blinded. Quote (page 3): "Image analysis....was conducted by an investigator who was unaware of treatment assignments."
Incomplete outcome data	Low risk	Intention-to-treat analysis was used in the primary analysis and was further complemented by per-protocol analysis. Intervention- A: 6 dropouts (reasons: consent withdrawal (3), side effects (2), and noncompliance (1).) Control- B: 2 dropouts due to consent withdrawal.

Satyanarayan 2013

Methods	Randomised, within-participant study lasting 6 months.
Participants	**Inclusion criteria of the trial** • Generalised vitiligo • Skin type III to VI • 5% to 50% body surface area • Stable disease (<10% change in the last 6 months) **Exclusion criteria of the trial** • Nil reported 25 participants were randomised, 13 male and 12 female. The age range was from 14 to 36 years. 4 patients were lost to follow-up: 2 developed new lesions, 1 did not respond after 8 weeks of therapy and 1 was lost to follow-up. There was no intention-to-treat analysis.
Interventions	**Intervention** **A:** NB-UVB and Tacrolimus ointment 0.1%. Tacrolimus applied once daily at night on the lesions on one half of the body. Light therapy was administered thrice weekly.This was for 6 months or till complete repigmentation of study lesions if the same occurred earlier.

Satyanarayan 2013 *(Continued)*

	Control Intervention **B:** Light therapy alone thrice weekly. This was for 6 months or till complete repigmentation of study lesions if the same occurred earlier.
Outcomes	Primary outcomes of the trial 1) Percentage of repigmentation. This was graded as absent: 0%, minimal: < 25%, mild: 26% to 50%, moderate: 51% to 75%, marked to complete: > 75%. 2) Adverse effects All outcomes were measured at baseline and at 2, 4, 6, 8, 12, 16, 20 and 24 weeks.
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page not known): "Tacrolimus ointment (Topgraf) 0.1% was dispensed to the patients and advised to apply once daily at night on the lesions on one half of the body, which was randomly chosen by a randomization table."
Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	High risk	Participants were not blinded. Comment: This study is open as stated in the title.
Blinding (performance bias and detection bias) clinician	High risk	Clinicians were not blinded. Comment: This study is open as stated in the title.
Blinding (performance bias and detection bias) assessor	High risk	Outcome assessors were not blinded. Comment: This study is open as stated in the title.
Incomplete outcome data	High risk	Intention-to-treat analysis was not used. Because it is a within-participant study there were 4 dropouts in both groups (Reasons: developed new lesions (2); did not respond even after 8 weeks of therapy (1); lost to follow-up (1)).

Schallreuter 2002

Methods	Randomised, placebo-controlled, parallel group study lasting 21 days.
Participants	**Inclusion criteria of the trial** • Vitiligo determined by clinical examination, including Wood's lamp. • Skin type III (Fitzpatrick classification) **Exclusion criteria of the trial** • None reported.

Schallreuter 2002 *(Continued)*

	59 participants (14 men, 45 female) with skin type III, aged between 18 and 62 years old (mean 38.6) with generalised (86%) or acrofacial (14%) vitiligo. The duration of the disease varied from 3 to 53 years (mean 16.7). This study was conducted in Israel.
Interventions	**A:** Dead Sea climatotherapy alone. Participants bathed for 15 minutes in the Dead Sea twice daily then showered without soap to wash off the salt. Group A (10 participants) exposed the whole body directly to the sun, **B:** Placebo cream and climatotherapy. Participants bathed for 15 minutes in the Dead Sea twice daily then showered without soap to wash off the salt. group B (10 participants) and group C (39 participants) applied their creams to the entire body surface prior to sun exposure. The time in the sun was gradually increased to 1 hour and treatment took place in morning between 7.30 and 10.30 and in the afternoon between 2.30 and 5.30. Participants recorded their exposure times. **C:** Pseudocatalase (PC-KUS) cream with climatotherapy. Participants bathed for 15 minutes in the Dead Sea twice daily then showered without soap to wash off the salt. group B (10 participants) and group C (39 participants) applied their creams to the entire body surface prior to sun exposure. The time in the sun was gradually increased to 1 hour and treatment took place in morning between 7.30 and 10.30 and in the afternoon between 2.30 and 5.30. Participants recorded their exposure times.
Outcomes	**Primary outcomes of the trial** 1) Clinician-rated repigmentation: 0 (no signs of repigmentation), 1+ (minimal follicular repigmentation), 2+ (follicular repigmentation < 50% of the involved areas), and 3+ (> 50% follicular/confluent repigmentation of involved areas). Measured pre- and post-treatment (21 days).
Notes	This was a very short study which only assessed the speed of repigmentation and did not seek to establish the efficacy either of PC-KUS or climatotherapy.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 484): "The clinical observation was based on a randomised three-arm study." Comment: Insufficient detail was reported about the method used to generate the allocation sequence.
Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	High risk	This was not stated.
Blinding (performance bias and detection bias) clinician	High risk	This was not stated.
Blinding (performance bias and detection bias) assessor	High risk	This was not stated.
Incomplete outcome data	Low risk	Intention-to-treat analysis was used.

Schallreuter 2002 *(Continued)*

	No dropouts.

Sharquie 2005

Methods	Randomised, placebo-controlled, within-participant study lasting 6 months.
Participants	**Inclusion criteria of the trial** • People with localised vitiligo in a non-exposed area and at least four patches. **Exclusion criteria of the trial** • Not reported 46 participants with localised vitiligo in a non-exposed area and at least 4 vitiligo patches. Participants were aged between 3 and 30 years old (mean 17.29, SD 6.64) and 3 were male and 14 female. 29 participants were lost at follow-up resulting in 17 evaluated. This study was conducted in Iraq.
Interventions	**A:** topical 15% lactic acid. The lactic acid was applied to the affected area twice a week. **B:** UVA. Exposure to UVA lasted for 10 minutes and was delivered twice a week. **C:** topical 15% lactic acid plus UVA. The lactic acid was applied to the affected area twice a week. **D Control group:** tap water
Outcomes	**Primary outcomes of the trial:** 1) Repigmentation: grade 0: no response, grade 1: slight response (when a quarter of size of patches or less showed repigmentation), grade 2: moderate response (when half of patches or less showed repigmentation), grade 3: marked response (when more than half of the patches showed repigmentation).
Notes	A very large percentage (63%) of unexplained dropouts.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 1013): "The patches were divided into four groups randomly according to the type of treatment." Comment: Insufficient detail was reported about the method used to generate the allocation sequence.
Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	High risk	Participants were not blinded. Comment: No information given but unlikely because 4 different interventions and lesions assessed.
Blinding (performance bias and detection bias) clinician	High risk	Clinicians were not blinded. Comment: No information given but unlikely because 4 different interventions and lesions assessed.

Sharquie 2005 *(Continued)*

Blinding (performance bias and detection bias) assessor	High risk	This was not stated.
Incomplete outcome data	High risk	Intention-to-treat analysis was not used. Because it is a within-participant study there were 29 dropouts in both groups (the reasons for dropouts were not reported).

Sheth 2012

Methods	This is a randomised, within-participant study lasting 12 weeks.
Participants	**Inclusion criteria** - Patients with stable vitiligo on the forearms and hands, defined as no more than 10% reported change in lesion size over the previous 6 months, - Lack of improvement with topical immunomodulators or corticosteroids for 6 months, - Not receiving more than 12 previous phototherapy treatments. **Exclusion criteria** Patients that have received more than 12 previous phototherapy treatments 13 patients were included in the study, each with two target lesions.
Interventions	**A:** Five 1.5-mm minigrafts were harvested from hip skin and placed in each of two target lesions per patient. One week after transplantation, the MEL(Monochromatic Excimer Light) device was used on one target lesion for 12 weeks **B:** 1.5 mm minigrafts plus hand-foot NBUVB device (Hand/Foot II NBUVB system was used on the other target lesion, National Biological Corp) 3 times weekly on the other target lesion for 12 weeks.
Outcomes	The primary outcome measure was improvement in target lesion size performed by a blinded investigator using Scion Image J measurement software (National Institutes of Health, Bethesda, MD) on baseline and week-12 images. These images were taken under standardised conditions. Adverse events were noted
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 318): "Treatment assignments were based on a computer-generated randomization code."
Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	High risk	Participants were not blinded. Comment: As the devices were different it is unlikely they could blind clinician or participants.

Sheth 2012 *(Continued)*

Blinding (performance bias and detection bias) clinician	High risk	Clinicians were not blinded. Comment: As the devices were different it is unlikely they could blind clinician or participants.
Blinding (performance bias and detection bias) assessor	Low risk	Outcome assessor was blinded. Quote (page 318-319): "The primary outcome measure was improvement in target lesion size performed by a blinded investigator."
Incomplete outcome data	High risk	Intention-to-treat analysis was not used. Because it is a within-participant study there were 3 dropouts. The reasons for dropouts were not reported, although as quoted on page 319 "The remaining 3 did not have any adverse effects before dropping out."

Shi 2008

Methods	Randomised parallel-group study, lasting 3 months.
Participants	**Inclusion criteria of the trial** • Vitiligo of qi-stagnancy and blood-stasis (VQB) type. • Participants willing to receive TCM and who offered active co-operation **Exclusion criteria of the trial** • Excluded those with abnormal function of the liver or kidney • With organic diseases • Taken other drugs for vitiligo treatment in the last month. 86 participants which included 65 participants with vitiligo and 21 healthy participants. The intervention group consisted of 35 participants (14 male/20 female) aged between 13 and 52 years old (mean 30.6, SD 9.2). Participants in this group had been affected by vitiligo for between 2 months and 5 years in 14 cases, between 6 and 10 years in 16 cases and between 11 and 15 years in 4 cases. The placebo control group consisted of 31 participants (13 male/18 female) aged between 11 and 52 years old (mean 29.4, SD 10.6). Participants in this group had been affected by vitiligo for between 3 months and 5 years in 13 cases, 6 and 10 years in 14 cases and 11 and 15 years in 4 cases. The healthy volunteer control group consisted of 9 males and 12 females. This study was conducted in China.
Interventions	**A:** 5 Zengse pills and 2 cobamamide tablets orally 3 times a day and topical psoralea tincture 3 times a day. The Zengse pill contained 5 herbal drugs: Chinese angelica root, red sage root, chaunxiong, spatholobus stem and safflower. **B:** 2 cobamamide tablets orally 3 times a day and topical psoralea tincture 3 times a day. The healthy volunteer group received no intervention. **C:** The healthy volunteer group received no intervention.
Outcomes	**Primary outcomes of the trial** 1) Repigmentation: cured (complete disappearance of white patches, the colour of skin becoming normal), markedly effective (area of the skin lesion has disappeared or has shrunk by less than 50%), ineffective (no skin pigment appears or the skin lesion even expands). 2) Determination of T-lymphocyte subsets and immunological indexes.

Shi 2008 *(Continued)*

	3) Adverse effects. Measured pre- and post-intervention (3 months).
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 304): "They were randomised using the digital table method into two groups."
Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	High risk	This was not stated.
Blinding (performance bias and detection bias) clinician	High risk	This was not stated.
Blinding (performance bias and detection bias) assessor	High risk	This was not stated.
Incomplete outcome data	Low risk	Intention-to-treat analysis was used. No dropouts.

Shi 2013

Methods	Randomised, within-participant, left/right comparison study lasting 7 weeks.
Participants	**Inclusion criteria** • Patients with at least 2 symmetrical vitiligo lesions of less than 10 cm^2, active or stable vitiligo, evolving for at least 3 months **Exclusion criteria** • History of photosensitive disorder • History of skin cancer • History of psychological disorders • Pregnancy and breastfeeding 14 participants, 7 males and 7 females, with 48 symmetrical vitiligo lesions were included in this study.
Interventions	**A:** 308 nm excimer lamp, three sessions on non-consecutive days every week until 20 sessions in total **B:** 308-nm excimer laser, three sessions on non-consecutive days every week until 20 sessions in total For both modalities, Initial dose 200mJ (150 mJ if < 16 y). Dose increased 20% from treatment 1 to 10, 10% from treatment 11 to 13, 5% from treatment 14 to 16, and 2% from treatment 17 to 20. If sympto-

Shi 2013 *(Continued)*

	matic erythema or blistering developed, treatment was withheld (once or twice) until resolution; when the treatment was resumed, the dose was reduced to the last well-tolerated dose
Outcomes	**Primary outcomes of the trial** 1) Repigmentation. Based on a clinical examination and photography evaluation in a blinded manner at the baseline pretreatment visit and once a month thereafter until the end of the study. Assessment of repigmentation was performed by two physicians who did not follow the course of phototherapy. Repigmentation was graded on a 5-point scale: score 0, no repigmentation; score 1, poor repigmentation (up to 25% of the affected area); score 2, moderate repigmentation (between 26% and 50%); score 3, good repigmentation (between 51% and 75%); and score 4, excellent repigmentation (between 76% and 100%). The efficacy of treatment was assessed based on the following endpoints: average repigmentation scores at five treatment intervals, the repigmentation rate of at least 50%, the repigmentation rate of at least 75%, the mean time to obtain the appearance of repigmentation, and the response rates of the vitiligo lesions at various sites. 2) Safety assessment. Any potential side effects were also noted.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 28): "The lesion to be treated with the 308 nm excimer lamp was selected according to a left–right randomization table."
Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	High risk	Participants were not blinded.
Blinding (performance bias and detection bias) clinician	High risk	Clinicians were not blinded.
Blinding (performance bias and detection bias) assessor	Low risk	Outcome assessors were blinded. Quote (page 27): "This was an investigator-blinded study."
Incomplete outcome data	Low risk	Intention-to-treat analysis was used. No dropouts.

Shin 2012

Methods	Randomised, within-participants, left/right comparison study lasting 4 months.
Participants	**Inclusion criteria** • Adult patients with non-segmental vitiligo (NSV) without improvement despite more than a year of conventional treatment including NB-UVB phototherapy, topical steroids and calcineurin inhibitors **Exclusion criteria** • Patients with new, spreading lesions within the preceding 1 year.

Shin 2012 *(Continued)*

	10 participants were included in this study, 3 males and 7 females.
Interventions	**Intervention** **A:** Fractional CO_2 laser followed by NB-UVB therapy. Two sessions of fractional CO_2 laser therapy using a 10 600 nm eCO_2 laser on lesions of half of the body were performed at a 2-month interval. The treatment settings were a pulse energy of 100 mJ and a spot density of 150 spots cm^{-2} in the static mode; two passes were delivered using a 300-density tip. After the laser treatments, only mupirocin ointment was applied to the wounds for 1 week without any dressing. NB-UVB phototherapy was re-administered 5 days after each laser treatment using two-thirds of the most recent NBUVB dose administered before enrolment in the study (mean ± SD restarting dose: 2452 ± 859.8 mJ cm^{-2}). The sequential phototherapies were performed twice a week for 2 months, elevating the treatment dose by 15% each time. After the second laser treatment, phototherapy was performed according to the same protocol. **Control Interventoin** **B:** NB-UVB therapy alone
Outcomes	**Primary outcomes of the trial** 1)Repigmentation. - Clinical assessments were made by two blinded dermatologists using a quartile grading scale (grade 0 = no improvement; 1,1% to 25% = minimal; 2, 26% to 50% = moderate; 3, 51% to 75% = good; and 4, > 75% = excellent). - Also, 2 months after the last treatment, patients were questioned about their overall satisfaction using a 10-point visual analogue scale (VAS, 0–10) 2) Safety assessment. 2 months after the last treatment, patients were questioned about side effects of the treatment.
Notes	Dosage and irradiation for NB-UVB alone not clearly reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 659): "Each side of the body was randomly assigned to one of two groups..." Comment: Insufficient detail was reported about the method used to generate the allocation sequence.
Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	High risk	Participants were not blinded.
Blinding (performance bias and detection bias) clinician	High risk	Clinicians were not blinded.
Blinding (performance bias and detection bias) assessor	Low risk	Outcome assessors were blinded.

Shin 2012 *(Continued)*

		Quote (page 659): "Objective clinical assessments were made by two blinded dermatologists using a quartile grading scale..."
Incomplete outcome data	Low risk	Intention-to-treat analysis was used. No dropouts.

Siddiqui 1994

Methods	Randomised, double-blind, placebo-controlled, parallel group study lasting 6 months
Participants	**Inclusion criteria of the trial** • Patients with disseminated vitiligo over large parts of the body (10% to 40%) **Exclusion criteria of the trial** • Vitiligo on distal extremities or acrofacial vitiligo only Participants with vitiligo; 149 in the open trial and 32 in the double-blind trial. Participants in the open trial did not take part in the double-blind trial. Average age 30.6 years (range 18 to 56). Duration of the disease was 1 to 33 years (9.6 average), 60% of them had vitiligo for 5 to 10 years. 8 participants dropped out of the trial; 5 from the placebo group and 3 from the intervention group. This study was conducted in the Netherlands.
Interventions	**Intervention** **A:** L-Phe (L-phenylalanine) plus UVA exposure. The L-Phe was taken daily with water after or during a low protein breakfast and were told not to eat or drink for 1 hour afterwards. UVA was given twice or 3 times weekly 30 to 40 minutes after L-Phe ingestion. Frequency of exposure was reduced to once a week in the last 6 months. Minimum exposure was given according to skin type, maximum did not exceed 9 J/cm^2 for skin types I-III and 12 J/cm^2 for skin types IV-V. **Control Intervention** **B:** placebo without UVA. The placebo was taken daily with water after or during a low protein breakfast and were told not to eat or drink for 1 hour afterwards.
Outcomes	**Primary outcomes of the trial** 1) Repigmentation: partial (25% to 40%), incomplete (> 40% to 60%), and good (> 60% to 80%). 2) Cessation of spread of vitiligo.(stability) Measured pre- and post-treatment (6 months).
Notes	Participants were randomly assigned to the open trial so it was assumed they were also randomised in the double-blind study.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 215): "One hundred and forty-nine vitiligo patients were randomly divided into three groups." Comment: Insufficient detail was reported about the method used to generate the allocation sequence. Moreover, 2 studies reported in the paper. This

Siddiqui 1994 *(Continued)*

		quote described larger open trial. Assumed smaller double-blind study lasting 6 months was also randomised.
Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	Unclear risk	Participants were blinded. Comment: States that the trial was double-blinded but no details given as to how blinding was maintained for participants (e.g. no information about markings on packets of medication given to participants).
Blinding (performance bias and detection bias) clinician	Unclear risk	Clinicians were blinded. Comment: States that the trial was double-blinded but no details given as to how blinding was maintained for clinicians.
Blinding (performance bias and detection bias) assessor	High risk	No separate outcome assessor mentioned.
Incomplete outcome data	High risk	Intention-to-treat analysis was not used. In the blind trial (32 participants): Intervention- A: 3 dropouts (reasons: lost to follow-up (1), and personal reasons (2).) Control- B: 5 dropouts (the reasons for dropouts were not reported.)

Singh 2013

Methods	Randomised, parallel group study lasting 16 weeks.
Participants	**Inclusion criteria of the trial** • Stable vitiligo for a period of 1 year and not responding to medical therapy **Exclusion criteria of the trial** • Patients aged < 10 years • Those with actively spreading vitiligo • A history of Köebnerisation • Hypertrophic and keloidal scars • A bleeding disorder and pregnant patients 30 patients were randomised, there were no losses to follow-up. The study included 10 males and 20 females. The study was conducted in India.
Interventions	**A:** Autologous non-cultured epidermal cell suspension (NCES) - surgical procedure using non-cultured epidermal cell suspension. Patients were asked to lie down for 1 hour after procedure and then they were allowed to go home. The dressing was removed after 7 days at the first follow-up visit at the hospital. Patients were asked to expose the area to sunlight at home starting from 5 min and up to a maximum of 30 min daily. **B:** Autologus non-cultured extracted hair follicle outer root sheath cell suspension (NCORSHFS) - Surgical procedure using non-cultured extracted hair follicle outer root sheath suspension. Patients were

Singh 2013 *(Continued)*

	asked to lie down for 1 hour after procedure and then they were allowed to go home. The dressing was removed after 7 days at the first follow-up visit at the hospital. Patients were asked to expose the area to sunlight at home starting from 5 min and up to a maximum of 30 min daily.
Outcomes	**Primary outcomes of the trial** 1) Degree of repigmentation: <50% = poor repigmentation; 50% to 74% = fair repigmentation; 75% to 89% = good repigmentation; 90% to 100% = excellent repigmentation. 2) Change in Dermatology Life Quality Index (DLQI) score. 3) Adverse effects.
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 4): "All the patients were randomly divided into two groups using a randomization table."
Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	High risk	Participants were not blinded.
Blinding (performance bias and detection bias) clinician	High risk	Clincians were not blinded. Comment: Clinicians could not be blinded since they extracted cells from the epidermis or hair follicles.
Blinding (performance bias and detection bias) assessor	High risk	Outcome assessors were not blinded.
Incomplete outcome data	Low risk	Intention-to-treat analysis was used. No dropouts.

Souto 1997

Methods	Randomised, double -blind, placebo-controlled, parallel group study lasting 6 months.
Participants	**Inclusion criteria of the trial** • Patients with vitiligo (clinical diagnosis) **Exclusion criteria of the trial** • Use of topical or systemic medication 2 months before the treatment. 20 participants: 10 randomised to treatment group and 10 to placebo group. 16 females and 4 males. Age range from 6 to 66 years, predominantly in the 40 year age group. Participants who had used topical or systemic medication in the previous 2 months were excluded from the trial. No other criteria applied. 1 participant withdrew from the placebo group.

Souto 1997 *(Continued)*

	This study was conducted in Brazil.
Interventions	**Intervention** **A:** Melagenina (a topical human placental extract) 3 times a day at 8-hourly intervals. During 1 of the applications the participants were exposed to infra-red light (250 watts) for 15 minutes, during which time the medication was applied every 5 minutes. The distance of the treated areas from the light source was 40 cm. **Control Intervention** **B:** placebo cream 3 times a day at 8-hourly intervals. During 1 of the applications the participants were exposed to infra-red light (250 watts) for 15 minutes, during which time the medication was applied every 5 minutes. The distance of the treated areas from the light source was 40 cm.
Outcomes	**Primary outcomes of the trial** 1) Repigmentation: improvement (presence of focal or diffuse areas of repigmentation on the edges of the white patches), deterioration (if the existing lesion increased in size), and no change (the appearance of new lesions was not taken into account). 2) Adverse effects.
Notes	Authors suggest a longer treatment period may give different results but note that it might be difficult to find participants willing to do this using placebo. Poor study with small number of participants, unclear outcome measures, apparently decided subjectively by participants. Measured pre- and post-treatment (6 months).

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Translated quote (page 237): "A total of 20 patients were included in this double-blind, randomized study" Comment: Insufficient detail was reported about the method used to generate the allocation sequence.
Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	Unclear risk	Participants were blinded. Comment: Study reported as double-blind (estudo dople cego) but no details given as to how blinding was maintained for participants.
Blinding (performance bias and detection bias) clinician	Unclear risk	Clinicians were blinded. Comment: Study reported as double-blind (estudo dople cego) but no details given as to how blinding was maintained for clinicians.
Blinding (performance bias and detection bias) assessor	High risk	This was not stated.
Incomplete outcome data	Low risk	Intention-to-treat analysis was used despite the poor results and poor tables. Intervention- A: 0 dropouts Control- B: 1 dropout due to intolerance.

Stinco 2009

Methods	Randomised parallel-group study, lasting 6 months
Participants	**Inclusion criteria** - Patients over 18 years old with vitiligo for almost 1 year (chronic) - Without any new depigmented patches in the past 12 months (stable) **Exclusion criteria** - Nursing or pregnant women and - Patients under 18 - patients affected infections, neurological or psychiatric disorders, autoimmune disease, immune defects, heart deficiency, kidney failure, previous or current history of neoplasms 44 patients were recruited and examined by the same dermatologist at baseline (T0) and every three weeks for 24 (T24) weeks.
Interventions	Patients were randomised on basis of a computer-generated randomisation schedule into three groups (A, B and C) corresponding to three different therapeutic programs: **A:** NB-UVB phototherapy **B:** pimecrolimus 1% cream **C:** tacrolimus 0.1% ointment.
Outcomes	- The area of repigmentation was analysed by serial mapping of body lesions. Based on the area of repigmentation, treatment outcome was calculated for each anatomical site according to a scale ranging from 0 to 4 and classified as “0, absent” (0), “1, poor” (1% to 25%), “2, moderate” (26% to 50%), “3, good” (51% to 75%), and “4, excellent” (> 75%). - Possible side effects were recorded during the whole period of the study
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 589): "The patients were randomized on basis of a computer-generated randomization schedule into three groups (A, B and C)..."
Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	High risk	Participants were not blinded. Quote (page 589): "We performed a randomized, open study..."
Blinding (performance bias and detection bias) clinician	High risk	Clinicians were not blinded. Quote (page 589): "We performed a randomized, open study..."
Blinding (performance bias and detection bias) assessor	Low risk	Outcome assessors were blinded.

Stinco 2009 *(Continued)*

		Comments: Base on the quote (page 589) "Estimation of response was performed visually by 2 clinicians not involved in the study." although omitting the term "blind" we assumed that the fact that they were not involved in the study made them blind.
Incomplete outcome data	High risk	Intention-to-treat analysis was not used. Intervention - A: 0 dropouts Intervention - B: 2 dropouts due to personal reasons. Intervention - C: 4 dropouts (reasons: personal (3); Herpes simplex on lips (1))

Tegta 2006

Methods	Randomised parallel group study lasting 3 months.
Participants	**Inclusion criteria of the trial** • Clinical diagnosis of vitiligo vulgaris or segmental vitiligo • Stable for >1 year **Exclusion criteria of the trial** • Age < 10 years • Unstable disease • Lesions on mucosa, palms, and soles • Patients with keloids • Pregnancy 22 participants with vitiligo vulgaris or segmental vitiligo, which had been stable for more than 1 year. Intervention group 1 consisted of 11 participants aged between 11 and 54 years old (mean 20.8). 6 were male and 4 were female and had been affected with vitiligo for between 2 and 13 years (mean 5.85). Intervention group 2 comprised of 11 participants aged between 10 and 40 years old (mean 21.7). 4 were male and 6 were female and had been affected by vitiligo for between 1.5 and 13 years (mean 6.25). 2 participants were lost at follow-up, which resulted in 20 evaluated participants. This study was conducted in India.
Interventions	**A:** autologous transplantation of epidermal suspension from skin graft approximately ⅓ of the size of the recipient area. Single transplantation applied to blister or dermabraded skin. Oral ciprofloxacin (500 mg) was taken twice a day for 5 days. Dressing was retained for 7 days. **B:** autologous transplantation of epidermal suspension from skin graft approximately ⅕ the size of the recipient area. Single transplantation applied to blister or dermabraded skin. Oral ciprofloxacin (500 mg) was taken twice a day for 5 days. Dressing was retained for 7 days.
Outcomes	**Primary outcomes of the trial** 1) Repigmentation: no response (0% to 25%), mild repigmentation (26% to 51%), moderate repigmentation 51% to 75%), and marked repigmentation (> 75%). 2) Colour matching of repigmentation: somewhat darker, somewhat lighter, and the same. 3) Mean time to initial repigmentation. 4) Adverse effects. Measured pre- and post-treatment (3 months).

Tegta 2006 *(Continued)*

Notes	singe intervention dose dependent

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 107): "Twenty-two patients fulfilling the criteria were randomly assigned to Groups A and B (11 patients each)." Comment: Insufficient detail was reported about the method used to generate the allocation sequence, thus we e-mailed the authors who responded that "Randomization was done by using random table number."
Allocation concealment (selection bias)	Unclear risk	This was not stated. Comment: No details given as to whether or not random table was kept concealed.
Blinding (performance bias and detection bias) participant	High risk	Participants were not blinded. Comment: Blinding not possible because different areas of skin were used to provide the epidermal suspension.
Blinding (performance bias and detection bias) clinician	High risk	Clinicians were not blinded. Comment: Blinding not possible because different areas of skin were used to provide the epidermal suspension.
Blinding (performance bias and detection bias) assessor	High risk	No separate outcome assessor mentioned.
Incomplete outcome data	High risk	Intention-to-treat analysis was not used. Intervention- A: 1 dropout (the reason for the dropout was not reported.) Control- B: 1 dropout (the reason for the dropout was that the participant developed a bacterial infection at the recipient site 2 days after grafting and although he was prescribed systemic antimicrobials, he was lost to follow-up.)

Tjioe 2002

Methods	Randomised parallel group study lasting 1 year.
Participants	**Inclusion criteria of the trial** • Aged 18 and above • Stable vitiligo vulgaris (at least one year no changes) • Fitzpatrick's skin type II–IV **Exclusion criteria of the trial** • Patients using any medical treatment for their vitiligo at the time of the study were excluded • Patients with a history of skin cancer or dysplastic naevus syndrome • Photosensitivity or using photosensitising medicines • Psychiatric or epileptic disorders • Known renal failure

Tjioe 2002 *(Continued)*

	• Known allergies to substances in the trial medication. 27 participants aged 18 or over with long-term stable (no change in the previous year) vitiligo vulgaris including skin type was II to IV. Participants using any medication for vitiligo at the time of recruitment were excluded as were those with a history of skin cancer or dysplastic naevus syndrome photosensitivity, psychiatric disorders, renal failure, or known allergies to substances in the trial medication. Ages ranged from 20 to 51 (mean 41.6) in the UVB-only group and 29 to 68 (mean 46.8) in the group using additional vitamins. Duration of the disease 1 to 30 years (mean 10.8). This study was conducted in the Netherlands.
Interventions	**A:** Narrowband (311 nm) UVB only 3 times a week, starting with 0.10 J/cm^2 increasing by 0.30 J/cm^2 at each visit. Affected areas were monitored monthly, including before and after photographs. If complete repigmentation was achieved before 1 year, treatment was discontinued. **B:** 1000 mg of slow release B_{12} tablets and 5 mg folic acid twice daily as well as UVB exposure 3 times a week, starting with 0.10 J/cm^2 increasing by 0.30 J/cm^2 at each visit. Affected areas were monitored monthly, including before and after photographs. If complete repigmentation was achieved before 1 year, treatment was discontinued.
Outcomes	**Primary outcomes of the trial** 1) Percentage of mean repigmentation. Measured pre- and post-intervention (1 year). Outcomes were measure visually as a percentage of repigmentation of the lesions.
Notes	This study appears to confirm the efficacy of narrow band UVB for vitiligo but additions of vitamin supplements B_{12} and folic acid did not improve results.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 370): "The patients were randomised in 2 narrow band UVB treatment groups." Comment: Insufficient detail was reported about the method used to generate the allocation sequence.
Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	High risk	Participants were not blinded. Quote (page 369): "Using a non-blinded approach..."
Blinding (performance bias and detection bias) clinician	High risk	Clinicians were not blinded. Quote (page 369). "Using a non-blinded approach..."
Blinding (performance bias and detection bias) assessor	High risk	This was not stated.
Incomplete outcome data	Low risk	Intention-to-treat analysis was used. No dropouts.

Van Geel 2004

Methods	Randomised, double-blind, placebo-controlled, within-participant, left/right comparison study, lasting 12 months.
Participants	**Inclusion criteria of the trial** • Generalised, stable (no new lesions or expansion of existing ones in previous 12 months) vitiligo **Exclusion criteria of the trial** • Age less then 15 years 28 participants (equal number of males and females) with generalised vitiligo. Participants were aged between 15 and 65 years old (mean 35.2) and 19 participants had stable vitiligo. The participants had been affected by the condition for between 18 and 324 months (mean 144) and the body surface area affected ranged from 0.2% to 20% (mean 4%). 2 participants were lost at first follow-up (3 months), 10 at second follow-up (6 months), and 12 at final follow-up (12 months) resulting in 26, 18, and 16 evaluated respectively. This study was conducted in Belgium.
Interventions	**Intervention** **A:** Cellular suspension (melanocytes medium plus hyaluronic acid plus epidermal cells). Using a hand dermatome, a shave biopsy specimen of approximately 2 cm^2 was taken from the participants' normally pigmented gluteal region. Hyaluronic acid was added in a 1:1 ratio to increase viscosity and obtain the gel. The lesion was covered with a sterile dressing, dry gauze, and adhesive tape, and participants were asked to limit movement of the treated region for 3 to 7 days. 1 week later the bandage was changed and left in place for another week. UVB or PUVA started 3 weeks later. UVB or PUVA was administered twice a week for approximately 2 months. UVB started with 0.1 J/cm^2 and increased by 0.1 J/cm^2 each session until a slight erythema appeared. UVA started with 0.5 J/cm^2 and increased by 0.5 J/cm^2 each session until a slight erythema appeared. **Control Intervention** **B:** Placebo (melanocytes medium plus hyaluronic acid).Using a hand dermatome, a shave biopsy specimen of approximately 2 cm^2 was taken from the participants' normally pigmented gluteal region. Hyaluronic acid was added in a 1:1 ratio to increase viscosity and obtain the gel. The lesion was covered with a sterile dressing, dry gauze, and adhesive tape, and participants were asked to limit movement of the treated region for 3 to 7 days. 1 week later the bandage was changed and left in place for another week. UVB or PUVA started 3 weeks later. UVB or PUVA was administered twice a week for approximately 2 months. UVB started with 0.1 J/cm^2 and increased by 0.1 J/cm^2 each session until a slight erythema appeared. UVA started with 0.5 J/cm^2 and increased by 0.5 J/cm^2 each session until a slight erythema appeared.
Outcomes	**Primary outcomes of the trial** 1) Percentage of repigmentation. 2) Repigmentation pattern. Measured pre-treatment and at 3, 6, and 12 months follow-up.
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 1204): "Treatment with either a cellular suspension..or a placebo..was randomised by a lottery system."

Van Geel 2004 *(Continued)*

		Comment: Insufficient detail was reported about the method used to generate the allocation sequence, thus we e-mailed the authors who responded that "Randomisation: in each person individually (left/right lottery ticket)."
Allocation concealment (selection bias)	Low risk	This was not stated. Comment: we e-mailed the authors who responded that "In each person individually (left/right lottery ticket). This was performed by the laboratory co-worker."
Blinding (performance bias and detection bias) participant	Low risk	Participants were blinded. Comment: we e-mailed the authors who responded that "The patient and the investigator were blinded. It was not possible to distinguish the active from the placebo treatment. Both sides were treated in the same way, with the preparation and the same suspension. The cells inside the cell suspension- were not visible."
Blinding (performance bias and detection bias) clinician	Low risk	Clinicians were blinded. Comment: we e-mailed the authors who responded that "The patient and the investigator were blinded. It was not possible to distinguish the active from the placebo treatment. Both sides were treated in the same way, with the preparation and the same suspension. The cells inside the cell suspension were not visible."
Blinding (performance bias and detection bias) assessor	Low risk	No outcome assessor in this study. Email response: "There was not an independent outcome assessor. All measurements were carried out by the clinician who was blinded for the treatment and did not know at all what the actively or placebo treated site was."
Incomplete outcome data	Low risk	Intention-to-treat analysis was used. No dropouts.

Vasistha 1979

Methods	Randomised, placebo-controlled, parallel group study lasting 8 weeks.
Participants	**Inclusion criteria of the trial** • Patients with vitiligo **Exclusion criteria of the trial** • None reported 35 participants, 18 males 17 females with at least 1 patch of vitiligo for a minimum of 1 year (8 participants). This study was conducted in India.
Interventions	**Intervention** **A:** Injections of 10 mg/ml triamcinolone acetonide suspension were given to 25 participants. 0.1 ml of the drug was injected into each site leaving 2 cm between 2 injections. Treatment was given at weekly intervals for 8 weeks and participants were followed-up for 4 weeks. **Control Intervention**

Vasistha 1979 *(Continued)*

	B: injections of distilled water into each site leaving 2 cm between 2 injections. Treatment was given at weekly intervals for 8 weeks and participants were followed-up for 4 weeks.
Outcomes	**Primary outcomes of the trial** 1) Repigmentation: no response (no improvement), fair response (slight improvement), good response (increase in the size of new pigmented spots or decrease in the size of the lesion), and excellent response (considerable increase in the size of pigmented spots and decrease in the size of the lesion). 2) Adverse effects. Measured pre- and post-treatment (8 weeks).
Notes	The authors conclude that this treatment cannot be recommended as a substitute or alternative to psoralen therapy. It may have some use in treating recalcitrant patches or when participants have a photo-allergy to psoralens. Side effects included atrophy in 9 participants, telangiectasia in 2, 1 had an infection, and one had intradermal haemorrhage. There was no statistical difference between the use of triamcinolone and distilled water.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 308): "Patients were randomly selected, considering the comparability of the two groups." Comments: Insufficient detail was reported about the method used to generate the allocation sequence. However, according to the response letter, on 08.10.2002: "Patients belonging to random number of statistical random number table were given inj. triamcinolone and patients belonging to remaining number were given inj. aqua distillata." Note: The very unequal numbers of participants in each group suggests that this was not true randomisation, but we have accepted that a random number table was used.
Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	High risk	This was not stated.
Blinding (performance bias and detection bias) clinician	High risk	This was not stated.
Blinding (performance bias and detection bias) assessor	High risk	This was not stated.
Incomplete outcome data	Low risk	Intention-to-treat analysis was used. No dropouts.

Verhaeghe 2011

Methods	Randomised, within-participant study lasting 12 weeks.

Verhaeghe 2011 *(Continued)*

Participants	**Inclusion criteria of the trial** • Patients aged 18 years or older with established generalised vitiligo for at least 3 months • Presence of at least 3 vitiligo patches or at least 1 lesion of ≥ 15 cm^2 **Exclusion criteria of the trial** • A history of melanoma or other skin cancer • Severe Köebner reactions after sun exposure • Pregnancy or lactation • Vitiligo patches on the face or hands • Phototherapy for the last month • Vitiligo treatment on the selected lesions less than 1 month prior to the study • Use of photosensitising drugs • Herbal supplements, perfumes or cosmetics that could influence the susceptibility to UV light 11 patients were randomised, this included 3 males and 8 females. The mean age was 41.2 years, the age range was 22 to 57 years. The average duration of disease was 13.11 years and the range was 1 to 40 years. This study was conducted in Belgium.
Interventions	**A:** NB-UVB given twice a week for 12 weeks. The initial dose was 400 mJ/cm^2. At each treatment session, the dose was increased by 100 mJ/cm^2. If minimal asymptomatic erythema appeared, the dose was kept constant. If symptomatic erythema (burning, pain) or blistering developed, treatment was interrupted until clearance of the symptoms and resumed at a dose 100 mJ/cm^2 less than that of the last treatment session. **B:** 308-nm monochromatic excimer light MEL given twice a week for 12 weeks. The initial dose was 400 mJ/cm^2. At each treatment session, the dose was increased by 100 mJ/cm^2. If minimal asymptomatic erythema appeared, the dose was kept constant. If symptomatic erythema (burning, pain) or blistering developed, treatment was interrupted until clearance of the symptoms and resumed at a dose 100 mJ/cm^2 less than that of the last treatment session. **C:** Placebo - MEL device, while the lamp was shielded by a metal shutter.
Outcomes	**Primary outcomes of the trial** 1) Percentage of repigmentation. Repigmentation was expressed as absolute numbers and afterwards classified into 5 scores: < 0% repigmentation (score 0), 0% to 25% repigmentation (score 1), 25% to 50% repigmentation (score 2), 50% to 75% repigmentation (score 3), > 75% repigmentation (score 4). 2) Adverse effects. All outcomes were measured at baseline, after 12 sessions and after 24 sessions (12 weeks).
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 2): "Randomization and allocation were carried out by patients drawing lots out of an opaque container containing identical cards with the treatment code."
Allocation concealment (selection bias)	Low risk	Quote on page 344: “same opaque container where the generation of the randomisation sequence was carried out which contained identical cards with the treatment code”

Verhaeghe 2011 *(Continued)*

Blinding (performance bias and detection bias) participant	High risk	Participants were not blinded.
Blinding (performance bias and detection bias) clinician	High risk	Clinician were not blinded.
Blinding (performance bias and detection bias) assessor	Low risk	Outcome assessor was blinded. Quote (page 2): "The allocated treatment was concealed from the assessor who analysed the data and measured repigmentation, and was revealed only to the treating physician."
Incomplete outcome data	Low risk	Intention-to-treat analysis was used. No dropouts. Comment: However, data of 1 patient at session 24 was excluded from surface measurement analysis due to incorrect lesion contours caused by a wrong positioning of the patient.(see page 3).

Wazir 2010

Methods	Randomised parallel-group study, lasting 6 months
Participants	**Inclusion criteria** • Patients of both sex aged older than 5 years and had stable vitiligo • Involvement of less than 30% of the body surface area. • Patients showed no evidence of spontaneous repigmentation • Duration of disease of less than five years • No treatment for last one month **Exclusion criteria** • Patients with lip-tip type of vitiligo or mucosal involvement • Patients with known hypersensitivity to tacrolimus or mometasone. Patients who had history of autoimmune disease, impaired liver or renal function, hypercalcaemia, hypercalciuria, urolithiasis, thyroid or parathyroid disease, photosensitivity,cataract, hypertension, cardiovascular or malignant disease, arsenic exposure, pregnancy, lactation, concomitant use of vitamin D, calcium and any other drug that can affect calcium homeostasis were also excluded. Sixty patients, 30 in each group, suffering from vitiligo with Fitzpatrick skin type IV completed the study. There were 14 males and 16 females in group I and 12 males and 18 females in group II respectively. The duration of disease was < 5 years in both groups, with a mean of 1.7+1.5 years in group I and 1.8+1.4 years in group II. In all patients, the extent of involvement was < 30%.
Interventions	**A:** Topical mometasone furoate 0.01% ointment **B:** Topical tacrolimus 0.03% ointment and mometasone furoate 0.01%
Outcomes	**Primary outcomes of the trial**

Wazir 2010 *(Continued)*

	1) Repigmentation measured by comparing the treated areas with pretreatment photographs with Responses graded on a scale from 0-5. The improvement was evaluated by comparing the treated areas with pretreatment photographs. Responses were graded on a scale from 0 to 5: Grade Improvement (%) 0 = No response 1 = 1% to 25% 2 = 26% to 50% 3 = 51% to 75% 4 = 76% to 95% Grade 0 = ineffective, grade 1 to 3 = partially effective, grade 4 to 5 = effective 2) Adverse effects No side effects reported. "The main point was the absence of atrophy and other side effects in lesions treated with tacrolimus and mometasone" Patients were assessed weekly during the first month and then fortnightly for the next five months for pigmentation and adverse effects. Photographs of vitiliginous skin were taken at first visit and after three and six months.
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 89): "All the patients were randomly divided into two equal groups using random number table."
Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	Unclear risk	Participants were blinded. Comment: Insufficient detail was reported about blinding of participants. We e-mailed the authors who responded on 26/06/2013 that only participants were blinded.
Blinding (performance bias and detection bias) clinician	High risk	Clinicians were not blinded.
Blinding (performance bias and detection bias) assessor	High risk	Outcome assessors were not blinded.
Incomplete outcome data	Low risk	Intention-to-treat analysis was used. No dropouts.

Westerhof 1999

Methods	Randomised, parallel group, left/right comparison study lasting 9 months.
Participants	**Inclusion criteria of the trial** • 18 to 80 years of age • Vitiligo with long-term stable or active lesions • No spontaneous repigmentation • 2 almost symmetrical lesions on legs, arms or trunk **Exclusion criteria of the trial** • Vitiligo on face, hands or feet only • Use of immunosuppressive agents • Use of topical steroids in the 2 weeks before study initiation • Use of systemic steroids in the 6 weeks before study initiation • Known hypersensitivity to FP • Abnormal reactions to UV-A radiation • Signs of skin atrophy • Pregnancy 135 participants enrolled in the study and 96 were evaluated at the end of the study. Reasons for stopping included not enough repigmentation (23), lack of motivation(11), and protocol violations (5). Participants of either sex were affected on arms, legs, and trunk and had symmetrical patches. Ages ranged from 18 to 80 years and the disease could be of any duration. This study was conducted in the Netherlands.
Interventions	**A:** Fluticasone propionate 0.5% (FP) alone on 1 side of the body and FP + UVA on the other. The FP cream was applied daily half an hour before retiring to bed. The UVA exposure was 10 J/cm^2 for 20 minutes twice a week. participants were assessed at 3, 6, and 9 monthly intervals. **B:** UVA alone on one side, and FP + UVA on the other. The FP cream was applied daily half an hour before retiring to bed. The UVA exposure was 10 J/cm^2 for 20 minutes twice a week. participants were assessed at 3, 6, and 9 monthly intervals. Participants were divided randomly into 2 groups, 1 group using FP alone on 1 side of the body, and FP + UVA on the other, the other group using UVA alone on one side, and FP + UVA on the other.
Outcomes	**Primary outcomes of the trial** 1) Repigmentation: 0% (no response), 75% (successful significant response), 100% (complete repigmentation). 2) Adverse effects No side effects reported. "The main point was the absence of atrophy and other side effects in lesions treated with tacrolimus and mometasone" Measured pre-treatment and at 3, 6, and 9 months.
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 1062): "This randomised, controlled, left-right comparative study..."

Westerhof 1999 *(Continued)*

		Comment: Insufficient detail was reported about the method used to generate the allocation sequence.
Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	High risk	Participants were not blinded. Comment: Not stated in text but probably not done because of 3 different interventions.
Blinding (performance bias and detection bias) clinician	High risk	Clinicians were not blinded. Comment: Not stated in text but probably not done because of 3 different interventions.
Blinding (performance bias and detection bias) assessor	Unclear risk	Quote (page 1062): "Repigmentation was assessed by a single dermatologist." Comment: It was not clear whether the outcome assessor was blinded or not.
Incomplete outcome data	Low risk	Intention-to-treat analysis was used. Intervention- A: 23 dropouts (reasons: violation of the protocol (4), decreased motivation (7), and because of insufficient repigmentation in their opinion (12).) Control- B: 16 dropouts (reasons: violation of the protocol (1), decreased motivation (4), and because of insufficient repigmentation in their opinion (11).)

Wind 2011

Methods	This is a randomised, within-participant study lasting 6 months.
Participants	**Inclusion criteria of the trial** • Patients over > 18 years with non-segmental vitiligo that has been stable for at least 1 year **Exclusion criteria of the trial** • A history of hypertrophic scarring and/or keloid • History of allergic/phototoxic reaction (Lidocaine, Tegaderm, Suture strips, sunlight) • A negative minigrafting test • A personal or a family history of skin cancer (non-melanoma skin cancer: first degree family members, melanoma: any family member) • A personal history of photosensitivity and/or phototoxicity disorders • Skin type I (according to Fitzpatrick classification I-VI) • Pregnancy • Taking medications known to cause photosensitivity and/or phototoxicity and chronic or very frequent use of any medication that can influence the UVB response (e.g..tetracycline, retinoids, sulfonamides, psoralens, NSAID's) • With other skin diseases that would impair evaluation of repigmentation, such as psoriasis and eczema. • Patients not able to have 2 times weekly NB-UVB/Excimer therapy. • Patients taking local immunosuppressive treatment within 6 weeks prior to enrolment. For these patients a washout period of 6 weeks will be required. 6 participants were randomised, this included 2 males and 4 females. The mean age was 43.

Wind 2011 *(Continued)*

	This study was conducted in The Netherlands.
Interventions	**A:** Punch grafts alone, no other treatment. The total trial duration was 3 months. **B:** Punch grafts and BB-UVA. Following the punch grafts, UVA (BB-UVA; 320–400 nm) facial tanner was used at a power density of 8 mW/cm^2 twice weekly on non-consecutive days. The exposure-time was increased from 4 to 8 to 12 min in the first three sessions. From the fourth session onwards, exposure-time remained 14.5 min. During each phototherapeutic treatment, a tinfoil template was used to prevent irradiation of the other three test regions. The total trial duration was 3 months. **C:** Punch grafts and NB-UVB. Following the punch grafts, a 311 nm NB-UVB hand-held device was used at a power density of 8 mW/cm^2 twice weekly on non-consecutive days. Treatment was started at 0.1 J/cm^2. This dose was increased by 0.1 J/cm^2 at each treatment if no side-effects were reported. During each phototherapeutic treatment, a tinfoil template was used to prevent irradiation of the other three test regions. The total trial duration was 3 months. **D:** Punch grafts and Helium-Neon (HeNe) laser. Following the punch grafts, a continuous wave HeNe laser with an average power of 1.0 mW was used for 30 s per punch graft at an average distance of 10 cm. This was given twice weekly on non-consecutive days. During each phototherapeutic treatment, a tinfoil template was used to prevent irradiation of the other three test regions. The total trial duration was 3 months.
Outcomes	**Primary outcomes of the trial** • Degree of repigmentation. Directly after the last phototherapeutic treatment (T_1), and at three and 6 months follow-up (T_2 and T_3), a blinded physician measured the largest (d_1) and its perpendicular diameter (d_2) of each punch graft. The (re)pigmented surface area A was calculated by A = 0.25 π x d1 x d2.
Notes	Additional information was obtained via email correspondence regarding inclusion/exclusion criteria and baseline characteristics of patients.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (page 1236): "A randomized controlled observer-blinded study was performed in six patients" Comment: Insufficient detail was reported about the method used to generate the allocation sequence.
Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	High risk	Participants were not blinded.
Blinding (performance bias and detection bias) clinician	High risk	Clinicians were not blinded.
Blinding (performance bias and detection bias) assessor	Low risk	Outcome assessor was blinded. Quote (page 1236): "randomized controlled observer-blinded study was performed in six patients"
Incomplete outcome data	Low risk	Intention-to-treat analysis was used.

Wind 2011 *(Continued)*

	No dropouts.

Yaghoobi 2011

Methods	This is a randomised parallel group study lasting 4 months.
Participants	**Inclusion criteria of the trial** • The localized and generalised types of vitiligo • Vitiligo for less than 5 years • Normal or low serum zinc • Normal other laboratory tests • Taking no zinc during 4 weeks prior to referring **Exclusion criteria of the trial** • Segmental vitiligo • History of systemic disorder • Pregnancy • History of drug administration 35 patients were randomised in this trial. 5 patients were lost to follow-up: 1 from group A because of discontinuation of treatment and 4 from group B 3 patients refuted reference and 1 patient had a rise in serum zinc level. This study was conducted in Iran.
Interventions	**A:** Topical corticosteroid as 0.05% clobetasol propionate cream in isopropyl alcohol 65° preparation (in equal proportion) for the body and 0.1% triamcinolone acetonide cream for the face and flexures, used twice daily for 4 months. **B:** Topical corticosteroid as 0.05% clobetasol propionate cream in isopropyl alcohol 65° preparation (in equal proportion) for the body and 0.1% triamcinolone acetonide cream for the face and flexures with oral zinc sulphate capsules. The topical steroids were applied twice daily and patients were given 2 capsules of the 220mg zinc sulphate capsule. For children, 10 mg/kg of a capsule or syrup was given.
Outcomes	**Primary outcomes of the trial** • Percentage of repigmentation, assessed at 1, 3, 4 months after beginning of treatment.
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 2): "Then, the patients were divided in two groups, randomly; randomization in the two groups of therapy and control was performed by computerized number tables."
Allocation concealment (selection bias)	Unclear risk	This was not stated.
Blinding (performance bias and detection bias) participant	High risk	This was not stated.

Yaghoobi 2011 *(Continued)*

Blinding (performance bias and detection bias) clinician	High risk	This was not stated.
Blinding (performance bias and detection bias) assessor	High risk	This was not stated.
Incomplete outcome data	High risk	Intention-to-treat analysis was not used. Intervention - A: 1 dropout due to treatment discontinuation. Intervention - B: 4 dropouts (reasons: refuting reference (3), rising of serum zinc level (3))

Yones 2007

Methods	Randomised, double-blind, placebo-controlled, parallel group study lasting 12 months.
Participants	**Inclusion criteria of the trial** • Non-segmental vitiligo affecting 2% to 70% of the body surface area. **Exclusion criteria of the trial** • Age < 18 years or older than 70 years, • Previous skin malignancy • Previous failure of intolerance to photochemotherapy • > 100 sessions of photochemotherapy in the patient's lifetime • Treatment for vitiligo within the last 3 months (phototherapy, systemic therapy, or topical therapy with corticosteroids agents • Vitamin D analogues, or tacrolimus) • Pregnancy or lactation • Renal or hepatic disease • Lupus erythematosus • A history of photosensitivity or administration of a drug known frequently to cause photosensitization. 56 participants with symmetrical vitiligo affecting 2% to 70% of their body surface area were recruited and 50 commenced treatment. There were an equal number of participants in each group and 48% were male in the intervention group and 68% in the control group. In the intervention group, participants were aged between 18 and 70 years old (mean 26), had been affected by vitiligo for between 1 and 36 years (mean 6) and vitiligo affected 3% to 64% of their body surface area (mean 8.4). In the control group, participants were aged between 18 and 64 years old (mean 38), had been affected by vitiligo for between one and 47 years (mean 10) and vitiligo affected 2% to 55% of their body surface area (mean 6.9). This study was conducted in the UK.
Interventions	**A:** PUVA. The dose of 8-methoxypsoralen was determined according to the participant's body surface area, namely, 25 mg/m^2, and ranged from 30 to 60 mg. The dose was taken 2 hours before irradiation. Participants intolerant of 8-methoxypsoralen were instead given identical-appearing 5-methoxypsoralen tablets, 3 hours before irradiation. **B:** NB-UVB.
Outcomes	**Primary outcomes of the trial**

Yones 2007 *(Continued)*

	1) Patient-rated quality of life: Dermatology Life Quality Index and Visual Analogue Scale 2) Repigmentation: < 0% (deterioration in vitiligo), 0% to 25%, 25% to 50%, 50% to 75%, and > 75%. 3) Adverse effects. Measured pre- and post-treatment (1 year).
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (page 579): "Patients were randomly allocated to receive either PUVA or NB-UVB therapy by means of a sequentially numbered list held in the pharmacy."
Allocation concealment (selection bias)	Low risk	Quote (page 579): "Sequentially numbered list held in the pharmacy."
Blinding (performance bias and detection bias) participant	Low risk	Participants were blinded. Quote (page 579):"The phototherapy cabinet labels were concealed and two hours before treatment all patients ingested identical appearing tablets."
Blinding (performance bias and detection bias) clinician	High risk	Clinicians were not blinded. Quote (page 579): "Nursing and pharmacy staff conducting the treatment were necessarily aware of them." (i.e. treatment allocations.)
Blinding (performance bias and detection bias) assessor	Low risk	Outcome assessor was blinded. Quotes (page 579): "The dermatologist conducting the assessments was blinded to the treatment allocations." and "All assessments were made by one blinded investigator."
Incomplete outcome data	Low risk	Intention-to-treat analysis was used only for all those who commenced therapy who included regardless of withdrawal for any reason thereafter. Six patients withdrew before commencement of treatment and were not considered further: Intervention- A: 3 dropouts (the reasons for dropouts were due to non-attendance of treatment but the reasons were unknown) Control- B: 3 dropouts (the reasons for dropouts were due to non-attendance of treatment but the reasons were unknown)

BB-UVA: broadband ultraviolet A light
BB-UVB: broadband ultraviolet B light
BSA: body surface area
IU: international units
NB-UVB: narrowband ultraviolet B light
NSAIDs: non-steroidal anti-inflammatories
NSV: non-segmental vitiligo
PUVA: psoralen and UVA
SD: standard deviation
TCM: Traditional Chinese Medicine
VASI score: vitiligo area scoring index

VETF score: Vitiligo European Task Force
VIDA score: vitiligo disease activity score

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Babu 2008	Participants were randomly selected but not randomly allocated to groups
Bahmani 2011	States randomised in the abstract but in email correspondence, authors admitted the study was not randomised
Du 1996	Listed as RCT in the search which Cochrane Skin Group checked with their translator who concluded that it was not randomised
El Mofty 2001	Claimed to be randomised but methodology showed the study is not randomised
El Mofty 2006b	Not a RCT. Report of two right–left comparative studies carried out simultaneously, Participants were randomly allocated to either study. Lesions (not participants) were assessed but were non-randomised
El Zawahry 1997	This study was classified as a CCT by the Skin Group in their register
Ghosh 1994	Participants were randomly selected but not randomly allocated to groups
Godse 2008	Claimed to be randomised but methodology showed the study is not randomised
Shi 1995	Listed as RCT in the search which Cochrane Skin Group checked with their translator who concluded that it was not randomised
Sun 1996	Listed as RCT in the search which Cochrane Skin Group checked with their translator who concluded that it was not randomised
Suo 2010	Study in Chinese. Randomisation unclear and study confirmed as not randomised by translator
Xu 1992	Listed as RCT in the search which Cochrane Skin Group checked with their translator who concluded that it was not randomised
Zhang 2008	Listed as RCT in the search which Cochrane Skin Group checked with their translator who concluded that it was not randomised

CCT: controlled clinical trial
RCT: randomised controlled trial

Characteristics of studies awaiting assessment *[ordered by study ID]*

Al Rubaie 2002

Methods	Randomised controlled trial.
Participants	39 participants enrolled in the study, 20 males and 19 females, with generalised vitiligo and of skin type IV and V, aged 9 to 65 years with a mean duration of disease 4.36 years. 33 completed the treatment and follow-up.
Interventions	NB-UVB vs PUVA plus calcipotriol vs PUVA alone.
Outcomes	Repigmentation.

Al Rubaie 2002 *(Continued)*

Notes	Conclusion: NB-UVB superior to PUVA. PUVA plus calcipotriol gives faster results than PUVA alone. Old study but still not published. Kept in this table for information as study could have provided useful information.

Awasthi 2011

Methods	Randomised within participant trial.
Participants	Participants with recent (within 1 year) stable lesions.
Interventions	Cold trypsinisation for preparing non-cultured epidermal cell suspension vs warm trypsinisation in non-cultured melanocyte transplantation for stable vitiligo.
Outcomes	The effect on repigmentation of cold vs warm trypsinisation in melanocyte transplantation for stable, early onset vitiligo.
Notes	Conclusion: Cold trypsinisation gives a better result. Study still not retrieved from sources of published studies.

Baldo 2014

Methods	Randomised controlled trial.
Participants	48 patients in 4 groups of 12 with bilateral vitiligo.
Interventions	NB-UVB twice weekly on one side and tacrolimus ointment twice daily on the other side.
Outcomes	Repigmentation and quality of life measured with Dermatology Life Quality Index (DLQI).
Notes	Conclusion: Study confirmed the efficacy of NB-UVB as comparable to tacrolimus.

Budania 2014

Methods	Randomised controlled trial.
Participants	63 participants with 80 stable vitiligo lesions.
Interventions	Autologous non-cultured epidermal cell suspension (NCES), suction blister epidermal grafting (SBEG) and split thickness skin grafting (STSG).
Outcomes	Repigmentation, colour match, change in Dermatology Life Quality Index (DLQI) and patient satisfaction.
Notes	Cocnlusion: NCES was found to be significantly superior to SBEG (P = 0.002) and STSG (P = 0.001). Good repigmentation (> 75%) was seen in 89% of lesions in the NCES group, 85% in the SBEG group and 73% in the STSG group.

Caballero 2011

Methods	Randomised controlled trial.
Participants	Participants with vitiligo for less than 2 years with facial or hand involvement, aged 18 to 40 years, without systemic diseases and mild to moderate levels of depression. 38 enrolled 20 dropouts, therefore 18 were assessed.
Interventions	Control group received topical clobetasol and the experimental group also received psychotherapy. Clobetasol was applied once a day for 2 months and experimental group had 8 weekly psychological sessions. There was a 2-month follow-up.
Outcomes	Improvement but not specified. Evaluated by an iconographic analysis and SPSS.
Notes	Result not statistically significant although slightly better results found in combination group. High number of dropouts.

Daniel 2011

Methods	Randomised controlled within-participant trial.
Participants	14 participants with chronic stable vitiligo sites of lesions randomised to minigrafting or non-cultured epidermal cell suspension (NCES) using ReCell technique.
Interventions	Minigrafting versus NCES.
Outcomes	Percentage repigmentation after 3,6 and 12 months Cosmetic acceptability of repigmentation.
Notes	This is an interim result on only 14 patients and so the results are not conclusive.

De la Fuente-Garcia 2014

Methods	Randomised cross-over trial
Participants	Forty-four adults with non-segmental vitiligo affecting 20% or less of the body surface area
Interventions	Topical clobetasol propionate 0.05% cream (group 1) or placebo (group 2) for 12 weeks
Outcomes	To establish the role of ACTH test before, during, and after treatment with high potency topical steroids; to determine if adrenal insufficiency occurs secondary to the use of high potency topical steroids in patients with vitiligo and intact cutaneous barrier; and also to determine response to treatment and side effects.
Notes	Conclusion: Doses of 50 g or less per week of clobetasol during a period of 12 weeks are safe on adult vitiligo patients, although local side effects are possible. Repigmentation rates were incomplete with single steroid therapy, making combined therapy a better option

De Leeuw 2011

Methods	Randomised? within-participant, controlled, blinded study.
Participants	19 participants,12 women and seven men, mean age 44 years, 25 to 68 years).

De Leeuw 2011 *(Continued)*

Interventions	Combining blister roof transplantation (BRT) with khellin in liposomes and ultraviolet light (KLUV).
Outcomes	Repigmentation, patient satisfaction, adverse effects.
Notes	Randomisation unclear, not described and only mentioned once in the text. "In each patient, two lesions were selected to be suited for BRT. Of these lesions, one was randomly chosen..." Clarificatoin sought but no response.

Ediriweera 2009

Methods	Clinical study on efficacy of the traditional Sri Lankan oil,"The Kakodumbaradi Taila" with selected ayurvedic preparations on Shvitra.
Participants	70 patients in total divided into groups of 25,10 and 35, randomisation not described or stated.
Interventions	Ayurvedic medicines vs placebo 5 were given orally and the 6th was applied topically in both groups.
Outcomes	Percentages of symptomatic relief for shvitra, ayurvedic condition which includes loss of pigment as well as other symptoms.
Notes	Study assessed outcomes which were not of interest, being part of the ayurvedic system of medicine. They actually reported on percentage of symptomatic relief based on ayurvedic criteria. In addition, author did not respond to two emails to establish proper randomisation, which we doubted due to extreme differences in numbers of participants in the 3 groups (25,10, 35).

Eleftheriadou 2014

Methods	Feasibility, double-blind, randomised, placebo-controlled, parallel group, multi-centre trial.
Participants	29 participants
Interventions	Hand-held NB-UVB phototherapy vs dummy devices for the treatment of vitiligo at home.
Outcomes	The primary outcome measure was the proportion of eligible participants who were willing to be randomised. The secondary outcomes included proportion of participants expressing interest in the trial and fulfilling eligibility criteria, withdrawal rates and missing data, proportion of participants adhering to and satisfied with the treatment, and incidence of NB-UVB short-term adverse events.
Notes	This study was not found in the standard search but as a result of a monthly PubMed update received by the lead author

Fatemi-Naeini 2014

Methods	Pilot randomised placebo-controlled trial.
Participants	23 participants with 2 symmetrical lesions each (46 lesions evaluated).
Interventions	Pseudocatalase/superoxide dismutase (PSD) as a topical gel vs placebo gel

Fatemi-Naeini 2014 *(Continued)*

Outcomes	Lesion area and degree of pigmentation were assessed at baseline and 2, 4, and 6 months later.
Notes	Conclusion: The results indicated no significant therapeutic effect for pseudocatalase/superoxide dismutase in vitiligo.

Ghorbanibirgani 2014

Methods	Randomised double blind clinical trial.
Participants	96 participants with vitiligo, from which 52 eligible patients were selected and allocated to two groups with equal size.
Interventions	*Nigella sativa* and fish oil. The study medications were applied twice a day by patients on their lesions.
Outcomes	Improvement in the lesions and adverse effects.
Notes	Conclusion: *Nigella sativa* oil and fish oil were effective in reducing the size of patient's lesions; however, *Nigella sativa* was more effective in comparison to the fish oil. Therefore, using *Nigella sativa* with the major drugs in the treatment of vitiligo is recommended. Randomisation needs to be confirmed for this study.

Gimenez-Azcarate 2013

Methods	Randomised intraindividually controlled double-blind clinical trial.
Participants	30 participants with at least one year stable vitiligo lesions.
Interventions	Autologous melanocyte seeded amniotic membrane vs melanocyte cell suspension. Three lesions randomised for each participant to receive either melanocyte cells in suspension, melanocyte cells in amniotic membrane, placebo group (no melanocyte cells) All three groups were recommended sun exposure.
Outcomes	Repigmentation.
Notes	Conclusion: transplantation of autologous melanocytes cultured using amniotic membrane superior to suspension melanocytes in the treatment of stable vitiligo.

Kalafi 2014

Methods	Randomised, double-blind, placebo-controlled, within-participant study
Participants	30 participants with two lesions of similar size on right and left sides of the body
Interventions	Topical tetracycline applied twice daily to one lesion and the other was treated with placebo twice daily. Both lesions were exposed to NB UVB two to three times a week
Outcomes	Repigmentation assessed by VASI score

Kalafi 2014 *(Continued)*

Notes	No significant improvement in repigmentation in treated lesions compared to placebo. Study found as a result of PUbMed alert received by Lead Author

Li 2010

Methods	Randomised monocentric study.
Participants	14 participants with two vitiligo lesions.
Interventions	One lesion was treated with 308-nm excimer laser and the other with 308-nm excimer light. Lesions were treated 2 or 3 times weekly with 5% to 20% increased dose on both sides.
Outcomes	Repigmentation.
Notes	The two treatments showed similar efficacy in treating vitiligo.

Martin 2007

Methods	Prospective intra-patient randomised controlled trial.
Participants	Participants had chronic stable vitiligo.
Interventions	Minigrafting (transplantation of multiple miniature full thickness punch grafts) and non-cultured epidermal suspension (using the ReCell Kit) are performed on each participant on anatomically matched sites.
Outcomes	Percentage repigmentation at 6 months. Participant assessment of cosmetic outcome.
Notes	Conclusion: Restoration of normal pigmentation is the ultimate goal of vitiligo research and management, and minigrafting and non-cultured epidermal suspension show promising clinical utility. Moreover these techniques are relatively simple and could feasibly be incorporated into routine clinical practice in an outpatient setting.

Naini 2012

Methods	Pilot randomised, double-blind, placebo-controlled trial.
Participants	23 participants with 46 symmetrical lesions.
Interventions	Pseudocatalase/superoxide dismutase (PSD) as a topical gel vs placebo gel.
Outcomes	Lesion area and degree of pigmentation were assessed at baseline, 2, 4, and 6 months.
Notes	There were no significant changes in lesion area and perifollicular pigmentation in each group (P >.05. Conclusion : The results indicated no significant therapeutic effect for PSD in vitiligo. Study claimed to be randomised but randomisation needs to be confirmed.

Nitayavardhana 2014

Methods	Single-blind randomised pilot study.
Participants	Twenty participants with symmetrical, non-acral vitiligo.
Interventions	0.1% mometasone furoate cream or 0.1% topical tacrolimus ointment twice daily for 6 months.
Outcomes	Repigmentation.
Notes	At the end of the study, there was no statistical significant difference in repigmentation. The only adverse event was telangiectasia. Conclusion: 0.1% Tacrolimus ointment and 0.1%mometasone furoate cream are effective in treatment of vitiligo; however, 0.1% tacrolimus ointment has fewer adverse effects.

Pacifico 2009

Methods	Randomised prospective study.
Participants	57 participants with generalised vitiligo.
Interventions	480 mg oral *Polypodium leucotomos* once daily plus NB UVB vs NB-UVB alone. All participants used NB-UVB twice weekly. Duration of treatment was 6 months.
Outcomes	Repigmentation.
Notes	Conclusion: *Polypodium leucotomos* added to NBUVB exposure might enhance repigmentation.

Passeron 2011

Methods	Monocentric prospective randomised trial with intraindividual comparison.
Participants	18 participants with non-segmental vitiligo with at least two symmetrical lesions of more than 4cm^2 located on bony areas and/or extremities.
Interventions	Erbium laser dermabrasion on one side(randomly assigned) After 48 hours hydrocortisone 17-butyrate cream applied daily for 12 weeks on both sides plus 2 sessions of NB UVB per week for 12 weeks.
Outcomes	At least 50% repigmentation one month after the end of treatment.
Notes	Conclusion: Laser dermabrasion improves repigmentation rate in vitiligo patients. However, side effects strongly limit its use. However, action of dermabrasion may provide future clues for treatment of vitiligo.

Phiske 2011

Methods	Randomised controlled trial.

Phiske 2011 *(Continued)*

Participants	52 cases of localised stable vitiligo.
Interventions	0.1% tacrolimus vs 1% pimecrolimus.
Outcomes	Repigmentation.
Notes	Conclusion: Tacolimus showed best results -moderate to excellent results in 39% as opposed to 8% in Pimecrolimus group. Better response in early onset cases. Maximum repigmentation on trunk (62%) in tacrolimus group and on lower extremities in Pimecrolimus group. Side effects were burning and pruritus in both groups (6% equally).

Ramaiah 2011

Methods	Multi-centre, randomised, double-blind phase IV clinical trial.
Participants	30 participants with stable non-segmental vitiligo on non sun-exposed areas.
Interventions	Nb-UVB vs NBUVB plus topical bFGF related deca peptide as a lotion. Trial duration was 3 months.
Outcomes	Repigmentation.
Notes	This trial was presented at the IPCC conference in 2011 but was conducted in 2009 in Delhi. Conclusion: the combination treatment got better results.

Rondon Lugo 1987

Methods	Randomised double-blind comparative study.
Participants	24 participants of both sexes, different age groups and variable grade of disease severity according to the extent of lesions and time evolution of the disease.
Interventions	EP-50 Melagenina P (human placenta extract) vs placebo.
Outcomes	In all participants a clinical evaluation was performed and also a study of lymphocyte subpopulations in peripheral blood was conducted. They evaluated the lymphoproliferative response to phytohemagglutinin (PHA) and Concanavalin A, at the start and at end of the study.
Notes	This very old study was of poor quality and we were unable to contact the author to get more information. We are now unable to get hold of the full paper and so cannot make a judgment about the study's suitability. No further efforts will be made to get further information although its inclusion might have contributed to the review.

Seckin 2007

Methods	Prospective, double-blind clinical study.
Participants	16 participants were enrolled in the study. In each participant, 2 lesions similar in size and time of disease were selected to be applied either 1% pimecrolimus or 0.05% clobetasol propionate twice a day.

Seckin 2007 *(Continued)*

Interventions	Topical 1% pimecrolimus vs topical 0.05% clobetasol propionate applied twice a day in a double blind randomised way.
Outcomes	Percentages of repigmentation and the adverse effects were compared at the end of the study.
Notes	-

Shah 2014

Methods	Randomised controlled study.
Participants	75 participants randomised to three groups.
Interventions	The intervention was based on a cognitive behavioural (CBT) model of social anxiety and incorporates CBT techniques presented in a leaflet form. The leaflet included psycho-education, relaxation and attentional refocusing. The cognitive behavioural self-help intervention (CBSH) had three parts: (i) psycho-education, including a description of how social anxiety is likely to be maintained in vitiligo; (ii) symptom monitoring with an emphasis on the recognition of self-focused attention and triggers of anxiety; and (iii) guided imagery based relaxation and techniques for switching attention. In the enhanced cognitive behavioural self-help condition (CBSH+) guidance was also provided on forming specific if-then plans aimed at increasing the use of the interventions. Participants in the control group did not receive any intervention for the duration of the study but received the intervention (CBSH+) after completion of the study.
Outcomes	Clinically significant reduction in social anxiety associated with vitiligo. Improvement in quality of life
Notes	This study did not measure repigmentation but measured another primary outcome, quality of life. Study found as a result of PubMed alert received by lead author.

Singh 2014

Methods	Randomised controlled study.
Participants	50 patients with actively spreading vitiligo.
Interventions	Minocycline100 mg/day (Group I - 25 patients) or OMP 2.5 mg dexamethasone on 2 consecutive days in a week (Group II - 25 patients) for 6 months.
Outcomes	Mean vitiligo disease activity score (VIDA) and mean Vitiligo Area Scoring Index (VASI) were assessed in all patients in addition to the photographic comparison before and after treatment.
Notes	Study found as a result of PubMed alert received by lead author.

Syed 2006

Methods	Randomised, double-blind, parallel groups.
Participants	Preselected participants (n = 120, 89M/31F) aged 15 to 70 years showing visible clinical signs of vitiligo.

Syed 2006 *(Continued)*

Interventions	5% polyphenone (-EGCg, epigallocatechin gallate) incorporated in a hydrophilic cream. Participants applied active cream or placebo twice a day for 8 weeks.
Outcomes	Repigmentation assessed with photographs or optical techniques at baseline and weekly thereafter.
Notes	-

Verma 2014

Methods	Randomised controlled trial.
Participants	100 patches of vitiligo in patients were randomly allocated into 2 groups to receive either of the interventions.
Interventions	The melanocytes were harvested as an autologous melanocyte rich cell suspension from a donor split thickness graft. Cultured or non-cultured melanocytes were then transplanted to the recipient area that had been superficially dermabraded.
Outcomes	An excellent response was seen in 62.17% cases with the autologous melanocyte rich cell suspension technique and in 52% with the melanocyte culture technique.
Notes	It would appear that vitiligo patches, no participants, were assessed. However, study found as a result of PubMed alert received by lead author and information taken from abstract as it was not possible to acquire full text. Therefore data incomplete.

Wu 2013

Methods	Randomised, within-participant, left/right study.
Participants	Participants with progressive and symmetric vitiligo on face or neck.
Interventions	Excimer laser therapy (10 times a month) or 0.03 % tacrolimus (twice a day topically) was randomly assigned to the bilateral patches for 3 months. Systemic betamethasone injection was administered once a month (3 times).
Outcomes	Of the 27 patients who finished the trial, 15 (55.55 %) achieved more than 75 % repigmentation and 10 (37.04 %) achieved 51%˜75 % repigmentation after 308-nm excimer laser treatment. In comparison, only 7 patients (25.93 %) achieved over 75% repigmentation and 11 (40.74%) achieved 51%˜75 % repigmentation after 0.03 % tacrolimus treatment. Slight erythema was observed in both treatment sides. Pricking, burn, or itching was also observed in tacrolimus side.
Notes	Conclusion: The combination treatment of 308-nm excimer laser and systemic betamethasone injection is effective and safe for progressive vitiligo on face and neck.

Yan 2013

Methods	Randomised, open, parallel group study.
Participants	288 participants with skin type III-IV and aged 4 to 63 years (151M/137F) with vitiligo.

Yan 2013 *(Continued)*

Interventions	308-nm excimer laser vs 311 nm NB-UVB twice a week, three days interval, 10 sessions per course (total of 3 courses) for 4 months.
Outcomes	Percentages of repigmentation were compared at the end of the study.
Notes	Characteristics of participants at baseline was not provided.

Zhang 2013

Methods	Randomised, open, parallel group study.
Participants	93 participants with generalised vitiligo and aged 7 to 60 years (48M/45F). Duration of vitiligo no longer than 10 years.
Interventions	Fire needle plus NB-UVB (3 punctures for each acupoint, seven days per session, for sessions per course for a total of 3 courses) vs. NB-UVB (two sessions per week, 3 to 4 days interval, eight sessions per course for a total of 3 courses) for 3 months.
Outcomes	Percentages of repigmentation and the adverse effects were compared at the end of the study.
Notes	-

Zhang 2014

Methods	Randomised controlled study
Participants	437 participants with stable vitiligo enrolled and randomised to four groups
Interventions	Cultured, autologous, melanocyte transplantation. Group 1 underwent 20 sessions of NB-UVB treatment before transplantation; Group 2 underwent 30 sessions of NB-UVB treatment after transplantation; Group 3 underwent 20 sessions of NB-UVB treatment before transplantation and 30 sessions after transplantation;.Group 4 underwent only transplantation.
Outcomes	Repigmentation - the effect of different modalities of narrow-band ultraviolet B (NB-UVB) therapy on the outcome of cultured autologous melanocyte transplantation in treating vitiligo.
Notes	Study found as a result of PubMed alert received by lead author.

ACTH: adrenocorticotropic hormone
bFGF: basic fibroblast growth factor
NB-UVB: narrowband ultraviolet B light
PUVA: psoralen and UVA

Characteristics of ongoing studies *[ordered by study ID]*

ACTRN12607000635460

Trial name or title	The use of melanocyte/keratinocyte co-suspension for the re-pigmentation of amelanotic patches in vitiligo
Methods	Randomised, double-blind study. The site to receive the cell suspension (A or B) is randomised by sealed envelopes produced before the commencement of the study. The randomisation will be

ACTRN12607000635460 *(Continued)*

	double-blinded to surgeon and participant, known only to the technicians preparing the treatment samples.
Participants	Target sample size: 15 Age minimum: 18 years Age maximum: 0 (no limit) Gender: both males and females **Inclusion criteria:** • Participants must have established vitiligo of any duration (an idea of the efficacy of the treatment in early, active vitiligo must be gained). • Participants must be > 18 years old and must be able and willing to provide consent to all aspects of the study following verbal and written explanation of the study by the investigating clinician. • Participants must have a leukodermic patch for study, which is outside cosmetically sensitive areas such as the face i.e. low back, medial thigh, medial arm etc. • Participants must have no documented previous reaction to local anaesthetic agents. **Exclusion criteria:** • Any contraindication to surgery/anaesthesia. • Any failure of consent process
Interventions	**A:** dermabrasion using diamond-tipped burr plus medium with keratinocyte/melanocyte cell suspension. Patch will be sited in leukodermic area. The 3 treatment areas, A, B and C will be subcutaneously infiltrated with 0.25% bupivacaine with 1:400,000 adrenaline; for local anaesthesia, participant comfort post-operatively and to ensure a bloodless bed for study dressing application. **B:** dermabrasion using diamond-tipped burr plus medium alone. Patch will be sited entirely within the leukodermic area. with medium alone. Which patch receives the cell suspension will be randomised and double-blinded. Post-dermabrasion, the test areas will be covered with individual adhesive, occlusive, transparent film dressings (TegadermTM, 3M Healthcare, St Paul, Minnesota, USA). A sterile 25 G (orange-hubbed) needle will be used to puncture the film over the dermabraded area and the treatment fluid will be injected until the dermabraded area is completely covered. Area C will be located so that the dermabraded area overlaps the edge of the patch onto normally-pigmented skin and will be treated by dermabrasion alone and similarly covered with TegadermTM. A gentle compression dressing will be applied over the whole treatment area to prevent reactive haemorrhage at the treatment sites and consequent haematoma formation under the occlusive dressings. **C:** area C will be located so that the dermabraded area overlaps the edge of the patch onto normally-pigmented skin and will be treated by dermabrasion alone - this process performed at the same surgical episode as the treatment application and assessed at the same time-points with the same outcome measures. It is a 'one-off' process. The duration of the control is until the end of the trial period.
Outcomes	Primary outcomes of the trial 1) Repigmentation - The Visual Pigmentation Scoring Scale (VPSS) will be used to assess repigmentation (see below for description of scoring scale). KP-No pigmentation (previously pigmented area) 0-No pigmentation (vitiligo area) 1-Minimal pigmentation 2-Slight pigmentation 3-Normal pigmentation 4-Slight hyperpigmentation 5-Marked hyperpigmentation KP = Koebner Phenomenon. Measurement of colour change will also be performed using a miniature fibre-optic spectrometer (StellarNet Inc., Oldsmar, 34677, USA), and supporting digital photographs will be taken at each time point using a Sony 5.2 megapixel camera with macro lens. Secondary outcomes of the trial 1) Rate of re-epithelialisation by direct clinical visualisation supported by colour digital photography.

ACTRN12607000635460 *(Continued)*

Starting date	February 2005
Contact information	Name: John Greenwood Address: Burns Unit, Royal Adelaide Hospital, North Terrace, Adelaide, SA 5000, Australia Phone number:0422 000809 Email: john.greenwood@health.sa.gov.au
Notes	Study complete.

ACTRN12610000581066

Trial name or title	A randomised controlled trial of Light Amplification by Stimulated Emission of Radiation (LASER) application and ultraviolet application on decreasing the area affected by vitiligo
Methods	Randomised, controlled, parallel study.
Participants	22 participants aged 20 to 60 years **Inclusion criteria** • vitiligo disease **Exclusion criteria** • other dermatology diseases • exposed by sun frequently • under medication
Interventions	**A:** Helium Neon LASER (HeNe) density 6j/cm2, pontual technique 1 minute and 15 s per point. The total points and session was area-dependent. It was about 15 minutes. The LASER was applied transcutaneously for 2 sessions per week, totalling 10 sessions. The patients were re-evaluated after 10 sessions. **B:** NB UVB applied twice a week, during 5 weeks, totalling 10 sessions. The dose of ultraviolet was determined by Saidman test. The duration of session was about 5 minutes.
Outcomes	Primary outcomes of the trial: Measure of area that lost pigment. A photograph machine was used to take a picture of the area and the autocad programme was used to measure the area - 1st session and 10th session.
Starting date	July 2010
Contact information	Name: Ana Carolina Brandt de Macedo Address:Aristides pereira da cruz street, 1. complement 57. Portao. CEP: 80330290. Curitiba, Parana,BRAZIL Telephone:+55 41 33297058 Email: acbrandt@bol.com.br
Notes	Study now closed but follow-up continuing.

Chictr-TRC-12002584

Trial name or title	NB-UVB plus placebo vs. NB-UVB plus lipoic acid tablets for the treatment of the sporadic treatment quiescent vitiligo: efficacy and safety of the multi-centre, randomized, double-blind, parallel-group clinical trials
Methods	Randomised parallel control study - computer-generated
Participants	500 participants in each arm of the study = 1000 aged 14 to 65 years **Inclusion criteria** • age 14 to 65 years old, inpatient or outpatient, male or female; • meet the diagnostic criteria of clinically diagnosed primary sporadic quiescent (resting stage standard, see Annex 2) patients with vitiligo; • patients volunteered to participate, required to sign an informed consent form; • leukoplakia dispersed in three or more anatomical zones, at least a maximum diameter of greater than 2 cm, with a total area of > 1% of body surface area. **Exclusion criteria** • pregnant and lactating women; • serious heart, liver, renal insufficiency; • pre-cancerous skin lesions; • systemic lupus erythematosus (SLE), dermatomyositis ultraviolet treatment contraindications; • diabetes; • with immunosuppressive therapy; • the eye, vulva, and other parts of skin lesions in patients; nearly 2 months; • received glucocorticoid NB-UVB excimer laser treatment, nearly one month to accept any treatment, at the same time to participate in other clinical trials; • secondary vitiligo (secondary to discoid lupus erythematosus, chronic eczema, vitiligo); • cannot adhere to treatment.
Interventions	**Intervention** **A:** NB-UVB plus lipoic acid tablets **Control Intervention** **B:** NB-UVB plus placebo
Outcomes	Primary outcomes of the trial 1) Lesion change
Starting date	September 2012
Contact information	name: Yun-fei Cai email: cyf_epi@163.com telephone:+86 13664124644 address: Department of Dermatology (national key department, Ministry of Education, China), The First Hospital of China Medical University, No.155, Nanjing St. Shenyang, 110001, China
Notes	Multi-centre trial

Chictr-TRC-12002593

Trial name or title	Dot matrix laser plus betamethasone compound Injection/triamcinolone acetonide plus NB-UVB vs dipropionate betamethasone cream plus NB-UVB for the treatment of the acral type (including the subcarinal parts) of vitiligo: the efficacy and safety of the multi-center, open, randomized controlled clinical trial.
Methods	Randomised parallel control - computer-generated
Participants	500 participants in each arm of the study = 1000 aged 14 to 65 years **Inclusion criteria:** • age 14 to 65 years old, inpatient or outpatient, male or female; • meet the diagnostic criteria of clinically diagnosed primary acral or sporadic in patients with acromegaly leukoplakia, or skin lesions symmetrically distributed in the sacral iliac carina parts; • patients volunteered to participate, required to sign an informed consent form; • whether or not the body with or without white spots, hands back or carina parts (such as sacral iliac sudden Long) needs with white markings and basic symmetrical on both sides at least there is a greater than 1 cm; • All cases must for the progress of patients; • regardless of previous treatment. **Exclusion criteria:** • pregnant and lactating women; • serious heart, liver, renal insufficiency; • pre-cancerous skin lesions; • systemic lupus erythematosus (SLE), dermatomyositis ultraviolet treatment contraindications; • with immunosuppressive therapy; • hand infection or past treatment caused skin damage is not significant improvement or treatment; • secondary vitiligo (secondary to discoid lupus erythematosus, chronic eczema, vitiligo); • can not adhere to treatment.
Interventions	**A:** dot matrix Laser plus compound betamethasone injection / triamcinolone acetonide injection plus NB-UVB **B:** Betamethasone cream plus NB-UVB
Outcomes	Primary outcomes of the trial 1) Lesion change
Starting date	September 2012
Contact information	Name: Yun-fei Cai Address: Department of Dermatology (national key department, Ministry of Education, China), The First Hospital of China Medical University, No.155, Nanjing St. Shenyang, 110001, China Telephone:+86 13664124644 Email: cyf_epi@163.com
Notes	Multi-centre trial

Chictr-TRC-12002594

Trial name or title	308-nm excimer laser plus betamethasone compound Injection vs. tacrolimus ointment plus betamethason compound Injection for the treatment of advanced face and neck vitiligo: efficacy and safety of the multi-center, randomized, open, parallel, self-controlled clinical trials
Methods	Randomised parallel control - computer-generated
Participants	500 participants in each arm of the study = 1000 with advanced face and neck vitiligo **Inclusion criteria:** • age 10 to 70 years old, inpatient or outpatient, male or female; • meet the diagnostic criteria of clinically diagnosed with primary advanced (advanced standards, see Annex 2); • patients with vitiligo of the face and neck; • patients volunteered to participate, required to sign an informed consent form; • leukoplakia spread in the neck of the double-side, with at least one lesions greater than 1 cm in diameter. **Exclusion criteria:** • pregnant and lactating women; • serious heart, liver, renal insufficiency; • pre-cancerous skin lesions; • systemic lupus erythematosus (SLE), dermatomyositis ultraviolet treatment contraindications; • with immunosuppressive therapy; nearly 2 months; • received corticosteroids, calcineurin inhibitors, NB-UVB excimer laser treatment, any treatment received nearly January, at the same time to participate in clinical trials; • cannot adhere to treatment; • tacrolimus sensitive; • secondary vitiligo (secondary to discoid lupus erythematosus, chronic eczema, vitiligo).
Interventions	**A:** 308-nm excimer laser plus compound betamethasone injection **B:** Tacrolimus ointment plus compound betamethasone injection
Outcomes	Primary outcomes of the trial 1) Lesion change
Starting date	September 2012
Contact information	name: Yun-fei Cai email: cyf_epi@163.com telephone:+86 13664124644 address: Department of Dermatology (national key department, Ministry of Education, China), The First Hospital of China Medical University, No.155, Nanjing St. Shenyang, 110001, China
Notes	Multi-centre trial

Chictr-TRC-12002595

Trial name or title	308-nm excimer laser vs tacrolimus ointment for the treatment of the stationary phase surface neck vitiligo: the efficacy and safety of multi-center, randomized, open, parallel, self-controlled clinical trials.
Methods	Randomised parallel control - computer-generated
Participants	500 participants in each arm of the study = 1000 **Inclusion criteria:** • age 14 to 65 years old, inpatient or outpatient, male or female; • meet the diagnostic criteria of clinically diagnosed primary quiescent face and neck vitiligo patients; • patients volunteered to participate, required to sign an informed consent form; • leukoplakia spread in the neck of the double-side, with at least one lesions greater than 1 cm in diameter; **Exclusion criteria:** • pregnant and lactating women; • serious heart, liver, renal insufficiency; • pre-cancerous skin lesions; (4), systemic lupus erythematosus (SLE), dermatomyositis ultraviolet treatment contraindications; • with immunosuppressive therapy; nearly 2 months; • received corticosteroids, calcineurin inhibitors, NB-UVB excimer laser treatment, any treatment received nearly January, at the same time to participate in clinical trials; • tacrolimus sensitive; • secondary vitiligo (such as secondary to discoid lupus erythematosus, chronic eczema, vitiligo); • cannot adhere to treatment.
Interventions	**A:** 308-nm excimer laser **B:** tacrolimus ointment
Outcomes	**Primary outcomes of the trial:** 1) Lesion change **Secondary outcomes of the trial:** Not reported
Starting date	September 2012
Contact information	Name: Yun-fei Cai Address: Department of Dermatology (national key department, Ministry of Education, China), The First Hospital of China Medical University, No.155, Nanjing St. Shenyang, 110001, China Telephone:+86 13664124644 Email: cyf_epi@163.com
Notes	Multi-centre trial

Chictr-TRC-12002596

Trial name or title	NB-UVB plus lipoic acid tablets plus compound times betamethasone injection vs. NB-UVB plus placebo plus compound betamethasone injection for the treatment of sporadic progress vitiligo: efficacy and safety of the multi-center, randomized, double-blind, parallel-group clinical trial.
Methods	Randomised, double-blind, parallel-group clinical trial.
Participants	500 participants in each arm of the study = 1000 **Inclusion criteria:** • (1) age 14 to 65 years old, inpatient or outpatient, male or female; • (2) meet the diagnostic criteria of clinically diagnosed advanced primary sporadic vitiligo patients; • (3) participants volunteered to participate, required to sign an informed consent form; • (4) leukoplakia dispersed in the three anatomical district, there is at least one greater than 2 cm, with a total area of > 1% of body surface area. **Exclusion criteria:** • (1) pregnant and lactating women; • (2) serious heart, liver, renal insufficiency; • (3) pre-cancerous skin lesions; • (4) systemic lupus erythematosus (SLE), dermatomyositis ultraviolet treatment contraindications; • (5) diabetes; • (6) with immunosuppressive therapy; nearly 2 months; • (7) received glucocorticoid NB-UVB excimer laser treatment, nearly one month to accept any treatment, at the same time to participate in other clinical trials; • (8) secondary vitiligo (such as secondary to discoid lupus erythematosus, chronic eczema, vitiligo); • (9) cannot adhere to treatment.
Interventions	**Intervention** **A:** NB-UVB plus lipoic acid tablets plus Compound times betamethasone injection **Control Intervention** **B:** NB-UVB plus placebo plus compound betamethasone injection
Outcomes	**Primary outcomes of the trial:** 1) Lesion change **Secondary outcomes of the trial:** Not reported
Starting date	September 2012
Contact information	Name: Yun-fei Cai Address: Department of Dermatology (national key department, Ministry of Education, China), The First Hospital of China Medical University, No.155, Nanjing St. Shenyang, 110001, China Telephonel:+86 13664124644 Email: cyf_epi@163.com
Notes	Multi-centre trial

CTRI/2012/03/002531

Trial name or title	Double-blind, randomized study to evaluate the ability of H-009 and Arsenic-sulphuricum-flavum in stimulating pigmentation in vitiligo and examining safety in patients
Methods	Randomised, parallel-group trial Method of generating randomisation sequence: Computer-generated randomisation. Method of allocation concealment: Pre-numbered or coded identical containers. Blinding and masking: Participant- and investigator-blinded.
Participants	108 participants **Inclusion criteria:** • Patients with focal vitiligo. Focal vitiligo: this type is characterised by one or more lesions in single area. • Patient is willing and able to give written informed consent • Vitiligo stable for 3 months, that is, there should have been no increase of spots in number or size, during last three months. • Patient having vitiligo spots, size up less than 15 cm x 15 cm. **Exclusion criteria:** • Patient having extensive vitiligo, bilateral symmetrical or having only mucocutaneous junction (such as lips, genitals, finger-tips, etc.) affection. • Any form of systemic, injectable or topical treatment (conventional, homeopathic, Ayurvedic, Cuben, phototheraphy, surgical, laser, etc.) during the last 2 months • Patients having uncontrolled or untreated under active thyroid. (To be ruled out by meauring TSH.) • Patients who are on or have consumed in last three months any anti-cancer (conventional) medication. • Women of childbearing age who had tested positive for pregnancy, or who do not use acceptable contraceptive method, or do not agree to practice reliable contraception during the study. • Current participation or participation in last 3 months period, in any clinical trial. • Any finding of clinical observation (anamnesis and physical exam) laboratory abnormality, disease (for example, liver, cardiovascular system, lung) or therapy that, in opinion of the investigator may endanger the participant or interfere with the endpoints of study.
Interventions	**A:** arsenic-sulphuricum-flavum: Homeopathy pills 30c potency for three months. Dose- 6 pills three times daily. **B:** H-009: Homeopathy pills 30c potency for three months. Dose- 6 pills three times daily.
Outcomes	**Primary outcomes of the trial:** 1) To evaluate ability of potentized preparation H-009 and Arsenic-sulphuricum-flavum in stimulating pigmentation on vitiligo patches using 30c and 50c potencies.Timepoint: Efficacy end points at week 6 and week 12 **Secondary outcomes of the trial:** 1) Percentage of pigmentation produced by the medicine on vitiligo patches. Comparative study in terms of improvement in vitiligo patches, 2) Change in vital signs 3) Laboratory evaluations (blood chemistry, haematology, urinalysis) Electrocardiogram (ECG), to examine toxic effects of the IP, if any. Timepoint: Efficacy end points at week 6 and week 12.

CTRI/2012/03/002531 *(Continued)*

Starting date	March 2012
Contact information	Name: Dr Rajesh Shah Address: Life Force Center 411 Krushal Commercial Complex, Amarmahal, Chembur, Mumbai MAHARASHTRA 400089 India Life Force Center 411 Krushal Commercial Complex, Amarmahal, Chembur, Mumbai MAHARASHTRA 400089 India 400089 Mumbai, MAHARASHTRA India Telephone: 02266888888 Email: rajesh@lifeforce.in
Notes	Title registered retrospectively

CTRI/2012/11/003157

Trial name or title	Pharmaceutical standardization of two different dosage form of Apamarg Kshara Yoga and Their clinical efficacy on Shvitra (vitiligo)
Methods	Randomised, parallel-group trial Method of generating randomisation sequence: Computer-generated randomisation. Method of allocation concealment: An Open list of random numbers. Blinding and masking: Not Applicable
Participants	30 participants **Inclusion criteria:** • Patients having signs and symptoms of Shvitra (vitiligo). • Patient between the age of 16 to 60 years. • Patients with chronicity of less than 5 years. **Exclusion criteria:** • Patients with chronicity of more than 5 years • Patients having serious cardiac, renal, hepatic diseases, major illness such as insulin-dependent diabetes mellitus (IDDM), non-insulin-dependent diabetes mellitus (NIDDM), patches due to burning, chemical exposure, • any other serious systemic illness. • Gravid and lactating women.
Interventions	**A:** Ointment of Apamargaksharyoga: Dose: QS for local application, once a day in the morning. Duration: 8 weeks Follow-up: 4weeks **B:** Lepa of Apamargaksharyoga: Dose: QS for local application, once a day in the morning. Duration: 8 weeks Follow-up: 4weeks
Outcomes	**Primary outcomes of the trial:** 1) Improvement in the signs and symptoms will be appraised on the basis of special adopted scoring pattern for scrutinising the symptomatology. The effect will be assessed on the basis of subjective and objective criteria. The score will be given on the basis of site, size, colour, numbers, and chronicity of the patches etc. Timepoint: 8weeks 2) The effect will be assessed on the basis of subjective and objective criteria after 4 weeks **Secondary outcomes of the trial:**

CTRI/2012/11/003157 *(Continued)*

	Not reported
Starting date	December.2012
Contact information	Name: Dr Galib Address: Department of RS BK I P G T and R A Gujarat ayurved university Jamnagar 361008 361008 Jamnagar, GUJARAT India Telephone: 9428315733 Email: prajapati.pradeep1@gmail.com
Notes	-

EUCTR2008-006903-22-NL

Trial name or title	Narrow band UV-B phototherapy and fluticasone proprionate versus narrow band UV-B phototherapy and placebo for the treatment of active vitiligo: a randomized double blind controlled trial - UVBVIT
Methods	Randomised, controlled, double-blind, parallel-group trial
Participants	**Inclusion criteria:** • Patients with active vitiligo, eligible for NB-UVB phototherapy; • Patients attending the outpatient department of the SNIP; • Adult patients: 18 to 64 years; • Participant is willing and able to give written informed consent. **Exclusion criteria:** • With a personal or a family history of skin cancer (non-melanoma skin cancer: first degree family members, melanoma: any family member) • With a personal history of photosensitivity and/or phototoxicity disorders • With skin type I (according to Fitzpatrick classification I-VI) • Who are pregnant • Who are taking medications known to cause photosensitivity and/or phototoxicity and chronic or very frequent use of any medication that can influence the UVB response (e.g. tetracycline, retinoids, sulphonamides, psoralens, NSAID's) • With other skin diseases that would impair evaluation of repigmentation, such as psoriasis and eczema. • Who are not able to have 2 times weekly NB-UVB phototherapy • With local immunosuppressive treatment or 6 weeks prior to enrolment. For these patients a washout period of 6 weeks will be required.
Interventions	**Intervention** **A:** Narrow band UVB phototherapy and fluticasone propionate **Control Intervention** **B:** Narrow band UVB and placebo
Outcomes	**Primary outcomes of the trial:** 1) onset and degree of repigmentation

EUCTR2008-006903-22-NL *(Continued)*

	Secondary outcomes of the trial: Not reported
Starting date	July 2009
Contact information	No information provided
Notes	No details of duration of trial or number of participants

EUCTR2010-019994-13-FR

Trial name or title	Exploratory study to evaluate the safety and efficacy of CXD07387 solution in patients with vitiligo
Methods	Randomised, single-blind, placebo-controlled trial
Participants	36 participants **Inclusion criteria:** • Male or a female participant, aged 18 to 65 years old inclusive. • Female participant should be of non-childbearing potential, i.e. female presenting with hysterectomy or bilateral ovariectomy, or having a bilateral tubal ligation, or postmenopausal female (absence of menses for at least 1 year without an alternative medical cause). • The patient has a clinical diagnosis of non-segmental (generalised) symmetrical vitiligo, with stable plaques on the trunk for more than 3 months (no change in pigmentation or size over the last 3 months for the plaque(s) to be treated). **Exclusion criteria:** • The participant has an underlying known disease, a surgical or medical condition (i.e. cardiovascular, endocrinological, psychiatric, neurological,...) that, in the opinion of the investigator might put the person at risk. • The participant has an underlying dermatological disease (i.e.: history of atopic dermatitis, eczema, psoriasis), which, in the judgment of the investigator, could interfere with the study assessments.
Interventions	Product Code: CD07387 Pharmaceutical Form: Cutaneous solution vs placebo cutaneous solution
Outcomes	**Primarty outcomes of the trial:** 1) Evaluation of the local tolerance of CD07387 solution on vitiligo skin 2) Evaluation of the systemic safety by adverse events recording, physical examination (including body weight), vital signs, ECG and laboratory safety tests **Secondary outcomes of the trial:** 1) Pharmacodynamic assessments: quantification of melanin and determination of the presence of epidermal melanocytes on zones treated by CD07387 solution vs vehicle (skin biopsies)
Starting date	September 2010
Contact information	GALDERMA R&D. No contact details given
Notes	-

IRCT138808212704N1

Trial name or title	308-nm excimer laser plus topical calcipotriol in the treatment of vitiligo
Methods	Randomised, single-blind, placebo-controlled trial
Participants	70 participants **Inclusion criteria:** • Patients that suffer from localised or generalised vitiligo at least for one year or stable vitiligo • All phenotypes of skin colour **Exclusion criteria:** • Pregnancy • Lactation • Allergy to calcipotriol • Renal insufficiency • Abnormality in bone or calcium metabolism • Light-sensitive dermatoses • Photodermatoses • Phototoxic systemic or topical medication • Previous history of arsenic exposure
Interventions	**Intervention** **A:** 308-nm excimer laser two times weekly for 12 weeks plus calcipotriol ointment (Daivonex®) twice daily **Control Intervention** **B:** 308-nm excimer laser two times weekly for 12 weeks plus Vaseline twice daily
Outcomes	**Primary outcomes of the trial:** 1) Repigmentation. Timepoint: first visit,12 weeks after starting therapy. Method of measurement: Visual scale software **Secondary outcomes of the trial:** 1) Adverse effects: irritant contact dermatitis. Timepoint: 2 times per week (in each phototherapy session). Method of measurement: clinical examination
Starting date	December 2010
Contact information	Name: Somayeh Khezri Address: Razi Hospital, Vahdat_e_eslami st. 1199663911 Tehran, Islamic Republic of Iran Telephone: 00982155609951 Email:khezri@razi.tums.ac.ir
Notes	-

IRCT138904081159N6

Trial name or title	Comparative evaluation of efficacy of dermabrasion alone, injection of melanocyte suspension and autologous melanocyte suspension transfer in the treatment of vitiligo
Methods	Randomised, controlled, parallel, unblinded trial
Participants	70 participants,both male and female **Inclusion Criteria:** • Having no treatment within past 6 months • Men or women of 11 to 60 years old • Have a diagnosis of vitiligo with depigmented patch more than 5 cm despite receiving at least 3 months active treatment • Stable vitiligo for at least 1 year • No infection at recipient site • No history of keloid and or Koebner phenomenon • No history of active hepatitis B or C, or AIDS • Not pregnant or breast-feeding • No active uncontrolled chronic systemic disease **Exclusion Criteria:** • Vitiligo patients with active or progressive disease within last 12 months.
Interventions	**A:** Dermabrasion alone: One time dermabrasion with cone-shaped head of high speed mini craft dermabrader until appearance of pinpoint bleeding in depigmented patch **B:** Injection of melanocyte suspension (only in phosphate-buffered saline (PBS)): One time 0.4 cc sub cutis injection of melanocyte suspension in phosphate-buffered saline with tenfold dilution **C:** Combined dermabrasion and melanocyte suspension in PBS: One time dermabrasion with cone-shaped head of high speed mini craft dermabrader until appearance of pinpoint bleeding in depigmented patch and one time transfer of 0.4 cc melanocyte suspension in phosphate-buffered saline with tenfold dilution **D:** Combined dermabrasion and melanocyte suspension in media: One time dermabrasion with cone-shaped head of high speed mini craft dermabrader until appearance of pinpoint bleeding in depigmented patch and 1 time transfer of 0.4 cc cell suspension in patient serum with replacement of patient serum with any dilution at the end of cell suspension preparation
Outcomes	**Primary outcomes of the trial:** 1) Pigmentation. Before intervention and 1 week, 3 weeks, 1 month and 3 months after transplantation. Observation, wood lamp, visioface software **Secondary outcomes of the trial:** Not reported
Starting date	June 2012
Contact information	Name: Fariba Jaffary Address: Skin Diseases and Leishmaniasis Research Center, Isfahan University of Medical Sciences, Sedigheh Tahereh (AS) Research Centers Complex, Khorram Ave., Isfahan, Iran Telephone: 00983113373736 00989133137166

IRCT138904081159N6 *(Continued)*

	Email: jaffary@pharm.mui.ac.ir
Notes	-

IRCT201107317160N1

Trial name or title	Evaluation of the efficacy of topical ethyl vanillate in treatment of vitiligo
Methods	Randomised, double-blind, placebo-controlled trial
Participants	25 participants **Inclusion criteria:** • Patients with bilateral generalised depigmented lesions selected among phototherapy patients **Exclusion criteria:** • Pregnant women • Children under 6 years of age • Patients with past history of skin cancer • Patients taking immunosuppressive medications
Interventions	**Intervention** **A:** Topical ethyl vanillate 20% on the lesion of one side, twice daily for 3 months. **B:** Topical Eucerin (placebo) on the other side (same place) twice daily for 3 months.
Outcomes	**Primary outcomes of the trial:** 1) Pigmentation of lesions. Timepoint: before intervention 1, 2, 3 months after intervention. Method of measurement: vitiligo area severity index scale **Secondary outcomes of the trial:** 2) Adverse effects: erythema of lesion. Timepoint: at the end of months 1, 2, 3 after intervention. Method of measurement: taking photo
Starting date	March 2012
Contact information	Name: Amir Kalafi Shotorbani Address: Dermatology clinic, Faghihi hospital, Zand street 7134844119 Shiraz, Islamic Republic of Iran, Telephone:00987112319049 Email:kalafia@sums.ac.ir , amirkalafi@yahoo.com
Notes	-

IRCT201108017160N3

Trial name or title	Evaluation of efficacy of topical tetracycline in enhancing the effect of phototherapy against vitiligo

IRCT201108017160N3 *(Continued)*

Methods	Double-blind, randomised, placebo-controlled, parallel, clinical trial
Participants	30 participants with generalised stable vitiligo aged 8 to 70 years, both male and female **Inclusion criteria:** • Patients with generalised stable vitiligo (more than 20% of body surface area) **Exclusion criteria:** • Pregnant or lactating women • Children under 8 years old
Interventions	**Intervention** **A:** Tetracycline ointment twice daily plus phototherapy 2 to 3 times weekly on one lesion **Control Intervention** **B:** Placebo (yellow Vaseline) on the other while taking phototherapy 2 to 3 times weekly. Then according to photos taken and VASI scores, lesions are evaluated.
Outcomes	**Primary outcomes of the trial:** 1) Lesion pigmentation, monthly photo and VASI score **Secondary outcomes of the trial:** 1) Adverse effects: erythema, monthly photo
Starting date	June 2013
Contact information	Name: Amir Kalafi,MD Address:Shiraz University of Medical Sciences, Faghihi hospital, Karim Khan Zand blvd, Shiraz, Fars, Islamic Republic of Iran, Telephone: 00987112319049 Email: amirkalafi@yahoo.com
Notes	Retrospective registration, recruitment complete

IRCT201201025069N5

Trial name or title	Efficacy of *Nigella sativa* oil and fish oil in vitiligo patients in Iran
Methods	Randomised, double-blind, parallel control
Participants	52 participants Age minimum: 0 Age maximum: 150 (as listed on website) Gender: Both male and female **Inclusion criteria:**

IRCT201201025069N5 *(Continued)*

	• Known case of vitiligo • Not using of *Nigella sativa* or fish oil during last 3 months • Not pregnant **Exclusion criteria:** • Pregnancy women • Using of *Nigella sativa* or fish oil during last 3 months.
Interventions	**A:** *Nigella sativa* oil, 100 g twice a day for 6 months in first intervention group Intervention 2: **B:** Fish oil, 100 g twice a day for 6 months in second intervention group.
Outcomes	**Primary outcomes of the trial:** (Presume improvement of vitiligo but not stated on form) Timepoint: before intervention and every month for sixth months. Method of measurement: Vitiligo Area Scoring Index (VASI) **Secondary outcomes of the trial:** Not reported
Starting date	June 2011
Contact information	Name: Alireza Ghorbani Birgani Address:Academic Complex (Site)-Islamic Azad University 75817 Gachsaran, Islamic Republic Of Iran Telephone:00987423334600 Email: alenc5@gmail.com
Notes	-

IRCT201203108567N1

Trial name or title	Effects of transplantation (non-cultured autologous melanocytes) in stable vitiligo plaques
Methods	Randomised, double-blind, placebo-controlled trial
Participants	10 participants **Inclusion criteria:** • At least 4 years have passed since the onset of their disease • At least 6 months of stable disease and no new lesions • The patient's lesions are bilateral symmetric • There is not an appropriate response to other therapies • There is no history of disease such as hypothyroidism, hyperthyroidism, diabetes, asthma, atopic dermatitis, rhinitis, psoriasis, ulcerative colitis, lupus, alopecia areata, pernicious anaemia • Not currently being treated with other methods **Exclusion criteria:** • Pregnant women • The incidence of these diseases (compare above in inclusion criteria)

IRCT201203108567N1 *(Continued)*

	• Parts of the body that are routinely exposed to light • "Patients who once responded to NB-UVB return is after the break" • Keloid
Interventions	**A:** "initially a small areas of the head selected by lidocaine with epinephrine anaesthetic is then using a punch 5 mm in the area occipital removed and the bulge and outer root sheet and dermal papilla may be extracted by suspension of the procurement 3 is injected into the area". Scheme used in this study: a block design capacity is 3 for each block. The patient in this study, is considered a block and a third treatment is performed on each patient. Block designs, random allocation of treatments in each block must be done. Plaque in the first two of which will be created later dermal abrasion with needle are traumatized. a - The main area where melanocytes Dermal papilla and outer Root sheet plus the Bulge area into the area.. **B:** with the other, as seen in the control and the treatment will not be around either. **C:** with the other, just insert a needle to create trauma and respond to trauma .
Outcomes	**Primary outcomes of the trial:** 1) Repigmentation. Timepoint: One month. Method of measurement: Size and photo **Secondary outcomes of the trial:** 2) Adverse effects. Timepoint: During study. Method of measurement: Observation
Starting date	March 2012
Contact information	Name: Dr. Shakoei Address: Shohada hospital shahrdari St. Tajrish Sq.198993414 Tehran, Islamic Republic of Iran Telephone: 00982122741507 Email:dr.shakoei@gmail.com
Notes	-

IRCT201205029618N1

Trial name or title	Formulation and clinical trial of a traditional dosage form for skin depigmentation and comparison to a marketed preparation in two groups of patients suffering from vitiligo.
Methods	Randomised, double-blind, placebo-controlled trial
Participants	30 participants **Inclusion criteria:** • Vitiligo patients aged from 20 to 60 years **Exclusion criteria:** • Receiving any vitiligo treatment
Interventions	**Intervention** **A:** In the Intervention group the formulation under study is used twice a day as a camouflage for 40 days

IRCT201205029618N1 *(Continued)*

	Control Intervention **B:** In the control group the marketed cosmetic product is used twice a day as a camouflage for 40 days .
Outcomes	**Primary outcomes of the trial:** 1) Quality of life of patients. Timepoint: before and after intervention in 10-day intervals to 40 days. Method of measurement: use of DLQI questionnaire **Secondary outcomes of the trial:** 1) Change of skin patches colour. Timepoint: before and after intervention in 10-day intervals to 40 days. Method of measurement: imaging and use of the software
Starting date	August.2012
Contact information	Name: Ayda Hosseinkhani Address: Akbar aabad, Shiraz School of Pharmacy, Shiraz, Islamic Republic of Iran Telephone: 00987112424255 Email: hoseinkhan@sums.ac.ir
Notes	-

IRCT201208144269N4

Trial name or title	Comparative efficacy of 0.1% tacrolimus ointment versus 0.005% Calcipotriol ointment in perifollicular pigmentation in patients with hand and facial vitiligo
Methods	Randomised, double-blind, parallel group
Participants	70 participants Age minimum: 2 years Age maximum: 85 years Gender:Both male and female **Inclusion criteria:** • Older than 2 years • Vitiligo patients in which less than 20% of the face and hands are affected • Willing to participate in the study **Exclusion criteria:** • History of herpes, dermatitis herpetiformis and any kind of active skin infections • Patients with autoimmune hepatitis • Patients with coeliac disease • Patients with immune system deficiency • Pregnant or lactating women • Patients with unknown systemic disorders • Having simultaneous skin diseases other than vitiligo, malignancies or renal disorders

IRCT201208144269N4 *(Continued)*

Interventions	**A:** Tacrolimus ointment (0.1%) manufactured by "Quality Care" which will be rubbed on the lesions once every night for one year. The weekly dosage used will be less than 100 g. **B:** Calcipotriol ointment (0.005%) with the trade name of "Daivonex" manufactured by "Quality Care" which will be rubbed on the lesions once every night for one year. The weekly dose of the ointment will be less than 100 g to avoid probable hypercalcaemia.
Outcomes	**Primary outcomes of the trial:** 1) Perifollicular pigmentation. Timepoint: At baseline and monthly for one year. Method of measurement: Photographs will be taken from the patients using a 12.1 mega pixel Cannon camera which has a lens zoom of 15*4 **Secondary outcomes of the trial:** 1) Number of the lesions. Timepoint: At baseline and monthly for one year. Method of measurement: Counting visually 2) Size of the lesions. Timepoint: At baseline and monthly for one year. Method of measurement: Evaluating the photographs taken from the lesions
Starting date	November 2012
Contact information	Name:Farideh Golfroushan Address: Golgasht Ave., Daneshgah St., Tabriz, Islamic REepublic of Iran Telephone: 00984115406612 Email:golfroushanf@tbzmed.ac.ir
Notes	-

IRCT201212059800N3

Trial name or title	Evaluation of efficacy of microdermabrasion in association with tacrolimus ointment plus elocome ointment in compare with pimecrolimus ointment plus elocome ointment in patients with vitiligo
Methods	Single-blind, randomised clinical trial
Participants	47 participants, both male and female **Inclusion criteria:** • Age range 18 to 70 years • Existence of 2 vitiligo symmetrical patches on both sides of body • Not taking local drugs from 2 weeks before the study • No photo therapy from one month before the study • Stable for 6 months prior to study **Exclusion criteria:** • Evidence of local infection at the site of testing • Evidence of spontaneous repigmentation • Abnormal liver function tests & thyroid tests • Pregnant and lactating mothers • No satisfaction to participate at any stage of the study

IRCT201212059800N3 *(Continued)*

Interventions	**Intervention** **A:** microdermabrasion combined with two topical creams (Tacrolimous plus Elocome) **Control Intervention** **B:** combination of two topical creams (Tacrolimous plus Elocome)
Outcomes	**Primary outcomes of the trial:** 1) Patient clinical healing in the weeks 0, 2, 4, 6 & 8 according to two dermatologist assessment based on digital photos of therapeutic sessions (score 0 to 4). **Secondary outcomes of the trial:** Not reported
Starting date	August 2013
Contact information	Name: Dr. Parvin Mansouri Address: Skin Ward, Imam Khomeini hospital, Kheshavarz BLV. Tehran, Islamic Republic of Iran, 1417653761 Telephone:00982166595911 00989121241636 Email: mansorip@sina.tums.ac.ir
Notes	-

ISRCTN51633881

Trial name or title	A prospective within-patient randomised controlled trial of the treatment of vitiligo with the 308-nm excimer laser: a pilot study
Methods	Not provided.
Participants	17 to 48 participants.
Interventions	308-nm laser.
Outcomes	**Primary outcomes of the trial:** 1) Repigmentation achieved with this treatment. 2) Monitoring the side effects of the treatment if any. 3) To determine if the repigmentation achieved is sustained over a duration of time. **Secondary outcomes of the trial:** Not reported
Starting date	April 2003
Contact information	Name: Dr S W Lanigan Address:

ISRCTN51633881 *(Continued)*

	Department of Dermatology City Hospital Dudley Road Biringhm B18 7QH Telephone: +44 0121 554 3801 Email: Sean.Lanigan@swbh.nhs.uk
Notes	Study complete. Anticipated end date June 2005. No information on comparator intervention/placebo provided

NCT00615355

Trial name or title	Efficacy of narrow-band UVB treatment after transplantation of harvested epidermal cells in vitiligo
Methods	Randomised, single-blind (outcomes assessor), dose comparison, single group assignment, efficacy study.
Participants	11 participants Age minimum: 18 years Age maximum: 70 years Gender: both **Inclusion Criteria:** • 11 female or male vitiligo participants between the age of 18 and 70 • Stable vitiligo for at least 1 year **Exclusion Criteria:** • Progressive disease within the last 12 months • Sporadic repigmentation of single patches within the last 12 months • Participants with contraindications for UV-treatment • Participants with anticoagulant treatment or bleeding disorders • Participants with prolonged wound healing in the history • History of hypertrophic scarring, or keloids or Koebner phenomenon • Reduced general health status • Participants with allergic reactions to local anaesthesia • Topical steroids or calcineurin inhibitors in the last 4 weeks before study entry - UV exposure in the last 4 weeks before study entry • Pregnancy or lactation
Interventions	**Intervefntion** **A:** UVB 311 nm radiation randomised to one half of the transplanted vitiligo lesion given 2 times a week for 3 months. **B:** no radiation to the other half of the transplanted lesion.
Outcomes	**Primary outcomes of the trial:** 1) Percentage of repigmentation. **Secondary outcomes of the trial** :

NCT00615355 *(Continued)*	
	2) Stability of the achieved repigmentation [Time Frame: 1 year after transplantation].
Starting date	February 2008
Contact information	Study ID: NCT00615355 Angelika Hofer Medical Univsersity of Graz, Department of Dermatology, Austria Telephone: +43/216-385 Email: angelika.hofer@meduni-graz.at
Notes	-

NCT00622180	
Trial name or title	The efficacy of hand-foot narrow-band UVB versus Focal 308-nm treatment in inducing repigmentation of vitiligo after minigrafting on the dorsal hands
Methods	Treatment, randomised, single-blind (Investigator), active control, single-group assignment, safety/efficacy study.
Participants	25 participants **Inclusion Criteria:** • Male and female participants 18 years of age or older • Skin type III-VI - vitiligo on both dorsal hands • History of stable vitiligo (no new lesions and no more than 10% enlargement of existing lesions) for 6 months with an absence of Koebner phenomenon (new lesions appearing after trauma to the skin) • Refractory to topical steroids and immunomodulators **Exclusion Criteria:** • Pregnant and/or breast-feeding females • History of skin cancer • History of taking photosensitising medications • History of recent phototherapy (light therapy) or topical medications within 1 month prior to enrolment • History of organ transplantation • History of failed vitiligo skin transplantation • History of segmental vitiligo • History of 12 or more continuous light treatments
Interventions	**A:** Daavlin Spectra UVB Hand/Foot Box **B:** Excilite Focal 308-nm light
Outcomes	**Primary outcomes of the trial:** 1) Percentage repigmentation of individual surviving grafts. 2) Percentage repigmentation of all surviving grafts per hand. 3) Percentage repigmentation of lesional skin with each light source.

NCT00622180 *(Continued)*

	Secondary outcomes of the trial: 1) Time to initial 10% repigmentation per graft. 2) Time to initial 10% repigmentation per lesion. 3) The physician global repigmentation assessment. 4) An assessment of the safety of each treatment [Time Frame: 25 weeks].
Starting date	January 2008
Contact information	Study ID: NCT00622180 Amit Pandya, M.D. UT Southwestern MedicalCenter at Dallas - Department of Dermatology
Notes	The recruitment status of this study is unknown because the information has not been verified recently.

NCT01006421

Trial name or title	Oral *Ginkgo biloba* and narrow band UVB in the treatment of vitiligo
Methods	Double-blind randomised, observational, case-control, prospective trial.
Participants	Estimated enrolment: 160 Age minimum: 12 yeats Age maximum: 65 years Gender: both males and females **Inclusion criteria:** • Any person (age 12 years and above) with non-segmental Vitiligo • Body surface area (BSA) involvement ≥ 3% **Exclusion criteria:** • Unable to give consent • Segmental vitiligo • Any topical, systemic, or phototherapy for vitiligo in the previous 2 months • Pregnancy, breast feeding • Liver or kidney disease
Interventions	**Intervention** **A:** oral *Ginkgo biloba* (2 tablets of 60 mg twice daily) with NB-UVB twice weekly. **Control Intervention** **B:** placebo tablets (identical in size, shape, and colour) to *Ginkgo biloba* twice daily with NB-UVB twice weekly. Both groups will be treated for 6 months. Standard protocol of phototherapy will be used for both groups.
Outcomes	**Primary outcomes of the trial:**

NCT01006421 *(Continued)*

	1) Repigmentation (more than 50% from baseline) [Time Frame: 3, 6, and 9 months]. **Secondary outcomes of the trial:** 1) Quality of life [Time Frame: 3,6, and 9 months].
Starting date	January 2009
Contact information	Study ID: NCT01006421 Dr Khalid Alghamdi King Saud University, University Hospital, Saudi Arabia Telephone: 4690815 Email: kmgderm@yahoo.com
Notes	-

NCT01246921

Trial name or title	Effect of fluticasone proprionate 0.05% cream on narrow band UV-B Phototherapy in active vitiligo: a randomised single-blinded controlled trial
Methods	Controlled randomised assessor-blinded study
Participants	50 participants Age minimum: 18 years Age maximum: N/A Gender: Both **Inclusion criteria:** • Non-segmental vitiligo • Eligible for NB-UVB therapy • Patients attending the outpatient department of the SNIP • Patients > 18 years • Skin type II-V • Patients with active vitiligo: progression of older lesions or development of new lesion during the last 6 months • Patient is willing and able to give written informed consent **Exclusion criteria:** • Personal or a family history of skin cancer (non-melanoma skin cancer: first-degree family members, melanoma: any family members) • Personal history of photosensitivity and/or phototoxicity disorders • Pregnancy • Taking medication known to cause photosensitivity, phototoxicity, immune suppression and chronic or very frequent use of any medication that can influence the UVB response (e.g. tetracycline, retinoids, sulfonamids, psoralens) • Other skin diseases that would impair the evaluation of repigmentation • Not able to have 2 times weekly NB-UVB phototherapy • With local immunosuppressive treatment or 6 weeks prior to enrolment. For these patients a washout period of 6 weeks will be required

NCT01246921 *(Continued)*

	• Contact-allergy for any of the parts in fluticasone propionate
Interventions	**Intervention:** **A:** Fluticasone Propionate 0.05% plus NB UVB **Control Intervention** **B:** NB UVB alone
Outcomes	**Primary outcomes of the trial:** 1) Repigmentation of the vitiligo lesions [Time Frame: 15 months] **Secondary outcomes of the trial:** 2) Patients satisfaction [Time Frame: 15 months]
Starting date	September 2009
Contact information	Name: Marie Kroon Address: Telephone:+31205666955 Email: mwkroon@gmail.com
Notes	-

NCT01262547

Trial name or title	A randomized controlled pilot study to examine the use of micrografting, using a novel grafting technique for the repigmentation of vitiligo
Methods	Phase 2 randomised, controlled, assessor-blind trial
Participants	Number of participants not stated **Inclusion criteria:** • 18 to 80 years • Have a diagnosis of stable vitiligo as defined by Vitiligo Disease Activity Score of 0 or 1 • Has 3 comparable vitiliginous areas of trunk or extremities (excluding hands) each measuring at least 3 cm × 3 cm in size, with at least 80% of depigmentation, and anticipated equal sun exposure • Have not used any topical therapy to patches or Ultraviolet light therapy for at least 2 weeks (participants may restart phototherapy at week 10 if desired) • Be able to understand the requirements of the study, the risks involved, and be able to sign the informed consent form • Agree to follow and undergo all study-related procedures **Exclusion criteria:** • Female patients who are breastfeeding, pregnant, or planning to become pregnant • Patients with a history of hypertrophic scarring or keloids and psoriasis • Participants on any dose of coumadin, warfarin, Plavix or at least 325 mg aspirin • Concurrent use of immunosuppressive medications such as oral steroids, tacrolimus and other cytotoxic reagents within 2 weeks of grafting)

NCT01262547 *(Continued)*

	• Participant who received topical therapy or UV light (phototherapy)in last 2 weeks. Patients with a positive HIV status • Patients withDiabetes Mellitus with a haemoglobin A1C of more than 8 • Participants with dermatologic conditions that may Koebnerise such as psoriasis and lichen planus • Participation in another interventional study with potential exposure to an investigational drug within past 30 days
Interventions	**A:** dermabrasion-micrografting Several small pieces of skin, each measuring 1.75 mm in diameter will be harvested from a normal pigmented area using a commercially available suction blister device. This will be attached to a sterile elastomeric substrate and then placed on a recipient area prepared by epidermal dermabrasion (removal of the epidermis). **B:** dermabrasion Only dermabrasion (removal of epidermis) alone will be done at baseline. **C:** no intervention
Outcomes	**Primary outcomes of the trial:** 1) Percentage of change in pigmentation with UV photos at 10 weeks in sites undergoing grafts compared to control sites. [Time Frame: 10 weeks] **Secondary outcomes of the trial:** 1) Clinical assessment of change in pigmentation at 24 weeks using both regular and UV light evaluations in sites undergoing grafts compared to control sites [Time Frame: 24 weeks] [Designated as safety issue: No] 2) Incidence of adverse effects, including increased activity of vitiligo [Time Frame: 24 weeks] [Designated as safety issue: Yes]
Starting date	Sept 2011
Contact information	Name: Alexandra B Kimball, MD, MPH Address: Massachusetts General Hospital
Notes	This study has been terminated.(The study sponsor was acquired by a company that focuses on chronic wounds.) Sponsor:Massachusetts General Hospital

NCT01333410

Trial name or title	Comparison of the efficacy and safety of 0.1% tacrolimus ointment with 0.1% mometasone furoatecream in the treatment of adult vitiligo: A single blinded pilot study
Methods	Randomised, assessor-blinded trial
Participants	30 participants 18+ years, male and female **Inclusion criteria:** • Patients must be above 18 years old • Patients must have symmetrical vitiligo lesion on both sides of the body. Total vitiligo area is not exceeded 5% of the body surface area

NCT01333410 *(Continued)*

	• Discontinue any previous systemic medication or phototherapy for at least 3 months and discontinue any topical medication for at least 1 month before starting the study **Exclusion criteria:** • Patients who have the lesion on acral area (hands or feet) • Pregnancy or lactating patient
Interventions	**A:** Tacrolimus ointment 2 applications per days for 6 months. Other Name: protopic **B:** Mometasone furoate 2 applications per day for 6 months. Other Name: Elomet At first visit, patients will be randomised to receive 0.1% tacrolimus ointment to apply to vitiligo lesion on one side of the body. The lesion on the other side of the body will be treated with 0.1% mometasone furoate cream. Patients are instructed to apply 0.1% tacrolimus ointment and 0.1% mometasone furoate cream twice a day for 6 months Patients will be follow up at 2, 4 and 6 months for clinical improvement, side effects and photographs
Outcomes	**Primary outcomes of the trial:** 1) percent of repigmentation [Time Frame: 6 months] [Designated as safety issue: No] Percentage of patients who get repigmentation of the lesion after 0.1% tacrolimus ointment vs 0.1% mometasone furoate cream Percentage of repigmentation is defined as following a) No improvement (0 % repigmentation) b) Improved by 1% to 25% repigmentation c) Improved by 26% to 50% repigmentation d) Improved by 51% to 75% repigmentation e) Improved by 76% to 100% repigmentation **Secondary outcomes of the trial :** 2) possible side effect from topical 0.1% tacrolimus ointment and 0.1% mometasone furoate cream
Starting date	June 2009
Contact information	Name:Chanisada Wongpraparut, M.D Address: Department of Dermatology, Faculty of Medicine Siriraj Hospital, Bangkok, Thailand
Notes	-

NCT01377077

Trial name or title	Autologous punch grafting in vitiligo patients: the effect of punch depth and punch size
Methods	Prospective, observer-blinded, randomised controlled study
Participants	35 patients ≥ 18 years with segmental or stable non-segmental vitiligo

NCT01377077 *(Continued)*

	Inclusion criteria: • Patients with non-segmental and segmental vitiligo under medical treatment at the Netherlands Institute for Pigment Disorders • Age between 18 and 60 years • Patient is willing and able to give written informed consent • Vitiligo stable since 12 months without systemic therapy or 6 months without topical therapy as defined by the absence of new lesions and/or enlargement of existing lesions • Vitiligo lesions on the extremities or trunk larger than 5 cm x 5 cm **Exclusion criteria:** • UV therapy or systemic immunosuppressive treatment during the last 12 months • Local treatment of vitiligo during the last 6 months • Vitiligo lesions with follicular or non-follicular repigmentation • Skin type 1 • Hypertrophic scars • Keloid • Cardial insufficiency • Patients with a history of hypersensitivity to (UVB) light and allergy to local anaesthesia • Patients who are pregnant or breast-feeding • Patients not competent to understand what the procedures involved • Patients with a personal history of melanoma or non-melanoma skin cancer • Patients with a first degree relative with melanoma skin cancer • Patients with atypical nevi
Interventions	**A:** epidermal 1 mm grafting epidermal skin biopsies of 1 mm diameter **B:** dermal 1 mm grafting dermal skin biopsies of 1 mm diameter **C:** dermal 1.5 mm grafting dermal skin biopsies of 1.5 mm diameter **D:** epidermal 1.5 mm grafting epidermal skin biopsies of 1.5 mm diameter
Outcomes	**Primary outcomes of the trial:** 1) Repigmentaton. Outgrowth of pigment after six months. Time Frame: at 3 and 6 months after treatment]. Objective assessment of the repigmentation 3 and 6 months after punch grafting. Assessment will be done using a ruler on a dermatoscope to measure the diameter of the growth of the punch grafts. The surface of repigmentation will be calculated. **Secondary outcomes of the trial:** 1) Visual assessment of side effects at 3 and 6 months after treatment (hyperpigmentation, hypopigmentation, scar, cobblestone effect on a scale from 0 to 3) by a blinded investigator.
Starting date	June 2011
Contact information	Name: Charlotte Vrijman, MD Address:Netherlands Institute of PIgmentary Disorders, Amsterdam, Noord-Holland, Netherlands, 1105 AZ Telephone:0031205662575 Email:c.vrijman@amc.uva.nl
Notes	-

NCT01382589

Trial name or title	A phase II randomised pilot study to compare the efficacy and safety of subcutaneous, bioresorbable afamelanotide implants and Narrow-Band Ultraviolet B (NB-UVB) light in the treatment of non-segmental vitiligo
Methods	Randomised, open-label, phase 2 study
Participants	15 participants aged 18 to 75 years **Inclusion criteria:** • Male and female participants with a confirmed diagnosis of non-segmental vitiligo with 15% to 50% of total body surface involvement • Stable or slowly progressive vitiligo over a 3-month period • Aged 18 or more • Fitzpatrick skin types III-VI • Willing and able to comply with the conditions specified in this protocol and study procedures in the opinion of the Investigator • Providing written Informed consent prior to the performance of any study-specific procedure **Exclusion criteria:** • Fitzpatrick skin types I-II • Vitiligo involving the hands and feet only • Extensive leukotrichia, in the opinion of the Investigator • Vitiligo of more than 5 years duration • Allergy to afamelanotide or the polymer contained in the implant or to lignocaine/lidocaine or other local anaesthetic to be used during the administration of the implant • Previous treatment with topical immunomodulators (corticosteroids, calcineurin inhibitors) for vitiligo within 4 weeks prior to the Screening Visit • History of photosensitivity disorders • Claustrophobia • History of photosensitive lupus • Any active and/or unstable autoimmune disease judged to be clinically significant by the Investigator • History of melanoma or lentigo maligna • History of dysplastic nevus syndrome • Any malignant skin lesions • Any skin disease that may interfere with the study evaluation • Any evidence of organ dysfunction or deviation from normal in clinical or laboratory determinations judged to be clinically significant by the Investigator • History of systemic or psychiatric disease judged to be clinically significant by the Investigator and which may interfere with the study evaluation • Female who is pregnant (confirmed by positive β-HCG pregnancy test), or lactating • Female of child-bearing potential (pre-menopausal, not surgically sterile) not using adequate contraceptive measures (i.e. oral contraceptives, diaphragm plus spermicide, intrauterine device) during the trial and for a period of three months thereafter • Sexually active man with a partner of child-bearing potential not using barrier contraception during the trial and for a period of three months thereafter • Participation in a clinical trial for an investigational agent within 30 days prior to the screening visit • Use of any prior and concomitant therapy which may interfere with the objective of the study, including drugs that cause photosensitivity or skin pigmentation within 60 days prior to the screening visit • Participants assessed as not suitable for the study in the opinion of the Investigator

NCT01382589 *(Continued)*

Interventions	**Intervention** **A:** Afamelanotide plus NB-UVB Participant in this arm will receive both afamelanotide implants (one implant administered every 28 days, 6 implants in total) and NB-UVB light (administered thrice weekly, 72 treatments in total) **Control Intervention** **B:** NB-UVB alone Participants in this arm B will receive NB-UVB light only (administered thrice weekly, 72 treatments in total)
Outcomes	**Primary outcomes of the trial:** 1) To compare the efficacy of afamelanotide implants and NB-UVB light in the treatment of non-segmental vitiligo [Time Frame: 6 months] 2) Time to onset of repigmentation of full body, face, trunk and extremities 3) Pigmentation by VASI and VETF 4) Dermatology Life Quality Index (DLQI) 5) Safety of the treatment will be assessed by: For selected study sites, immunomodulatory assessment Full body anterior and posterior photography. Vitiligo lesion photography Examination of the skin and oral mucosa and digital photography. Ophthalmologic examination **Secondary outcomes of the trial:** 1) Maintenance of pigmentation achieved [Time Frame: 6 months]
Starting date	Sept 2011
Contact information	Clinuvel Pharmaceuticals Limited
Notes	Study completed Dec 2012

NCT01419964

Trial name or title	Phase III, multicenter, randomized, double-blind, placebo-controlled parallel group study of the efficacy and safety of ACH24 in the treatment of vitiligo
Methods	Randomised, double-blind, placebo-controlled trial
Participants	94 participants **Inclusion criteria:** • Patients of both sexes, aged between 18 and 65 years, remaining the feasibility of a legal guardian in accordance with need, able to understand and provide written informed consent and able to allow compliance at the treatment and the requirements of the protocol • Presence of generalised vitiligo • Able to comprehend and willing to provide written informed consent in accordance with institutional and regulatory guidelines **Exclusion Criteria:** • Inflammatory diseases

NCT01419964 *(Continued)*

	• Alopecia areata • Diabetes Type I • Asthma • Collagen disease • Atopic dermatitis • Psoriasis • Autoimmune thyroid disease (self-reported). Thyroid problems (represents 15% of people with vitiligo), exclude only those who need to do treatment with corticosteroid or immunosuppressive • Women of childbearing age who had tested positive for pregnancy, or who do not use acceptable contraceptive method, or do not agree to practice reliable contraception during the study • Woman in pregnancy or lactation period • Known allergic reaction against the phytomedicine as assessed by medical history • Patient that is taking any prohibited medication (Item 9.3) • Participation in last one year of clinical protocols, unless it can be direct benefit to participant • Any finding of clinical observation (anamnesis and physical exam) laboratory abnormality (e.g. blood glucose, blood count), disease (for example, liver, cardiovascular system, lung) or therapy that, in opinion of the investigator, may endanger the participant or interfere with the endpoints of study.
Interventions	**Intervention** **A;** ACH24 - Standardized extract of *Stachytarpheta cayensensis Vahl* (Verbenaceae) **Control Intervention** **B:** Placebo
Outcomes	**Primary outcomes of the trial:** 1) Repigmentation of the affected area assessed by VASI (vitiligo area scoring index). [Time Frame: Baseline compared to the end of 18 months of treatment It is considered successful treatment] a repigmentation of greater than or equal to 50% of the affected area assessed by VASI (vitiligo area scoring index). **Secondary outcomes of the trial:** 1) Quality of life questionnaire [Time Frame: Baseline and each 12 weeks of treatment (V0, V3, V6, V9, V12, V15, V18)] Dermatology Life Quality Index (DLQI) 2) Safety descriptive about occurrence of adverse events, evaluation of results of general physical examination. [Time Frame: Will be evaluated during whole study, at the baseline and after 18 months of treatment.] Collection of safety data throughout the whole study period
Starting date	January 2012
Contact information	Name:Ache Laboratorios Farmaceuticos S.A, Brazil
Notes	Study not yet recruiting

NCT01430195

Trial name or title	Proof of concept study to compare efficacy and safety of subcutaneous, bioresorbable Afamelanotide implants and Narrow-Band Ultraviolet B (NB-UVB) light versus NB-UVB light alone in the treatment of nons-egmental vitiligo
Methods	Randomised, open-label, parallel-group study

NCT01430195 *(Continued)*

Participants	56 participants **Inclusion Criteria:** • Male and female participants with a confirmed diagnosis non-segmental vitiligo with 15% to 50% of total body surface involvement • Stable or slowly progressive vitiligo over a 3-month period • Aged 18 or over • Fitzpatrick skin types III-VI • Willing and able to comply with the conditions specified in this protocol and study procedures in the opinion of the Investigator • Providing written Informed Consent prior to the performance of any study-specific procedure **Exclusion Criteria:** • Fitzpatrick skin types I-II • Vitiligo involving the hands and feet only • Extensive leukotrichia, in the opinion of the Investigator • Vitiligo of more than 5 years duration • Previous treatment with NB-UVB within 6 months prior to the screening visit • Patient not responsive to previous NB-UVB treatment, defined as a patient who has undergone at least 30 NB-UVB sessions with no or minimal clinically relevant pigmentary response, in the opinion of the Investigator • Allergy to afamelanotide or the polymer contained in the implant or to lignocaine/lidocaine or other local anaesthetic to be used during the administration of the implant • Previous treatment with topical immunomodulators (corticosteroids, calcineurin inhibitors) for vitiligo within 4 weeks prior to the Screening Visit • History of photosensitivity disorders • ClaustrophobiaHistory of photosensitive lupus • Any active and/or unstable autoimmune disease judged to be clinically significant by the Investigator • History of melanoma or lentigo maligna • History of dysplastic nevus syndrome • Any malignant skin lesions • Any skin disease that may interfere with the study evaluationAny evidence of organ dysfunction or deviation from normal in clinical or laboratory determinations judged to be clinically significant by the Investigator • History of systemic or psychiatric disease judged to be clinically significant by the Investigator and which may interfere with the study evaluation • Female who is pregnant (confirmed by positive β-HCG pregnancy test), or is lactating • Female of child-bearing potential (pre-menopausal, not surgically sterile) not using adequate contraceptive measures (i.e. oral contraceptives, diaphragm plus spermicide, intrauterine device) during the trial and for a period of three months thereafter • Sexually active man with a partner of child-bearing potential not using barrier contraception during the trial and for a period of three months thereafter • Participation in a clinical trial for an investigational agent within 30 days prior to the screening visit • Use of any prior and concomitant therapy which may interfere with the objective of the study, including drugs that cause photosensitivity or skin pigmentation within 60 days prior to the screening visit • Pparticipants assessed as not suitable for the study in the opinion of the Investigator
Interventions	**Intervention** **A:** Afamelanotide plus NB-UVB:

NCT01430195 *(Continued)*

	Pparticipants in this arm will receive both afamelanotide implants (one implant administered every 28 days, 4 implants in total) and NB-UVB light (administered thrice weekly, 72 treatments in total). **Control Intervention** **B:** NB UVB only Participants in this arm will receive NB-UVB light only (administered thrice weekly, 72 treatments in total).
Outcomes	**Primary outcomes of the trial:** 1) Pigmentation of full body, face, trunk and extremities using the VASI and VETF scores. [Time Frame: 6 months] **Secondary outcomes of the trial:** 1) Time to onset of repigmentation of full body, face, trunk and extremities. [Time Frame: 6 months] 2) Quality of life using the Dermatology Life Quality Index (DLQI) 3) Vitiligo biopsies assessments (optional, selected sites only) 4) Short-term safety of both treatments: Routine laboratory assessments - Full body anterior and posterior photography - Vitiligo lesion photography - Examination of the skin and oral mucosa and digital photography - Ophthalmologic examination 5) Maintenance of pigmentation using the VASI and VETF scores [Time Frame: 12 months]
Starting date	August 2011
Contact information	Name: Henry Lim, MD Address: Henry Ford Hospital, 3031 W. Grand Blvd., Suite 800, Detroit, MI 48202, USA
Notes	This study was completed Nov 2012

NCT01478945

Trial name or title	Pilot randomised controlled trial of hand held NB-UVB for the treatment of focal or early vitiligo at home
Methods	Randomised, double-blind, parallel pilot study
Participants	29 participants of both sexes 5 years or older **Inclusion criteria:** • Participants with a diagnosis of vitiligo confirmed by dermatologist. Participants with focal disease, less than 25% of body surface area • Age: children and adults (no upper age limit). The child has to be older than 5 years old and/or mature enough to understand that the eyes must be kept closed, and to stay still for the duration of treatment • No therapy for vitiligo in the previous 2 weeks and no other vitiligo treatment during the trial other than as per trial protocol • Participants with both spreading and stable disease

NCT01478945 *(Continued)*

- Participants able to give informed consent. We will aim to treat all vitiligo lesions, however the participant (and parent/legal guardian if the participant is a child) and research nurse will agree at the beginning of the trial if there are any lesions participants would not want to be treated, such as on non-exposed sites or areas difficult to reach to treat, e.g. back

Exclusion criteria:

- Segmental vitiligo
- Universal vitiligo
- Previous history of skin cancer
- Recent or concurrent radiotherapy
- Photosensitivity
- Use of immunosuppressive or photosensitive drugs
- Pregnant or lactating women
- Any major medical co-morbidities
- Vitiligo lesions on genitalia should not be treated

Interventions	**A:** Dermfix 1000 active 311 nm NB-UVB Active hand held NB-UVB unit: Manual device administering NB-UVB **B:** Waldmann active 311 nm NB-UVB Active hand held NB-UVB unit: Manual device administering NB-UVB **C:** Sham Comparator: Dermfix 1000 placebo Manual placebo hand held NB-UVB unit
Outcomes	**Primary outcomes of the trial:** 1) Proportion of eligible participants, willing to be randomised. [Time Frame: 4 to 6 months] [Designated as safety issue: No] 2)To establish the proportion of eligible participants and their willingness to be randomised to home NB-UVB **Secondary outcomes of the trial:** 1) Number of participants accepting the initial invitation to participate [Time Frame: 4 to 6 months] 2) Proportion of participants fulfilling trial eligibility criteria 3) Proportion of participants adhering to the treatment protocol [Designated as safety issue] To establish participants' adherence in using home phototherapy 4) Proportion of participants (or their parent/legal guardian) who are satisfied with the treatment and the hand held units. [Time Frame: 4 months] To establish participants' satisfaction in using home phototherapy 5) Proportion of participants for whom the blinding of the assessor and the allocated group is maintained [Time Frame: 4 months]. To assess success of blinding of both participants and outcome assessors by using an identical placebo unit with visible light fluorescence bulb instead of NB-UVB bulb. 6) Incidence of NB-UVB short term adverse events [Time Frame: 4 months] [Designated as safety issue: Yes] To manualise the treatment intervention, i.e. prepare package educating participants in how to use the intervention and to deal with possible side effects. To establish possible short term side effects i.e. if the device is suitable for home use with limited medical supervision 7) Outcome measures for the main large trial will also be tested. These will include: repigmentation rate of vitiliginous lesions, cessation of spreading of vitiligo, impact on the quality of life of participants.

NCT01478945 *(Continued)*

	8) To define and test the primary and secondary outcome measures and the methods of data collection for the main RCT
Starting date	Feb 2012
Contact information	Name: Viktoria Eleftheriadou, MD Address: Centre of Evidence-Based Dermatology, Queens Medical Centre, Nottingham Unversity Hospitals NHS Trust, Nottingham, UK, NG7 2UH
Notes	Comparison of light devices. Study complete

NCT01511965

Trial name or title	Study of applications of autologous epidermal cells in liquid phase in the treatment of vitiligo (Viticell)
Methods	Phase 1/2 randomised, open-label study
Participants	24 participants **Inclusion criteria:** • Elderly patients at least 18 years • Participants with a stable vitiligo (no new injury or lack of expansion of existing • Lesions in the last 12 months), with at least two vitiligo lesions of at least 10 cm2 • Located in the same anatomical location, and requiring treatment with UVB • Phototherapy. • Topic with vitiligo • Participants who agreed to have a blood research with human immunodeficiency virus (HIV), human T-lymphotropic virus - 1 (HTLV-1), hepatitis B, hepatitis C, and human Chorionic Gonadotropinfor (hCG) women • For women of childbearing age, the use of effective contraception (birth control pills or Intrauterine Device (IUD)) for the duration of the study • Topics able to participate and to respect it • Topics affiliated to social security • Topics that have signed a written informed consent before the start of the study **Exclusion criteria:** • Pregnant or nursing women • Participants with a history of keloid scarring • Participants with a history of melanoma • Participants with a photodermatitis • Participants taking photosensitising treatment • Participants who received treatment for vitiligo in the 4 weeks before enrolment • Participants with HIV testing, hepatitis B or hepatitis C positive • Major Topics protected by law
Interventions	**Intervention:** **A:** autologous cellular therapy plus light therapy **Control Intervention**

NCT01511965 *(Continued)*

	B: light therapy alone
Outcomes	**Primary outcomes of the trial:** 1) Rate of repigmentation of vitiligo lesion to 12 months [Time Frame: 12 months] The lesions defined by the investigator to Month 0, Month 3, Month 6 and Month 12 will be analysed by an image analysis system managed by a PC computer. Digital photos will be taken in order to illustrate the quantitative results above. **Secondary outcomes of the trial:** 1) Repigmentation> 70% of vitiligo lesion at 6 months [Time Frame: 6 months] 2) Side effects [Time Frame: 12 months] [Designated as safety issue: No] the frequency, severity and time of occurrence of side effects will be reported for each treatment. Side effects are classified into grades according to WHO criteria. 3) Patient satisfaction and tolerance will be studied using visual analogue scales graded from 0 to 10.
Starting date	May 2011
Contact information	Name: Philippe Bahadoran, PH Address: Centre Hospitalier Universitaire de Nice Telephone: Email: bahadoran.p@chu-nice.fr
Notes	-

NCT01517893

Trial name or title	A Phase-II, randomized, placebo-controlled trial of simvastatin in generalized vitiligo
Methods	Phase 2 randomised, double blind, parallel assignment, efficacy study
Participants	50 participants (male) **Inclusion criteria:** Male gender • Age 18 to 64 years • At least one vitiligo skin lesion measuring at least 2cm x 2 cm in size • Willing and able to understand and sign informed consent • Able to complete study and comply with study procedures **Exclusion criteria:** • History of segmental vitiligo • Allergy to statin medications • Use of statin medications due to cardiac risks. • Use of any medications contraindicated with use of simvastatin • Use of topical vitiligo treatments in past 4 weeks • Use of laser or light-based vitiligo treatments within the past 8 weeks- treatment with immunomodulating oral medications in the past 4 weeks

NCT01517893 *(Continued)*

	• Use of statin medications in the past 8 weeks • Evidence of hepatic dysfunction, personal or family history of non-alcoholic steatotic hepatitis, or personal history of hepatitis • Evidence of renal dysfunction • History of myopathy or rhabdomyolysis, or elevated baseline creatinine kinase • Recent history of alcohol or drug abuse • History of diabetes • Untreated hypothyroidism • Other conditions that require the use of interfering topical or systemic therapy • Other current conditions that might interfere with study assessments such as, but not limited to, atopic dermatitis and psoriasis • Clinically significant abnormal findings or conditions which might, in the opinion of the Principal Investigator, interfere with study evaluations or pose a risk to • Participant safety during the study
Interventions	**Intervention:** **A:** Simvastatin **Control Intervention** **B:** placebo
Outcomes	**Primary outcomes of the trial:** 1) Decrease in VASI score [Time Frame: Assessed at final study visit, 6 months after randomisation] **Secondary outcomes of the trial:** 1) Correlation among various outcome measures for vitiligo [Time Frame: Assessed at final study visit, 6 months after randomisation] 2) Decrease in CXCR3 expression on CD8+ T cells [Time Frame: Assessed prior to treatment and periodically while on treatment] 3) Decrease in Sentinel patch area [Time Frame: Assessed at final study visit, 6 months after randomisation] 4) Decrease in serum chemokines [Time Frame: Assessed prior to treatment and periodically while on treatment] 5) Increase in Investigator's global assessment score [Time Frame: Assessed at final study visit, 6 months after randomisation] 6) Increase in Patient's Global Assessment Score [Time Frame: Assessed at final study visit, 6 months after randomisation] 7) Increase in Quality of Life (QoL) Score [Time Frame: Assessed at final study visit, 6 months after randomisation] 8) Safety and tolerability of high-dose simvastatin use in vitiligo patients.[Time Frame: Assessed at every visit following randomisation (monthly for 6 months)]
Starting date	January 2012
Contact information	Name: Celia Hartigan, RN, MPH Addrress: Telephone: 508-856-3676

NCT01517893 *(Continued)*

	Email: Celia.Hartigan@umassmed.edu
Notes	-

NCT01629979

Trial name or title	Efficacy and tolerance of transplantation of harvested epidermal cells and narrow-band UVB in vitiligo
Methods	Randomised, parallel, intra-individual, open label trial
Participants	23 participants **Inclusion criteria:** • Age > 18 years • Stable vitiligo (no lesion since 12 months) • 2 symmetrical vitiligo patches of at least 10 cm2 • Vitiligo requiring UVB treatment • Women using a contraceptive **Exclusion criteria:** • History of keloids • History of skin cancer • Photosensitivity • Positive blood test for HIV, HBV, HVC, or HTLV1 • Pregnant or breastfeeding women
Interventions	**Intervention:** **A:** Grafting of autologous epidermal harvested cells and NBUVB **Control Intervention:** **B:** NBUVB
Outcomes	**Primary outcomes of the trial:** 1) Repigmentation rate at 12 months [Time Frame: 12months] [Designated as safety issue: No] **Secondary outcomes of the trial:** 2) Repigmentation > 70% at 12 months
Starting date	May 2011
Contact information	Centre Hospitalier Universitaire de Nice, Nice, France 060000
Notes	Study completed Nov 2012

NCT01640678

Trial name or title	Autologous cell suspension grafting using ReCell in vitiligo and piebaldism patients: a randomized controlled pilot study

NCT01640678 *(Continued)*

Methods	Randomised, controlled, parallel,assessor blinded, pilot study
Participants	10 participants **Inclusion criteria:** • Patient with piebaldism • Patients with segmental vitiligo, stable since 12 months without systemic therapy or topical therapy as defined by the absence of new lesions and/or enlargement of existing lesions • with at least three depigmented skin lesions on the proximal extremities or trunk larger than 3 cm x 3 cm or one lesion of at least 9 x 3 cm • Age >18 years • Willing and able to give written informed consent **Exclusion criteria:** • UV therapy or systemic immunosuppressive treatment during the last 12 months • Local treatment of vitiligo during the last 12 months • Vitiligo lesions with follicular or non-follicular repigmentation • Skin type I • Recurrent HSV skin infections • Hypertrophic scars • Keloid • Cardial insufficiency • Patients with a history of hypersensitivity to (UVB or UVA) light and/or allergy to local anaesthesia. • Patients who are pregnant or breast-feeding • Patients not competent to understand the procedures involved • Patients with atypical nevi • Patients with a personal history of melanoma or non-melanoma skin cancer
Interventions	**A:** CO2 laser ablation plus ReCell epidermal cell suspension grafting plus UV therapy **B:** CO2 laser abrasion plus UV-therapy **C:** No treatment plus UV therapy
Outcomes	**Primary outcomes of the trial:** Degree of repigmentation [Time Frame: 6 months]. Objective assessment of the degree of repigmentation 6 months after autologous epidermal cell suspension grafting. Assessment will be done by standardised photographs and a digital image analysis system. **Secondary outcomes of the trial:** 1. Visual assessment of side effects per treatment region (hyper pigmentation, hypo pigmentation and scar on a scale from 0 to 3) will be done by a blinded investigator 2. General outcome assessed by the patient per treatment region on a scale from 0 to 3 (Poor, Moderate, Good, and Excellent)
Starting date	June 2012
Contact information	Name; Lisa Komen, Drs. Address:The Netherlands Institute for pigment disorders, AMC,Amsterdam, Netherlands, 1105 AZ Telepjone: 0031 20 5667792 Email: l.komen@amc.uva.nl

NCT01640678 *(Continued)*

Notes	Type of UV therapy not reported. Study also includes piebald patients

NCT01766609

Trial name or title	Efficacy and safety of intralesional corticosteroids in the treatment of vitiligo: a prospective, double-blind, randomized controlled trial
Methods	Phase 2, prospective, double-blind randomised controlled trial
Participants	18 participants **Inclusion criteria:** • Age > 18 years • Localised or generalised vitiligo that involves a non-mucosal or acral site • Patients should have a patch of at least 5 cm in the smallest diameter that shows no more than 10% repigmentation as assessed visually **Exclusion Criteria:** • Patients who received treatment for vitiligo within the past 4 weeks • Hypersensitivity to TA or vehicle • Pregnancy or breast-feeding
Interventions	**Intervention** **A:** Triamcinolone Acetonide. Injections will be given within one half of a single vitiligo patch **Control Intervention:** **B:** normal saline. Bacteriostatic normal saline will be injected into one half of the vitiligo patch.
Outcomes	**Primary outcomes of the trial:** 1) Assessment of the degree of repigmentation based on the modified VASI score for each half. We will consider the treatment successful if there was = 50% change in modified VASI score from baseline. [Time Frame: 3 to 5 weeks after each treatment session] **Secondary outcomes of the trial:** 2) Assessment of side effects in each half including atrophy, telangiectasia, hyperpigmentation and hypopigmentation using a severity scale as follows: 0 = none, 1 = mild, 2 = moderate, 3 = severe. [Time Frame: 3 to 5 weeks after each treatment session]
Starting date	Jan 2013
Contact information	Name: Mohammed AlJasser, MD FRCPC Address:The Skin Care Center, Vancouver General Hospital, Vancouver, British Columbia, Canada, V5Z 4E8 Telephone:17788595522 Email: mj_derma@hotmail.com

NCT01766609 *(Continued)*

Notes	Mention of " single group assignment" and reference to "each half" suggest this is a within individual study. although this is not specifically stated.

NCT01787695

Trial name or title	UVA 1 phototherapy for vitiligo
Methods	Prospective assessor-blind randomised clinical trial
Participants	16 participants **Inclusiion criteria:** • Age > 18 years • Localised or generalized vitiligo that involves a non-mucosal or acral site • Patients should have a patch of at least 25 cm2 that shows no more than 10% repigmentation as assessed visually **Exclusion criteria:** • Patients who received treatment for vitiligo within the past 3 weeks • Patients known to have a photosensitivity disorder • History of previous skin cancer • History of severe medical illness or immunosuppression • Pregnancy or breast-feeding
Interventions	**Intervention:** **A:** UVA1 **Control Interevention** **B:** No treatment, control area covered by foil
Outcomes	**Primary outcomes of the trial:** 1) Change in the modified VASI score compared to baseline. [Time Frame: assessments at 2, 4, 6, and 8 weeks during treatment then at 4, 8, and 12 weeks post treatment] **Secondary outcomes of the trial:** 1) Assessment of side effects in each half including erythema, pruritus, and polymorphous light eruption [Time Frame: assessments at 2, 4, 6, and 8 weeks during treatment then at 4, 8, and 12 weeks post treatment] [Designated as safety issue: Yes]
Starting date	February 2013
Contact information	Name: Mohammed I AlJasser, MD, FRCPC Address: The Skin Care Center, Vancouver General Hospital, Vancouver, British Columbia, Canada, V5Z 4E8 Telephone: 17788595522 Email: mj_derma@hotmail.com
Notes	-

NCT01787708

Trial name or title	Efficacy of red light in vitiligo: a prospective, single-blind randomized controlled trial
Methods	Prospective, single-blind randomised controlled trial
Participants	16 participants **Inclusion Criteria:** • Age > 18 years • Localised or generalised vitiligo that involves a non-mucosal or acral site • Patients should have a patch of at least 25 cm2 that shows no more than 10% repigmentation as assessed visually **Exclusion Criteria:** • Patients who received treatment for vitiligo within the past 3 weeks • Patients known to have a photosensitivity disorder • History of previous skin cancer • History of severe medical illness or immunosuppression • Pregnancy or breast-feeding
Interventions	**A:** Low intensity red laser **B:** High intensity red light **C:** No Intervention: No treatment 1 (covered) **D:** No Intervention: No treatment 2 (covered) Patients with a vitiligo patch larger than 25 cm2 will be recruited. The target patch will be divided into four quadrants. Two opposite quadrants will be shielded by foil and served as control, the third quadrant will be exposed to low intensity red laser (at 3 J/cm¬2), and the fourth quadrant will be exposed to high intensity red light (at 37 J/cm¬2). Treatments will be given twice weekly for 10 weeks. This will be followed by assessments at 4, 8, and 12 weeks post-treatment.
Outcomes	**Primary outcomes of the trial:** 1) Repigmentation change in the modified VASI score compared to baseline.[Time Frame: assessments at 2, 4, 6, 8 and 10 weeks during treatment then at 4, 8, and 12 weeks post treatment] **Secondary outcomes of the trial:** Not reported
Starting date	February 2013
Contact information	Name: Mohammed I AlJaaser, MD FRCPC Address: The Skin Care Center, Vancouver General Hospital, Vancouver, British Columbia, Canada, V5Z 4E8 Telephone:17788595522 Email: mj_derma@hotmail.com
Notes	-

NCT01841008

Trial name or title	Maintenance treatment of non segmental vitiligo with tacrolimus ointment 0.1% versus control
Methods	Randomised, parallel double-blind (participant and investigator) study
Participants	50 participants **Inclusion criteria:** • Age > 18 years • Non-segmental vitiligo repigmented more than 75% with treatment (any type of treatment is accepted: NB-UVB, PUVA, lamp or excimer laser at 308-nm, topical steroids, topical tacrolimus, graft). The total area treated plates during maintenance treatment should not exceed 10% of the total body surface area • Affiliation to the Social Security • Informed consent signed by the patient **Exclusion criteria:** • Segmental vitiligo • Pregnant or breastfeeding women (pregnancy test will be conducted); effective contraception will be maintained for the duration of the study • Allergy to macrolide derivatives • Exposure to UV or concomitant exposure to the sun without protective shield • Concomitant immunosuppressive therapy or oral corticosteroids for topical (on the vitiligo lesions) or systemic
Interventions	**Intervention** **A:** Protopic (tacrolimus ointment 0.1%) applied twice per week (3 or 4 days apart) for 24 weeks. **Control Intervention** **B:** placebo (Diprobase)
Outcomes	**Primary outcomes of the trial:** 1) To assess the efficacy of maintenance therapy with topical tacrolimus vs placebo in the prevention of depigmentation in patients with vitiligo who responded to treatment. UV and direct light photographs. [Time Frame: At 6 months] Comparison of photographs between day 0 and 24 weeks by two independent-blinded dermatologists **Secondary outcomes of the trial:** 1) Adverse effects 2) Score of depigmentation, VASI score. Frequency and severity of adverse events. [
Starting date	December.2011
Contact information	Name: Thierry Passeron, PU-PHAddress: Service de Dermatologie - Hôpital de l'Archet - 151 Route de saint-antoine de ginestière 06200 Nice, FranceTelephone: +33492039224Email:passeron.t@chu-nice.fr
Notes	-

NCT01923142

Trial name or title	Double blind within-subject controlled study of autologous hair follicle outer-root-sheath melanocytes transplantation in the treatment of vitiligo
Methods	Randomised, double-blind (participant, investigator and assessor), parallel trial
Participants	20 participants aged 18 to 60 years **Inclusion criteria:** • Presence of symmetric lesions of vitiligo at the back of the hands with an extension >5 cm^2 • Vitiligo lasting at least one year at the backs of both hands • Stable vitiligo, defined as vitiligo that presents no evident evolution (appearance of new lesions or increase in the extension of lesions already present) for at least 6 months • Suspension for at least two months prior to the enrolment date of any systemic drug for vitiligo such as immunosuppressive treatment (cyclosporine, systemic steroids) or psoralen plus ultraviolet A therapy, phototherapy with ultraviolet B, and of any anticoagulant drug • Suspension of topical medications for at least 15 days prior to the enrolment date **Exclusion criteria:** • Presence of active vitiligo or Koebner phenomenon • Difference of more than 10% in the extension of symmetrical areas of vitiligo • Presence of systemic infections or infections localizsd to the tissues intended for transplantation • History of infections to the tissues intended for transplantation (herpes simplex, human papillomavirus infections, pityriasis versicolor, pityriasis alba) • Presence or history of malignancy • Chemotherapy or radiation therapy in progress • History of allergies or adverse reactions to local anaesthetics • Presence of transmissible diseases (human immunodeficiency virus, hepatitis B and C, human T-lymphotropic virus type I and II, syphilis, cytomegalovirus, Creutzfeldt-Jacob, tuberculosis) • Women who are pregnant or intend to become pregnant during the study period (including breastfeeding women)
Interventions	**Intervention** **A:** Outer-Root-Sheath Melanocytes Suspension **Control Intervention** **B:** placebo
Outcomes	**Primary outcomes of the trial:** 1) Repigmentation equal to or greater than 50% of the treated areas from baseline as assessed by image analysis. [Time Frame: 12 weeks] **Secondary outcomes of the trial:** 1) Repigmentation of the treated areas from baseline as assessed by physician according to an ordinal 6-point scale. [Time Frame: 6 weeks, 12 weeks] 2) Any repigmentation of the treated areas from baseline as assessed by patient according to an ordinal 6-point scale. [Time Frame: 6 weeks, 12 weeks] 3) Overall patient satisfaction to the proposed therapy as assessed by visual analogue scale. [Time Frame: 6 weeks, 12 weeks] 4) Any repigmentation of the treated areas from baseline as assessed by image analysis. [Time Frame: 6 weeks, 12 weeks]

NCT01923142 *(Continued)*	5) Any repigmentation of other areas affected by vitiligo from baseline as assessed by physician according to an ordinal 6-point scale (evaluation of a possible systemic effect)
Starting date	November 2013
Contact information	Luigi Naldi, MD (Principal Investigator) Name: Simone Cazzaniga (Contact)Address:Centro Studi GISEDTelephone: +390352278719Email: simone.cazzaniga@gissed.it
Notes	-

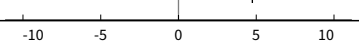
DATA AND ANALYSES

Comparison 1. TOPICAL CORTICOSTEROID: hydrocortisone 17-butyrate plus laser versus excimer laser

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Quality of life: Skindex-29	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
2 Percentage repigmentation (> 75%)	1		Risk Ratio (M-H, Random, 95% CI)	Subtotals only

Analysis 1.1. Comparison 1 TOPICAL CORTICOSTEROID: hydrocortisone 17-butyrate plus laser versus excimer laser, Outcome 1 Quality of life: Skindex-29.

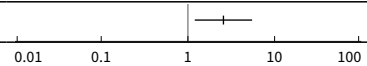
Study or subgroup	Hydrocort+laser N	Hydrocort+laser Mean(SD)	Laser N	Laser Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Sassi 2008	42	19 (14.9)	42	14.2 (14.6)		0%	4.75[-1.56,11.06]



Favours laser — Favours hydrocort+laser

Analysis 1.2. Comparison 1 TOPICAL CORTICOSTEROID: hydrocortisone 17-butyrate plus laser versus excimer laser, Outcome 2 Percentage repigmentation (> 75%).

Study or subgroup	Hydrocort+laser n/N	Laser n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Sassi 2008	18/42	7/42		0%	2.57[1.2,5.5]



Favours laser — Favours hydrocort+laser

Comparison 2. TOPICAL CORTICOSTEROID: clobetasol propionate versus 8-MOP plus sunlight

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Percentage repigmentation (> 75%)	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected

Analysis 2.1. Comparison 2 TOPICAL CORTICOSTEROID: clobetasol propionate versus 8-MOP plus sunlight, Outcome 1 Percentage repigmentation (> 75%).

Study or subgroup	Clobetasol propionate n/N	PUVAsol n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Khalid 1995	9/22	2/23		4.7[1.14,19.39]
		Favours PUVAsol	0.05 0.2 1 5 20	Favours clobetasol

Comparison 3. TOPICAL CORTICOSTEROID: mometasone furoate versus pimecrolimus

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Percentage repigmentation (>75%)	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected

Analysis 3.1. Comparison 3 TOPICAL CORTICOSTEROID: mometasone furoate versus pimecrolimus, Outcome 1 Percentage repigmentation (>75%).

Study or subgroup	Mometasone furoate n/N	Pimecrolimus n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Köse 2010	3/20	0/20		7[0.38,127.32]
		Favours pimecrolimus	0.01 0.1 1 10 100	Favours mometasone f.

Comparison 4. TOPICAL VITAMIN D ANALOGUE: tacalcitol plus sunlight versus placebo plus sunlight

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Percentage repigmentation (> 75%)	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected

Analysis 4.1. Comparison 4 TOPICAL VITAMIN D ANALOGUE: tacalcitol plus sunlight versus placebo plus sunlight, Outcome 1 Percentage repigmentation (> 75%).

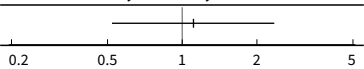
Study or subgroup	Tacalcitol plus sunlight n/N	Placebo plus sunlight n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Rodriguez-Martin 2009	0/32	1/32		0.33[0.01,7.89]

Comparison 5. TOPICAL VITAMIN D ANALOGUE: calcipotriol plus NB-UVB versus NB-UVB

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Percentage repigmentation (>75%)	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected

Analysis 5.1. Comparison 5 TOPICAL VITAMIN D ANALOGUE: calcipotriol plus NB-UVB versus NB-UVB, Outcome 1 Percentage repigmentation (>75%).

Study or subgroup	Calcipotriol + NB-UVB n/N	NB-UVB n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Arca 2006	6/13	10/24		1.11[0.52,2.35]

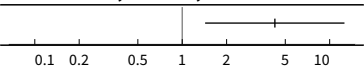


Comparison 6. TOPICAL VITAMIN D ANALOGUE: calcipotriol plus PUVA versus PUVA

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Percentage repigmentation (>75%)	1		Paired Odds Ratio (Random, 95% CI)	Totals not selected

Analysis 6.1. Comparison 6 TOPICAL VITAMIN D ANALOGUE: calcipotriol plus PUVA versus PUVA, Outcome 1 Percentage repigmentation (>75%).

Study or subgroup	Experimental N	Control N	log[Paired Odds Ratio] (SE)	Paired Odds Ratio IV, Random, 95% CI	Paired Odds Ratio IV, Random, 95% CI
Ermis 2001	0	0	1.4 (0.556)		4.25[1.43,12.64]

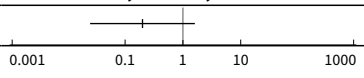


Comparison 7. TOPICAL: superoxide dismutase and catalase versus tacrolimus

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Percentage repigmentation (>75%)	1		Risk Ratio (M-H, Random, 95% CI)	Subtotals only

Analysis 7.1. Comparison 7 TOPICAL: superoxide dismutase and catalase versus tacrolimus, Outcome 1 Percentage repigmentation (>75%).

Study or subgroup	Superoxide dis+ catalase n/N	Tacrolimus n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Paracha 2010	1/30	5/30		0%	0.2[0.02,1.61]

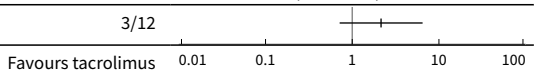


Comparison 8. TOPICAL CALCINEURIN INHIBITOR: pimecrolimus versus tacrolimus

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Percentage repigmentation (>75%)	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected

Analysis 8.1. Comparison 8 TOPICAL CALCINEURIN INHIBITOR: pimecrolimus versus tacrolimus, Outcome 1 Percentage repigmentation (>75%).

Study or subgroup	Pimecrolimus n/N	Tacrolimus n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Stinco 2009	7/13	3/12		2.15[0.72,6.48]

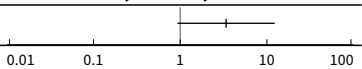


Comparison 9. TOPICAL CALCINEURIN INHIBITOR: pimecrolimus plus NB-UVB versus placebo plus NB-UVB

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Percentage repigmentation (> 75%)	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected

Analysis 9.1. Comparison 9 TOPICAL CALCINEURIN INHIBITOR: pimecrolimus plus NB-UVB versus placebo plus NB-UVB, Outcome 1 Percentage repigmentation (> 75%).

Study or subgroup	Pimecrolimus plus NB-UVB n/N	Placebo plus NB-UVB n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Esfandiarpour 2009	8/75	3/95		3.38[0.93,12.29]



Comparison 10. TOPICAL CALCINEURIN INHIBITOR: tacrolimus plus vitamin E with MEL versus vitamin E with MEL

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Percentage repigmentation (>75%)	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected

Analysis 10.1. Comparison 10 TOPICAL CALCINEURIN INHIBITOR: tacrolimus plus vitamin E with MEL versus vitamin E with MEL, Outcome 1 Percentage repigmentation (>75%).

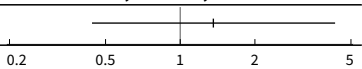
Study or subgroup	Tacrolimus n/N	Control n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Nistico 2012	6/20	5/20		1.2[0.44,3.3]

Comparison 11. ORAL: Vitamin E plus NB-UVB versus NB-UVB

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Percentage repigmentation (>75%)	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected

Analysis 11.1. Comparison 11 ORAL: Vitamin E plus NB-UVB versus NB-UVB, Outcome 1 Percentage repigmentation (>75%).

Study or subgroup	Vitamin E plus NB-UVB n/N	NB-UVB n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Elgoweini 2009	5/11	3/9		1.36[0.44,4.21]



Comparison 12. ORAL: ginkgo biloba versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Percentage repigmentation (> 75%)	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected

Analysis 12.1. Comparison 12 ORAL: ginkgo biloba versus placebo, Outcome 1 Percentage repigmentation (> 75%).

Study or subgroup	gingko n/N	placebo n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Parsad 2003b	10/25	2/22		4.4[1.08,17.95]
		Favours placebo	0.01 0.1 1 10 100	Favours ginkgo

Comparison 13. ORAL: oral minipulses of betamethasone (OMP) plus NB-UVB versus OMP

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Percentage repigmentation (> 75%)	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected

Analysis 13.1. Comparison 13 ORAL: oral minipulses of betamethasone (OMP) plus NB-UVB versus OMP, Outcome 1 Percentage repigmentation (> 75%).

Study or subgroup	OMP + NB-UVB n/N	OMP n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Rath 2008	10/27	1/20		7.41[1.03,53.26]
		Favours OMP	0.01 0.1 1 10 100	Favours OMP + NB-UVB

Comparison 14. ORAL: oral minipulses of betamethasone (OMP) plus 8-MOP plus UVA versus OMP

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Percentage repigmentation (> 75%)	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected

Analysis 14.1. Comparison 14 ORAL: oral minipulses of betamethasone (OMP) plus 8-MOP plus UVA versus OMP, Outcome 1 Percentage repigmentation (> 75%).

Study or subgroup	OMP + PUVA n/N	OMP n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Rath 2008	5/27	1/20		3.7[0.47,29.28]
		Favours OMP	0.01 0.1 1 10 100	Favours OMP + PUVA

Comparison 15. ORAL: oral minipulses of betamethasone (OMP) plus BB-UVB versus OMP

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Percentage repigmentation (> 75%)	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected

Analysis 15.1. Comparison 15 ORAL: oral minipulses of betamethasone (OMP) plus BB-UVB versus OMP, Outcome 1 Percentage repigmentation (> 75%).

Study or subgroup	OMP + BB-UVB n/N	OMP n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Rath 2008	1/12	1/20		1.67[0.11,24.26]

Favours OMP 0.01 0.1 1 10 100 Favours OMP + BB-UVB

Comparison 16. ORAL: azathioprine plus 8-MOP plus UVA versus 8-MOP plus UVA

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Percentage repigmentation (> 75%)	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected

Analysis 16.1. Comparison 16 ORAL: azathioprine plus 8-MOP plus UVA versus 8-MOP plus UVA, Outcome 1 Percentage repigmentation (> 75%).

Study or subgroup	Azathioprine plus PUVA n/N	PUVA n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Radmanesh 2006	9/30	0/28		17.77[1.08,291.82]

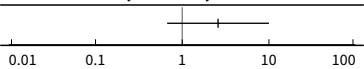
Favours PUVA 0.01 0.1 1 10 100 Favours azathioprine+PUVA

Comparison 17. ORAL: antioxidant pool (alpha lipoic acid, vitamins C and E and fatty acids) plus NB-UVB versus NB-UVB

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Percentage repigmentation (> 75%)	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected

Analysis 17.1. Comparison 17 ORAL: antioxidant pool (alpha lipoic acid, vitamins C and E and fatty acids) plus NB-UVB versus NB-UVB, Outcome 1 Percentage repigmentation (> 75%).

Study or subgroup	Antioxidant pool + NB-UVB n/N	NB-UVB n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Dell'Anna 2007	8/17	2/11		2.59[0.67,10]



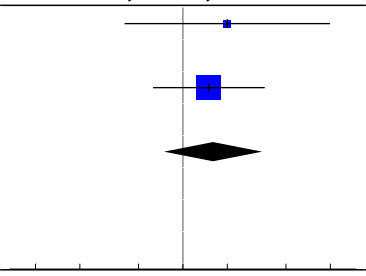
Favours NB-UVB — Favours antioxidant pool

Comparison 18. LIGHT THERAPY: NB-UVB versus Psoralen + UVA (PUVA)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Percentage repigmentation (>75%)	3	156	Risk Ratio (M-H, Random, 95% CI)	1.60 [0.74, 3.45]
2 Adverse events	3		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 Nausea	3	156	Risk Ratio (M-H, Random, 95% CI)	0.13 [0.02, 0.69]
2.2 Itching	2	106	Risk Ratio (M-H, Random, 95% CI)	0.57 [0.20, 1.60]
2.3 Erythema	2	106	Risk Ratio (M-H, Random, 95% CI)	0.73 [0.55, 0.98]

Analysis 18.1. Comparison 18 LIGHT THERAPY: NB-UVB versus Psoralen + UVA (PUVA), Outcome 1 Percentage repigmentation (>75%).

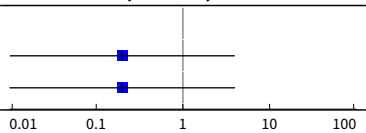
Study or subgroup	NB-UVB n/N	PUVA n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Bhatnagar 2007	4/25	2/25		22.79%	2[0.4,9.95]
Sapam 2012	0/28	0/28			Not estimable
Yones 2007	9/25	6/25		77.21%	1.5[0.63,3.59]
Total (95% CI)	**78**	**78**		**100%**	**1.6[0.74,3.45]**
Total events: 13 (NB-UVB), 8 (PUVA)					
Heterogeneity: Tau²=0; Chi²=0.1, df=1(P=0.76); I²=0%					
Test for overall effect: Z=1.21(P=0.23)					



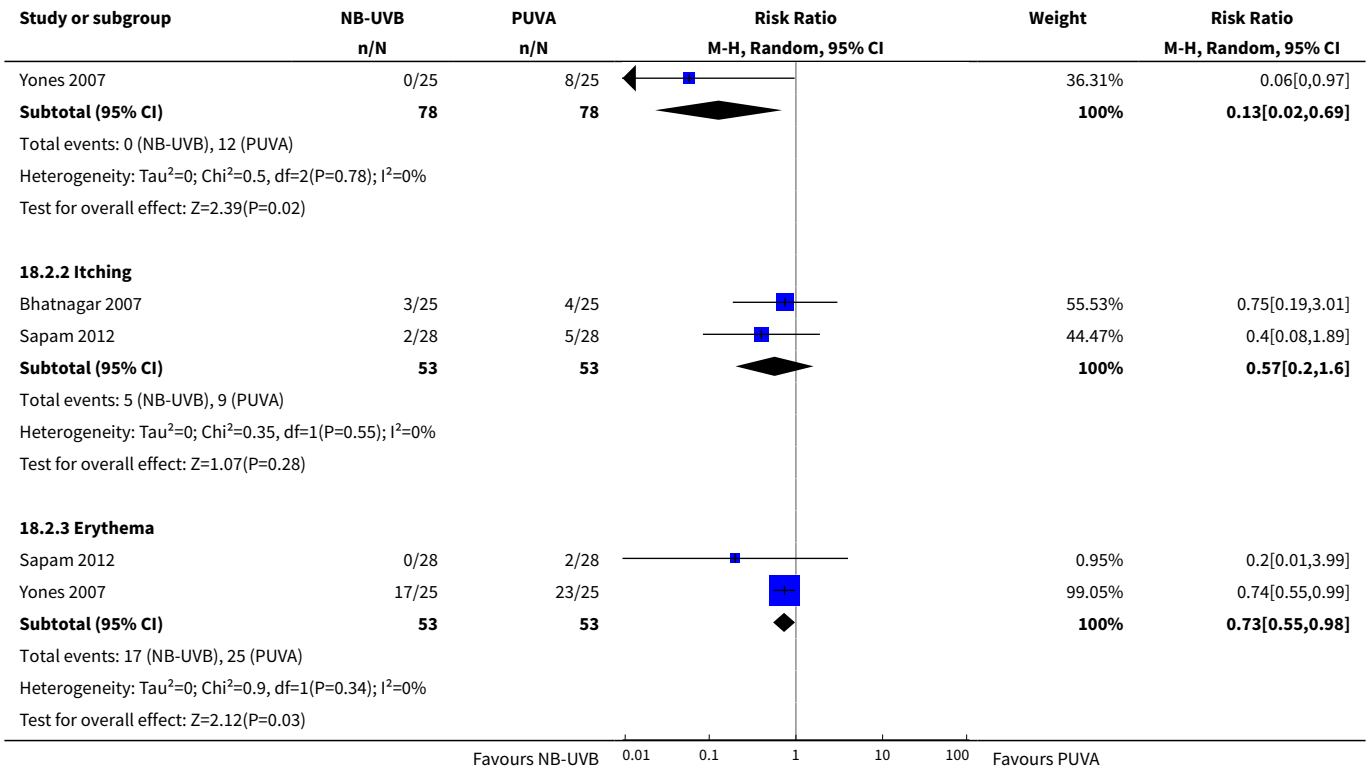
Favours PUVA — Favours NB-UVB

Analysis 18.2. Comparison 18 LIGHT THERAPY: NB-UVB versus Psoralen + UVA (PUVA), Outcome 2 Adverse events.

Study or subgroup	NB-UVB n/N	PUVA n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
18.2.1 Nausea					
Bhatnagar 2007	0/25	2/25		31.9%	0.2[0.01,3.97]
Sapam 2012	0/28	2/28		31.79%	0.2[0.01,3.99]



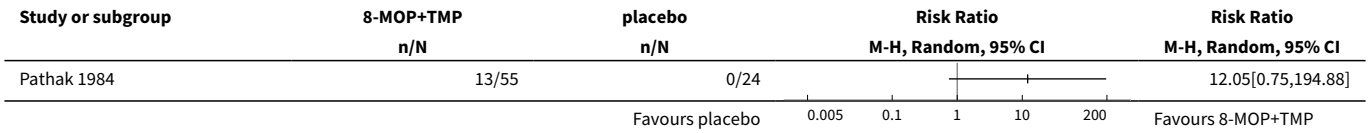
Favours NB-UVB — Favours PUVA



Comparison 19. LIGHT THERAPY: 8-MOP plus TMP plus sunlight versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Percentage repigmentation (> 75%)	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected

Analysis 19.1. Comparison 19 LIGHT THERAPY: 8-MOP plus TMP plus sunlight versus placebo, Outcome 1 Percentage repigmentation (> 75%).

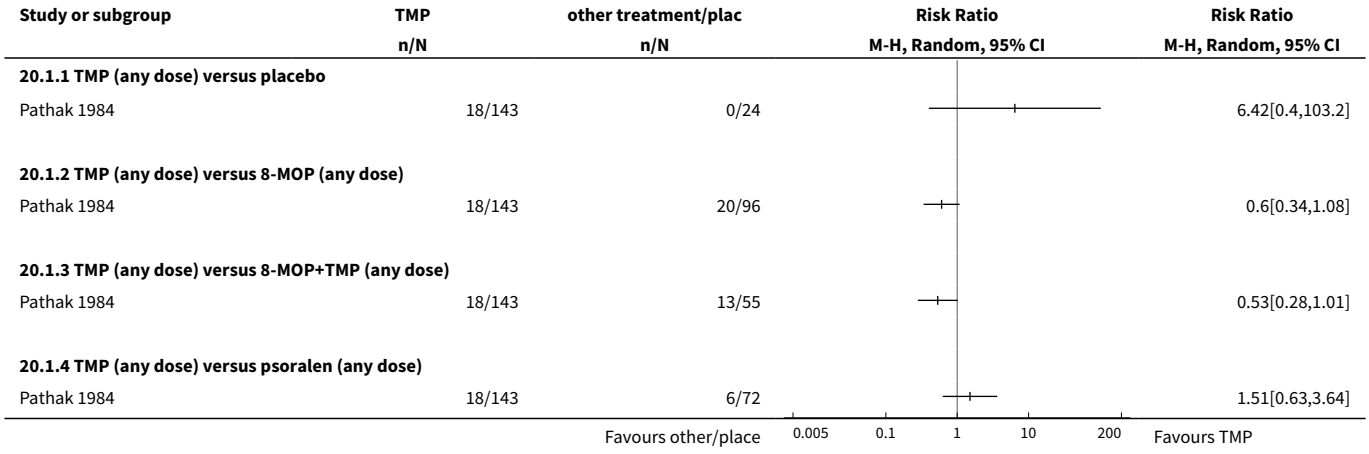


Comparison 20. LIGHT THERAPY: TMP plus sunlight versus other treatments/placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Percentage repigmentation (> 75%)	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 TMP (any dose) versus placebo	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
1.2 TMP (any dose) versus 8-MOP (any dose)	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
1.3 TMP (any dose) versus 8-MOP+TMP (any dose)	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
1.4 TMP (any dose) versus psoralen (any dose)	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]

Analysis 20.1. Comparison 20 LIGHT THERAPY: TMP plus sunlight versus other treatments/placebo, Outcome 1 Percentage repigmentation (> 75%).

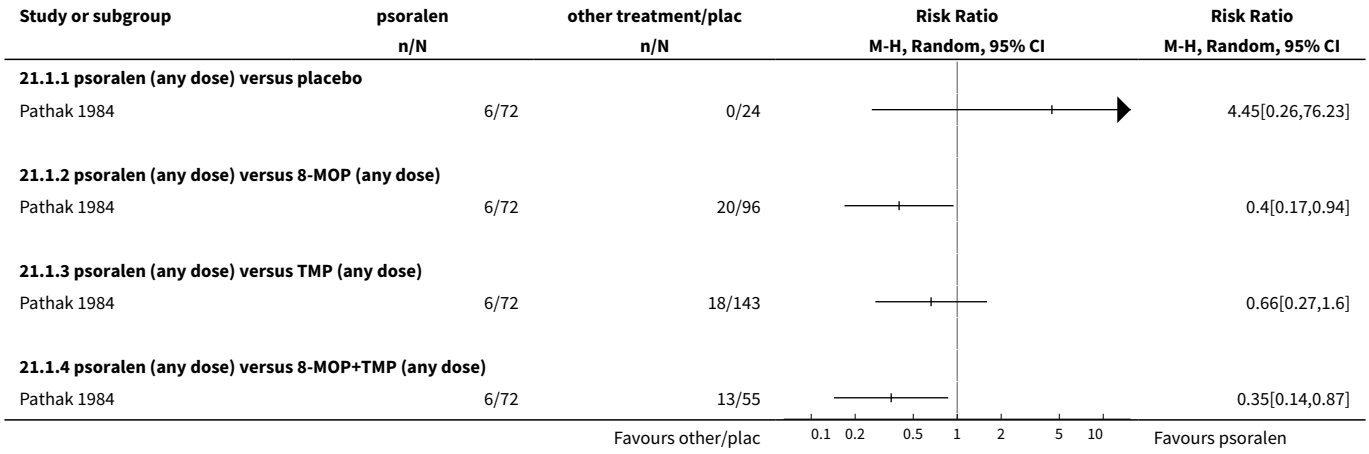


Comparison 21. LIGHT THERAPY: psoralen plus sunlight (PUVAsol) versus other treatments/placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Percentage repigmentation (> 75%)	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
1.1 psoralen (any dose) versus placebo	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
1.2 psoralen (any dose) versus 8-MOP (any dose)	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
1.3 psoralen (any dose) versus TMP (any dose)	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.4 psoralen (any dose) versus 8-MOP+TMP (any dose)	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]

Analysis 21.1. Comparison 21 LIGHT THERAPY: psoralen plus sunlight (PUVAsol) versus other treatments/placebo, Outcome 1 Percentage repigmentation (> 75%).

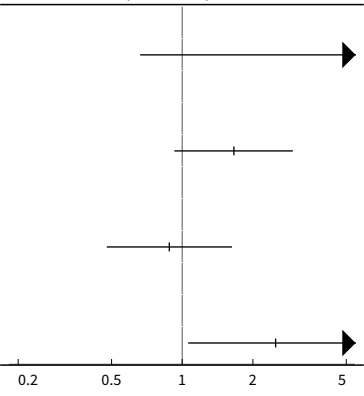


Comparison 22. LIGHT THERAPY: 8-MOP plus sunlight versus other treatments/placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Percentage repigmentation (> 75%)	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
1.1 8-MOP (any dose) versus placebo	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
1.2 8-MOP (any dose) versus TMP (any dose)	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
1.3 8-MOP (any dose) versus 8-MOP+TMP (any dose)	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
1.4 8-MOP (any dose) versus psoralen (any dose)	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]

Analysis 22.1. Comparison 22 LIGHT THERAPY: 8-MOP plus sunlight versus other treatments/placebo, Outcome 1 Percentage repigmentation (> 75%).

Study or subgroup	8-MOP n/N	other treatment/plac n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
22.1.1 8-MOP (any dose) versus placebo				
Pathak 1984	20/96	0/24		10.57[0.66,168.76]
22.1.2 8-MOP (any dose) versus TMP (any dose)				
Pathak 1984	20/96	18/143		1.66[0.92,2.96]
22.1.3 8-MOP (any dose) versus 8-MOP+TMP (any dose)				
Pathak 1984	20/96	13/55		0.88[0.48,1.63]
22.1.4 8-MOP (any dose) versus psoralen (any dose)				
Pathak 1984	20/96	6/72		2.5[1.06,5.91]

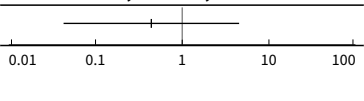


Comparison 23. ORAL: trimethylpsoralen plus sunlight/sun lamp versus placebo plus sunlight/sun lamp

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Percentage repigmentation (>75%)	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected

Analysis 23.1. Comparison 23 ORAL: trimethylpsoralen plus sunlight/sun lamp versus placebo plus sunlight/sun lamp, Outcome 1 Percentage repigmentation (>75%).

Study or subgroup	Trimethylpsoralen n/N	Placebo n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Ruiz-Maldonado 1975	1/25	2/22		0.44[0.04,4.53]

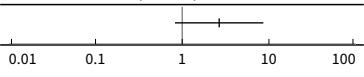


Comparison 24. LIGHT THERAPY: BB-UVA versus NB-UVB

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Percentage repigmentation (>75%)	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected

Analysis 24.1. Comparison 24 LIGHT THERAPY: BB-UVA versus NB-UVB, Outcome 1 Percentage repigmentation (>75%).

Study or subgroup	BB-UVA n/N	NB-UVB n/N	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
El Mofty 2013a	8/20	3/20		2.67[0.82,8.62]

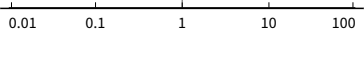


Comparison 25. SURGICAL: minipunch grafting plus 8-MOP plus sunlight versus split skin grafting plus 8-MOP plus sunlight

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Percentage repigmentation (> 75%)	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected

Analysis 25.1. Comparison 25 SURGICAL: minipunch grafting plus 8-MOP plus sunlight versus split skin grafting plus 8-MOP plus sunlight, Outcome 1 Percentage repigmentation (> 75%).

Study or subgroup	Split-skin graft+PUVAsol n/N	Minipunch+PUVAsol n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Khandpur 2005	25/30	15/34		1.89[1.25,2.85]

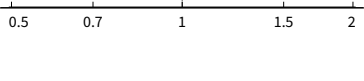


Comparison 26. SURGICAL: autologous noncultured epidermal cell suspension (NCES) versus autologous noncultured extracted hair follicle outer root sheath cell suspension (NCORSHFS)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Percentage repigmentation (>75%)	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected

Analysis 26.1. Comparison 26 SURGICAL: autologous noncultured epidermal cell suspension (NCES) versus autologous noncultured extracted hair follicle outer root sheath cell suspension (NCORSHFS), Outcome 1 Percentage repigmentation (>75%).

Study or subgroup	NCES n/N	NCORSHFS n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Singh 2013	22/24	18/23		1.17[0.92,1.5]

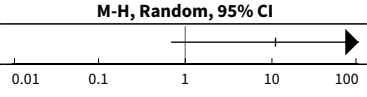


Comparison 27. SURGICAL: skin graft (1/3 the size of recipient area) versus skin graft (1/5 size)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Percentage repigmentation (> 75%)	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected

Analysis 27.1. Comparison 27 SURGICAL: skin graft (1/3 the size of recipient area) versus skin graft (1/5 size), Outcome 1 Percentage repigmentation (> 75%).

Study or subgroup	Skin graft (1/3 size) n/N	Skin graft (1/5 size) n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Tegta 2006	5/10	0/10		11[0.69,175.86]



Comparison 28. SURGICAL: melanocytes suspended in normal saline versus melanocytes suspended in patient's own serum

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Percentage repigmentation (>75%)	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected

Analysis 28.1. Comparison 28 SURGICAL: melanocytes suspended in normal saline versus melanocytes suspended in patient's own serum, Outcome 1 Percentage repigmentation (>75%).

Study or subgroup	Normal saline n/N	Patient's own serum n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Sahni 2011	12/18	17/18		0.71[0.5,1]

ADDITIONAL TABLES

Table 1. Glossary

ablation	a surgical procedure often used for acne, scars or tattoos which usually involves the use of a laser to remove the top layer of skin. In vitiligo it can be combined with topical or light treatment
acneiform papule	a small bump on the skin resembling those seen in acne, which is not a blackhead or whitehead and which does not contain pus
achromic fissuring	colourless cracks in the skin
analogue	a substance that has similar properties to, or mimics the action of, another

Table 1. Glossary *(Continued)*

atrophy	thinning (of the skin)
autologous	derived from the same individual
bullous eruptions	sudden appearance of blisters on the skin
cobblestoning	changes in skin texture that give the appearance of cobblestones
cryotherapy	treatment involving freezing of the skin
dermabrasion	surgical procedure that involves the controlled scraping away of the upper layers of the skin by using sandpaper or some other mechanical means
desquamation	peeling or shedding of the top layer of skin
Er-YAG laser	Erbium-doped yltrium-aluminium-garnet laser
erythema	redness (of the skin)
halo phenomenon	halo phenomenon, which is not the same as halo nevus, is a ring of white skin that surrounds a vitiligo patch which has been surgically treated and which persists despite repeated attempts to remove it. It should be considered as a side effect of surgery
hypertrichosis	excessive hairiness (of all or part of the body)
hyperpigmentation	increase in pigmentation (of the skin)
hypertrophic scarring	excessive scar tissue at the site of injury
intralesional	within an area of skin affected by vitiligo
koebner phenomenon/ koebnerisation	new skin lesions (including vitiligo patches) at the site of injury to the skin
lesion	area of the body which is damaged or affected by a disease process. In the case of vitiligo it is a vitiligo patch
micro-dermabrasion	a similar procedure to dermabrasion but does not need an anaesthetic as it is painless. It removes a very thin layer of the skin which can make it absorb topical preparations more easily. The procedure can be carried out by non-medically trained personnel.
milia	whiteheads, small white cysts just under the epidermis
monochromatic excimer light	a 308-nm radiation wavelength delivered in a targeted form by the xenon-chloride excimer laser and is also available in a non-laser form that is commonly referred to as the excimer lamp (MEL)
needling	a surgical procedure to insert a 30 G insulin needle at a 15 degree angle to reach the junction of the dermis (lower layer of skin) with the epidermis (top layer of skin) at several points, 1 cm apart. The underlying theory for the efficacy of the needling procedure is to introduce and push the active melanocytes (pigment producing cells), which are in the pigmented border of the vitiligo patches towards the centre of the white patches.
oedema	excessive fluid causing swelling in tissues
papule	small bump on the skin

Table 1. Glossary *(Continued)*

perilesional	occurring around a lesion (or white patch in the case of vitiligo)
phototoxicity	an adverse reaction to ultraviolet light or sunlight caused by medication or chemicals
phototype	Phototype is a method of describing the amount of melanin in the skin which relates to skin colour. It is used in determining the safe level of exposure to sunlight and other light therapy. There are 6 categories:- phototype I : burns easily, never tans phototype II : burns easily, tans with difficulty phototype III: burns moderately, tans moderately and uniformly phototype IV: tans moderately and easily phototype V: rarely burns, tans profusely phototype VI: never burns, tans profusely
pruritus	itching
striae	stretch marks
telangiectasia	thin, spidery blood vessels seen on the skin surface, sometimes called thread veins
tetrahydrocurcuminoid cream	a cream made from the colourless derivative of cucurmin, a component of the roots of the turmeric plant (cucurma longa), which is produced in a form which can be absorbed through the skin
vesicle	a small fluid-filled blister
vesiculation	formation of vesicles, blistering
xerosis	dryness (of the skin)

Table 2. Description of the Intervention

THERAPIES FOR VITILIGO	TYPES OF INTERVENTIONS	COMBINATIONS	REFERENCES FOR FURTHER INFORMATION
Topical Therapies	1. Corticosteroids 2. Intralesional corticosteroids 3. Pulsed steroids 4. Vitamin D analogues (tacalcitol, calcipotriol) 5. Calcineurin inhibitors (tacrolimus, pimecrolimus) 6. Khellin 7. Pseudocatalase 8. Other (melagenina, topical anti-oxidant gel containing pseudocatalase, superoxide, glutathione	All topical interventions can be combined with various forms of UV light. 5-FU has ben used immediately after dermabrasion and before onset of healing, followed by exposure to NB-UVB	References of included studies: (1) Westerhof 1999 (2) Vasistha 1979 (4) Rodriguez-Martin 2009 (5) Kathuria 2012 (6) Cestari 2001 (6) Procaccini 1995 (7) Bakis-Petsoglou 2009 (8) Sanclemente 2008 (8) Souto 1997

Table 2. Description of the Intervention *(Continued)*

	coenzyme Q10, carotenoids, vitamins A, E, C and selenium, plant-based topical catalase/dismutase superoxide, tetrahydrocurcuminoid cream, 5 fluorouracil (5-FU) cream)		Other references: (1) Kim 1999 (1) Kumari 1984 (1, 4, 5) Park 2012 (2)Goldstein 1992 (3) Seiter 2000
Oral Therapies	1. Oral psoralen 2. Oral levamisole 3. Polypodium Leucotomos 4. Oral *Ginkgo biloba* 5. Oral minipulse of betamethasone 6. Oral minipulse of dexamethasone 7. Oral azathioprine 8. Oral minocycline 9. Oral antioxidants including: B12, folic acid, L-phenylalanine, vitamin E, zinc sulphate	Oral psoralen is used in combination with UVA (PUVA) and sunlight and, more rarely, NB-UVB (only one study found). We assessed these with Light Therapies. Other oral therapies used with phototherapy include: *Polypodium leucotomos*, oral minipulse of betamethasone, oral azathioprine and vitamin E	References of included studies: (1) Bansal 2013 (2) Agarwal 2005 (3) Middelkamp-Hup 2007 (4) Parsad 2003b (5) Rath 2008 (7)Radmanesh 2006 (9) Dell'Anna 2007 (9) Tjioe 2002 (9) Siddiqui 1994 (9) Nistico 2012 (9) Yaghoobi 2011 Other references: (6, 8) Singh 2014
Light Therapies	1. PUVA (oral), PUVAsol (oral) 2. UVA (UVA-1,BB-UVA) 2. UVB (BB and NB) 3. Psoralen and NB-UVB 3. Laser Light devices including: excimer laser, helium neon laser 4. Non-laser monochromatic excimer light/lamp 5. Sunlight, including special light at the Dead Sea 6. Infra-red light	Both UVA and NB-UVB have been combined with oral or topical psoralen which potentiates the effect of the light. NB-UVB was combined with psoralen in one study. Excimer laser has been used in conjunction with topical therapies including corticosteroids, vitamin D analogues or tacrolimus. Helium neon laser has been combined with tacrolimus	References of included studies: (1, 2) Bhatnagar 2007 (2) El Mofty 2006a (2) El Mofty 2013a (2, 3) Wind 2011 (3) Sassi 2008 (3) de Macedo 2012 (3) Asawanonda 2008 (3) Bansal 2013 (4) Le Duff 2010 (5) Schallreuter 2002 (5) Rodriguez-Martin 2009 (6) Souto 1997 Other references:

Table 2. Description of the Intervention *(Continued)*

			(1-3) Hamzavi 2012
Surgical Therapies	1. Grafting (autologous), including punch grafts, mini-grafts, suction blister grafts, split thickness skin grafts 2. Melanocyte transplantation 3. Micropigmentation 4. Dermabrasion 5. Needling 6. ER-Yag laser 7. Fractional carbon dioxide (CO_2) laser 8. Autologous non-cultured epidermal cell suspension (NCES) 9. Autologous non-cultured extracted outer root sheath hair follicle cell suspension (NCORSHFS)	Punch grafts have been used in combination with BB-UVA, NB-UVB and PUVA ER-Yag laser and fractional CO_2 laser have been used with NB-UVB. Dermabrasion and needling have been used with NB-UVB. Transplantation NCES and NCORSHFS have been used with sunlight Cultured melanocyte transplantation combined with NB UVB was reported in a recent study	References of included studies: (1) Barman 2004 (1) Wind 2011 (1) Linthorst Homan 2012 (2) Czajkowski 2004 (4) Bayoumi 2012 (5) Mohaghegh 2012 (6) Anbar 2008 (8, 9) Singh 2013 Other references: (1, 2) Mulekar 2013 (2) Zhang 2014 (3) Francis 2013
Complementary Therapies	1. Human placental extract 2. Vitamins including vitamin E, vitamin B12, vitamin C, folic acid, L-phenylalanine 3. Indian/Chinese herbal medications (*Ginkgo Biloba*/Zengse pill) 4. Polypodium leucotomos 5. Topical lactic acid 6. Tetrahydrocurcuminoid	These treatments are often combined with light including infra-red (used with topical human placental extract), UVA, NB-UVB and sunlight.	References of included studies: (1) Souto 1997 (2) Siddiqui 1994 (2) Elgoweini 2009 (2) Dell'Anna 2007 (4) Middelkamp-Hup 2007 (5) Sharquie 2005 (6) Asawanonda 2010 Other references: (2-4) Szczurko 2008
Psychological Therapies	Cognitive behavioural therapy Patient-centred therapy	No combinations	References of included studies: Papadopoulos 2004

In the table some interventions may be found in more than one category e.g. tetrahydrocurcuminoid cream in Topical and Complementary; *Ginkgo biloba* in Oral and Complementary. Similarly, some references may appear in more than one category. The column of references are to point the reader to more information on the interventions and includes some of the studies included in the review. See also the Glossary (Table 1)

Table 3. Types of Interventions assessed in Included Studies

Study ID	Topical	Light	Oral	Surgical	Complementary
N=95*	N = 52	N = 65	N = 20	N =18	N = 8

Table 3. Types of Interventions assessed in Included Studies *(Continued)*

Agarwal 2005	Yes	No	Yes	No	No
Akdeniz 2013	Yes	Yes	No	No	No
Akhyani 2005	Yes	Yes	No	No	No
Anbar 2008	Yes	Yes	No	No	No
Arca 2006	Yes	Yes	No	No	No
Asawanonda 2008	No	Yes	No	No	No
Asawanonda 2010	Yes	Yes	No	No	Yes
Bakis-Petsoglou 2009	Yes	Yes	No	No	Yes
Bansal 2013	No	Yes	No	No	No
Barman 2004	Yes	Yes	No	Yes	No
Bayoumi 2012	Yes	Yes	No	Yes	No
Bhatnagar 2007	No	Yes	No	No	No
Budania 2012	No	Yes	No	Yes	No
Casacci 2007	No	Yes	No	No	No
Cestari 2001	Yes	Yes	No	No	No
Czajkowski 2004	No	Yes	No	Yes	No
Dawid 2006	Yes	No	No	No	No
de Macedo 2012	No	Yes	No	No	No
Dell'Anna 2007	No	Yes	Yes	No	Yes
El Mofty 2006a	No	Yes	No	No	No
El Mofty 2013a	No	Yes	No	No	No
El Mofty 2013b	No	Yes	No	No	No
Elgoweini 2009	No	Yes	Yes	No	Yes
El-Zawahry 2012	No	Yes	No	No	No
Ermis 2001	Yes	Yes	No	No	No
Esfandiarpour 2009	Yes	Yes	No	No	No
Farah 1967	No	No	Yes	No	No
Farajzadeh 2009	Yes	No	No	Yes	No

Table 3. Types of Interventions assessed in Included Studies *(Continued)*

Galarza 2009	Yes	No	No	No	Yes
Ghosh 2012	No	No	No	Yes	No
Goldinger 2007	Yes	Yes	No	No	No
Hamzavi 2004	No	Yes	No	No	No
Ho 2011	Yes	No	No	No	No
Hofer 2005	No	Yes	No	No	No
Hui-Lan 2009	Yes	Yes	No	No	No
Kandil 1974	Yes	No	No	No	No
Kathuria 2012	Yes	No	No	No	No
Kawalek 2004	Yes	Yes	No	No	No
Khalid 1995	Yes	Yes	No	No	No
Khandpur 2005	No	Yes	No	Yes	No
Klahan 2009	Yes	Yes	No	No	No
Köse 2010	Yes	No	No	No	No
Kumaran 2006	Yes	No	No	No	No
Le Duff 2010	No	Yes	No	No	No
Leone 2006	Yes	Yes	No	No	No
Lepe 2003	Yes	No	No	No	No
Lim-Ong 2005	Yes	Yes	No	No	No
Linthorst Homan 2012	No	Yes	No	Yes	No
Lu-Yan 2006	Yes	Yes	No	No	No
Mehrabi 2006	Yes	Yes	No	No	No
Middelkamp-Hup 2007	No	No	Yes	No	Yes
Mohaghegh 2012	No	Yes	No	Yes	No
Navarro 2002	No	No	Yes	Yes	No
Nistico 2012	Yes	Yes	Yes	No	No
Nordal 2011	Yes	Yes	No	No	No
Oh 2011	Yes	Yes	No	No	No

Table 3. Types of Interventions assessed in Included Studies *(Continued)*

Ozdemir 2002	No	No	No	Yes	No
Paracha 2010	Yes	No	No	No	No
Parsad 1998	Yes	No	Yes	No	No
Parsad 2003b	No	No	Yes	No	No
Passeron 2004	Yes	Yes	No	No	No
Pathak 1984	No	Yes	Yes	No	No
Procaccini 1995	Yes	Yes	No	No	No
Radakovic 2009	Yes	No	No	No	No
Radmanesh 2006	No	Yes	Yes	No	No
Rath 2008	No	Yes	Yes	No	No
Reyes 2006	No	Yes	Yes	No	No
Rodriguez-Martin 2009	Yes	Yes	No	No	No
Rojas-Urdaneta 2007	Yes	No	No	No	No
Ruiz-Maldonado 1975	No	Yes	Yes	No	No
Sahni 2011	No	No	No	Yes	No
Sanclemente 2008	Yes	No	No	No	No
Sapam 2012	No	Yes	Yes	No	No
Sassi 2008	Yes	Yes	No	No	No
Satyanarayan 2013	Yes	Yes	No	No	No
Schallreuter 2002	Yes	Yes	No	No	No
Sharquie 2005	Yes	Yes	No	No	No
Sheth 2012	No	Yes	No	Yes	No
Shi 2008	Yes	No	Yes	No	No
Shi 2013	No	Yes	No	No	No
Shin 2012	No	Yes	No	Yes	No
Siddiqui 1994	No	Yes	Yes	No	Yes
Singh 2013	No	No	No	Yes	No
Souto 1997	Yes	No	No	No	Yes

Table 3. Types of Interventions assessed in Included Studies *(Continued)*

Stinco 2009	Yes	Yes	No	No	No
Tegta 2006	No	No	No	Yes	No
Tjioe 2002	No	Yes	Yes	No	No
Van Geel 2004	No	No	No	Yes	No
Vasistha 1979	Yes	No	No	No	No
Verhaeghe 2011	No	Yes	No	No	No
Wazir 2010	Yes	No	No	No	No
Westerhof 1999	Yes	Yes	No	No	No
Wind 2011	No	Yes	No	Yes	No
Yaghoobi 2011	Yes	No	Yes	No	No
Yones 2007	No	Yes	Yes	No	No

N = 95 represents the number of studies in this table
*Papadopoulos 2004 is not included as it was the only study assessing psychological interventions, therefore, we did not include another column in this table due to space restrictions. Details of the study can be found in the 'Psychological Therapies' section of the review.

Table 4. Outcomes assessed in Included Studies

Study ID **N = 96**	**Primary outcomes**			**Secondary outcomes**
	QoL **N = 9**	**Percentage repigmentation >75%** **N = 53**	**Adverse effects** **N = 65**	**Cessation of spread of vitiligo** **N = 6**
Agarwal 2005	Yes	No	Yes	Yes
Akdeniz 2013	Yes	Yes (≥75%)	No	No
Akhyani 2005	No	No	No	No
Anbar 2008	No	Yes (>75%)	Yes	No
Arca 2006	No	No	Yes	No
Asawanonda 2008	No	Yes (76% to 100%)	No	No
Asawanonda 2010	No	Yes (76% to100%)	Yes	No
Bakis-Petsoglou 2009	No	No	No	No
Bansal 2013	No	No	Yes	No

Table 4. Outcomes assessed in Included Studies *(Continued)*

Barman 2004	No	No	Yes	Yes
Bayoumi 2012	No	Yes (≥75%)	Yes	No
Bhatnagar 2007	No	Yes (>75%)	No	No
Budania 2012	Yes	Yes (75% to 89%)	Yes	No
Casacci 2007	No	Yes (76% to 100%)	Yes	No
Cestari 2001	No	No	No	No
Czajkowski 2004	No	No	No	No
Dawid 2006	No	No	No	Yes
de Macedo 2012	No	No	No	No
Dell'Anna 2007	No	Yes (>75%)	No	No
El Mofty 2006a	No	No	No	No
El Mofty 2013a	No	Yes (>75%)	Yes	No
El Mofty 2013b	No	No (60% to 80%; >80%)	Yes	No
Elgoweini 2009	No	Yes (>75%)	Yes	No
El-Zawahry 2012	No	No (60% to 80%)	Yes	No
Ermis 2001	No	Yes (75% to 100%)	No	No
Esfandiarpour 2009	No	Yes (>75%)	Yes	No
Farah 1967	No	No	No	No
Farajzadeh 2009	No	Yes (75% to 99%)	Yes	No
Galarza 2009	No	No	Yes	No
Ghosh 2012	No	No	Yes	No
Goldinger 2007	No	No	No	No
Hamzavi 2004	No	Yes (76% to 99%)	Yes	No
Ho 2011	No	No	Yes	No
Hofer 2005	No	Yes (76% to 100%)	Yes	No
Hui-Lan 2009	No	Yes (≥75%)	Yes	No
Kandil 1974	No	No	Yes	No
Kathuria 2012	No	Yes (76% to 99%)	Yes	No

Table 4. Outcomes assessed in Included Studies *(Continued)*

Kawalek 2004	No	Yes (75%)	Yes	No
Khalid 1995	No	Yes (>75%)	Yes	No
Khandpur 2005	No	Yes (76% to 90%)	Yes	No
Klahan 2009	No	Yes (76% to 100%)	Yes	No
Köse 2010	No	Yes (>75%)	Yes	No
Kumaran 2006	No	Yes (>75%)	Yes	No
Le Duff 2010	No	Yes (76% to 100%)	Yes	No
Leone 2006	No	No	No	No
Lepe 2003	No	Yes (>75%)	Yes	No
Lim-Ong 2005	No	Yes (>75%)	Yes	Yes
Linthorst Homan 2012	No	Yes (>75%)	No	No
Lu-Yan 2006	No	Yes (75% to 100%)	Yes	No
Mehrabi 2006	No	No	Yes	No
Middelkamp-Hup 2007	Yes	No	Yes	No
Mohaghegh 2012	No	No	Yes	No
Navarro 2002	No	No	No	No
Nistico 2012	No	Yes (76%-100%)	Yes	No
Nordal 2011	No	No	Yes	No
Oh 2011	No	No	Yes	No
Ozdemir 2002	No	No	Yes	No
Papadopoulos 2004	Yes	No	No	No
Paracha 2010	No	Yes (76% to 100%)	Yes	No
Parsad 1998	No	Yes (75%)	Yes	No
Parsad 2003b	No	Yes (75%)	Yes	Yes
Passeron 2004	No	Yes (75% to 99%)	Yes	No
Pathak 1984	No	Yes (75% to 95%)	Yes	No
Procaccini 1995	No	Yes (75% to 100%)	No	No
Radakovic 2009	No	Yes (>75%)	No	No

Table 4. Outcomes assessed in Included Studies *(Continued)*

Radmanesh 2006	No	Yes (>75%)	No	No
Rath 2008	No	Yes (>75%)	No	No
Reyes 2006	No	No	No	No
Rodriguez-Martin 2009	No	Yes (>75%)	No	No
Rojas-Urdaneta 2007	No	No	Yes	No
Ruiz-Maldonado 1975	No	No	Yes	No
Sahni 2011	Yes	Yes (76% to 90%)	Yes	No
Sanclemente 2008	No	No	Yes	No
Sapam 2012	No	Yes (76% to 100%)	Yes	No
Sassi 2008	Yes	Yes (75%)	Yes	No
Satyanarayan 2013	No	Yes (>75%)	Yes	No
Schallreuter 2002	No	No	No	No
Sharquie 2005	No	No	No	No
Sheth 2012	No	No	Yes	No
Shi 2008	No	No	Yes	No
Shi 2013	No	Yes (76% to 100%)	Yes	No
Shin 2012	No	Yes >75%)	Yes	No
Siddiqui 1994	No	No	No	Yes
Singh 2013	Yes	Yes (75% to 100%)	Yes	No
Souto 1997	No	No	Yes	No
Stinco 2009	No	Yes (>75%)	Yes	No
Tegta 2006	No	Yes (>75%)	Yes	No
Tjioe 2002	No	No	No	No
Van Geel 2004	No	No	No	No
Vasistha 1979	No	No	Yes	No
Verhaeghe 2011	No	Yes (>75%)	Yes	No
Wazir 2010	No	Yes (76% to 95%)	Yes	No
Westerhof 1999	No	Yes (75%)	Yes	No

Table 4. Outcomes assessed in Included Studies *(Continued)*

Wind 2011	No	No	No	No
Yaghoobi 2011	No	No	No	No
Yones 2007	Yes	Yes (>75%)	Yes	No

For the >75% repigmentation outcome we included studies which stated in the text " 75%, >75%, more than 75%, 75% to 90%/100%, 76 to 90%/100% or ≥ 75%"
None of the studies assessed our outcome of long-term repigmentation (defined as no loss of pigment on treated areas two years or more after treatment) so this was not included in the table.
N represents the number of studies which reported the outcome.

Table 5. Light Therapies (NB-UVB studies)

Study ID (N = 35)	Interventions	QOL N = 4	Repigmentation >75% N = 20	Adverse effects N = 26	Cessation of spread (at least 2-year follow-up) N = 1
Akdeniz 2013	1. Topical calcipotriol + betamethasone + NB-UVB 2. Topical calcipotriol + NB-UVB 3. NB-UVB	Yes (DLQI)	Yes	No	No
Anbar 2008	1. Er-Yag laser ablation + 5 fluorouracil + NB-UVB 2. NB-UVB	No	Yes	Yes	No
Arca 2006	1. NB-UVB + topical calcipotriol 2. NB-UVB	No	No	Yes (did not say how many participants affected)	No
Asawanonda 2008	1. BB-UVB 2. NB-UVB	No	Yes	Yes	No
Asawanonda 2010	1. Targeted NB-UVB + tetrahydrocurcuminoid cream 2. Targeted NB-UVB	No	Yes	Yes	No
Bakis-Petsoglou 2009	1. Pseudocatalase + NB -UVB 2. Placebo + NB-UVB	No	No Used different scales Assessed patient - rated outcomes	Yes	No

Table 5. Light Therapies (NB-UVB studies) *(Continued)*

Bansal 2013	1. Psoralen +NB-UVB 2. NB-UVB	No	Yes	Yes	No
Bayoumi 2012	Laser dermabrasion + NB-UVB	No	Yes	Yes	No
Bhatnagar 2007	1. PUVA 2. NB-UVB	No	Yes >75% repigmentation only appeared after 6 months treatment	Yes	No
Casacci 2007	1. Monochromatic excimer light (MEL) 2. NB-UVB	No	No	Yes	No
Dell'Anna 2007	1. NB-UVB + antioxidant pool (alpha lipoic acid, vitamins C and E, polyunsaturated fatty acids) 2. NB-UVB.	No	Yes	No	No
Elgoweini 2009	1. NB-UVB + vitamin E 2. NB-UVB alone	No	Yes	Yes	No
El Mofty 2013a	1. BB-UVA 2. NB-UVB	No	Yes	Yes	No
El-Zawahry 2012	1. UVA-1 2. NB-UVB	No	No	Yes	No
Esfandiarpour 2009	1. NB-UVB + pimecrolimus 2. NB-UVB + placebo	No	Yes	No	No
Hamzavi 2004	1. NB-UVB (single intervention dose dependent study)	No	Yes (this study developed VASI scoring index)	No	No
Klahan 2009	1. Tacrolimus + NB-UVB 2. NB-UVB alone	No	No	No (minor side effects mentioned but not specified)	No
Leone 2006	1. Tacalcitol + NB-UVB 2. NB-UVB alone	No	No	Yes	No

Table 5. Light Therapies (NB-UVB studies) *(Continued)*

Lim-Ong 2005	1. Clobetasol propionate + NB-UVB 2. Placebo + NB-UVB	No	yes	Yes	No (only one year follow-up)
Linthorst Homan 2012	1. Punch graft + Excimer laser post graft 2. Punch graft + NB-UVB post graft	No	Yes	No	No
Mehrabi 2006	1. NB-UVB + tacrolimus 2. NB-UVB + placebo	No	No	Yes	No
Mid-delkamp-Hup 2007	1. *Polypodium leucotomos*+ NB-UVB 2.Placebo + NB-UVB	Yes (Skindex-29)	No	Yes	No
Mohaghegh 2012	1. NB-UVB with needling 2. NB-UVB alone	No	No	Yes	No
Nordal 2011	1. NB-UVB + tacrolimus 2. NB-UVB + placebo	No	No	Yes	No
Rath 2008	1. PUVA + OMP of betamethasone 2. NB-UVB + OMP 3. BB-UVB + OMP 3. OMP alone	No	Yes	Yes	No
Sapam 2012	1. PUVA 2. NB-UVB	No	Yes (assessed 76%-100%)	Yes	No
Satyanarayan 2013	1. NB-UVB + tacrolimus 2. NB-UVB aone	No	Yes .	Yes	No
Sheth 2012	1. Minigrafts + (MEL) 2. Minigrafts + hand-foot NB-UVB device	No	No	No	No
Shin 2012	1. Fractional CO2 laser ablation + NB-UVB 2. NB-UVB alone	No	Yes This out-come was as-sessed but no patient achieved more than 75% of repig-mentation	Yes	No
Stinco 2009	1. NB-UVB 2. Pimecrolimus	No	Yes	Yes	No

Table 5. Light Therapies (NB-UVB studies) *(Continued)*

	3. Tacrolimus				
Tjioe 2002	1. NB-UVB 2. Vitamin B12 tablets and folic acid + NB-UVB	Yes (DLQI)	No	No	No
Van Geel 2004	1.Cellular suspension with hyaluronic acid and epidermal cells + NB-UVB or PUVA 2. Placebo cellular suspension with hyaluronic acid + NB-UVB or PUVA	No	No	Yes (initial erythema)	No
Verhaeghe 2011	1. NB-UVB 2. MEL (Monochromtic excimer light) 3. Placebo MEL device with bulb covered	No	Yes	Yes	No
Wind 2011	1. Punch grafts alone 2. Punch grafts + BB-UVA 3. Punch grafts + NB-UVB 4. Punch grafts + Helium Neon (HeNe) laser	No	No	No	Yes
Yones 2007	1. PUVA 2. NB-UVB	Yes (DLQI)	No	Yes	No

Abbreviations: UVA = ultraviolet A; PUVA = psoralen plus ultraviolet A; BB-UVA = broadband ultraviolet A; NB-UVB = narrowband ultraviolet B; BB-UVB = broadband ultraviolet B; MEL = monochromatic excimer light; OMP = oral minipulse; N represents the number of NB-UVB studies which reported the outcome.

APPENDICES

Appendix 1. CENTRAL (The Cochrane Library) search strategy

#1 MeSH descriptor Vitiligo explode all trees
#2 (vitiligo) or (leucoderma) or (leukoderma)
#3 (#1 OR #2)

Appendix 2. MEDLINE (Ovid) search strategy

1. randomized controlled trial.pt.
2. controlled clinical trial.pt.
3. randomized.ab.
4. placebo.ab.
5. clinical trials as topic.sh.
6. randomly.ab.
7. trial.ti.
8. 1 or 2 or 3 or 4 or 5 or 6 or 7
9. (animals not (human and animals)).sh.
10. 8 not 9
11. vitiligo.mp.
12. leucoderma.mp.
13. leukoderma.mp.
14. exp Vitiligo/
15. 11 or 12 or 13 or 14
16. 10 and 15

Appendix 3. Embase (Ovid) search strategy

1. random$.mp.
2. factorial$.mp.
3. (crossover$ or cross-over$).mp.
4. placebo$.mp. or PLACEBO/
5. (doubl$ adj blind$).mp.
6. (singl$ adj blind$).mp.
7. (assign$ or allocat$).mp.
8. volunteer$.mp. or VOLUNTEER/
9. Crossover Procedure/
10. Double Blind Procedure/
11. Randomized Controlled Trial/
12. Single Blind Procedure/
13. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12
14. leucoderma.mp.
15. leukoderma.mp.
16. exp leukoderma/
17. vitiligo.mp. or exp vitiligo/
18. 14 or 15 or 16 or 17
19. 13 and 18

Appendix 4. PsycINFO (Ovid) search strategy

1. double-blind.tw.
2. random$ assigned.tw.
3. control.tw.
4. 1 or 2 or 3
5. vitiligo.mp.
6. leucoderma.mp.
7. leukoderma.mp.
8. 5 or 6 or 7
9. 4 and 8

NB: Lines 1-4 of this strategy are a therapy filter for PsycINFO (OVID) created by the Health Information Research Unit at McMaster University.

Appendix 5. AMED (Ovid) search strategy

1. randomized controlled trial$/
2. random allocation/
3. double blind method/
4. single blind method.mp.
5. exp Clinical trials/
6. (clin$ adj25 trial$).mp.
7. ((singl$ or doubl$ or trebl$ or tripl$) adj25 (blind$ or mask$ or dummy)).mp.
8. (placebo$ or random$).mp.
9. research design/ or clinical trials/ or comparative study/ or double blind method/ or random allocation/
10. prospective studies.mp.
11. cross over studies.mp.
12. Follow up studies/
13. control$.mp.
14. (multicent$ or multi-cent$).mp.
15. ((stud or design$) adj25 (factorial or prospective or intervention or crossver or cross-over or quasi-experiment$)).mp.
16. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15
17. vitiligo.mp.
18. leucoderma.mp.
19. leukoderma.mp.
20. 17 or 18 or 19
21. 16 and 20

Appendix 6. LILACS search strategy

vitiligo or leucoderma or leukoderma or leucodermia

Appendix 7. CINAHL (EBSCO) search strategy

S16 S12 and S15
S15 S13 or S14
S14 leucoderma or leukoderma
S13 (MM "Vitiligo") OR "vitiligo"
S12 S1 or S2 or S3 or S4 or S5 or S6 or S7 or S8 or S9 or S10 or S11
S11 TX ((singl* n1 blind*) or (singl* n1 mask*)) or TX ((doubl* n1 blind*) or (doubl* n1 mask*)) or TX ((tripl* n1 blind*) or (tripl* n1 mask*)) or TX ((trebl* n1 blind*) or (trebl* n1 mask*))
S10 "randomi#ed control* trial*"
S9 TX allocat* random*
S8 (MH "Quantitative Studies")
S7 (MH "Placebos")
S6 TX placebo*
S5 TX random* allocat*
S4 (MH "Random Assignment")
S3 TX (clinic* n1 trial*)
S2 PT clinical trial
S1 (MH "Clinical Trials+")

WHAT'S NEW

Date	Event	Description
9 September 2015	Amended	Author information (affiliation) updated

HISTORY

Protocol first published: Issue 4, 2001
Review first published: Issue 1, 2006

Date	Event	Description
2 March 2015	Amended	Edits made to the funding disclaimer
29 October 2014	New citation required but conclusions have not changed	New studies from search added to awaiting classification but conclusions not changed
29 October 2014	Amended	Review updated, new search studies included in tables
3 November 2011	Amended	The lead author's email address has been updated, and one minor change has been made to the 'Quality of the evidence' section.
14 June 2010	Amended	hydrocortisone 17-butyrate corrected
4 May 2010	Amended	Changes to text and amendments of some citations
9 November 2009	New citation required but conclusions have not changed	New authorship.
9 November 2009	New search has been performed	Review substantially updated with 38 new studies.
24 June 2009	Amended	MW and JLB reviewed effects of interventions
22 June 2009	Amended	Data synthesis sections amended by JLB

Date	Event	Description
29 January 2009	Amended	Risk of bias table headings inserted. ongoing studies identifiers added 290109
21 January 2009	Amended	Missing references for included studies, apart from El Mofty 2006, have been added. New draft of outcomes 210109 MW
25 November 2008	Amended	New study added to references but no details. Some studies added to Characteristics of included studies table. MW
2 November 2008	Amended	More changes to text and started inputting details of references for included studiesMW
24 October 2008	Amended	References added for new included studies. Changes to text including outcome measures MW.
11 September 2008	Amended	New included study identifiers added. Full refs for additional studies addedMP/MW
29 August 2008	Amended	Background amended. New additional references listed but not detailed MW
19 May 2008	Amended	Background updated MW/JB. Checked by all authors
15 April 2008	Amended	Converted to new review format.
15 November 2005	New citation required and conclusions have changed	Substantive amendment

CONTRIBUTIONS OF AUTHORS

MW was the contact person with the editorial base, MW co-ordinated contributions from the co-authors, and all co-authors contributed to the final draft of the review.
MW, JB, MP, and ZJ screened papers against eligibility criteria.
MW obtained data on ongoing and unpublished studies.
MP, ZJ, KE, and VE extracted data for the review, and MW sought additional information from study authors by email.
All authors assessed studies for risk of bias, and MP wrote this section of the review.
MW, JB, and UG checked data extraction forms for accuracy.
MW, MP, ZJ, JLB, and KE entered data into RevMan.
JLB and KE analysed and interpreted data.
All authors worked on the methods and discussion sections.
MW and JB drafted the clinical sections of the background and responded to the clinical comments of the referees.
JLB responded to the methodology and statistics comments of the referees.
MW was the consumer lead author and wrote the Plain language summary, checked the review for readability and clarity, as well as ensuring outcomes are relevant to consumers.
ALL authors are guarantors of the update.

Disclaimer

This project was supported by the National Institute for Health Research, via Cochrane Infrastructure funding to the Cochrane Skin Group. The views and opinions expressed therein are those of the authors and do not necessarily reflect those of the Systematic Reviews Programme, NIHR, NHS or the Department of Health.

DECLARATIONS OF INTEREST

Jonathan Batchelor: "I was an investigator on the HI-Light Pilot RCT, assessing hand-held NB-UVB units for early, focal vitiligo. I am Chief Investigator for the main HI-Light Trial (started recruiting in 2015), which will assess the combination of hand-held NB-UVB units and topical mometasone furoate ointment. I have attended or lectured at educational events that were partly or fully funded by sponsorship from a

number of pharmaceutical companies that produce topical treatments that can be used to treat vitiligo. These companies include Astellas, Dermal, Galderma, Leo, Pfizer, and Stiefel (a GSK company)."
Dr Viktoria Eleftheriadou: "I conducted and led a pilot HI-Light trial for home phototherapy for vitiligo in 2012, as part of my PhD funded by the NIHR. This trial is now published. In addition, I am also a co-applicant on a successful NIHR grant application for the conduct of a national trial on home phototherapy for vitiligo (HI-Light trial). This trial is currently in preparation."
Maxine Whitton: "I was involved in the HI-Light pilot trial and am currently involved in the multicentre trial assessing hand-held NB-UVB devices combined with topical corticosteroid for early onset vitiligo."
Mariona Pinart: nothing to declare.
Khaled Ezzedine: nothing to declare.
Jo Leonardi-Bee: nothing to declare.
Zainab Jiyad: nothing to declare.
Urbà González: nothing to declare.
Clinical referee, Dr Mauro Picardo: "I am the author of two papers reported in the review."

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Internal sources

- No sources of support supplied

External sources

- The Vitiligo Society, UK.
- The National Institute for Health Research (NIHR), UK.

  The NIHR, UK, is the largest single funder of the Cochrane Skin Group.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

In the original review we clarified the objectives, the studies, and the participant groups that we had stated in the published protocol. In terms of outcome measures, in the protocol we had divided these into patient-rated, doctor-rated, and adverse effects. In the review these were classified as primary and secondary outcomes.

Other changes in this updated review include the following.

- We have incorporated new information into the background section; and have now added objective measures to the primary outcome of 'quality of life' and to repigmentation from a clinical perspective. We have also limited the repigmentation to > 75% because anything less than that is likely to be visually still disfiguring from the patient perspective. In order to be consistent and objective in our assessments we have also defined our criteria for > 75% repigmentation as follows: 75%, > 75%, ≥ 75%, 75% to 90%/100% or 76% to 90%/100%
- We have transferred adverse events from secondary outcomes to primary outcomes.
- We have removed depigmentation because it is rarely offered as a treatment.
- We have added cessation of spread as a secondary outcome because of its importance to clinicians as well as to people with vitiligo, and have subdivided this outcome into 'no increase in size of lesions' and 'no new lesions', both within a period of a) less than one year or b) one year or more.
- We have calculated P values using Fisher's Exact test where small numbers of events were seen in the intervention groups.
- Where it was not possible to perform a meta-analysis, we summarised the data for each trial and have only presented forest plots for primary outcome measures.

In the original protocol and review we considered outcomes from a participant and clinical perspective. However, in this updated review we have decided to omit patient-rated repigmentation because this could not be measured objectively.

INDEX TERMS

Medical Subject Headings (MeSH)

Combined Modality Therapy [methods]; Ginkgo biloba; Lasers, Excimer [therapeutic use]; PUVA Therapy [methods]; Photosensitizing Agents [therapeutic use]; Phototherapy [methods]; Plant Extracts [therapeutic use]; Quality of Life; Randomized Controlled Trials as Topic; Skin Pigmentation; Skin Transplantation [methods]; Steroids [administration & dosage]; Vitiligo [*therapy]

MeSH check words

Humans