How effective is natural sunlight in achieving repigmentation of the skin in patients with vitiligo?
Original submitted uncertainties:
• Is natural sunshine beneficial or detrimental to vitiligo?
• Does sunlight exposure help?
• How much sun exposure is therapeutic and how much is dangerous/damaging?
• Using common sense about not burning one's skin could sun help to regain normal pigment?
• Does sunlight make vitiligo spread?
• Is sun bathing a good treatment long & short term?
• Does sunlight help the pigment come back in my vitiligo patches?
• Is morning and evening mild sunlight good for vitiligo?
• What is the effect of the sun on helping to cure existing patches of vitiligo?
• Some sunlight is necessary, but what should the balance be?

Non specific but related uncertainties - safety and effectiveness of light treatments: 57

• Top 20 for patients: yes (10th)
• Top 20 for health professionals: no
• Top 20 for BEM: no
• Systematic review yes
Is pseudocatalase cream more effective in treating vitiligo when combined with UVB light therapy?
The Steering group noted serious mismatch between number of times submitted as an Uncertainty and number of votes. Uncertainty included despite only 6 votes.

**Original submitted uncertainties:**
- What is the long term efficacy of topical catalase or pseudocatalase in treating vitiligo?
- Is the pseudocatalase treatment with light therapy effective?
- Pseudocatalase and UVB compared to UVB alone.
- Is pseudocatalase treatment any good?
- Is pseudocatalase proving to be effective in the treatment of vitiligo?
- Is pseudocatalase more effective than other treatments in respect of children?
- Overall effectiveness of pseudocatalase in the long term?

**DUETs:**
- Pseudocatalase cream for repigmentation in vitiligo

- Top 20 for patients: no
- Top 20 for health professionals: no
- Top 20 for BEM: yes (13th)
- Systematic review: yes

Non specific but related uncertainties - safety and effectiveness of light treatments: 57
Which treatment is more effective for vitiligo: PUVA or UVB light therapy?
Original submitted uncertainties:

• Comparison of efficacy and cost effectiveness of UVB and PUVA.
• How does TL01 compare with PUVA in the long term?
• Is UVB as effective as PUVA in providing sustained benefits?
• Patient satisfaction after treatment with UVB/PUVA i.e. not just % repigmentation - is repigmentation cosmetically useful?
• Is TL01 better than PUVA? What is the response rate and duration?
• Does PUVA repigment the skin more effectively than narrow band UVB?

• Top 20 for patients: no
• Top 20 for health professionals: yes (1st)
• Top 20 for BEM: yes (3rd)
• Systematic review: yes

Non specific but related uncertainties - safety and effectiveness of light treatments: 57
How effective is UVB light therapy when combined with creams or ointments (e.g. steroid creams) in treating vitiligo?
Original submitted uncertainties:

- Tacrolimus compared to placebo compared to tacrolimus+ NB-UVB
- Is there an additive benefit in using tacrolimus and phototherapy in the long term?
- Using phototherapy and Protopic: when and where does the physician decide enough is enough? Is there a time limit?
- TL01 and topical steroids
- Should protopic (tacrolimus) be used in conjunction with UV light (advice is often conflicting)?
- UVB+ topical khellin

Uncertainties from the updated systematic review 2010 “Interventions for vitiligo” and DUETs:

- Topical pimecrolimus plus NB-UVB for repigmentation in vitiligo
- Topical tacalcitol (Vitamin D analogue) plus NB-UVB for repigmentation in vitiligo
- Topical calcipotriol plus UV light for repigmentation in vitiligo

- Top 20 for patients: no
- Top 20 for health professionals: yes (13th)
- Top 20 for BEM: no
- Systematic review: yes

Non specific but related uncertainties - safety and effectiveness of light treatments: 5
Which treatments are more effective for improving the quality of life of patients with vitiligo: psychological interventions or cosmetic camouflage?
Original submitted uncertainties:

- What does support and counselling compared to camouflage do to improve patients quality of life?
- Top 20 for patients: no but 22\textsuperscript{nd}
- Top 20 for health professionals: yes (11\textsuperscript{th})
- Top 20 for BEM: yes (17\textsuperscript{th})
- Systematic review: no
Which treatment is more effective for improving the quality of life of patients with vitiligo: cosmetic camouflage or a treatment to aid repigmentation?
Original submitted uncertainties:

- What does current active treatment compared to camouflage do to improve patients quality of life?
- What are the changes in DLQ1 after camouflage vs topical steroids for 6/52 or tacrolimus for 3/12?
- Is camouflage treatment as effective as phototherapy in improving quality of life in vitiligo?

- Top 20 for patients: yes (6th)
- Top 20 for health professionals: yes (6th)
- Top 20 for BEM: no
- Systematic review: no
How much do psychological interventions (such as counselling) help people with vitiligo?
Uncertainty combined:
‘How effective are psychological interventions?’ and ‘How effective are psychological interventions when combined with other treatments?’

Original submitted uncertainties:
• Should money be diverted into psychological treatments/support for vitiligo
• Should psychological therapy be part and parcel of all treatment?
• Any treatment (psychological) for the disappointments when treatment fails?
• Does group therapy or one to one therapy help with the psychological impact of vitiligo?
• What psychological therapies are more effective to cope with vitiligo?
• Are there useful and validated methods to reduce the potential negative side effects of vitiligo such as low self esteem, body image issues?
• What is the evidence for psychological therapy to help cope with living with vitiligo?
• What is the impact of structures psychological interventions e.g. CBT on quality of life in vitiligo patients?
• Is counselling at earliest stage effective in building coping strategies?

DUETs
• Psychological interventions for improved quality of life in vitiligo

• Top 20 for patients: yes (6th )
• Top 20 for health professionals: yes (6th )
• Top 20 for BEM: no
• Systematic review : no
How much does depigmentation help vitiligo?
Reworded from: How effective is depigmentation in treating vitiligo?

**Original submitted uncertainties:**
- Does hydroquinone make any difference to vitiligo in children?
- Bleaching: when/what age/what stage is this a real option and how effective - psychological follow up?
- How effective is monobenzyl/ether of hydroquinone for depigmenting?

**DUETs**
- Depigmentation for improved quality of life in severe vitiligo

- Top 20 for patients: yes (18th)
- Top 20 for health professionals: yes (16th)
- Top 20 for BEM: no
- Systematic review: no
What role might gene therapy play in the treatment of vitiligo?
Votes combined with genetic engineering question as Steering Group felt these questions are the same

**Original submitted uncertainties:**

- What are the effects of gene therapy in the treatment of vitiligo?
- If heredity - why not look for the gene hence a cure?
- Will genetic engineering be the answer by way of cell therapy?

Non-specific but related uncertainty - safety of systemic treatments: yes (2nd)

- Top 20 for patients: yes
- Top 20 for health professionals: yes (4th)
- Top 20 for BEM: yes (20th)
- Systematic review: no
What role might stem cell therapy play in treating vitiligo?
Original submitted uncertainties:

• Can stem cells be use to re-introduce functional melanocytes into affected areas?
• Stem Cell research
• Is it/ will it be possible for stem cell technology to be used in both eradicating and curing vitiligo and other similar complaints?

Non specific but related uncertainty - safety of systemic treatments: 1

• Top 20 for patients: yes (4th)
• Top 20 for health professionals: yes (6th)
• Top 20 for BEM: yes (3rd)
• Systematic review: no
How effective are hormones that stimulate pigment cells (MSH analogues, afamelanotide) in treating vitiligo?
Original submitted uncertainties:

- Will drugs like AFAMELANOTIDE be researched as a possible treatment for vitiligo?
- Use of MSH (melanocyte-stimulating hormones) analogues.
- Are there any creams/tablets available which will stimulate the body's production of melanin?

Non specific but related - safety of systemic treatments: 1

- Top 20 for patients: yes (8th)
- Top 20 for health professionals: yes (16th)
- Top 20 for BEM: yes (5th)
- Systematic review: no
Is the treatment of underlying autoimmune conditions also effective for vitiligo in the same individual?
Includes the indicative uncertainty: Is taking drugs that suppress the immune system an effective way to treat vitiligo, such as cyclosporine, azathioprine etc?

**Original submitted uncertainties:**
- Would aggressive immunosuppressive therapy at the onset be beneficial?
- Azathioprine for early vitiligo.
- What is the role of systematic immunosuppressants in active vitiligo? oral cyclosporin, MTX (methotrexate)
- Will addressing the thyroid problem cure vitiligo/ prevent further loss of pigmentation?
- Would under active thyroid treatment (thyroxin) help to cure my vitiligo?
- Can vitiligo be cured by treating other medical conditions e.g. Hypothyroidism, vitamin B deficiency?
- Links to other conditions such as thyroid, diabetes, that prescribed medicines could help.
- Does treatment of autoimmune disease reduce the spread of vitiligo?

Non specific but unrelated - safety of systemic treatments: 1

- Top 20 for patients: yes (3rd)
- Top 20 for health professionals: no
- Top 20 for BEM: yes (4th)
- Systematic review: yes
Which treatment is more effective for vitiligo: calcineurin inhibitors (e.g. tacrolimus, pimecrolimus) or steroid cream?
Original submitted uncertainties:

- Which is more effective Dermovate or Protopic?
- Are calcineurin inhibitors as effective as topical steroids in treating vitiligo?
- Effectiveness of potent topical steroid or Protopic.
- First line treatment- what should it be? Topical steroids compared to topical calcineurin inhibitors.

Non specific related uncertainty - safety and effectiveness of topical treatments: 14

- Top 20 for patients: no
- Top 20 for health professionals: yes (2nd)
- Top 20 for BEM: yes (7th)
- Systematic review: yes
How effective is VITIX in treating vitiligo?
Original submitted uncertainties:

• Does VITIX really work?

VITIX gel
A patented plant complex with anti-oxidising properties.
Cucumis Melo (Melon) Fruit Extract

Non specific related uncertainty - safety and effectiveness of topical treatments: 14

• Top 20 for patients: yes (16th)
• Top 20 for health professionals: no
• Top 20 for BEM: yes (6th)

• Systematic review: no
How effective is piperine (black pepper) cream in treating vitiligo?
Votes combined with “side effects of piperine” question

Piperine is currently going through laboratory investigations on human melanocytes and safety checks for melanoma prior to a Phase 1 trial.

**Original submitted uncertainties:**
- Is it safe to apply black pepper oil (with base oil) on a daily basis?
- How effective is piperine in repigmenting the loss of skin colour?

**From DUETs**
- Black pepper for repigmentation in vitiligo

Non specific related uncertainties - safety and effectiveness of topical treatments: 14

- Top 20 for patients: yes 1\textsuperscript{st}
- Top 20 for health professionals: yes 7\textsuperscript{th}
- Top 20 for BEM: yes 1\textsuperscript{st}
- Systematic review: no
How effective is the transplant of pigment cells (autologous melanocyte transplantation) in treating vitiligo?
**Original submitted uncertainties:**

- Is transplantation of melanocytes helpful as monotherapy for cosmetically sensitive sites in vitiligo?

**From DUETs**

- Melanocyte transplantation for repigmentation in vitiligo

**Non specific related uncertainties - effectiveness of surgical treatments:** 11

- Top 20 for patients: yes (10th)
- Top 20 for health professionals: yes (3rd)
- Top 20 for BEM: no
- Systematic review: yes
How effective are steroid injections into the skin, in treating vitiligo?
Original submitted uncertainties:

- Is there any role of intra-lesional steroid injections?

Non specific but related uncertainties - effectiveness of surgical treatments: 11

- Top 20 for patients: yes (17th)
- Top 20 for health professionals: no
- Top 20 for BEM: no
- Systematic review: yes
What role does diet play in the management of vitiligo?
Original submitted uncertainties:

- Are there any dietary changes that can retard the spread of the condition?
- Is there anything in terms of diet vitiligo sufferers can do to supplement any treatment?
- Would diet assist in helping vitiligo improve?
- Does diet have an effect on vitiligo and or treatments
- Can dietary changes help avoid/reduce/treat vitiligo
- Are there any proven dietary treatments (e.g. celery) and what are the required quantities for effectiveness?
- Can diet help? a friend had seen that some Americans thought kelp may help.
- What role does diet have to play in the treatment (and/or prevention) of vitiligo
- Are there any natural foods which could trigger the production of melanin?
- Is diet in any way helping or hindering the condition?
- Do certain foods e.g. carrots which assist production of keratin assist in the treatment of vitiligo?
- Is there something in what we eat or drink (nutrients) that could help or hinder? diet related once vitiligo has occurred

- Top 20 for patients: yes (9th)
- Top 20 for health professionals: no
- Top 20 for BEM: no
- Systematic review no
What role do vitamins and supplements play in the management of vitiligo?
Original submitted uncertainties:

• Is anyone doing trials on basic supplements e.g. zinc?
• The correct medicines to help! ie zinc, vitamin B12.
• Does folic acid prevent vitiligo if taken before it appears and is known to be in the family? Does it help in any way if one already has vitiligo?
• The use of vitamins particularly of the B group.
• Using vitamins (B12 & folic acid) with UV or sun exposure.
• Is there any evidence that taking vitamins (especially B12) or folic acid have an effect on vitiligo?
• Are vitamins/minerals/antioxidants of any benefit in treating vitiligo?
• Does taking certain vitamins etc help when being treated?
• If dietary supplements can help in the treatment of vitiligo what are the safe doses?

- Top 20 for patients: yes (5th)
- Top 20 for health professionals: no
- Top 20 for BEM: yes (14th)
- Systematic review: yes (UVB in combination with folic acid and Vitamin B12)
How effective are homeopathic remedies in treating vitiligo?
Original submitted uncertainties:

- What role can homeopathy (and other complementary therapies) have in the treatment (and/or prevention) of vitiligo?
- Does/will homeopathic remedies play any part in the treatment of vitiligo?

- Top 20 for patients: yes 15th
- Top 20 for health professionals: no
- Top 20 for BEM: no
- Systematic review: no
Complementary and lifestyle

What role might lifestyle (e.g. stress, smoking) play in the management of vitiligo?
Original submitted uncertainties:

- Is anyone studying the stress caused by treatments and its affect on vitiligo?
- Is there any lifestyle that hinders or helps treatments of vitiligo?
- Is stress likely or not to exacerbate vitiligo condition?
- Would exercise assist in helping vitiligo improve?
- Can lifestyle changes help avoid/reduce/treat vitiligo?
- Does lifestyle (i.e. exercise, stress, smokers, drinkers etc) have an effect on vitiligo and the treatments?
- Is there anything in terms of diet, exercise or other things vitiligo sufferers can do to supplement any treatment?

- Top 20 for patients: yes (20th)
- Top 20 for health professionals: no
- Top 20 for BEM: no
- Systematic review: no
Which treatment is more effective for vitiligo: light therapy or calcineurin inhibitors (e.g. tacrolimus, pimecrolimus)?
Original submitted uncertainties:

• Is phototherapy more or less effective in inducing long term re pigmentation compared to tacrolimus ointment?

Non specific but related uncertainties - safety and effectiveness of light treatments: 57

Non specific but related uncertainties - safety and effectiveness of topical treatments: 14

• Top 20 for patients: no
• Top 20 for health professionals: yes (10th)
• Top 20 for BEM: yes (8th)
• Systematic review: yes
Which treatment is more effective for vitiligo: steroid cream or light therapy?
Original submitted uncertainties:

• Which is more effective for the treatment of vitiligo - light therapy or steroid creams?

Non specific but related uncertainties - safety and effectiveness of light treatments: 57

Non specific but related uncertainties - safety and effectiveness of topical treatments: 14

• Top 20 for patients: yes (10th)
• Top 20 for health professionals: yes (18th)
• Top 20 for BEM: no
• Systematic review: yes