British Association of Dermatologists guidelines for the management of people with vitiligo 2021

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Produced in 2008 by the British Association of Dermatologists
Reviewed and updated 2021

Key words: vitiligo, guidelines, management, diagnosis, treatment, GRADE, systematic review.

NICE has accredited the process used by the British Association of Dermatologists to produce clinical guidelines. The renewed accreditation is valid until 31 May 2021 and applies to guidance produced using the process described in Updated guidance for writing a British Association of Dermatologists clinical guidance – the adoption of the GRADE methodology 2016. The original accreditation term began on 12 May 2010. Accreditation renewal in progress at time of publication. More information on accreditation can be viewed at www.nice.org.uk/accreditation.

***Footnote**: This is an updated guideline prepared for the British Association of Dermatologists (BAD) Clinical Standards Unit, which includes the Therapy & Guidelines Sub-committee. Members of the Clinical Standards Unit that have been involved are: NJ Levell (Chair, Therapy & Guidelines sub-committee), B McDonald, SL Chua, G Petrof, P Laws, L Solman, H Frow, A Daunton, I Nasr, M Hashme [Information Scientist], LS Exton [Senior BAD Guideline Research

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1.0 Purpose and scope

The overall objective of the guideline is to provide up-to-date, evidence-based recommendations for the management of vitiligo. The document aims to:

- offer an appraisal of all relevant literature up to May 2019, focusing on any key developments
- address important, practical clinical questions relating to the primary guideline objective
- provide guideline recommendations and if appropriate research recommendations.

The guideline is presented as a detailed review with highlighted recommendations for practical use in both primary care and in a dermatology clinic in secondary care, in addition to an updated Patient Information Leaflet (PIL; available on the BAD website www.skinhealthinfo.org.uk/a-z-conditions-treatments/).

1.1 Exclusions

The guideline does not cover diagnosis of vitiligo or leukotrichia (piebaldism).

Nearly all the evidence supporting the recommendations relates to studies in adults. The guideline development group (GDG) is aware that the onset of vitiligo can occur before adulthood, however, due to the paucity of high-certainty evidence relating to vitiligo in those younger than 18 years of age, there are no specific recommendations that apply to children and young people. Please also refer to section 5.7 on the management of children and young people for further clarifications.

2.0 Methodology

This set of guidelines has been developed using the BAD's recommended methodology[1] with reference to the Appraisal of Guidelines Research and Evaluation (AGREE II) instrument [www.agreetrust.org][2] and the Grading of Recommendations Assessment, Development and Evaluation (GRADE) (Appendix L; see supporting information).[3] Recommendations were developed for implementation in the UK National Health Service (NHS).

The GDG, which consisted of seven consultant dermatologists, one dermatology specialist registrars, two clinical psychologists, two patient representatives and a technical team (consisting of an information scientist, two guideline research fellows and a project manager providing methodological and technical support), established several clinical questions pertinent to the scope of the guideline and a set of outcome measures of importance to patients, ranked by the patient representatives according to the GRADE methodology (see section 2.1 and Appendix A; see supporting information).

A systematic literature search of PubMed, MEDLINE, EMBASE, Cochrane and AMED databases was conducted to identify key articles on vitiligo from January 2007 up to May 2019 (Appendix L; see supporting information); studies included in the previous iteration of the guideline were evaluated for inclusion. Search terms and strategies are detailed in the supplementary information (Appendix M; see supporting information). Additional references relevant to the topic were also isolated from citations in reviewed literature. Data extraction and critical

appraisal, data synthesis, evidence summaries, lists of excluded studies and the PRISMA diagram were prepared by the technical team. Evidence from included studies was graded according to the GRADE system (high, moderate, low or very low certainty). Recommendations are based on evidence drawn from systematic reviews of the literature pertaining to the clinical questions identified. The summary of findings with forest plots (Appendix B; see supporting information), tables Linking the Evidence To the Recommendations (LETR) (Appendix C; see supporting information), GRADE evidence profiles indicating the certainty of evidence (Appendix D; see supporting information), summary of included studies (Appendix E; see supporting information), comparative studies without data in an extractable format (Appendix F; see supporting information), within-patient studies (Appendix G; see supporting information), non-comparative studies (Appendix H; see supporting information), PRISMA flow diagram (Appendix I; see supporting information), critical appraisal of systematic review using AMSTAR – 2 (Appendix J; see supporting information), and list of studies excluded from quantitative analysis (Appendix K; see supporting information) are detailed in the supplementary information. The strength of recommendation is expressed by the wording and symbols as shown in Table 1.

Table 1: Strength of recommendations

Strength	**Wording**	**Symbols**	**Definition**
Strong recommendation *for* the use of an intervention	"Offer" *(or similar, e.g. "Use", "Provide", "Take", "Investigate", etc.)*	↑↑	Benefits of the intervention outweigh the risks; most patients would choose the intervention whilst only a small proportion would not; for clinicians, most of their patients would receive the intervention; for policy makers, it would be a useful performance indicator.
Weak recommendation *for* the use of an intervention	"Consider"	↑	Risks and benefits of the intervention are finely balanced; most patients would choose the intervention, but many would not; clinicians would need to consider the pros and cons for the patient in the context of the evidence; for policy makers it would be a poor performance indicator where variability in practice is expected.
No recommendation		Θ	Insufficient evidence to support any recommendation.
Strong recommendation *against* the use of an intervention	"Do not offer"	↓↓	Risks of the intervention outweigh the benefits; most patients would *not* choose the intervention whilst only a small proportion would; for clinicians, most of their patients would *not* receive the intervention.

2.1 Clinical Questions and Outcomes

The GDG established a number of clinical questions pertinent to the scope of the guideline. See supporting information (Appendix A; see supporting information) for full review protocol. The GDG also established two sets of outcome measures of importance to patients (treatment) which were agreed and ranked according to the GRADE methodology, by the patient representatives,[4] data on which are extracted from included studies (Appendix E; see supporting information). The proposed outcomes were in agreement with the core outcomes set which was developed based on international consensus.[5] Outcomes ranked 7, 8 and 9 are critical for decision-making; those ranked 4, 5 and 6 are important, but not critical for decision-making; those ranked 3, 2 and 1 are least important for decision making.

In people with vitiligo, what is the clinical effectiveness and safety of interventions, including active therapies, compared with each other, placebo or in combination with other interventions? These interventions included:

- Topicals – e.g. corticosteroids, vitamin D analogues, calcineurin inhibitors
- Systemics
- Light – e.g. narrow band ultraviolet B (NB-UVB), psoralen-ultraviolet A (PUVA), PUVA-sol
- Laser – e.g. excimer laser
- Surgical
- Psychological
- Complementary

Critical

- Change in psychological well-being (e.g. signs of depression or anxiety) (9)
- Re-pigmentation ≥75% (9)
- Patient rating of appearance of vitiligo (patient global assessment/colour matching/cosmetic acceptability) (9)
- Harms of treatment (8)
- Quality of Life (7)

Important

- Re-pigmentation ≥50% (6)
- Cessation of spreading of vitiligo (6)
- Maintenance of gained re-pigmentation (6)
- Tolerability/burden of treatment (5)

In people with vitiligo, what is the clinical effectiveness and safety of one combination therapy compared to another combination therapy?

Critical

- Change in psychological well-being (e.g. signs of depression or anxiety) (9)
- Re-pigmentation ≥75% (9)
- Patient rating of appearance of vitiligo (patient global assessment/colour matching/cosmetic acceptability) (9)
- Harms of treatment (8)

- Quality of Life (7)

Important

- Re-pigmentation ≥50% (6)
- Cessation of spreading of vitiligo (6)
- Maintenance of gained re-pigmentation (6)
- Tolerability/burden of treatment (5)

In people with vitiligo, what is the clinical effectiveness of skin camouflage compared with placebo, other interventions or combination of skin camouflage plus other active therapies?

Critical

- Change in psychological well-being (e.g. signs of depression or anxiety) (9)
- Patient rating of appearance of vitiligo (patient global assessment/colour matching/cosmetic acceptability) (9)
- Harms of treatment (8)
- Quality of Life (7)

Important

- Tolerability/ burden of treatment (5)

In people with vitiligo, what is the clinical effectiveness and safety of depigmentation treatment compared with other active treatments or placebo?

Critical

- Change in psychological well-being (e.g. signs of depression or anxiety) (9)
- Degree of depigmentation (9)
- Patient rating of appearance (patient global assessment/colour matching/cosmetic acceptability) (9)
- Harms of treatment (8)
- Quality of Life (7)

Important

- Risk of re-pigmentation (6)
- Tolerability/ burden of treatment (5)

In people with vitiligo, who have received large doses of PUVA (more than 150 treatment sessions) or narrowband UVB (more than 150 treatment sessions) what is the risk of developing premalignant or malignant skin changes compared with people who have not received light therapies and which individuals are at particular risk?

Critical

- Melanoma (9)
- Squamous Cell Carcinoma (9)

Important

- Basal Cell Carcinoma (6)

- Other skin cancers (6)
- Intraepidermal carcinoma (Bowens disease/SCC in situ) (5)

Less important

- Actinic keratosis (3)

3.0 Summary of recommendations

The following recommendations and ratings were agreed upon unanimously by the core members of the GDG and patient representatives. For further information on the wording used for recommendations and strength of recommendation ratings see section 2.0. The GDG is aware of the lack of high-certainty evidence for some of these recommendations, therefore strong recommendations with an asterisk (*) are based on available evidence, as well as consensus and specialist experience. Good practice point (GPP) recommendations (R) are derived from informal consensus.

GENERAL RECOMMENDATIONS

R1 (GPP) Undertake a full history for people with vitiligo including the site and type of vitiligo (**segmental, non-segmental**), disease extent (affected body surface area), disease stability, speed of onset, trigger factors, quality of life, psychological/psychosocial impact, and personal and family history of associated thyroid dysfunction or other autoimmune disease.

R2 (GPP) Screen for anti-thyroid antibodies and thyroid function in people with vitiligo (including children) to identify those at high risk of developing autoimmune thyroid disease.

R3 (GPP) Discuss with people with vitiligo (including children) the psychosocial impact of living with the condition, emphasizing the relationship between the skin and the mind.

R4 (GPP) Refer people with suspected vitiligo to a healthcare professional experienced in managing the condition (secondary care specialist or general physicians with enhanced role, GPwER) if:

- the condition is progressing rapidly.
- there is diagnostic uncertainty.
- the condition has a significant psychosocial impact.
- the condition is not responding to topical treatment.

R5 (↑↑) Assess* and monitor the QoL and level of psychological distress associated with living with vitiligo. Assessment tools that can be used include Patient Health Questionnaire-4 (PHQ-4)[6], Patient Health Questionnaire 9 (PHQ9),[7] Generalized Anxiety Disorder 7 (GAD7),[8] Dermatology Life Quality Index (DLQI),[9] and more specifically the vitiligo impact patient scale (VIPs)[10] or vitiligo-specific quality of life (VitiQoL).[11]

R6 (GPP) Provide people with vitiligo (including children) with a patient information leaflet on the condition and prescribed treatments (e.g. British Association of Dermatologists PILs www.skinhealthinfo.org.uk/a-z-conditions-treatments/).

R7 (GPP) Consider measuring serum vitamin D levels in people with vitiligo who are avoiding all sun exposure. If levels are reduced or deficient, advise that they may wish to consider

taking supplementary vitamin D3 (10-25 micrograms per day) and increasing their intake of foods high in vitamin D, such as oily fish, eggs, meat, fortified margarines, and cereals.

R8 (GPP) Monitor the skin of people with vitiligo for treatment response (or rapid progression) via medical photography (digital imaging) taken at the beginning of treatment and at regular intervals of approximately 3-6 months. Alternatively, body surface area (BSA) and areas affected by vitiligo should be documented or patients could use personal devices to take photographs if medical photography is not available or not practical. Please refer to the vitiligo calculator www.vitiligo-calculator.com.

R9 (GPP) Offer sunscreen with 4* or 5* UVA rating and SPF 50 to people with vitiligo, applied to affected patches and surrounding skin before going outdoors into the sun.

TOPICAL THERAPIES

R10 (↑↑) Offer a potent or very potent topical corticosteroid once daily to minimize potential side effects to people with vitiligo as the first-line treatment in primary or secondary care, avoiding the periocular area.

R11 (GPP) Discuss with people with vitiligo the amount of topical corticosteroids to be used, the site of application, and the safe use of a potent or very potent topical steroid when used correctly.

R12 (↑) Consider topical tacrolimus 0.1% ointment twice daily in people with **facial vitiligo** as an alternative to potent or very potent topical corticosteroids.

R13 (↑) Consider topical tacrolimus 0.1% ointment twice daily **under occlusion** on photo-exposed areas only in people with **non-facial vitiligo** as an alternative to potent or very potent topical corticosteroids.

R14 (GPP) Consider an intermittent regimen of once daily application of potent or very potent topical corticosteroids with or without topical calcineurin inhibitors (more evidence for tacrolimus), factoring the risks and benefits, in people with vitiligo especially in areas with thinner skin, e.g. periocular region, genital area and skin flexures. Examples of intermittent regimens would include:

- 1 week of potent or very potent corticosteroids and at least 1 week off
- 1 week of potent or very potent topical corticosteroids alternating with ≥ 1 week of topical calcineurin inhibitor.

Topical corticosteroids could be used for longer than 1 week in the intermittent regimen, after consideration of the risks and benefits.

R15 (GPP) Reassess the use of topical treatments (**R10**-**R14**) every 3-6 months in people with vitiligo to check for improvement. The use of periodic medical photographs may help assess these changes.

Θ There is insufficient evidence to recommend topical vitamin D analogues in people with vitiligo.

DEPIGMENTATION THERAPIES

R16 (GPP) Consider depigmentation therapies in people with **extensive vitiligo** on visible sites, in whom the condition is having a negative psychological impact. This should be done after adequate psychological assessment and/or intervention. Please refer to the supplementary information document for further details.

SYSTEMIC THERAPIES

R17 (↑) Consider oral betamethasone 0.1 mg/kg twice weekly on two consecutive days for 3 months followed by tapering of the dose by 1 mg/month for a further 3 months in combination with NB-UVB in people with **rapidly progressive vitiligo** to arrest activity of the disease after careful consideration of risks and benefits (see **R18** and Table 3 for definition of rapidly progressive vitiligo).

R18 (GPP) Consider an equivalent dose of alternative oral corticosteroids in people with **rapidly progressive vitiligo** if betamethasone is not available.

R19 (↓↓) Do not offer azathioprine in combination with PUVA (and NB-UVB) to people with vitiligo due to the risk of malignancy.

Θ There is insufficient evidence to recommend any currently available systemic treatments as monotherapy for people with **stable vitiligo**. However, there is some evidence for their use in combination with other treatments for **rapidly progressive vitiligo** (see **R17** and **R18**, and Table 3 for definition of rapidly progressive vitiligo).

Θ There is insufficient evidence to recommend minocycline, methotrexate or tofacitinib for people with vitiligo.

LIGHT AND LASER MONO- AND COMBINATION THERAPIES

R20 (↑↑) Offer NB-UVB (whole body or localised, e.g. home-based hand-held) as first-line phototherapy to people with vitiligo who have an inadequate response to topical therapy and/or with **extensive** or **progressive** disease. This may be combined with topical calcineurin inhibitor[†] (more evidence for tacrolimus) or potent topical corticosteroid,[‡] for localised sites. Counsel patients on the significant risk of loss of response upon treatment cessation.

[†] Prior to combination NB-UVB and topical tacrolimus treatment, advise patients that there is a theoretical increased risk of skin cancer with this combination of treatment. A shared decision should be made with the person with vitiligo, taking into account other alternatives, the individual's personal and family history of skin cancer risk and the impact of the vitiligo.
[‡] The evidence for potent topical corticosteroid is limited. Prior to this combination, consider the risk/benefit ratio of the prolonged use of potent topical corticosteroid.

R21 (GPP) Inform people with vitiligo who are eligible for NB-UVB therapy of the requirements (depending on local protocols: a pre-therapy assessment, medical photographs taken prior to and during follow-ups 3-6 months, two to three sessions weekly possible for up to 1 year), and the likely response depending on the affected anatomical site (e.g. the face and trunk usually achieve better repigmentation than acral sites). Alternatively, body surface

area (BSA) and areas affected by vitiligo should be documented or patients could use personal devices to take photographs if medical photography is not available or not practical. Please refer to vitiligo calculator www.vitiligo-calculator.com.

R22 (↑) Only consider PUVA/PUVAsol in adults with vitiligo if treatment with NB-UVB is unavailable or has been ineffective.[§]

[§] For contraindications refer to BAD PUVA guidelines 2016[12]

R23 (↑) Consider excimer laser or light in people with **localised vitiligo** in combination with topical calcineurin inhibitors (more evidence for tacrolimus). Prior to treatment, advise patients that there is a theoretical increased risk of skin cancer with this combination of treatment. This treatment is not widely available on the NHS but in a limited number of centres with a specialist interest.

R24 (↑) Consider CO_2 laser in combination with 5-fluorouracil in adults with **non-segmental vitiligo** on **hands and feet** if other treatments have been ineffective (apply 5-fluorouracil once daily for 7 days per month for 5 months; CO_2 laser treatments once a month for 5 months). This treatment is not widely available on the NHS but in a limited number of centres with a specialist interest.

Θ There is insufficient evidence to recommend combination treatment of potent or very potent topical steroid with NB-UVB plus CO_2 laser for people with vitiligo.

SURGICAL THERAPIES

R25 (↑) Consider cellular grafting, e.g. blister grafting or cell suspension, in people with **stable**, **segmental,** or **non-segmental** vitiligo that is unresponsive to other treatments, and who remain distressed by the condition (see Table 3 for definition of stable vitiligo). This treatment is not widely available on the NHS but in a limited number of centres with a specialist interest.

Θ There is insufficient evidence to recommend mini-punch grafting in people with vitiligo.

PSYCHOLOGICAL THERAPIES

R26 (↑↑) Offer* information on self-help (e.g. leaflets, books, websites, apps) to people with vitiligo with mild psychological distress.

R27 (↑↑) Offer* referral to psychological services for group or/and individual cognitive behavioural therapy (CBT) to people with vitiligo with moderate-to-severe psychological distress.

SKIN CAMOUFLAGE THERAPIES

R28 (↑) Consider a skin camouflage consultation in people with vitiligo who would like to explore this option.

COMPLEMENTARY THERAPIES

Θ There is insufficient evidence to recommend a specific complementary therapy for people with vitiligo.

FUTURE RESEARCH RECOMMENDATIONS

FRR1 A national registry for people with vitiligo undergoing systemic or light therapy to identify outcomes and safety.

FRR2 A prospective, randomized controlled trial evaluating the safety and efficacy of topical tacrolimus combined with NB-UVB compared with commonly used interventions.

FRR3 A prospective, randomized controlled trial evaluating the safety and efficacy of topical 5-fluorouracil compared with commonly used interventions in adults with vitiligo.

FRR4 Prospective, randomized controlled trials are needed to evaluate the safety and efficacy of oral JAK-inhibitors, alone or in combination, compared with commonly used interventions in people with vitiligo.

FRR5 Prospective, randomized controlled trials are needed to evaluate the safety and efficacy of topical JAK-inhibitors, alone or in combination, compared with commonly used interventions in people with vitiligo.

FRR6 Prospective, randomized controlled trials evaluating the safety and efficacy of CO_2 laser for vitiligo compared with commonly used interventions in adults with vitiligo.

FRR7 Prospective randomized controlled trials evaluating the safety and efficacy of afamelanotide compared with commonly used interventions in adults with vitiligo.

FRR8 Prospective randomized controlled trials evaluating the effectiveness of psychological interventions in people with vitiligo.

FRR9 A cost-effectiveness analysis of treatments for people with vitiligo within a U.K. healthcare setting.

4.0 Algorithm

The recommendations, discussions in the LETR (Appendix C; see supporting information) in the supplementary information and consensus specialist experience were used to inform the algorithm/pathway of care (Figure 1).

Figure 1: Management pathway for people with vitiligo

5-FU, 5-fluorouracil; BD, twice daily; BSA, body surface area; CBT, cognitive behavioural therapy; DLQI, Dermatology Life Quality Index;[9] GAD7, Generalized Anxiety Disorder 7;[8] PHQ4, Patient Health Questionnaire-4;[6] PHQ9, patient health questionnaire 9;[7] PIL, patient information leaflet; NB-UVB, narrow band ultraviolet B; QoL, quality of life; UVA, ultraviolet A; VIPs,[10] vitiligo impact scale; VitiQoL, vitiligo specific quality of life.[11]

5.0 Background

5.1 Definition

Vitiligo is an acquired chronic depigmentation disorder, which results in a loss of functional melanocytes. Vitiligo affects between 0.5-1% of population worldwide,[13] although higher

incident of 8.8% has been reported India.[14] Adults and children of both sexes are equally affected. Almost 50% of people with vitiligo present before the age of 20 years and nearly 70-80% before the age of 30 years old.[15]

5.2 Classification

The most common form, non-segmental vitiligo, is symmetrical and can initially has an acrofacial distribution, but may spread to involve the entire body surface. In contrast, segmental vitiligo is unilateral and characterised by rapid stabilisation (Table 2).[16] The term vitiligo can be used as an umbrella term for all non-segmental forms of vitiligo.[17,18] Classification and disease stability in vitiligo are important prognostic factors (**17**

Table *3*).

Where vitiligo is classical, the diagnosis is straight forward and can be made in primary care; however challenging cases require assessment by a dermatologist.[19] Several depigmenting or hypopigmenting disorders should be considered in the differential diagnosis of vitiligo (Table 4).

Table 2: Classification of vitiligo[a]

	Subtype	**Definition**
Vitiligo/NSV	Acrofacial	Involved sites are usually limited to face, head, hands, feet
	Generalised	Acrofacial vitiligo may later progress to include other body sites
	Universal	Most extensive form of vitiligo. This term is used when depigmentation is over 80% of total body surface.
	Mucosal	Usually refers to the involvement of oral and/or genital mucosae
	Mixed	Concomitant occurrence of NSV and SV
	Rare variants	• Follicular • Vitiligo minor (incomplete defect in pigmentation with a pale skin colour compared to healthy skin) • Vitiligo punctata (1-1.5 mm sharply demarcated macules)
Segmental vitiligo	Uni-, bi-, or pluri-segmental	Presence of one or more depigmented macules distributed on one side of the body
Undetermined/ unclassified vitiligo	Focal	Small, isolated patch, which has not evolved into NSV after a period of at least 2 years nor fits into a segmental distribution
	Mucosal	One mucosal site in isolation

NSV, non-segmental vitiligo; SV, segmental vitiligo

[a]Adapted from the revised classification of vitiligo: the vitiligo Global Issues Consensus Conference.[17]

Table 3: Definition of disease stability in vitiligo[a]

Vitiligo (NSV and SV)	Definition	Recommendations
Stable	The following criteria should be met:[**] • No new lesions developing within the last 12 months • Lack of progression of old lesions within the last 12 months	**Assessment of overall stability is inaccurate and unreliable, whereas individual lesion stability is more reliable. Ideally, stability should be assessed using patient self-reporting, clinical scoring system (e.g. VASI or VETF) and serial digital imaging or specific lesions.
Progressive	New lesions developing or old vitiliginous lesions progressing within the last 12 months[**]	
Regressive	Spontaneous repigmentation of existing vitiliginous lesions	

NSV, non-segmental vitiligo; SV, segmental vitiligo; VASI, vitiligo area scoring index; VETF Vitiligo European Task Force

[a] Adapted from the revised classification of vitiligo: the vitiligo Global Issues Consensus Conference.[17]

Table 4: Differential diagnosis of vitiligo

Inherited/genetic induced hypomelanoses	Piebaldism Tuberous sclerosis Hypomelanosis of Ito Waardenburg syndrome Hermanski-Pudlak syndrome Griscelli syndrome Menkes syndrome
Post-inflammatory hypomelanoses	Atopic eczema Psoriasis Lichen planus Pityriasis alba Genital/extragenital lichen sclerosus Allergic contact dermatitis
Para-malignant hypomelanoses	Mycosis fungoides Melanoma associated depigmentation
Occupational/drug induced hypomelanoses	Potent topical steroids Imiquimod Phenolic derivatives Systemic drugs (chloroquine, physostigmine, imatinib)
Melasma	Normal skin contrasting with melasma might appear hypopigmented
Post traumatic leukoderma	Deep burns Post-scars

Para-infectious hypopigmentation	Tinea versicolor Leprosy Leishmaniasis
Nevus depigmentosus	Congenital or detectable in the first year of life

5.3 Assessment, monitoring and early treatment

During initial consultation with a vitiligo patient, it is important to document the following:

- type of vitiligo
- extent of the disease (affected body surface area)
- skin phototype
- age of onset of disease
- disease stability
- type and duration of previous treatments
- history of autoimmune diseases.

The clinical assessment of vitiligo involves an estimation of the affected body surface area. Recently, global Vitiligo Extent Score (VES) was introduced. This user-friendly depigmentation measurement instrument allows clinician to monitor accurately and easily the affected body surface area in a standardised way.[20] Vitiligo calculator (online version of VES) is a freely available, useful online tool, which utilises pictures that reflect the extent of the vitiligo lesions (www.vitiligo-calculator.com). Other scores also have been used such as Vitiligo Area Soring Index (VASI)[21] and the VETF scoring system.[16]

Digital photographs (or if available UV photographs) taken on the initial consultation provide a useful benchmark for monitoring disease progression and treatment effectiveness.

During treatment, digital photographs, extent of vitiligo, quality of life and level of psychological distress should ideally be evaluated and recorded every 3-4 months. In a clinical setting, treatment response at 3-4 months is usually an indicator to continue treatment.[19]

In addition, some evidence exists that recent onset vitiliginous lesions respond better to treatments such as topical tacrolimus, phototherapy. Early treatment of generalised vitiligo including acral areas may enhance the chance of successful repigmentation.[22-24]

5.4 Psychological and quality of life impact

People living with vitiligo report experiencing stigmatisation, including prejudice, and in some cases actual discrimination.[25-27] Learning to deal with such reactions takes time and is emotionally demanding. Perhaps unsurprisingly high levels of social anxiety have been reported.[28] Studies have shown that people with vitiligo exhibit social anxiety and adopt coping techniques such as concealment and/or avoidance. Perceived stigma was significantly related to the extent to which vitiligo affected social activities and distress.[29]

A recent systematic review and meta-analysis reported a pooled prevalence of anxiety and depression using depression-specific and anxiety-specific questionnaires of [RR 0.29 (95% CI 0.21–0.38)] and [RR 0.33 (95% CI 0.18–0.49)], respectively. Prevalence was found to be lower for clinically diagnosed depression [RR: 0.21 (95% CI 0.15–0.28)] and anxiety [RR: 0.15 (95%

CI 0.06–0.24)].[30] An earlier systematic review also commented on the negative impact on quality of life, increased levels of self-consciousness, lower self-esteem and the potential negative impact on intimacy and sexual functioning.[31]

From the evidence we recommend routine screening for quality of life and psychosocial distress and referral for psychological therapy or recommending sources of self-help when necessary (see **R1**, **R3**, **R5**).

5.5 Associations: vitiligo, autoimmunity, and thyroid disease

Autoimmunity is considered a contributor to pathogenesis of vitiligo.

Vitiligo has been shown to be associated with other autoimmune diseases such as thyroid disorders, pernicious anaemia, Addison disease, atopic dermatitis and diabetes amongst others.[32,33]

Studies have reported that the incidence of thyroid disease is up to 52% in patients with vitiligo, and that 3%-90% of vitiligo patients have antithyroid antibodies. Patients with vitiligo were at increased risk of Graves' disease, Hashimoto thyroiditis and thyroid cancer compared to general population.[34]

A systematic review of studies on the prevalence of thyroid disease in patients in vitiligo found high rates of thyroid disease, autoimmune thyroid disease, and presence of thyroid specific autoantibodies, 15.1%, 14.3%, and 20.8%, respectively. The risk for patients with vitiligo to develop (any) thyroid diseases is almost twice as high compared with patients without vitiligo. The risk for patients with vitiligo to develop autoimmune thyroid disease is even higher (2.5-fold) compared with patients without vitiligo and the risk of elevated thyroid antibodies in patients with vitiligo is more than fivefold higher compared with patients without vitiligo.[35]

A large, recently conducted systematic review and meta-analysis assessing the prevalence of thyroid disorders in patients with vitiligo showed that 6 thyroid disorders (subclinical hyperthyroidism, overt hyperthyroidism, subclinical hypothyroidism, overt hypothyroidism, Graves' disease, and Hashimoto thyroiditis) have various prevalence in vitiligo. The highest prevalence was in subclinical hypothyroidism, and the lowest was in subclinical hyperthyroidism or Graves' disease. The authors suggested that screening vitiligo patients for thyroid disorders seem reasonable, in an effort to detect potential thyroid diseases or to assess the risk of future onset.[36]

Another study of 363 paediatric patients found significant incidence of thyroid dysfunction in paediatric patients with non-segmental vitiligo and concluded that vitiligo usually appears before the development of thyroid disease.[37]

From this evidence we suggest the routine screening of anti-thyroid antibodies and thyroid function should be performed in all vitiligo patients (for affected children if it is appropriate to their age) to identify those at high risk of developing autoimmune thyroid disease (see **R2**).

5.6 Vitiligo and skin cancer

Recently, it has been shown that vitiligo has an inverse relationship with melanoma, which means that people with vitiligo are less likely to develop melanoma.[38] A recent systematic review and meta-analysis looking into the risk of skin cancer in people with vitiligo showed that compared with people without vitiligo, people with vitiligo had a significantly lower risk of non-melanoma skin cancer; the crude odds ratio (OR) was 0·29 [95% confidence interval (CI) 0·14–0·58, I^2 = 75·9%]. The same pattern occurred for melanoma, but the crude OR was not statistically significant (OR 0·52, 95% CI 0·15–1·78, I^2 = 85·3%).[39] Forest plots are available on request to the corresponding author. This review supports the current view that vitiligo may be protective of skin cancer. This could be due to the genetic and autoimmune profile of vitiligo, or the fact that patients with vitiligo are more careful regarding sun protection than those without vitiligo. However, this review was limited by the small number of included studies and high heterogeneity due to methodological and clinical differences between the included studies. Once more appropriate research has been conducted in this field, clinicians may be able to reassure people with vitiligo that they are not at increased risk of skin cancer.

5.7 Children and young people

Childhood onset vitiligo is common and affects around 30% of patients. Research showed that the majority of paediatric patients with vitiligo (89%) had a disease onset after the age of four.[40] In most aspects, vitiligo is very similar in children and adolescents compared with adults, including treatment approaches. There are, however, a few important management aspects to consider when seeing paediatric and adolescent patients:

1. There is very little published evidence for treatment interventions in children under 12 years.
2. The impact of vitiligo on children will depend on age and developmental level. Treatment decisions, including deciding not to actively treat should take into account the child's own level of concern about the condition and its impact on them. Potential future impact may also be considered.
3. Phototherapy
   Excess UV exposure may have different biological effect in young children compared to adults with childhood sunburn episodes increasing the risk of melanoma.[41-43] More caution should be exercised in recommending phototherapy treatment in children. Phototherapy is logistically difficult in young children and is generally not offered to children under the age of 5.
4. Topical corticosteroid treatment
   Young children are more at risk from skin atrophy especially on delicate areas such as the face. Non-steroid options such as tacrolimus should be considered first line alongside potent topical corticosteroid in children. Topical potent and very potent steroid are more likely to have a systemic effect due to increased surface area to volume ration in young children and caution should be exercised regarding their use, especially in generalised widespread disease.
5. Oral corticosteroids
   Systemic corticosteroid treatment can affect growth in children and more caution should be exercised when recommending their use in children.

6.0 Recommended audit points

In the last 20 consecutive people with vitiligo, is there clear documentation of:

1. the extent of their disease and quality of life recorded at initial assessment?
2. the type of vitiligo, disease stability and skin type recorded at initial assessment?
3. a psychological assessment following referral to secondary care?
4. thyroid antibody screening?
5. a potent topical corticosteroid being offered to treat the condition (if clinically appropriate)?

The audit recommendation of 20 cases per department is to reduce variation in the results due to a single patient and allow benchmarking between different units (See Appendix N; supporting information). However, departments unable to achieve this recommendation may choose to audit all cases seen in the preceding 12 months.

7.0 Stakeholder involvement and peer review

The draft document and supporting information were made available to the BAD membership, the British Photodermatology Group (BPG) membership, British Dermatological Nursing Group (BDNG), Primary Care Dermatological Society (PCDS) the British Society for Paediatric Dermatology (BSPD), the British Society for Dermatological Surgery (BSDS), the Royal Pharmaceutical Society, and the Vitiligo Society for comments, which were actively considered by the GDG. Following further review, the finalized version was sent for peer-review by the Clinical Standards Unit of the BAD, made up of the Therapy & Guidelines Sub-committee (T&G), prior to submission for publication.

8.0 Limitations of the guideline

This document has been prepared on behalf of the BAD and is based on the best data available when the document was prepared. It is recognized that under certain conditions it may be necessary to deviate from the guidelines and that the results of future studies may require some of the recommendations herein to be changed. Additionally, it is acknowledged that limited cost effectiveness data in the context of U.K. healthcare setting may impact the availability of a given therapy within the NHS, despite evidence of efficacy. Failure to adhere to these guidelines should not necessarily be considered negligent, nor should adherence to these recommendations constitute a defence against a claim of negligence. Limiting the systematic review to English language references was a pragmatic decision but the authors recognize this may exclude some important information published in other languages.

9.0 Plans for guideline revision

The proposed revision date for this set of recommendations is scheduled for 2026; where necessary, important interim changes will be updated on the BAD website.

Acknowledgments

We are very grateful to Dr Robert Dawe, Consultant Dermatologist at NHS Tayside for his input on phototherapy treatments for vitiligo, both patient representatives Ms Emma Rush and Mr Jeetesh Patel for their input in formulating the clinical question, ranking of the outcomes, reviewing of the evidence and subsequent draft guideline, Miss Alina Constantin (BAD Guideline Research Fellow) for assisting with the final stages, as well as those who commented on the draft during the consultation period.

Declarations of interest

VE: (1) investigator and trial development group member on the HI-Light Trial (specific); (2) Lead investigator on the pilot HI-Light trial, medical advisory panel member of the Vitiligo Society UK. **JB**: (1) chief Investigator on the HI-Light Vitiligo Trial (specific); (2) unpaid position on the medical advisory panel of the Vitiligo Society (specific). **BMcD**: (1) Invited speaker – Genus Pharmaceuticals, sponsored by Abbvie to attend the American Academy of Dermatology (non-specific), and a Hidradenitis suppurativa course (non-specific). **JR**: (1) investigator on the HI-Light Vitiligo Trial (specific). **RS**: (1) consultant for Dove, Unilever, a spokesperson for a Leo Pharma project, workshop fees from Novartis (non-specific); (2) has provided consultancy to Pegasus, Leo Pharma and Exorex (non-specific); (3) advisor to the National Eczema Society (non-specific); (4) clinical psychologist for the Psychodermatology UK executive committee (specific). **AT**: (1) honorarium from Crawford for presenting at an event relating to psoriasis and eczema (non-specific); (2) trustee for Changing Faces (non-specific); (3) unpaid member of the UK Vitiligo Scientific Advisory board (specific); (4) previously supported the Vitiligo Support and Awareness Foundation on a volunteer basis (specific).

RA, **LN**, **JP**, **ER**, **DS**, **LS**, **MH**, **LSE**, **MFMM** and **LM** have no interests to declare.

Supporting information

Additional supporting information may be found in the online version of this article at the publisher's website:
Appendix A: Review protocol
Appendix B: Forest plots
Appendix C: Linking Evidence to Recommendation (LETR)
Appendix D: GRADE evidence tables
Appendix E: Summary of included comparative studies
Appendix F: Comparative studies with no extractable data
Appendix G: Narrative findings from within-patient studies
Appendix H: Narrative findings from non-comparative studies
Appendix I: PRISMA diagram – study selection
Appendix J: Critical appraisal of included systematic reviews – AMSTAR 2
Appendix K: Papers excluded from quantitative analysis
Appendix L: Methodology
Appendix M: Search strategy
Appendix N: Audit standards, data items and data collection methodology

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