ASSESSMENT METHODS IN VITILIGO

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7th MASTERCLASS ON VITILIGO AND PIGMENTARY DISORDERS, ISTANBUL 2014
I HAVE NO FINANCIAL RELATIONSHIPS TO DISCLOSE
INITIAL EXTENT AND SEVERITY OF VITILIGO

PROGNOSIS

THERAPEUTIC CHOICES

TREATMENT EFFICACY
Interventions for vitiligo.

Whitton ME¹, Pinart M, Batchelor J, Lushey C, Leonardi-Bee J, González U.

Author information

Abstract

BACKGROUND: Around one per cent of the world’s population has vitiligo, a disease which causes white patches on the skin. There are a variety of treatments available, most of which are unsatisfactory.

OBJECTIVES: To assess all interventions used to manage vitiligo.

SEARCH STRATEGY: In November 2009 we updated searches of the Cochrane Skin Group Specialised Register, the Cochrane Central Register of Controlled Trials in The Cochrane Library (Issue 4, 2009), MEDLINE, EMBASE, AMED, PsycINFO, LILACS and ongoing trials databases.

SELECTION CRITERIA: Randomised controlled trials (RCTs).

DATA COLLECTION AND ANALYSIS: At least 2 review authors independently assessed study eligibility and methodological quality, and carried out data extraction. Two of the 57 included studies could be combined for meta-analysis.

MAIN RESULTS: In this update, 57 trials, including 19 from the original review, were assessed with 3139 participants. Most of the RCTs, which covered a wide range of interventions, had fewer than 50 participants. All of the studies assessed repigmentation, 6 measured cessation of spread, and 5 investigated the effect of treatment on quality of life. Most of the studies assessed combination therapies which generally reported better results. New interventions include monochromatic excimer light (MEL), Polyพอodium leucotomos, melanocyte transplantation, oral antioxidants, Chinese zengse pill, and pimecrolimus. We analysed the data from 28 studies that met our outcome criteria of improvement in quality of life and greater than 75% repigmentation. Fifteen analyses from studies comparing various interventions showed a statistically significant difference between the proportions of participants achieving more than 75% repigmentation. The majority of analyses showing statistically significant differences were from studies that assessed combination interventions which generally included some form of light treatment. Topical preparations, in particular corticosteroids, reported most adverse effects. However, in the combination studies it was difficult to ascertain which treatment caused these effects. None of the studies was able to demonstrate long-term benefits. Very few studies were conducted on children or included segmental vitiligo. We found one study of psychological interventions and none 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.
Which outcomes should we measure in vitiligo? Results of a systematic review and a survey among patients and clinicians on outcomes in vitiligo trials.

Eleftheriadou V, Thomas KS, Whitton ME, Batchelor JM, Ravenscroft JC.

Abstract

BACKGROUND: Relevant and reliable outcomes play a crucial role in the correct interpretation and comparison of the results of clinical trials. There is a lack of consensus around methods of assessment and outcome measures for vitiligo, which makes it difficult to compare results of randomized controlled trials (RCTs) and perform meta-analysis.

OBJECTIVES: To describe the heterogeneity in outcome measures used in published RCTs of vitiligo treatments, and to report the most desirable outcomes from patients’ and clinicians’ perspectives.

METHODS: We conducted a systematic review of outcome measures used in RCTs as well as a survey of the most desirable outcomes identified by patients and clinicians as part of a Vitiligo Priority Setting Partnership.

RESULTS: Outcomes from 54 eligible trials were analysed and compared with outcomes suggested by patients and clinicians. In the systematic review, 25 different outcomes were reported. Only 22% of trials had clearly stated primary outcome measures. Repigmentation was the most frequently reported outcome in 95% of trials and was measured using 48 different scales. Only 9% of trials assessed quality of life. Thirteen per cent measured cessation of spreading of the disease and 17% of studies reported patients’ opinions and satisfaction with the treatment. In contrast, out of 438 suggestions made by patients and clinicians, cosmetically acceptable repigmentation (rather than percentage of repigmentation) was the most desirable outcome (68%), followed by cessation of spread of vitiligo (15%), quality of life (8%) and maintenance of repigmentation (4%).

CONCLUSIONS: We propose that future vitiligo trials should include repigmentation, cosmetic acceptability of results, global assessment of the disease, quality of life, maintenance of repigmentation, stabilization of vitiligo and side-effects. International consensus among clinicians, researchers and patients is needed to establish an agreed core outcome set for future vitiligo trials.
quintiles (e.g. 0–24, 25–50, 51–74, 75–100), percentages (e.g. 0–40, 40–60, 60–100; 0–30, 31–50, 51–75, 75–100), mean difference in lesion size in millimetres. Five trials (9%) used more than one scale to measure repigmentation.

In total, repigmentation was measured using 48 different scales in 54 eligible trials. Although 30% of the trials used quartiles (16/54), 14 different scales were created including differences in the definition of quartiles and the names of the corresponding categories. For example, Kumaran et al.\textsuperscript{11} and Bhatnagar et al.\textsuperscript{12} both used the ‘0–24%, 25–50%, 50–75%, 76–100%’ quartiles, but one trial\textsuperscript{11} reported moderate improvement as 25–50% repigmentation and the other\textsuperscript{12} as 50–75% repigmentation of vitiliginous lesions. The definition of excellent repigmentation or success varied from trial to trial and included values from ‘any repigmentation’ to 100% repigmentation of vitiliginous lesions.

Trials assessed repigmentation by combination of clinical assessment and other methods such as digital images, paper tracing, planimetry (29/54; 54%) or clinically only (17/54; 31%). Eleven per cent of trials (6/54) used only objective methods in assessing repigmentation such as digital images, planimetry, and image analysis of reflected ultraviolet photographs. Only two trials (4%) incorporated patient-assessed repigmentation.

section or the results section only. Perifollicular and peripheral/perifollicular patterns were mentioned in 4% (2/54) and 9% (5/54) of the trials, respectively. Four per cent of the trials reported all patterns (perifollicular, marginal and diffuse) of repigmentation (Table 3).

Change in colour (colorimetry) and colour matching of vitiliginous lesions were assessed in 6% (3/54) and 2% (1/54) of trials, respectively. These were assessed by either clinicians only\textsuperscript{12,13} or combination of clinical assessment and photographs\textsuperscript{14} or by using digital images.\textsuperscript{15} Patient assessment of colour matching was not included in any of the trials (Table 3).

Response to the treatment in light vs. dark skin types was reported in one trial (2%) and was measured clinically.

Cessation of disease activity

Thirteen per cent (7/54) of RCTs measured the cessation of spreading of vitiligo during the treatment period; only 7% (4/54) stated the scale used.

Stability of gained repigmentation

MEASURES OF EXTENT OF DEPIGMENTATION/DISEASE ACTIVITY

- **VISUAL ASSESSMENT**
  - Physician’s Global Assessment
  - Visible Light Photography
  - UV Light Photography

- **VITILIGO AREA SCORING INDEX (VASI) (2004)**

- **VITILIGO EUROPEAN TASK FORCE assessment (VETF)a (2007)**

- **POINT-COUNTING METHOD**

- **VITILIGO DISEASE ACTIVITY SCORE (VIDA SCORE) (1999)**

- **POTENTIAL REPIGMENTATION INDEX (PRI) (2013)**

- **VITILIGO ACTIVITY INDEX (VAI) (2007)**

- **VITILIGO EXTENT TENSITY INDEX (VETI) (2014)**

- **DIGITAL PLANIMETRY**
  - Image Pro Plus 4.5
  - AutoCad 2000
  - Photoshop
  - Corel Draw...

- **REFLECTANCE TRISTIMULUS CIE COLORIMETRY**

- **SPECTROPHOTOMETRY**

- **REFLECTANCE CONFOCAL MICROSCOPY**
MEASURES OF EXTENT OF DEPIGMENTATION/DISEASE ACTIVITY

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- SPECTROPHOTOMETRY
- REFLECTANCE CONFOCAL MICROSCOPY
Parametric modeling of narrowband UV-B phototherapy for vitiligo using a novel quantitative tool: the Vitiligo Area Scoring Index.

Hamzavi I1, Jain H, McLean D, Shapiro J, Zeng H, Lui H.

Abstract

BACKGROUND: There is currently no quantitative tool for evaluating vitiligo treatment response using parametric methods.

OBJECTIVE: To develop and apply a simple clinical tool, the Vitiligo Area Scoring Index (VASI), to model the response of vitiligo to narrowband UV-B (NB-UV-B) phototherapy using parametric tests.

DESIGN: Prospective, randomized, controlled, bilateral left-right comparison trial.


PATIENTS: Patients older than 18 years with stable vitiligo involving at least 5% of their total body surface in a symmetric distribution.

INTERVENTION: Treatment with NB-UV-B was given 3 times a week to half of the body on all patients for either 60 treatments or 6 months. The contralateral side served as a no-treatment control.

MAIN OUTCOME MEASURE: Repigmentation was assessed using the VASI, which was based on a composite estimate of the overall area of vitiligo patches at baseline and the degree of macular repigmentation within these patches over time. The VASI was validated separately against physician and patient global assessments. The overall reductions in VASI for NB-UV-B and control groups were modeled by multilevel regression with random effects and compared parametrically.

RESULTS: The VASI scoring correlated well with both patient and physician global assessments (P = .05 and P < .001, respectively, using ordinal logistic regression). The extent of repigmentation after 6 months on the treated side was 42.9% (95% confidence interval, 26.7%-59.0%) vs 3.3% (95% confidence interval -19.3% to 30.0%) on the untreated side (P < .001). A significant difference between control and NB-UV-B groups was apparent within the first 2 months of therapy. The legs, trunk, and arms were much more likely to repigment than the feet and hands.

CONCLUSIONS: The VASI is a quantitative clinical tool that can be used to evaluate vitiligo parametrically. Patients treated with NB-UV-B can be expected to achieve approximately 42.9% repigmentation of their vitiligo after 6 months of treatment, with the greatest response being achieved over the trunk and nonacral portions of the extremities.
THE HEAD/NECK AREA ARE NOT INCLUDED IN THE OVERALL EVALUATION

HANDS

UPPER EXTREMITIES (including axillary regions)

TRUNK

LOWER EXTREMITIES (including inguinal regions and buttocks)

FEET

PALMAR METHOD
(PATIENT’S PALM)

SURFACE OF THE PATIENT’S HAND INCLUDING FINGERS ~ 1% OF THE TOTAL BODY SURFACE AREA

VITILIGO AREA SCORING INDEX (VASI)

- 100% → NO PIGMENT
- 90% → SPECKS OF PIGMENT
- 75% → THE DEPIGMENTED AREA EXCEEDS THE PIGMENTED AREA
- 50% → THE DEPIGMENTED AND PIGMENTED AREAS ARE EQUAL
- 25% → THE PIGMENTED AREA EXCEEDS THE DEPIGMENTED AREA
- 10% → ONLY SPECKS OF DEPIGMENTATION

VITILIGO AREA SCORING INDEX (VASI)

VASI = \( \sum \) [HAND UNITS] \( \times \) [RESIDUAL DEPIGMENTATION] 
ALL BODY SITES

1 X 1.00 = 1
+ 0.5 X 1.00 = 0.5
+ 2 X 0.75 = 1.5
+ 0.5 X 1.00 = 0.5
+ 1 X 0.10 = 0.10

\[ \rightarrow 3.6 \]

Taieb A1, Picardo M; VETF Members.

Abstract
Vitiligo is the most common depigmenting disorder, which affects 0.5-1% of the worldwide population, causing disfigurement and serious disturbances in well being. There is a current lack of consensus in definition and methods of assessment of this disorder, which makes it generally impossible to compare the outcomes of different studies of the same treatment. This report summarizes the work carried out by the Vitiligo European Task Force to propose a consensus definition of the disease and to assess treatment outcomes using a system which combines analysis of extent, stage of disease (staging), and disease progression (spreading). In summary, extent is evaluated using the rule of 9. Staging is based on cutaneous and hair pigmentation in vitiligo patches, and the disease is staged 0-3 (revised version) on the largest macule in each body region, except hands and feet, which are assessed separately and globally as one unique area. Assessment of spreading is based on Wood's lamp examination of the same largest macule in each body area. Wood's lamp is useful for a combined assessment of staging and spreading in the same selected area. This study reports a workshop which validated the clinical use of the assessment form performed at several European University clinics, and showed an overall good concordance among panelists using the proposed scoring system. This system can be easily handled in clinical practice. However, variations between scorer profiles indicate a need for training to decrease interobserver variability. Further steps are envisaged, namely: (i) build a global index including staging and spreading for the initial assessment of vitiligo patients, usable as a guidance for therapeutic indications and prognosis, which could be interpreted as an equivalent of the TNM (tumor, node, metastasis) system for cancer; (ii) implement large-scale tests necessary for clinical trials (to check reproducibility and sensitivity); (iii) carry out studies of automated devices to assess extent more accurately; (iv) set up a teaching tool for scoring vitiligo, which could be posted on a website; and (v) set up an international conference on classifying, staging and scoring vitiligo, through the IFPCS Special Interest Group on Vitiligo.
**I. EXTENT**

**II. STAGE OF DISEASE (STAGING)**

**III. DISEASE PROGRESSION (SPREADING)**

<table>
<thead>
<tr>
<th>AREA</th>
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<tbody>
<tr>
<td>HEAD/NECK</td>
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<tr>
<td>TRUNK</td>
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<tr>
<td>ARMS</td>
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<tr>
<td>LEGS</td>
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<tr>
<td>HANDS/FEET</td>
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<tr>
<td>AREA</td>
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<tr>
<td>---------------------</td>
</tr>
<tr>
<td>HEAD/NECK (0-9%)</td>
</tr>
<tr>
<td>TRUNK (0-18%)</td>
</tr>
<tr>
<td>ARMS (0-36%)</td>
</tr>
<tr>
<td>LEGS (0-36%)</td>
</tr>
<tr>
<td>HANDS/FEET</td>
</tr>
<tr>
<td>TOTALS (0-100%)</td>
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</tbody>
</table>

HANDS AND FEET ARE INCLUDED IN EVALUATION OF EXTENT IN ARMS AND LEGS

### STAGE OF DISEASE (STAGING)

**STAGE 0:** Normal pigmentation (no depigmentation in area graded)

**STAGE 1:** Incomplete depigmentation (including spotty depigmentation, trichrome, and homogeneous lighter pigmentation)

**STAGE 2:** Complete depigmentation (may include hair whitening in a minority of hairs, <30%)

**STAGE 3:** Complete depigmentation plus significant hair whitening (>30%)

**STAGE 4:** Complete hair whitening

#### AREA | STAGING* (0-4)
---|---
HEAD/NECK |  
TRUNK |  
ARMS |  
LEGS |  
HANDS/FEET |  
**TOTALS** | **0-20**

*The largest macule in each body region

**HANDS AND FEET ARE EVALUATED SEPARATELY AND GLOBALLY FOR STAGING**
**DISEASE PROGRESSION (SPREADING)**

<table>
<thead>
<tr>
<th>AREA</th>
<th>SPREADING* (-1) (+1)</th>
</tr>
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<tbody>
<tr>
<td>HEAD/NECK</td>
<td></td>
</tr>
<tr>
<td>TRUNK</td>
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<tr>
<td>ARMS</td>
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<td>LEGS</td>
<td></td>
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<tr>
<td>HANDS/FEET</td>
<td></td>
</tr>
<tr>
<td>TOTALS</td>
<td>(-5)-(+5)</td>
</tr>
</tbody>
</table>

*SPREADING IS ASSESSED BY COMBINING WOOD’S LAMP AND ELECTRIC LIGHT EXAMINATIONS IN A DARK ROOM

+1: PROGRESSIVE

0: STABLE

−1: REGRESSIVE

*The largest macule in each body area

HANDS AND FEET ARE EVALUATED SEPARATELY AND GLOBALLY FOR STAGING
### VITILIGO EUROPEAN TASK FORCE assessment (VETF)α

<table>
<thead>
<tr>
<th>Area</th>
<th>% Area</th>
<th>Staging* (0–4)</th>
<th>Spreading* (−1 +1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head and neck (0–9%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trunk (0–36%)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Arms (0–18%)</td>
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</tr>
<tr>
<td>Legs (0–36%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hands and feet</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Totals (0–100%)</td>
<td></td>
<td>0–20</td>
<td>(−5 +5)</td>
</tr>
</tbody>
</table>

*largest patch in each area

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VASI - VETF

SEMIOBJECTIVE

WELL DESCRIBED

EASY AND QUICK IN USE

USEFULL IN WIDESPREAD VITILIGO
The VASI and the VETF assessment: reliable and responsive instruments to measure the degree of depigmentation in vitiligo.

Komen L¹, da Graca V, Wolkerstorfer A, de Rie MA, Terwee CB, van der Veen JP.

Author information

Abstract

BACKGROUND: Vitiligo is a common skin disorder causing depigmented macules that can impair a patient's quality of life. Currently, there are no standardized outcome measures to assess the degree of depigmentation. Moreover, there is limited knowledge on the measurement properties of outcome measures in vitiligo.

OBJECTIVE: To assess the reliability and responsiveness of the VASI and the VETFa, two well described clinician reported outcomes.

METHODS: We included three vitiligo patient groups. In one group of 31 patients, the inter-observer reliability was assessed by three observers. In 27 patients the intra-observer reliability was assessed by two repeated measures by one of the observers. To assess the responsiveness the repigmentation was calculated after six months of phototherapy in 33 patients and tested against hypotheses.

RESULTS: The inter-observer reliability was high for the VASI (ICC 0.93) and VETFa depigmentation (ICC 0.88). The intra-observer reliability was high for the VASI (ICC 0.93) and VETFa depigmentation (ICC 0.97). The smallest detectable change (SDC) was 7.1% and 10.4% for the inter-observer reliability and 4.7% and 2.9% for the intra-observer reliability in the VASI and VETFa depigmentation, respectively. All four responsiveness hypotheses formulated a priori were confirmed.

CONCLUSIONS: The VASI and the VETFa are reliable and responsive instruments to assess the degree of depigmentation in vitiligo. The VASI and the VETFa for depigmentation are potential instruments for vitiligo research in the future. However, for the use in individual patient care, caution is needed when interpreting change scores in individual patients because of the relatively large SDC. This article is protected by copyright. All rights reserved.
STABLE vs PROGRESSIVE
Table 1. Vitiligo Disease Activity (VIDA) Score on a 6-Point Scale*

<table>
<thead>
<tr>
<th>Disease Activity†</th>
<th>VIDA Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active, in the past 6 wk</td>
<td>+4</td>
</tr>
<tr>
<td>Active, in the past 3 mo</td>
<td>+3</td>
</tr>
<tr>
<td>Active, in the past 6 mo</td>
<td>+2</td>
</tr>
<tr>
<td>Active, in the past 1 y</td>
<td>+1</td>
</tr>
<tr>
<td>Stable for at least 1 y</td>
<td>0</td>
</tr>
<tr>
<td>Stable, for at least 1 y and spontaneous repigmenting</td>
<td>−1</td>
</tr>
</tbody>
</table>

*CONSISTS OF SCORING OF THE PATIENT’S OWN OPINION OF THE PRESENT DISEASE ACTIVITY WITHIN THE TIMES
†ACTIVE REFERS TO EXPANSION OF EXISTING LESIONS OR APPEARANCE OF NEW LESIONS

A LOW VIDA SCORE INDICATE LESS VITILIGO ACTIVITY

Vitiligo Potential Repigmentation Index: a simple clinical score that might predict the ability of vitiligo lesions to repigment under therapy.

Benzekri L, Eziedine K, Gauthier Y.

...lated for every patient by establishing the ratio between the number of lesions with an expected good response rate (type A + type B) and the number of usually refractory lesions (type C + type D). Thus, $PRI = \frac{\text{type A + type B}}{\text{type C + type D}}$. Nb-UVB therapy was performed twice weekly for 6 months. We started with $0.2 \text{ J cm}^{-2}$, independent of the skin type, and increased the dose by 20% every session until we reached the minimal erythema dose, which caused mild erythema that disappeared the next day of the session. At each follow-up visit, every lesion was photographed and the rate of repigmentation was evaluated under natural light and Wood’s lamp examination. The response to therapy for every single lesion was classified as positive ($\geq 75\%$ repigmentation) or negative ($< 75\%$ repigmentation). The global response for each individual was classified as good ($\geq 70\%$ of lesions with over $75\%$ repigmentation), mild ($50-70\%$ of lesions with over $75\%$ repigmentation) or poor ($< 50\%$ of lesions with over $75\%$ repigmentation). Two-paired Student tests were used to compare...

...The description of our population is given in Table 1. In brief, 30 patients were enrolled, of whom 18 were men and 12 were women. In all patients, no new patches developed during the study. The PRI values and the description of the lesions before and after treatment are given in Table 2. There was a significant difference for higher PRI between patients who achieved good vs. poor repigmentation ($P = 0.03$), mild vs. poor repigmentation ($P = 0.0003$) and mild and good vs. poor repigmentation ($P = 0.001$). Patients who achieved good repigmentation tended to have a higher PRI than those who achieved mild repigmentation ($P = 0.08$). Overall, there was a strong correlation between PRI and the percentage of repigmentation, and patients with higher PRI were more prone to achieve higher repigmentation rates ($r = 0.8, P < 0.0001$).
Only lesions exceeding 10 cm²

PRI = (TYPE A + TYPE B) / (TYPE C + TYPE D)

POTENTIAL REPIGMENTATION INDEX IS A PREDICTIVE INDEX FOR REPIGMENTATION, IT IS NOT A NUMERICAL INDEX FOR MEASURING THE EXTENT AND SEVERITY OF VITILIGO
• There are a large number of different approaches for the assessment of the disease severity and treatment response

• Currently there is a lack of consensus in the methods of assessment used in clinical trials and daily practice

• It is difficult to compare the efficacy of different treatment modalities, because measurement of repigmentation is not standardized