




## ORIGINAL ARTICLE

# Assessing the dynamic changes in vitiligo: reliability and validity of the Vitiligo Disease Activity Score (VDAS) and Vitiligo Disease Improvement Score (VDIS)

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## Abstract

**Background** The assessment of the individual evolution of vitiligo is important for therapeutic decision making in daily practice. A fast, simple and validated physician-reported score to assess clinical changes in depigmentation over time in separate parts (activity and improvement) is currently missing.

**Objective** The main objective of the study was to develop and validate the Vitiligo Disease Activity Score (VDAS) and Vitiligo Disease Improvement Score (VDIS).

**Methods** The Vitiligo Disease Activity Score (VDAS) and Vitiligo Disease Improvement Score (VDIS) were evaluated based on a photo set of 66 patients with two different time points. In the first (short) version, only the number of changing body regions was counted based on 15 predefined areas (VDAS<sub>15</sub> and VDIS<sub>15</sub>), while in the second (extensive) version the degree of worsening or improvement from +4 to -4 for each body area was added for a more detailed assessment (VDAS<sub>60</sub> and VDIS<sub>60</sub>). Content and construct validity were tested. In addition inter-, intrarater reliability and feasibility were evaluated by 7 (test) and 5 (retest) physicians.

**Results** Evidence for content and construct validity was provided. Overall, VDAS<sub>15</sub>, VDIS<sub>15</sub>, VDAS<sub>60</sub> and VDIS<sub>60</sub> demonstrated good to excellent inter-rater reliability [intraclass correlation (ICC): VDAS: range = 0.797–0.900; VDIS: range = 0.726–0.798]. The intrarater reliability ICCs were 0.865 and 0.781 for the VDAS<sub>15</sub> and VDIS<sub>15</sub>, respectively. Similar results were obtained for the VDAS<sub>60</sub> and VDIS<sub>60</sub> (ICC = 0.913 and 0.800, respectively). Completion time was short (median: 122 s/patient (first round); 95 s/patient (second round)).

**Limitations** Single tertiary centre mainly of skin phototype 2 to 3.

**Conclusion** The VDAS and VDIS appear to be valid, reliable and feasible instruments to score the evolution of vitiligo lesions. This accommodates the current urgent need for a simple, standardized and practical assessment of vitiligo activity and improvement over time.

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## Introduction

Vitiligo is a common (prevalence of 1–2%), acquired skin disease characterized by sharply demarcated depigmented lesions localized on any part of the body.<sup>1</sup> The unpredictable and variable disease course, including periods of disease stability and activity, seriously impacts the quality of life of the patient.<sup>2</sup> In clinical practice, the management of vitiligo is challenging and primarily based on the disease extent and the disease activity.<sup>3,4</sup>

This assessment should preferably be based on validated instruments. With regard to disease extent, the VASI is a commonly used tool. More recently the ‘Vitiligo Extent Score’ (VES) and VESplus are developed as fast and accurate scoring instruments to measure the affected Body Surface Area (BSA) of patients with vitiligo.<sup>5–7</sup> In addition to disease extent, the evaluation of disease activity is at least equally important.<sup>8</sup> International guidelines provide specific interventions for patients with active vitiligo, while other interventions are indicated in stable vitiligo only.<sup>1,9</sup> However, there is currently no agreed consensus on the grading of disease activity or on preferred instrument(s) for

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measuring the degree of disease activity. This is especially important in the light of the development of new immunomodulating topical and systemic treatments for vitiligo.<sup>10,11</sup>

To date, disease activity is often assessed by asking the patient about recent progression of vitiligo. However, there is an urgent need for a better and standardized way to determine disease activity, as the initiation and choice of vitiligo treatment is highly depending on this. Disease activity can be assessed as disease progression over time (i.e. 'dynamic' assessment) or at a single time point (i.e. 'static' assessment) by examining visible clinical signs associated with disease activity. For the latter, we introduced recently the Vitiligo Signs of Activity Score (VSAS).<sup>12</sup> It is based on the assessment of three clinical visible signs in vitiligo (e.g. confetti-like depigmentations, Koebner phenomenon and hypochromic areas/borders).<sup>13-15</sup> To assess vitiligo activity over time, a comparison between two time points ('dynamic' assessment) with the aid of clinical pictures is most commonly used. In this study, we developed and validated the Vitiligo Disease Activity Score (VDAS) and Vitiligo Disease Improvement Score (VDIS) to assess the progression (activity) and repigmentation (improvement) in a standardized way. The combination of this new score with the VSAS will provide a complete set of information related to the quantification of the disease activity signs ('static' assessment) as well as changes over time ('dynamic' assessment).

## Materials and methods

### Study design, ethics and construction of the scoring system

This study was performed at the department of dermatology, Ghent University Hospital. During a preparatory phase, the scoring system was developed, evaluated and modified based on experience in clinical practice. Key factors kept in mind during development were relevance for patients, feasibility and usefulness both in clinical practice and in trials. Two pilot sessions were performed including 7 and 5 raters, respectively. Based on these pilot sessions some modifications were included resulting in a first (short) and a second (more extensive) version of the instrument. To score the course of the disease between two time points, a paper version of the instruments was used (see Fig. 1).

The study has been approved by the ethics committee (reference number Ghent: B670201421409). The COnsensus-based Standards for the selection of health Measurement Instruments (COSMIN) checklist was used as a guide for designing and reporting our study.

### Raters and participants

All raters were clinicians at the dermatology department of the Ghent University Hospital with different levels of experience, including dermatology residents (5), dermatologists (1) and a vitiligo expert (1). 3 of 7 raters were involved in the preceding

pilot sessions using the same 66 patients. However, to avoid any recall bias between the pilot sessions and the final scoring rounds, an interval of many months (>3) was included between the scoring rounds.

Patients who were visiting our clinic and who provided written informed consent in the period between September 2018 and September 2019 were selected. Patients of all ages, with and without treatment were included, with the clinical diagnosis of non-segmental vitiligo and having at least two clinical photo sets with 6 ( $\pm 2$ ) or 12 ( $\pm 2$ ) months of interval. Patients with segmental vitiligo were excluded.

### Selection of photographs

For each patient, two clinical photo sets were selected with 4–14 months of interval. In those who had multiple photo sets meeting this criterion, one of both intervals [6 ( $\pm 2$ ) or 12 ( $\pm 2$ ) months] was randomly assigned in order to obtain an equal number of patients for each interval. The selected photo sets were placed on Microsoft Powerpoint slides with each slide containing two photographs of one body area affected by vitiligo on two different dates. Only body areas present in both photo sets were used. Photographs were taken in a standardized manner during clinical practice and could consist of both UV and non-UV images.

### Scoring sessions

The sequence of the slideshows was randomly picked (Research Randomizer: <https://www.randomizer.org>) for repeating scoring rounds. All assessors received a training session of at least 15 min before the start of the first scoring round and a document with written instructions was provided.

### Reliability

To check the reliability of the scoring system, the inter- and intrarater reliability were assessed. The scoring rounds were repeated by the raters with an interval of at least 2 weeks.

### Validity

Evidence for content validity for the items included in the VDAS and VDIS was provided by the opinion of vitiligo experts based on a VGICC workshop in Rome 2016 (Nov 30-Dec 3rd).<sup>16</sup> A questionnaire was filled out individually by 28 vitiligo experts. The question included in the questionnaire was referring to what items one suggests to include in a disease activity instrument based on a 'dynamic' assessment (difference between two time points). A five-point scale was used to provide an answer. For the interpretation of the results per item, a 'consensus' was defined as: 'if at least 70% "agreement" or "strong agreement" was reached'.

As no gold standard exists to evaluate criterion validity, the evaluation of construct validity was performed by testing against hypotheses. A draft of the hypotheses was formulated by two investigators (NvG and RS) both involved in the preceding pilot studies and partial analyses of this trial. To avoid a possible bias,

Date:..... This assessment is based on an interval of .....months

Mark an X (for paper version) or click (for digital version) on the location(s) of involvement with vitiligo, location(s) of improvement (repigmentation) and location(s) of worsening (activity) in this patient with vitiligo. One X/click per demarcated body area is sufficient. Palm of the hands and sole of the feet can be marked on the opposite side of the same body area (back of hand/dorsum of feet).

<p><b>Indicate the AREAS INVOLVED with vitiligo in this patient</b></p> <p><input type="checkbox"/> There are no vitiligo lesions anymore</p>	<p><b>Is there any IMPROVEMENT (repigmentation)?</b></p> <p><input type="checkbox"/> Yes; mark/click below  <input type="checkbox"/> No, there has been no improvement  <input type="checkbox"/> I don't know</p>	<p><b>Is there any WORSENING (activity)?</b></p> <p><input type="checkbox"/> Yes; mark/click below  <input type="checkbox"/> No, there has been no worsening  <input type="checkbox"/> I don't know</p>						
<p>Optional: Add the level of 'improvement' and/or 'worsening' of the vitiligo in each area according to the following scale(s):</p>	<p>Completely improved (no vitiligo anymore) (4+)                  Much improved (3+)                  Moderately improved (2+)                  Slightly improved (1+)                  Stable (0)                  Slightly worse (1-)                  Moderately worse (2-)                  Much worse (3-)                  Very much worse (4-)</p>	<table border="1"> <tr> <td>Number of locations involved with vitiligo</td> <td>...../15</td> </tr> <tr> <td>Number of locations with improvement</td> <td>...../15</td> </tr> <tr> <td>Number of locations with worsening</td> <td>...../15</td> </tr> </table>	Number of locations involved with vitiligo	...../15	Number of locations with improvement	...../15	Number of locations with worsening	...../15
Number of locations involved with vitiligo	...../15							
Number of locations with improvement	...../15							
Number of locations with worsening	...../15							

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**Figure 1** (a) Instrument used to score the VDAS<sub>15</sub>, VDIS<sub>15</sub>, VDAS<sub>60</sub> and VDIS<sub>60</sub> (based on original combined English/Dutch version; Dutch part not included).

the draft of the hypotheses was subsequently evaluated by an external investigator (AW) not familiar with any previous data or results, and the magnitude of the relations was set. This investigator consulted a second external investigator (AL) for the final approval. Some of the hypotheses were based on a comparison (correlation) between the median VDAS<sub>(15 or 60)</sub> or VDIS<sub>(15 or 60)</sub> of all raters and an expert Physician's Global Assessment (PGA) score for clinical disease evolutions (performed by one expert, who was not involved in the scoring sessions). This PGA score included a five-point scale ranging from no disease activity/no improvement to very severe disease activity/very much improved. Sufficient evidence for construct validity was assumed if ≥75% of the hypotheses were in agreement with the results.

**Feasibility**

The completion time per patient was recorded by each rater to evaluate the feasibility of this scoring system. After completion of the scoring rounds, all raters evaluated the user-friendliness on a five-point scale.

**Statistics and data analysis**

All statistical analyses were performed using IBM SPSS Statistics version 26 and Medcalc 19.8. For interrater reliability, a two-way random, absolute agreement, single-measures intra-class correlation coefficient (ICC) was used, and for intrarater reliability a two-way mixed, absolute agreement, single-measures ICC. For both inter-rater and intrarater reliability, an ICC of 0.75 or more was considered as excellent, between 0.6 and 0.74 as good, between 0.4 and 0.6 as fair and lower than 0.4 as poor. To test construct validity, Spearman's rho correlation was used. To compare average completion times between the first and second rounds, a Wilcoxon signed-rank test was used.

**Results**

**Development of the VDAS and VDIS**

The scoring tools were constructed using similar designs for scoring activity (VDAS) and improvement (VDIS) (Fig. 1). The

assessor has to identify all the involved body areas in the first figure (0–15) and then indicate in the second and third figures (follow-up figures) if this vitiligo area shows activity (progression) and/or improvement (repigmentation) (= VDAS<sub>15</sub> and VDIS<sub>15</sub>, respectively). The main numeric outputs obtained are the overall VDAS and VDIS values, ranging from 0 to 15. An additional option was added in each area showing the grade of difference, ranging from -4 to +4 (very much worsened or improved), resulting in a score of 0–60 (VDAS<sub>60</sub> and VDIS<sub>60</sub>).

### Raters and participants

The first scoring round was performed by seven raters and the retest by five raters. A total of 66 patients were included for the scoring rounds [Fitzpatrick skin type II: 14 (21.2%), III: 39 (59.1%), IV: 2 (3.0%), V: 1 (1.5%) and VI: 1 (1.5%), unknown: 9 (13.6%); female/male: 57.6%/42.4%]. The interval between both photo sets was 6 ( $\pm$ 2) months in 34 patients and 12 ( $\pm$ 2) months in 32 patients. The total body surface area affected (measured by the VESplus) varied between the patients [range: 0.01% - 36.43%, median (mean) VES: 1.3% (3.2%)]. The mean age at inclusion was 37 (median: 39).

### Validity

- a) **Content validity** Content validity for the items included in the VDAS and VDIS was provided based on the results obtained during the VGICC workshop with vitiligo experts.<sup>16</sup> Agreement on the items to include in a dynamic assessment of vitiligo disease activity were 'Evolution in disease extent' (e.g. worsening-stable-improved) (agree-strongly agree: 96%), 'Number of active body locations' (agree-strongly agree: 88%) and 'Time interval of the 2 different time points' (agree-strongly agree: 85%). As a possible indirect item 'disease activity index' was also scored but did not reach >70% agreement: 'Number of active body locations/total number of affected body locations' (agree-strongly agree: 65%).
- b) **Construct validity** All hypotheses with the corresponding results can be found in Tables 1 and 2. For VDAS<sub>15</sub>, VDAS<sub>60</sub>, VDIS<sub>15</sub> and VDIS<sub>60</sub>, sufficient evidence for construct validity was provided as all hypotheses for construct validity were confirmed. Very strong correlations with the PGA expert were found for all scores [ $\rho$  (range) = 0.757–0.864]. The VDAS<sub>15</sub> and VDAS<sub>60</sub> correlated strongly with the relative percentage of worsening between 2 time points as measured by the VESplus score ( $\rho$  = 0.791 and  $\rho$  = 0.795, respectively) while moderate correlations were found with the improvement (repigmentation) scores (VDIS<sub>15</sub>:  $\rho$  = 0.372 and VDIS<sub>60</sub>:  $\rho$  = 0.486). Patients with a longer follow-up interval (12  $\pm$  2 months vs. 6  $\pm$  2 months) and more involved body locations had higher VDAS<sub>15</sub> and VDAS<sub>60</sub> scores.

### Reliability

- a) **Inter-rater reliability** The median (mean) total scores (first round) were 6 (6; range 1–14, IQR 3–8) for the areas of involvement, 1 (1.56; range 0–9; IQR: 0–2) for areas with activity/worsening (VDAS<sub>15</sub>) and 1 (1.15; range 0–7; IQR: 0–1) for areas with improvement/repigmentation (VDIS<sub>15</sub>), respectively. The median total scores for grading the changes was 0.75 (2.44; range 0–23; IQR: 0–4) for activity/worsening (VDAS<sub>60</sub>) and 1 (1.71; range 0–10; IQR: 0–2.5) for improvement/repigmentation (VDIS<sub>60</sub>) (Fig. 2). The inter-rater reliability for the number of involved areas was excellent (first round: ICC = 0.975; 95% CI = 0.965–0.983; second round: ICC = 0.971; 95% CI = 0.958–0.981). The inter-rater reliabilities for the VDAS<sub>15</sub> and VDIS<sub>15</sub> were good to excellent for both for the first and second round [VDAS<sub>15</sub>: ICC = 0.797 (95% CI = 0.730–0.856) and 0.861 (0.806–0.905); VDIS<sub>15</sub>: ICC = 0.726 (95% CI: 0.645–0.801) and 0.793 (95% CI: 0.722–0.855), respectively]. Inter-rater agreement for grading the changes within the involved areas (grade 0 to 4) were in the first and second round good to excellent for VDAS<sub>60</sub> (ICC = 0.856; 95% CI 0.804–0.901 and ICC = 0.900; 95% CI = 0.857–0.933, respectively) and for VDIS<sub>60</sub> (ICC = 0.766; 95% CI = 0.692–0.833 and ICC = 0.798; 95% CI: 0.724–0.860, respectively).
- b) **Intrarater reliability** The intraclass correlation coefficient for intrarater reliability between the first and second scoring round was excellent for the number of involved areas (ICC = 0.983; 95% CI = 0.979–0.986), as well as for VDAS<sub>15</sub> (ICC = 0.865; 95% CI: 0.834–0.890), and VDIS<sub>15</sub> (ICC = 0.781; 95% CI: 0.735–0.820). Excellent results were also found for the VDAS<sub>60</sub> (ICC = 0.913; 95% CI: 0.891–0.931) and VDIS<sub>60</sub> (ICC = 0.800, 95% CI: 0.752–0.839). The Bland–Altman plots showed no signs of proportional or systematic error (Fig. 3).

### Feasibility

**Completion time** In the first scoring round, the total completion time per patient which includes both filling out the scoring instruments (involved areas, VDAS and VDIS) and the degree of changes as well as the calculation of the score, was 122.4 (135.9) seconds/patient [median (mean)] (range 36.6–344.6). In the second round, this was 94.6 (92.5) seconds/patient [median (mean)] (range 25.8–192.6). A Wilcoxon signed-rank test showed a significant difference between the median completion times of both rounds ( $P < 0.001$ ).

In addition, the median (mean) completion of the instruments and score calculation was analysed separately (assessed by four raters) and was 34.0 (36.0) seconds/patient (range: 8.25–92.5) for filling out the instrument (15 anatomic areas) and 73.5 (88.97) seconds/patient (range: 17.3–272) to calculate the scores, respectively (first round).

**Table 1** Hypotheses for construct validity concerning the Vitiligo Disease Activity Score 0–15 (VDAS<sub>15</sub>) and Vitiligo Disease Improvement Score 0–15 (VDIS<sub>15</sub>)

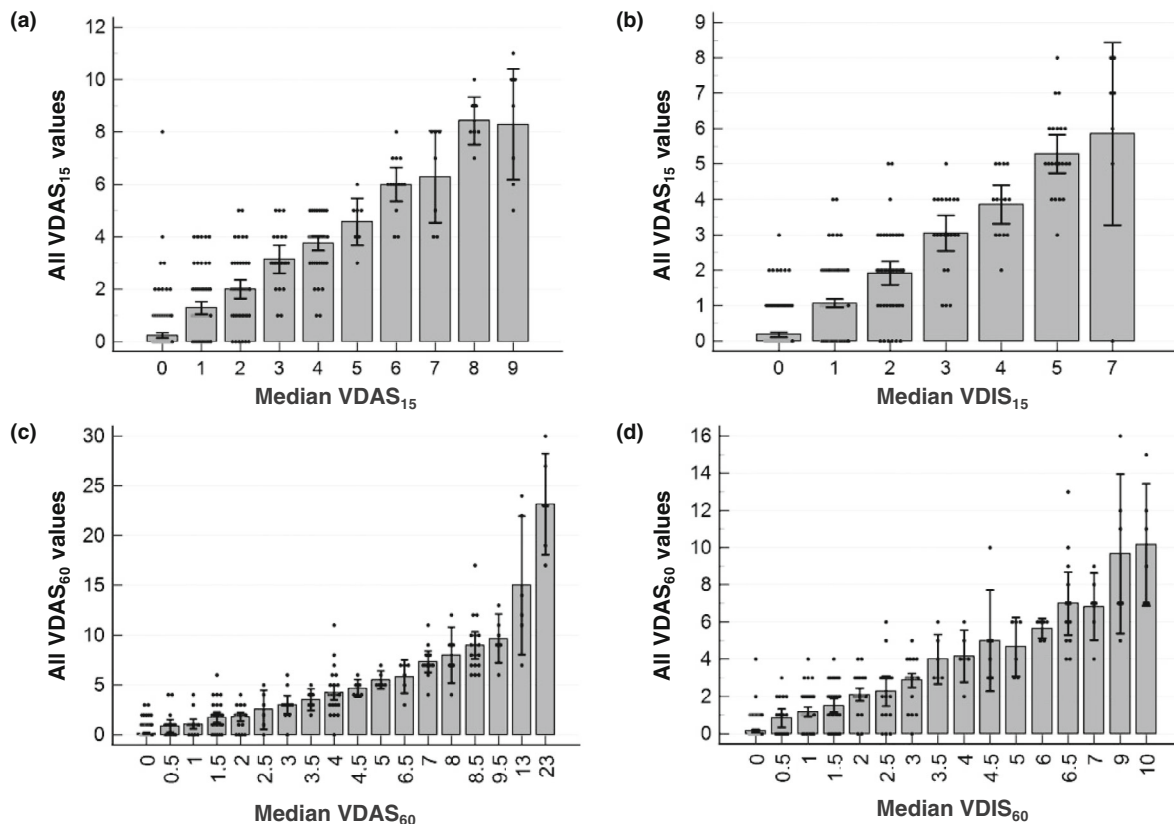
Hypothesis	Result	Confirmed (C) or failed (F)
<b>VDAS<sub>15</sub></b>		
1. We expect a rank correlation coefficient of at least 0.5 between the overall* VDAS <sub>15</sub> and the PGA expert global disease progression score	Rho = 0.831 (95% CI: 0.734–0.895)	C
2. We expect a rank correlation coefficient of at least 0.3 between the overall* VDAS <sub>0-15</sub> and the relative percentage worsening (in %) between 2 time points of the VESplus score	Rho = 0.791 (95% CI: 0.675–0.869)	C
3. Patients with a follow-up (FU) interval of 12 (± 2) months will have an at least 5% mean higher* VDAS <sub>15</sub> than patients with an interval of 6 (± 2) months	FU 6 (± 2) months: VDAS <sub>15</sub> = 0.794 FU 12(±2) months VDAS <sub>15</sub> = 2.375199% higher	C
4. We expect that patients with more than 5 involved body locations* will have an at least 10% higher VDAS <sub>15</sub> * compared to patients with less than 6 involved body locations	N ≤ 5: VDAS <sub>15</sub> = 0.625 N > 5: VDAS <sub>15</sub> = 2.4412291% higher	C
<b>VDIS<sub>15</sub></b>		
1. We expect a rank correlation coefficient of at least 0.5 between the overall* VDIS <sub>0-15</sub> and the PGA expert repigmentation score	Rho = 0.757 (95% CI: 0.627–0.847)	C
2. We expect a rank correlation coefficient of at least 0.3 between the overall* VDIS <sub>0-15</sub> and the relative percentage improvement (in %) between 2 time points of the VESplus score	Rho = 0.372 (95% CI: 0.135–0.568)	C
3. In patients with an overall* VDIS <sub>0-15</sub> of ≥5/15, the answer of the PGA expert global disease repigmentation scores will be at least 'slightly improved (or more)' in at least 50% of cases.	100% of cases	C
4. We expect that the mean repigmentation score on the face [(total sum score* for face/number of cases with involvement of the face)] will be ≥20% higher compared to the mean repigmentation score on the hands [total sum score* for hands/number of cases with involvement of the hands]	69% higher	C

\* Median of all raters.

**Table 2** Hypotheses for construct validity concerning the Vitiligo Progression Score 0–60 (VDAS<sub>60</sub>) and Vitiligo Repigmentation Score 0–60 (VDIS<sub>60</sub>)

Hypothesis	Result	Confirmed (C) or failed (F)
<b>VDAS<sub>60</sub></b>		
1. We expect a rank correlation coefficient of at least 0.5 between the overall* VDAS <sub>0-60</sub> and the PGA expert global disease progression score	Rho = 0.864 (95% CI: 0.784–0.916)	C
2. We expect a rank correlation coefficient of at least 0.3 between the overall* VDAS <sub>0-60</sub> and the relative percentage worsening (in %) between 2 time points of the VESplus score	Rho = 0.795 (95% CI: 0.680–0.871)	C
3. Patients with a follow-up (FU) interval of 12 (±2) months will have an at least 5% mean higher* VDAS <sub>0-60</sub> than patients with an interval of 6 (±2) months	211% higher	C
4. We expect that patients with more than 5 involved body locations* will have an at least 10% higher VDAS <sub>0-60</sub> * compared to patients with less than 6 involved body locations	303% higher	C
<b>VDIS<sub>60</sub></b>		
1. We expect a rank correlation coefficient of at least 0.5 between the overall* VDIS <sub>0-60</sub> and the PGA expert repigmentation score	Rho = 0.822 (95% CI: 0.721–0.889)	C
2. We expect a rank correlation coefficient of at least 0.3 between the overall* VDIS <sub>0-60</sub> and the relative percentage improvement (in %) between 2 time points of the VESplus score	Rho = 0.486 (95% CI: 0.270–0.656)	C
3. In patients with an overall* VDIS <sub>0-60</sub> of ≥5/60, the answer of the PGA expert global disease repigmentation scores will be at least 'slightly improved (or more)' in at least 50% of cases	100% of cases	C
4. We expect that the mean repigmentation score on the face [(total sum score* for face/number of cases with involvement of the face)] will be ≥20% higher compared to the mean repigmentation score on the hands (total sum score* for hands/number of cases with involvement of the hands)	93% higher	C

\* Median of all raters.



**Figure 2** Vitiligo Disease Activity Score [VDAS<sub>15</sub> (A), VDAS<sub>60</sub> (C)] and Vitiligo Disease Improvement Score [VDIS<sub>15</sub> (A) and VDIS<sub>60</sub> (C)] values according to the median scores.

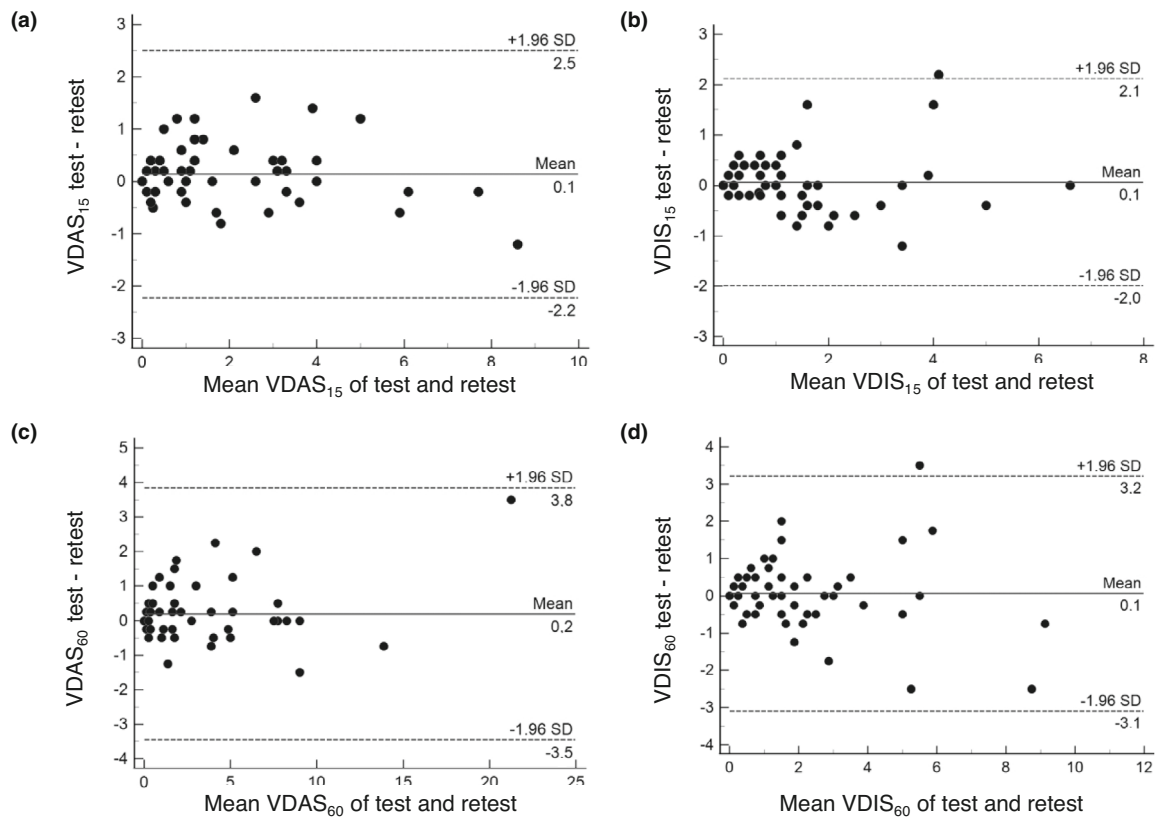
**User-friendliness** The median (mean) user-friendliness (scale 0–10) was 8.5 (8.5) for the VDAS<sub>15</sub> and 8.5 (8.5) for the VDIS<sub>15</sub>. The user-friendliness for the separate additional grading scale +4 to –4 (one scale for both VDAS<sub>60</sub> and VDIS<sub>60</sub>) was slightly lower but still excellent [= 8 (7.7)].

## Discussion

Based on this study, the VDAS and VDIS appear to be valid, reliable and user-friendly measurement instruments to score the dynamic changes in depigmentation of vitiligo. This accommodates the current urgent need for a simple, standardized and practical assessment of activity and improvement over time. The large majority of dermatologists and patients agreed that cessation of spread should be part of a core domain set for vitiligo.<sup>17</sup> It has been demonstrated that cessation of spread (= disease stability) is a valuable treatment goal for patients and should therefore be measured accordingly.<sup>8</sup> For this, we developed a simple instrument (VDAS) to measure disease activity over time. Similar to other disorders, it seems logic to measure disease activity in vitiligo on a single continuous scale ranging from ‘worse’ to

‘improved’. However, areas with activity (worsening) and improvement (repigmentation) can occur in the same patient during follow-up, sometimes even in the same body area. In our cohort, 19/66 (28.8%) of patients displayed areas of repigmentation while other lesions progressed. As such, disease activity is not fully reflected by measuring the difference in disease extent between two time points. Valuable information concerning the dynamic changes in vitiligo patients would be lost without separate assessments of improvement (repigmentation) and activity (worsening). Different from other skin diseases, the improvement (repigmentation) of vitiligo not only needs a favourable immune environment but requires also additional stimulation of (precursor) melanocytes, usually by ultraviolet light.<sup>18</sup> Additionally, as most treatments exert only an immunomodulating effect, their efficacy is not well reflected by the amount of repigmentation.<sup>19</sup> Therefore, the VDAS and VDIS were developed and validated separately allowing to monitor the different aspects of disease evolution and the efficacy of treatments reliably.

The content validity, defined by an international group of experts, showed that an evolution score should contain



**Figure 3** Bland–Altman plots of the intrarater of score difference between the first and second round per rater plotted against the average score between both rounds per rater for the Vitiligo Disease Activity Score [VDAS<sub>15</sub> (a); VDAS<sub>60</sub> (c) and Vitiligo Disease Improvement Score (VDIS<sub>15</sub> (b); VDIS<sub>60</sub> (d)].

information on the number of changing locations. Additionally, as the efficacy of treatments depends strongly on the body location, the identification of which areas are changing is crucial.<sup>20</sup> The VDAS and VDIS allow for an easy and rapid evaluation of the overall change while retaining specific information on each body location which is ideally suited for clinical practice. With new drugs for vitiligo on the horizon, it is essential to have a comprehensive set of validated measurement instruments to assess the extent and evolution of vitiligo lesions both in trials and clinical practice.<sup>21</sup> A simple and validated scoring tool to measure the multi-dimensional changes (worsening and improvement) in vitiligo was missing. The VDAS and VDIS are supported by a scoring sheet including a visual representation of the areas to be scored, which will allow a more standardized assessment. This further supports the comprehensibility and comprehensiveness of the tool. The final score as well as the scores per region can easily be implemented in any medical record (see example Fig. 1).

For each instrument, we validated two versions varying in items and scale dimensions (from 0 to 15 or 0 to 60). The first (VDAS<sub>15</sub> and VDIS<sub>15</sub>) involves the total number of body

locations with changes (activity or improvement) and can be useful for clinical practice due to its simplicity. The second version (VDAS<sub>60</sub> and VDIS<sub>60</sub>) includes the option to grade the degree of activity/improvement per area and can be more interesting for clinical trials. The outcome of the 0–15 scale (= sum of the changing body areas) has the advantage of a direct clinical meaning while the option of grading the magnitude of change (VDAS<sub>60</sub> and VDIS<sub>60</sub>) offers more details on the degree of improvement or worsening. For all scores, a good-to-excellent inter- and intrarater reliability was found. Construct validity was successfully tested by confirming all the predefined hypotheses.

Currently, the Vitiligo Disease Activity (VIDA) Scale, albeit in its original as a patient-reported outcome measure or a modified patient or physician-reported version, is a frequently used instrument that maps the last time when activity (worsening) of the vitiligo lesions was observed.<sup>22</sup> However, the VIDA offers no information on the magnitude of the change. Moreover, the assessment of the disease evolution by patients can have limitations in vitiligo due to recall bias, slow changes over time and differences in skin tone depending on sun exposure in fair-skin

patients.<sup>23</sup> The potential value of the assessment of disease activity by patients in clinical practice still needs to be further investigated and confirmed.

A limitation of this study is the low number of patients with dark skin types. Moreover, photographic material used in this study was suboptimal which could have negatively affected the results for the reliability testing. In addition, as this study was conducted in one centre, the observed changes might not be generalizable to the global population of vitiligo patients.

In conclusion, this study introduces and validates measurement instruments for both activity and improvement in vitiligo. These scores can be used both in clinical practice as in trials combining good reliability, content validity, construct validity, user-friendliness and favourable timing.

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### Conflict of interest

NvG: Consultancy and/or investigator: Pfizer, Incyte, Sunpharma and Abbvie. NvG was involved in the preparative phase (e.g. design and pilot testing) of the scores used. The co-authors Virginie Vandaele, Laura Mertens, Jérôme Van Causenbroeck, Sofie De Schepper, Laura Van Coile, Astrid Van Reempts, Ann-Sophie De Vos, Jorien Papeleu, Isabelle Hoorens, Delphine Mertens, Albert Wolkerstorfer, Janny E Lommerts, Reinhart Speeckaert declare no conflict of interest related to the content of the paper.

### Data availability statement

The design, material and methods that support the findings of this study are available from the corresponding author upon request. The database is not available due to privacy or ethical restrictions.

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