Reliability of the Vitiligo Area Scoring Index measurement tool for vitiligo

Aunna Pourang, MD,[a] Indermeet Kohli, PhD,[a,b] Nneamaka Ezekwe, MD,[a,c] Angela Parks-Miller, CCRP,[a] Tasneem F. Mohammad, MD,[a] Richard H. Huggins, MD,[a] Henry W. Lim, MD,[a] Linda S. Deal, MS,[d] Tatjana Lukic, MD, MSc,[d] Fan Zhang, PhD,[e] and Iltefat Hamzavi, MD[a]

Background: A reliable instrument is needed to assess vitiligo severity and treatment response.

Objective: To assess inter- and intrarater variability and accuracy of the Vitiligo Area Scoring Index among trained raters and to evaluate a proposed Vitiligo Area Scoring Index using equidistant 10% depigmentation increments (VASI 10%).

Methods: In this prospective study, 12 raters evaluated images of 10 participants with vitiligo on 2 occasions using total body Vitiligo Area Scoring Index (T-VASI) and facial Vitiligo Area Scoring Index (F-VASI) scores after training. Inter- and intrarater reliabilities and accuracy vs digital scores were determined using intraclass correlation coefficients. VASI 10% scores were evaluated separately for interrater reliability and accuracy.

Results: F-VASI interrater reliability improved from "moderate" to "good" between time points, while T-VASI was "good" at both time points. Intrarater reliability ranged from "good" to "excellent" for T-VASI and "poor" to "excellent" for F-VASI. Accuracy intraclass correlation coefficient was "good" to "excellent" for most raters. Interrater reliability using VASI 10% was "moderate" for both T-VASI and F-VASI.

Limitations: Small participant population and number of raters; participants were not assessed in person; no repeated VASI 10% measures.

Conclusion: Vitiligo Area Scoring Index generally provides good to excellent reliability for assessment of vitiligo by raters who receive standardized training. (JAAD Int 2024;16:206-13.)

Key words: measurement tool; reliability; reproducibility; validation; validity; VASI; VASI 10%; vitiligo.

INTRODUCTION

Vitiligo is an autoimmune disease with underlying immuno-inflammatory pathogenesis that leads to skin depigmentation secondary to autoimmune destruction of melanocytes.[1,2] Affecting approximately 0.5% to 2.0% of the population,[3-5] vitiligo is associated with psychological comorbidities and has a major impact on quality of life.[3,6] A substantial need exists for effective vitiligo treatments as no available therapy can consistently stabilize or repigment vitiligo lesions.[7,8] Several medications are currently in development to address this unmet need,[8,9] and a reliable instrument for assessing the extent of disease and response to treatment is needed.

Several instruments have been developed to measure the extent of depigmentation in vitiligo, including the Vitiligo Area Scoring Index (VASI),[10] Vitiligo Extent Severity scale,[11] and Vitiligo European

Task Force scale.[12] The VASI is a clinician-reported outcome (ClinRO) tool used to measure changes in vitiligo over time, has been validated in research, and is most commonly used for assessing vitiligo in clinical trials.[13-15] With the VASI, the area of depigmented lesions within each affected region can be assessed by using the patient's hands and fingers or fingertip units (FTUs) as anatomic measurement units (ie, the vitiligo surface area "rulers") for precise measurement of body surface area (BSA) affected.[16] The area from the distal interphalangeal joint to the tip of the second, third, or fourth digit = 1 FTU, corresponding to approximately 0.03% of the total BSA. This unit of measurement is appropriate for small facial lesions not easily measured by a hand unit.[16] A VASI score is calculated by multiplying the estimated BSA affected by vitiligo by the percentage of depigmentation in granular values of 0, 10%, 25%, 50%, 75%, 90%, or 100% and summing across all lesions within the body regions.[10,13,16]

In the current era of patient-focused drug development, the US Food and Drug Administration has emphasized the importance of clinical outcomes assessments measuring outcomes of importance to patients living with a condition, that is, content validity. Content validity evidence for the VASI was established recently through direct input from individuals living with vitiligo and those who treat them.[17] Further, the US Food and Drug Administration patient-focused drug development guidance describes the importance of additional "fit-for-purpose" evidence to support the use of clinical outcomes assessment—based end points for registration and labeling. For ClinROs in particular, intrarater reliability (high agreement in ratings made by the same rater at different times) is important in clinical trials to ensure confidence that any longitudinal changes from baseline are credible. Additionally, interrater reliability (also known as consensus reliability) evidence supports an acceptable level of agreement/consensus among a group of raters scoring the same patient at the same time point after receiving the same training.

While previous efforts found that the VASI is a sensitive method to detect treatment responses among patients with vitiligo,[10] challenges for establishing reliability evidence include inconsistent use,

CAPSULE SUMMARY

- Reliable tools are needed for the clinical assessment of vitiligo. We evaluated the reliability of the Vitiligo Area Scoring Index and a modification with Vitiligo Area Scoring Index using equidistant 10% depigmentation increments.

- High reliability of the Vitiligo Area Scoring Index from digital photos supports the use of this tool in clinical trials evaluating vitiligo treatments.

limited depigmentation values (0%, 10%, 25%, 50%, 75%, 90%, and 100%), and subjectivity of measurements. For mitigation of these issues in this study, a standardized training program for the VASI was created, and raters with a broad distribution of previous experience in VASI measurements were trained. The primary objective of this prospective study was to assess inter- and intrarater reliability of the total body Vitiligo Area Scoring Index (T-VASI) and facial Vitiligo Area Scoring Index (F-VASI) from digital images in participants with vitiligo. For preliminary evaluation of a plausibly more precise VASI measurement tool in a separate related study, a newly proposed Vitiligo Area Scoring Index using equidistant 10% depigmentation increments (VASI 10%) was also evaluated.

METHODS

Study population

This prospective study (Fig 1) was conducted from February to October 2021 and included 10 otherwise healthy participants with vitiligo as confirmed by a board-certified dermatologist. Participants had a total vitiligo-affected BSA of <60%. All participants were screened for eligibility at the Henry Ford Health Department of Dermatology clinic and provided written informed consent prior to participation.

Assessments

This study assessed the inter- and intrarater reliability of T-VASI and F-VASI assessments for participants with vitiligo as scored by raters who received standardized training for the VASI, using the original depigmentation increments. A second smaller study was conducted to determine interrater reliability of a VASI measurement tool using equidistant depigmentation increments of 10% (0 = no depigmentation or fully pigmented and 100% = fully depigmented or no pigmentation) (VASI 10%; Fig 2). The accuracy and precision of both the VASI and VASI 10% were confirmed by comparing rater scores with digital analyses of participant images.

Photography and presentations

Photographs of study participants were obtained using the published guidelines for uniform and standardized acquisition of photos specific to

vitiligo.[18] Photographs were taken using a standard Canon single-lens reflex camera with a polarizer, ring flash, and tripod stand. To better visualize lesions for patients with lighter skin types, UV pictures were captured under Wood's lamp illumination. All photos contained a calibration marker of known size. Microsoft PowerPoint presentations of images of each participant were created for rater assessments. Each photo was scaled using ImageJ software (National Institutes of Health) using the calibration marker. For facilitation of quantitative assessments of the VASI, images of the hand, FTUs, and 3-finger units (second through fourth fingers) were scaled for each image.

VASI training and rater assessments

Raters assessed clinical photographs of the study participants. A training presentation was created by Iltefat Hamzavi, MD, a vitiligo expert who originally helped create the VASI, and the Henry Ford Dermatology team in conjunction with Pfizer, Inc. This training was administered to raters with different levels of prior experience using the VASI. Of 12 raters, 5 were experts (experience with VASI measurements in clinical trials), 4 were intermediate raters (some knowledge of the VASI), and 3 were novice raters (no prior exposure to the VASI). Raters performed VASI scoring on images contained in the Microsoft PowerPoint slide decks using the scaled measurement tools.

The VASI 10% was assessed by novice and expert raters. A group of 5 novice raters evaluated the 10 participant slide decks as above after receiving standardized training for VASI 10%. This group consisted of the 3 novice raters who participated in the initial VASI study and 2 additional novice raters with no training on the original VASI. Additionally, 5 expert raters evaluated a subset of 5 participant slide decks after viewing the same standardized VASI 10% training materials provided to the novice raters. The 5 participant slide decks selected for expedient review by expert raters were representative of the original 10 slides across age, vitiligo severity, and Fitzpatrick skin phototype (FST).

Raters entered their assessments into a case report form that assessed BSA and T-VASI and F-VASI using algorithmically programmed scoring mathematics. T-VASI and F-VASI scores were determined for all 10 participants (round 1), and scoring was repeated 7 days later (round 2) to assess intrarater variability. VASI 10% ratings were collected at a single time point. Interrater variability was assessed for novice raters using scores for all 10 participants; for expert raters, interrater reliability was based on scores from image slide decks of 5 participants. Cumulative interrater reliability for the VASI 10% was evaluated using novice and expert rater scores from the 5 participant slide deck subset.

Statistical analysis

For characterization of the inter- and intrarater reliability, intraclass correlation coefficients (ICCs) calculated in a 2-way mixed model with absolute agreement and reported as a single measure were evaluated. Interrater reliabilities of the separate VASI 10% were determined by their ICCs calculated in a 1-way mixed model. ICC values of <0.5, 0.5 to 0.75, 0.75 to 0.9, and >0.9 are indicative of poor, moderate, good, and excellent reliability, respectively.[19] Lesions on hands were analyzed digitally by ImageJ, and rater assessment scores for VASI and VASI 10% were compared with digital scores by calculating ICCs.

RESULTS
Participants

Demographics of the 10 participants are summarized in Table I. Participants ranged in age from 34 to 73 years. Six participants (60%) were female. FSTs ranged from II (lighter skin color) to VI (darker skin color).

Inter- and intrarater reliability of the VASI

With previously established ICC interpretations defined above,[19] the overall interrater reliability of the initial ratings across all raters was "good" for T-VASI (ICC = 0.843; 95% CI, 0.697-0.949) and "moderate" for F-VASI (ICC = 0.542; 95% CI, 0.327-0.808). Upon repeat assessment after 7 days, interrater reliability remained "good" for T-VASI (ICC = 0.837; 95% CI, 0.690-0.947) and improved to "good" for F-VASI (ICC = 0.811; 95% CI, 0.652-0.957) (Table I).

In a comparison of the reliability among the experience levels of the raters, interrater reliability for the T-VASI was "good" among all experience levels at round 1 (all ICC ≥0.750) and ranged from "moderate" to "good" at round 2 (all ICC ≥0.744)
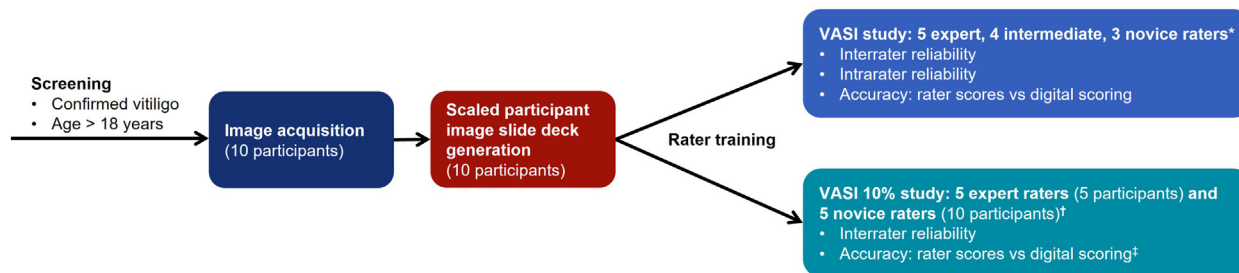
Fig 1. Design of the studies. *VASI*, Vitiligo Area Scoring Index; *VASI 10%*, Vitiligo Area Scoring Index using equidistant 10% depigmentation increments.
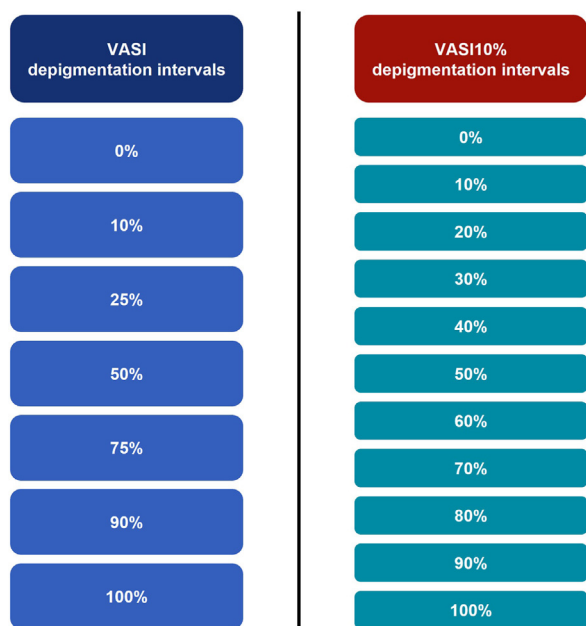

Fig 2. Comparison of lesion depigmentation intervals used in the assessment of Vitiligo Area Scoring Index and Vitiligo Area Scoring Index using equidistant 10% depigmentation increments. *VASI*, Vitiligo Area Scoring Index; *VASI 10%*, Vitiligo Area Scoring Index using equidistant 10% depigmentation increments.

Table I. Demographics of participants included in the participant slide decks

Participant	Age, y	Sex	Race/ethnicity	Fitzpatrick skin phototype*
1	39	F	White	II
2	50	M	White	III
3	62	M	White	III
4	62	F	White	II
5	40	F	White	III
6	73	F	Black	VI
7	67	M	Black	VI
8	67	F	Black	VI
9	34	F	Hispanic	IV
10	58	M	White	III

*UV images of lesions in participants with lighter skin light skin were captured to enhance contrast between depigmented and normally pigmented areas; however, scoring was performed on standard photographs for all patients, consistent with clinically perceptible vitiligo-affected body surface area.

(Table II). F-VASI interrater reliability remained consistently "good" among intermediate levels at both time points (round 1: ICC = 0.812; 95% CI, 0.602-0.941; round 2: ICC = 0.837; 95% CI 0.646-0.950), varied between "excellent" and "good" for experienced raters (round 1: ICC = 0.911; 95% CI, 0.803-0.973; round 2: ICC = 0.836; 95% CI, 0.662-0.949), and improved from "poor" to "good" for novice raters (round 1: ICC = 0.134; 95% CI, −0.143 to 0.566; round 2: ICC = 0.793; 95% CI, 0.533-0.937) (Table II).

Overall intrarater reliability ranged from "good" to "excellent" for both T-VASI and F-VASI, with the exception of 1 novice rater, who returned a "poor" intrarater score for the F-VASI (Table III). ICC was calculated between rater scores for images of hands

and corresponding digital scores obtained from ImageJ analysis of the same images. Accuracy ranged from "poor" to "excellent" for round 1 and from "moderate" to "excellent" for round 2 (Table IV).

Inter- and intrarater reliability of the VASI 10%

Interrater reliabilities among novice raters scoring 5 participant slide decks using VASI 10% were "excellent" for T-VASI (ICC = 0.957; 95% CI, 0.827-0.990) and "moderate" for F-VASI (ICC = 0. 552; 95% CI, 0.174-0.878) (Table V). Expert raters who evaluated a subset of 5 participant slide decks achieved "poor" reliability for T-VASI (ICC = 0.443; 95% CI, 0.106-0.842) and "good" reliability for F-VASI (ICC = 0.788; 95% CI, 0.429-0.948) (Table V). The overall interrater consensus reliability across novice raters and expert raters for this subset of 5 participant slide decks was "moderate" for both T-VASI (ICC = 0.721; 95% CI, 0.365-0.921) and F-VASI (ICC = 0.691; 95% CI, 0.330-0.910) (Table V).

When ICC was calculated between novice-rater scores and corresponding digital scores obtained using ImageJ for images of hands from all 10

Table II. Interrater reliability results using the validated VASI (overall and by rater experience category)

Assessment	Scoring round*	ICC	95% CI	Reliability
Overall				
T-VASI	Round 1	0.843	0.697-0.949	Good
	Round 2	0.837	0.690-0.947	Good
F-VASI	Round 1	0.542	0.327-0.808	Moderate
	Round 2	0.811	0.652-0.957	Good
By rater experience level				
T-VASI				
Experienced	Round 1	0.884	0.734-0.965	Good
	Round 2	0.857	0.693-0.956	Good
Intermediate	Round 1	0.750	0.473-0.920	Good
	Round 2	0.744	0.474-0.918	Moderate
Novice	Round 1	0.868	0.651-0.963	Good
	Round 2	0.895	0.724-0.970	Good
F-VASI				
Experienced	Round 1	0.911	0.803-0.973	Excellent
	Round 2	0.836	0.662-0.949	Good
Intermediate	Round 1	0.812	0.602-0.941	Good
	Round 2	0.837	0.646-0.950	Good
Novice	Round 1	0.134	−0.143 to 0.566	Poor
	Round 2	0.793	0.533-0.937	Good

F-VASI, Facial Vitiligo Area Scoring Index; *ICC*, intraclass correlation coefficient; *T-VASI*, total body Vitiligo Area Scoring Index; *VASI*, Vitiligo Area Scoring Index.
*Scoring rounds were separated by 7 days.

Table III. Intrarater reliability results based on 2 VASI assessments scored 7 days apart

Assessment	Rater	ICC	95% CI	Reliability
T-VASI	A	0.972	0.893-0.993	Excellent
	B	0.918	0.721-0.979	Excellent
	C	0.978	0.916-0.995	Excellent
	D	0.872	0.578-0.966	Good
	E	0.869	0.416-0.969	Good
	F	0.891	0.628-0.972	Good
	G	0.993	0.971-0.998	Excellent
	H	0.998	0.993-1	Excellent
	I	0.968	0.881-0.992	Excellent
	J	0.961	0.849-0.990	Excellent
	K	0.869	0.546-0.966	Good
	L	0.999	0.993-1	Excellent
F-VASI	A	0.989	0.960-0.997	Excellent
	B	0.930	0.750-0.982	Excellent
	C	0.996	0.985-0.999	Excellent
	D	0.971	0.892-0.993	Excellent
	E	0.175	−0.339 to 0.676	Poor
	F	0.768	0.341-0.936	Good
	G	0.996	0.983-0.999	Excellent
	H	0.999	0.997-1	Excellent
	I	0.908	0.687-0.976	Excellent
	J	0.803	0.414-0.947	Good
	K	0.953	0.828-0.988	Excellent
	L	0.991	0.964-0.998	Excellent

F-VASI, Facial Vitiligo Area Scoring Index; *ICC*, intraclass correlation coefficient; *T-VASI*, total body Vitiligo Area Scoring Index; *VASI*, Vitiligo Area Scoring Index.

Table IV. Accuracy ICC comparing rater VASI scores with digital scores for images of hands

Scoring round*	Rater	ICC	95% CI	Reliability
Round 1	A	0.863	0.543-0.964	Good
	B	0.757	0.278-0.934	Good
	C	0.675	0.169-0.906	Moderate
	D	0.755	0.246-0.934	Good
	E	0.773	0.305-0.939	Good
	F	0.435	−0.250 to 0.824	Poor
	G	0.816	0.309-0.954	Good
	H	0.815	0.446-0.950	Good
	I	0.860	0.548-0.963	Good
	J	0.916	0.707-0.978	Excellent
	K	0.892	0.633-0.972	Good
	L	0.876	0.587-0.968	Good
Round 2	A	0.844	0.486-0.959	Good
	B	0.775	0.336-0.939	Good
	C	0.843	0.505-0.958	Good
	D	0.702	0.092-0.921	Moderate
	E	0.863	0.520-0.965	Good
	F	0.643	0.096-0.896	Moderate
	G	0.830	0.436-0.956	Good
	H	0.829	0.478-0.954	Good
	I	0.922	0.727-0.980	Excellent
	J	0.946	0.803-0.986	Excellent
	K	0.879	0.609-0.968	Good
	L	0.876	0.602-0.967	Good

ICC, Intraclass correlation coefficient; *VASI*, Vitiligo Area Scoring Index.
*Scoring rounds were separated by 7 days.

Table V. Interrater consensus reliability results using VASI 10%*

Assessment	Novice raters			Expert raters			Combined		
	ICC	95% CI	Reliability	ICC	95% CI	Reliability	ICC	95% CI	Reliability
T-VASI	0.957	0.827-0.990	Excellent	0.443	0.106-0.842	Poor	0.721	0.365-0.921	Moderate
F-VASI	0.552	0.174-0.878	Moderate	0.788	0.429-0.948	Good	0.691	0.330-0.910	Moderate

F-VASI, Facial Vitiligo Area Scoring Index; *ICC*, intraclass correlation coefficient; *T-VASI*, total body Vitiligo Area Scoring Index; *VASI 10%*, Vitiligo Area Scoring Index scored with 10% depigmentation intervals.
*ICC data are based on assessments of a subset of 5 participant slide decks (participants 2, 4, 7, 8, and 10).

Table VI. Accuracy ICC comparing novice rater VASI 10% scores with digital VASI 10% scores for images of hands*

Rater	ICC	95% CI	Reliability
1	0.929	0.741-0.982	Excellent
2	0.894	0.652-0.972	Good
3	0.900	0.660-0.974	Excellent
4	0.828	0.445-0.954	Good
5	0.817	0.326-0.954	Good

ICC, Intraclass correlation coefficient; *VASI 10%*, Vitiligo Area Scoring Index scored with 10% depigmentation intervals.
*Novice raters scored all 10 participant slide decks in a single round.

participant slide decks, accuracy ranged from "good" to "excellent." (Table VI)

DISCUSSION

In the current prospective study, both inter- and intrarater reliabilities of VASI assessments were generally high among raters of all experience levels, presumably due to standardized VASI training provided at the beginning of the study. The VASI 10%, investigated here as a plausibly more precise VASI measurement using equidistant 10% depigmentation increments, provided "moderate" reliability across a combined group of novice and experienced raters. Using VASI 10%, we observed excellent reliability for T-VASI and moderate reliability for F-VASI measurements for novice raters; however, expert raters achieved only "poor" interrater reliability when T-VASI was measured. Novice raters may have benefitted more from standardized VASI 10% training than experts, as experts likely had previous measurement habits to overcome. Accuracy ICC results comparing rater-generated VASI and VASI 10% scores with those from digital analysis of the same images showed at least good reliability. These results indicate that raters can adequately assess surface area affected by vitiligo and the extent of depigmentation using the VASI, although these results are preliminary and have not been validated.

The current study supports both the use of FTUs assessed from digital photographs and centralized scoring of photographs for the reliable determination of VASI and VASI 10%.[16] The high degree of VASI reliability observed here is consistent with other studies,[13,20] suggesting that centralized photographic assessment of VASI is consistent with the reported construct validity for assessing the extent of vitiligo.[17] An evaluation of VASI reliability as measured in the clinic found an interrater reliability from 3 raters (ICC = 0.93) to be somewhat higher than we observed.[13] A recent study evaluating the assessment of vitiligo using digital photography also found high inter- and intrarater reliability of the VASI and F-VASI; however, this study used specialized equipment (a Fotofinder employing primarily UV photography rather than the readily available and standard cross-polarized camera used here, which limits comparisons between studies), and did not evaluate VASI 10% or rater accuracy vs digitally scored images.[20]

Vitiligo-affected surface area can be challenging to measure accurately and consistently across participants with different FSTs, particularly lighter types.[21,22] The current study evaluated participants spanning an adequate representation of FSTs (II-VI) using standard photographs, consistent with clinically perceptible vitiligo.

Several limitations are important to consider when interpreting these results. Given the circumstances of the COVID-19 pandemic, raters assessed clinical photographs of study participants rather than participants in person; however, the assessment of images proved to be novel and important. Images may be difficult for raters to fully visualize and may not adequately represent 3-dimensional area. Also, images may not capture all vitiligo lesions, although this study collected additional images outside of the standard 15 areas proposed.[18] Potential resizing of images and the measuring tools used by raters may have resulted in more conservative assessments of ICCs than those obtained from in-person assessments; however, raters were instructed to avoid resizing and images were eventually locked. Future studies comparing the reproducibility of VASI scores from digital images with those acquired in person are necessary. Another limitation of this study was that VASI 10% was only evaluated on a subset of 5

representative participant slide decks by novice and expert raters. The VASI 10% may improve clinicians' ability to detect small changes in vitiligo distribution during treatment vs the standard VASI; however, the current study included a limited number of raters and did not evaluate intrarater reliability. Replication of VASI 10% measurement in multicenter clinical trials is needed to confirm interrater reliability and evaluate intrarater reliability.

Regulatory agencies, including the US Food and Drug Administration, require ClinROs to be "fit for purpose" for inclusion as registration end points in clinical trials. For ClinROs in particular, inter- and intrarater reliability are critical to ensuring accurate readings among all raters and providing confidence in any beneficial treatment-related outcomes obtained from clinical trials.[23,24] Establishing the reproducibility of the VASI from scaled digital images will improve the utility of the VASI as a clinical trial efficacy end point and allow for identification of raters who may benefit from further training.

CONCLUSIONS

Based on inter- and intrarater reliability of T-VASI and F-VASI assessments in the current study, VASI from scaled digital photos was a reliable tool for the assessment of vitiligo severity. VASI 10% showed promise as a potentially more sensitive assessment compared with VASI for a novice user group; however, VASI 10% requires evaluation in further studies. Standardized VASI training will likely improve reproducibility among raters of different experience levels.

Conflicts of interest

Dr Kohli has served as an investigator for Ferndale, Estée Lauder, La Roche Posay Dermatologique, Unigen, Johnson and Johnson, Allergan, Pfizer, and Bayer; has received support from the American Skin Association for a vitiligo project; has served as a consultant for Pfizer,

Johnson and Johnson, Beiersdorf (previously known as Bayer), and ISDIN; and has received salary support from the Dermatology Foundation through a research career development award. Dr Mohammad has served as an investigator for Avita Medical, Clinuvel, Pfizer, Incyte, National Institute for Allergy and Immunology, Ferndale Laboratories, Estée Lauder, Johnson and Johnson, and Allergan; and has received honoraria as an advisory board member for Ferndale Laboratories. Dr Huggins is an investigator for Pfizer, Incyte, Arcutis, Clinuvel, and the Immune Tolerance Network. Dr Lim is an investigator for Incyte, L'Oréal, Pfizer, and PCORI; is a consultant for Pierre Fabre, ISDIN, La Roche-Posay, and Beiersdorf; and has served as a speaker for educational sessions for La Roche-Posay, Cantabria Labs, Pierre Fabre, and Bioderma. Author Deal, and Dr Lukic are employees of Pfizer, Inc and hold shares in Pfizer, Inc. Dr Zhang was an employee of Pfizer, Inc, at the time of this analysis and holds shares in Pfizer, Inc. Dr Hamzavi received honoraria as an advisory board member for Aclaris and is a consultant and investigator for Pfizer, Abbvie, Incyte, Avita, and Clinuvel. Dr Pourang, Dr Ezekwe, and Author Parks-Miller have no conflicts of interest to declare.

REFERENCES

1. Bergqvist C, Ezzedine K. Vitiligo: a review. *Dermatology*. 2020; 236(6):571-592.
2. Chen J, Li S, Li C. Mechanisms of melanocyte death in vitiligo. *Med Res Rev*. 2021;41(2):1138-1166.
3. Elbuluk N, Ezzedine K. Quality of life, burden of disease, comorbidities, and systemic effects in vitiligo patients. *Dermatol Clin*. 2017;35(2):117-128.
4. Krüger C, Schallreuter KU. A review of the worldwide prevalence of vitiligo in children/adolescents and adults. *Int J Dermatol*. 2012;51(10):1206-1212.
5. Gandhi K, Ezzedine K, Anastassopoulos KP, et al. Prevalence of vitiligo among adults in the United States. *JAMA Dermatol*. 2022;158(1):43-50.
6. Sarkar S, Sarkar T, Sarkar A, Das S. Vitiligo and psychiatric morbidity: a profile from a vitiligo clinic of a rural-based tertiary care center of eastern India. *Indian J Dermatol*. 2018; 63(4):281-284.
7. Narayan VS, Uitentuis SE, Luiten RM, Bekkenk MW, Wolkerstorfer A. Patients' perspective on current treatments and demand for novel treatments in vitiligo. *J Eur Acad Dermatol Venereol*. 2021;35(3):744-748.
8. Kubelis-López DE, Zapata-Salazar NA, Said-Fernández SL, et al. Updates and new medical treatments for vitiligo. *Exp Ther Med*. 2021;22(2):797.
9. Karagaiah P, Valle Y, Sigova J, et al. Emerging drugs for the treatment of vitiligo. *Expert Opin Emerg Drugs*. 2020;25(1):7-24.
10. Hamzavi I, Jain H, McLean D, Shapiro J, Zeng H, Lui H. Parametric modeling of narrowband UV-B phototherapy for vitiligo using a novel quantitative tool: the Vitiligo Area Scoring Index. *Arch Dermatol*. 2004;140(6):677-683.
11. van Geel N, Lommerts J, Bekkenk M, et al. Development and validation of the Vitiligo Extent Score (VES): an international collaborative initiative. *J Invest Dermatol*. 2016;136(5):978-984.
12. Kohli I, Veenstra J, Hamzavi I. Vitiligo assessment methods—Vitiligo Area Scoring Index and vitiligo European Task Force assessment. *Br J Dermatol*. 2015;172(2):318-319.
13. Komen L, da Graça V, Wolkerstorfer A, de Rie MA, Terwee CB, van der Veen JP. Vitiligo Area Scoring Index and Vitiligo

European Task Force assessment: reliable and responsive instruments to measure the degree of depigmentation in vitiligo. *Br J Dermatol.* 2015;172(2):437-443.

14. Alghamdi KM, Kumar A, Taïeb A, Ezzedine K. Assessment methods for the evaluation of vitiligo. *J Eur Acad Dermatol Venereol.* 2012;26(12):1463-1471.

15. Kawakami T, Hashimoto T. Disease severity indexes and treatment evaluation criteria in vitiligo. *Dermatol Res Pract.* 2011;2011:750342.

16. Bae JM, Zubair R, Ju HJ, et al. Development and validation of the fingertip unit for assessing facial Vitiligo Area Scoring Index. *J Am Acad Dermatol.* 2022;86(2):387-393.

17. Kitchen H, Wyrwich K, Carmichael C, et al. Meaningful changes in what matters to individuals with vitiligo: content validity and meaningful change thresholds of the Vitiligo Area Scoring Index (VASI). *Dermatol Ther.* 2022;12(7):1623-1637.

18. van Geel N, Hamzavi I, Kohli I, et al. Standardizing serial photography for assessing and monitoring vitiligo: a core set of international recommendations for essential clinical and technical specifications. *J Am Acad Dermatol.* 2020;83(6):1639-1646.

19. Koo TK, Li MY. A guideline of selecting and reporting intraclass correlation coefficients for reliability research. *J Chiropr Med.* 2016;15(2):155-163.

20. Merhi R, Canu D, Barnetche T, et al. Assessment of Vitiligo Area Scoring Index (VASI), facial-VASI and vitiligo extent score using standardized photography of patients with vitiligo. *Br J Dermatol.* 2022;187(3):422-424.

21. Gawkrodger DJ, Ormerod AD, Shaw L, et al. Guideline for the diagnosis and management of vitiligo. *Br J Dermatol.* 2008; 159(5):1051-1076.

22. Kumar Jha A, Sonthalia S, Lallas A, Chaudhary RKP. Dermoscopy in vitiligo: diagnosis and beyond. *Int J Dermatol.* 2018; 57(1):50-54.

23. US Food and Drug Administration. Methods to identify what is important to patients & select, develop or modify fit-for-purpose clinical outcomes assessments. Accessed April 12, 2022. https://www.fda.gov/media/116277/download

24. Powers JH, Patrick DL, Walton MK, et al. Clinician-reported outcome assessments of treatment benefit: report of the ISPOR clinical outcome assessment emerging good practices Task Force. *Value Health.* 2017;20(1):2-14.