Supplementary Online Content

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eAppendix. Supplementary Methods

eTable 1. Vitiligo Impact Patient Scale

eReferences.

eTable 2. Characterization of Participant Survey Respondents

eFigure 1. Global VIPs Scores by Country

eFigure 2. Impact of Vitiligo on Self-Esteem, Relationships, and Careers Overall and by Affected BSA

eFigure 3. Formal Mental Health Diagnoses Among Patients With Vitiligo

eFigure 4. Moderate-to-Severe Depressive Symptoms as Assessed by the PHQ-9 in Patients With Vitiligo by Country

eFigure 5. Moderate-to-Severe Depressive Symptoms as Assessed by the PHQ-9 in Patients With Vitiligo by Geographic Region, Affected BSA, Fitzpatrick Skin Types, and Location of Lesions

This supplementary material has been provided by the authors to give readers additional information about their work.

eAppendix. Supplementary Methods

Study Design and Patients

Patients were recruited from a network of potential participants in 17 countries across several regions (Africa/Middle East [Egypt, Saudi Arabia, South Africa], Asia [China, India, Japan, Philippines, Thailand], Australia, Brazil, Canada, Europe [France, Germany, Italy, Spain, United Kingdom], and the United States). In-person interviews were permitted in markets where the internet was less accessible to achieve the desired sample size. Patients who completed the survey could receive compensation for their time.

This study was conducted in accordance with Good Clinical Practice and the principles embodied by the Declaration of Helsinki. All patients provided electronic or written consent before completing the survey and were allowed to withdraw consent at any time. The study protocol received an exemption from the Western Institutional Review Board based on survey procedures and the use of deidentified data.

Survey Instrument

The survey was designed by Envision Health Partners and Incyte, with input and refinement from a VALIANT steering committee, and translated into local languages using a forward-backward method that was reviewed by a native speaker. Questions were translated verbatim, and the translation was certified; however, questions and were not adapted to be culturally sensitive. The self-administered online screener was designed to capture high-level demographics (eg, age and sex), confirmation of diagnosed vitiligo, and patient consent before patients continued on to the full survey, which took approximately 25 minutes. Patients proceeding to the full survey were asked about the history of their condition and details pertaining to clinical characteristics and emotional well-being, including self-assessment of the extent of vitiligo using the validated Self Assessment Vitiligo Extent Score (SA-VES) tool, 1 which

uses an array of validated images for the patient to self-select, indicating how many vitiligo lesions are on each location of the body, and estimates the affected body surface area.

Survey questions covered the emotional well-being domain, to understand the impact of vitiligo on various behavioral metrics, including daily life and activities, self-esteem, depression, anxiety, and stigmatization. The 12-item short-form Vitiligo Impact Patient scale, a cross-culturally validated tool encompassing several areas where a patient's life may be impacted because of their vitiligo was also administered (6-point scale ranging from 0 [never] to 5 [all the time] with total score ranging from 0–60, with higher scores indicating greater burden).² For simplicity, survey participants were administered all questions, regardless of the Fitzpatrick skin type (ie, fair vs dark skin), and analysis was conducted based on the validated fair and dark skin short-forms (12-items each, some overlapping; eTable³). Finally, assessment of symptoms consistent with depression was conducted using the Patient Health Questionnaire-Depression screener (PHQ-9; scores range from 1 to 27, with scores ≥10 indicating moderate-to-severe depression).⁴ Additional questions regarding emotional well-being, with domains of self-esteem/stigma, relationships, and careers, were assessed on a 5-point scale (range, 1 [strongly disagree] to 5 [strongly agree]).

Statistical Analyses

The target sample size for the survey was approximately 3500 patients. Replacement of patients was allowed following screening failures, with brief demographic characteristics collected to ensure fair representation. To minimize selection bias, characteristics that would allow for comparison of demographics with the expected distributions in the various countries were collected. Respondents retained the right to discontinue the survey for any reason; those who did not complete the entire survey were not included in the analysis set. Respondents were removed from the analysis set for issues of data quality (eg, straight-lining, nonsensical responses, speeding through the survey [ie, completion in <8 minutes]).

The study was not powered to test any formal hypotheses, and reported analyses were considered hypothesis-generating in nature. Mean (SD) or median (range) was reported for continuous variables and percentages were reported for discrete variables. We used *t*-tests for comparisons of means and chi-square tests for categorical counts. Significance was conferred at the level of *P*<0.05; no corrections were made for multiple testing.

eTable 1. Vitiligo Impact Patient scale³

Item*	Parameter	VIPs-12-	VIPs-12-
		FS	DS
1.	I feel discouraged because of my vitiligo	Х	
2.	My vitiligo has repercussions on my physical appearance	Χ	
3.	The progression of my vitiligo worries me (makes me anxious)	Χ	
4.	My reflection in the mirror makes me anxious	X	
5.	I dread nice weather because of my vitiligo	Χ	
6.	Questions about my vitiligo bother me, disturb me	X	
7.	I tend to withdraw into myself because of my vitiligo	X	X
8.	I dread first meetings because of my vitiligo	Χ	X
9.	I dip into my savings to treat my vitiligo	X	X
10.	I make sacrifices to afford my vitiligo treatments	Χ	X
11.	Managing my vitiligo on a daily basis is a burden	Χ	Χ
12.	I often tell myself that my life would be very different without vitiligo		Χ
13.	I experience my vitiligo as a daily handicap		Χ
14.	My vitiligo has a negative impact on my libido (sexual desire)		X
15.	My vitiligo is an obstacle (a barrier) to my sexuality	X	
16.	In the evening, once I've applied all the creams, I feel depressed		X
17.	I have had to change my vacations, leisure activities because of my vitiligo		X
18.	I am ashamed of the consequences of my vitiligo		X
19.	I feel that medicine has abandoned me		Χ
20.	The looks I get from children because of my vitiligo are hurtful		

DS, dark skin; FS, fair skin; VIPs-12, Vitiligo Impact Patient scale 12-item.

^{*} The 20 questions were used for a further factor analysis of the VIPs tool (data not shown).

eReferences

- van Geel N, Lommerts JE, Bekkenk MW, et al. Development and validation of a patientreported outcome measure in vitiligo: the Self Assessment Vitiligo Extent Score (SA-VES). J Am Acad Dermatol. 2017;76(3):464-471.
- 2. Ezzedine K, Ahmed M, Tovar-Garza A, et al. Cross-cultural validation of a short-form of the Vitiligo Impact Patient scale (VIPs). *J Am Acad Dermatol.* 2019;81(5):1107-1114.
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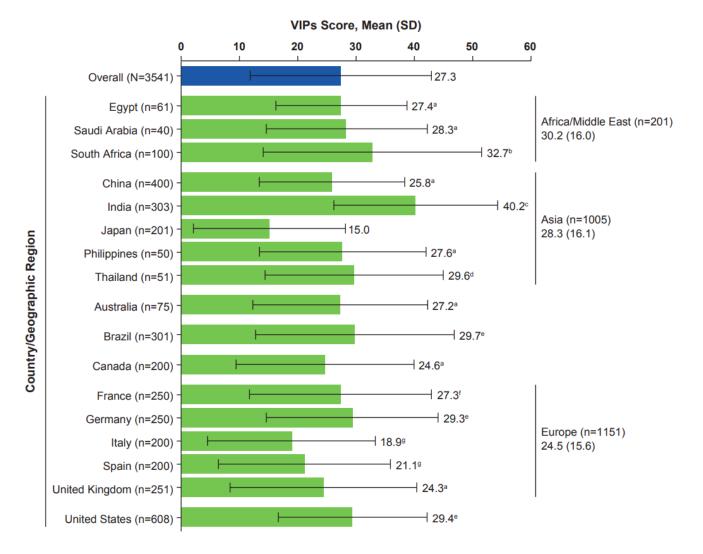
eTable 2. Characterization of Participant Survey Respondents

	Invited Participants
Patients, n (%)	(N=881,522)
Responded to invitation	197,858 (22.4)
Not eligible	194,317 (98.2)
Quota already filled*	1454 (0.7)
Ineligible response	165,479 (85.2)
Did not have vitiligo	162,862 (98.4)
Was not diagnosed with vitiligo by a medical professional	2083 (1.3)
Did not consent to survey	156 (0.1)
Data quality issues [†]	378 (0.2)
Survey not completed	26,476 (13.6)
Clicked the survey but did not proceed or finish the screener	21,422 (80.9)
Did not finish the screener	4789 (18.1)
Qualified in the screener but did not complete the survey	265 (1.0)
Age <18 y	908 (0.5)
Eligible adult patients included in analysis	3541 (1.8)

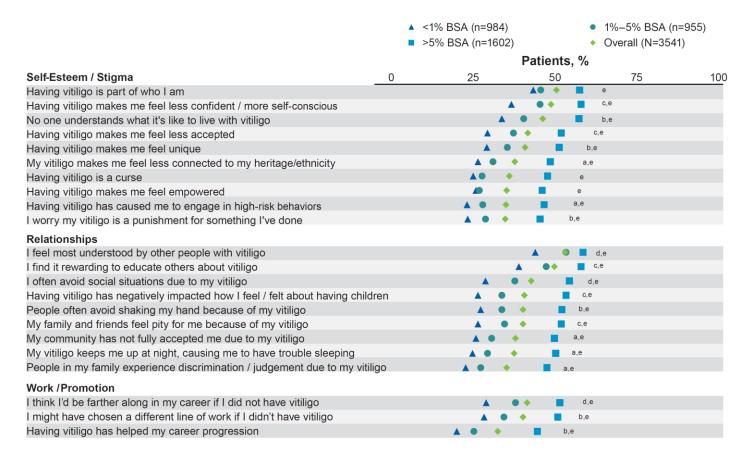
^{*} Census-based quota for age and sex were already filled.

† Patients met all eligibility criteria but were removed for the following data quality issues: (1) n=248: completed the 25-minute survey in <8 minutes and/or provided identical ratings on scale questions for 2 entire questions (42 attributes); (2) n=130: incongruous/nonsensical responses.

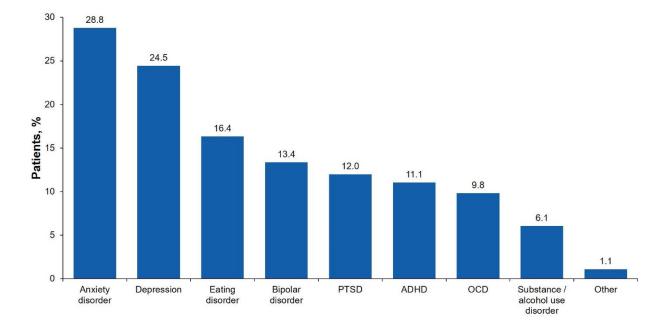
eFigure 1. Global VIPs Scores by Country. VIPs, Vitiligo Impact Patient scale. ^a *P*<0.05 vs Spain, Italy, and Japan; ^b *P*<0.05 vs United Kingdom, France, Spain, Italy, Canada, Australia, Japan, China, and Egypt; ^c *P*<0.05 vs all other countries; ^d *P*<0.05 vs United Kingdom, Spain, Italy, Canada, Japan, and China; ^f *P*<0.05 vs United Kingdom, Spain, Italy, and Japan; ^g *P*<0.05 vs Japan.



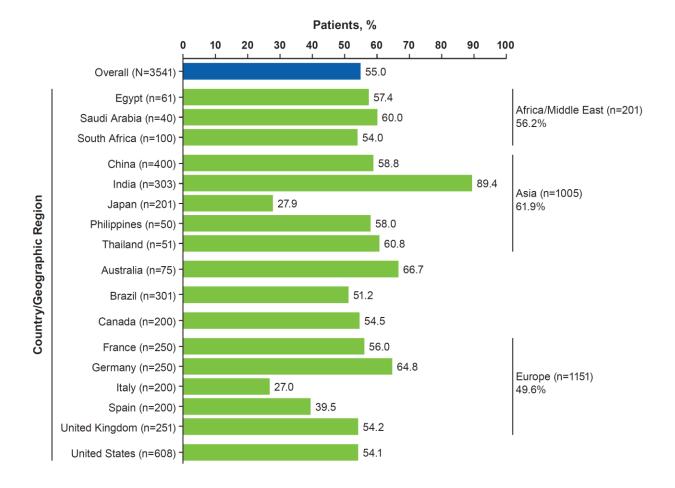
eFigure 2. Impact of Vitiligo on Self-Esteem, Relationships, and Careers Overall and by Affected BSA*†. BSA, body surface area; SA-VES, Self Assessment Vitiligo Extent Score. * Includes patients who responded to these questions with "agree" or "strongly agree." † BSA was determined using the SA-VES. ^a *P*<0.05 vs <1% BSA for 1%–5% BSA. ^b *P*<0.01 vs <1% BSA for 1%–5% BSA. ^d *P*<0.0001 vs <1% BSA for 1%–5% BSA. ^d *P*<0.0001 vs <1% BSA for 1%–5% BSA.



eFigure 3. Formal Mental Health Diagnoses Among Patients With Vitiligo.* ADHD, attention-deficit/hyperactivity disorder; OCD, obsessive-compulsive disorder; PTSD, posttraumatic stress disorder. * Multiple answers were accepted.



eFigure 4. Moderate-to-Severe Depressive Symptoms as Assessed by the PHQ-9 in Patients With Vitiligo by Country. Significance between countries was not determined for the combination of moderate (score, 10–14), moderately severe (score, 15–19), and severe (score 20–27) symptoms of depression.



eFigure 5. Moderate-to-Severe Depressive Symptoms as Assessed by the PHQ-9 in Patients With Vitiligo by Geographic Region, Affected BSA, Fitzpatrick Skin Types, and Location of Lesions. BSA, body surface area; PHQ-9, Patient Health Questionnaire-Depression screener. * Fitzpatrick skin types I–III were characterized as fairer and types IV–VI as darker skin types. † Patients with 0% affected BSA (n=87) were excluded from analysis. a P<0.01 vs Brazil, Europe, and United States. b P<0.05 vs Brazil, Europe, and United States. P<0.001 vs Reponded P<0.0001 vs -1% BSA. P<0.0001 vs -1% BSA. P<0.0001 vs no facial lesions. P<0.0001 vs no hand lesions. P<0.0001 vs no facial or hand lesions.

