

Drivers of depression and anxiety in US nonsegmental vitiligo patients

Babak Mohit¹; Sean Fleming¹; Joanne Brady¹; Simran Marwaha²; Jenny Austin²; Emily Quinones²; Chloe Middleton-Dalby²

¹Merck & Co., Inc., Rahway, NJ USA; ²Adelphi Real World, Bollington, UK

Background

- Nonsegmental vitiligo (NSV) is an immune-mediated disorder of pigmentation which is most often characterized by prominent white patches on the skin¹
- While NSV is predominantly defined by its cosmetic presentation, it can be detrimental to patients’ psychosocial health, with over half of all NSV-diagnosed patients experiencing feelings of depression and anxiety²⁻⁴
- There is limited real-world evidence investigating the burden of disease in patients with vitiligo in the United States (US)
- In this study, we used a machine learning technique to explore the multidimensional factors, beyond clinical features, that may be associated with feelings of depression and anxiety in NSV patients

Methods

- Data source**
- Data were drawn from the Adelphi Vitiligo Disease Specific Programme (DSP™)⁵⁻⁷, a cross-sectional survey (from October 2021 to April 2022) of dermatologists and their adult and adolescent NSV patients in the US
 - Dermatologists reported patient demographics and clinical characteristics, including assessment of patient’s current severity and treatment history, for their next 8 consulting NSV patients (6 adults, and 2 adolescents aged 12-17 years)
 - These same patients were invited to complete a voluntary questionnaire on feelings about their vitiligo and its impact on their lives, including the Vitiligo Noticeability Scale (VNS, assessing noticeability of lesions since starting treatment⁸) and the Hospital Anxiety and Depression Scale (HADS)⁹
 - The HADS is a validated, 14-item self-reported scale assessing patients’ feelings of depression (7 items) and anxiety (7 items) over the past 7 days. Scoring for each item ranges from zero to three, with three denoting the highest depression or anxiety level. The total subscale score ranges from 0-21 where a higher score indicates higher distress, however the HADS does not offer a confirmed diagnosis and is only valid for screening purposes^{9,10}

- Study analysis**
- Elastic net regressions were conducted to identify important predictors of HADS depression scores and HADS anxiety scores, from 87 possible variables
 - Elastic net is a machine learning technique that identifies variables which have an impact on an outcome using a combination of L1 (LASSO) and L2 (Ridge) regularization techniques. This method does not provide p-values or confidence intervals for the predictors due to the use of machine learning
 - Patients with HADS depression and anxiety scores, and valid, non-missing responses for all covariates added to the model were included in the analysis
 - Data were managed and analyzed using Stata version 18.0¹¹

Disclosures

Merck did not influence the original survey through either contribution to the design of questionnaires or data collection. The analysis described here used data from the Adelphi Real World Vitiligo DSP. The DSP is a wholly owned Adelphi Real World product. Merck is one of multiple subscribers to the DSP. Publication of survey results was not contingent on the subscriber’s approval or censorship of the publication.

Babak Mohit, Sean Fleming, and Joanne Brady are employees of Merck. Simran Marwaha, Jenny Austin, Emily Quinones, and Chloe Middleton-Dalby are employees of Adelphi Real World.

References

- Joge R, et al. Vitiligo: A Narrative Review. *Cureus*. 2022;14(9):e29307.
- Ezzedine K, et al. Vitiligo is not a cosmetic disease. *J Am Acad Dermatol*. 2015;73(5):893-895.
- Morrison B, et al. Quality of life in people with vitiligo: a systematic review and meta-analysis. *Br J Dermatol*. 2017;177(6):e338-e339.
- Osinubi, O., et al. (2018). The prevalence of psychological comorbidity in people with vitiligo: a systematic review and meta-analysis. *British Journal of Dermatology*, 178(4), 863-878.
- Anderson P, et al. Real-world physician and patient behaviour across countries: disease specific programmes – a means to understand. *Curr Med Res Opin*. 2008;24:3063–307
- Babineaux SM, et al. Evidence for validity of a national physician and patient-reported, cross-sectional survey in China and UK: the Disease Specific Programme. *BMJ Open*. 2016;6(8):e010352.
- Higgins V, et al. Trends in medication use in patients with type 2 diabetes mellitus: a long-term view of real-world treatment between 2000 and 2015.
- Batchelor, et al. (2022). Using the Vitiligo Noticeability Scale in clinical trials: construct validity, interpretability, reliability and acceptability. *British Journal of Dermatology*, 187(4), 548-556.
- Snath, R.P. The Hospital Anxiety And Depression Scale. *Health Qual Life Outcomes* 1, 29 (2003). <https://doi.org/10.1186/1477-7525-1-29>
- Rishi, P, et al. (2017). Hospital anxiety and depression scale assessment of 100 patients before and after using low vision care: A prospective study in a tertiary eye-care setting. *Indian journal of ophthalmology*, 65(11), 1203–1208. https://doi.org/10.4103/ijo.IJO_436_17
- StataCorp. 2023. Stata Statistical Software: Release 18. College Station, TX: StataCorp LLC

Results

- Of the 112 NSV patients included in this analysis, 54.5% were female, 59.8% were white, mean age was 35 years old, and 33.9% of patients reported at least one concomitant condition (**Table 1**)
- Table 1** shows 9.8% of patients had severe NSV at the time of data collection, 48.1% had moderate, and 42.0% had mild NSV, while approximately 50.9% had vitiligo affecting their face

Table 1. Patient demographics and clinical characteristics

	NSV patients (n=112)
Age , mean (SD)	35.3 (33.0)
Proportion of ≥18 years, n (%)	96 (85.7)
Proportion of 12-17 years, n (%)	16 (14.3)
Sex , female, n (%)	61 (54.5)
Ethnicity , n (%)	
White/Caucasian	67 (59.8)
African American	26 (23.2)
Mixed race	12 (10.7)
Employed , n (%)	(n=96)
Working full time	71 (74.0)
Working part time	3 (3.1)
Time since diagnosis , months	(n=82)
Mean	34.9
Median (IQR, interquartile range)	22.9 (7.7, 42.9)
Physician-reported current severity , n (%)	
Mild	47 (42.0)
Moderate	54 (48.1)
Severe	11 (9.8)
Face affected currently , n (%)	57 (50.9)
Concomitant conditions (top 3), n (%)	
Thyroid condition	14 (12.5)
Inflammatory bowel disease	9 (8.0)
Diabetes without chronic complications	3 (2.7)
No concomitant conditions	74 (66.1)
Fitzpatrick skin type , n (%)	
Type I/II	32 (28.6)
Type III/IV	52 (46.4)
Type V/VI	28 (25.0)

- Figure 1** reports the frequency of HADS depression and anxiety scores. For the depression subscale, n=72 had no feelings of depression, while n=40 reported to some extent at least one behavior related to depressive feelings, with n=7 classified as borderline abnormal. For the anxiety subscale, n=50 reported no feelings of anxiety, while n= 62 reported at least one behavior related to feelings of anxiety, with n=18 classified as borderline abnormal/abnormal

Figure 1. HADS anxiety and depression scores

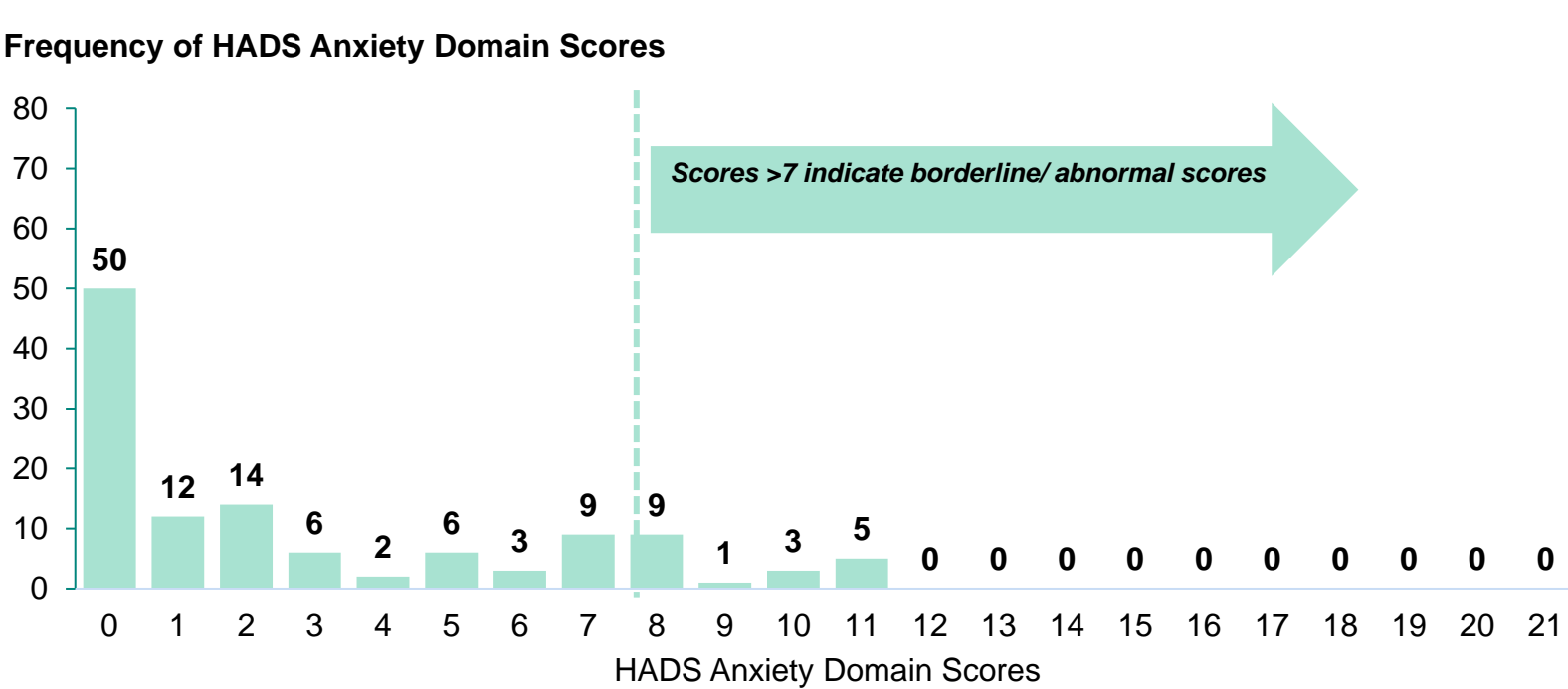
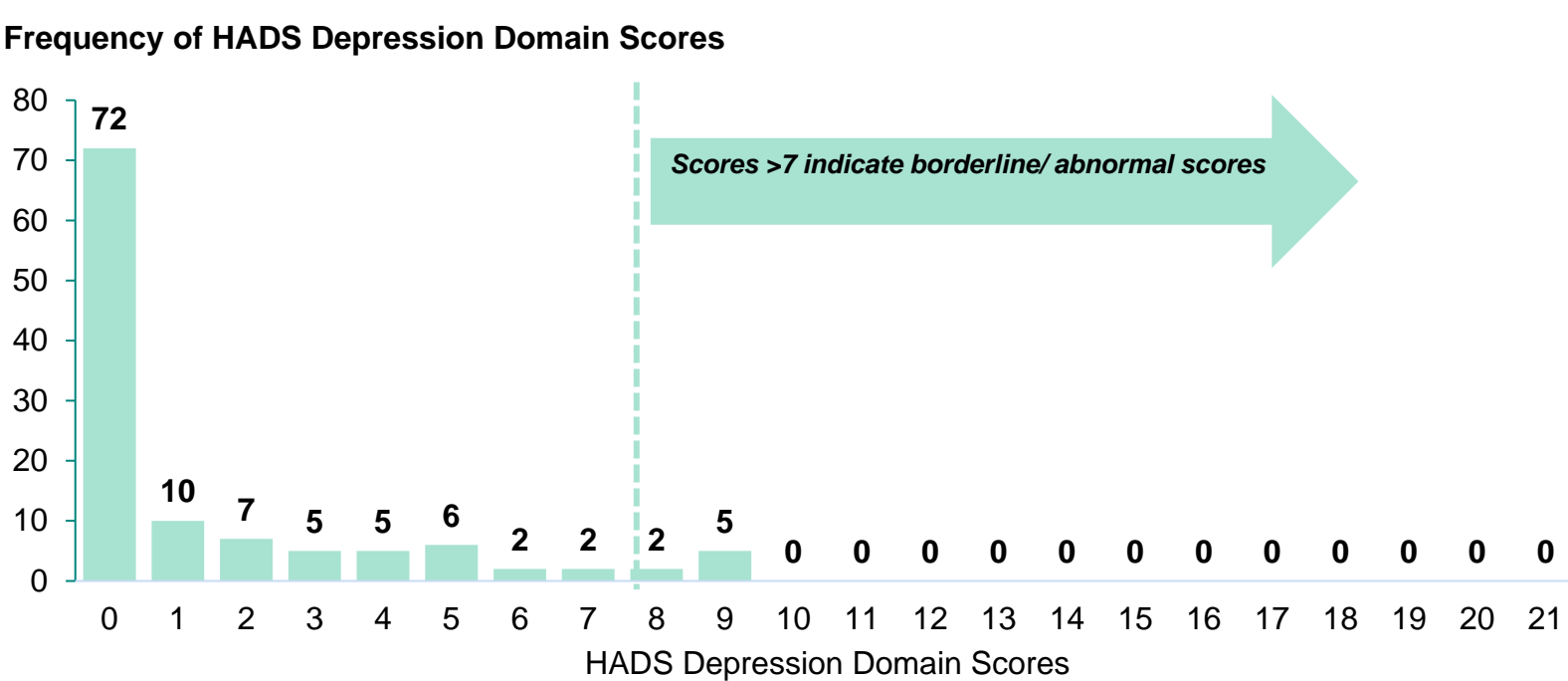
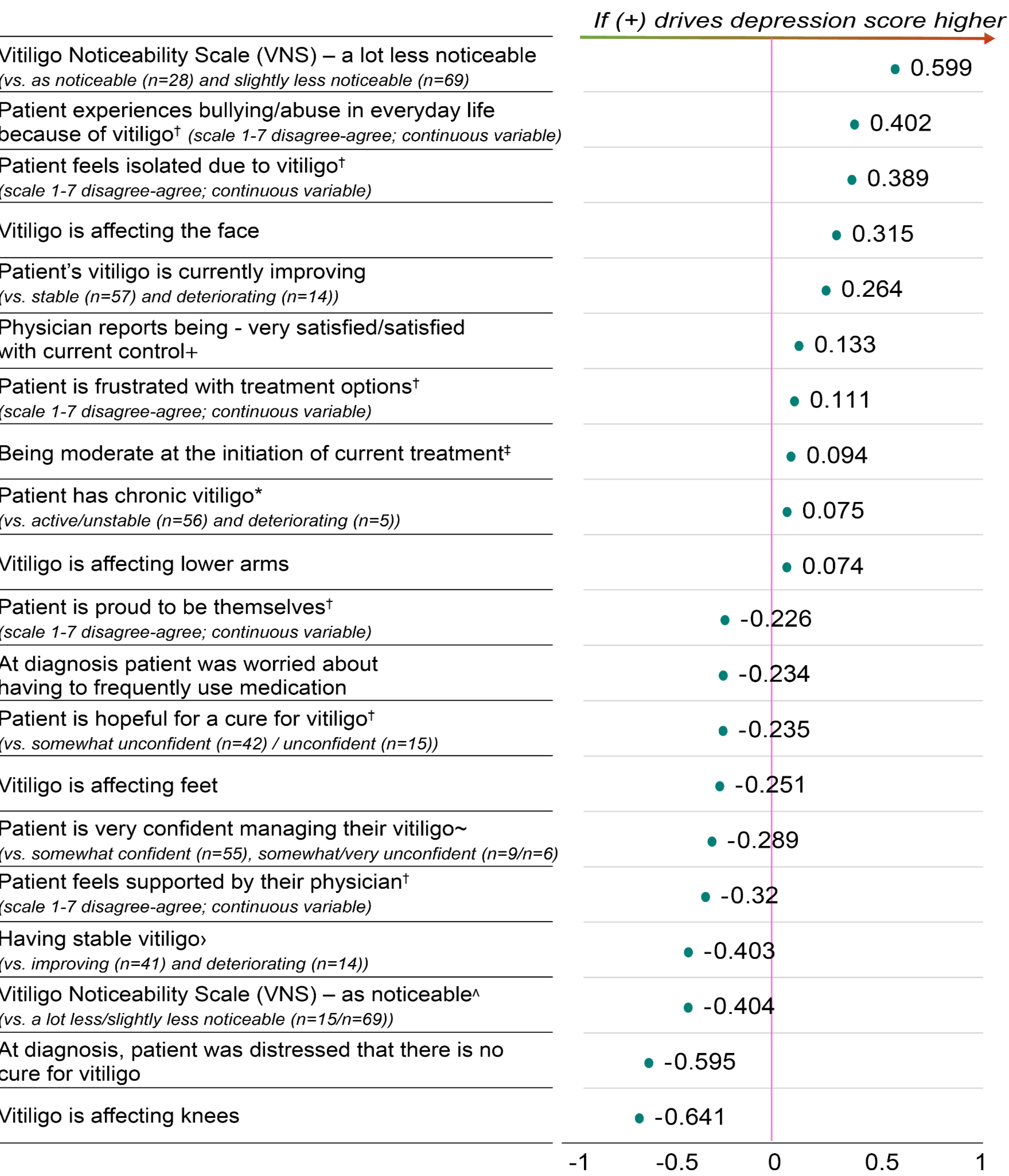


Figure 1 HADS domain categorization cutoffs define scores 8-10 borderline abnormal and scores 11-21 as abnormal, scores 0-7 are classified as normal. For any score above 0, the patient must have indicated that they are at least to some extent experiencing a feeling related to depression or anxiety for at least one item on the respective subscale

- Figure 2** shows that vitiligo reported as a lot less noticeable since starting current treatment (vs. as noticeable or slightly less noticeable) ($\beta = 0.599$), experiencing bullying in everyday life due to their vitiligo ($\beta = 0.402$), feeling isolated due to their vitiligo ($\beta = 0.389$), and vitiligo affecting their face ($\beta = 0.315$) were all associated with increased feelings of depression assessed through the HADS depression subscale

Figure 2. Top 20 predictors of HADS depression from the elastic net regression



- Figure 2.** General themes of 87 cofounder variables - selected predictor groups for HADS depression: Fitzpatrick skin type; physician/patient-reported affected body areas; type of vitiligo; disease progression; severity at initiation of current treatment; VNS; feelings at diagnosis; physician-reported satisfaction; general feelings towards vitiligo; confidence in disease management

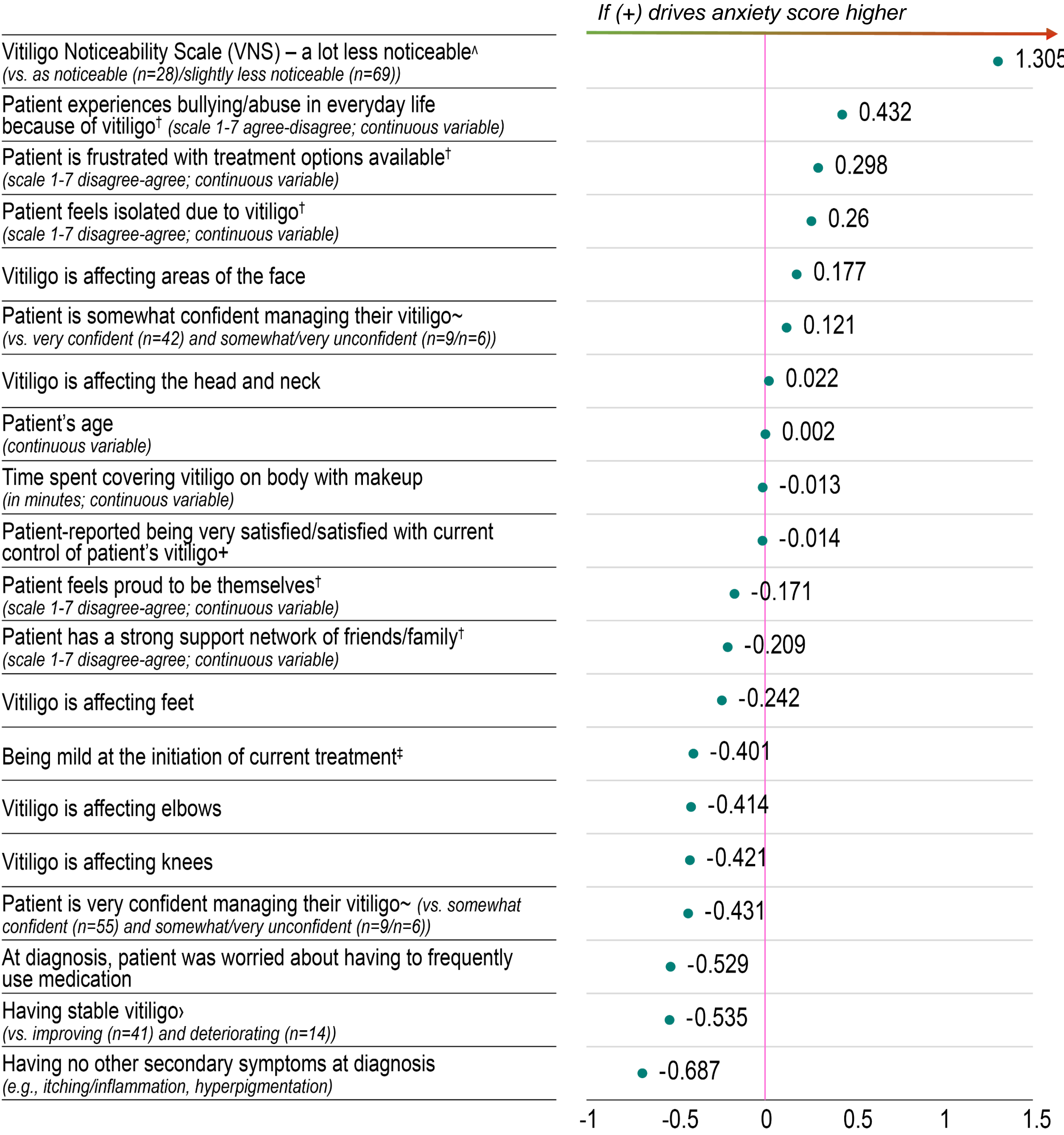
[†]Patient-reported feeling on a 1-7 scale, where 1=completely disagree and 7=completely agree. As patients move towards completely agreeing with statements, HADS domain score increases if coefficient is positive and decreases if negative.
~Patient-reported confidence in management: very confident (n=42) somewhat confident (n=55), somewhat unconfident (n=9), very unconfident (n=6).
*Type of vitiligo: active/unstable – depigmenting 1-2% per month (n=51), chronic – depigmentation for ≥1 year (n=56), refractory – responds poorly to treatment (n=5).
+Physician reported satisfaction on a 5-point likert scale, where 1=very satisfied and 5=very dissatisfied: 1-2=satisfied (n=76), 3=neither satisfied/dissatisfied (n=30), 4-5=dissatisfied (n=6).
^Severity at initiation of current treatment: mild (n=29), moderate (n=67), severe (n=16).
^VNS: no longer noticeable (n=0), more noticeable (n=0), as noticeable (n=28), slightly less noticeable (n=69), a lot less noticeable (n=15).
>Vitiligo disease progression: improving (n=41), stable (n=57), deteriorating (n=14).

Conclusions

- The elastic net regression identified multiple factors that may predict anxiety and depression in patients with NSV
- Some of these factors including patients’ vitiligo being less noticeable and improvement in disease severity were identified as drivers of feelings of depression and anxiety. These findings may have been confounded by latent factors, e.g., baseline disease severity or time since diagnosis, which were not included in the elastic net models
- Other factors such as feelings of societal isolation and stigmatization due to NSV, vitiligo with facial involvement, and frustration with treatment options were found to be associated with increased feelings of depression and anxiety in line with expectations
- Further finetuning of the machine learning model may be needed to conclusively establish associations between potential predictors and feelings of anxiety and depression in patients with vitiligo

- Figure 3** shows that vitiligo being reported as a lot less noticeable since starting current treatment (vs. as noticeable or slightly less noticeable) ($\beta = 1.305$), experiencing bullying in everyday life due to vitiligo ($\beta = 0.432$), frustration with treatment options ($\beta = 0.298$), feeling isolated due to vitiligo ($\beta = 0.260$), and vitiligo affecting their face ($\beta = 0.177$) were all key drivers of increased feelings of anxiety assessed through the HADS anxiety subscale

Figure 3. Top 20 predictors of HADS anxiety from the elastic net regression



- Figure 3.** General themes of 87 cofounder variables - selected predictor groups for HADS anxiety: Patient’s age; physician-reported affected body areas; symptoms at diagnosis; patient-reported affected body areas; disease progression; severity at initiation of current treatment; VNS; feelings at diagnosis; patient-reported satisfaction; general feelings towards vitiligo; confidence in disease management.

[†]Patient-reported feeling on a 1-7 scale, where 1=completely disagree and 7=completely agree. As patients move towards completely agreeing with statements, HADS domain score increases if coefficient is positive and decreases if negative.
~Patient-reported confidence in management: very confident (n=42) somewhat confident (n=55), somewhat unconfident (n=9), very unconfident (n=6).
*Patient-reported satisfaction on a 5-point likert scale, where 1=very satisfied and 5=very dissatisfied: 1-2=satisfied (n=77), 3=neither satisfied/dissatisfied (n=24), 4-5=dissatisfied (n=11).
^Severity at initiation of current treatment: mild (n=29), moderate (n=67), severe (n=16).
^VNS: no longer noticeable (n=0), more noticeable (n=0), as noticeable (n=28), slightly less noticeable (n=69), a lot less noticeable (n=15).
>Vitiligo disease progression: improving (n=41), stable (n=57), deteriorating (n=14).

Limitations

- The DSP patient sample is representative of the consulting patient population, but may not accurately represent the total vitiligo patient population
- The cross-sectional methodology cannot be used to demonstrate cause and effect
- In elastic net models, analysis is data-driven not theory-driven. This can lead to unintuitive findings which require more research to understand why certain variables are having an impact
- In the study sample, most NSV patients reported low scores on the HADS subscales. However, due to the analytic method using continuous HADS scores, it may allow us identify factors that drive feelings of depression and anxiety higher