



ORIGINAL ARTICLE

Patients' perspective on current treatments and demand for novel treatments in vitiligo

V.S. Narayan,*  S.E. Uitentuis,  R.M. Luiten, M.W. Bekkenk, A. Wolkerstorfer

Department of Dermatology, Netherlands Institute for Pigment Disorders, Amsterdam Infection and Immunity Institute, Amsterdam University Medical Center, Amsterdam, the Netherlands

*Correspondence: V.S. Narayan. E-mail: v.s.narayan@amsterdamumc.nl

Abstract

Background The treatment of non-segmental vitiligo (NSV) remains a challenge. Current treatments often achieve sub-optimal clinical results. To improve these treatment results, several new therapies are being developed and investigated. There is, however, little evidence on the actual need for novel therapies.

Objective To assess patients' perspective on current and novel therapies for vitiligo.

Methods A prospective questionnaire study was conducted in a large cohort of vitiligo patients that consecutively visited the outpatient clinic of the Amsterdam University Medical Centre between April 2017 and January 2019. Patients were requested to fill in a digital questionnaire on patient characteristics, disease burden, quality of life, efficacy and satisfaction of current treatments and aspects regarding new treatments.

Results A total of 325 vitiligo patients completed the questionnaire (60% response rate). Of the respondents, 94% believed that new and improved treatments are needed and 86% would be willing to participate in clinical trials investigating a new therapy. Sixty-nine per cent would agree on taking weekly injections if it led to effective treatment results. Of the patients that had received therapy before, 49% reported that the current treatments were not effective and 50% was not satisfied with the current treatments. Sixty-seven per cent of the patients experienced facial lesions as an extreme burden, whereas this was, 25%, 12% and 10% for lesions on the hands, trunk and feet, respectively. The emotional burden score was significantly higher in dark skin types compared with light skin types (respectively, 8 vs 5, $U P < 0.05$).

Conclusion There is a substantial need for new vitiligo therapies. A considerable number of patients in our study are dissatisfied with current treatments and are emotionally burdened by the disease. Moreover, the vast majority demands novel treatments and is willing to participate in clinical trials.

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Conflicts of Interest

None declared.

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None.

Introduction

Vitiligo is the most common depigmenting skin disease affecting approximately 1% of the world population, regardless of gender, ethnicity or skin type.¹ Although problems like itch and a history of sunburns are common, vitiligo generally does not lead to physical complaints.² However, the disease is strongly associated with a significant negative effect on the quality of life, as many of the patients feel stressed and stigmatized by their condition.^{3,4}

To date, there is no curative treatment available for vitiligo. For many years, now vitiligo therapy consists of topical agents, phototherapy and surgical techniques, which all aim to minimize

disease progression and/or stimulate repigmentation.⁵ So far, current treatment results vary between patients and a considerable number of patients do not sufficiently benefit from treatment.

To improve these suboptimal treatment results, several new therapies are being developed and investigated.⁵⁻⁸ However, for the clinical implementation of these new treatments it is crucial to know the vitiligo patients' need for novel treatment modalities. What are these novel therapies worth to a patient? And how satisfied are patients in fact with the current treatments? More knowledge of these factors could be of great value to various

stakeholders, such as physicians, policymakers and pharmaceutical companies.

Furthermore, many studies have shown that vitiligo is associated with a substantial disease burden, using various measurement tools.^{9–11} In addition, a few studies have related psychological complaints and quality of life to the location of the vitiligo lesions, showing a higher impact on exposed areas, such as the face.^{12–14} However, various other studies indicate that other body regions have larger impact on the quality of life and/or disease burden. For example, Linthorst Homan et al. showed that vitiligo particularly on the chest had an impact on the health-related quality of life, whereas lesions on the hands and face did not.² Another study found that lesions on the genital area were associated with a high burden.¹¹ Florez-Pollack et al. illustrated that lesions on the hands were even more bothersome compared with the face and neck.¹⁵ We hypothesize that the disease burden and its relation to the location of the various vitiligo lesions could be correlated with the demand for new therapies.

To address these issues, we performed a cross-sectional prospective survey. The aim of this study was to assess the patients' perspective on current and novel therapies for vitiligo. Furthermore, we aimed to compare demographic features, such as gender, skin type and location of lesions (e.g. facial vs. non-facial) in relation to the primary outcomes on satisfaction of current treatments, disease burden and demand for new therapies.

Patients and methods

Patients

This prospective questionnaire study was conducted in a cohort of vitiligo patients at the Netherlands Institute for Pigment Disorders (NIPD) of the Amsterdam University Medical Centre (UMC). This institute is a centre of expertise for vitiligo and has a nation-wide patient population. All patients with non-segmental vitiligo (NSV), aged 16 years or older that had consecutively visited our outpatient clinic between April 2017 and January 2019, were approached. Patients with segmental, focal and universal vitiligo were not included, since these subtypes differ in management, treatment and prognosis and cannot be compared to NSV for this study purpose.

Patients of whom the email address was registered in the electronic patient system received an email with a secured online questionnaire carried out by LimeSurvey version 2.6.7. Patients of whom the email addresses were not registered were not additionally contacted. If a patient did not respond, a reminder was sent after 1 month. Only fully completed responses were included in the final analysis. This study was not subject to the WMO (Medical Research Involving Human Subjects Act) as confirmed by the Medical Ethical Committee of the Amsterdam UMC (EC number W17_349).

Questionnaire

We developed an online questionnaire consisting of questions regarding; (i) demographics, (ii) disease burden, (iii) current treatment results, (iv) novel therapies and (v) quality of life (Appendix S1).

Demographic questions included age, gender, location of the vitiligo lesions and the vitiligo disease activity (VIDA) score. Patients were requested to indicate the disease burden of their vitiligo lesions in relation to the location of these lesions. Furthermore, they were asked to score their emotional disease burden on a visual analogue scale from 0 to 10 (where 0 means no burden at all and 10 means an extreme burden). Patients were asked two questions in total about the effectiveness and satisfaction of current therapies. Three questions were included regarding novel therapies. First, patients were asked if they thought new and improved therapies for vitiligo are needed. Secondly, patients were requested to indicate whether they would accept vitiligo therapy if it consisted of weekly injections. A third question was included about the willingness to participate in a clinical trial investigating a new vitiligo therapy, if patients would not receive any payments for participation and if this would be free of treatment costs. Finally, 10 questions of the Dermatology Life Quality Index (DLQI) were included to assess the quality of life.

Statistical analysis

Only fully completed responses were included in the final analysis. Descriptive statistics were used to analyse the demographics of the study population. To compare means and medians, respectively, t-tests and Mann–Whitney *U* tests (*U*) were performed. Spearman rank correlation coefficient (r_s) was used for correlation analysis, and Pearson chi-square tests (χ^2) were used to analyse categorical data. A *P*-value of <0.05 was considered statically significant. All statistical analyses were performed in SPSS version 25.0 (IBM, Armonk, NY).

Results

Of the 920 patients with NSV, aged 16 or older that visited our outpatient clinic, 542 patients had a functioning email address that was available to us. Questionnaires were sent to a total of 542 patients of whom 377 (70%) responded. Of these, 325 (60%) patients fully completed the questionnaire, 7 patients declined (1%) and 45 (9%) patients started the questionnaire, but did not complete it. Patient and vitiligo characteristics are presented in Table 1.

Primary survey outcomes

The primary survey outcomes are shown in Table 2. Of all patients, 94% indicated that new and improved treatment modalities are needed for vitiligo. Half of the patients were not or little satisfied with the current therapies, and 49% indicated that the current treatments were not or little effective. The

Table 1 Patient and vitiligo characteristics

Characteristics	
Male: female ratio	133: 192
Mean age \pm SD (min-max) in years	41 \pm 14 (16–77)
Mean age of onset \pm SD (min-max) in years	31 \pm 16 (0–76)
Disease duration median in years [IQR]	7 [3–16]
Parameter	N (%)
Vitiligo disease activity (VIDA score)	
Activity in past 6 weeks	31 (10)
Activity in past 3 months	37 (11)
Activity in past 6 months	33 (10)
Activity in past year	104 (32)
Stable at least for 1 year	69 (21)
Stable for 1 year and spontaneous repigmentation	51 (16)
Skin type	
I	11 (3)
II	202 (62)
III	58 (18)
IV	20 (6)
V	25 (8)
VI	9 (3)
Previous treatments	
Has had treatment before for vitiligo	323 (99)
Use of creams	322 (99)
Use of NB-UVB light therapy	221 (68)
Skin transplantations	25 (8)

demand for new treatments did not significantly differ between males and females ($\chi^2 P = 0.305$). No association was found between the location of vitiligo lesions and the demand for new therapies (Fisher's exact test $P = 0.558$). Dark skin type patients (Fitzpatrick 4–6) did not have a higher need for new therapies than light skin type patients (Fitzpatrick 1–3) (Fisher's exact test $P = 0.217$). However, darker patients were significantly more willing to receive a new effective treatment if it consisted of weekly injections ($\chi^2 p = 0.029$). No relations were found for gender, location of lesions and skin type with regard to the willingness to participate in clinical trials.

Satisfaction with current treatments

The lesser satisfied patients were with current treatments, the more they indicated a need for new and improved therapies ($r_s = -0.18$, $P = 0.002$). The satisfaction is significantly correlated with the effectiveness from patients view of current treatments ($r_s = 0.778$, $P = 0.00$). Patients who had received UVB therapy were significantly more satisfied with treatment than patients who had not received UVB therapy ($\chi^2 P = 0.001$). The same applies to skin transplantation treatment ($\chi^2 P = 0.001$). No relation was found between skin type and satisfaction with current therapies ($\chi^2 P = 0.19$). Patients with facial vitiligo were significantly more satisfied with treatments than patients that

Table 2 Primary survey outcomes

Parameter	N (%)
Effectiveness of current treatments	
Not effective	56 (17)
Little effective	104 (32)
Effective	93 (29)
Very effective	55 (17)
Not applicable	17 (5)
Satisfaction regarding current treatments	
Not satisfied	63 (19)
Little satisfied	99 (31)
Satisfied	96 (30)
Very satisfied	45 (14)
Not applicable	22 (7)
Need for novel treatments: yes	305 (94)
Study participation: yes	281 (87)
New effective treatment if consisted of weekly injections: yes	224 (69)

did not have facial lesions ($\chi^2 P = 0.003$). No difference in satisfaction was found between males and females ($\chi^2 P = 0.321$).

Disease burden and Dermatology Life Quality Index

The median of the emotional disease burden score during lifetime was 5 [IQR 3–8] and over the past week was 3 [IQR 1–6] (Fig. 1). The burden score over the past week was significantly lower than the score during lifetime (Wilcoxon signed-rank test, $P = 0.000$). Of all our patients, 28% had a DQLI total score higher than 5, which indicates a moderate-to-severe impaired quality of life (Fig. 2). The emotional burden score of the past week was significantly correlated with the total scores of the DLQI ($r_s = 0.607$ $P = 0.000$). The lifetime emotional burden score was significantly higher in darker skin types compared with lighter skin types (median 8 vs 5, $U P = 0.000$). In addition, female patients had a significantly higher emotional burden score than male patients (t -test, $P = 0.002$).

In Figure 3, the burden of the disease is shown for each body region. Sixty-seven per cent of the patients experienced their facial lesions as an extreme burden, whereas this was 25%, 12% and 10% for lesions on the hands, trunk and feet, respectively. Patients that experienced facial lesions as an extreme burden were significantly more convinced that new and improved vitiligo treatments are needed ($\chi^2 P = 0.033$). Furthermore, the emotional burden score of the past week had a significant relation with (i) the demand for novel treatment ($r_s = 0.147$ $P = 0.002$), (ii) the willingness to participate in clinical trials ($r_s = 0.131$ $P = 0.018$) and (iii) the acceptance of taking invasive therapy ($r_s = 0.263$ $P = 0.000$). The same applies to the DLQI total scores with the demand for new treatment ($r_s = 0.226$ $P = 0.000$), willingness to participate in clinical trials ($r_s = 0.175$ $P = 0.002$) and acceptance of taking invasive therapy ($r_s = 0.327$ $P = 0.000$). An overview of the statistical differences and correlations can be found in Table S1.

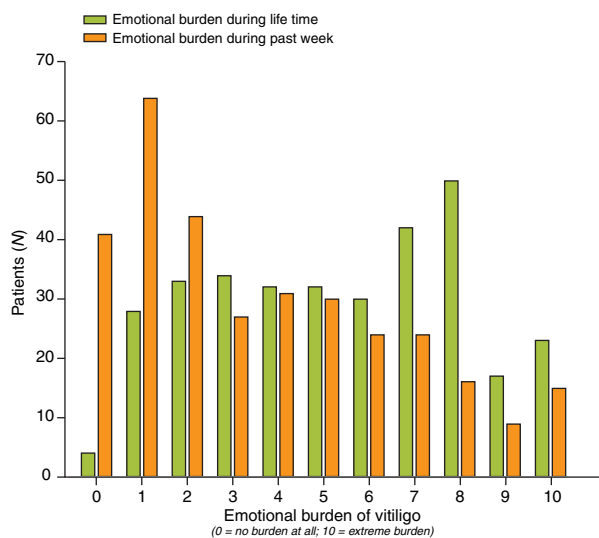


Figure 1 Emotional burden of vitiligo. The bar graph represents the emotional burden that vitiligo patients have experienced during their lifetime (black bars) and during the past week (white bars). On the x-axis, the numbers are shown for the degree of emotional burden (0 is no burden at all, 10 is an extreme burden). The y-axis represents the number of patients.

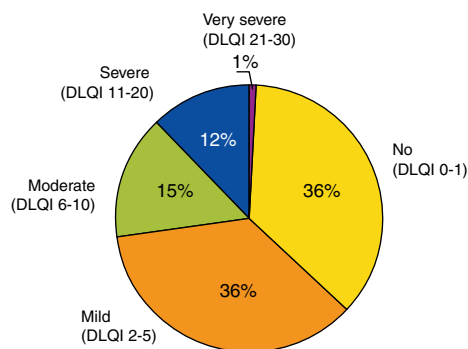


Figure 2 Dermatology Quality Life Index total scores. Dermatology Life Quality Index (DLQI) total scores distribution between the patients. Percentage of total number of patients ($n = 325$) shown. DLQI total scores of 0–1 represent no effect at all on patient’s life, 2–5 represent a mild effect, 6–10 represent a moderate effect, 11–20 a severe effect and 21–30 a very severe effect on a patient’s life.

Discussion

Our study clearly demonstrates the substantial demand of vitiligo patients for new therapies. Ninety-four per cent of the vitiligo patients included in this study indicate that new and better treatments are needed for vitiligo. Consequently, a majority of these patients is willing to participate in clinical trials for

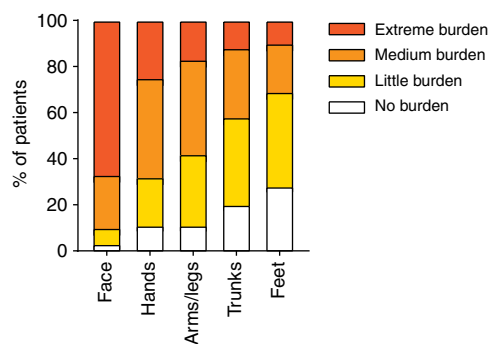


Figure 3 Patient burden of disease per location. The stacked bar chart shows the patient burden of disease per body region. On the x-axis, the specific body regions are shown, and the y-axis represents the percentage of total number of patients ($n = 325$).

improvement of vitiligo therapy. Moreover, approximately half of the patients felt that their current treatment was not effective and was not satisfied with it.

We analysed factors with potential influence on patient satisfaction. We found that patients who had received UVB therapy were significantly more satisfied than patients who had only received topical treatment, which is in line with previous studies.^{16,17} Patients with facial vitiligo also seemed to be more satisfied with current treatments. This could be clarified by the fact that facial lesions often respond better to therapy than lesions on other body regions.¹⁸

Our results also show that patients that are little or not satisfied with current treatments are more demanding for new treatments. It is, however, remarkable that even patients, who were (very) satisfied with current treatments, still expressed the opinion that new treatments are needed for vitiligo.

Moreover, we found that the emotional burden was significantly higher in dark skin type patients (Fitzpatrick skin types 4–6). This is in accordance with our previous study which showed that vitiligo particularly has more impact on the quality of life of patients with dark skin than patients with a light skin (Fitzpatrick skin types 1–3).² In addition, our results show a clear difference in experiencing burden of vitiligo lesions related to their location. The majority of the patients reported that they experienced their facial lesions as an extreme burden, followed by lesions on the hands in a quarter of the patients. This is not unexpected, since these body sites are usually exposed areas. On the contrary, lesions on the feet and on the trunk are experienced as little or no burden at all by the majority of the patients, probably since these usually involve covered areas. Thus, the degree of burden seems to be correlated with the visibility of the specific body region, which is in line with previous studies.^{12–14,19} Furthermore, this study shows that a higher burden and impaired quality of life were significantly associated with a

higher demand for new therapies, but also with a higher willingness to participate in clinical trials and a higher acceptance of invasive treatment for their vitiligo.

To our knowledge, our study is the first to analyse the demand for new therapies in a large cohort of vitiligo patients in the Netherlands. Similarly, the majority of vitiligo patients participating in a UK survey study reported the main priority of finding a cure or an effective lasting treatment.²⁰ As our collected data were recent up to October 2019, our study represents an up-to-date view of patients' perspective. The strength of our study is that all patients were approached consecutively from our outpatient department, thereby including patients from daily practice. Moreover, this survey is completed by a relatively large cohort of patients all over the Netherlands. However, there are some limitations to this study. Firstly, this questionnaire was constructed specifically for this study and was not validated. Secondly, the response rate was 70% but only 60% completed the full questionnaire, which may raise a bias, due to the lack of data available on the non-responding patients. Moreover, since patients were included at a national referral centre for pigment disorders, the population of vitiligo patients in this study may have a relative high disease burden and may not fully reflect the larger community of people with vitiligo who do not seek care or are not referred to our expert centre. In addition, 65% of our participants had skin types I and II, which is not fully representative for the global vitiligo population.

The results of this exploratory study underline the demand for improved and novel vitiligo therapies. A considerable fraction of patients in our study is dissatisfied with current treatments and emotionally burdened by the disease. In addition, the disease burden seems to be dependent on the visibility of the location of the vitiligo lesion. Moreover, the vast majority of all patients included demands novel treatments and is willing to participate in clinical trials.

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Supporting information

Additional Supporting Information may be found in the online version of this article:

Table S1. Summary of statistical correlations.

Appendix S1. Short survey vitiligo treatment.