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Review Article

Quality of Life Assessments Utilized in Vitiligo Clinical Trials

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Introduction. Vitiligo is an acquired autoimmune disease associated with high psychosocial burden. As novel treatments are being developed in clinical trials, assessing vitiligo disease burden extends beyond physical manifestations. Including quality of life (QoL) measures in vitiligo clinical trials can better capture disease-specific psychosocial concerns and facilitate cross comparisons amongst interventions. *Objective*. To determine the frequency and types of QoL measures utilized in vitiligo clinical trials and comment on how this has changed longitudinally. *Methods*. A search of vitiligo clinical trials using clinicaltrials.gov was conducted. Phase 2 and phase 3 trials published in English from January 2000 to July 2023 were eligible for this review. Characteristics of clinical trial parameters were compared to those of non-QoL reporting clinical trials using Pearson's χ^2 tests (or Fisher's if low n). *Results*. A total of 60 clinical trials were eligible for this review, of which 40% included a QoL measure in their study design. Phase 3 clinical trials ($p = 0.002$), larger (100+ participants) trials ($p = 0.063$), U.S. trials ($p = 0.029$), and pharmaceutical interventions ($p = 0.022$) were more likely to include QoL measures in their design. The number of clinical trials has been increasing over time, with 8 trials from 2000 to 2010, 32 total trials from 2011 to 2020, and 20 trials from 2021 to 2023. The most commonly used QoL measures were the Dermatology Life Quality Index (DLQI, 55.2%), Children's Dermatology Life Quality Index (CDLQI, 13.8%), and Vitiligo-specific quality of life instrument (VitiQoL, 13.8%). Over time, the VitiQoL and CDLQI have been used more frequently. *Conclusion*. Although vitiligo is associated with high psychological and emotional burden, less than half of vitiligo trials utilize QoL measures. The general dermatology QoL measures, namely the DLQI and CDLQI, are the most commonly used QoL assessments. As the number of clinical trials is increasing, vitiligo-specific questionnaires may better capture unique vitiligo-specific concerns. Standardizing the types of and implementation of QoL questionnaires in clinical trials can aid in assessing outcome measures across clinical trials worldwide and allow for better data interpretation, comparability, and clinical application of results.

1. Introduction

Vitiligo is an acquired autoimmune disease characterized by symmetrically distributed white patchy skin depigmentation due to selective autoimmune damage to melanocytes [1]. Patients with vitiligo experience a multitude of psychological and emotional trauma due to the disease's cosmetic effects, particularly in the skin of color (SOC) patients. The skin's altered appearance in vitiligo often leads to poor self-esteem, lack of confidence, and social isolation. Consequently, affected patients have higher rates of major depressive disorder, social anxiety, and cognitive impairment [2].

Treatments such as corticosteroid creams, immunosuppressives, biologics (ruxolitinib), and procedural modalities (phototherapy, lasers, and surgical transplant) reduce inflammation and restore pigment [3]. Assessing objective measures of disease severity may not capture important information on how well those changes improve patients' lives. Assessing quality of life (QoL) measures in clinical trials may better capture psychosocial effects to further determine treatment efficacy.

QoL is defined as an individuals' perception of their status or position in life in the context of the culture and values they hold in relation to their goals, expectations, standards, and concerns. QoL is determined by physical functioning, psychological state, and social interaction [4]. Common dermatology-specific QoL tools include the Dermatology Life Quality Index (DLQI) and Children's Dermatology Life Quality Index (CDLQI). More vitiligo-specific QoL tools include the Vitiligo-specific quality of life instrument (VitiQoL) and the vitiligo impact scale (VIS) [5].

Characterizing the utilization of QoL measures in vitiligo clinical studies is important since these validated scales may effectively capture the disease-specific psychosocial concerns that vitiligo patients face. In addition, analyzing trends in vitiligo QoL measures may guide future QoL tool selection in future clinical trials to allow for better agent cross comparisons and compilation of data for more informed therapeutic decision making for clinicians [5]. In this review, we aim to characterize the use of QoL measures in past and current vitiligo clinical trials (using clinicaltrials.gov) and comment on the trends in their longitudinal use.

2. Methods

A search of past and current vitiligo clinical trials was conducted using clinicaltrials.gov. The search term vitiligo was applied in "condition or disease," and only interventional studies (clinical trials) published in English from January 2000 to July 2023 were included. Clinical trials of any "status" of recruitment were included, and clinical trials of any age and sex group were also eligible. Studies with and without results were included, and only phase 2 and phase 3 clinical trials were evaluated, as trials in earlier phases may be primarily "proof of concept" or "safety" oriented clinical trials in which capturing QoL may not be reasonable or expected. In the event of multiple clinical phases, at least one of the phases must be 2 or 3 to be included and stratified independently. Studies were included regardless of the intervention type (pharmaceutical or procedural).

When commenting on trends in QoL measures, only studies that assessed at least one QoL measure were included. Scales that included some component of patient satisfaction or QoL were also included. Studies not published in English, not pertinent to vitiligo, or that were phase 1 or proof of concept studies were excluded. Clinical trials that were missing information regarding primary/secondary outcomes measured were also excluded. Characteristics of the respective clinical trial parameters were compared to non-QoL reporting clinical trials patients using Pearson's χ^2 tests (or Fisher's if low n). A p value of less than 0.05 was considered statistically significant.

Parameters of interest included: specific indication, clinical trial's current status, year the trial was posted, enrollment (or projection), patient age group in trial, gender of patients, phase of trial (pharmaceutical or procedural), specific intervention, geographic location of the trial (US or outside US), QoL collected (yes/no), number of QoL instruments used (if applicable), QoL as the type of outcome measure (primary/secondary/other), and what specific QoL tool was utilized. Data collected were cross-checked by two authors (G.N.P. and V.N.) independently and any discrepancies were resolved by consensus.

3. Results

A search of vitiligo clinical trials using clinicaltrials.gov was conducted, and a total of 165 total clinical trials were identified. After excluding trials that were not interventional, not in English, or were not phase 2 or 3, there were a total of 62 trials that met inclusion criteria. An additional two studies were excluded because they were missing information regarding outcome measures and/or other parameters of interest. A total of 60 interventional clinical trials were included in this medical literature review.

All of the clinical trials included adult vitiligo patients, 18.33% of trials evaluated both children and adults, and no trials exclusively evaluated children with vitiligo (Table 1). The majority of the identified clinical trials were phase 2 (60%), while phase 3 (20%) and mixed (phase 2 and 3) (20%) comprised the minority. QoL outcome measures were assessed in 24 (40%) of all the trials identified, and 47% of phase 2 and 58% of phase 3 trials included a QoL or patient satisfaction questionnaire. The number of clinical trials has been increasing over time, with 8 trials from 2000 to 2010, 32 total trials from 2011 to 2020, and 20 trials from 2021 to 2023. Validated QoL tools, such as DLQI and CDLQI, were used in 83% of the trials that assessed QoL in their study design.

Phase 3 clinical trials were more likely to include a QoL measure, whereas phase 2 and mixed phase clinical trials were less likely ($p = 0.002$). Vitiligo was the most common indication in trials including QoL measures and clinical trials not including QoL measures studied (75% and 86%, respectively), with nonsegmental vitiligo being the most common specific indication (25% in QoL studies and 11% in non-QoL studies). The specific indication did not differ across studies reporting QoL ($p = 0.288$). The size of enrollment did not vary across studies; in trials with 100+ patients, QoL was more frequently collected (8 studies vs. 4 that did not include QoL in study design) ($p = 0.063$).

Clinical trials for pharmaceutical interventions comprised the majority of studies with QoL measures in their study design (75%). Conversely, trials evaluating only a procedural intervention did not commonly assess QoL (1/13 or 8%). Overall, studies evaluating pharmaceutical interventions were more likely to include QoL tools compared to procedure-only trials ($p = 0.022$). The majority of studies evaluating QoL were in the US (67%), whereas most

Table 1: Proportion of clinical trials assessing QoL measures.

Number of clinical trials by indication ($n = 60$)	Proportion that assessed a QoL	Breakdown by the trial type (total)	Percent of trials that assessed a QoL by the trial type:	Number of trial per year range
Adult: 60 Children: 0 Both: 11	Adult: 18 (30%) Children: 0 (0%) Both: 6 (54.55%)	Phase 1/2*: 4 Phase 2:36 Phase 3:12 Phase 2/3*: 8	Phase 1, 2:0 (0%) Phase 2:17 (47.22%) Phase 3:7 (58.33%) Phase 2, 3:0 (0%)	2000–2005:1 2006–2010:7 2011–2015:17 2016–2020:15 2021–2023:20

QoL = quality of life. Number of studies that used validated QoL: 20/24 = (83.33%). *Clinical trials were listed as both listed phases on clinicaltrials.gov.

Table 2: Breakdown of included vitiligo clinical trials assessing QoL measures.

Parameter of interest	Outcome in QoL studies	Outcome in non-QoL studies	p value using Fischer's exact test
Number of clinical trials	24 total studies	36 total studies	$p = 0.002$
Phase 2: n (%)	17 (47.22%)	19 (55.88%)	
Phase 3: n (%)	7 (58.33%)	5 (13.89%)	
Unspecified*: n (%)	0 (0.00%)	12 (33.33%)	
Specific indication			$p = 0.288$
Vitiligo, n (%)	18 (75.00%)	31 (86.11%)	
Nonsegmental vitiligo, n (%)	6 (25.00%)	4 (11.11%)	
Unspecified/other, n (%)	0 (0.00%)	1 (2.78%)	
Gender			$p = 0.400$
All	23 (95.83%)	36 (100.00%)	
Male only	1 (4.17%)	0 (0.00%)	
Female only	0 (0.00%)	0 (0.00%)	
Enrollment, n			$p = 0.063$
0–20	7 (29.17%)	8 (22.22%)	
20–50	8 (33.33%)	16 (44.44%)	
50–100	1 (4.17%)	8 (22.22%)	
100+	8 (33.33%)	4 (11.11%)	
Date of clinical trial			$p = 0.199$
2000–2005	1 (4.17%)	0 (0.00%)	
2006–2010	0 (0.00%)	7 (19.44%)	
2011–2015	6 (25.00%)	11 (30.56%)	
2016–2020	8 (33.33%)	7 (19.44%)	
2021–present	9 (37.50%)	11 (30.56%)	
Type of intervention			$p = 0.022$
Medication (pharmaceutical)	18 (75.00%)	19 (52.78%)	
Laser/photo/other (nonpharmaceutical)	1 (4.17%)	12 (33.33%)	
Medication + laser/photo/other (both)	5 (20.83%)	5 (13.89%)	
Location			$p = 0.029$
Within US	16 (66.67%)	13 (36.11%)	
Outside US	7 (29.17%)	22 (61.11%)	
Unknown	1 (4.17%)	1 (2.78%)	
QoL as outcome measure		N/A	N/A
Primary measure, n (%)	1 (4.17%)		
Secondary measure, n (%)	22 (91.67%)		
Other, n (%)	1 (4.17%)		
Number of QoL measures assessed		N/A	N/A
One	19 (79.17%)		
Two	5 (20.83%)		
QOL measurement used	29 total	N/A	N/A
DLQI, n (%)	16 (55.17%)		
CDLQI, n (%)	4 (13.79%)		
VitiQoL, n (%)	4 (13.79%)		
VIS, n (%)	1 (3.45%)		
Patient satisfaction, n (%)	2 (6.90%)		
Patient global assessment, n (%)	1 (3.45%)		
Unspecified, n (%)	1 (3.45%)		

*Includes trials listed as phase 1 and 2 and phase 2 and 3. QoL = quality of life; DLQI = Dermatology Life Quality Index; CDLQI = Child Dermatology Life Quality Index; VitiQoL = Vitiligo Quality of Life Index; VIS = vitiligo impact scale.

studies not evaluating QoL were conducted outside the US (61%) (Table 2). When QoL was assessed, it was most commonly a secondary outcome (92% of trials) and generally only one QoL tool was utilized (79% of studies including QoL measures) (Table 2).

The DLQI was the most commonly used QoL measurement tool (55%), followed by CDLQI (14%) and VitiQoL (14%). The vitiligo impact scale (VIS) was only used in one clinical trial (3.45%). Patient satisfaction questionnaires were collected in 7% of the QoL trials, and patient global assessments and/or unspecified QoL metrics were both present in 3% of trials each (Table 2). Before 2010, only 1 of the 8 trials assessed some aspect of patients' QoL/satisfaction. However, after 2011, the implementation of QoL metrics in clinical trial design became more common. The DLQI and CDLQI became much more popular longitudinally and became the most commonly used QoL metrics. The vitiligo-specific VitiQoL and VIS questionnaires increased in use since 2011 but consist a minority of QoL measures used. The general QoL tools (Global Assessment, unspecified QoL tool) and satisfaction metrics have comprised the minority of assessments and have been on the decline since 2015 (Figure 1).

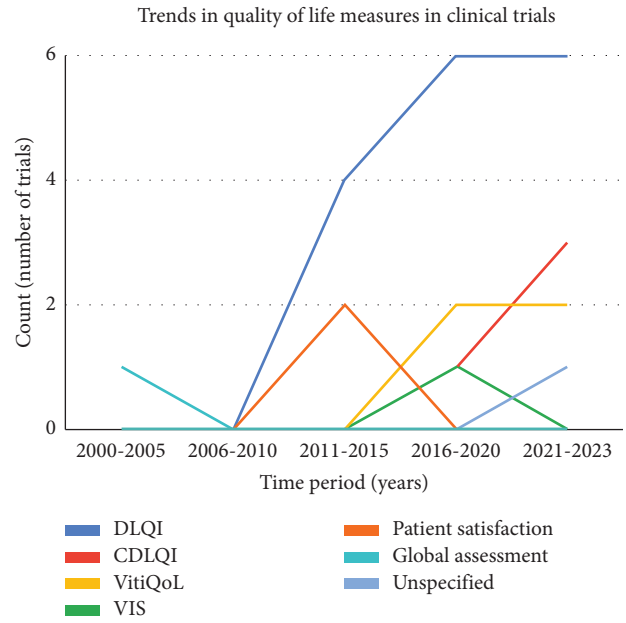

Figure 1: Trends in quality of life instruments in 5 year increments.

4. Discussion

Although vitiligo greatly impacts psychosocial well-being, less than 50% of the total identified clinical trials included QoL measures in their study design. Phase 3 clinical trials were more likely to include QoL measures compared to phase 2 trials, likely because previous trials have already established initial treatment efficacy. Although there was no relationship with the patient enrollment size and whether the trial captured QoL measures, most of the trials with 100+ patients had QoL measures. This may be because smaller trials often assess specific subpopulations of patients or novel medications and have less incentive to explore QoL within such a small population [6]. The lack of QoL assessment in nonpharmaceutical interventions in clinical trials is surprising given the rise in laser, surgical, and phototherapy treatments in vitiligo studies and their associated disfiguring adverse effects (hyper/hypopigmentation, scars, etc.). Likewise, the increasing number of vitiligo clinical trials is likely a reflection of increased research in biologics and small-molecule inhibitors that are emerging as therapeutics for various autoimmune conditions.

Majority of the QoL measurement tools utilized were validated outcome measures, which include the DLQI, CDLQI, VitiQoL, and VIS [7–9]. The DLQI and CDLQI are dermatology-specific QoL tools that evaluate psychosocial impacts of dermatologic conditions and have been extensively studied in other conditions including psoriasis, alopecia, and vitiligo [10]. Specifically, the DLQI is a 10-question survey that assesses physical, psychological, and social aspects of QoL through a series of dermatology-focused disease effects. High DLQI scores equate to high QoL impairment (range: 0–30) [11]. The CDLQI is a similar questionnaire used for children [12]. Advantages to using these general dermatology QoLs are that they have great established validity, have greater awareness and widespread use, and they allow for easier cross comparisons between vitiligo and other dermatologic diseases [13, 14]. In addition, they are short questionnaires that are simple and quick to complete, with a high success rate of accurate completion [15].

A key potential disadvantage of DLQI/CDLQI use in vitiligo is that they do not specifically capture vitiligo-specific elements of QoL that validated vitiligo-specific QoL measures assess. For example, the Vitiligo Impact Scale 22 (VIS 22) is a vitiligo-specific questionnaire developed in India that captures specific cultural concerns for vitiligo. This may better address cultural-specific vitiligo QoL concerns [9]. This questionnaire is a series of 22 questions with each item ranging from 0 (not at all) to 3 (very much) assessing several domains including self-confidence, anxiety, depression, marriage, and family worries [16]. Although this QoL tool may better assess disease-specific concerns, our analysis finds that it is not a commonly used metric. This may be due to its relative novelty (developed in 2013) and its documented use primarily in India. Other potential disadvantages of the VIS include being a longer questionnaire, the potential community-specific differences in scores, and lack of validity due to its inconsistent use, thereby limiting cross-trial comparisons for treatment monitoring and outcome endpoints [9, 16].

The VitiQoL is a validated vitiligo-specific QoL instrument that was also developed in 2013. It is a 16-question survey, with each item scored from 0 (not at all) to 6 (all the time). This survey emphasizes the stigma and psychosocial burden of vitiligo [17]. Advantages of this instrument include more thorough assessment of vitiligo patient-specific psychosocial concerns; however, limited studies have utilized the VitiQoL in their clinical trial design compared to

the use of the DLQI and CDLQI. The longer length of the questionnaire and novelty may also attribute to its less frequent use. Nonetheless, given its recent development and increased use longitudinally, the VitiQoL may continue to increase in use in the near future.

Given that the development of vitiligo-specific QoL occurred in the early 2010s, their recent increase in popularity within clinical trials may be more gradual. Similar trends are seen in other dermatologic disease indications, such as hidradenitis suppurativa (HS), in which general dermatology QoL's such as the DLQI were reported most frequently but disease-specific QoL measures were gaining popularity more recently [18]. Surprisingly, the DLQI and CDLQI were developed in 1994, yet were only routinely used recently in vitiligo clinical trials. This may be due to recent recognition that QoL is a disease-severity instrument for patient evaluation and treatment [19].

Limitations of this review include that only clinical trials registered on clinicaltrials.gov were included and other publication types including cohort studies, case-control studies, cases series, and case reports were excluded. Some evaluated measures, including the CDLQI, may be underreported due to the majority of trials not assessing pediatric patients. The low frequency of reported QoL measures in vitiligo make evaluating trends in specific QoL use more difficult. The recent development of vitiligo-specific questionnaires makes cross comparisons between longitudinal trends in usage compared to older questionnaires (DLQI) more challenging.

5. Conclusion

Vitiligo is associated with high psychosocial and emotional burden with substantial reductions in QoL. As various novel pharmacotherapeutic and procedural treatments are being developed to treat vitiligo, the number of vitiligo clinical trials is increasing and changes in QoL may better evaluate treatment efficacy and patient-reported outcomes. However, the majority of current vitiligo clinical trials do not assess QoL measures. QoL was more commonly included in phase 3 clinical trials, larger patient clinical trials, medication-related interventions, and trials conducted in the US. QoL measures were most commonly reported as secondary outcome measures, and the DLQI was the most commonly used QoL metric. The use of QoL in clinical trials has increased since 2010, and vitiligo-specific questionnaires including the VitiQoL are recently increasing in popularity. Vitiligo is associated with a negative stigma and high comorbidity, and utilization of more validated vitiligo-specific questionnaires may better capture and address the unique patient-specific burdens of vitiligo. Additionally, both limiting the number of QoL questionnaires in use and standardizing its implementation can aid in assessing outcome measures across clinical trials worldwide and allow for better data interpretation, comparability, and clinical application of results.

Data Availability

No data were used to support this study.

Conflicts of Interest

Feldman has received research, speaking, and/or consulting support from AbbVie, Accordant, Almirall, Alvotech, Amgen, Arcutis, Arena, Argenx, Biocon, Boehringer Ingelheim, Bristol-Myers Squibb, Dermavant, Eli Lilly and Company, Eurofins, Forte, Galderma, Helsinn, Janssen, Leo Pharma, Micreos, Mylan, Novartis, Ono, Ortho Dermatology, Pfizer, Regeneron, Samsung, Sanofi, Sun Pharma, UCB, Verrica, Voluntis, and vTv Therapeutics. He is the founder and part owner of Causa Research and holds stock in Sensal Health. All other authors have no conflicts of interest to declare. Rao is a speaker for Incyte.

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