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## SYSTEMATIC REVIEW

# The humanistic burden of vitiligo: a systematic literature review of quality-of-life outcomes

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## Abstract

Despite historical mischaracterization as a cosmetic condition, patients with the autoimmune disorder vitiligo experience substantial quality-of-life (QoL) burden. This systematic literature review of peer-reviewed observational and interventional studies describes comprehensive evidence for humanistic burden in patients with vitiligo. PubMed, EMBASE, Scopus and the Cochrane databases were searched through February 10, 2021, to qualitatively assess QoL in vitiligo. Two independent reviewers assessed articles for inclusion and extracted data for qualitative synthesis. A total of 130 included studies were published between 1996 and 2021. Geographical regions with the most studies were Europe (32.3%) and the Middle East (26.9%). Dermatology-specific instruments, including the Dermatology Life Quality Index (DLQI; 80 studies) and its variants for children (CDLQI; 10 studies) and families (FDLQI; 4 studies), as well as Skindex instruments (Skindex-29, 15 studies; Skindex-16, 4 studies), were most commonly used to measure humanistic burden. Vitiligo-specific instruments, including the Vitiligo-specific QoL (VitiQoL; 11 studies) instrument and 22-item Vitiligo Impact Scale (VIS-22; 4 studies), were administered in fewer studies. Among studies that reported total scores for the overall population, a majority revealed moderate or worse effects of vitiligo on patient QoL (DLQI, 35/54 studies; Skindex, 8/8 studies; VitiQoL, 6/6 studies; VIS-22, 3/3 studies). Vitiligo also had a significant impact on the QoL of families and caregivers; 4/4 studies reporting FDLQI scores indicated moderate or worse effects on QoL. In general, treatment significantly ( $P < 0.05$ ) improved QoL, but there were no trends for types or duration of treatment. Among studies that reported factors significantly ( $P \leq 0.05$ ) associated with reduced QoL, female sex and visible lesions and/or lesions in sensitive areas were most common. In summary, vitiligo has clinically meaningful effects on the QoL of patients, highlighting that greater attention should be dedicated to QoL decrement awareness and improvement in patients with vitiligo.

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## Conflicts of interest

MP has served as a consultant for Incyte Corporation and Pfizer, a principal investigator for Pfizer and PPM, and received non-restricted research grants from Pierre Fabre and PPM. RHH has served as a principal investigator for Incyte Corporation and Pfizer and a subinvestigator for Immune Tolerance Network. HJ was an employee and shareholder of Incyte Corporation when the study was conducted. RM and MO are employees and shareholders of Incyte Corporation. JS has received grants and/or honoraria from AbbVie, Calypso Biotech, Bristol Myers Squibb, Incyte Corporation, LEO Pharma, Eli Lilly, Novartis, Pfizer, Pierre-Fabre, Sanofi, Sun Pharmaceuticals and Viela Bio; and has patents on MMP9 inhibitors and uses thereof in the prevention or treatment of a depigmenting disorder, and three-dimensional model of depigmenting disorder.

## Funding sources

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## Introduction

Vitiligo is an autoimmune depigmentation disorder<sup>1</sup> for which there is no cure or approved medical treatment for repigmentation of lesions.<sup>2</sup> Vitiligo lesions are characterized by a progressive loss of pigmentation caused by the destruction of functioning melanocytes in the epidermis.<sup>3</sup> The process of repigmentation is typically slow, and acral body areas (i.e. hands and feet) tend to be more refractory to repigmentation.<sup>4</sup> Patients experience a high quality-of-life (QoL) burden,<sup>5</sup> including significant psychological comorbidity.<sup>6,7</sup> Vitiligo onset typically occurs before 30 years of age,<sup>8</sup> and patients with a family history of vitiligo exhibit earlier disease onset.<sup>9</sup> The risk of vitiligo has been attributed to heritable genetic factors (approximately 80%) and environmental factors (approximately 20%).<sup>1</sup> Physical, environmental and psychosocial stressors not only contribute to vitiligo onset but are also involved in disease progression.<sup>10</sup>

Quality of life is a multidimensional concept based on subjective perceptions of health, comfort and happiness in psychosocial and physical domains, among others.<sup>11</sup> Although patients with vitiligo may have comparatively lower levels of symptomatic impairment versus atopic dermatitis and psoriasis, the psychosocial impact of vitiligo is vast and distressing.<sup>12</sup> Studies investigating willingness to pay (WTP) in dermatological diseases have shown that WTP among patients with vitiligo is higher than in atopic dermatitis and psoriasis.<sup>13–15</sup> Evidence of substantial reduction in overall QoL, together with high WTP among patients, highlights the significant patient burden of this disease.

The objective of this systematic literature review was to describe the evidence for humanistic burden (a holistic concept including impact on health-related QoL, activities of daily living, caregiver health and QoL, as well as treatment benefit or satisfaction<sup>16</sup>) in patients with vitiligo, including the instruments used to assess burden and factors affecting burden.

## Methods

### Literature search

PubMed, EMBASE, Scopus and the Cochrane database were searched for articles from the earliest entry in respective databases through February 10, 2021. The search string (Appendix S1), which was limited to articles published in English, included the keywords *vitiligo*, *leucoderma*, *leukoderma*, *quality of life* and *patient-reported outcomes*. No limitations were placed on interventions. Duplicate results from the separate databases were removed before assessment of article eligibility. Subsequent to the searches, additional articles were identified from other sources, including through appraisal of existing systematic reviews and meta-analyses.

Peer-reviewed primary publications, including interventional and observational studies, were selected for inclusion. Two independent reviewers (WvdS and KW) performed title and abstract

review as well as a full-text review and data extraction. Studies excluded during these processes were reviews, editorials and commentaries, study protocols, articles with content irrelevant to general QoL in vitiligo, data sets that had <5 participants (e.g. patients with vitiligo or their caregivers), and retracted articles. The reviewers independently assessed the risk of bias in a qualitative manner and resolved disagreements by discussion.

This systematic literature review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.<sup>17</sup> No institutional review board approval was required for the study because all data were collected from published articles. The study protocol was registered with PROSPERO (CRD42021260138).

### Data extraction and analysis

Extracted data included study design, geographical region of the study, sample sizes, detailed patient demographics, clinical characteristics of vitiligo, QoL measures and outcomes, factors associated with QoL burden, the effect of treatment on QoL and caregiver burden. Where available, data reporting the burden of vitiligo in comparison with healthy controls and other skin diseases were also collected. All outcomes were analysed in a descriptive manner.

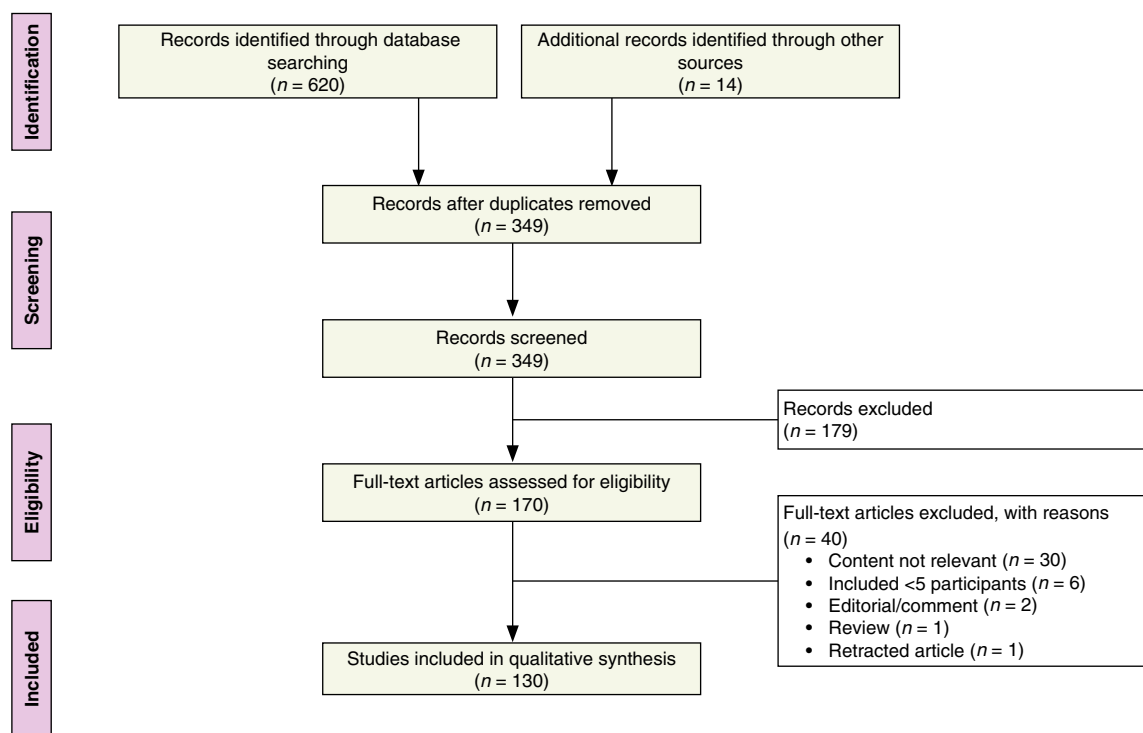
## Results

### Literature search

Initial database searches yielded 620 results, of which 285 were duplicate records that were excluded from screening; 14 records were identified through other sources. Screening resulted in the exclusion of 179 articles during title and abstract review; an additional 40 articles were excluded upon full-text review due to irrelevant content ( $n = 30$ ), inclusion of <5 patients with vitiligo or their caregivers ( $n = 6$ ), editorials/commentaries ( $n = 2$ ), reviews ( $n = 1$ ) and retracted articles ( $n = 1$ ). A total of 130 articles were retained for data extraction and inclusion in qualitative synthesis (Fig. 1).

### Study characteristics

Included studies were published between 1996 and 2021, with 78% published since 2010 (Fig. S1). Studies were characterized as observational ( $n = 97$ , 74.6%) or interventional ( $n = 33$ , 25.4%); including studies reporting pharmaceutical treatment, phototherapy, photochemotherapy, surgical treatment, climatotherapy, homeopathic/natural treatment, camouflage and counselling); paediatric and adult populations were represented. Study characteristics and sample sizes are presented in Table 1. Studies representing populations from most geographical regions were included (Fig. S2); regions with the most studies were Europe (32.3%) and the Middle East (26.9%). All studies were qualitatively assessed to minimize the risk of bias and were deemed to be of acceptable quality for inclusion in the systematic literature review.



**Figure 1** PRISMA flow diagram. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

### Per-instrument QoL burden in patients with vitiligo

Dermatology-specific instruments were most commonly used to measure humanistic burden (including QoL and patient satisfaction or benefit), followed by vitiligo-specific instruments and generic tools. Study characteristics and findings from observational and interventional study assessments that reported results in the overall population are summarized in Table 2 (dermatology- and vitiligo-specific instruments) and Table S1 (generic tools). Several studies reported differences between the QoL in patients with vitiligo and other groups. Compared with healthy controls, QoL in patients with vitiligo was significantly reduced ( $P \leq 0.05$ ) in 13 studies<sup>18–30</sup> and similar in six studies.<sup>31–35</sup> Compared with other dermatological diseases, QoL in patients with vitiligo was significantly worse ( $P \leq 0.05$ ) compared with melasma<sup>36</sup> and significantly better ( $P \leq 0.05$ ) compared with psoriasis<sup>21,37–39</sup>; reports of QoL impairment in vitiligo compared with atopic dermatitis were inconsistent.<sup>19,26</sup> Below, data for instruments measuring QoL are presented by decreasing order of use among included studies.

**Dermatology Life Quality Index** The majority of studies (91/130) used the Dermatology Life Quality Index (DLQI) and/or its variants for children (CDLQI) and family (FDLQI), all of which have possible scores that range from 0 to 30, with higher scores indicating worse QoL.<sup>40–42</sup> DLQI-based instruments are scored

as follows: total score of 0–1 translates to no effect at all on a patient's life; 2–5, small effect; 6–10, moderate effect; 11–20, very large effect; 21–30, extremely large effect.

The DLQI was administered in 80 studies<sup>15,21,22,25,26,28,30,35–39,43–110</sup>; the instrument can be administered to patients  $\geq 16$  years old. Among studies that reported a total DLQI mean score for the overall population, mean scores ranged from 1.82 to 15.0<sup>15,21,22,26,28,35–39,44,46–48,50,51,57–62,64–68,70,71,74,75,77–80,83–85,89,91,94,97,99,100,103–105,107,110</sup>; as such, vitiligo effects on the lives of patients ranged from no effects to very large effects (Fig. 2a). In general, QoL was least impaired among patients from Italy (DLQI total scores, 1.82 and 4.3)<sup>74,75</sup> and Singapore (4.0 and 4.4)<sup>58,59</sup> and most impaired among patients from Saudi Arabia (9, 10.6 and 14.7)<sup>46,47,51</sup> and Egypt (9.52 and 12.5).<sup>50,65</sup>

The CDLQI, utilized in 10 studies,<sup>19,23,24,43,55,111–115</sup> is administered to patients 5 to 16 years old. Among studies that reported CDLQI total mean scores in the overall population, scores ranged from 2.76 to 11.7<sup>19,23,24,112–114</sup>; vitiligo scores indicated that the disease had small to very large effects on patients' lives (Fig. 2a). One additional study used a modified DLQI questionnaire<sup>116</sup> that included items on marriageability and spirituality to fit the cultural context of the Iranian study population, with higher scores indicating worse QoL. Female patients had significantly worse QoL than their male counterparts ( $P = 0.002$ ).<sup>116</sup>

**Table 1** Summary of study characteristics

Characteristic	Number of studies, n (%) N = 130
Study type	
Observational	97 (74.6)
Interventional*	33 (25.4)
Geographical region†	
Africa	2 (1.5)
Europe	42 (32.3)
Eastern Asia‡	18 (13.8)
Southern Asia	21 (16.2)
Middle East	35 (26.9)
North America	12 (9.2)
South America	5 (3.8)
Age group of patients with vitiligo§	
Adult only (≥18 years)	58 (44.6)
Paediatric only (<18 years)	14 (10.8)
Mixed¶	50 (38.5)
Number of patients with vitiligo	
≤50	42 (32.3)
51–150	59 (45.4)
151–250	14 (10.8)
>250	15 (11.5)

QoL, quality of life.

\*Interventions included pharmaceutical treatment, phototherapy, photochemotherapy, surgical treatment, climatotherapy, homeopathic/natural treatment, camouflage and counselling.

†Multinational studies conducted in 2 geographical regions are listed under both regions (Europe/Middle East, 2 studies; Europe/North America, 2 studies; Southern Asia/North America, 1 study).

‡Includes Northeast Asia and Southeast Asia.

§Patient age groups were not reported for 8 (6.2%) studies.

¶Studies with mixed populations often included patients ≥16 years of age, who are considered to be adults for the application of some QoL instruments.

**Skindex** Skindex instruments were used in 19 studies; scores range from 0 to 100 on both the 29-item (Skindex-29) and 16-item (Skindex-16) instruments, with higher scores indicating reduced QoL.<sup>117</sup> The Skindex total score can be interpreted as having very little effect (score ≤ 5), mild effect (scores 6–17), moderate effect (scores 18–36) and severe effect (scores ≥ 37) on QoL.<sup>118</sup> The Skindex-29 was administered in 15 studies.<sup>33,39,118–130</sup> Among studies that reported mean global scores in the overall population, scores ranged from 20.8 to 33.1<sup>39,121–123,125</sup>; these scores indicate that vitiligo had moderate effects on patients' lives (Fig. 2b). The Skindex-16 was administered in four studies.<sup>67,81,82,131</sup> Among studies that reported mean global scores in the overall population, scores were 32.0 and 39.4,<sup>67,131</sup> indicating that patients experienced moderate to severe effects (Fig. 2b).

**Vitiligo-specific QoL instrument** The Vitiligo-specific Quality of Life (VitiQoL) instrument, with scores that range from 0 to 90, was employed in 11 studies<sup>49,53,55,82,85,120,132–136</sup>; higher scores indicate poorer QoL. One study shared an interpretation

of VitiQoL scores with 0–5 representing no effect, 6–20 mild effect, 21–38 moderate effect and ≥39 severe effect.<sup>49</sup> Among studies that reported mean total scores for the overall population, the range was 30.5 to 40.0,<sup>53,85,133,135</sup> suggesting that patients with vitiligo experienced moderate to severe QoL impairment (Fig. 2c).

**Vitiligo Impact Scale** The Vitiligo Impact Scale (VIS) was used in six studies, two of which employed the original 27-item questionnaire (scores ranging from 0–8<sup>81,135</sup> and four of which employed the abbreviated 22-item questionnaire (VIS-22; scores ranging from 0–66).<sup>60,67,68,80</sup> Although no ratings of severity have been recognized for VIS scores, higher scores indicate poorer psychosocial QoL. VIS-22 scores can be interpreted as follows: 0–5, no effect; 6–15, mild effect; 16–25, moderate effect; 26–40, large effect and 41–66, very large effect.<sup>68</sup> One study presented a VIS mean total score of 23.9 in the overall population.<sup>135</sup> VIS-22 mean total scores ranged from 16.4 to 26.5,<sup>67,68,80</sup> indicating moderate to large effects of vitiligo on QoL (Fig. 2d).

**Vitiligo Life Quality Index** Only one study reported results of the Vitiligo Life Quality Index (VLQI),<sup>97</sup> which is a vitiligo-specific version of the DLQI. The mean score on the VLQI was 44.0,<sup>97</sup> which was shown to correlate significantly with the DLQI and with the perceived severity of vitiligo (both  $P < 0.001$ ).

**Generic instruments** The Short-Form 36 (SF-36) health survey questionnaire was used in nine studies,<sup>29,33,35,37,39,66,124,125,137</sup> one of which used version 2 of the questionnaire<sup>29</sup>; on this instrument, higher scores indicate better QoL. Among studies that reported mean mental and physical component scores of the SF-36 in the overall population, physical component scores ranged from 53.6 to 54.9,<sup>29,33,125</sup> and mental component scores ranged from 46.3 to 48.1<sup>29,33,125</sup>; overall, it appears that patients with vitiligo experience more mental than physical impairment. This was also demonstrated in one study that used the abbreviated Short-Form 12 (SF-12) questionnaire.<sup>64</sup>

The Pediatric Quality of Life (PedsQL) inventory was completed in three studies,<sup>27,32,34</sup> two of which also administered the proxy questionnaire to parents of patients with vitiligo<sup>27,32</sup>; scores range from 0 to 100, with higher total scores indicating better QoL.<sup>138</sup> Questionnaires administered to paediatric patients and their parents yielded relatively similar total scores regarding the perception of vitiligo impact on children/adolescents; mean scores among children/adolescents ranged from 76.5 to 90.2,<sup>27,32,34</sup> and parent's mean scores ranged from 72.3 to 73.5.<sup>27,32</sup>

The 60-item General Health Questionnaire (GHQ) was used in two studies,<sup>76,103</sup> and the abbreviated 28-item questionnaire (GHQ-28) was used in two studies<sup>20,52</sup>; higher scores indicate worse QoL. GHQ total scores in patients who reported that

**Table 2** Dermatology- and vitiligo-specific quality-of-life assessment tools and outcomes among studies that reported total scores in the overall population

Study	Country	Sample size at baseline	Total score, mean (SD)	Total score, median (Range)	Estimated effect on QoL*
<b>DLQI*</b>					
Aghaei 2004 <sup>44</sup>	Iran	70	7.05 (5.13)	–	Moderate
Al Robaee 2007 <sup>46</sup>	Saudi Arabia	109	14.7 (5.17)	–	Very large
Al-Shobaili 2015 <sup>47</sup>	Saudi Arabia	134	10.6 (4.3)	–	Moderate
Amatya 2019 <sup>48</sup>	Nepal	100	4.13 (3.74)	3 (0–17)	Small
Anaba 2020 <sup>49</sup>	Nigeria	29	–	5 (IQR, 2–10)	Small
Bassiouny 2021 <sup>50</sup>	Egypt	100	12.5 (4.2)	–	Very large
Bin Saif 2013 <sup>51</sup>	Saudi Arabia	141	9 (6.5)	– (0–25)	Moderate
Boza 2015 <sup>53</sup>	Brazil	74	–	3 (IQR, 1–7)	Small
Catucci Boza 2016 <sup>55</sup>	Brazil	93	–	3.00 (IQR, 1.00–6.50)	Small
Chahar 2018 <sup>57</sup>	India	54	9.64 (4.32)	–	Moderate
Chan 2012 <sup>59</sup>	Singapore	145	4.4 (4.5)	3.0 (0–23)	Small
Chan 2013 <sup>58</sup>	Singapore	222	4.0 (4.4)	–	Small
Chen 2019 <sup>60</sup>	China	884	5.83 (5.75)	– (0–30)	Small
Dabas 2019 <sup>36</sup>	India	95	10.3 (6.65)	–	Moderate
Doiruk Kaçar 2014 <sup>61</sup>	Turkey	34	6.02 (2.55)	– (2–14)	Moderate
Dolatshahi 2008 <sup>62</sup>	Iran	100	8.16 (5.42)	– (0–28)	Moderate
Ezzedine 2015 <sup>64</sup>	France	261	8.7 (6.2)	7.0 (0–28.0)	Moderate
Fawzy 2013 <sup>65</sup>	Egypt	104	9.52 (5.88)	– (1–24)	Moderate
Ghaderi 2014 <sup>66</sup>	Iran	70	8.40 (5.80)	–	Moderate
Ghajarzadeh 2012 <sup>37</sup>	Iran	100	8.4 (6.9)	–	Moderate
Gupta 2014 <sup>67</sup>	India	161	8.25 (6.93)	–	Moderate
Gupta 2019 <sup>68</sup>	India	382	7.8 (6.6)	– (0–28)	Moderate
Hartmann 2005 <sup>71</sup>	Germany	9	13 (6.1)	– (8–25)	Very large
Hartmann 2008 <sup>70</sup>	Germany	30	12.4 (6.5)	– (2–27)	Very large
Ingordo 2012 <sup>75</sup>	Italy	47	1.82 (2.95)	–	No effect
Ingordo 2014 <sup>74</sup>	Italy	161	4.3 (4.9)	– (0–22)	Small
Karelsen 2013 <sup>21</sup>	Estonia	54	4.7 (–)	– (0–22)	Small
Kent 1996 <sup>77</sup>	United Kingdom	614	4.82 (4.84)	– (0–26)	Small
Kiprono 2013 <sup>78</sup>	Tanzania	88	7.2 (4.8)	–	Moderate
Kostopoulou 2009 <sup>79</sup>	France	48	7.17 (4.8)	– (0–18)	Moderate
Kota 2019 <sup>80</sup>	India	150	7.02 (5.58)	–	Moderate
Kruger 2015 <sup>22</sup>	Germany	96	4.9 (–)	–	Small
Mashayekhi 2010 <sup>83</sup>	Iran	83	7.54 (4.97)	– (0–20)	Moderate
Mishra 2014 <sup>84</sup>	India	100	6.86 (–)	–	Moderate
Morales-Sanchez 2017 <sup>85</sup>	Mexico	150	5.2 (5.4)	–	Small
Noh 2013 <sup>26</sup>	South Korea	60	7.61 (–)	–	Moderate
Ongenaë 2005a <sup>38</sup>	Belgium	102	4.95 (–)	– (0–8)	Small
Ongenaë 2005b <sup>89</sup>	Belgium	78	6.9 (5.6)	– (0–20)	Moderate
Parsad 2003 <sup>91</sup>	India	150	10.7 (4.56)	– (2–21)	Moderate
Radtke 2009 <sup>15</sup>	Germany	1023	7.0 (5.9)	– (0–27)	Moderate
Salman 2016 <sup>94</sup>	Turkey	37	5.6 (5.1)	–	Small
Sangma 2015 <sup>28</sup>	India	100	9.08 (4.46)	–	Moderate
Senol 2013 <sup>97</sup>	Turkey	183	15.0 (4.6)	14.0 (IQR, 11.0–17.0)	Very large
Silpa-Archa 2020 <sup>99</sup>	Thailand	104	7.46 (6.06)	6 (0–26)	Moderate
Silverberg 2013 <sup>100</sup>	United States	1541	5.9 (5.5)	–	Small
Tejada 2011 <sup>102</sup>	Brazil	16	–	13 (IQR, 9–15.5)	Very large
Temel 2019 <sup>103</sup>	Turkey	50	4.70 (5.33)	–	Small
Udaya Kiran 2020 <sup>104</sup>	India	14	12.4 (4.48)	–	Very large
van Geel 2006 <sup>105</sup>	Belgium	40	6.95 (6.68)	4.5 (0–21)	Moderate
van Geel 2021 <sup>106</sup>	Belgium	315	–	2 (0–21)	Small

Table 2 Continued

Study	Country	Sample size at baseline	Total score, mean (SD)	Total score, median (Range)	Estimated effect on QoL*
Wang 2011 <sup>35</sup>	China	101	8.41 (7.31)	–	Moderate
Wong 2012 <sup>107</sup>	Malaysia	102	6.4 (–)	– (0–20)	Moderate
Xu 2017 <sup>39</sup>	South Korea	37	4.49 (3.97)	–	Small
Zandi 2011 <sup>110</sup>	Iran	124	9.09 (6.2)	–	Moderate
<b>CDLQI*</b>					
Catucci Boza 2016 <sup>55</sup>	Brazil	24	–	3 (IQR, 1.3–7.3)	Small
Dertlioglu 2013 <sup>19</sup>	Turkey	50	11.7 (6.54)	–	Very large
Kruger 2014 <sup>24</sup>	Germany, United States	74	2.8 (–)	–	Small
Kruger 2018 <sup>23</sup>	Germany, United States	85	2.81 (3.65)	– (0–17)	Small
Manzoni 2012 <sup>111</sup>	Brazil	43	–	2 (IQR, 1–6)	Small
Njoo 2000 <sup>112</sup>	Netherlands	51	5.6 (3.8)	–	Small
Ramien 2014 <sup>113</sup>	Canada	9	5.0 (–)	–	Small
Savas Erdogan 2020 <sup>114</sup>	Turkey	29	2.76 (2.39)	– (0–8)	Small
Silverberg 2014 <sup>115</sup>	United States	336	–	3.0 (IQR, 5)	Small
<b>FDLQI*</b>					
Andrade 2020 <sup>149</sup>	United States	118	13.1 (3.5)	–	Very large
Bin Saif 2013 <sup>51</sup>	Saudi Arabia	141	10.3 (6.4)	– (range, 0–26)	Moderate
Handjani 2013 <sup>151</sup>	Iran	15	14.4 (5.08)	–	Very large
Saeedeh 2019 <sup>152</sup>	Iran	150	6.1 (6.1)	5 (0–24)	Moderate
<b>Skindex-29†</b>					
Choi 2010 <sup>121</sup>	South Korea	57	21.8 (–)	–	Moderate
Kim 2009 <sup>122</sup>	South Korea	133	30.7 (19.2)	–	Moderate
Komen 2015 <sup>123</sup>	Netherlands	60	20.8 (–)	–	Moderate
Linthorst Homan 2009 <sup>125</sup>	Netherlands	245	22.8 (17.1)	–	Moderate
Sanclemente 2017 <sup>129</sup>	Colombia	99	– (16.2)	21.5 (–)	Moderate
Xu 2017 <sup>39</sup>	South Korea	37	33.1 (12.4)	–	Moderate
<b>Skindex-16†</b>					
Essa 2018 <sup>131</sup>	Egypt	21	39.4 (19.2)	–	Severe
Gupta 2014 <sup>67</sup>	India	161	32.0 (23.1)	–	Moderate
<b>VitiQoL‡</b>					
Anaba 2020 <sup>49</sup>	Nigeria	29	–	38 (IQR, 17–54)	Moderate
Boza 2015 <sup>53</sup>	Brazil	74	40.0 (27.3)	–	Severe
Catucci Boza 2016 <sup>55</sup>	Brazil	93	–	37.0 (IQR, 17.0–64.5)	Moderate
Hedayat 2016 <sup>133</sup>	Iran	173	30.5 (14.5)	31 (0–60)	Moderate
Morales-Sanchez 2017 <sup>85</sup>	Mexico	150	32.1 (22.7)	–	Moderate
Pun 2021 <sup>135</sup>	Nepal	22	37.2 (24.2)	–	Moderate
<b>VIS</b>					
Pun 2021 <sup>135</sup>	Nepal	22	23.9 (15.9)	–	–
<b>VIS-22§</b>					
Gupta 2014 <sup>67</sup>	India	161	26.5 (14.5)	–	Large
Gupta 2019 <sup>68</sup>	India	391	24.8 (14.0)	– (0–61)	Moderate
Kota 2019 <sup>60</sup>	India	150	16.4 (9.57)	–	Moderate
<b>VLQI</b>					
Senol 2013 <sup>97</sup>	Turkey	183	44.0 (12.1)	43.0 (IQR, 35.0–52.0)	–

CDLQI, Children's Dermatology Life Quality Index; DLQI, Dermatology Life Quality Index; FDLQI, Family Dermatology Life Quality Index; IQR, interquartile range; QoL, quality of life; VIS, Vitiligo Impact Scale; VitiQoL, Vitiligo-specific Quality of Life; VLQI, Vitiligo Life Quality Index.

\*Interpretation of total scores based on mean. If mean was not available, median was used for interpretation.

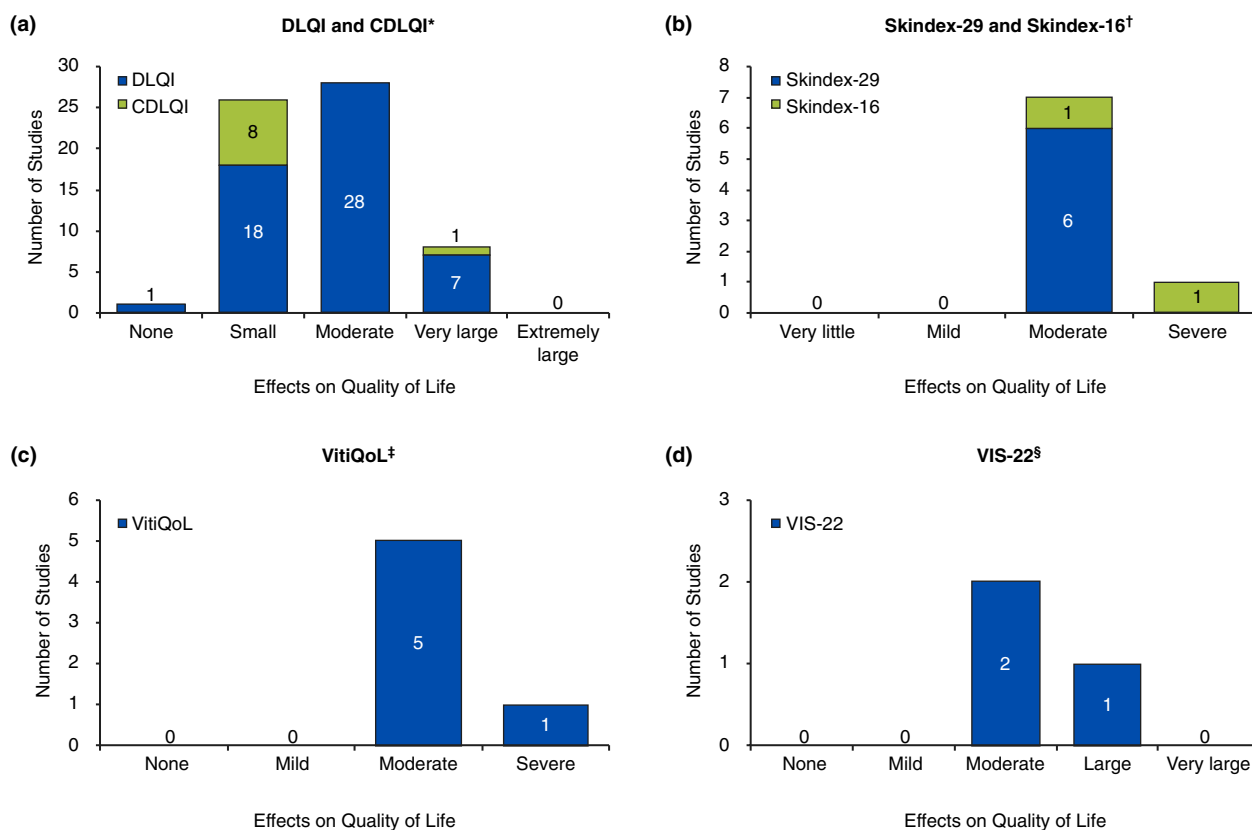
†DLQI/CDLQI/FDLQI total score interpretation: 0–1, no effect at all on patient's life; 2–5, small effect on patient's life; 6–10, moderate effect on patient's life; 11–20, very large effect on patient's life; 21–30, extremely large effect on patient's life.

‡Skindex total score interpretation: ≤5, very little effect; 6–17, mild effect; 18–36, moderate effect; ≥37, severe effect.

§VitiQoL total score interpretation: 0–5, no effect; 6–20, mild effect; 21–38, moderate effect; ≥39, severe effect.

¶VIS-22 total score interpretation: 0–5, no effect; 6–15, mild effect; 16–25, moderate effect; 26–40, large effect; and 41–66, very large effect.



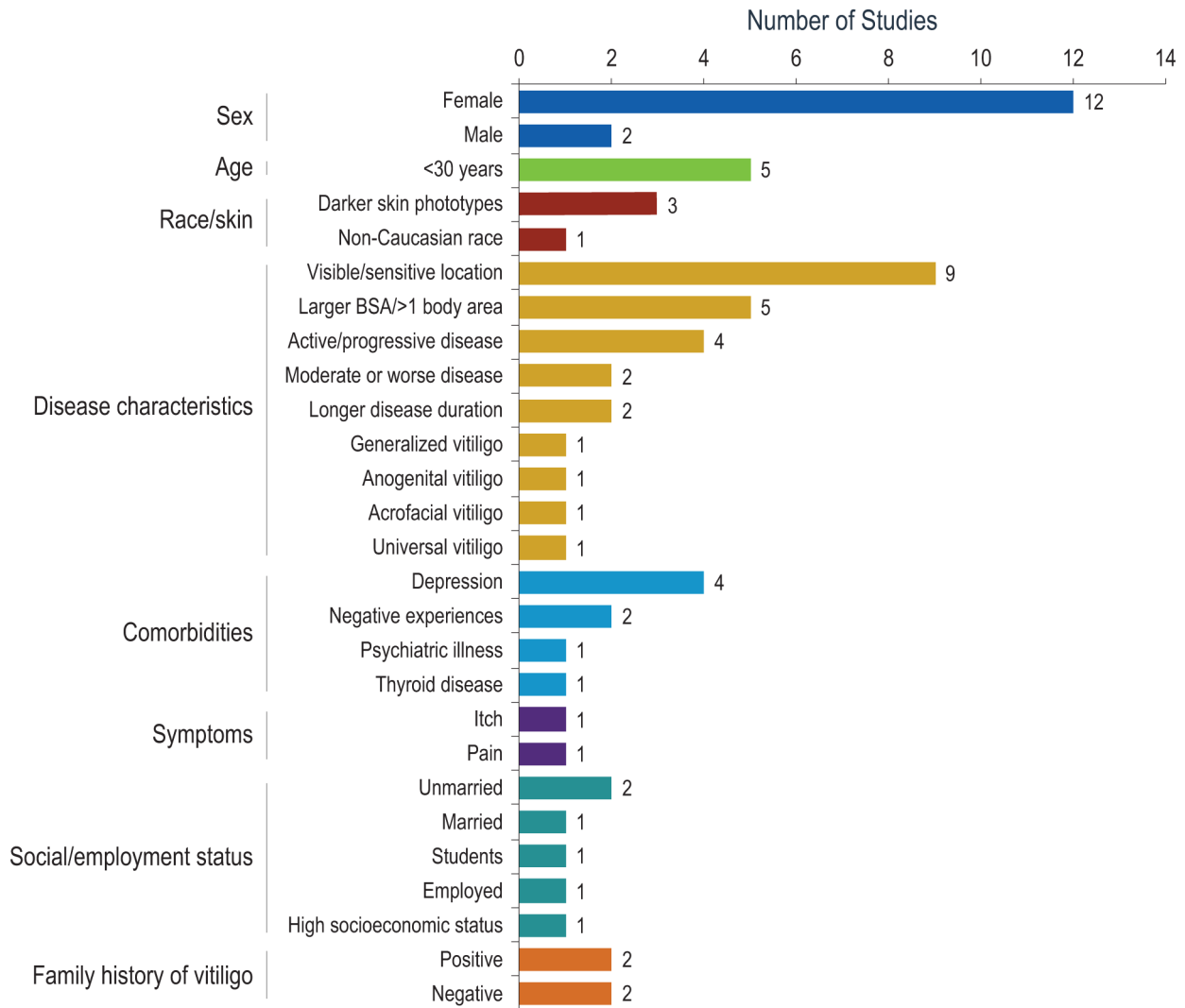


**Figure 2** Categorization of mean total scores for (a) DLQI and CDLQI,\* (b) Skindex-29 and Skindex-16,† (c) VitiQoL,‡ and (d) VIS-22. § CDLQI, Children's Dermatology Life Quality Index; DLQI, Dermatology Life Quality Index; VIS, Vitiligo Impact Scale; VitiQoL, Vitiligo-specific Quality of Life. \* DLQI/CDLQI total score interpretation: 0–1, no effect at all on patient's life; 2–5, small effect on patient's life; 6–10, moderate effect on patient's life; 11–20, very large effect on patient's life; 21–30, extremely large effect on patient's life. † Skindex total score interpretation: ≤5, very little effect; 6–17, mild effect; 18–36, moderate effect; ≥37, severe effect. ‡ VitiQoL total score interpretation: 0–5, no effect; 6–20, mild effect; 21–38, moderate effect; ≥39, severe effect. § VIS-22 total score interpretation: 0–5, no effect; 6–15, mild effect; 16–25, moderate effect; 26–40, large effect; and 41–66, very large effect.

vitiligo had an effect on their lives during the past 3 weeks were significantly higher ( $P < 0.001$ ) versus those who reported no effects on their lives.<sup>76</sup> Other generic questionnaires used in studies included the EuroQol 5-Dimension (EQ-5D; 2 studies),<sup>15,31</sup> EQ-5D five level (EQ-5D-5L; 1 study),<sup>120</sup> Child Health Utility 9-Dimension (CHU-9D; 1 study),<sup>120</sup> Perceived Health Status (PHS; 1 study),<sup>103</sup> Self-Rated Health Measurement Scale (SRHMS; 1 study),<sup>18</sup> World Health Organization Quality of Life Brief (WHOQOL-BREF; 1 study),<sup>43</sup> ENRICH marital inventory (1 study)<sup>35</sup> and generic study-specific QoL questionnaires (6 studies).<sup>139–144</sup> Measures of patient-perceived severity of vitiligo included the Visual Analog Scale (VAS; 4 studies),<sup>45,47,67,73</sup> generic questionnaires (5 studies,<sup>54,93,105,145,146</sup> including one that used a VAS-based questionnaire<sup>145</sup>), the Patient Benefit Index (PBI [2 studies]<sup>63,147</sup> and PBI 2.0 [1 study]<sup>148</sup>) and EuroQol VAS (EQ-VAS; 1 study).<sup>31</sup>

### Factors that reduced QoL in patients with vitiligo

Several articles discussed factors that significantly ( $P \leq 0.05$ ) reduced QoL; Fig. 3 summarizes factors that affected total scores on the previously discussed instruments. Women generally had worse QoL,<sup>37,38,50,52,55,60,65,81,83,133,139,145</sup> although two studies showed significantly poorer QoL in men.<sup>46,116</sup> QoL was reduced in patients with visible lesions (i.e. face, neck, hands) and/or lesions in sensitive areas (i.e. genital, anogenital)<sup>15,24,30,50,60,75,85,107,132</sup>; patients <30 years old (especially adolescents)<sup>50,60,80,115,133</sup>; patients with involvement of a larger body surface area or lesions on several body areas,<sup>15,75,89,110,149</sup> including those with moderate or worse vitiligo<sup>81,121</sup>; and in patients with active and/or progressive disease.<sup>36,50,75,99</sup> Darker skin phototypes<sup>62,64,99</sup> and non-Caucasian race<sup>77</sup> (notably, some studies reported no significant differences among patients with fairer or darker skin phototypes<sup>22,50,65,133</sup>); longer disease duration<sup>15,133</sup>;



**Figure 3** Factors significantly associated with reduced QoL. BSA, body surface area; QoL, quality of life.

as well as generalized,<sup>58</sup> anogenital,<sup>60</sup> acrofacial<sup>65</sup> and universal vitiligo<sup>85</sup> were associated with reduced QoL. General QoL was reduced in patients with reported psychosocial burden including psychiatric illness,<sup>55</sup> depression,<sup>21,58,59,99</sup> and negative experiences due to vitiligo<sup>33,76</sup>; patients with thyroid disease<sup>58</sup>; and patients who reported symptoms including itching and pain.<sup>60</sup> Employment status and socioeconomic status also affected QoL; worse QoL was seen in students versus employed patients<sup>50</sup> and employed versus unemployed patients,<sup>107</sup> as well as patients with high versus middle or low socioeconomic status.<sup>50</sup> Marital status showed inconsistent results, with two studies showing reduced QoL in unmarried patients<sup>36,92</sup> and one study showing reduced QoL in married individuals.<sup>62</sup> Family history of vitiligo also

showed inconsistent results; positive family history reduced QoL in two studies,<sup>62,65</sup> whereas negative family history reduced QoL in two studies.<sup>24,107</sup>

#### Effects of interventions on QoL in patients with vitiligo

Tables 3 and S2 summarize findings from interventional studies (in dermatology- and vitiligo-specific and generic instruments respectively), including the effects of pharmaceutical treatment, phototherapy, photochemotherapy, surgical treatment, climatotherapy, homeopathic/natural treatment, camouflage and counselling on QoL. In general, most interventions significantly improved QoL at end of follow-up compared with baseline<sup>25,43,45,47,50,54,57,70–73,86,89,90,93,104,105,108,112,134,136,144</sup>; however,

**Table 3** Dermatology- and vitiligo-specific quality-of-life assessment tools and outcomes in interventional studies

Study	Country	Sample size at baseline	Treatment group	Baseline		Follow-up		P value vs comparator	
				Total score	Median (range), I (O–I)	Last follow-up	Total score		P value vs baseline
<b>DLQI</b>									
Agarwal 2005 <sup>43</sup>	India	25	Levamisole	Median (range), 4 (0–18)	Median (range), 1 (0–7)	6 months	Median (range), 1 (0–14)	0.003	NS
		17	Placebo	Median (range), 3.5 (0–15)	Median (range), 1 (0–14)	6 months	Median (range), 1 (0–14)	0.025	Ref
Akdeniz 2014 <sup>45</sup>	Turkey	15	NB-UVB + topical calcipotriol + betamethasone	Mean (SD), 7.67 (0.50)	Mean (SD), 2 (0.64)	6 months	Mean (SD), 2 (0.54)	<0.01*	NA
		15	NB-UVB + topical calcipotriol	Mean (SD), 8.40 (0.39)	Mean (SD), 2 (0.54)	6 months	Mean (SD), 2 (0.54)	<0.01*	NA
		15	NB-UVB	Mean (SD), 9.93 (0.63)	Mean (SD), 4 (0.71)	6 months	Mean (SD), 4 (0.71)	<0.01*	NA
Al-Shobaili 2015 <sup>47</sup>	Saudi Arabia	134	Monochrome excimer light	Mean (SD), 10.6 (4.3)	Mean (SD), 4.5 (3.9)	16 weeks	Mean (SD), 4.5 (3.9)	<0.001*	NA
Bassiouny 2021 <sup>50</sup>	Egypt	40	Camouflage	Mean (SD), 13.4 (3.6)	Mean (SD), 7.5 (3.7)	1 month	Mean (SD), 7.5 (3.7)	<0.001*	NA
		60	None	Mean (SD), 11.9 (4.5)	Mean (SD), 10.6 (4.2)	1 month	Mean (SD), 10.6 (4.2)	<0.001	NA
Budania 2012 <sup>54</sup>	India	21	Non-cultured epidermal cell suspension grafting	Mean, 11.5	Mean, 2.24	16 weeks	Mean, 2.24	<0.001*	0.045†
		20	Suction blister epidermal grafting	Mean, 9.7	Mean, 2.9	16 weeks	Mean, 2.9	<0.001*	Ref
Cavaille 2015 <sup>56</sup>	France	16	Placebo	Mean (SD), 6.48 (2.80)	Mean (SD), 4.59 (3.53)	6 months	Mean (SD), 4.59 (3.53)	NS	NA
		19	Tacrolimus	Mean (SD), 4.79 (3.58)	Mean (SD), 3.54 (2.91)	6 months	Mean (SD), 3.54 (2.91)	NS	NA
Chahar 2018 <sup>57</sup>	India	54	NB-UVB	Mean (SD), 9.64 (4.32)	Mean (SD), 4.86 (2.15)	6 months	Mean (SD), 4.86 (2.15)	<0.001*	NA
Eleftheriadou 2014 <sup>63</sup>	United Kingdom	19	Hand-held NB-UVB	Mean (SD), 2.8 (3.2)	Mean (SD), 3.2 (2.3)	16 weeks	Mean (SD), 3.2 (2.3)	NS	NS
		10	Placebo	Mean (SD), 3.8 (3.2)	Mean (SD), 3.7 (3.8)	16 weeks	Mean (SD), 3.7 (3.8)	NS	Ref
Hartmann 2005 <sup>71</sup>	Germany	9	UVB (narrow-band or broadband) + calcipotriol ointment (right side of body) or placebo ointment (left side of body)	Mean (SD), 13 (6.1)	Mean (SD), 9.4 (4.9)	12 months	Mean (SD), 9.4 (4.9)	<0.05	NA
Hartmann 2008 <sup>70</sup>	Germany	30	Tacrolimus 0.1% ointment	Mean (SD), 12.4 (6.5)	Mean (SD), 9.3 (5.6)	12 months	Mean (SD), 9.3 (5.6)	0.001	NA
Hosseinkhani 2015 <sup>72</sup>	Iran	15	Sabgh formulation for camouflage	Mean (SD), 12.9 (5.68)	Mean (SD), 9.60 (4.32)	8 weeks	Mean (SD), 9.60 (4.32)	<0.001	NA
		15	Exuviance formulation for camouflage	Mean (SD), 12.8 (7.22)	Mean (SD), 10.3 (6.18)	8 weeks	Mean (SD), 10.3 (6.18)	0.006	NA

Table 3 Continued

Study	Country	Sample size at baseline	Treatment group	Baseline Total score	Follow-up Last follow-up	Total score	P value vs baseline	P value vs comparator
Ibrahim 2020 <sup>73</sup>	Egypt	19	MBEH 20%	Mean (SD), 11.9 (6.11)	12 months	Mean (SD), 2.39 (4.39)	<0.001*	NA
		20	MBEH 40%	Mean (SD), 11.2 (6.27)	12 months	Mean (SD), 1.70 (3.73)	<0.001*	NA
Kruger 2011 <sup>25</sup>	Germany, Jordan	71	Climatotherapy with PC-KUS (year 1)	Mean, 7.8	Day 20 (year 1)	Mean, 1.9	<0.001*	Ref
		33	Climatotherapy with PC-KUS (year 2)	Mean, 6.2	Day 20 (year 2)	Mean, 2.1	<0.001*	NS
Mou 2016 <sup>86</sup>	China	37	Oral compound glycyrrhizin	Mean (SD), 4.8 (4.5)	6 months	Mean (SD), 2.9 (2.6)	<0.001	NA
		36	NB-UVB	Mean (SD), 6.3 (4.8)	6 months	Mean (SD), 3.1 (2.4)	<0.001	NA
		42	Oral compound glycyrrhizin + NB-UVB	Mean (SD), 5.6 (3.2)	6 months	Mean (SD), 1.8 (1.5)	<0.001	NA
Ongenaes 2005b <sup>89</sup>	Belgium	62	Camouflage	Mean (SD), 7.3 (5.6)	≥1 month	Mean (SD), 5.9 (5.2)	0.006	NA
Papadopoulos 1999 <sup>90</sup>	United Kingdom	8	Cognitive behavioural therapy-based counselling	NA	5 months	NA	<0.001	NA
Parsad 2003 <sup>91</sup>	India	91	PUVA/OMP betamethasone (treatment success)	NA	12 months	Mean, 7.06	NA	<0.0001
		50	PUVA/OMP betamethasone (treatment failure)	NA	12 months	Mean, 13.12	NA	Ref
Sahni 2011 <sup>93</sup>	India	13	Non-cultured melanocyte transplant + saline	Mean, 8.85	16 weeks	Mean, 3.62	0.002*	Ref
		12	Non-cultured melanocyte transplant + serum	Mean, 11.42	16 weeks	Mean, 2.17	0.002*	0.005†
Shah 2014 <sup>98</sup>	United Kingdom	24	Enhanced cognitive behavioural self-help leaflet	Mean (SD), 5.43 (6.17)	8 weeks	Percentage change from baseline, -53%	NA	NS
		25	Cognitive behavioural self-help leaflet	Mean (SD), 6.75 (5.31)	8 weeks	Percentage change from baseline, -58%	NA	NS
		26	None	Mean (SD), 6.73 (5.98)	8 weeks	Percentage change from baseline, -46%	NA	Ref
Tanioka 2010 <sup>101</sup>	Japan	21	Cosmetic camouflage lessons	Mean, 5.90	1 month	Mean, 4.48	NA	0.005†
		11	None	Mean, 3.18	1 month	Mean, 4.36	NA	Ref
Udaya Kiran 2020 <sup>104</sup>	India	14	Cosmetic camouflage + camouflage lessons	Mean (SD), 12.42 (4.48)	30 days	Mean (SD), 3.78 (1.52)	<0.0001*†	NA

Table 3 Continued

Study	Country	Sample size at baseline	Treatment group	Baseline		Follow-up		P value vs baseline	P value vs comparator
				Total score	Mean (SD), 6 or 12 months	Last follow-up	Total score		
van Geel 2006 <sup>105</sup>	Belgium	40	Non-cultured epidermal cellular graft surgery	Mean (SD), 6.95 (6.68)	Mean (SD), 3.85 (4.13)	6 or 12 months	Mean (SD), 3.85 (4.13)	0.016	NA
Yones 2007 <sup>108</sup>	United Kingdom	25	NB-UVB	Median, ~6	Median, ~3	End of treatment (median, 97 sessions)	Median, ~3	<0.001	0.8
		25	PUVA	Median, ~10	Median, ~4	End of treatment (median, 47 sessions)	Median, ~4	<0.001*	Ref
<b>CDLQI</b>									
Agarwal 2005 <sup>43</sup>	India	7	Levamisole	Median (range), 1.5 (0-6)	Median (range), 1 (0-6)	6 months	Median (range), 1 (0-6)	0.17	NS
		11	Placebo	Median (range), 3 (0-8)	Median (range), 1 (0-2)	6 months	Median (range), 1 (0-2)	0.57	Ref
Njoo 2000 <sup>112</sup>	Netherlands	51	NB-UVB	Mean (SD), 5.6 (3.8)	Mean (SD), 2.1 (2.0)	12 months	Mean (SD), 2.1 (2.0)	<0.001	NA
Ramien 2014 <sup>113</sup>	Canada	9	Cosmetic camouflage	Mean, 5.0	Mean, 3.2	6 months	Mean, 3.2	NS†	NA
<b>Skindex-29</b>									
Batchelor 2020 <sup>120</sup>	United Kingdom	133	Topical corticosteroids	Mean (SD), 22.8 (15.7)	Mean (SD), 22.5 (16.5)	21 months	Mean (SD), 22.5 (16.5)	NA	Ref
		130	NB-UVB	Mean (SD), 21.4 (18.6)	Mean (SD), 19.1 (16.6)	21 months	Mean (SD), 19.1 (16.6)	NA	NS
		135	Topical corticosteroids + NB-UVB	Mean (SD), 23.8 (18.7)	Mean (SD), 25.9 (17.5)	21 months	Mean (SD), 25.9 (17.5)	NA	NS
Middelkamp-Hup 2007 <sup>126</sup>	Netherlands	24	<i>Polydodium leucotomos</i> + NB-UVB	-	Change from baseline, 4	26 weeks	Change from baseline, 4	NA	NS
		24	Placebo + NB-UVB	-	Change from baseline, 2	26 weeks	Change from baseline, 2	NA	Ref
Sassi 2008 <sup>130</sup>	Italy	42	Excimer laser	Mean (SEM), 19.4 (2.53)	Mean (SEM), 14.2 (2.25)	12 weeks	Mean (SEM), 14.2 (2.25)	NA	0.727
		42	Excimer laser + topical hydrocortisone	Mean (SEM), 23.7 (2.18)	Mean (SEM), 19.0 (2.30)	12 weeks	Mean (SEM), 19.0 (2.30)	NA	Ref
<b>VitiQoL</b>									
Batchelor 2020 <sup>120</sup>	United Kingdom	133	Topical corticosteroids	Mean (SD), 34.7 (21.8)	Mean (SD), 36.1 (21.1)	21 months	Mean (SD), 36.1 (21.1)	NA	Ref
		130	NB-UVB	Mean (SD), 33.3 (23.8)	Mean (SD), 31.1 (22.8)	21 months	Mean (SD), 31.1 (22.8)	NA	NS
		135	Topical corticosteroids + NB-UVB	Mean (SD), 35.6 (23.3)	Mean (SD), 38.4 (23.6)	21 months	Mean (SD), 38.4 (23.6)	NA	NS
Liu 2020 <sup>134</sup>	China	52	Home-based NB-UVB	Mean (SD), 42 (1.10)	Mean (SD), 19.0 (1.14)	20 weeks	Mean (SD), 19.0 (1.14)	<0.001	NS
		48	Hospital-based NB-UVB	Mean (SD), 42.2 (3.69)	Mean (SD), 14.6 (2.84)	20 weeks	Mean (SD), 14.6 (2.84)	<0.001	Ref

Table 3 Continued

Study	Country	Sample size at baseline	Treatment group	Baseline		Follow-up		P value vs comparator	
				Total score	Mean (SD),	Last follow-up	Total score		
Zhang 2019 <sup>136</sup>	China	48	Home-based NB-UVB	Mean (SD), 68.3 (10.8)	Mean (SD), 32.4 (5.4)	6 months	Mean (SD), 31.0 (5.8)	<0.01	0.22
		48	Outpatient NB-UVB	Mean (SD), 65.9 (10.8)	Mean (SD), 31.0 (5.8)	6 months	Mean (SD), 31.0 (5.8)	<0.01	Ref

CDLQI, Children's Dermatology Life Quality Index; DLQI, Dermatology Life Quality Index; MBEH, monobenzyl ether of hydroquinone; NA, not available/applicable; NB-UVB, narrow-band ultraviolet B; NS, not significant; OMP, oral minipulse; PC-KUS, narrow-band ultraviolet B-activated pseudocatalase; PUVA, psoralen plus ultraviolet A; UVB, ultraviolet B; VitiQoL, VitiQoL. VitiQoL-specific Quality of Life.

\*Achieved meaningful score changes (4-point score reduction) in DLQI score.

†P value based on change from baseline.

differences between treatment comparators within studies were rarely reported as significant. DLQI was used in the majority (23/33) of interventional studies<sup>25,43,45,47,50,54,56,57,63,70–73,86,89–91,93,98,101,104,105,108</sup>; meaningful score changes (4-point score reduction)<sup>150</sup> were achieved with  $\geq 1$  treatment arm in 10 studies.<sup>25,45,47,50,54,57,73,93,104,108</sup> Among studies that assessed patient satisfaction or patient benefit with previous or current treatment (8 interventional studies<sup>45,47,54,63,73,93,105,145</sup> and 5 observational studies<sup>31,67,146–148</sup>), approximately half showed significant improvement in patient satisfaction with their vitiligo after treatment.<sup>45,47,54,73,93,145</sup>

### Humanistic burden of caregivers

The FDLQI was used in four studies<sup>51,149,151,152</sup>; the instrument can be administered to family members  $\geq 16$  years old. All studies reported mean scores in the overall population, which ranged from 6.1 to 14.4,<sup>51,149,151,152</sup> indicating moderate to very large effects of vitiligo on families and/or caregivers. The Dermatitis Family Impact (DFI) questionnaire was used in one study,<sup>18</sup> which showed significantly reduced QoL in parents of patients with vitiligo versus parents of healthy controls ( $P = 0.000$ ). The Quality of Life in a Child's Chronic Disease Questionnaire (QLCCDQ) for caregivers<sup>149</sup> and the Dermatological Family Impact Scale (DeFIS)<sup>114</sup> were each used in one study.

### Discussion

This systematic literature review highlights the significance of QoL burden in patients with vitiligo. Despite no limitations on publication date, included studies addressing QoL in vitiligo were first published in 1996, indicating that interest in vitiligo-related QoL only emerged in the last 25 years. Furthermore, only one-quarter of included studies were interventional, showing limitation in the evaluation of patient perceptions in studies investigating treatment options.

Instruments used to quantify QoL included questionnaires (i.e. validated or study-specific questionnaires) and visual analogue scales. The widespread use of validated instruments including the VitiQoL and DLQI enabled qualitative appraisal of burden in this systematic review. The most common instruments used to measure QoL in patients with vitiligo were dermatology-specific, including the DLQI and CDLQI, as well as Skindex tools. Dermatology-specific tools including the DLQI and Skindex account for physical symptoms such as itching, burning/stinging and pain,<sup>40,117</sup> which may not be present in patients with vitiligo, and may lack sensitivity for application in vitiligo. Vitiligo-specific instruments were used in comparatively fewer studies, with the VitiQoL and VIS-22 being the most common. Among studies that reported interpretable scores, vitiligo was estimated to have moderate or worse effects on patient QoL in a majority of studies (i.e. DLQI, 35/54 studies; Skindex, 8/8 studies; VitiQoL, 6/6 studies; VIS-22, 3/3 studies). Vitiligo also had a significant impact on the QoL of families and/or

caregivers; interpretable scores indicated moderate or worse effects of vitiligo on their QoL (i.e. FDLQI, 4/4 studies). Factors that were most commonly associated with reduced QoL in patients with vitiligo were female sex and lesions in visible or sensitive areas. It is notable that none of the aforementioned instruments were designed to differentiate among skin phototypes; this limitation is evident in the inconsistent reports of differences in QoL burden among patients with fair and dark skin phototypes. Another vitiligo-specific instrument, the Vitiligo Impact Patient scale (VIPs; including the 29-item VIPs and the 12-item short-form VIPs), includes response models for fair and dark skin.<sup>153,154</sup> However, the VIPs has not been applied in published studies beyond initial development and validation. Future studies quantifying QoL in vitiligo may benefit from the use of this cross-culturally validated tool.

In interventional studies, treatment was generally shown to lessen the impact of vitiligo on QoL, but there were no trends indicating superiority of any type of treatment or longer treatment duration. A 2021 study showed that 94% of patients indicated the need for new and improved treatment modalities; half of the patients were not satisfied with currently available therapies and did not find them effective.<sup>88</sup> It follows that the impact of interventions on vitiligo is still limited and warrants further investigation. Repigmentation of vitiligo lesions is typically a slow process, and psychosocial stress together with previous treatment failure can affect long-term treatment adherence.<sup>4</sup> The complexity of treatment regimens (including time taken to treat and experience satisfactory results) is expected to compound the burden experienced by patients and their caregivers.<sup>155</sup> Additionally, the likelihood of repigmentation is dependent on lesion location, with facial lesions being more responsive to treatment than lesions on the hands and feet.<sup>156,157</sup> It is also generally accepted that patient satisfaction is associated with near-complete ( $\geq 80\%$ ) repigmentation.<sup>158,159</sup> It follows that QoL improvements may be minimal with less complete repigmentation, particularly in patients with lesions in visible and/or sensitive areas. Therefore, more effective treatments and an emphasis on patient well-being and coping mechanisms are needed.

Limitations to this systematic review include the heterogeneity of studies and instruments used to determine QoL, particularly considering that included studies were published over a period of 25 years (1996–2021). Differences in reporting among studies, especially with regard to reporting of total scores versus subscales of instruments measuring QoL, limited the interpretation of results among studies. Furthermore, differences across geographical regions, cultures, skin colour, or gender perceptions of vitiligo and the subsequent impact on QoL were not always considered in studies.

In summary, vitiligo has clinically meaningful effects on the overall QoL of patients. Several studies using instruments with interpretable scores indicate that a majority of patients experience moderate to severe effects of vitiligo on their QoL.

Although a breadth of instruments are used to measure QoL, the use of vitiligo-specific instruments in the literature is limited. These findings highlight that greater attention should be dedicated to QoL decrement awareness and improvement of burden in patients with vitiligo.

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### Author contributions

All authors (MP, RHH, HJ, RM, MO and JS) contributed to the study design, developed the search strategy for the literature review, and took part in the development and drafting of the study and PROSPERO protocols. RM served as a contact for the PROSPERO protocol submission. All authors contributed to the interpretation of extracted data, drafting and critical appraisal of the manuscript and approved the final version for submission. All authors agree to be accountable for all aspects of the work.

### Data availability statement

All data were collected from published articles available in the public domain.

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### Supporting information

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

**Appendix S1.** Search strategy.

**Figure S1.** Number of studies by year of publication\*.

**Figure S2.** Number of studies by country and geographic region\*.

**Table S1.** Generic quality-of-life assessment tools and outcomes among studies that reported total scores in the overall population.

**Table S2.** Generic quality-of-life assessment tools and outcomes in interventional studies.