American Journal of Clinical Dermatology (2021) 22:757–774
https://doi.org/10.1007/s40257-021-00631-6

SYSTEMATIC REVIEW

Psychosocial Effects of Vitiligo: A Systematic Literature Review

Khaled Ezzedine[1] · Viktoria Eleftheriadou[2] · Heather Jones[3] · Kristen Bibeau[3] · Fiona I. Kuo[3] · Daniel Sturm[3] · Amit G. Pandya[4,5]

Accepted: 27 July 2021 / Published online: 23 September 2021

Abstract

Background Patients with vitiligo experience reduced quality of life.

Objective To comprehensively describe the available evidence for psychosocial burden in vitiligo.

Methods A systematic review of observational studies and clinical trials identified using PubMed, EMBASE, Scopus, and the Cochrane databases was performed through 1 March, 2021, to assess psychosocial comorbidities in vitiligo. Two independent reviewers performed an assessment of articles and extracted data for qualitative synthesis.

Results Included studies ($N = 168$) were published between 1979 and 1 March, 2021; 72.6% were published since 2010. Disorders including or related to depression (41 studies, 0.1–62.3%) and anxiety (20 studies, 1.9–67.9%) were the most commonly reported. The most prevalent psychosocial comorbidities were feelings of stigmatization (eight studies, 17.3–100%), adjustment disorders (12 studies, 4–93.9%), sleep disturbance (seven studies, 4.6–89.0%), relationship difficulties including sexual dysfunction (ten studies, 2.0–81.8%), and avoidance or restriction behavior (12.5–76%). The prevalence of most psychosocial comorbidities was significantly higher vs healthy individuals. Factors associated with a significantly higher burden included female sex, visible or genital lesions, age < 30 years (particularly adolescents), and greater body surface area involvement, among others. The most commonly reported patient coping strategy was lesion concealment.

Limitations Available studies were heterogeneous and often had limited details; additionally, publication bias is possible.

Conclusions The results of this systematic review show that vitiligo greatly affects psychosocial well-being. The extent of psychosocial comorbidities supports the use of multidisciplinary treatment strategies and education to address the vitiligo-associated burden of disease.

Protocol Registration PROSPERO (CRD42020162223).

Graphic Abstract

Digital Features for this article can be found at https://doi.org/10.6084/m9.figshare.15058539.

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Key Points

Vitiligo has been associated with depression and anxiety; however, other psychosocial comorbidities have not been comprehensively investigated.

A wide variety of psychosocial comorbidities are prevalent in patients with vitiligo; multidisciplinary treatment strategies and education about vitiligo are vital to addressing the burden of this disease.

1 Introduction

Vitiligo is a chronic inflammatory autoimmune disease that results in skin depigmentation due to the loss of melanocytes [1–3]. Lesions can appear at any age, but onset usually occurs at ≤ 30 years of age [2, 4, 5]. Global prevalence is approximately 0.5–2.0% and varies geographically [6]. Similar prevalence rates have been reported for adult populations as well as children and adolescents [6].

Vitiligo is commonly misinterpreted as a cosmetic disease [2]. Patients with vitiligo experience a higher level of burden [7, 8] compared with healthy controls [7], as reflected by quality-of-life (QoL) indicators. Quality-of-life impairment may be comparable to dermatologic (e.g., atopic dermatitis) [7, 8] and non-dermatologic diseases (e.g., cancer) [9]. Importantly, the QoL burden of vitiligo may be largely affected by the presence of psychosocial comorbidities [10–12]. In recent years, a large focus has been placed on depression and/or anxiety in vitiligo [10–12]. The purpose of this systematic literature review was to comprehensively describe the evidence for psychosocial burden in patients with vitiligo, including the prevalence and types of psychosocial comorbidities, factors associated with psychosocial burden, patient coping strategies, perceptions toward vitiligo, and caregiver burden.

2 Methods

2.1 Literature Search

The search strategy was established and agreed upon by the authors during protocol development (Appendix 1 of the Electronic Supplementary Material [ESM]). PubMed, EMBASE, Scopus, and the Cochrane database were searched for articles from their earliest available entries through 1 March, 2021. The search string, which was limited to articles published in English, included the keywords *vitiligo*, *quality of life*, *burden*, *psychosocial*, and *anxiety*, as well as variants of *depression*, *stigma*, *psychology*, and *psychiatry*. Duplicate results from the separate databases were subsequently discarded.

Peer-reviewed primary publications, including clinical trials and observational studies (cross-sectional, case-control, prospective, and retrospective analyses), were included. Two independent reviewers (WvdS and KW) performed the title and abstract review; reviews and articles with irrelevant content were excluded. The same reviewers performed the full-text review and data extraction; reviewers independently assessed the risk of bias and resolved any disagreement through discussion. Studies excluded at the full-text review included data sets with fewer than five participants (e.g., patients with vitiligo or their caregivers), editorials, commentaries, articles with irrelevant content (including those that focused only on general QoL and/or that did not report instrument subscales that could be related to psychosocial comorbidity), and articles not available in English. Articles that included the same patient populations but reported different outcomes were retained.

Because data were collected from published articles, no institutional review board approval was required for the study. The study protocol was registered with PROSPERO (CRD42020162223).

2.2 Data Extraction and Analysis

Extracted data included study design, geographic region, sample size, detailed patient demographics, prevalence and types of psychosocial comorbidities, extent of psychosocial burden (vs healthy controls and/or patients with other skin diseases), factors associated with psychosocial burden, endpoints (scales) used to assess psychosocial burden, patient coping strategies, perceptions toward vitiligo (by patients and non-patients), and caregiver burden. A qualitative synthesis of evidence was performed to summarize the findings from included primary publications.

3 Results

3.1 Literature Search

Initial database searches yielded 2288 articles, of which 1111 were duplicate records that were excluded from screening; one additional article was identified through other sources. Screening resulted in the exclusion of 919 articles during the title and abstract review; an additional 91 articles were excluded on the full-text review. A total of 168 articles were retained for data extraction and inclusion in the qualitative synthesis (Fig. 1).

3.2 Study Characteristics

Included studies were published between 1979 and 2021, with 72.6% published between 2010 and 2021 [4, 5, 9, 13–177]. Most included studies were observational (96.4%), with only six clinical trials (3.6%) containing data specific to psychosocial comorbidity in vitiligo; child, adolescent, and adult populations were represented in the included studies (Table 1). Studies representing populations from most geographic regions were included (Fig. 2); regions with the most studies included the Middle East (29.8%), Europe (28.6%), and Southern Asia (15.5%). All studies included in the systematic review were qualitatively assessed to minimize the risk of bias; included studies were deemed to be of acceptable quality.

3.3 Instruments Measuring QoL

Among QoL instruments assessing general health, total and/or component scores were most frequently reported for the adult and child versions of the Dermatology Life Quality Index (DLQI, 53 studies) [4, 13, 14, 18, 19, 22, 25, 33, 35–38, 45, 64, 65, 67–70, 74, 77, 81–83, 87, 89, 90, 92, 93, 96, 99, 100, 102, 104, 112, 115, 119, 120, 122, 123, 140, 143, 144, 146, 148, 151, 156, 161, 162, 164–166, 168], Children's DLQI (seven studies) [24, 67, 73, 101, 103, 110, 152], 36-Item Short Form Health Survey (SF-36, eight studies) [9, 82, 83, 105–107, 161, 162], General Health Questionnaire (eight studies) [14, 30, 65, 93, 95, 113, 114, 124], and Skindex-29 (eight studies) [29, 71, 98, 106, 107, 162, 174, 175].

The DLQI is widely used across dermatologic diseases. Fifty studies that reported DLQI mean scores for patients with vitiligo were further examined. Mean scores did not differ vastly by region, but there were trends for higher mean scores (i.e., increased burden of disease) in the Middle East (4.7–14.7) [14, 45, 64, 74, 82, 83, 87, 104, 112, 140, 144, 164, 166], Southern Asia (4.1–12.4) [18, 22, 38, 100, 120, 143, 146, 168], and Eastern Asia (4.0–8.4) [35, 68–70, 119, 156, 161, 162] compared with Europe (1.8–8.7) [4, 77, 89, 90, 92, 93, 96, 99, 102, 104, 122, 123, 148] and North America (5.2–6.6) [115, 151, 165]. The lowest DLQI mean scores were reported in Italy (1.8 [89] and 4.3 [90]), Singapore (4.0 [69] and 4.4 [68]), and Nepal (4.1 [38]), whereas the highest DLQI mean scores were reported in Saudi Arabia (14.7 [45] and 9.0 [64]) and Egypt (13.0 [144], 12.4 [87], 12.2 [25], and 11.2–11.9 [19]). Factors affecting DLQI scores were not examined.

In contrast, the Vitiligo-specific QoL (VitiQoL) instrument has only been reported in eight studies [13, 16, 29,

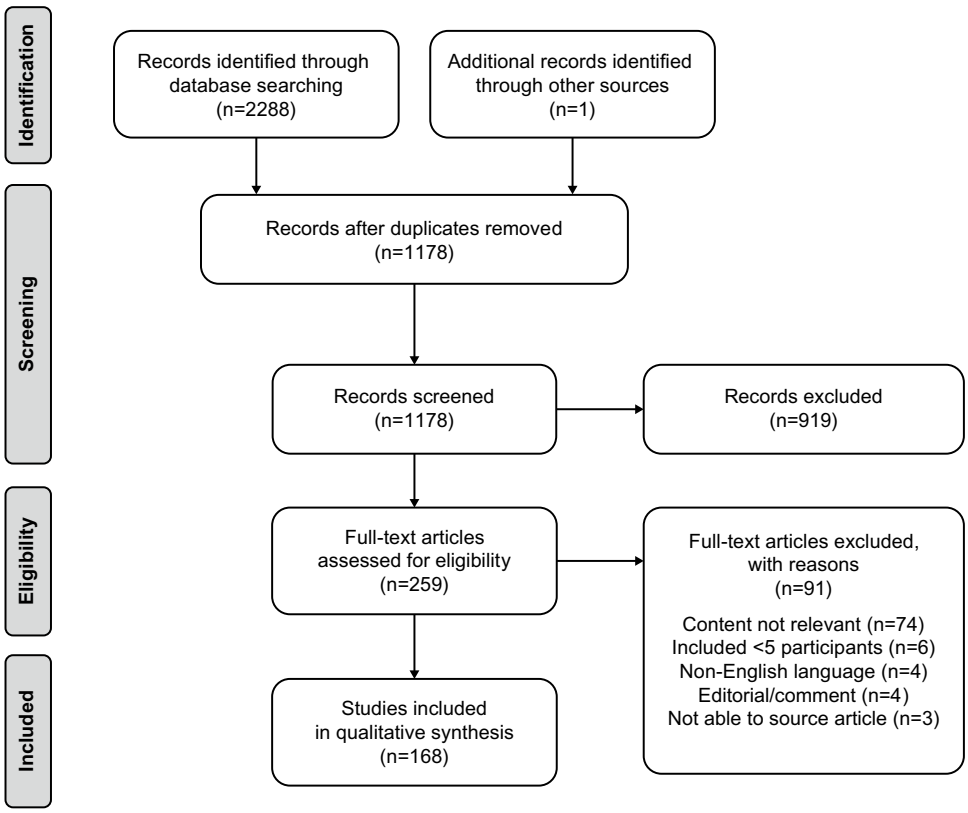

Fig. 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram

Table 1 Summary of study characteristics

Characteristic	Number of studies, *n* (%) *N* = 168
Year of publication	
1979–1999	13 (7.7)
2000–2009	33 (19.6)
2010–2021	122 (72.6)
Study type	
Observational	162 (96.4)
Clinical trial	6 (3.6)
Geographic region[a]	
Africa	4 (2.4)
Europe	48 (28.6)
Eastern Asia[b]	18 (10.7)
Southern Asia	26 (15.5)
Middle East	50 (29.8)
North America	20 (11.9)
South America	6 (3.6)
Age group of patients with vitiligo, years[c]	
Child only (< 12)	1 (0.6)
Adolescent only (12–17)	1 (0.6)
Adult only (≥ 18)	87 (51.8)
Child and adolescent (≤ 17)	13 (7.7)
Adolescent and adult (≥ 12)	42 (25.0)
All age groups (≥ 0)	15 (8.9)
Number of patients with vitiligo[d]	
≤ 25	15 (8.9)
26–100	77 (45.8)
101–200	38 (22.6)
> 200	30 (17.9)

[a]Multinational studies conducted in 2 geographic regions are listed under both regions

[b]Includes East (Northeast) Asia and Southeast Asia

[c]Patient age groups were not reported for 9 (5.4%) studies

[d]The number of patients with vitiligo was not available for 8 studies, which reported on the perceptions of others toward patients with vitiligo ($n = 5$) and caregiver burden ($n = 3$)

32, 67, 80, 88, 115] using our search parameters; half were published in the past year, of which two were clinical trials. There were no notable regional differences in VitiQoL scores among studies, which were conducted in each of the seven geographic regions, with two in North America. Another instrument specific to vitiligo, the Vitiligo Impact Scale (VIS), was only used in three studies, with two published in the past year. One study used the original 27-item VIS [32], and two used the abbreviated 22-item scale (VIS-22) [36, 100]; all studies were conducted in Southern Asian populations. Although the use of vitiligo-specific scales has increased recently, there remains an unmet need for a widely utilized, vitiligo-specific QoL instrument that has been validated in large interventional studies.

3.4 Psychosocial Comorbidities

3.4.1 Prevalence of Psychosocial Comorbidities

A summary of studies that reported psychosocial comorbidities is presented in Table 2 (complete information presented in Table 1 of the ESM). Nine studies noted the presence of any (unspecified) psychosocial comorbidity in 32.6–90.0% of patients with vitiligo [22, 23, 34, 39, 42–44, 138, 145, 173]. Depression and anxiety were the most commonly reported psychosocial comorbidities. Forty-one studies reported depression or depressive disorders (including major depressive disorder, bipolar disorder, and dysthymic disorder) in patients with vitiligo, with a prevalence range from 0.1–62.3% [15, 17, 22, 23, 28, 30, 32, 34, 35, 39, 40, 43, 44, 46, 48, 50, 57, 68, 69, 71, 92, 100, 104, 113–115, 131, 137, 138, 142, 143, 145, 146, 150, 154, 155, 158–160, 163, 177]. Twenty studies reported anxiety or anxiety-related disorders (including generalized anxiety disorder, agoraphobia, social phobia [not social avoidance], and panic disorder), with a prevalence of 1.9–67.9% [22, 23, 30, 34, 39, 43, 44, 46, 50, 57, 92, 115, 137, 138, 150, 154, 155, 158, 159, 175]. Among studies that used the same rating scales for determining the prevalence of depression or anxiety, ranges were more narrow (Table 2). Concomitant depression and anxiety was reported in four studies (4.9–33.3%) [34, 43, 44, 159].

Other psychosocial comorbidities were also widely reported and included feelings of stigmatization (eight studies, 17.3–100%) [32, 101, 102, 131–133, 136, 169], sleep disturbance (seven studies, 4.6–89.0%) [92, 109, 117, 143, 150, 154, 167], alexithymia (four studies, 23.8–46.7%) [72, 108, 129, 142], anger (six studies, 14–36.9%) [40, 46, 141, 142, 145, 158], and somatoform disorder (three studies, 6.3–9.4%) [22, 137, 150]. Various impairments were noted, including emotional impairment (11 studies, 6–65.0%) [13, 23, 32, 40, 46, 56, 131–133, 141, 145]; cognitive impairment (three studies, 0.3–50.8%) [23, 137, 145]; and behavioral impairments that included avoidance or restriction behavior (nine studies, 12.5–76%) [32, 57, 61, 100, 102, 109, 130, 141, 146], attention-deficit/hyperactivity disorder (one study, 20.0%) [34], obsessive disorders (five studies, 0.1–19.5%) [23, 39, 137, 138, 154], and binge-eating disorder (one study, 7.4%) [22]. Alcohol dependence or abuse was reported in three studies (2.4–7.6%) [22, 57, 137]. Patients were affected by adjustment disorders, such as stress associated with vitiligo and worry about spread (12 studies, 4–93.9%) [13, 30, 32, 40, 100, 109, 113, 114, 131, 141, 142, 149], and also experienced aspects of self-consciousness, including embarrassment (eight studies, 24–66.7%) [13, 32, 131–133, 135, 142, 145] and low self-esteem (four

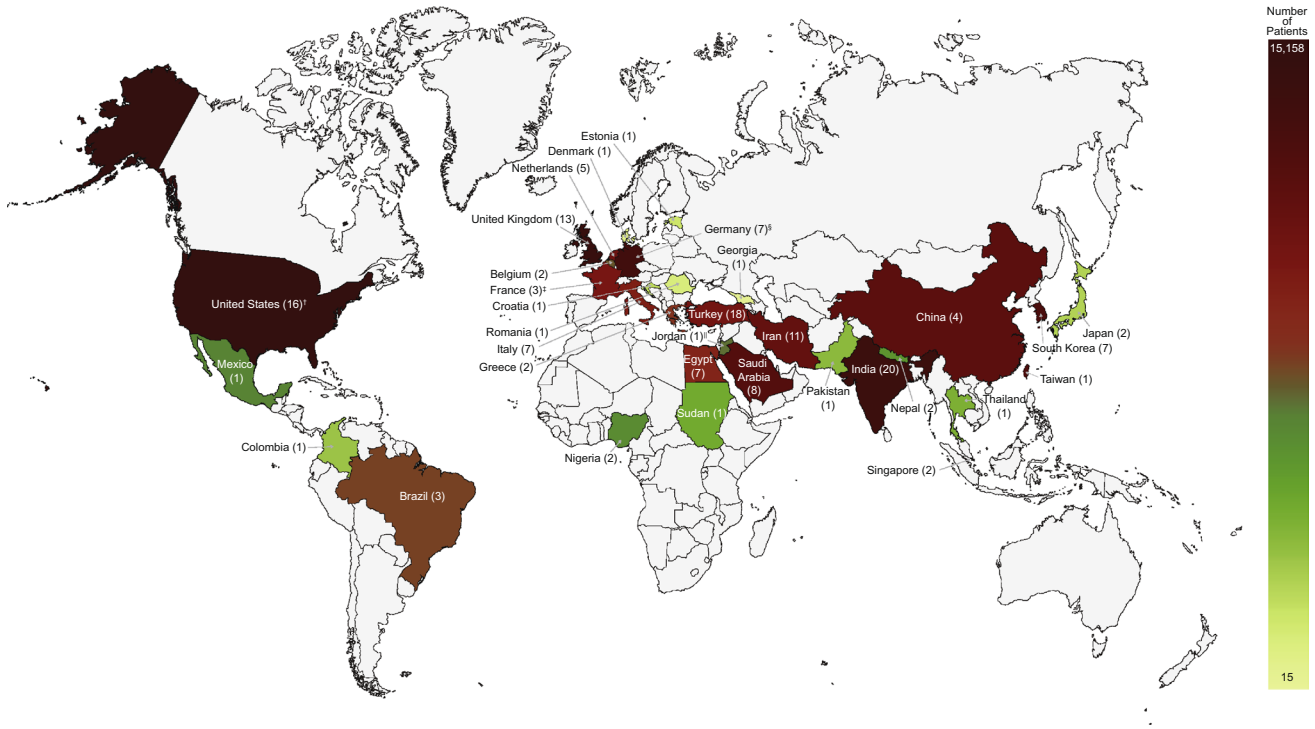

Fig. 2 Number of patients with vitiligo in included studies by country and number of studies. * Number of patients is the sum of patients across studies from each country with multiple populations from the same patient population excluded; the number of unique studies is shown in parentheses after the name of each country. † Includes three studies with populations in the USA and a European country (France, one study [n = 442]; Germany, two studies [n = 85 and n = 74]). Within each study, the number of patients in each country was not available in the published studies; thus, the full population is included in both countries on this map. ‡ Includes one study with a population in France and the USA (n = 442). The number of patients in each country was not available in the published study; thus, the full population is included in both countries on this map. § Includes two studies with populations in Germany and the USA (n = 85 and n = 74) and one study with a population in Germany and Jordan (n = 167). Within each study, the number of patients in each country was not available in the published studies; thus, the full population is included in both countries on this map. ‖ Includes one study with a population in Jordan and Germany (n = 167). The number of patients in each country was not available in the published study; thus, the full population is included in both countries on this map

studies, 6.2–72.7%) [32, 68, 69, 141]. Relationship difficulties including sexual dysfunction were reported over a wide range of patients (ten studies, 2.0–81.8%) [32, 43, 97, 109, 131, 132, 135, 154, 155, 167]. Suicidality was reported among patients with vitiligo, including unspecified suicidality (one study, 28.3%) [138], suicidal ideation (six studies, 3–25.0%) [32, 100, 131, 143, 150, 154], and suicide attempts (two studies, 3.3–3.7%) [150, 154].

3.4.2 Degree of Psychosocial Burden

Compared with controls, psychosocial comorbidities noted to be significantly ($p \leq 0.05$) associated with vitiligo were depression (11 studies) [23, 28, 33, 34, 55, 63, 128, 140, 143, 145, 155], anxiety (ten studies) [23, 30, 33, 34, 55, 63, 119, 128, 140, 155], emotional or behavioral impairment (six studies) [9, 23, 34, 128, 140, 161], adjustment disorder (four studies) [15, 30, 37, 128], low self-esteem (three studies) [57, 65, 134], relationship and sexual dysfunction (three studies) [33, 155, 161], sleep disturbance (two studies) [55, 117], suicidality (one study) [128], self-consciousness (one study) [119], embarrassment (one study) [145], alexithymia (one study) [108], and alcohol abuse or addiction (one study) [128]. Five studies reported that depression [30, 84, 85, 102, 164] and/or anxiety [84, 164] scores measured by Beck Inventory scales were not significantly different in patients with vitiligo vs controls.

The QoL and/or psychosocial burden of vitiligo was most frequently compared with psoriasis (26 articles) [4, 9, 27, 58, 60, 76, 83, 84, 87, 92, 110, 111, 113, 118, 123, 130, 134, 136, 137, 150, 154, 159, 162, 173, 174], alopecia areata (13 articles) [14, 24, 58, 60, 75, 76, 83, 109, 118, 154, 159, 173, 174], acne (11 articles) [14, 58, 76, 117, 118, 137, 140, 154, 159, 174, 175], atopic dermatitis (ten articles) [27, 58, 73, 76, 110, 111, 119, 154, 173, 174], and urticaria (nine articles) [27, 58, 76, 137, 154, 155, 173–175]. Table 3 lists the prevalence of psychosocial

Table 2 Prevalence of psychosocial comorbidity in patients with vitiligo

Psychosocial comorbidity	Comorbidity screening tool	Number of patients with vitiligo	Prevalence, %	Country
Depression or depressive disorders	Any	6–7104	0.1–62.3	Egypt [154], Estonia [92], Georgia [159], Germany [104], India [22, 28, 43, 100, 113, 114, 137, 138, 143, 145, 146, 150, 177], Italy [142], Iran [30], Japan [163], Jordan [104], South Korea [71], Mexico [115], Nepal [32], Nigeria [44], Saudi Arabia [17, 46, 48, 50], Singapore [68, 69], Taiwan [23], Thailand [35], Turkey [34, 39, 57, 155, 158], UK [40, 160], USA [15, 131]
Depression	BDI	100–308	30.3–54.5	Germany [104], India [146], Iran [30], Jordan [104], Mexico [115], Saudi Arabia [17, 48]
	CES-D	54–222	16.2–27.8	Japan [163], South Korea [71], Singapore [68, 69]
	HADS	15–102	7.8–60.0	Georgia [159], Nigeria [44], Saudi Arabia [50]
	PHQ-9	6–104	37.5–50.0	Thailand [35], India [177]
	Other[a]	22–3962	2.7–62.3	Egypt [154], Estonia [92], India [22, 28, 100, 113, 114, 137, 143, 145, 150], Italy [175], Nepal [32], Saudi Arabia [46], Turkey [39, 158], UK [40], USA [15, 131]
Bipolar disorder	Diagnosed during screening	53	7.6	India [137]
	Diagnosis on file	1432	0.1	Taiwan [23]
Dysthymic disorder	Diagnosed during screening	113	0.9–1.8	India [113, 114]
	SCID-I	42–50	4.8–26.0	Turkey [57, 155]
MDD	Other[a]	42–7104	3.5–56.6	India [22, 43, 138], Taiwan [23], Turkey [57], UK [160]
Unspecified depressive disorder	K-SADS-PL	30	23.4	Turkey [34]
Anxiety or anxiety-related disorders	Any	15–1432	1.9–67.9	Egypt [154], Estonia [92], Georgia [159], India [22, 43, 137, 138, 150], Italy [175], Iran [30], Mexico [115], Nigeria [44], Saudi Arabia [46, 50], Taiwan [23], Turkey [34, 39, 57, 155, 158]
Anxiety	BAI	100–150	60.0–66.0	Iran [30], Mexico [115]
	HADS	15–102	18.6–66.7	Georgia [159], Nigeria [44], Saudi Arabia [50]
	Other[a]	30–1432	3.3–57	Egypt [154], Estonia [92], India [22, 43, 137, 150], Saudi Arabia [46], Taiwan [23], Turkey [39, 155, 158]
Agoraphobia	PAS	100	2.0	India [43]
GAD	Other[a]	30–42	4.8–10.0	Turkey [34, 57]
Panic disorder	Other[a]	53–95	1.9–11.3	Estonia [92], India [22, 138]
Social phobia	Other[a]	42–181	2.4–67.9	Estonia [92], India [43, 138], Italy [175], Turkey [57]
Depression and anxiety	Any	15–102	4.9–33.3	Georgia [159], India [43], Nigeria [44], Turkey [34]
	HADS	15–102	4.9–33.3	Georgia [159], Nigeria [44]
	Other[a]	30–100	5–10.0	India [43], Turkey [34]

Table 2 (continued)

Psychosocial comorbidity	Comorbidity screening tool	Number of patients with vitiligo	Prevalence, %	Country
Stigmatization	Other[a]	7–326	17.3–100	Germany [101, 102], India [136], Nepal [32], UK [169], USA [101, 131, 132]
Adjustment disorders	Any	22–326	4–93.9	Egypt [149], Germany [141], Italy [142], India [100, 113, 114], Iran [30], Nepal [32], Nigeria [13], Romania [109], UK [40], USA [131]
Adjustment disorder	Diagnosed during screening	113	10.6–11.5	India [113, 114]
Helplessness	VIS	22	9.1	Nepal [32]
Hopelessness	BHS	100	60.0	Iran [30]
Stress	Holmes and Rahe Social Readjustment Rating Scale	30–32	65.6–93.9	Egypt [149], Romania [109]
	Freiburger Personality Inventory	117	28.2	Germany [141]
Unhappiness	Self-report	22	68.2	Nepal [32]
Worry about others' thoughts	VitiQoL	22–29	31.8–40.9	Nepal [32], Nigeria [13]
Worry about spread	VitiQoL	22–29	68.2–75.9	Nepal [32], Nigeria [13]
	Other[a]	22–326	4–88.0	India [100], Italy [142], Nepal [32], UK [40], USA [131]
Sleep disturbances	Other[a]	30–116	4.6–89.0	Egypt [154], Estonia [92], Greece [117], India [143, 150], Romania [109], UK [167]
Behavioral impairment	Any	22–1432	0.1–76	Egypt [154], France [61], Germany [102, 141], India [22, 100, 130, 137, 138, 146], Nepal [32], Romania [109], Taiwan [23], Turkey [34, 39, 57], USA [61]
ADHD	K-SADS-PL	30	20.0	Turkey [34]
Binge-eating disorder	PRIME-MD PHQ	95	7.4	India [22]
Obsessive disorders	Diagnosed during screening	53–113	7.6–19.5	Egypt [154], India [137], Turkey [39]
	Diagnosis on file	1432	0.1	Taiwan [23]
	Not specified	53	3.8	India [138]
Social and situational avoidance/restriction	Participation Scale	100–150	17.3–48.0	India [130, 146]
	Other[a]	22–442	12.5–76	France [61], Germany [102, 141], India [100], Nepal [32], Romania [109], Turkey [57], USA [61]
Self-consciousness	Any	22–326	6.2–72.7	Germany [141], India [145], Italy [142], Nepal [32], Nigeria [13], Singapore [68, 69], USA [131–133, 135]
Embarrassment	VitiQoL	22–29	27.3–55.5	Nepal [32], Nigeria [13]
	Other[a]	22–326	24–66.7	India [145], Italy [142], Nepal [32], USA [131–133, 135]
Low self-esteem	RSES	145–222	6.2–6.8	Singapore [68, 69]
	Other[a]	22–117	30–72.7	Germany [141], Nepal [32]
Emotional impairment	Any	22–1432	6–65.0	Germany [141], India [145], Nepal [32], Nigeria [13], South Korea [56], Saudi Arabia [46], Taiwan [23], UK [40], USA [131–133]
	VitiQoL	22–29	18.2–55.2	Nepal [32], Nigeria [13]
	Other[a]	61–1432	6–65.0	Germany [141], India [145], South Korea [56], Saudi Arabia [46], Taiwan [23], UK [40], USA [131–133]

Table 2 (continued)

Psychosocial comorbidity	Comorbidity screening tool	Number of patients with vitiligo	Prevalence, %	Country
Cognitive impairment	Any	53–1432	0.3–50.8	India [137, 145], Taiwan [23]
Schizophrenia	Diagnosed during screening	53	3.8	India [137]
	Diagnosis on file	1432	0.3	Taiwan [23]
Unspecified	Skindex-61	61	50.8	India [145]
Relationship difficulties and sexual dysfunction	Any	22–326	2.0–81.8	Egypt [154], India [43], Nepal [32], South Korea [97], Romania [109], Turkey [155], UK [167], USA [131, 132, 135]
Relationships	Other[a]	22–326	4.5–81.8	Nepal [32], USA [131, 135]
Sexual	Other[a]	32–167	2.0–48.2	Egypt [154], India [43], South Korea [97], Romania [109], Turkey [155], UK [167], USA [132, 135]
Alexithymia	TAS-20	30–181	23.8–46.7	Iran [72, 108], Italy [129, 142]
Anger	Any	61–181	14–36.9	Germany [141], India [145], Italy [142], Saudi Arabia [46], Turkey [158], UK [40]
	IPQ	100–164	29.0–34	Saudi Arabia [46], Turkey [158]
	Other[a]	61–181	14–36.9	Germany [141], India [145], Italy [142], UK [40]
Suicidality	Any	30–326	3–28.3	Egypt [154], India [100, 138, 143, 150], USA [131]
Attempts	Diagnosed during screening	30–108	3.3–3.7	Egypt [154], India [150]
Ideation	Other[a]	22–326	3–25.0	Egypt [154], India [100, 143, 150], Nepal [32], USA [131]
Unspecified	Not specified	53	28.3	India [138]
Somatoform disorder	Other[a]	30–95	6.3–9.4	India [22, 137, 150]
Alcohol dependence or abuse	Other[a]	42–95	2.4–7.6	India [22, 137], Turkey [57]

ACS Adjustment to Chronic Skin Disorders Questionnaire, *ADHD* attention-deficit/hyperactivity disorder, *ASEX* Arizona Sexual Experience Scale, *BAI* Beck Anxiety Inventory, *BDI* Beck Depression Inventory, *BHS* Beck Hopelessness Scale, *CES-D* Center for Epidemiologic Studies Depression Scale, *DLQI* Dermatology Life Quality Index, *ES-Q* Emotional State Questionnaire, *GAD* generalized anxiety disorder, *GHQ* General Health Questionnaire, *GHQ-H* Hindi version of the General Health Questionnaire, *HADS* Hospital Anxiety and Depression Scale, *HDRS* Hamilton Depression Rating Scale, *IPQ* Illness Perception Questionnaire, *K-SADS-PL* Schedule for Affective Disorders and Schizophrenia for School Age Children-Present and Lifetime Version, *MDD* major depressive disorder, *PAS* Psychiatric Assessment Schedule, *PHQ-9* Patient Health Questionnaire-9, *PRIME-MD PHQ* Primary Care Evaluation of Mental Disorders–Patient Health Questionnaire, *QIDS-SR-16* Quick Inventory of Depressive Symptomatology-Self Report, *RSES* Rosenberg Self-Esteem Scale, *SCID-I* Structured Clinical Interview for DSM-IV Axis I Disorders, *SDS* Sheehan Disability Scale, *SRE* Schedule of Recent Experience, *TAS-20* Toronto Alexithymia Scale-20, *VIS* Vitiligo Impact Scale, *VIS-22* Vitiligo Impact Scale 22, *VitiQoL* Vitiligo-specific Quality of Life

[a]Reporting based on diagnosis or self-report, an unspecified tool, or a tool used in only 1 study for each comorbidity; if a comorbidity only included data from 1 study, the specific tool (including diagnosis or self-report) was listed. For "diagnosis on file" and "diagnosed during screening," formal diagnosis or diagnostic criteria/codes (i.e., Diagnostic and Statistical Manual of Mental Disorders IV/V or International Classification of Diseases 9/10) suggestive of a formal diagnosis were provided in the article. Tools used in only 1 study per comorbidity include ACS (stigmatization, social and situational avoidance/restriction), ASEX (sexual dysfunction), DLQI (sleep disturbances), ES-Q (depression, anxiety, panic disorder, social phobia, sleep disturbances), Freiburger Personality Inventory (social and situational avoidance/restriction, low self-esteem, emotional impairment, anger), GHQ-H (sleep disturbances, somatoform disorder), HDRS (depression, MDD, suicidal ideation), Holmes and Rahe Social Readjustment Rating Scale (sleep disturbances, social and situational avoidance/restriction, sexual dysfunction), IPQ (depression, emotional impairment), K-SADS-PL (GAD, depression and anxiety), Participation Scale (stigmatization), PAS (MDD, anxiety, social phobia, depression and anxiety, sexual dysfunction), PRIME-MD PHQ (depression, MDD, anxiety, panic disorder, somatoform disorder, alcohol dependence or abuse), QIDS-SR-16 (depression, suicidal ideation), SCID-I (MDD, anxiety, GAD, social phobia, alcohol dependence or abuse), SDS (social and situational avoidance/restriction), Skindex-29 (depression, social phobia, worry about spread, embarrassment, emotional impairment, anger), Skindex-61 (depression, embarrassment, emotional impairment, anger), SRE (sleep disturbances, sexual dysfunction), VIS (depression, worry about spread, social and situational avoidance/restriction, embarrassment, relationship difficulties, suicidal ideation), VIS-22 (worry about spread, social and situational avoidance/restriction), and VitiQoL (social and situational avoidance/restriction). Additional details are available in Table 1 of the ESM

Table 3 Psychosocial comorbidity burden in patients with vitiligo compared with other skin diseases

Psychosocial comorbidity, %	Vitiligo vs acne	Vitiligo vs alopecia areata	Vitiligo vs atopic dermatitis	Vitiligo vs psoriasis	Vitiligo vs urticaria	Vitiligo vs eczema
Depression	**46.3 vs 18.9** [154]	*46.3 vs 55.3* [154]	**46.3 vs 35.5** [154]	**46.3 vs 42.3** [154]	**46.3 vs 35.5** [154]	**60.0 vs 56.6** [159]
	47.2 vs 19.6 [137]	**60.0 vs 50.0** [159]		**47.2 vs 34.8** [137]	**47.2 vs 43.6** [137]	
	60.0 vs 54.1 [159]			*60.0 vs 69.4* [159]		
				10.0 vs 23.3 [150]		
				4.4 vs 6.8 [113]		
Anxiety	*31.5 vs 55.3* [154]	**31.5 vs 19.7** [154]	*31.5 vs 43.6* [154]	**31.5 vs 24.3** [154]	*31.5 vs 43.6* [154]	*66.7 vs 73.3* [159]
	11.3 vs 24.7 [137]	**66.7 vs 64.3** [159]		*11.3 vs 13.5* [137]	*11.3 vs 11.5* [137]	
	66.7 vs 78.4 [159]			*66.7 vs 83.3* [159]	*6.0 vs 30.0* [155] ($p = 0.003$)	
				3.3 vs 3.3 [150]		
Depression and anxiety	**33.3 vs 21.6** [159]	**33.3 vs 21.4** [159]		*33.3 vs 38.8* [159]		**33.3 vs 26.7** [159]
Sleep disturbances	**4.6 vs 1.9** [154]	**4.6 vs 2.4** [154]	*4.6 vs 51.8* [154]	*4.6 vs 22.0* [154]	*4.6 vs 51.8* [154]	
				20.0 vs 56.7 [150]		
Suicide						
Ideation	**25.0 vs 11.7** [154]	*25.0 vs 38.5* [154]	**25.0 vs 19.1** [154]	**25.0 vs 10.0** [154]	**25.0 vs 19.1** [154]	
				10.0 vs 26.6 [150]		
Attempt	**3.7 vs 2.4** [154]	*3.7 vs 4.3* [154]	**3.7 vs 0** [154]	*3.7 vs 4.3* [154]	**3.7 vs 0** [154]	
Sexual dysfunction	**48.2 vs 6.8** [154]	**48.2 vs 20.2** [154]	**48.2 vs 21.8** [154]	**48.2 vs 40.0** [154]	**48.2 vs 21.8** [154]	
					36.0 vs 58.0 [155]	
Somatoform disorder	**9.4 vs 8.3** [137]			**9.4 vs 5.6** [137]	**9.4 vs 9.0** [137]	
Adjustment disorder	*0 vs 10.3* [137]			*0 vs 4.5* [137]	*0 vs 7.7* [137]	
				11.5 vs 14.6 [113]		
Obsessive-compulsive disorder	**18.5 vs 3.9** [154] *7.6 vs 11.3* [137]	**18.5 vs 2.9** [154]	**18.5 vs 2.7** [154]	**18.5 vs 2.7** [154] **7.6 vs 2.3** [137]	**18.5 vs 2.7** [154] **7.6 vs 2.6** [137]	
Bipolar affective disorder	**7.6 vs 2.1** [137]			**7.6 vs 3.4** [137]	**7.6 vs 3.9** [137]	
Schizophrenia	**3.8 vs 3.1** [137]			*3.8 vs 5.6* [137]	**3.8 vs 2.6** [137]	
Alcohol dependence syndrome	**7.6 vs 2.1** [137]			*7.6 vs 11.2* [137]	**7.6 vs 5.1** [137]	
Dysthymia				**1.8 vs 1.0** [113]	*26.0 vs 46.0* [155] *(p = 0.04)*	
Stigma				*17.3 vs 28.0* [136]		
Stress[a]		*65.6 vs 68.9* [109]				
Participation restriction				*17.3 vs 28.0* [130]		
Unspecified psychiatric comorbidity		**79.2 vs 60.0** [173]	**79.2 vs 56.3** [173]	*79.2 vs 80.0* [173] *16.7 vs 53.3* [150] *(p = 0.003)*	**79.2 vs 70.6** [173]	

Bolded cells indicate a higher prevalence in vitiligo; italics cells indicate a lower prevalence in vitiligo

[a]Stress includes stressful events that stem from family, personal, work, and financial problems

Fig. 3 Heat map showing the references that report factors significantly associated with psychosocial comorbidity. Significance was conferred at $p \leq 0.05$. *Darker red shading* indicates a larger number of studies reporting significant associations

comorbidity in vitiligo compared with other skin diseases. In general, psychosocial comorbidities were more prevalent in vitiligo compared with acne, alopecia areata, atopic dermatitis, and urticaria but less prevalent vs psoriasis. Regarding non-dermatologic diseases, one study reported comparable SF-36 mental component scores in patients with vitiligo vs chronic lung disease, arthritis, cancer, and congestive heart failure [9].

3.4.3 Factors Associated with Psychosocial Burden

Factors that were significantly associated with higher psychosocial (Fig. 3) or overall QoL burden were female sex (30 studies) [15, 21, 25, 28, 30, 45, 46, 49, 51, 57, 62, 66–68, 70, 88, 90, 99, 104, 107, 109, 112, 113, 120, 123, 132, 143, 146, 154, 158], lesion location in visible areas (e.g., face, hands [17 studies]) [4, 25, 35, 37, 49, 62, 70, 80, 89, 90, 92, 101, 122, 123, 138, 143, 151] or genitals (eight studies) [70, 89, 97, 105, 115, 122, 144, 151], younger age (16 studies; particularly those aged <30 years and more so in adolescents) [17, 25, 30, 48, 49, 62, 67, 68, 70, 88, 100, 113, 119, 132, 151, 160], and extensive body area involvement (13 studies) [4, 25, 63, 65, 70, 89, 92, 96, 98, 107, 151, 152, 166]. Unmarried and/or single relationship status (nine studies) [17, 22, 48, 49, 62, 70, 93, 113, 138], longer disease duration (nine studies; particularly duration >5 years) [4, 25, 30, 62, 65, 68, 88, 107, 119], progressive disease (seven studies) [22, 25, 35, 89, 92, 107, 143], Fitzpatrick skin phototype IV–VI (five studies) [21, 35, 37, 77, 107], lower education status (five studies; particularly high school or lower level of education) [17, 48, 49, 108, 136], non-segmental vitiligo (three studies; vs segmental or focal vitiligo) [97, 115, 143], non-Caucasian race (three studies) [93, 96, 133], positive family history of vitiligo (two studies) [98, 101], being employed (one study; compared with being students, unemployed, or retired) [35], and higher socioeconomic level (one study) [25] were also significantly associated with increased burden. Four studies reported that comorbid depression significantly reduced overall QoL [35, 92, 100, 115]. Management strategies [107] including camouflage [18, 25, 102, 122, 156], cognitive behavioral therapy [26, 125, 127, 148, 168], phototherapy [51, 52, 157], and depigmentation cream (in patients with extensive vitiligo) [19] were associated with decreased vitiligo-associated burden.

3.5 Coping Strategies Among Patients with Vitiligo

The most commonly discussed coping strategies in studies included the use of concealing clothing (six studies, 8.3–78.3% of patients) [25, 74, 101, 102, 131, 157], camouflage (four studies, 14.6–62.0% of patients) [25, 74, 102, 131], and altered body movements (three studies, 5.9–8.1% of patients) [74, 101, 102]. Other coping strategies included vitiligo acceptance [42, 132, 170], avoidance behavior [101, 102, 170], and psychotherapy or support groups [42, 61, 170].

3.6 Perceptions Toward Vitiligo

Perceptions toward vitiligo were discussed in 13 articles; seven articles focused on perceptions of patients toward their vitiligo [32, 46, 79, 126, 158, 165, 172], and six focused on perceptions of others toward patients with vitiligo [31, 47, 54, 78, 91, 171]. Several articles covered aspects of knowledge or beliefs about vitiligo, including attitudes and behaviors. Common misperceptions included thinking that vitiligo is contagious [31, 47, 54, 91, 172] and that vitiligo is caused by external forces (e.g., "evil eye," witchcraft/sorcery, evil spirits/Jinn, chance/fate) [31, 32, 46, 47, 79, 158], lack of hygiene [47, 91], or infection with germs or viruses [47, 54, 79, 158]. In three studies that investigated attitudes toward patients with vitiligo, participants with sufficient knowledge of vitiligo vs insufficient knowledge reported a lower prevalence of negative attitudes and a higher prevalence of positive attitudes [31, 78, 91]. In four studies that reported a willingness to have a relationship with or marry someone with vitiligo, 6.7–43.9% of participants responded in the affirmative [31, 47, 54, 78]; reasons for refusing marriage included social reasons, the impact of vitiligo on appearance, and that vitiligo is believed to be inherited or contagious [31, 47].

3.7 Caregiver Burden

Caregiver (e.g., parents, sibling, spouse) burden and associated factors were discussed in ten articles [20, 24, 53, 64, 86, 103, 111, 121, 139, 172], although only four provided prevalence rates [64, 86, 103, 111] for aspects of psychosocial burden. Overall QoL among caregivers was impaired, with depression, anxiety, emotional distress, and impaired social life commonly mentioned. There were no notable consistencies across studies regarding factors affecting caregiver burden. Two studies reported significant parental depression vs controls [24, 121], and one study showed that caregiver depression and anxiety significantly reduced QoL among patients with vitiligo [111].

4 Discussion

In the past decade, interest in and publication of the overall and psychosocial QoL of patients with vitiligo have increased tremendously, highlighting the QoL burden in vitiligo. Several recent studies have reported meta-analyses of depression and/or anxiety in patients with vitiligo [10–12], with less focus on other psychosocial comorbidities experienced by patients with vitiligo. We sought to comprehensively review the prevalence of any psychosocial comorbidity reported by patients in peer-reviewed scientific articles.

Studies in this systematic review reported wide ranges (likely owing to differing assessment tools and geographically heterogeneous populations) for the majority of psychosocial comorbidities. Psychosocial comorbidities reported in >50% of patients in any study were depression, major depressive disorder, anxiety, social phobia, feelings of stigmatization, adjustment disorders, sleep disturbances, avoidance and restriction behavior, self-consciousness, emotional impairment, relationship difficulties, and cognitive impairment. Psychosocial comorbidities reported in >25% of patients included coexistent depression and anxiety, sexual dysfunction, alexithymia, anger, suicidality (unspecified suicidality and suicidal ideation), and dysthymic disorders. The breadth and severity of these comorbidities and the resulting effect on QoL in patients with vitiligo extend beyond what has previously been dismissed as a cosmetic disease.

Factors that were most commonly associated with significantly higher psychosocial burden included female sex, visible or genital lesions, age < 30 years (particularly adolescents), and extensive body area involvement, among others. The implementation of facial vitiligo as a primary outcome measure in recent clinical studies [178–181] is supported by the gravity of the association between facial lesions and a higher psychosocial burden reported here. Some of the factors significantly associated with a higher psychosocial burden have been associated with a greater willingness to pay, although the association between willingness to pay and lesion location was not assessed [4].

In many cases, studies reported findings using broad QoL instruments that are not specific to vitiligo. Generic QoL instruments may not reflect the true burden of vitiligo, in part because of instrument design. For example, the DLQI includes an item for physical symptoms (i.e., itch, soreness, pain, or stinging) [182], which tend to be more pronounced in patients with atopic dermatitis or psoriasis, possibly leading to an underestimation of burden in vitiligo vs other dermatologic diseases [183, 184]. In addition, the heterogeneity of studies included in this review may further complicate direct comparisons of general QoL in vitiligo with other dermatologic diseases. Interestingly, a recent study in South Korea showed that willingness to pay was highest in vitiligo compared with other dermatologic diseases including atopic dermatitis and psoriasis, despite lower median DLQI scores in patients with vitiligo [27]. The application of widely used generic QoL instruments in vitiligo may therefore be better suited for comparison across demographic or clinical characteristics. In our analysis, there were regional trends in DLQI scores, with a lower QoL burden among European and North American populations and a higher QoL burden noted among Middle Eastern and Asian populations, consistent with

findings from another review [185]. Future studies should assess QoL instruments for cultural sensitivity/influence. Psychosocial morbidity should also be examined to further elucidate the effect of culture on vitiligo burden, which is an important consideration for dermatologists caring for diverse patients. During the past decade, the VitiQoL was developed specifically for measuring QoL in patients with vitiligo [184], although it does not differentiate between skin types (i.e., fair and dark skin), and its use has not been widespread. Our search criteria identified only eight studies that reported aspects of psychosocial comorbidity using the VitiQoL instrument [13, 16, 29, 32, 67, 80, 88, 115], two of which were clinical trials published in the past year [16, 29]. Further research using vitiligo-specific QoL instruments is warranted.

It is well recognized that more effective treatment strategies are needed for vitiligo. The results of this systematic review raise the urgency for strategies (including better treatments, counseling, and cognitive behavioral therapy) to improve the overall QoL and psychosocial health of patients. Although not directly assessed in this systematic review, the significant association of longer disease duration with poorer psychosocial and general QoL supports the possibility that delayed interventions could exacerbate disease burden. Furthermore, this review highlights the unmet need for a widely used vitiligo-specific instrument to assess psychosocial burden and reinforce that vitiligo is not a purely cosmetic disease. A cross-culturally validated, vitiligo-specific instrument, the 12-item short-form of the Vitiligo Impact Patients scale (VIPs-12), was recently developed to address QoL burden, including psychological effects on daily life and items specifically related to skin type; however, the instrument still awaits testing in prospective studies for responsiveness [186]. In addition to psychotherapy and/or counseling for patients, general education about vitiligo in the unaffected population may help lessen the stigma associated with vitiligo and assist in improving the psychosocial well-being of patients and their caregivers. In surveys among people without vitiligo, participants with sufficient knowledge of the disease were more likely to display positive attitudes toward patients with vitiligo compared with people who had insufficient disease knowledge [31, 78, 91]. The most commonly reported coping strategy among patients in our analysis was concealment of lesions through clothing choices, camouflage, and altered body movements. It may follow that if patients were made to feel more comfortable in their own skin and around others, and if nonpatients were educated to be more accepting, the psychosocial burden among patients with vitiligo and their caregivers could be lessened.

Limitations to this study include the heterogeneity of studies (together with differences in methods used to quantify the presence of psychosocial comorbidities), the paucity of details available in some publications, and restriction to English language in the search criteria. Additionally, inclusion of only peer-reviewed publications may be associated with publication bias [187].

5 Conclusions

Vitiligo has a significant and broad effect on psychosocial well-being, an aspect of QoL that may not be accurately or fully captured by currently available QoL instruments. The extent of the psychosocial comorbidities summarized in this systematic review indicates that multidisciplinary approaches to treatment strategies (including medical and psychological treatment) and education about vitiligo are needed to address the burden of this disease.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s40257-021-00631-6.

Acknowledgements Writing assistance was provided by Wendy van der Spuy, PhD, and Ken Wannemacher, PhD, of ICON (North Wales, PA, USA) and was funded by Incyte Corporation (Wilmington, DE, USA).

Declarations

Funding The study was funded by Incyte Corporation, Wilmington, DE, USA.

Conflicts of Interest/Competing Interests KE is a consultant for AbbVie, Incyte Corporation, La Roche-Posay, Pfizer, Pierre Fabre, Sanofi, and Viela Bio. VE has nothing to disclose. HJ and FIK were employees and shareholders of Incyte Corporation when the study was conducted. KB and DS are employees and shareholders of Incyte Corporation. AGP has served as an investigator for Aclaris Therapeutics, Immune Tolerance Network, Incyte Corporation, and Pfizer; a consultant for Arcutis, Avita, Chromaderm, Immune Tolerance Network, Incyte Corporation, Pfizer, Viela Bio, and Villaris; and a board member who also holds stock options for Clarify Medical and Tara Medical.

Ethics Approval Because data were collected from published articles, no ethical approval was required for the study.

Consent to Participate Not applicable.

Consent for Publication Not applicable.

Availability of Data and Material All data were collected from published articles available in the public domain.

Code availability Not applicable.

Authors' Contributions KE, VE, HJ, KB, FIK, DS, and AGP contributed to the study design, including formulation of the search strategy, had access to extracted data, and contributed to data interpretation. KE, VE, HJ, KB, FIK, DS, and AGP were involved in drafting the manuscript. KE, VE, HJ, KB, FIK, DS, and AGP approved the final version for submission and agree to be accountable for all aspects of the work.

Prior Presentations Data in this article were previously presented, in part, at the European Academy of Dermatology and Venereology 2020 Virtual Congress (29–31 October, 2020) and the Vitiligo International Symposium 2020 Virtual Conference (5–6 December, 2020).

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Authors and Affiliations

Khaled Ezzedine[1] · Viktoria Eleftheriadou[2] · Heather Jones[3] · Kristen Bibeau[3] · Fiona I. Kuo[3] · Daniel Sturm[3] · Amit G. Pandya[4,5]

✉ Khaled Ezzedine
khaled.ezzedine@aphp.fr

[1] Department of Dermatology, Henri Mondor University Hospital and Université Paris-Est Créteil Val de Marne, 51 Avenue du Maréchal de Lattre de Tassigny, Créteil, 94010 Paris, France

[2] Department of Dermatology, Queen Elizabeth Hospital, Birmingham, UK

[3] Incyte Corporation, Wilmington, DE, USA

[4] Palo Alto Foundation Medical Group, Mountain View, CA, USA

[5] University of Texas Southwestern Medical Center, Dallas, TX, USA