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# The prevalence of psychological co-morbidity in people with vitiligo: a systematic review and meta-analysis

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**What's already known about this topic?**

- Vitiligo can have a profound psychosocial impact
- People with vitiligo are more likely to suffer depression than those without vitiligo

**What does this study add?**

- People with vitiligo experience a range of psychological symptoms/disorders.
- Approximately one in four people with vitiligo suffer from depression however the prevalence of anxiety is unclear as it varies substantially according to the screening tool used.
- Validation of psychological outcome screening tools in the field of dermatology should be considered.

## Abstract

Background: Vitiligo is a chronic disorder causing skin depigmentation with global prevalence varying from 0.2 to 1.8%. UK guidelines recommend assessment of psychological state during clinical evaluation of vitiligo. However, the prevalence of psychological co-morbidity in people with vitiligo has not been described.

Objectives: We aimed to establish the prevalence of psychological symptoms or disorders in people with vitiligo and describe the psychological outcome measures used.

Methods: We performed a comprehensive search of MEDLINE, Embase, CINAHL and PsychInfo to identify observational studies assessing the prevalence of psychological symptoms/disorders (December 2016). DerSimonian and Lard random-effects models were utilized to estimate the overall pooled prevalence.

Results: We identified 29 studies with 2530 people with vitiligo. Most studies included a measure of either depression (n=25) or anxiety (n=13).The commonest tools were the Hospital Anxiety and Depression Scale and the Centre for Epidemiology Studies Depression Scale. Ten studies provided information on thirteen other psychological symptoms/disorders. The pooled prevalence using depression-specific and anxiety-specific questionnaires was 0.29 (95%CI 0.21, 0.38) and 0.33 (95%CI 0.18, 0.49) respectively. The prevalence was lower for clinically diagnosed depression (0.21; 95%CI 0.15, 0.28) and anxiety (0.15; 95%CI 0.06, 0.24). When non-specific tools were used the prevalence remained similar for depression (0.27; 95%CI 0.08, 0.46) but increased for anxiety (0.46; 95% CI 0.39, 0.52). High heterogeneity was observed.

Conclusions: A range of psychological symptoms or disorders are common in people with vitiligo. The prevalence of anxiety was notably influenced by type of screening tool, suggesting the need for validated screening tools in this group of patients.

## Introduction

Vitiligo is an acquired chronic disorder of skin pigmentation caused by the selective destruction of melanocytes.[1] It causes milky-white patches or macules on the skin, most commonly in exposed areas of the body such as the hands and face.[2] Vitiligo occurs equally in both genders and all ethnicities, and may develop at any age, although it most commonly presents in children and young adults.[1] The global prevalence varies from 0.2 to 1.8%.[3]

The aetiology of vitiligo is not fully understood. Autoimmune, genetic and environmental factors probably combine to give a mixed aetiology.[4-6] A recent Cochrane systematic review concluded that there is currently no cure for the condition although there are various treatments/interventions available to manage vitiligo such as topical corticosteroids, calcineurin inhibitors, phototherapy and camouflage.[7]

Although vitiligo is typically asymptomatic it may substantially affect the psychological wellbeing of people living with the condition.[8-12] This may be due to the burden associated with the visibility of vitiligo and its consequent impact on interactions with others.[13] Another reason may be the unpredictable prognosis and the current lack of a cure. The British Association of Dermatologists recommends assessment of the psychological state and quality of life during clinical evaluation of people with vitiligo.[2] Furthermore, a recent systematic review has shown that people with vitiligo are significantly more likely to suffer from depression and impaired general health, compared to those without vitiligo.[14] However, there is a lack of knowledge of the other types of psychological symptoms/disorders that people with vitiligo experience. Such information may help the development of future trials of psychological interventions in people with vitiligo. A Cochrane Review found only one randomised controlled trial on the effectiveness of psychological interventions in people with vitiligo.[7] Evaluating the

effectiveness of psychological interventions for this patient group was one of the top ten research priorities identified by the James Lind Alliance's vitiligo Priority Setting Partnership.[15]

To date, no systematic review on the prevalence of psychological co-morbidity in people with vitiligo has been conducted. Therefore, this review aimed to synthesise all available evidence from observational studies on the prevalence of psychological symptoms/disorders in people living with vitiligo.

## Methods

The study protocol was registered with National Institute for Health Research International prospective register of systematic reviews (PROSPERO) on 21st of March 2016 and is available at http://www.crd.york.ac.uk/prospero (registration number CRD42016036193). We initially planned to look at two primary outcomes (i) psychological co-morbidity and (ii) quality of life within the same study. However, due to the number of studies found and the theoretical difference between quality of life and psychological symptoms, it was decided it would be more appropriate to assess these outcomes separately. The systematic review on quality of life in people with vitiligo has been published.[16] The methods used for this review were reported in accordance with the PRISMA statement.[17]

### Literature search

On 21st of December 2016, a literature search in MEDLINE (OVID), Embase (OVID), PsychINFO and CINAHL was performed. Records from the inception of each database were accessed. The search strategy was developed by O.O. after consultation with an information specialist with experience in dermatology (D.G.). The strategy included the search terms 'vitiligo', 'leucoderma', 'leukoderma', 'psychology', 'depression', 'anxiety' and 'mental health' (see Supplementary Table 1). The use of these search terms was appeared sufficient in capturing psychological co-morbidity and it was consequently deemed as unnecessary to conduct searches using all known diagnostic categories.

Grey literature was searched at this website:

http://www.bl.uk/reshelp/findhelprestype/theses/ethos/index.html.

**Eligibility Criteria**

We included observational studies (cohort, case-control, cross-sectional and case series) that reported data on the prevalence or incidence of any psychological outcome in people with vitiligo. Ecological studies, policy statements, editorials/reviews and randomised controlled clinical trials involving any form of intervention were excluded. Trials were excluded as people included in trials may not be representative of people from everyday clinical practice and to keep this work manageable within the timeframe available.[18] There was no restriction on age, sex, type of vitiligo, ethnicity or publication language. Vitiligo had to have been diagnosed clinically by a clinician or dermatologist. The psychological outcomes of interest were any form of psychological symptom or disorder that was either self-reported or clinically diagnosed.

**Selection**

Two authors (O.O., S.R.) independently assessed studies for eligibility using a two-stage sifting process. The titles and abstracts were reviewed simultaneously and subsequently the full text copies of potentially relevant studies were screened. Results of the independent assessments by each author were compared and differences were resolved through discussion. A citation search using Google Scholar and reference lists of key papers were searched by hand for relevant studies to increase the sensitivity of our search.

**Data extraction**

Two authors (O.O., L.H.) independently extracted information from the included studies using a piloted template and any disparity was resolved by discussion. The translation and data extraction of the Spanish, French and Italian papers were conducted by researchers proficient in these languages.

**Evaluation of methodological quality of the included studies**

The methodological quality of the included studies was evaluated by combining and adapting the Newcastle-Ottawa[19] and the National Heart Lung and Blood Institute scales.[20-21] Modification of the Newcastle-Ottawa scale was required due to concerns about the vagueness of decision rules in relation to the focus of our review and the National Heart Lung and Blood Institute scale was used to include a tool for cross-sectional studies (Supplementary Tables 2a & 2b). Quality assessment was conducted independently by three of the researchers (O.O., L.H., S.R.). A score of ≥70% was rated as good, 50-69% as fair and <50% as poor.

**Data Analysis**

Pooled prevalence (expressed as a proportion) of depression and anxiety according to depression/anxiety-specific, non-depression/non-anxiety specific questionnaires and psychiatric diagnosis was calculated. For controlled studies, studies were pooled to determine relative risk when there were a sufficient number of studies ≥3. Random-effects model of DerSimonian and Lard was used to account for variance between and within studies.[22] Heterogeneity between studies was assessed using I-squared statistic, with values of 25%, 50% and 75% considered low, moderate and high heterogeneity respectively.[23] All analyses were performed using Stata version 14.0 (StataCorp, College Station, TX). For psychological outcomes which were not included in the meta-analysis, a narrative synthesis was conducted.

## Results

### Study selection

The execution of the search strategy initially resulted in 1000 studies after duplicates were removed. After screening titles and abstracts, 98 studies were obtained for full review. Of these, 24 fulfilled the inclusion criteria for the systematic review (Figure 1). A search through the grey literature database identified no further studies. However, a citation search using Google Scholar identified two further eligible papers and reference tracking identified three eligible studies, giving a total of 29 included studies.

### Description of included studies

Table 1 summarises the general characteristics of the 29 eligible studies (2530 vitiligo patients in total). Twenty-six of the studies were cross-sectional and three studies were case-control. Eleven studies included comparator groups; these consisted of participants diagnosed with other dermatological diseases such as acne, psoriasis, albinism, alopecia areata, skin cancer, neurodermatitis, eczema, or healthy participants that were either related to or accompanying the participants to the clinics/hospitals, or hospital staff. There were seven studies conducted in Europe, thirteen studies from Asia, three studies from the Americas, three studies from the Middle East and the remaining three studies were from Africa. Sample size ranged from 9 to 326 people. The participants were recruited from either hospitals (n=24) or dermatology clinics (n=4) or from both (n=1).

### Psychological outcomes

The most common psychological outcomes in the studies reviewed was depression (n=25 studies) (Table 2). Anxiety was reported in 13 studies; two of these reported generalised anxiety (Table 3). Ten studies reported on 13 other less commonly reported outcomes: substance abuse, suicidal attempts, panic disorder, social phobia, dysthymic

disorder, adjustment disorder, alcohol addiction, asthenia, interpersonal conflict, insomnia, obsessive compulsive disorder, specific phobia and agoraphobia. (Table 4). The focus of our analysis is on depression and anxiety as these are the two most common outcomes.

**Outcome measurement tools**

Nineteen different outcome tools were used in total including depression-specific or anxiety-specific questionnaires (e.g. Centre for Epidemiology Studies Depression Screening Index (CES-D) or ) non-depression or non-anxiety specific questionnaires (e.g. General Heath Questionnaire (GHQ)) and clinical diagnostic tools (e.g. International Classification of Disease 10$^{th}$ version (ICD-10)) (Table 1). Of the 29 included studies, only nine[26,28-30,33,34,40,42,51] included clinical assessment (only one study reported the use of a structured interview[42]), and four of these did so after screening with the general health questionnaire (Table 1).[28-30,40]

**Quality of studies**

A score of ≥70% was rated as good, 50-69% as fair and <50% as poor. Of the 29 studies, n=4 (14%) were of poor quality, n=13 (45%) were of fair quality and n=12 (41%) of were of good quality (Table 1).

**Prevalence of depression**

A total of 25 studies including 2071 vitiligo patients reported data on the prevalence of depression. Table 2 summarises the general characteristics of each study. A total of fourteen different outcome tools were used to assess depression including five depression-specific tools (n=11 studies) and four non-depression specific tools (n=4 studies); clinical examination was conducted in nine studies using the ICD-10 or Diagnostic and Statistical Manual of Mental Disorders, 4$^{th}$ Edition (DSM-IV) or tool not

stated. One study used a questionnaire but did not provide further details (and has been classified as a non-depression specific questionnaire). In two studies clinical examination was conducted only for patients within a certain GHQ threshold (this is why the total number of patients in Table 2 is greater than 2071).[28,30]

The pooled prevalence of depression among vitiligo patients based on depression-specific questionnaires was 0.29 (95% CI 0.21, 0.38), as shown in Figure 2. There was substantial heterogeneity between the studies (I-squared=89%, p<0.001). Using non-depression specific questionnaires, the pooled prevalence was similar 0.27 (95% CI 0.08, 0.46) with higher heterogeneity (I-squared=97.5%, p<0.001); using clinical diagnosis, the pooled prevalence was lower 0.21 (95% CI 0.15, 0.28) with lower heterogeneity (I-squared 66.7%, p=0.004).

Eleven studies presented the prevalence of depression in a comparator group. The most common comparator was people with psoriasis with five studies including 172 vitiligo patients. Only the study conducted by Mattoo et al.[28], matched the control and the vitiligo participants (by sex and education). The overall risk of depression was less in people with vitiligo compared to those with psoriasis; pooled relative risk was 0.66 (95% CI 0.48, 0.90); there was no heterogeneity (Figure 3).

The second most common comparator was healthy controls (n=4 studies; but only two of these reported the prevalence of depression in the comparator groups).[42,51] In both studies, the prevalence of depression was higher in vitiligo patients compared to the healthy controls. The healthy controls and vitiligo participants were similar in age and sex in the study conducted by Balaban et al.[42] but not in the study by Karia et al.[51]

**Prevalence of anxiety**

Thirteen studies including 866 vitiligo patients reported data on the prevalence of anxiety. Table 3 summarises the general characteristics of each study. A total of five different outcome tools were used to assess this disorder including three anxiety-specific tools (n=5 studies) and two non-anxiety tools (n=2 studies); and clinical examination by a psychiatrist was conducted in six studies.

The pooled prevalence of anxiety among vitiligo patients based on anxiety-specific questionnaires was 0.33 (95% CI 0.18, 0.49), as shown in Figure 4. There was substantial heterogeneity between the studies (I-squared=89.2%, p<0.001). Using non-anxiety specific questionnaires, the pooled prevalence was higher at 0.46 (95% CI 0.39, 0.52) with higher heterogeneity (I-squared=96.2%, p<0.001). Using clinical diagnosis, the prevalence was substantially lower at 0.15 (95% CI 0.06, 0.24) but heterogeneity was still very high (I-squared 88.7%, p<0.001).

Nine studies presented the prevalence of anxiety in a comparator group. The most common comparator was psoriasis with four studies including 119 vitiligo patients. Only the study conducted by Mattoo et al.[28] matched the control group and the vitiligo participants by sex. The pooled relative risk of anxiety in people with vitiligo compared to those with psoriasis was 0.80 (95% CI 0.57, 1.13) and there was no heterogeneity (Figure 5).

The second most common comparator was healthy controls.[42,51] The prevalence of anxiety was higher in vitiligo patients compared to the healthy controls. The control group was matched on age and sex in the study conducted by Balaban et al.[42]

**Prevalence of other psychological symptoms or disorders**

Ten studies including 577 patients with vitiligo provided data on 13 less commonly reported psychologicaloutcomes . Table 4 summarises the general characteristics of each

study. The majority of these studies were based in Asia (n=6 studies). The most commonly reported psychological symptom was social phobia (n=4 studies); the prevalence varied from 2.4% to 67.9%; two studies used psychiatric clinical examination and two used self-reported questionnaires.

Seven studies presented the prevalence of other psychological outcomes in a comparator group. The most common comparator was people with psoriasis (n=4 studies). Apart from dysthymic disorder, the prevalence of the psychological symtoms was the same or lower, in those with vitiligo compared to those with psoriasis. Only two studies matched the vitiligo and comparator groups. Matto et al.[28] matched in terms of sex and education while Balaban et al.[42] matched on age and sex.

## Discussion

### Main findings

To our knowledge, this is the first systematic review that synthesises the prevalence of different psychological outcomes in people with vitiligo. We demonstrated that people with vitiligo experience a range of outcomes on the spectrum of psychological symptoms or disorders including substance abuse and suicidal attempts.. The two most commonly reported outcomes were depression and anxiety which were assessed using either self-reported questionnaires or clinical diagnosis made by a psychiatrist.

Historically vitiligo has been classed as a cosmetic problem; this is clearly not the case.[53] Qualitative studies indicate that vitiligo can have a huge psychological burden on people.[54,55] According to our review, approximately a quarter of vitiligo patients reported depression symptoms using depression-specific or general/mental-health questionnaires and almost a fifth of them had clinical depression. However, they were significantly less likely to show symptoms of depression than people with psoriasis. The pooled prevalence of anxiety did differ depending on whether the diagnosis was made using anxiety-specific

or general/mental health questionnaires ranging from 33% to 46%. However, it was substantially lower when diagnosed clinically (15%). Similar to depression, the risk of anxiety was lower in those with vitiligo compared to those with psoriasis, but this result was not statistically significant.

**Strengths and Limitations**

The major strength of this review is the broad overview of the different psychological outcomes experienced by people with vitiligo. Searching four databases, including PsychInfo, helped ensure our search was comprehensive and improves on similar previous published work.[14] Including non-English papers, as far as possible, has reduced the potential for bias. We have also been able to conduct a meta-analysis to quantify the difference in depression and anxiety between people with vitiligo and those with psoriasis. Such information has not been reported previously.

The main limitation of this review is the high heterogeneity between the included studies. This may be due to the broad inclusion criteria. We have attempted to address study heterogeneity by employing a random-effects model. However, due to substantial heterogeneity, the results may not be generalizable to all vitiligo patients. Information on the type and severity of vitiligo, which can be potential sources of heterogeneity, were not available in most studies. Also, the majority of the included studies did not have adequate controls, making the results susceptible to the effect of confounding factors. All studies were hospital or clinic-based, which could also result in selection bias. Due to the small number of studies, we were not able to conduct separate meta-analyses for different measurement tools when comparing the prevalence of depression and anxiety to those seen in people with psoriasis. We were also limited to comparing vitiligo with psoriasis and not other skin conditions, or healthy controls. Finally, we had insufficient studies to assess publication bias.

**Comparison with other studies**

The most relevant study to compare our findings with is that of Lai et al.[14] The authors conducted a systematic review to investigate the prevalence of depression and general health in people with vitiligo worldwide. Among studies reporting the prevalence of depression based on ICD codes, the pooled prevalence of depression among vitiligo patients was 0.253 (95% CI: 0.161 to 0.345). Using DSM-IV criteria, the pooled prevalence decreased to 0.122 (95% CI: 0.046 to 0.197) and using self-reported questionnaires the prevalence of depressive symptoms was 0.336 (95% CI: 0.248-0.424). Their results, like ours, showed that use of questionnaires provided higher estimates of prevalence than clinical diagnosis. This is because questionnaires such as HADS (Hospital Anxiety and Depression Scale) and CES-D are often used to measure the presence of depressive symptomatology rather than the presence of the full criteria for a diagnosis of clinical depression to be made. The same rational is applicable in the explanation as to why the prevalence of clinically diagnosed anxiety that we found was substantially lower than that reported by questionnaires.

Lai et al. combined broad mental-health and depression-specific self-reported questionnaires, which may explain why their pooled estimate of the risk of depression was higher than ours (0.34 vs. 0.29). We only combined questionnaires specific to measuring depression, as we believe this provides a more accurate estimate. We did not report prevalence separately for ICD and DSM-IV tools, as Lai et al. did, but reported prevalence for clinical diagnosis overall as it was unclear in some papers which tool was used.[26,34] Finally, similar to Lai et al. we report that those with vitiligo are at higher risk of depression than healthy controls (without adjustment for confounders). Lai et al. did not compare the prevalence of depression in people with vitiligo with those with other skin conditions.

**Research implications**

This review has established that there are currently no large or population-based studies exploring the psychological impact of vitiligo. With the current availability of linked large routinely collected healthcare datasets such as the Clinical Practice Research Datalink and Hospital Episode Statistics and Mental Health Dataset[54] there is an opportunity for researchers to conduct large cost-effective studies at population level with comparable controls which will provide more generalizable and less biased results in this field.

This review has shown the range of psychological screening tools not all of which were validated being used. Lack of sensitivity of the measurement tools and variability in the tool use may greatly increases the risk of producing inaccurate estimates of the prevalence of anxiety. . It has been argued that the Patient Health Questionnaire-version 9 and the Generalised Anxiety Disorder Assessment-version 7 are useful pragmatic measures as they are free and widely used in primary care to assess depression and anxiety amongst people with skin conditions.[55-56] Nevertheless, our findings indicate that there is a case for developing dermatology specific validated scales.

**Clinical implications**

As approximately one in four people with vitiligo appear to have depression and at least one in seven have anxiety, assessment of psychological state during clinical evaluation of vitiligo patients, as suggested by the British Association of Dermatology guidelines[2], is essential. The same can be said for clinical evaluation of people with other skin conditions.

**Conclusion**

People living with vitiligo experience a range of psychologicalsymptoms/disorders. The prevalence of depression did not vary substantially by screening tool whereas the prevalence of anxiety did, suggesting the need for dermatological specific validated

screening tools in this group of patients. Population-based studies in this field are also required to provide more generalizable results.

# TABLE 1: CHARACTERISTICS OF INCLUDED STUDIES

| STUDY/ LOCATION | STUDY DESIGN | NUMBER OF VITILIGO PARTICIPANTS | M/F | SETTING | ADULTS/ CHILDREN | MEAN AGE (YEARS) | OUTCOME | OUTCOME MEASUREMENT TOOL | QUALITY RATING |
|---|---|---|---|---|---|---|---|---|---|
| **Porter 1987** (24) **USA** | Cross Sectional | 326 | Not stated | Clinic | Adults + children | 34 | Depression | Questionnaire | Fair |
| **Delfino 1988** (25) **Italy** | Case Control | 10 | 5/5 | Hospital | Adults | Not stated | Depression, Psychopathic personality, Hysteria | MMPI | Fair |
| **Vilella 1998** (26) **Cuba** | Case Control | 22 | 8/14 | Hospital | Children | Not stated | Depression, Anxiety, ADHD, | Clinical examination by psychiatrist, Machover test | Poor |
| **Picardi 2000** (27) **Italy** | Cross Sectional | 32 | Not stated | Hospital | Adults | Not stated | Psychiatric morbidity | GHQ 12 (Italian version) | Fair |
| **Mattoo 2001** (28) **India** | Cross Sectional | 113 | 62/51 | Hospital | Not stated | 30.1 (SD: 12.49) | Adjustment Disorder, Depressive episodes, Dysthymia | GHQ 12 (Hindi version), CPRS (which comprises of MADRS and ASI), ICD-10 | Good |
| **Sharma 2001** (29) **India** | Cross Sectional | 30 | 17/13 | Hospital | Adults | Not stated | Depression, Anxiety, Sleep Disturbance | GHQ 12 (Hindi version) prior to Psychiatric assessment using DSM – IV criteria | Good |
| **Mattoo 2002**(30) **India** | Cross Sectional | 113 | 62/51 | Hospital | Adults + children | 30.1(SD:12.49) | Adjustment Disorder, Depressive episodes | GHQ 12 (Hindi version), CPRS (which comprises of MADRS and ASI), ICD-10 | Good |
| **Sampogna 2004** (31) **Italy** | Cross Sectional | 29 | Not stated | Hospital | Not Stated | Not Stated | Psychiatric morbidity | GHQ 12 | Fair |
| **Mechri 2006** (32) **France** | Case Control | 60 | 32/28 | Hospital | Adults + children | 38.9 (SD:25.7) | Depression, Anxiety | CPRS(MADRS), HAM-A | Fair |
| **Ahmed 2007** (33) **Pakistan** | Cross Sectional | 100 | 38/62 | Hospital | Adults + children | 24.6 years | Major Depression. Generalized Anxiety, Social Phobia, Agoraphobia, Sexual Dysfunction | GHQ 12 (urdu version) prior to PAS (urdu Version) DAQ | Good |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Arycan 2008** (34) **Turkey** | Cross Sectional | 113 | 53/60 | Hospital | Adults + children | Males: 29.2, Females: 33.4 | Depression, Anxiety, Personality Disorder, Neurotic symptoms, Obsession | Clinical examination by psychiatrist | Poor |
| **Saleh 2008** (35) **Egypt** | Cross Sectional | 50 | 25/25 | Hospital | Adults | Not stated | Psychiatric morbidity, Anxiety, Depression, Suicidal thoughts, Suicidal attempts | GHQ 28 (Arabic version), Taylor manifest anxiety scale (Arabic version), SDS questionnaire. | Good |
| **Sampogna 2008** (36) **Italy** | Cross Sectional | 180 | 57/123 | Clinic | Adults + children | Not stated | Depression | GHQ 12 | Fair |
| **Nogueira 2009** (37) **Brazil** | Cross Sectional | 100 | Not stated | Hospital | Adults + children | Not stated | Psychological complaints | Questionnaire (cut off score not stated) | Poor |
| **Osman 2009** (38) **Sudan** | Cross Sectional | 111 | 46/65 | Hospital | Adults + children | Not stated | Psychological morbidity | GHQ 12 | Good |
| **AlGhamdi 2010** (39) **Saudi Arabia** | Cross Sectional | 164 | 91/70 | Hospital | Adults + children | 27 (SD:13) | Depression, Anxiety | IPQ | Good |
| **Bashir 2010** (40) **Pakistan** | Cross Sectional | 9 | Not stated | Hospital | Adults | Not stated | Depression | GHQ– 12 (Urdu version), PSE, ICD-10 | Fair |
| **Choi 2010** (41) **Korea** | Cross Sectional | 57 | 27/30 | Hospital | Children | 15.4 (SD:1.8) | Depression | CES-D | Good |
| **Balaban 2011** (42) **Turkey** | Cross sectional | 42 | 19/23 | Clinic | Adults | 39.70 (SD: 12.90), | Major Depression (MD), Generalised Anxiety Disorder (GAD), Dysthymic Disorder, Social Phobia, Specific Phobia, | HADS, SCID -1, LSAS | Good |
| **Chan 2011** (43) **Singapore** | Cross Sectional | 145 | 72/73 | Hospital | Adults | 47.4 (SD:15.0) | Depression | CES-D | Good |
| **Yamamoto 2011** (44) **Japan** | Cross Sectional (Pilot) | 54 | Not stated | Hospital/Clinic | Not stated | Not stated | Depression | CES-D | Poor |
| **Karelson 2012** (45) **Estonia** | Cross Sectional | 54 | 22/32 | Clinic | Not stated | 36.6 | Depression, Anxiety, Panic disorders, Social Phobia, Insomnia | ES-Q | Fair |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Chan 2013 (46) Singapore** | Cross Sectional | 222 | 105/117 | Hospital | Adults | 48.4 (SD:14.9) | Depressive Symptoms | CES-D | Good |
| **Ajose 2014 (47) Nigeria** | Cross Sectional | 102 | 51/51 | Hospital | Adults + children | 35.9 (SD: 13.65) | Depression. Anxiety | HADS | Good |
| **Ramakrishna 2014 (48) India** | Cross Sectional | 53 | 12/41 | Hospital | Not stated | Not stated | Major Depressive Disorder, Social Phobia, Panic Disorder, Obsessive Compulsive Disorder, Social Phobia and major Depression | HDRS | Fair |
| **Alshahwan 2015 (49) Saudi Arabia** | Cross Sectional | 64 | Not stated | Hospital | Adults | Not stated | Depression, Anxiety | HADS | Fair |
| **Mahsa 2015 (50) Iran** | Cross Sectional | 110 | 48/62 | Hospital | Adults + children | Not stated | Depression | HDRS | Fair |
| **Karia 2015 (51) India** | Cross Sectional | 50 | 22/28 | Hospital | Adults | 33.60 | Depression, Anxiety disorder, Schizophrenia, Substance Abuse | GHQ 28, DSM – IV | Fair |
| **Tsintsadze 2015 (52) Georgia** | Cross Sectional | 15 | 9/6 | Hospital | Adults + children | Not stated | Anxiety, Depression | HADS | Fair |

Centre for Epidemiologic Studies Depression Scale (CES-D), Hamilton Depression Rating Scale (HDRS), Hamilton Anxiety Rating Scale f(HAM – A), Hospital Anxiety and Depression Scale (HADS), General Health Questionnaire (GHQ) Emotional State Questionnaire (ES-Q), Structured clinical interview for DSM – IV Axis 1 Disorders (Clinical Version) (SCID-1), Liebowitz Social Anxiety Scale (LSAS), Present State Examination (PSE), Sheehan Disability Scale (SDS), Illness Perception Questionnaire (IPQ), Taylor Manifest Anxiety Scale (TMAS), Self rating Depression Scale (SDS), Rosenberg Self Esteem Scale (RSES), Dysfunction Analysis Questionnaire (DAQ), Impact of Skin Disease Scale (IMPACT), Comprehensive Psychopathological Rating Scale (CPRS) (which comprises of Montgomery Asberg Depression Rating Scale (MADRS) and Anxiety Severity Index (ASI)), Multi-factorial Method for Personality Investigations(MMPI), International statistical Classification of Disease version 10 (ICD)-10, Psychiatric Assessment Schedule (PAS), Standard Deviation (SD).

## TABLE 2: PREVALENCE OF DEPRESSION

| OUTCOME SCREENING TOOL | STUDY | COUNTRY | SAMPLE SIZE (VITILIGO PARTICIPANTS) | PREVALENCE | COMPARATOR | SAMPLE SIZE (COMPARATORS) | PREVALENCE IN COMPARATORS |
|---|---|---|---|---|---|---|---|
| HADS | Ajose 2014 (47) | Nigeria | 102 | 30% | Albinism with severe skin complications | 34 | 27% |
| | | | | | Albinism without severe skin complications | 53 | 2% |
| | Alshahwan 2015 (49) | Saudi Arabia | 64 | 14.1% | | | |
| | Tsintsadze 2015 (52) | Georgia | 15 | 60% | Acne | 37 | 54% |
| | | | | | Alopecia Areata | 28 | 50% |
| | | | | | Psoriasis | 36 | 69.4% |
| | | | | | Neurodermatitis | 18 | 18% |
| | | | | | Scabies | 23 | 21.7% |
| | | | | | Eczema | 30 | 56.6% |
| DSM-IV/SCID-1 | Balaban 2011(42) | Turkey | 42 | 14.3% | Healthy controls | 33 | 6.1% |
| | Sharma 2001 (31) | India | 30 | 10% | Psoriasis | 30 | 23.3% |
| | Karia 2015 (51) | India | 50 | 20% | Healthy controls | 50 | 0% |
| CES-D | Choi 2010 (41) | Korea | 57 | 22.8% | | | |
| | Chan 2011 (43) | Singapore | 145 | 17.2% | | | |
| | Yamamoto 2011 (44) | Japan | 54 | 27.8% | | | |
| | Chan 2013 (46) | Singapore | 222 | 16.2% | | | |
| GHQ | Sampogna 2008 (36) | Italy | 180 | 31% | | | |
| ICD-10 | Mattoo 2001 (28) | India | 113 | 21.7% | Psoriasis | 103 | 29.16% |
| | Mattoo 2002 (30) | India | 113 | 18.8% | | | |
| | Bashir 2010 (40) | Pakistan | 9 | 44.4% | | | |
| PAS (Urdu version) | Ahmed 2007 (33) | Pakistan | 100 | 15% | | | |
| SDS | Saleh 2008 (35) | Egypt | 50 | 24% | Psoriasis | 50 | 30% |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | | | | Alopecia Areata | 50 | 16% |
| HDRS | Ramakrishna 2014 (48) | India | 53 | 56.6% | | | |
| | Mahsa 2015 (50) | Iran | 110 | 52.7% | | | |
| CLINICAL EXAMINATION BY A PSYCHIATRIST | Vilella 1998 (26) | Cuba | 22 | 40.9% | Neurotic controls | 22 | 13.6% |
| | Arycan 2008 (34) | Turkey | 113 | 32.7% | | | |
| CPRS (MADRS) | Mechri 2006 (32) | France | 60 | 18.3% | Non vitiligo dermatoses | 60 | 0% |
| MMPI | Delfino 1988 (25) | Italy | 10 | 20% | Alopecia Areata | 30 | Not Stated |
| | | | | | Acne | 10 | Not Stated |
| | | | | | Psoriasis | 10 | Not Stated |
| | | | | | Healthy controls | 10 | Not Stated |
| IPQ | AlGhamdi 2010 (39) | Saudi Arabia | 164 | 54% | | | |
| ES-Q | Karelson 2012 (45) | Estonia | 54 | 20% | Psoriasis | 57 | 42% |
| | | | | | Healthy controls | 57 | Not Stated |
| QUESTIONNAIRE (NO FURTHER DETAILS GIVEN) | Porter 1987 (24) | USA | 326 | 7% | | | |

Centre for Epidemiologic Studies Depression scale (CES-D), Hamilton Depression Rating Scale (HDRS), Hospital Anxiety and Depression Scale (HADS), General Health Questionnaire (GHQ) Emotional State Questionnaire (ES-Q), Structured clinical interview for DSM – IV Axis 1 Disorders (Clinical Version) (SCID-1), Sheehan Disability Scale (SDS), Illness Perception Questionnaire (IPQ), Self rating Depression Scale (SDS), Impact of Skin Disease Scale (IMPACT), Comprehensive Psychopathological Rating Scale (CPRS) (which comprises of Montgomery Asberg Depression Rating Scale (MADRS), MMPI (a Multi-factorial Method for Personality Investigations), International statistical Classification of Disease version 10 (ICD)-10, Psychiatric Assessment Schedule (PAS), Multi-factorial Method for Personality Investigations(MMPI).

## TABLE 3: PREVALENCE OF ANXIETY

| OUTCOME SCREENING TOOL | STUDY | COUNTRY | VITILIGO PARTICIPANTS (SAMPLE SIZE) | PREVALENCE | COMPARATORS | SAMPLE SIZE (COMPARATORS) | PREVALENCE IN COMPARATORS |
|---|---|---|---|---|---|---|---|
| HADS | Ajose 2014 (47) | Nigeria | 102 | 48% | Albinism (with severe complications) | 34 | 54% |
| | | | | | Albinism (without severe complications) | 53 | 4% |
| | Alshahwan 2015 (49) | Saudi Arabia | 64 | 26.6% | | | |
| | Tsintsadze 2015 (52) | Georgia | 15 | 66.7% | Acne | 37 | 78.4% |
| | | | | | Alopecia Areata | 28 | 64.3% |
| | | | | | Psoriasis | 36 | 83.3% |
| | | | | | Neurodermatosis | 18 | 55.5% |
| | | | | | Scabies | 23 | 39% |
| | | | | | Eczema | 30 | 73.3% |
| DSM-IV/SCID-1 | Balaban 2011 (42) | Turkey | 42 | 4.8% | Healthy comparators | 33 | 3.0% |
| | Sharma 2001 (29) | India | 30 | 3.3% | Psoriasis | 30 | 3.3% |
| | Karia 2015 (51) | India | 50 | 8% | Healthy Comparators | 50 | 4% |
| HAM-A | Mechri 2006 (32) | France | 60 | 20% | Non Vitiligo dermatoses | 60 | 0% |
| CLINICAL EXAMINATION BY PSYCHIATRIST | Vilella 1998 (26) | Cuba | 22 | 68.1% | Neurotic controls | 22 | 31.8% |
| | Arycan 2008 (34) | Turkey | 113 | 15.9% | | | |
| PAS (Urdu version) | Ahmed 2007 (33) | Pakistan | 100 | 10% | | | |
| TAYLOR MANIFEST ANXIETY SCALE (ARABIC VERSION) | Saleh 2008 (35) | Egypt | 50 | 14% | Psoriasis | 50 | 12% |
| | | | | | Alopecia Areata | 50 | 24% |
| IPQ | AlGhamdi 2010 (39) | Saudi Arabia | 164 | 57% | | | |
| ES-Q | Karelson 2012 (45) | Estonia | 54 | 22% | Psoriasis | 57 | 33% |
| | | | | | Healthy Comparators | 57 | Not Stated |

Hospital Anxiety and Depression Scale (HADS), Hamilton Anxiety Rating Scale f(HAM – A), , Emotional State Questionnaire (ES-Q), Diagnostic and Statistical Manual of mental disorders, 4th Edition (DSM – IV) criteria, Structured clinical interview for DSM – IV Axis 1 Disorders (Clinical Version) (SCID-1), Illness Perception Questionnaire (IPQ), Psychiatric Assessment Schedule (PAS), Taylor Manifest Anxiety Scale (TMAS),

# TABLE 4: PREVALENCE OF OTHER PSYCHOLOGICAL SYMPTOMS/DISORDERS

| DISORDERS | STUDY | COUNTRY | VITILIGO PARTICIPANTS (SAMPLE SIZE) | PREVALENCE | COMPARATORS | SAMPLE SIZE (COMPARATORS) | PREVALENCE (COMPARATORS) | OUTCOME SCREENING TOOL |
|---|---|---|---|---|---|---|---|---|
| SUBSTANCE ABUSE | Karia 2015 () | India | 50 | 10% | Healthy Comparators | 50 | 0% | DSM – IV criteria |
| SUICIDAL ATTEMPTS | Sharma 2001 (29) | India | 30 | 3.3% | Psoriasis | 30 | 3.3% | DSM – IV |
| | Saleh 2008 (35) | Egypt | 50 | 2% | Psoriasis | 50 | 4% | DSM – IV |
| | | | | | Alopecia Areata | 50 | 2% | |
| PANIC DISORDER | Karelson 2012 (45) | Estonia | 54 | 2% | Psoriasis | 57 | Not Stated | ES-Q |
| | | | | | Healthy Comparators | 57 | Not Stated | |
| | Ramakrishna 2014 (48) | India | 53 | 11.3% | | | | RSES |
| SOCIAL PHOBIA | Ahmed 2007 (33) | Pakistan | 100 | 8% | | | | GHQ. PAS (Urdu Version) |
| | Balaban 2011(42), | Turkey | 42 | 2.4% | Healthy Comparators | 33 | 0% | GHQ, SCID-I |
| | Karelson 2012 (45), | Estonia | 54 | 7% | Psoriasis | 57 | Not stated | ES-Q |
| | | | | | Healthy comparators | 57 | Not Stated | |
| | Ramakrishna 2014 (48) | India | 53 | 67.9% | | | | RSES |
| DYSTHMIC DISORDER | Mattoo 2001 (28) | India | 113 | 8.7% | Psoriasis | 103 | 4.2% | GHQ, CPRS(MADRS), ICD-10 |
| | Mattoo 2002 (30) | India | 113 | 6.25% | | | | GHQ, CPRS(MADRS), ICD-10 |
| | Balaban 2011 (42) | Turkey | 42 | 4.8% | Healthy Comparators | 33 | 0% | GHQ, SCID-I |
| ADJUSTMENT DISORDER | Mattoo 2001 (28) | India | 113 | 56.52% | Psoriasis | 103 | 62.5% | GHQ, CPRS(MADRS), ICD-10, DAQ, IMPACT |
| | Mattoo 2002 (30), | India | 113 | 75% | | | | GHQ, CPRS(MADRS), ICD-10, DAQ, IMPACT |
| ALCOHOL ADDICTION | Balaban 2011 (42) | Turkey | 42 | 2.4% | Healthy Comparators | 33 | 0% | GHQ, SCID-I |
| ASTHENIA | Karelson 2012 (45) | Estonia | 54 | 41% | Psoriasis | 57 | 65% | ES-Q |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | Healthy Comparators | 57 | Not Stated | |
| INTERPERSONAL CONFLICT | Sharma 2001 (29) | India | 30 | 3.3% | Psoriasis | 30 | 3.3% | GHQ, DSM – IV |
| INSOMNIA | Vilella 1998 (26) | Cuba | 22 | 22.7% | Neurotic controls | 22 | 9% | Clinical examination by psychiatrist |
| | Sharma 2001 (29) | India | 30 | 20% | Psoriasis | 30 | 56.7% | GHQ |
| | Karelson 2012 (45) | Estonia | 54 | 30% | Psoriasis | 57 | Not stated | ES-Q |
| | | | | | Healthy Comparators | 57 | Not Stated | |
| OBSESSIVE COMPULSIVE DISORDER | Ramakrishna 2014 (48) | India | 53 | 51% | | | | RSES |
| SPECIFIC PHOBIA | Balaban 2011 (42) | Turkey | 42 | 2.4% | Healthy Comparators | 33 | 0% | GHQ, SCID-I |
| AGORAPHOBIA | Ahmed 2007 (33) | Pakistan | 100 | 2% | | | | GHQ, PAS, DAQ |

Hospital Anxiety and Depression Scale (HADS), Diagnostic and Statistical Manual of mental disorders, 4th Edition (DSM – IV) criteria, Comprehensive Psychopathological Rating Scale (CPRS) (which comprises of Montgomery Asberg Depression Rating Scale (MADRS), Dysfunction Analysis Questionnaire (DAQ), Impact of Skin Disease Scale (IMPACT), International statistical Classification of Disease and related health problems (ICD)-10, General Health Questionnaire (GHQ), Structured Clinical Interview for DSM – IV Axis 1 Disorders (Clinical Version) (SCID-1), Rosenberg Self Esteem Scale (RSES), Psychiatric Assessment Schedule (PAS), Emotional State Questionnaire (ES-Q ).

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**Supporting Information**

## SUPPLEMENTARY TABLE 1: SEARCH TERMS FOR MEDLINE (OVID MEDLINE (R) IN PROCESS AND OTHER NON-INDEXED CITATIONS AND OVID MEDLINE (R) 1946 TO PRESENT)

| S/NO | SEARCH TERM |
|---|---|
| 1 | Exp vitiligo/ |
| 2 | Vitiligo.mp. |
| 3 | Leucoderma.mp. |
| 4 | Leukoderma.mp. |
| 5 | 1 or 2 or 3 or 4 |
| 6 | Exp "Quality of life"/ |
| 7 | Exp mental health/ |
| 8 | Exp psychology/ |
| 9 | Exp depression/ |
| 10 | Exp depressive disorder/ |
| 11 | Exp anxiety/ |
| 12 | Exp social stigma/ |
| 13 | Depress*.mp |
| 14 | Antidepress*.mp |
| 15 | Anti-depress*.mp |
| 16 | Psychosocial*.mp. |
| 17 | Psychology.mp. |
| 18 | Psychological*.mp. |

| | |
|---|---|
| 19 | "Quality of Life".mp. |
| 20 | Depression.mp. |
| 21 | Anxiety.mp. |
| 22 | Stigma* |
| 23 | 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 |
| 24 | 5 and 23 |

## SUPPLEMENTARY TABLE 2A: QUALITY ASSESSMENT TOOL (COHORT AND CROSS SECTIONAL STUDIES)

| S/NO | CRITERIA | YES | NO | NA, NR, CD* |
|---|---|---|---|---|
| 1 | Was the research question or objective in the paper clearly stated? | | | |
| 2 | Was the study population clearly specified and defined? | | | |
| 3 | Was the sample somewhat or a true representative of the average vitiligo affected population in that environment/community? | | | |
| 4 | Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Was there a description of the derivation of the non exposed cohort? | | | |
| 5 | Were inclusion and exclusion criteria for being in the study pre-specified and applied uniformly to all participants? | | | |
| 6 | Was a sample size justification, power description, or variance and effect estimates provided? | | | |
| 8 | Was there sufficient timeframe to be able to see an association between the exposure and the outcome? | | | |
| 8 | Was there a demonstration that the outcome of interest was not present before the manifestation of vitiligo? | | | |
| 9 | Did the study examine different levels/proportion of the vitiligo as related to the outcome (e.g., categories/severity of outcome)? | | | |
| 10 | Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants? | | | |
| 11 | Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants? | | | |
| QUALITY RATING (GOOD, FAIR OR POOR) | | | | |
| Reviewer #1 | | | | |
| Reviewer #2 | | | | |

*CD, cannot determine; NA, not applicable; NR, not reported

## SUPPLEMENTARY TABLE 2B: QUALITY ASSESSMENT TOOL (CASE CONTROL STUDIES)

| S/NO | CRITERIA | YES | NO | NA, NR, CD* |
|---|---|---|---|---|
| 1 | Was the research question or objective in the paper clearly stated? | | | |
| 2 | Was the study population clearly specified and defined? | | | |
| 3 | Was there a clear definition of the cases? Were they differentiated from controls? | | | |
| 4 | Did the authors include a sample size justification? | | | |
| 5 | Were controls selected or recruited from the same or similar population that gave rise to the cases (including the same timeframe)? Were they clearly defined? | | | |
| 6 | Were the definitions, inclusion and exclusion criteria, algorithms or processes used to identify or select cases and controls valid, reliable, and implemented consistently across all study participants? | | | |
| 7 | If less than 100 percent of eligible cases and/or controls were selected for the study, were the cases and/or controls randomly selected from those eligible? | | | |
| 8 | Were the investigators able to confirm that the exposure/risk occurred prior to the development of the condition or event that defined a participant as a case? | | | |
| 9 | Were the measures of exposure clearly defined, valid, reliable, and implemented consistently (including the same time period) across all study participants? | | | |
| 10 | Was there use of concurrent controls? | | | |
| 11 | Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants? | | | |
| QUALITY RATING (GOOD, FAIR OR POOR) | | | | |
| Reviewer #1 | | | | |
| Reviewer #2 | | | | |

*CD, cannot determine; NA, not applicable; NR, not reported

## Figure Legends

**Figure 1: Summary of study selection process**

**Figure 2: Meta-analyses of the prevalence of depression measured by (1) Depression-specific tools; (2) Non-depression specific tools and (3) Clinical Examination**

**Figure 3: Meta-analysis of the prevalence of depression in people with vitiligo compared to those with psoriasis**

**Figure 4: Meta-analyses of the prevalence of anxiety measured by (1) Anxiety-specific tools; (2) Non-anxiety specific tools and (3) Clinical Examination**

**Figure 5: Meta-analysis of the prevalence of anxiety in people with vitiligo compared to those with psoriasis**