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The mental health associations of vitiligo: UK population-based cohort study

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Background

Vitiligo is an acquired, autoimmune depigmenting skin disorder that may affect psychological well-being.

Aims

To determine the risk and impact of psychological comorbidity in people with new-onset vitiligo.

Method

We conducted a retrospective observational study, using UK general practice data (2004–2020). Adults diagnosed with vitiligo ($n = 7224$) were matched 1:4 with controls ($n = 28\,880$). Associations within 2 years of diagnosis were assessed for psychological conditions: recurrent depressive disorder (RDD), depressive episodes, non-phobia-related anxiety disorder, social phobia, adjustment disorder, substance misuse, self-harm and suicide attempts. Healthcare utilisation, time off work and unemployment within 1 year were compared in those with and without a mental health condition at vitiligo diagnosis.

Results

At diagnosis, people with vitiligo had a similar prevalence of mental health conditions as controls, except for anxiety disorder (cases 7.9%, controls 7.0%; $P = 0.014$). Incident RDD and anxiety disorder were more common in people with vitiligo (RDD: adjusted hazard ratio (aHR) 1.25, 95% CI 1.01–1.55; anxiety disorder: aHR 1.23, 95% CI 1.00–1.51). Risk was highest in Black and minority ethnic individuals (RDD: aHR 1.72, 95% CI 1.06–2.79; depressive episodes: aHR 1.56, 95% CI 1.03–2.37). No association was found with other mental health conditions. People with vitiligo and psychological comorbidity had more primary care encounters, more time off workand higher unemployment.

Conclusions

People with vitiligo have a higher incidence of RDD and anxiety disorder than controls, and this risk increase may be greatest in Black and minority ethnic populations.

Keywords

Depressive disorders; anxiety disorders; vitiligo; epidemiology; comorbidity.

Vitiligo is an acquired autoimmune skin disorder characterised by depigmented patches of skin that may appear in a localised or more generalised distribution. Vitiligo is estimated to affect 0.5–2% of the global population, with a similar incidence between genders and across different ethnic groups.[1] Human society places a profound significance on aesthetics, including skin pigmentation,[2] and so although vitiligo is typically asymptomatic, it may substantially affect the psychological well-being of people living with the condition.[3] This may be exacerbated by the unpredictable prognosis, current lack of a cure and visibility of lesions.[4]

Reliable population-based estimates of the psychological burden associated with vitiligo are important to gain a better understanding of the condition, and to ensure patients are provided with appropriate psychological support following diagnosis. Recent systematic reviews suggest that people with vitiligo are significantly more likely to suffer from depression[3,5,6] and anxiety,[3,7,8] although there is a lack of knowledge regarding other psychological conditions.[9] However, these reviews noted high heterogeneity between studies, which have typically involved small patient numbers and are mostly from non-representative cohorts such as secondary care patients. There have been few population-based studies providing representative estimates of the risks of psychological comorbidities associated with vitiligo. A recent observational study in the UK[10] investigated the burden of major depressive disorder in people with vitiligo, and noted a bidirectional relationship between the conditions. However, the study did not explore the associations of other mental health conditions or adjust for ethnicity. The only other large population-based study found that people of Asian ethnicity with vitiligo had a near threefold increase in risk of developing psychiatric disorders, including depression and anxiety, but did not evaluate other ethnic groups.[11]

Method

We performed a retrospective observational cohort study in the UK to determine the risks of depression, anxiety and other potential psychological complications in adults with vitiligo (cases), compared with a matched control population without vitiligo. We also stratified risk by age, gender, ethnicity and, in those of working age, employment, and explored potential impacts on healthcare utilisation.

The protocol was specified *a priori* and preregistered as an observational study (ClinicalTrials.gov identifier: NCT04953338). Required changes and *post hoc* additions to the protocol were minor (Supplementary File 1).

Data source

We used routinely collected and collated electronic health record data from the Optimum Patient Care Research Database (OPCRD). OPCRD currently incorporates pseudonymised primary care records from around 850 general practitioner (GP) practices distributed across England, Wales, Scotland and Northern Ireland. The current OPCRD cohort size is over 5 million actively registered people, with historic records available for over 12 million people.

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Study population

All eligible adults (≥18 years of age) contributing data to OPCRD between 1 January 2004 and 31 December 2020 were eligible for inclusion.

Definition of people with new-onset vitiligo

We identified all people diagnosed with new-onset vitiligo over the study period, using clinical codes specific to vitiligo (Supplementary Table 1.1 available at https://doi.org/10.1192/bjo.2022.591). We excluded anyone with a diagnosis code for an alternative depigmenting disorder (Supplementary Table 1.2) coded within 6 months of their vitiligo diagnostic code. The index date for people with vitiligo was set as the date of vitiligo diagnosis.

Definition of matched controls without vitiligo

Each person with vitiligo was matched at their index date with up to four unaffected controls without a history of vitiligo before the index date, selected from the pool of eligible people registered in the same GP practice. Time-dependent propensity score matching, without replacement, was based on age (exact category and then nearest neighbour continuous age within each age category), gender (exact), ethnicity (exact White/Black and minority ethnic) and duration of practice registration (nearest neighbour), using a rolling time window so that controls were only eligible for matching if they were actively registered with the same GP practice on the index date of the case in question. After matching, the index date for each control was set to the index date of their matched counterpart.

Mental health outcomes

Primary outcomes comprised recurrent depressive disorder (RDD), depressive episodes and non-phobia-related anxiety disorder, chosen because they represent the most common mental health conditions presenting to primary care,[12] and defined according to the ICD-10 classifications.[13] Each condition was identified by algorithms validated for use in UK primary care, using a combination of diagnosis codes and treatments,[14] reported in Supplementary Tables 1.3 and 1.4. We also identified less common mental health conditions as secondary outcomes: social phobia, adjustment disorder, substance misuse, self-harm, overdose and suicide attempt or parasuicide (for specific diagnostic codes, see Supplementary Tables 1.3 and 1.4).

Healthcare utilisation outcomes

Healthcare utilisation was examined in people with vitiligo compared with controls, and among people with vitiligo with and without mental health conditions. Measures of healthcare utilisation comprised primary care encounters and dermatology referrals in the year after the index date.

Time off work and unemployment outcomes

To investigate work-related effects in people with vitiligo and mental health conditions, time off work was defined by the issue of Med 3 certificates of fitness for work,[15] which indicate absenteeism as they are issued to provide employers with evidence of the individual being medically unable to perform usual work activities. Unemployment was defined by the presence of a clinical code relating to unemployment or issue of a IB113 or ESA113 form to indicate incapacity from work.[15] We did not evaluate whether time off work or unemployment was related specifically to vitiligo or mental health, as this specific information is not coded in the primary care record.

Recorded clinical features

We extracted clinical information on age, gender, socioeconomic status and ethnicity. Socioeconomic status was defined with the official national deprivation measure, Index of Multiple Deprivation,[16] derived from patient postcode at the point of data extraction. Ethnicity was grouped into major UK census ethnic groups: White, Black/African/Caribbean/Black British, Asian/Asian British, mixed/multiple ethnic groups and other ethnic groups.[17,18] Other clinical covariates comprised body mass index category, smoking status, alcohol use and common comorbidities (hypertension, hyperlipidaemia, type 2 diabetes, atrial fibrillation, angina, myocardial infarction, stroke, heart failure, chronic kidney disease stages 3–5, chronic obstructive pulmonary disease, asthma, chronic liver disease and dementia). We used the missing indicator variable method where body mass index, Index of Multiple Deprivation, alcohol use or smoking status were not recorded, as missing data were considered likely not to be missing at random, meaning multiple imputation approaches may lack validity.[19]

Statistical analyses

Prevalence of mental health conditions

Prevalence of the three common mental health conditions (RDD, depressive episodes and anxiety disorder) and secondary outcomes (social phobia, adjustment disorder, substance misuse, self-harm and suicide attempt or parasuicide) was estimated at the index date for cases and matched controls. For RDD, depressive episodes and anxiety disorder, we further examined prevalence in subgroups defined by age category (18–49 years, ≥50 years), gender and ethnicity (White, Black and minority ethnic).

Incidence of new-onset mental health conditions

Incidence of all primary and secondary new-onset mental health conditions was assessed prospectively up to 2 years from the index date. A 2-year period was chosen to ensure we captured a sufficient number of new-onset mental health conditions. The relative risk of developing each mental health condition in vitiligo cases versus controls was examined with Cox proportional hazards models, stratified by matched set, to provide hazard ratios as summary estimates for the association of the presence of vitiligo with the time to each mental health condition. Proportional hazards assumptions were tested by visual inspection of Schoenfeld residuals. Unadjusted, age- and gender-adjusted, and fully adjusted (adjusted for the full feature set as described in 'Recorded clinical features') models were sequentially fitted. For each individual, the end of follow-up was defined as the earliest of the following: study end date (31 December 2020), date of patient transfer from an included general practice, date of death, date an individual first developed a mental health condition of interest or 2 years after the index date. We then estimated associations for the three primary outcomes (RDD, depressive episodes and anxiety disorder) in the same age-, gender- and ethnicity-defined subgroups as for prevalence.

Healthcare utilisation

We prospectively examined primary care encounter frequency and dermatology referral rates within 1 year of index date in vitiligo cases with and without prevalent depression or anxiety. For primary care visits, Poisson regression (using the same covariate set as for mental health outcomes) was used to model visit rates. For secondary care referrals, the proportion of people with a referral was estimated as the cumulative 1-year incidence by using the Kaplan–Meier method, and relative associations were estimated

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with adjusted Cox models (using the same covariate set as for mental health outcomes).

Time off work and unemployment

In people of normal working age (18–65 years), risk of either being issued a time off work certificate or having a first record of unemployment within 1 year was examined in vitiligo cases and matched controls, and in people with vitiligo with and without prevalent depression or anxiety. As for referrals, outcome proportions were estimated with the Kaplan–Meier method, and relative associations were estimated with adjusted Cox models.

Sensitivity analysis

A subgroup analysis was performed with data restricted to the most recent 10-year period, to ensure no influence of temporal changes in clinical care. To evaluate the magnitude of potential bias from including people who are registered with GP practices but do not attend their practice as matched controls, we also repeated the primary analysis including only controls with a least one primary care consultation in the year preceding their index date. A final *post hoc* sensitivity analysis was added to explore the influence of the definition of mental health conditions on the outcomes. The main analyses were repeated with RDD, depressive episodes and anxiety disorder defined by diagnosis codes only, rather than the more stringent definition requiring both diagnosis codes and treatment codes, and repeated once more, excluding patients who had been previously diagnosed with RDD, depressive episodes or anxiety disorder.

Statistical analyses were performed with R statistical package software, version 4.2.1 for Linux (R Core Team, https://www.r-project.org/). The study was conducted in line with RECORD (Reporting of Studies Conducted using Observational Routinely Collected Data) guidelines.[20]

Ethics and consent

The National Health Service Health Research Authority (NHS HRA) has approved OPCRD for clinical research purposes (reference number 20/EM/0148). The protocol for this project was approved by the OPCRD affiliated study approvals committee (ADEPT0721) on 15 June 2021. The study did not require formal research ethics committee as it used anonymised, routinely collected healthcare data based on outputs from the NHS HRA research decision tool (http://www.hra-decisiontools.org.uk/research/). No patient identifiable information was available to researchers. All patients who chose to opt out of data sharing did not have their data processed. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

Results

A total of 7224 people had an incident vitiligo diagnosis during the study period and met the study inclusion criteria (see Supplementary Fig. 1). Cases had a median age of 44 years and 53% were female (Table 1). Cases were age-, gender- and ethnicity-matched to 28 880 controls (Table 1). Other clinical characteristics of cases and controls were similar, although controls were slightly more likely to be recorded as current smokers (Supplementary Table 2.1).

Table 1 Demographic and clinical characteristics of people newly diagnosed with vitiligo (vitiligo cases) and matched controls without vitiligo

	Matched controls	Vitiligo cases	SMD
Total number of patients	28 880	7224	
Age, median [IQR]	44.0 [32.0–58.0]	44.0 [33.0–58.0]	0.004
Age group, years, *n* (%)			0.005
18–29	5534 (19.2)	1377 (19.1)	
30–40	6087 (21.1)	1526 (21.1)	
40–49	5822 (20.2)	1463 (20.3)	
50–59	5006 (17.3)	1251 (17.3)	
60–69	3647 (12.6)	918 (12.7)	
70–79	2155 (7.5)	534 (7.4)	
≥80	629 (2.2)	155 (2.1)	
Gender, *n* (%)			<0.001
Male	13 576 (47.0)	3396 (47.0)	
Female	15 304 (53.0)	3828 (53.0)	
Ethnicity, *n* (%)			0.126
White	14 013 (48.5)	3504 (48.5)	
Asian or Asian British	3200 (11.1)	1060 (14.7)	
Black, African, Caribbean or Black British	556 (1.9)	170 (2.4)	
Mixed or multiple ethnic groups	238 (0.8)	66 (0.9)	
Other ethnic groups	1155 (4.0)	259 (3.6)	
Not stated	949 (3.3)	199 (2.8)	
Missing	8769 (30.4)	1966 (27.2)	

For additional baseline clinical characteristics, see Supplementary Table 2.1.
SMD, standardised mean difference; IQR, interquartile range.

Prevalence of pre-existing mental health conditions are similar in vitiligo cases and matched controls

Before vitiligo diagnosis, prevalence of pre-existing depression in cases was similar to controls (Table 2), whereas there was a slightly higher prevalence of anxiety in cases (7.9 *v.* 7.0%, $P = 0.014$). The differences in prevalent mental health conditions between cases and controls were consistent with the overall findings in all subgroups (stratified by gender, age and ethnicity) (Supplementary Table 2.2). In both cases and controls, males (compared with

Table 2 Baseline prevalence of primary and secondary mental health outcomes in people newly diagnosed with vitiligo and matched controls

	Matched controls, *n* (%)	Vitiligo cases, *n* (%)	*P*-value
Total number of patients	28 880	7224	–
Primary mental health outcomes			
Recurrent depressive disorder	4305 (14.9)	1093 (15.1)	0.647
Depressive episodes	4007 (13.9)	1018 (14.1)	0.647
Anxiety disorder	2031 (7.0)	569 (7.9)	0.014*
Secondary mental health outcomes[a]			
Adjustment disorder	232 (0.8)	62 (0.9)	0.696
Substance misuse	900 (3.1)	195 (2.7)	0.070
Self-harm	215 (0.7)	46 (0.6)	0.374
Parasuicide	236 (0.8)	61 (0.8)	0.876

Data are number (percent) of the total number of patients with the condition in each subgroup.
a. Social phobia prevalence is not reported because fewer than five events were recorded in vitiligo cases.
* $P < 0.05$.

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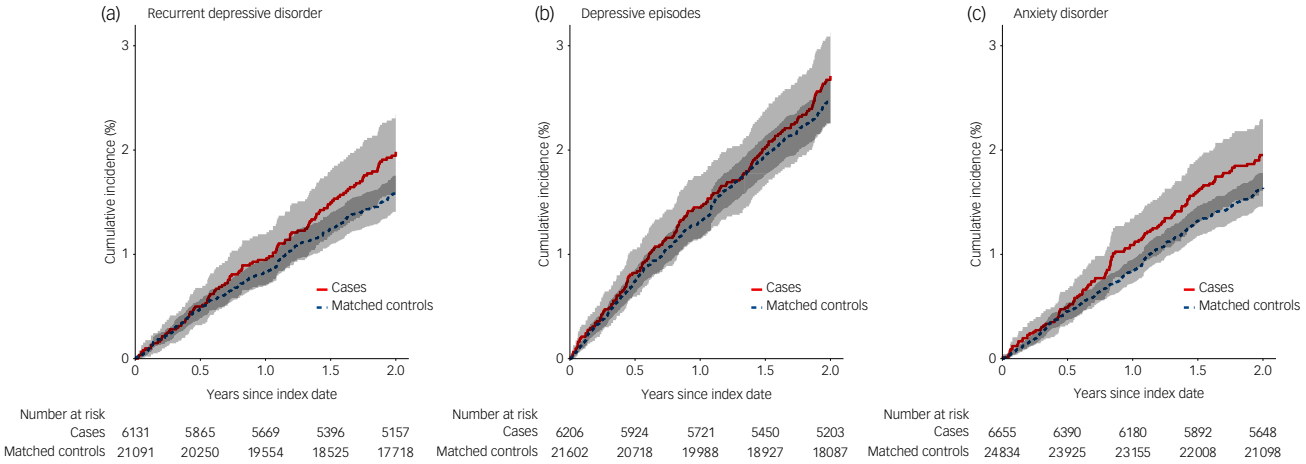

Fig. 1 Kaplan–Meier plots of the cumulative incidence of new-onset depression and anxiety in the 2 years after study index date, in vitiligo cases and matched controls without vitiligo. Median follow-up time for RDD, depressive episodes and anxiety disorder: 2.0 (interquartile range 2.0–2.0) years.

females) and Black and minority ethnic individuals (compared with those of White ethnicity) were less likely to have pre-existing depression or anxiety. Prevalence of adjustment disorder, substance misuse, self-harm and parasuicide were low, and were similar in cases and controls (Table 2). Prevalence of social phobia was not evaluated as five or fewer events were recorded in cases before vitiligo diagnosis.

New-onset mental health conditions are more common in people with vitiligo than controls, and risk is highest in Black and minority ethnic individuals

Over 2 years of follow-up, 2.0% of vitiligo cases developed new-onset RDD, 2.7% developed new-onset depressive episodes and 2.0% developed new-onset anxiety disorder, a slightly higher proportion than controls (RDD 1.6%, depressive episodes 2.5%, anxiety disorder 1.6%) (Fig. 1). There was no evidence of a higher incidence in the period immediately post-vitiligo diagnosis compared with later periods. In adjusted analysis, risk in vitiligo cases versus controls was increased by 25% for RDD (adjusted hazard ratio [aHR] 1.25, 95% CI 1.01–1.56) and 23% for anxiety disorder (aHR 1.23, 95% CI 1.01–1.51), but there was no significant risk increase for depressive episodes (aHR 1.11, 95% CI 0.92–1.32) (Table 3).

In subgroup analysis, the increased risk of new-onset RDD in vitiligo cases versus controls was greater among Black and minority ethnic individuals (Black and minority ethnic: aHR 1.72, 95% CI 1.06–2.79; White: aHR 1.26, 95% CI 0.93–1.70). A similar pattern was seen for depressive episodes (Black and minority ethnic: aHR 1.56, 95% CI 1.03–2.37; White: aHR 1.13, 95% CI 0.88–1.44), but not anxiety disorder (Black and minority ethnic: aHR 1.28, 95% CI 0.78–2.10; White: aHR 1.25, 95% CI 0.95–1.65) (Supplementary Tables 2.3–2.5).

In vitiligo cases, new-onset adjustment disorder ($n = 7$), substance misuse ($n = 35$), self-harm ($n = 6$) and parasuicide ($n < 5$) were uncommon, and there was no evidence of an increased risk compared with controls (Supplementary Table 2.6).

Primary care healthcare utilisation is greater in people with vitiligo and pre-existing mental health conditions

Comparing people diagnosed with vitiligo with and without pre-existing anxiety and depression, those with pre-existing mental health comorbidity had a 20% higher rate of primary care encounters in the year after vitiligo diagnosis (adjusted incidence rate ratio 1.20, 95% CI 1.18–1.23), but were not more likely to be referred to secondary care for dermatological review (13.3% of those with a

Table 3 Associations between vitiligo and risk of new-onset common mental health conditions

	Number of people	Person-years at risk	Events	Unadjusted hazard ratio (95% CI)	Gender- and age-adjusted hazard ratio (95% CI)	Fully adjusted hazard ratio[a] (95% CI)
Recurrent depressive disorder						
Matched controls	21 091	38 876	312	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
Vitiligo cases	6131	11 277	113	1.25 (1.01–1.55)*	1.24 (1.00–1.53)	1.25 (1.01–1.56)*
Depressive episodes						
Matched controls	21 602	39 746	501	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
Vitiligo cases	6206	11 392	157	1.09 (0.91–1.31)	1.08 (0.91–1.30)	1.11 (0.92–1.32)
Anxiety disorder						
Matched controls	24 834	46 038	382	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
Vitiligo cases	6655	12 297	122	1.20 (0.98–1.47)	1.19 (0.97–1.46)	1.23 (1.01–1.51)*

a. Adjusted for age, gender, ethnicity, social deprivation quintile, body mass index, smoking status, alcohol use and comorbidities (hypertension, hyperlipidaemia, type 2 diabetes, atrial fibrillation, angina, myocardial infarction, heart failure, stroke, chronic kidney disease stages 3–5, chronic obstructive pulmonary disease, asthma, chronic liver disease and dementia).
* $P < 0.05$.

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Table 4 Healthcare utilisation, time off work and unemployment post-vitiligo diagnosis in people with and without pre-existing anxiety or depression

	Vitiligo cases with mental health condition		Vitiligo cases without mental health condition		Adjusted relative risk (with versus without mental health condition)[a]
	n	Estimate (95% CI)	*n*	Estimate (95% CI)	
Primary care encounters (rate per person-year)[b]	950	12.8 (12.5–13.0)	3687	9.7 (9.6–9.8)	1.21 (1.18–1.23)***
Dermatology referral (% of people referred)	1398	13.3% (12.4–14.1)	5826	12.7% (11.0–14.5)	1.03 (0.87–1.22)
Time off work (% with time off work recorded)[c]	1205	12.7% (10.8–14.6)	4997	5.8% (5.1–6.5)	2.13 (1.72–2.63)***
Unemployment (% with unemployment recorded)[c]	1205	2.1% (1.2–2.9)	4997	0.8% (0.5–1.0)	2.12 (1.22–3.68)**

This analysis includes only the subset of cases with prevalent recurrent depressive disorder, depressive episodes or anxiety disorder at the date of vitiligo diagnosis. For primary care encounters, absolute estimates represent the encounter rate per person-year in the year after vitiligo diagnosis. For dermatology referrals, absolute estimates represent the proportion of people within each group with the outcome of interest within 1 year of vitiligo diagnosis.
a. Adjusted for age, gender, ethnicity, social deprivation quintile, body mass index, smoking status, alcohol use and comorbidities (hypertension, hyperlipidaemia, type 2 diabetes, atrial fibrillation, angina, myocardial infarction, heart failure, stroke, chronic kidney disease stages 3–5, chronic obstructive pulmonary disease, asthma, chronic liver disease and dementia).
b. In people followed up from 2010 onward.
c. In people of working age (18–65 years).
$^{**}P < 0.01$, $^{***}P < 0.001$.

mental health condition compared with 12.7% of those without; aHR 1.03, 95% CI 0.87–1.22) (Table 4).

Time off work and unemployment are greater only in people with vitiligo and pre-existing anxiety and depression

Of those with vitiligo and mental health comorbidity who were of working age (18–65 years), 12.7% had a record for time off work, meaning that they were twice as likely to have time off work as people with vitiligo without a mental health comorbidity (aHR 2.13, 95% CI 1.72–2.63) (Table 4). Recorded unemployment was similarly higher in those with vitiligo and mental health comorbidity (aHR 2.12, 95% CI 1.22–3.68) (Table 4). Comparing vitiligo cases and controls, overall proportions for time off work (cases: 7.1%, 95% CI 6.5–7.8; controls: 6.8%, 95% CI 6.4–7.1; aHR 1.08, 95% CI 0.97–1.20) and unemployment (cases: 1.0%, 95% CI 0.8–1.3; controls: 1.0%, 95% CI 0.9–1.1; aHR 1.00, 95% CI 0.75–1.33) were similar.

Sensitivity analysis

Associations between vitiligo and new-onset anxiety and depression were consistent when the analysis was restricted to those diagnosed in the most recent 10-year period to reduce the likelihood of any temporal changes influencing findings (Supplementary Table 2.7), when the analysis was further restricted to controls with at least one primary care consultation within the year before cohort entry (Supplementary Table 2.8), when the outcome conditions were defined using diagnosis codes only (Supplementary Tables 2.9 and 2.10) and when we excluded patients previously diagnosed with RDD, depressive episodes or anxiety disorder (Supplementary Table 2.11).

Discussion

In a large, population-based UK study, we demonstrate that people newly diagnosed with vitiligo have an increased risk of subsequently being diagnosed with new-onset depression (25%) and anxiety (23%) compared with the general population, and that this risk increase may be greatest in Black and minority ethnic populations (up to 72% risk increase for RDD). This is important as there is some evidence for vitiligo being associated with stigmatisation in people of British South Asian heritage.[21] We also found that people with both vitiligo and a mental health comorbidity have increased use of primary care services, and are twice as likely to have recorded time off work requests and unemployment. We found no evidence of an association with adjustment disorder, social phobia, substance misuse, self-harm or parasuicide, although event numbers were too small to exclude an increased risk. Further, other studies have found higher rates of social anxiety,[22] and it might be possible that more nuanced psychiatric diagnoses are not being considered in general practice assessment of patients with vitiligo.

To date, there have only been two other population-based studies investigating mental health conditions in those with vitiligo. Vallerand et al[10] investigated the temporal associations between vitiligo and RDD in UK primary care patients. This study did not use matching, made no adjustment for ethnicity, did not exclude people with coded other depigmenting conditions (present in 24.6% of those with a vitiligo code in our analysis) and did not use a validated definition for RDD. However, compared with controls, patients with vitiligo had a higher risk of being diagnosed with RDD (hazard ratio 1.27, 95% CI 1.16–1.40), consistent with our estimate. No other mental health conditions were assessed. Chen et al[11] investigated a much broader set of psychiatric conditions, including depression and anxiety, in those with and without vitiligo, in Taiwanese patients. They also observed that patients with vitiligo were more likely to have co-existing psychiatric disorders than matched controls. Overall, they found a three-fold increased risk for new-onset psychological conditions (aHR 2.93, 95% CI 2.64–3.24), and marked associations for major depressive disorder (aHR 3.72, 95% CI 3.36–4.11) and anxiety (aHR 3.85, 95% CI 3.48–4.25). Although the magnitude of these risk increases suggests a potential important difference by ethnic group and/or country, unadjusted risk differences between the Taiwanese matched groups were similar to our results (risk ratios of 1.12 for all psychological conditions, 1.43 for anxiety and 1.48 for major depressive disorder), suggesting that differences in methodology, in particular confounder adjustment, could be a potential explanation for the variation in effect sizes between studies.

Strengths and limitations

The key strengths of our study are the large cohort size drawn from a GP network covering the whole of the UK; the use of a matching algorithm that included matching patients within GP practices (to account for differences in clinical practice) and matching using clinical features; the use of validated definitions for primary mental health outcomes; the development of extensive codes lists for the outcomes where no validated definition was available and the assessment of multiple potential confounders, including ethnicity. Although previous small-scale studies have suggested, in people with darker skin, vitiligo is correlated with a worse quality of life,[23,24] we are not aware of any prior study of people with vitiligo that has assessed associations between ethnicity and diagnoses of mental health conditions.

There are key limitations related to the universal challenges of using routinely collected health data for research. Although we have utilised individual-level matching and adjustment for a wide range of potential confounders, we are unable to determine causality

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and cannot exclude residual confounding as an explanation of our findings. A further limitation, as indicated above, is the possibility of both misdiagnosis and under-capture of diagnoses that have not been recognised in primary care, and this might be a particular issue for both social anxiety and adjustment disorder. That said, it is important to note that to minimise the potential impact of misdiagnosis, we utilised a prespecified case definition that involved identification of all cases with vitiligo-specific codes and exclusion of people with codes for other depigmenting conditions that could have potentially been initially misdiagnosed as vitiligo. Our use of a validated algorithm to identify the primary mental health outcomes ensures that only people with those outcomes are identified, but there remains the risk of under-capture either because of lack of correct coding in primary care or lack of a clinical diagnosis at all. However, the prevalence of diagnosed depression and anxiety in our vitiligo cohort are similar to those in studies in which these data have been actively captured, with rates of clinically diagnosed depression of 8–25%[5,6,9] and rates of clinically diagnosed anxiety of 12–15%.[7,8] A further potential limitation is the risk of capture bias, whereby people interacting more frequently with primary care are more likely to have a recorded diagnosis of both vitiligo and mental health conditions. We explored this in our sensitivity analysis by excluding controls with no primary care interaction in the year preceding their index date (cases have at least one interaction by definition), which did not alter effect estimates.

Additional limitations are that phototherapy data and both lesion extent and location were not available in the primary care record, and therefore we were not able to explore potential severity or modifying effects of these factors. Existing data show that location of vitiligo lesions may also influence well-being, although findings are inconsistent; a small number of studies showed that patients had a more significant quality-of-life impairment when lesions were located on visible sites (e.g. face, neck and hands),[25,26] whereas other studies did not find any relationship.[27,28] Finally, our results cannot be extended to dissimilar populations or to children.

In conclusion, our study suggests that vitiligo is associated with an approximately 25% increase in risk of new-onset depression and anxiety within the 2 years after vitiligo diagnosis.

Primary care clinicians and policy makers should be aware of this increased risk. Given the increased healthcare utilisation, time off work and unemployment in this group, further study is required to evaluate the potential benefit of screening for mental health conditions in people with vitiligo, in particular to identify people who might benefit from early psychological support following vitiligo diagnosis.

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Supplementary material

Supplementary material is available online at https://doi.org/10.1192/bjo.2022.591

Data availability

Data from the OPCRD are available under licence for clinical research, which is subject to relevant approvals. For additional information, please visit opcrd.co.uk.

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Author contributions

The study concept and design were conceived and developed by A.R.T., V.E. and J.N. The study was performed and written under the direction of A.R.T., V.E. and J.N., including creation of the study population. All authors approved the final submitted version. J.N. attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

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Declaration of interest

A.R.T. is a scientific advisor to the Vitiligo Society and has been an advisor to the AllParty Parliamentary Group on Skin. V.E. is a member of the scientific committee for the Vitiligo Society UK and the Global Vitiligo Foundation. J.N. is an employee of Pfizer Ltd. and stockholder of Pfizer Inc.

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