

José Luis LÓPEZ ESTEBARANZ¹
 Carlos MALDONADO
 GONZÁLEZ-MONTAGUT²
 Jacob GONZÁLEZ²
 Inmaculada APARICIO GARCÍA
 SAN MIGUEL²
 Veronica GARCIA-RECIO³
 Daniel CALLEJO³
 Anna DE PRADO³
 Carine DELATTRE⁴

¹ Hospital Universitario Fundación Alcorcón, C. Budapest, 1, 28922 Alcorcón, Madrid, Spain

² Incyte Biosciences Iberia SL, Plaza De La Encina 10-11, Núcleo 5, Planta 2^a, Módulo A, 28760 Tres Cantos, Madrid, Spain

³ IQVIA Information SA, Juan Esplandiú, 11 - 6° 28007 Madrid, Spain

⁴ Incyte Biosciences International Sàrl, Rue Docteur-Yersin 12, 1110 Morges, Switzerland

Reprints: José Luis López Estebanzanz <jlestebanzanz@salud.madrid.org>

Real-world evidence for vitiligo using an electronic medical records database in Spain: the REVEAL-ES study

Background: The European prevalence of vitiligo diagnosis is 0.2%–0.8%, with country-specific and methodological differences. Although vitiligo profoundly impacts quality of life, limited studies have evaluated disease burden and treatment patterns. **Objectives:** This real-world study describes the prevalence, incidence, characteristics, and treatment patterns of vitiligo among patients in Spain during 2015–2021. **Materials & Methods:** This retrospective observational study using the IQVIA Electronic Medical Records database in Spain included patients with vitiligo (International Classification of Diseases, Ninth Revision codes 709.01/374.53). Incident and prevalent cohorts comprised registered patients with vitiligo diagnoses during and before 2015–2021, respectively. Patient characteristics and treatment data were extracted. **Results:** Vitiligo incidence was 0.016 (95% CI: 0.014–0.018) per 100 person-years, and prevalence was 0.19% (95% CI: 0.18%–0.19%) in 2021. Females were more affected than males (0.16% vs 0.13%, respectively). Among 1,400 incident patients, mean (SD) age was 40.7 (19.7) years; most were female (53.9%). The most common comorbidities after vitiligo diagnosis were eczema (20.8%), hypercholesterolaemia/hypertriglyceridaemia (17.9%), anxiety (10.9%), thyroid disorders (9.1%), and diabetes (6.4%). In 2021, 78.6% of prevalent patients did not receive vitiligo-related treatments. The most prescribed vitiligo-related treatments were topical calcineurin inhibitors (13.9%) and topical corticosteroids (13.0%); 11.9% had a record of psychiatric medications. **Conclusion:** This study confirms the association between vitiligo and comorbidities (e.g., eczema, thyroid disorders) and high disease burden. The prevalence in Spain in 2021 (0.19%) was within the lower band of European estimates based on surveys/medical screenings. Most patients are not receiving vitiligo-related treatment and could benefit from new, effective treatments.

Key words: burden of disease, electronic medical records, prevalence, real-world evidence, Spain, vitiligo

Article accepted on 03/03/2024

Vitiligo is a chronic autoimmune disease characterised by the destruction of melanocytes, which leads to pigment loss and the development of white patches on the skin [1]. The condition can affect any area of the skin but commonly appears on the face, neck, and hands, as well as in skin creases [2, 3]. The pathogenesis of vitiligo is complex, but different studies suggest a combination of genetic and environmental factors as well as oxidative stress as initiating events [1, 4–6]. Immunological changes, including increases in proinflammatory cytokines and chemokines as well as alterations in cell populations within the skin, drive inflammation and autoimmune destruction of melanocytes through recruitment of autoreactive CD8+ T cells [7]. Moreover, patients affected by vitiligo are commonly prone to other autoimmune diseases such as

type 1 diabetes, pernicious anaemia, and autoimmune thyroiditis, supporting the role of autoimmunity in the development of vitiligo [5].

The prevalence of vitiligo diagnosis in the European general population (including adults and children) ranges from 0.2% to 0.8%, with differences attributable to variability in countries and study methodology [8, 9]. Although vitiligo may appear at any age, onset mostly occurs before the age of 30 and affects both sexes equally [1].

Although vitiligo is considered to be a non-life-threatening disease, the overall disease burden is underestimated. This disease has a significant psychological impact, as well as a profound and permanent effect on patients' quality of life (QoL), especially when visible areas are affected [9–12]. Patients with vitiligo report

loneliness, isolation, stigmatisation, depression, anxiety, and suicidal ideation, as well as other psychosocial comorbidities [12, 13].

Ruxolitinib cream was approved by the European Commission in 2023 for the treatment of nonsegmental vitiligo with facial involvement in adults and adolescents aged 12 years and older [14]. Before 2023, there were no approved treatments for vitiligo in Spain; pharmacotherapy options relied upon the off-label use of topical corticosteroids and topical calcineurin inhibitors, although there are limited randomised trials evaluating the efficacy and safety of these treatments in patients with vitiligo [15]. According to the Spanish Association of Vitiligo Patients (ASPAVIT), up to 90% of patients with vitiligo do not receive any treatment [16].

Spanish studies examining the burden of vitiligo are currently lacking. The REVEAL-ES study aimed to retrospectively determine the prevalence and incidence of vitiligo among patients in Spain over the study period of 2015 to 2021, as well as describe the demographics, clinical characteristics, comorbidities, and treatment patterns in real-world settings in Spain.

Materials and methods

Database source

This was an observational, retrospective, longitudinal cohort study of patients with vitiligo conducted using the IQVIA Electronic Medical Records (EMR) database in Spain, which has collected anonymised patient data since 2008 from general practitioners and specialists. The IQVIA EMR database represents around 3% of the Spanish population (*i.e.*, 1.2 million people from three geographical regions, including all sexes and age groups). The protocol was approved (reference number HCB/2022/0759) by the Clinical Research Ethics Committee of the Hospital Clínic de Barcelona (Barcelona, Spain). The study was conducted in accordance with the ethical principles of the Helsinki Declaration (64th World Medical Association General Assembly, Fortaleza, Brazil, October 2013) and good pharmacoepidemiology practises, as well as applicable laws and regulations of Spain (Law 14/2007, of 3rd July, on Biomedical Research).

Study design and population

Patients of all ages diagnosed with vitiligo (as determined by International Classification of Diseases, Ninth Edition [ICD-9] codes 709.01 and 374.53) from 1st January 2015 to 31st December 2021 were identified in the database and included in the study. Patients were excluded if they were diagnosed with pigmentation disorders different from vitiligo (pinta [ICD-9 103.2] or dyschromia [ICD-9 709.00 or 709.09]). The incident study population was defined as those patients who had a first diagnosis of vitiligo (index date) between 2015 and 2021 (registered with a general practitioner for any length of time during the study period) with 12 months of data available before the index date; who had no previous diagnosis of vitiligo in the EMR database since

2008; and were followed until loss to follow-up or the end of the study period, whichever came first. The prevalent study population included all patients with a vitiligo diagnosis during the data availability period (2008-2021) and documented in the EMR database during the study period (2015-2021).

Demographic and clinical characteristics were derived from available data at the index date. Vitiligo-related treatments (topical corticosteroids, topical calcineurin inhibitors, oral corticosteroids, topical vitamin D and associated analogues, systemic psoralene, and methoxsalen) and psychiatric treatments for depression and anxiety (selective serotonin reuptake inhibitors [*e.g.*, escitalopram], serotonin and norepinephrine reuptake inhibitors [*e.g.*, duloxetine], and tricyclics [*e.g.*, amitriptyline]) were documented from the index date to the end of follow-up (the earliest between end date, death date, or last collection date). To assess comorbidities in patients with vitiligo, all conditions were documented during the last five years before vitiligo diagnosis (not reported here) and five years after diagnosis, except for mental health conditions, which were documented for the two years before diagnosis, two years before the index date, two years after the index date, and two years after diagnosis to the end of follow-up. These time frames were not mutually exclusive (*i.e.*, a patient could be included in a comorbid category in both time frames). Finally, the number of prescriptions was determined to study the medical and psychiatric treatment of patients with vitiligo.

Statistical analysis

Descriptive analyses were performed to obtain counts and proportions with a 95% CI for categorical variables, and the mean with SD and median with interquartile range for continuous variables. As part of the analysis, a description of missing data for each variable of interest was provided.

The crude annual incidence rate of vitiligo was calculated for each calendar year from 2015 to 2021 and presented as per 100 person-years, and the annual prevalence rate of vitiligo was calculated for each calendar year from 2015 to 2021 and presented per 100 people. If patients were followed for one person-year, they contributed one person-year to the denominator.

Prespecified subgroup analyses were performed based on age group category (0-11, 12-17, 18-24, 25-39, 40-65, >65 years), sex (male, female), and vitiligo-related treatment status (active, non-active, no treatment). Age group categories were selected to distinguish between children (0-11 years), adolescent (12-17 years), and adult (≥ 18 years) population subgroups. The active vitiligo-related treatment group included any patient treated for vitiligo during the last 12 months. The non-active vitiligo-related treatment group included any patient treated for vitiligo more than 12 months ago, and no treatment in the last 12 months. The no-treatment vitiligo group included any patient with no treatment for vitiligo recorded in their EMR database records.

Standardised incidence rates were calculated by applying direct age standardisation to the 2022 European

population [17] using the same prespecified age group categories.

Results

Incidence of vitiligo in Spain

Of the total population registered in the IQVIA EMR database ($N=1,226,129$), 3,656 patients with vitiligo were identified over the study period (2015-2021). Of these patients, 10 were excluded because of a diagnosis of pinta and 1,096 because of another type of dyschromia. Among the 2,550 patients with eligible records of vitiligo, 1,069 were excluded because their first recorded diagnosis of vitiligo occurred before 2015, and 81 were

excluded because they did not have at least one year of baseline data. Finally, 1,400 patients with complete data and meeting all criteria were included in the incident cohort (*supplementary figure 1*).

The aggregate annual incidence of vitiligo cases was 0.017 (95% CI: 0.016-0.018) per 100 person-years between 2015 and 2021. The same incidence was observed for adolescents and adults (aged ≥ 12 years). The aggregate age-standardised incidence rate between 2015 and 2021 using the European population was similar (0.017 [95% CI, 0.015-0.019] per 100 person-years). The annual incidence rate was mainly stable until 2019 and decreased during the COVID-19 period, as shown in *figure 1A*. In 2021, 197 patients were diagnosed with vitiligo, and the incidence rate increased from the previous year to 0.016 (95% CI: 0.014-0.018) per 100 person-years. The 2021 age-standardised incidence rate

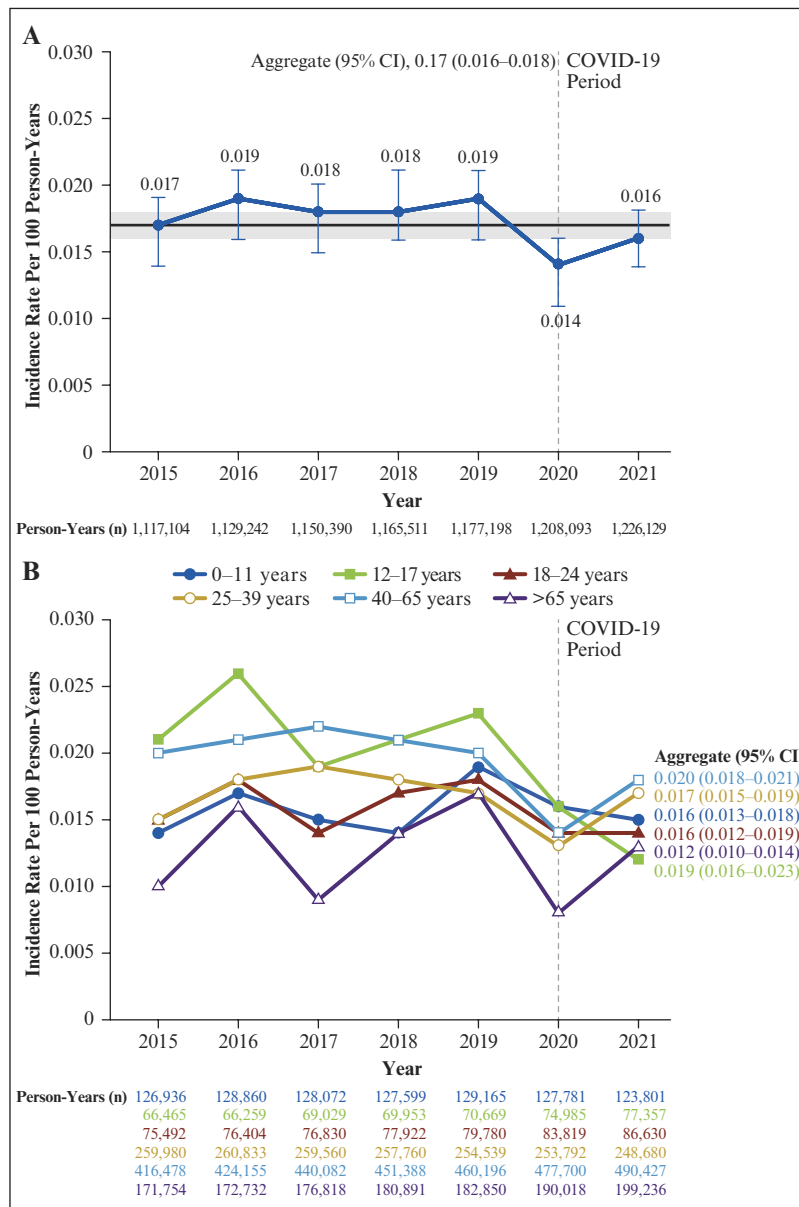


Figure 1. Annual incidence rates of vitiligo in Spain during the analysis period (2015-2021) overall* (A) and by age group (B). *Aggregate incidence across the study period is shown with a black line; the shaded region (grey) indicates the 95% CI.

was 0.016 (95% CI: 0.011-0.021) per 100 person-years. Most patients were aged 40 to 65 years (44.0%) at diagnosis, with an aggregate incidence rate of 0.020 (95% CI: 0.018-0.021) per 100 person-years (figure 1B). However, vitiligo occurred in any age group as evidenced by diagnosis in 141 children (10.1%; aged 0-11 years), with an aggregate incidence rate of 0.016 (95% CI: 0.013-0.018) per 100 person-years. Peak incidence was observed among 301 patients (21.5%) aged 25 to 39 years, with an aggregate incidence rate of 0.017 (95% CI: 0.015-0.019) per 100 person-years.

Prevalence of vitiligo in Spain

A total of 2,286 patients with vitiligo were identified in the prevalence study population in Spain in 2021. The

average annual point prevalence of vitiligo in 2021 was 0.19% (95% CI: 0.18%-0.19%), and an incremental increase was observed between 2015 and 2021 (figure 2A). The overall annual point prevalence for adolescent and adult patients (aged ≥ 12 years) in 2021 was also 0.19% (95% CI: 0.18%-0.19%). Adults aged 25 years and older experienced a slightly higher prevalence rate in 2021 (0.22% in patients aged 25-39 years and 0.20% in patients aged 40-65 years) than adolescents (12-17 years; 0.18%), and the lowest prevalence rate was observed in the >65-year age group (0.11%) (figure 2B). A higher prevalence rate in 2021 was observed in female compared with male patients (0.20% [95% CI: 0.19%-0.21%] vs 0.17% [95% CI: 0.16%-0.18%], respectively).

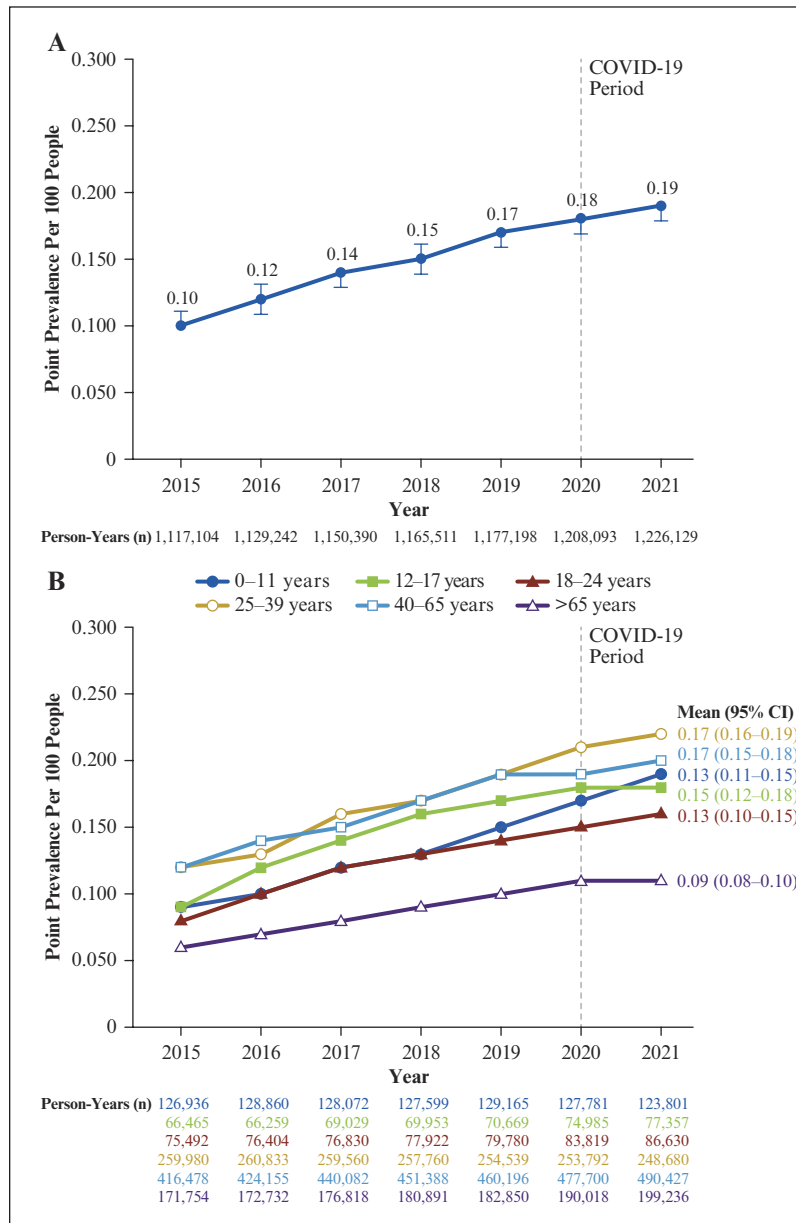


Figure 2. Annual prevalence rates of vitiligo in Spain during the analysis period (2015-2021) overall (A) and stratified by age (B).

Demographic and clinical characteristics of patients diagnosed with vitiligo in Spain during the study period (2015-2021)

Among the 1,400 patients with vitiligo in the incident cohort, 83.0% were adults (aged ≥ 18 years) at diagnosis, 10.1% were children (0-11 years), and 6.9% were adolescents (12-17 years) (table 1). The mean (SD) age at vitiligo diagnosis was 40.7 (19.7) years, and the median (interquartile range) age was 42.0 (28.0) years; a slightly higher proportion of patients with vitiligo were female (53.9%). The active-treatment group (*i.e.*, treated in the last 12 months) was older compared with the non-active-treatment group at diagnosis (mean [SD] age: 42.1 [21.5] vs 39.9 [19.5] years) (supplementary table 1). There were more female patients in the active- (61.7%) and non-active-treatment groups (53.1%), whereas the no-treatment group had more male patients (55.4%). More than two-thirds of the overall population presented with no comorbidities (Charlson Comorbidity Index [CCI] score of 0), and 0.6% presented with a severe CCI score (≥ 5); of note, 89.3% of the no-treatment group showed a CCI score of 0, compared with 73.4% in the active-treatment group.

The most common comorbidities in the five years after vitiligo diagnosis (excluding mental health conditions) were eczema (20.8% [including up to seven different ICD-9 codes, but not identifiable by type of eczema]), hypercholesterolaemia and hypertriglyceridaemia (17.9%), thyroid disorders (9.1%), other skin diseases (7.6%), diabetes (6.4%), and asthma (5.8%) (table 2).

Among children (aged 0-11 years), the most commonly observed comorbidities in the five years after vitiligo diagnosis were eczema (29.1%) and asthma (6.4%). Eczema, acne, asthma, thyroid disorders,

hypercholesterolaemia and hypertriglyceridaemia, and diabetes were also frequent in the other age categories (supplementary table 2).

A higher proportion of male versus female patients had diabetes (7.1% vs 5.7%, respectively) and other skin diseases (8.2% vs 7.1%, respectively) in the five years after vitiligo diagnosis; thyroid disorders (2.8% vs 14.4%), eczema (17.7% vs 23.4%), and hypercholesterolaemia and hypertriglyceridaemia (17.1% vs 18.7%) were more common in female patients (supplementary table 3).

Overall, the active-treatment group had more comorbidities in the five years after diagnosis than the non-active- and no-treatment groups. Eczema was the most prevalent comorbidity in the active vitiligo-related treatment group after diagnosis (37.8%), followed by hypercholesterolaemia and hypertriglyceridaemia (23.0%), diabetes (9.0%), and thyroid disorders (8.6%). Thyroid disorders occurred more frequently in the non-active-treatment group (10.2%) (supplementary table 4).

In the two years after vitiligo diagnosis, the most common mental health comorbidities were anxiety (10.9%), sleep disturbance (5.1%), and depression (2.6%), and rates were similar to those observed in the two years before vitiligo diagnosis (figure 3A). Anxiety was highest among patients aged 40 to 65 years (15.1%), whereas sleep disturbance was highest among patients aged >65 years (17.1%) and increased after vitiligo diagnosis (figure 3B). More female patients were diagnosed with anxiety (13.8%) and depression (3.4%) than male patients after vitiligo diagnosis (figure 3C), and more patients on active vitiligo-related treatment presented with mental health comorbidities than those not receiving active treatment (figure 3D).

Table 1. Demographic and clinical characteristics among patients with vitiligo (incident cohort).

Characteristic	Incident cohort N=1,400
Age at diagnosis,* y	
Mean (SD)	40.7 (19.7)
Median (IQR)	42.0 (28.0)
Age group,* y, n (%)	
0-11	141 (10.1)
12-17	96 (6.9)
18-24	87 (6.2)
25-39	301 (21.5)
40-65	616 (44.0)
>65	158 (11.3)
Sex, n (%)	
Male	645 (46.1)
Female	755 (53.9)
CCI category, n (%)	
0	1087 (77.6)
Mild (1-2)	270 (19.3)
Moderate (3-4)	34 (2.4)
Severe (≥ 5)	9 (0.6)

CCI: Charlson Comorbidity Index; IQR: interquartile range.

*Data missing from one patient.

Annual treatment patterns during the study period (2015-2021) for vitiligo and mental health conditions among patients with vitiligo (prevalent cohort)

During the study period, the majority of patients with vitiligo did not receive any vitiligo-related treatments (figure 4). In 2015, 71.7% of patients in the prevalent cohort did not receive vitiligo-related treatments. Among patients with vitiligo in the prevalent cohort in 2015, topical calcineurin inhibitors, topical corticosteroids, and oral corticosteroids were prescribed to 19.3%, 17.5%, and 8.8% of patients, respectively (figure 5). In 2021, the proportion of patients who did not receive vitiligo-related treatments increased to 78.6% (compared with 71.7% in 2015). Among patients with vitiligo in the prevalent cohort in 2021, topical calcineurin inhibitors were prescribed to 13.9% of patients with vitiligo, followed by topical corticosteroids (13.0%) and oral corticosteroids (8.0%), similar to the previous year. From 2015 to 2016, a slight decrease was observed in the proportion of patients with vitiligo who were prescribed psychiatric medications (8.2% to 7.9%). However, from 2017 to 2021, the rates of psychiatric medication prescriptions increased from 8.3% to 11.9% (figure 4). Escitalopram, amitriptyline, paroxetine, and fluoxetine were among the most prescribed psychiatric treatments in the prevalent cohort.

Table 2. Overall comorbidities after vitiligo diagnosis (incident cohort).

Comorbidities, n (%)	Incident cohort N=1,400
Autoimmune and metabolic comorbidities*	
Hypercholesterolaemia and hypertriglyceridaemia (ICD-9 272.0, 272.1, 272.3–272.5)	251 (17.9)
Thyroid disorders (ICD-9 42.0X, 242.1X, 242.2X, 242.3X, 242.4X, 242.8X, 242.9X, 244.8–244.9, 245.2, 780.1)	127 (9.1)
Diabetes (ICD-9 249.XX–250.XX)	89 (6.4)
Asthma (ICD-9 493.X)	81 (5.8)
Dermatological comorbidities†	
Eczema (ICD-9 690.12, 690.8, 691.8, 692.XX, 695.89, 696.5, 705.81)	291 (20.8)
Other skin diseases (ICD-9 110.1, 110.4, 111.0, 686.00, 686.01, 704.41, 704.08, 228.0, 228.0X, 454.0, 456.3, 448.0, 757.32, 214.0, 702.11, 288.4, 216.0, 215.0)	104 (7.6)
Acne (ICD-9 706.0–706.1)	37 (2.6)
Psoriasis (ICD-9 694.3, 696.0, 696.1, 696.2)	34 (2.4)
Inflammatory skin diseases (ICD-9 690.1X, 695.3)	30 (2.1)
Mental health comorbidities†	
Anxiety (ICD-9 293.84, 300.0X, 300.2X, 309.21)	153 (10.9)
Sleep disturbance (ICD-9 307.4X, 327.XX, 780.5X)	71 (5.1)
Depression (ICD-9 296.2X, 296.3X)	37 (2.6)
Other comorbidities	
Other superficial mycoses (ICD-9 117.9)	23 (1.7)

ICD-9: International Classification of Disease, Ninth Revision.

* Comorbidities >5% are included.

† Comorbidities >2.0% are included.

Discussion

To our knowledge, this is the first study to evaluate the incidence and prevalence of vitiligo in Spain based on EMR data in the last few years. In contrast to other studies, this study only included patients diagnosed with vitiligo as determined by the ICD-9 codes 709.01 and 374.53 [9, 18].

This is the largest study of physician-diagnosed patients with vitiligo in Spain, and the prevalence rates are in the lower range of rates seen in other European studies [8, 9], likely because of differences in study methodologies as well as the potential for a subset of patients with lower disease burden who may not seek medical advice. In this analysis, the incidence of vitiligo during the study period was stable, although a decrease in incidence was observed during the COVID-19 pandemic period in 2020. The decrease observed in vitiligo disease incidence in 2020 is reflective of the Spanish COVID-19 pandemic experience, in which other diseases also showed decreases in diagnoses [19–21].

In this study, there were slightly more female patients with vitiligo, which is consistent with findings from other European studies [9, 22]. The prevalence rate of vitiligo was similar among all age groups during the study period, except for the rate in adults aged >65 years, which was considerably lower (0.11% in 2021). Vitiligo can affect patients at any age. Previous studies indicate that most patients (~60%) experience disease onset before age 30 years, although initial manifestations later in life are also common [3, 23]. Our findings indicate that vitiligo is more common in slightly older adults among the Spanish population (44.0% of patients were aged

40–65 years at diagnosis). This finding may be attributable to the composition of the IQVIA database, which includes data from mostly general practitioners and, therefore, indicate a lower incidence of paediatric vitiligo.

This study shows that a higher proportion of female patients than male patients had received vitiligo-related treatment either before or during the study period. Similarly, Ali *et al.* (2016) showed that adherence to treatment was higher among female patients compared with male patients [24]. Ezzedine *et al.* (2021) found a higher psychosocial and overall QoL burden associated with female patients [12], which could indicate that female patients are more likely to seek medical attention and receive treatment, as found in our study. Additionally, although this study did not analyse vitiligo severity, patients with active vitiligo-related treatment presented with more comorbidities and a higher CCI score compared with those with no vitiligo-related treatment. These results suggest that these patients may have more severe disease and, therefore, are more likely to seek medical care or stay on treatment.

Previous studies have shown a strong association between vitiligo and autoimmune, dermatological, and ocular disorders [25]. In this study, we found that 9.1% of patients with vitiligo had diagnoses of thyroid disorders, which is in line with results from a retrospective US study, wherein more cases of hypothyroidism were reported among patients with vitiligo (10.6%) versus the general population [26]. Diabetes (6.4%) and hypercholesterolaemia and hypertriglyceridaemia (17.9%) were also common comorbidities in our study. In a comprehensive review by Dahir and Thomsen (2018), diabetes

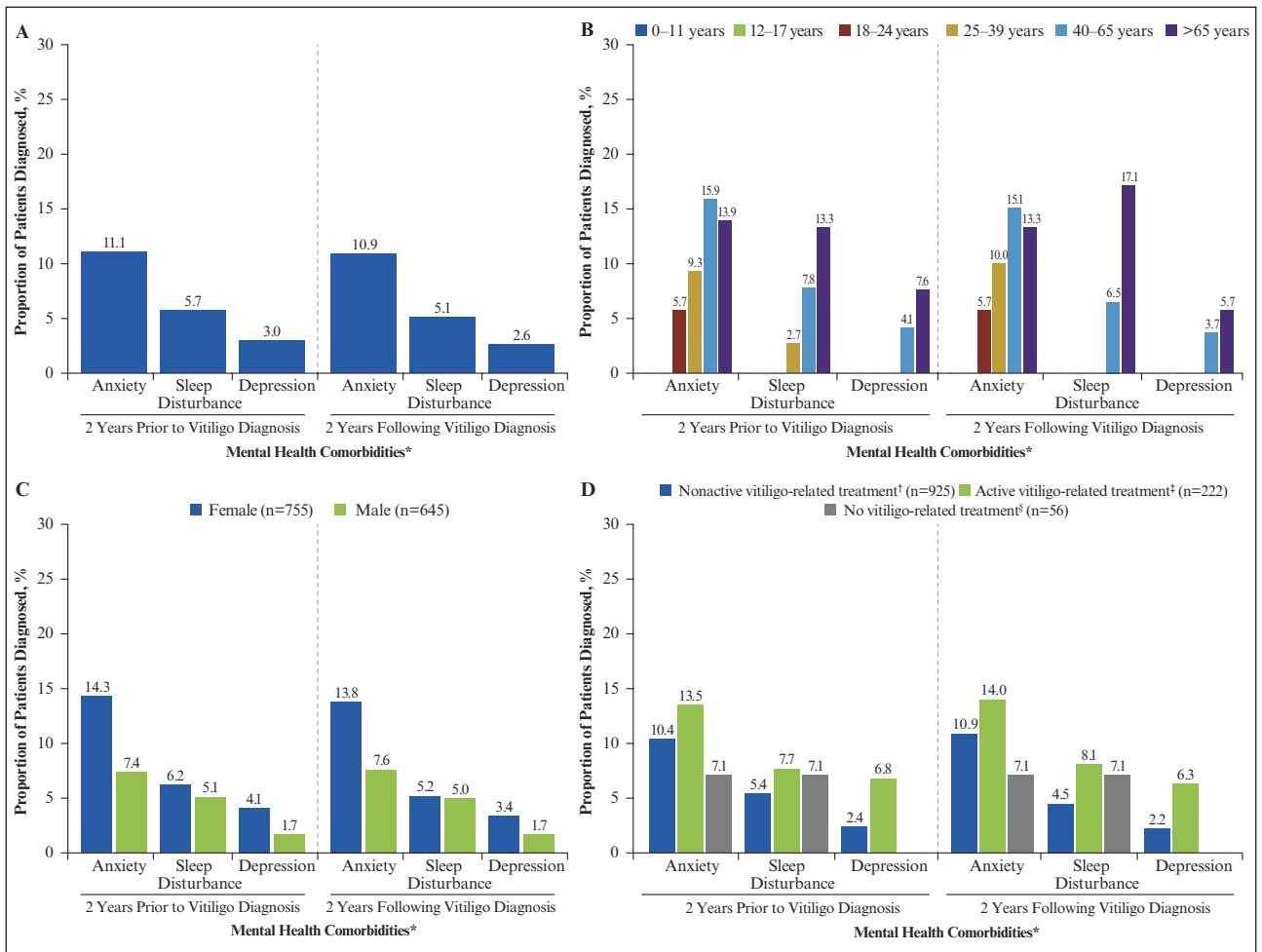


Figure 3. Proportion of patients with mental health comorbidities in the two years before and after vitiligo diagnosis overall (A), and stratified by age (B), sex (C), and vitiligo-related treatment group (D).

*The most frequent mental health comorbidities are reported; data from categories in which there were less than five patients are not shown owing to privacy considerations.

‡Patients with vitiligo-related treatment prescriptions during the last year of follow-up within the study period.

†Patients with vitiligo-related treatment prescriptions in the database and no vitiligo-related treatment prescriptions during the last year of follow-up within the study period.

§Patients who did not receive any vitiligo-related treatment prescriptions.

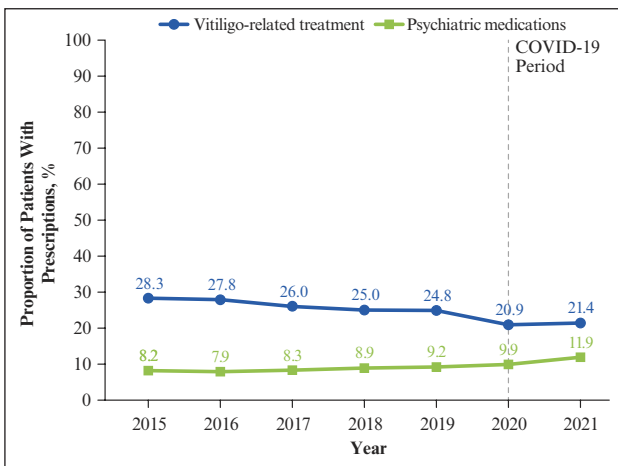


Figure 4. Proportion of patients in the prevalent cohort receiving vitiligo-related treatment and psychiatric medication.

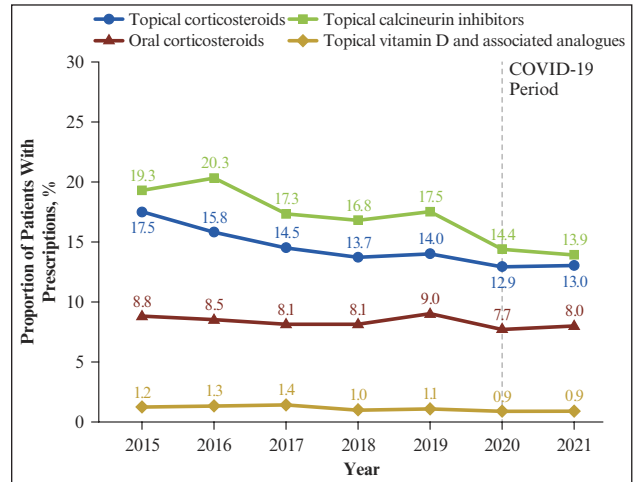


Figure 5. Vitiligo-related treatment patterns among patients with vitiligo in the prevalent cohort.

and thyroid disease were also the most common comorbid conditions reported among patients with vitiligo [25], and Sharma *et al.* (2017) found significantly higher levels of triglycerides in patients with vitiligo than in controls [27]. Eczema was the most common dermatological comorbidity reported in our study and may have contributed to the use of corticosteroids and calcineurin inhibitors. Additionally, our findings indicated that mental health comorbidities, such as anxiety and depression, were commonly reported following vitiligo diagnosis, occurring in 10.9% and 2.6% of patients with vitiligo, respectively. This is higher than the approximately 5.4% and 1.1% of patients in the general population in Spain diagnosed with anxiety and depression, respectively, over an approximately 12-month time frame, although this time frame included data from the COVID-19 lockdown period, during which diagnoses were slightly lower than expected [28]. Meta-analyses have demonstrated that depression [29] and anxiety [30] are often reported in patients with vitiligo. Furthermore, our study found that 11.9% of patients with vitiligo in 2021 were treated with psychiatric medications, which also suggests that mental health comorbidities contribute to the healthcare burden in patients with vitiligo. It is notable that the frequencies of mental health conditions were similar in the periods before and after vitiligo diagnosis. This finding may be due to a delay in vitiligo diagnosis relative to onset of the first vitiligo lesion [31]. Taken together, our findings suggest that patients with vitiligo and comorbidities have a high disease burden beyond those healthcare needs that are specific to vitiligo.

The percentage of patients with vitiligo who did not receive vitiligo-related treatments increased during the study period, with 78.6% of patients not receiving treatment in 2021. This suggests an unmet medical need and may be attributable to a lack of treatment effectiveness, supporting the need for treatments with better outcomes [3, 32, 33]. In our study, the most frequently prescribed vitiligo-related treatments in Spain were topical calcineurin inhibitors, topical corticosteroids, and oral corticosteroids. This is consistent with other analyses (some in other geographic regions), in which the main treatment used for vitiligo is topical tacrolimus, followed by oral corticosteroids [34-38]. It is reported that early treatment initiation may result in better outcomes for patients [39].

This study is based on the use of a national database with large healthcare coverage, containing data on approximately 3% of the current Spanish population. However, it is possible that these data are not fully representative of the general population and all patients with vitiligo in Spain. The study has additional limitations owing to the retrospective nature of the design and the use of the IQVIA EMR database as a data source, which include missing data, heterogeneity of terms of data quality, the frequency of data capture, and coverage for key study-related parameters. For certain demographic variables, not all patients had complete records. Although a few patients reported psoriasis, the number of cases was low, and data on phototherapy as vitiligo-related treatment, race, disease severity, segmentation, and light and laser therapy were not documented in the database.

The EMR database provides longitudinal data across both primary and secondary care environments; therefore, full care pathways can be observed. The database captures patients with vitiligo who seek medical assistance and describes the patient journey from diagnosis to referral to a dermatologist. The results of this study are generalisable owing to the large representation of the data.

The information available on vitiligo is limited, and further evidence-based information needs to be collected regarding patient-reported outcomes and vitiligo-specific measures.

Conclusion

This real-world study using EMR data confirms that vitiligo is associated with relevant comorbidities, such as diabetes, thyroid disorders, anxiety, and depression. The prevalence rate in Spain in 2021 (0.19%) represents the number of patients seeking medical help, which is on the lower end of European estimates (0.2%-0.8%). Most patients were not taking any vitiligo-related treatments, and approximately 1 in 10 patients were taking medications for mental health comorbidities, indicating a high unmet need for both vitiligo as well as associated comorbidities. In summary, patients with vitiligo in Spain have limited treatment options and would benefit from more effective treatments with a good safety profile. The effect of the recent approval (2023) of ruxolitinib cream in Europe on treatment patterns and real-world outcomes remains to be seen. ■

***Acknowledgements:** the study was carried out with funding from Incyte Corporation. Incyte Corporation participated in the design and data analysis of the study, as well as in the drafting of the manuscript. No honoraria or authorship payments were made. Editorial support was provided by Valerie Kinchen, PhD, from The Curry Rockefeller Group, a Citrus Health Group, Inc., company (Chicago, IL), and was funded by Incyte Corporation.*

***Disclosures:** JLLE has served as a consultant or speaker for AbbVie, Bristol Myers Squibb, Galderma, Incyte Corporation, Isdin, Janssen Cilag, Naos, Novartis, and UCB. CMG-M, JG, and IAGSM are employees and shareholders of Incyte Biosciences Iberia. VGR, DC, and AdP are employees of IQVIA Information SA. CD is an employee and shareholder of Incyte Biosciences International Sàrl.*

References

1. Bergqvist C, Ezzedine K. Vitiligo: a review. *Dermatology* 2020 ; 236 : 571-92.
2. Ezzedine K, Lim HW, Suzuki T, *et al.* Revised classification/nomenclature of vitiligo and related issues: the vitiligo global issues consensus conference. *Pigment Cell Melanoma Res* 2012 ; 25 : E1-13.

3. Talsania N, Lamb B, Bewley A. Vitiligo is more than skin deep: a survey of members of the Vitiligo Society. *Clin Exp Dermatol* 2010 ; 35 : 736-39.
4. Colucci R, Dragoni F, Moretti S. Oxidative stress and immune system in vitiligo and thyroid diseases. *Oxid Med Cell Longev* 2015 ; 2015 : 631927.
5. Rashighi M, Harris JE. Vitiligo pathogenesis and emerging treatments. *Dermatol Clin* 2017 ; 35 : 257-65.
6. Marchioro HZ, Silva de Castro CC, Fava VM, Sakiyama PH, Dellatorre G, Miot HA. Update on the pathogenesis of vitiligo. *An Bras Dermatol* 2022 ; 97 : 478-90.
7. Seneschal J, Boniface K, D'Arino A, Picardo M. An update on vitiligo pathogenesis. *Pigment Cell Melanoma Res* 2021 ; 34 : 236-43.
8. Mohr N, Petersen J, Kirsten N, Augustin M. Epidemiology of vitiligo - a dual population-based approach. *Clin Epidemiol* 2021 ; 13 : 373-82.
9. Bibeau K, Pandya AG, Ezzedine K, et al. Vitiligo prevalence and quality of life among adults in Europe, Japan and the USA. *J Eur Acad Dermatol Venereol* 2022 ; 36 : 1831-44.
10. Rodríguez-Cerdeira MdC, Arenas-Guzmán R. El vitiligo, una enfermedad estigmática: un recorrido a través de su historia [Vitiligo, a stigmatic disease: a journey through its history]. *Med Cutan Ibero Lat Am* 2011 ; 39 : 278-82.
11. Ezzedine K, Sheth V, Rodrigues M, et al. Vitiligo is not a cosmetic disease. *J Am Acad Dermatol* 2015 ; 73 : 883-5.
12. Ezzedine K, Eleftheriadou V, Jones H, et al. Psychosocial effects of vitiligo: a systematic literature review. *Am J Clin Dermatol* 2021 ; 22 : 757-74.
13. Grimes PE, Miller MM. Vitiligo: patient stories, self-esteem, and the psychological burden of disease. *Int J Womens Dermatol* 2018 ; 4 : 32-7.
14. Incyte Biosciences Distribution BV. *Opzelura (ruxolitinib cream)*. Amsterdam, Netherlands: Summary of Product Characteristics, 2023.
15. Taieb A, Alomar A, Böhm M, et al. Guidelines for the management of vitiligo: the European Dermatology Forum consensus. *Br J Dermatol* 2013 ; 168 : 5-19.
16. Asociación Española de Pacientes de Vitiligo (ASPAVIT). *ASPAVIT*; 2016. Available at aspavit-vitiligo.blogspot.com (accessed June 16, 2022).
17. Eurostat. *Eurostat Data Browser*; 2024. Available at https://ec.europa.eu/eurostat/databrowser/view/demo_pjan__custom_9844689/default/table?lang=en (accessed February 13, 2024).
18. Boisseau-Garsaud AM, Garsaud P, Calès-Quist D, Hélénon R, Quénehervé C, Claire RC. Epidemiology of vitiligo in the French West Indies (Isle of Martinique). *Int J Dermatol* 2000 ; 39 : 18-20.
19. Nagy E, Infantino M, Bizzaro N, et al. The impact of the COVID-19 pandemic on autoimmune diagnostics in Europe: a lesson to be learned. *Autoimmun Rev* 2021 ; 20 : 102985.
20. Ruiz-Medina S, Gil S, Jimenez B, et al. Significant decrease in annual cancer diagnoses in Spain during the COVID-19 pandemic: a real-data study. *Cancers (Basel)* 2021 ; 13 : 3215.
21. Ribes J, Pareja L, Sanz X, et al. Cancer diagnosis in Catalonia (Spain) after two years of COVID-19 pandemic: an incomplete recovery. *ESMO Open* 2022 ; 7 : 100486.
22. Krüger C, Schallreuter KU. A review of the worldwide prevalence of vitiligo in children/adolescents and adults. *Int J Dermatol* 2012 ; 51 : 1206-12.
23. Radtke MA, Schafer I, Gajur A, Langenbruch A, Augustin M. Willingness-to-pay and quality of life in patients with vitiligo. *Br J Dermatol* 2009 ; 161 : 134-9.
24. Ali MA, Abou-Taleb DA, Mohamed RR. Treatment adherence and beliefs about medicines among Egyptian vitiligo patients. *Dermatol Ther* 2016 ; 29 : 413-18.
25. Dahir AM, Thomsen SF. Comorbidities in vitiligo: comprehensive review. *Int J Dermatol* 2018 ; 57 : 1157-64.
26. Hadi A, Wang JF, Uppal P, Penn LA, Elbuluk N. Comorbid diseases of vitiligo: a 10-year cross-sectional retrospective study of an urban US population. *J Am Acad Dermatol* 2020 ; 82 : 628-33.
27. Sharma Y, Bansal P, Menon S, Prakash N. Metabolic syndrome in vitiligo patients among a semi-urban Maharashtrian population: a case control study. *Diabetes Metab Syndr* 2017 ; 11 : S77-80.
28. Raventos B, Pistillo A, Reyes C, et al. Impact of the COVID-19 pandemic on diagnoses of common mental health disorders in adults in Catalonia, Spain: a population-based cohort study. *BMJ Open* 2022 ; 12 : e057866.
29. Wang G, Qiu D, Yang H, Liu W. The prevalence and odds of depression in patients with vitiligo: a meta-analysis. *J Eur Acad Dermatol Venereol* 2018 ; 32 : 1343-51.
30. Kussainova A, Kassym L, Akhmetova A, et al. Vitiligo and anxiety: a systematic review and meta-analysis. *PLoS One* 2020 ; 15 : e0241445.
31. Londono-Garcia A, Arango Salgado A, Orozco-Covarrubias ML, et al. The landscape of vitiligo in Latin America: a call to action. *J Dermatolog Treat* 2023 ; 34 : 2164171.
32. Ahmed A, Steed L, Burden-Teh E, et al. Identifying key components for a psychological intervention for people with vitiligo - a quantitative and qualitative study in the United Kingdom using web-based questionnaires of people with vitiligo and healthcare professionals. *J Eur Acad Dermatol Venereol* 2018 ; 32 : 2275-83.
33. Narayan V, Uitentuis S, Luiten R, Bekken M, Wolkerstorfer A. Patients' perspective on current treatments and demand for novel treatments in vitiligo. *J Eur Acad Dermatol Venereol* 2021 ; 35 : 744-48.
34. Kim YC, Kim YJ, Kang HY, Sohn S, Lee ES. Histopathologic features in vitiligo. *Am J Dermatopathol* 2008 ; 30 : 112-6.
35. Rumbo-Prieto J, Palomar Llatas F. Therapeutic interventions on quality of life for adult vitiligo patients. Best practice information sheets for health professionals (BPIS) 2011 ; 15 : 1-4. In Spanish. Accessed at: http://scielo.isciii.es/scielo.php?script=sci_arttext&pid=S1988-348X2017000100010
36. Palomino OM. Current knowledge in *Polypodium leucotomos* effect on skin protection. *Arch Dermatol Res* 2015 ; 307 : 199-209.
37. Cavalieri M, Ezzedine K, Fontas E, et al. Maintenance therapy of adult vitiligo with 0.1% tacrolimus ointment: a randomized, double blind, placebo-controlled study. *J Invest Dermatol* 2015 ; 135 : 970-4.
38. Almeida P, Borrego L, Rodríguez-López J, Luján D, Cameselle D, Hernández B. Vitiligo. Tratamiento de 12 casos con tacrolimus tópico. *Actas Dermosifiliogr* 2005 ; 96 : 159-63.
39. Eleftheriadou V, Atkar R, Batchelor J, et al. British association of dermatologists guidelines for the management of people with vitiligo 2021. *Br J Dermatol* 2022 ; 186 : 18-29.