Eur J Dermatol 2024; 34(2): 163-175

Sergio VAÑÓ-GALVÁN[1]
Ignasi FIGUERAS-NART[2]
Esther ARTIME[3]
Silvia DÍAZ-CEREZO[3]
Mercedes NÚÑEZ[3]
Carlos IGLESIAS[4]
Maite ARTÉS[5]
Teresa HUETE[3]

[1] Servicio de Dermatología del Hospital Ramón y Cajal Hospital, IRYCIS, Universidad de Alcalá, Clínica Grupo Pedro Jaen, Madrid, Spain
[2] Servicio de Dermatología de Hospital Universitario de Bellvitge, Hospitalet de Llobregat, Barcelona, Spain
[3] Lilly, España, Alcobendas, Madrid, Spain
[4] Cegedim Health Data Spain, Barcelona, Spain
[5] Adelphi Targis, Barcelona, Spain

Reprints: Esther Artime
<artime_esther@lilly.com>

Article accepted on 07/01/2024

Epidemiological, clinical and economic burden of alopecia areata in Spain: a real-world retrospective study. The PETALO study

Background: Alopecia areata (AA) is a chronic autoimmune disease that causes non-scarring hair loss. Data are lacking on the epidemiology and clinical and economic burden of AA in Spain. *Objectives:* To estimate the prevalence and incidence of AA in Spain and describe sociodemographic and clinical characteristics, treatment patterns, healthcare resource utilization (HCRU) and associated costs. *Materials & Methods*: This was an observational, retrospective, descriptive study based on the Health Improvement Network (THIN®) database (Cegedim Health Data, Spain). Patients with ICD9-Code 704.01 for AA, registered between 2014 and 2021, were identified. Prevalence (%) and incidence rates per 1,000 patient-years (IR) of AA were calculated and clinical characteristics, treatment characteristics and HCRU/costs were assessed. *Results*: A total of 5,488 patients with AA were identified. The point prevalence of AA in 2021 was 0.44 (95% confidence interval [CI]: 0.43–0.45) overall, 0.48 (0.47–0.49) in adults, and 0.23 (0.21–0.26) in children ≤12 years. The 2021 IR for AA in adults was 0.55 (0.51–0.60). Of 3,351 adults with AA, 53.4% were female, mean (standard deviation [SD]) age was 43.1 (14.7) years, and 41.6% experienced comorbidities. Among adults, 2.7% used systemic treatment (0.5% immunosuppressants, 2.5% oral corticosteroids, 0.3% both). Laboratory tests and health care professional visits were the principal drivers of cost, which was €821.2 (1065.6)/patient in the first year after diagnosis. *Conclusion*: The epidemiology of AA in Spain is comparable with that reported for other countries, being more prevalent among adults. There is a significant burden of comorbidities and cost for patients, with limited use of systemic treatments, suggesting an unmet treatment need in this population.

Key words: alopecia areata, incidence, prevalence, comorbidities, systemic treatment, healthcare resources

Alopecia Areata (AA) is a chronic autoimmune disease that causes non-scarring hair loss, with no sex or racial predilection, and is the second most common cause of hair loss after androgenetic alopecia. Hair loss can occur on the scalp or anywhere on the face or body [1–3]. AA can progress from a localised manifestation to encompass total scalp hair loss (alopecia totalis) or extend to complete body hair loss across the entire body (alopecia universalis). The estimated worldwide prevalence of AA is between 0.1% and 0.2% with a lifetime risk of 2% [4, 5]. However, studies examining the prevalence of AA are limited and results are variable [6]. The onset of AA may occur at any age; it is a highly unpredictable condition with high rates of recurrence [2, 7–9]. Children constitute approximately 20% of patients with AA while 20% of patients are aged >40 years. The mean age at onset is between 25 and 36 years [2, 7, 9].

AA is associated with poor quality of life, as well as sleep and mood disturbances that affect the social, emotional and functional spheres of patients' lives [10]. AA also imposes a significant financial burden on patients and healthcare systems [1, 7, 11–14].

The pathophysiology of AA is poorly understood. Genetic and environmental factors are thought to contribute to the development of AA [11, 15–19]. The immune system is also involved and patients with AA frequently present with comorbid immune-mediated diseases such as atopic dermatitis, vitiligo and thyroid diseases [2, 4, 19–21]. Features associated with a poor prognosis in patients with AA include a long duration of hair loss, young age at initial onset (pre-pubescent), extensive hair loss, a positive family history, a pattern of ophiasis, associated nail lesions, and the presence of comorbid autoimmune disease [4].

doi:10.1684/ejd.2024.4654

To cite this article: Vañó-Galván S, Figueras-Nart I, Artime E, Díaz-Cerezo S, Núñez M, Iglesias C, Artés M, Huete T. Epidemiological, clinical and economic burden of alopecia areata in Spain: a real-world retrospective study. The PETALO study. *Eur J Dermatol* 2024; 34(2): 163-175 doi:10.1684/ejd.2024.4654

Current management of AA is difficult as there is no cure and few approved treatments are available [1, 22, 23]. Localised and systemic agents can be used based on patient age and disease severity [2, 4, 24]. Such treatments include intralesional and topical steroids for mild or moderate disease. For severe cases, the use of treatments, such as phototherapy, oral corticosteroids and immunosuppressant therapy, has been reported, although evidence for their efficacy is limited [25]. In most severe cases, an extended period of therapy of at least 12 months is required and maintenance therapy is recommended [26, 27]. The prognosis and response to treatment are variable and unpredictable. While the majority of patients with mild forms of AA will recover within a year with spontaneous hair regrowth and a good response to treatment, a significant proportion of patients will experience more than one episode of hair loss and their condition often becomes chronic [2, 4, 9, 12, 19, 28].

Few studies describe the burden of AA in Spain [3, 10, 29]. Therefore, there is a need for large scale population-based studies to characterise the epidemiological, clinical and economic burden of AA in Spain. This study aimed to estimate the prevalence and incidence of AA, with a focus on the sociodemographic and clinical characteristics, treatment patterns, healthcare resource utilization (HCRU), and associated costs in patients with AA in Spain.

Methods

The PETALO study is an observational, retrospective, descriptive study based on the Health Improvement Network (THIN®) database (Cegedim Health Data, Spain). The THIN® database is a longitudinal, patient-level, anonymized database of Electronic Medical Records that incorporates data via 1,900 general practitioners and 2,500 specialists (including 45 dermatologists) for a population of approximately 1.9 million patients in Spain since 2014. It represents approximately 4% of the Spanish national population and the patient distribution of diagnoses is closely aligned with national demographic and clinical data for Spain [30–33].

Ethical approval for the study was provided by the ethics committees of Ramón y Cajal University Hospital and Hospital Clínic de Barcelona.

Study population

The 'full analysis population' consisted of all patients included in the database (adults, adolescents [13 to 17 years] and children [≤12 years]) with at least one recorded diagnosis of AA (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] code 704.01) between 1st January 2014 and 31st December 2021. Patients with an ICD-9-CM record of other hair loss disorders (including trichotillomania, telogen effluvium, tinea capitis, tinea barbae, other alopecia, other specified hair loss pathologies) in the subsequent 365 days after the first AA recording were excluded. Incident cases were defined as those having a recorded diagnosis of AA between 1st January 2015 and 31st December 2021 and no documented diagnosis before.

Due to the potential impact of the COVID-19 pandemic, data on treatment patterns and HCRU for years 2020 and 2021 were excluded from these analyses. A sub-population of prevalent AA patients on 31st December 2018 was selected as the 'current study population' (*figure 1*). Patients were stratified according to the use of systemic treatment (including immunosuppressants [IS] and oral corticosteroids [OC]) for AA (*see supplementary table 1*

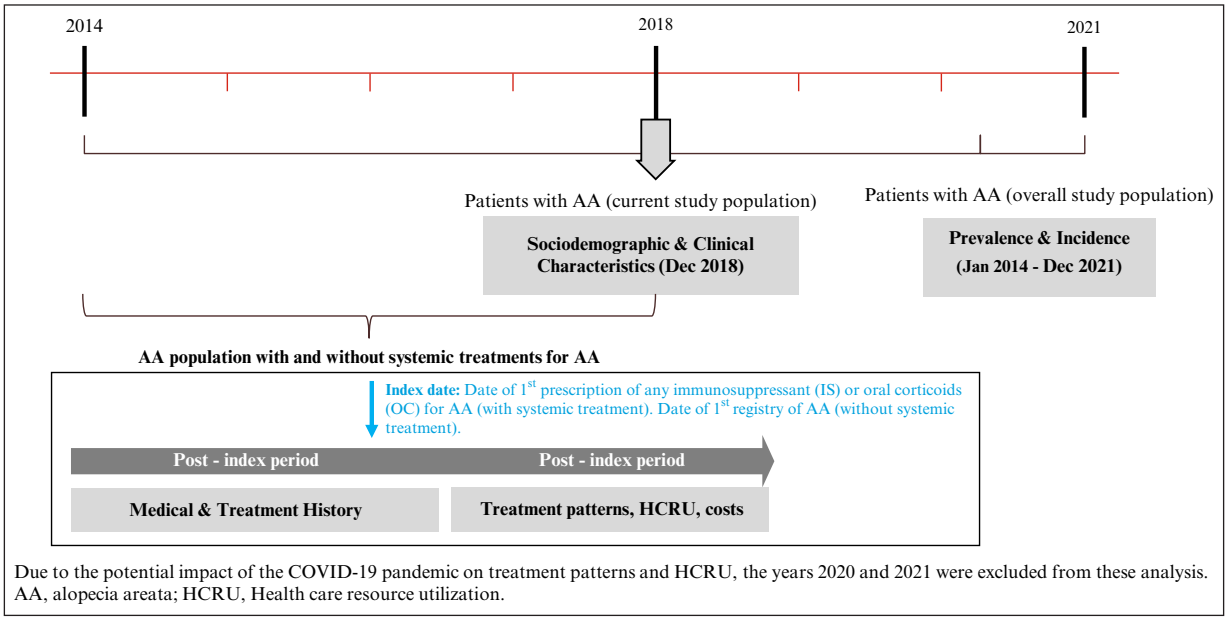


Figure 1. Study design

for more detail). For patients with no record of systemic treatment, the index date was defined as the date of the first record of AA diagnosis between 1st January 2014 and 31st December 2018. For patients with documented use of systemic treatment, the index date was defined as the date of the first recorded prescription between 1st January 2014 and 31st December 2018. To address treatment patterns, HCRU and associated costs, patients were required to have at least one year of follow-up between the index date and 31st December 2019 (*figure 1*).

Study variables and outcomes

Sociodemographic and clinical characteristics measured on 31st December 2018 included sex, age, body mass index (BMI), time from AA diagnosis, and comorbidities (presence of ICD-9-CM any time prior to or at index date). Data regarding referral to a dermatologist and time from AA diagnosis to referral were obtained. When the date of referral to a dermatologist coincided with the date of the first diagnosis of AA, it was assumed that the diagnosis was made by the dermatologist.

Systemic and non-systemic treatments linked to a diagnostic code for AA were captured (*supplementary table 1*). Systemic treatments over the follow-up period were described for patients with documented use of IS or OC for AA. Systemic monotherapy was defined as prescription of a single systemic treatment for AA with no record of other systemic treatments on the same date. A combination of systemic treatments was defined as prescription of more than one systemic treatment on the same date. Treatment sequences were defined as starting on the first registered prescription date for each systemic treatment (IS or OC) and numbered consecutively to the date of the last prescription of an IS or OC for AA. The duration of each treatment sequence was calculated as the time in days until change of prescribed treatment. A treatment switch was defined when a new systemic treatment for AA was initiated within 90 days of the end of the prior systemic treatment for AA. The number of patients who received a prescription of each type of non-systemic and concomitant treatment and the mean number of non-systemic and concomitant treatments during the pre-index period and during the post-index period were also analysed.

HCRU in the 365 days following the index date were measured based on general practitioner (GP) visits (all-cause), specialist visits (all-cause), laboratory tests requested for AA, systemic treatments prescribed for AA, non-systemic treatments prescribed for AA, and concomitant treatments prescribed for comorbid conditions.

Statistical analyses

Prevalence and incidence were estimated overall and stratified by age and sex.

The period prevalence (%) of AA was calculated based on the full study population and the total number of patients registered in the database at the median point for the same period. To determine the period prevalence according to age groups, the age at first AA diagnosis was considered.

The 2021 point prevalence (%) was calculated based on the number of patients with a diagnosis of AA on 31st December 2021 over the total number of patients registered in the database at the same time point. In the case of annual prevalence according to age groups, the patient's age was calculated on the 31st December 2021.

The incidence rate (IR) of AA (in 1,000 patient-years) was estimated based on the number of incident AA cases. To determine the annual incidence according to age group, age on the 1st January 2021 was used.

Descriptive analyses were performed to describe sociodemographic and clinical characteristics, and treatment patterns. For continuous variables, the number, mean, standard deviation (SD), and minimum and maximum values were calculated. For categorical variables, the count, frequency, and percentage (excluding missing values) were determined. HCRU was estimated by determining the utilisation of resources used at the individual patient level for one year following the index date. Unit costs for each healthcare resource were obtained from different sources and converted to Euros using published cost-price indices for 2022 from the National Institute of Statistics (*supplementary table 2*). The associated cost was estimated by multiplying patient level HCRU by the unit cost. The average cost per patient and per year and the 95% confidence intervals (CI) were estimated for total costs and by cost type (visits, tests, and treatments).

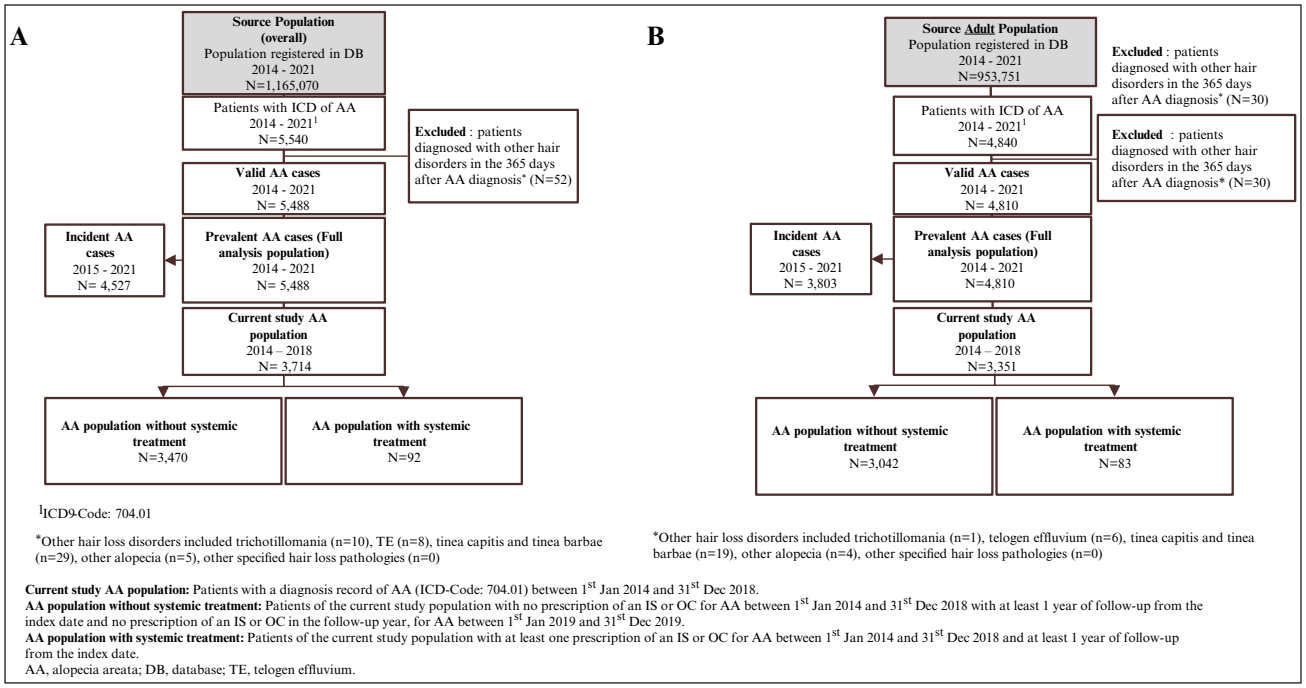
Results are presented overall and separately for adults only, given the small number of adolescents and children who received systemic treatment.

Results

The disposition of the overall and adult population of the study is presented in *figure 2*. Of a total of 1,165,070 patients registered in the THIN® database between 1st January 2014 and 31st December 2021, 5,488 were prevalent and 4,527 were incident cases of AA (*figure 2A*). Among the 953,751 adults registered in the THIN® database for this period, 4,810 were prevalent cases of AA and 3,803 were incident cases (*figure 2B*). In addition, among the 69,590 adolescents registered, 207 were prevalent cases and 215 were incident cases. Regarding the 141,729 children registered in the database, 471 were prevalent cases and 509 were incident cases of AA.

AA prevalence and incidence

The prevalence of AA between 2014 and 2021 was 0.47% (95% CI: 0.46–0.48) with an annual point prevalence of 0.44% (95% CI: 0.43–0.45) in 2021 (*table 1*). The prevalence of AA was similar among males (0.45%; 95% CI: 0.43–0.47) and females (0.49%; 95% CI: 0.47–0.51). AA was more prevalent among adults (0.50%; 95% CI: 0.49–0.52) than children ≤12 years of age (0.33%; 95% CI: 0.30–0.36) or adolescents aged 13 to ≤17 years of age (0.30%; 95% CI: 0.26–0.34). In 2021, the IR of AA was 0.52 (95% CI: 0.48–0.56) per 1,000 patient-years with a higher incidence among adults.



[1]ICD9-Code: 704.01

*Other hair loss disorders included trichotillomania (n=10), TE (n=8), tinea capitis and tinea barbae (n=29), other alopecia (n=5), other specified hair loss pathologies (n=0)

*Other hair loss disorders included trichotillomania (n=1), telogen effluvium (n=6), tinea capitis and tinea barbae (n=19), other alopecia (n=4), other specified hair loss pathologies (n=0)

Current study AA population: Patients with a diagnosis record of AA (ICD-Code: 704.01) between 1st Jan 2014 and 31st Dec 2018.
AA population without systemic treatment: Patients of the current study population with no prescription of an IS or OC for AA between 1st Jan 2014 and 31st Dec 2018 with at least 1 year of follow-up from the index date and no prescription of an IS or OC in the follow-up year, for AA between 1st Jan 2019 and 31st Dec 2019.
AA population with systemic treatment: Patients of the current study population with at least one prescription of an IS or OC for AA between 1st Jan 2014 and 31st Dec 2018 and at least 1 year of follow-up from the index date.
AA, alopecia areata; DB, database; TE, telogen effluvium.

Figure 2. Disposition of the overall (A) and adult (B) population.

Table 1. Prevalence and incidence of AA in Spain (2014 to 2021).

Metric (95% CI)	Prevalence (%) 1st Jan 2014–31st Dec 2021	Point prevalence (%) 31st Dec 2021	Incidence rate (per 1,000 patient-years) 1st Jan 2021- 31st Dec 2021
Overall	0.47 (0.46–0.48)	0.44 (0.43–0.45)	0.52 (0.48–0.56)
By sex			
Males	0.45 (0.43–0.47)	0.42 (0.40–0.43)	0.50 (0.44–0.56)
Females	0.49 (0.47–0.51)	0.46 (0.44–0.48)	0.54 (0.49–0.60)
By age interval			
0 to ≤12 years	0.33 (0.30–0.36)	0.23 (0.21–0.26)	0.39 (0.29–0.51)
13 to ≤17 years	0.30 (0.26–0.34)	0.24 (0.20–0.27)	0.36 (0.23–0.52)
≥18 years	0.50 (0.49–0.52)	0.48 (0.47–0.49)	0.55 (0.51–0.60)

CI: confidence interval.

Sociodemographic, clinical and treatment characteristics

The sociodemographic, clinical and treatment characteristics of the current study population (overall [*n*=3,714] and adult [*n*=3,351]) are shown in *table 2*. In the overall AA population, the mean (SD) age on 31st December 2018 was 39.9 (17.1) years and 53.4% were female. Among the adult population, 2.7% used systemic treatment (0.5% IS, 2.5% OC, 0.3% both) and 53.5% used non-systemic treatments for AA. IS used included methotrexate 0.2%, cyclosporine 0.2% and azathioprine 0.1% (*figure 3*).

Regarding AA diagnosis and referrals to dermatology, 1,560 patients (50.8%) were referred following a diagnosis of AA or were directly diagnosed by the dermatologist, with a mean interval between diagnosis and first dermatology referral of 129.6 days (SD: 290.1). From these, 870 adult patients (28.3%) were diagnosed with AA in 2018 by a dermatologist (*table 4*).

Patients with systemic treatment (n=92)

The mean age at initiation of the first systemic treatment (index date) was 39.5 years (SD: 15.1; males: 37.3 [SD 11.5], females: 41.0 [SD 17.2]) (*figure 4*). The mean age at diagnosis was 39.0 years (SD 15.2) with a mean time from AA diagnosis to index date of 208.8 days (SD: 324.6). Comorbidities were present in 39.1% of patients; contact dermatitis and other eczema (unspecified cause), cardiometabolic, dermatological immune-mediated systemic inflammatory disease and psychiatric diseases were the most frequently reported comorbid conditions (*figure 5, table 3*).

Of 83 adult patients, 51 (61.4%) were referred to a dermatologist following diagnosis, with a mean interval between diagnosis and referral of 192.8 days (SD: 367.4) (*table 4*).

Table 2. Sociodemographic and clinical characteristics of the current study population of AA patients on 31st December 2018.

Characteristics	Overall AA population (2018) N=3,714	Adult AA population (2018) N=3,351	0-12 years AA population (2018) N=238	13-17 years AA population (2018) N=125
Sex, n (%)				
Male	1,730 (46.6)	1,560 (46.6)	109 (45.8)	61 (48.8)
Female	1,984 (53.4)	1,791 (53.4)	129 (54.2)	64 (51.2)
Age, mean (SD)	39.9 (17.1)	43.1 (14.7)	7.8 (2.8)	14.9 (1.3)
BMI, mean (SD)	25.9 (6.9)	28.9 (5.6)	17.9 (3.7)	22.3 (3.6)
Time since AA diagnosis, mean years (SD)	2.7 (1.5)	2.7 (1.5)	2.6 (1.4)	2.6 (1.5)
Treatment for AA 2014 to 2018, n (%)				
Non-systemic	1,943 (52.3)	1,792 (53.5)	91 (38.2)	60 (48.0)
Systemic	94 (2.5)	89 (2.7)	1 (0.4)	4 (3.2)

AA: alopecia areata; BMI: body mass index; SD: standard deviation.

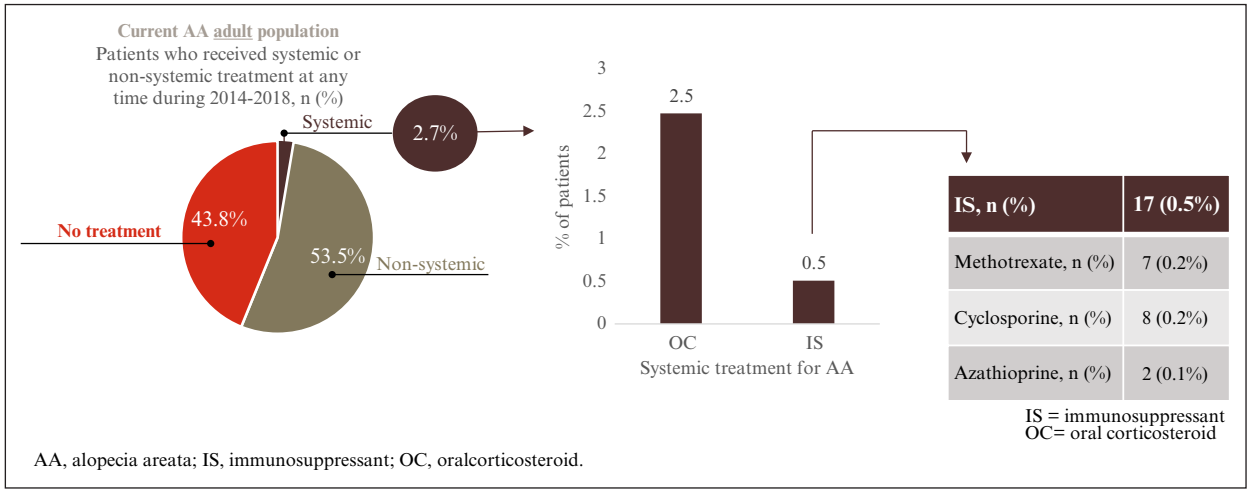


Figure 3. Systemic and non-systemic treatments for AA among adults in Spain (2014 to 2018).

Patients without systemic treatment (n=3,470)

The mean age at diagnosis (index date) was 37.2 years (SD: 17.1; males: 34.3 years [SD: 14.9], females: 39.8 years [SD: 18.5]). The mean follow-up time for this group was 5.8 years (SD: 1.5) (*figure 4*). In the overall population, comorbidities were present in 26.6% of those who did not receive systemic treatment for AA (*figure 5, table 3*).

Overall, a total of 1,624 adult patients (53.4%) were referred to a dermatologist following a diagnosis of AA with a mean interval of 283.8 days (SD: 548.4) between diagnosis and first dermatology referral (*table 4*).

Treatment patterns among adults prescribed systemic treatment (n=83)

Systemic treatment patterns

Among adults prescribed systemic monotherapy as their first treatment for AA (*n*=83), 89.2% received OC and 10.8% received IS (*figure 6*). For subsequent lines of therapy, 16.9%, 8.4% and 3.6% of adults were prescribed OC monotherapy as second, third and fourth line, respectively (*figure 6, table 5*). Non-systemic treatments were prescribed in combination with OC for 26.5% of adults, the most frequent combinations being dexamethasone in combination with mineral supplements (9.6% of adults) and prednisone in combination with topical corticosteroids (8.4% of adults) (*supplementary table 3*). Cyclosporine and methotrexate were the most commonly used IS (in 6.0% and 3.6% of adults, respectively) (*supplementary table 4*). Methotrexate in combination with iron preparations was the most frequently prescribed first-line IS combination regimen (in 2.4% of adults) (*supplementary table 3*).

At one and two years post-index date, 25.3% and 20.5% of adults, respectively, continued to be prescribed a systemic treatment for AA.

Non-systemic treatment patterns

The percentage of adults who received non-systemic treatment for AA was 76.7% pre-index and 62.7% post-index. (*figure 7, table 6*). Topical corticosteroids were

Table 3. Comorbid conditions among patients with AA with and without systemic treatment at the index date*.

	Patients without systemic treatment for AA						Patients with systemic treatment for AA					
Comorbid conditions, n (%)	**Overall N= 3,470**	**Female N=1,861**	**Male N=1,609**	**≤12 years N=296**	**13–17 years N=132**	**≥18 years N=3,042**	**Overall N= 92**	**Female N=53**	**Male N=39**	**≤12 years N=2**	**13 –17 years N=7**	**≥18 years N=83**
Any	923 (26.6)	593 (31.9)	330 (20.5)	90 (30.4)	19 (14.4)	814 (26.8)	36 (39.1)	23 (43.4)	13 (33.3)	1 (50.0)	3 (42.9)	32 (38.6)
Non-dermatological immune-mediated systemic inflammatory disease	18 (0.5)	13 (0.7)	5 (0.3)	0 (0.0)	1 (0.8)	17 (0.6)	1 (1.1)	1 (1.9)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)
Rheumatoid arthritis	5 (0.1)	3 (0.2)	2 (0.1)	0 (0.0)	0 (0.0)	5 (0.2)	1 (1.1)	1 (1.9)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)
SLE	8 (0.2)	7 (0.4)	1 (0.1)	0 (0.0)	0 (0.0)	8 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Ankylosing spondylitis	1 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Ulcerative colitis	3 (0.1)	2 (0.1)	1 (0.1)	0 (0.0)	0 (0.8)	2 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Crohn's disease	1 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Dermatological immune-mediated systemic inflammatory disease	143 (4.1)	77 (4.1)	66 (4.1)	41 (13.9)	6 (4.6)	96 (3.2)	7 (7.6)	5 (9.4)	2 (5.1)	1 (50.0)	2 (28.6)	4 (4.8)
Psoriasis	4 (0.1)	1 (0.1)	3 (0.2)	0 (0.0)	0 (0.0)	4 (0.1)	1 (1.1)	0 (0.0)	1 (2.6)	0 (0.0)	0 (0.0)	1 (1.2)
Vitiligo	10 (0.3)	7 (0.4)	3 (0.2)	0 (0.0)	0 (0.0)	10 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (00)	0 (0.0)
Atopic dermatitis	129 (3.7)	69 (3.7)	60 (3.7)	41 (13.9)	6 (4.6)	82 (2.7)	6 (6.5)	5 (9.4)	0 (2.6)	1 (50.0)	2 (28.6)	3 (3.6)
Contact dermatitis and other eczema, unspecified cause	409 (11.8)	240 (12.9)	169 (10.5)	59 (19.9)	12 (9.1)	338 (11.1)	14 (15.2)	8 (15.1)	6 (15.4)	1 (50.0)	0 (0.0)	13 (15.7)
Cardiometabolic disease	311 (9.0)	236 (12.7)	75 (4.7)	0 (0.0)	2 (1.5)	309 (10.2)	13 (14.1)	11 (20.8)	2 (5.1)	0 (0.0)	1 (14.3)	12 (14.5)
Diabetes mellitus	25 (0.7)	15 (0.8)	10 (0.6)	0 (0.0)	0 (0.0)	25 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Dyslipidaemia	12 (0.4)	8 (0.4)	4 (0.3)	0 (0.0)	0 (0.0)	12 (0.4)	2 (2.2)	2 (3.8)	0 (0.0)	0 (0.0)	0 (0.0)	2 (2.4)
Hypertension	164 (4.7)	115 (6.2)	49 (3.1)	0 (0.0)	0 (0.0)	164 (5.4)	4 (4.4)	4 (7.6)	0 (0.0)	0 (0.0)	0 (0.0)	4 (4.8)
Hyperthyroidism	12 (0.4)	8 (0.4)	4 (0.3)	0 (0.0)	0 (0.8)	11 (0.4)	1 (1.1)	0 (0.0)	1 (2.6)	0 (0.0)	0 (0.0)	1 (1.2)
Hypothyroidism	131 (3.8)	117 (6.3)	14 (0.9)	0 (0.0)	1 (0.8)	130 (4.3)	7 (7.6)	6 (11.3)	1 (2.6)	0 (0.0)	0 (14.3)	6 (7.2)
Psychiatric disease	217 (6.3)	167 (9.0)	50 (3.1)	1 (0.3)	0 (0.0)	216 (7.1)	7 (7.6)	4 (7.6)	3 (7.7)	0 (0.0)	0 (0.0)	7 (8.4)
Depression	95 (2.7)	73 (3.9)	22 (1.4)	1 (0.3)	0 (0.0)	94 (3.1)	1 (1.1)	1 (1.9)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)
Anxiety	138 (4.0)	109 (5.9)	29 (1.8)	0 (0.0)	0 (0.0)	138 (4.5)	7 (7.6)	4 (7.6)	3 (7.7)	0 (0.0)	0 (0.0)	7 (8.4)

AA: alopecia areata; SLE: systemic lupus erythematosus.
**Date of diagnosis for patients without systemic treatment, and date of first systemic treatment for patients with systemic treatment.*

Table 4. Referrals to dermatology specialist since AA diagnosis for the AA adult population on 31st December 2018 and AA adult patients with and without systemic treatment during the whole study period.

		Adult AA population (2018) N=3,351
Patients diagnosed by dermatologist, n (%)		870 (28.3)
Patients referred to dermatologist since AA diagnosis or directly diagnosed by the dermatologist, n (%)		1,560 (50.8)
Time from first AA diagnosis to first referral to dermatologist, mean days (SD)		129.6 (290.1)
	Patients without systemic treatment (2014–2018) N=3,042	**Patients with systemic treatment (2014–2018) N=83**
Patients referred to dermatologist since AA diagnosis, n (%)	1,624 (53.4)	51 (61.4)
Time from first AA diagnosis to first referral to dermatologist, mean days (SD)	283.8 (548.4)	192.8 (367.4)

AA: alopecia areata; SD: standard deviation.

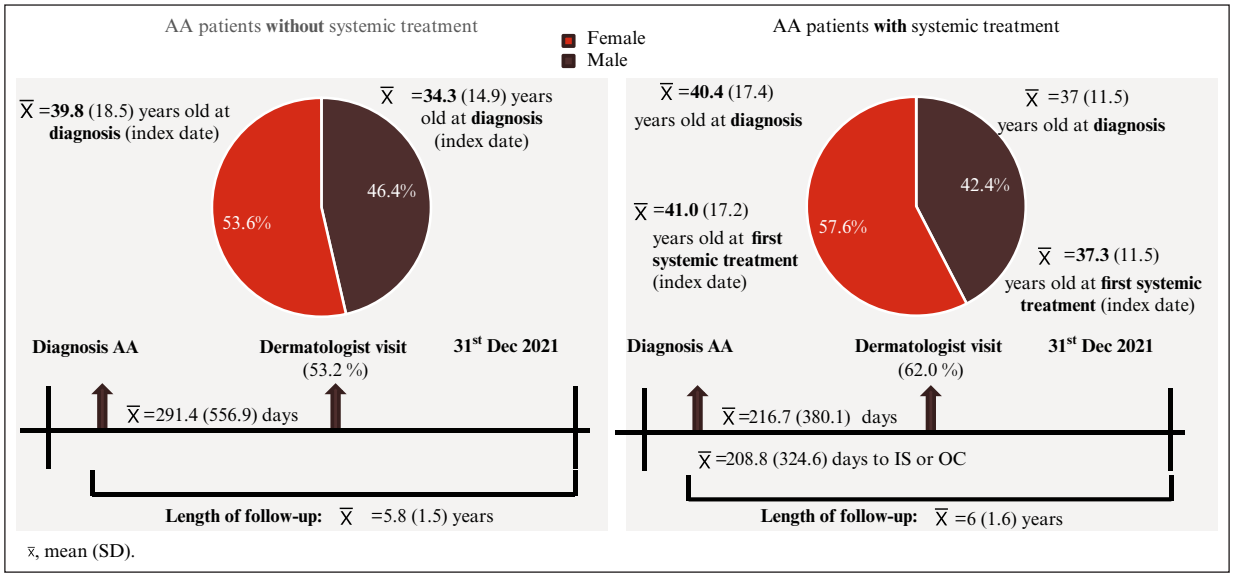


Figure 4. Age and sex at index date in patients with and without systemic treatment for AA.

the most frequently prescribed non-systemic treatment (31.3%).

Concomitant treatments

The percentage of patients who received concomitant treatments was 50% pre-index (43.3% psychiatric medications; 21.7% other) and 55.4% post-index (42.2% psychiatric medications; 30.1% other) (*figure 8, table 7*). The mean number of concomitant treatments prescribed per patient was 4.4 (SD: 8.6). Anxiolytics were the most frequently prescribed concomitant treatment (in 37.3% of adults).

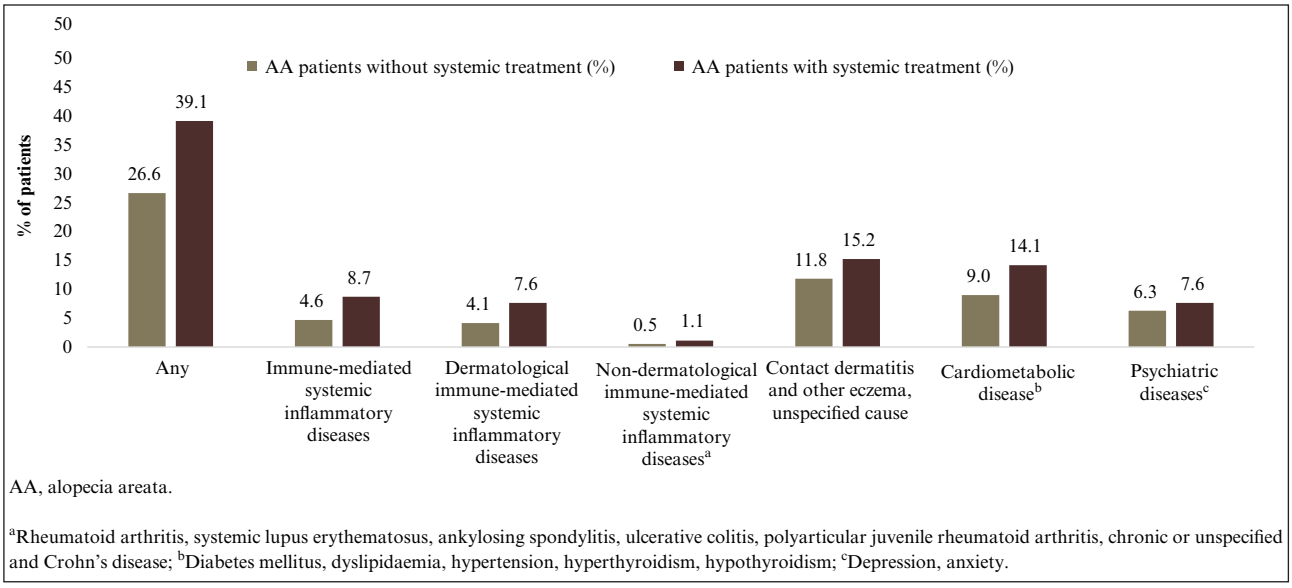
Healthcare resource utilization and associated costs

HCRU for adult patients who did and did not receive systemic treatment for AA during the study period is shown in *table 8*. A higher number of GP visits and greater use of non-systemic treatments for AA and concomitant treatments for comorbid conditions was observed among patients who received systemic treatment *versus* those who did not.

During the first year following the index date, the mean (SD) cost per patient was similar between those who did not receive systemic treatment (€821.2 [SD: 1,065.6]) and those who did receive systemic treatment for their AA (€ 881.4 [SD: 1,371.0]) (*supplementary table 5*). The numerical difference was mainly related to more frequent healthcare provider visits and greater concomitant treatment use among those who received systemic treatment for AA. Laboratory tests and health care professional (HCP) visits were the principal drivers of cost (*figure 9*).

Discussion

To our knowledge, PETALO is the first study to estimate the incidence and prevalence of AA in Spain. The study, based on the Spanish database THIN®, revealed a point



AA, alopecia areata.

[a]Rheumatoid arthritis, systemic lupus erythematosus, ankylosing spondylitis, ulcerative colitis, polyarticular juvenile rheumatoid arthritis, chronic or unspecified and Crohn's disease; [b]Diabetes mellitus, dyslipidaemia, hypertension, hyperthyroidism, hypothyroidism; [c]Depression, anxiety.

Figure 5. Comorbid conditions among patients with and without systemic treatment for AA.

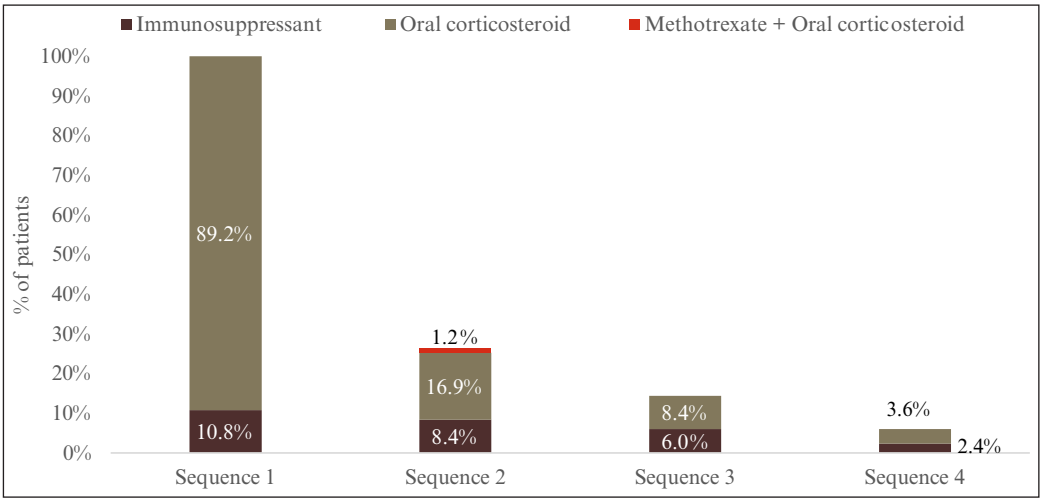


Figure 6. Systemic treatment for AA in adult patients and treatment sequence from index date to the end of follow up.

Table 5. Systemic treatments prescribed as first, second, third and fourth-line treatments for AA, from the index date to end of follow-up in patients with AA who received IS or OC.

	Line of treatment (n=83)			
Systemic treatment, n (%)	**1st (n=83)**	**2nd (n=22)**	**3rd (n=12)**	**4th (n=5)**
OC	74 (89.2)	14 (16.9)	7 (8.4)	3 (3.6)
IS	9 (10.8)	7 (8.4)	5 (6.0)	2 (2.4)
Methotrexate	3 (3.6)	4 (4.8)	3 (3.6)	0 (0.0)
Cyclosporine	5 (6.0)	2 (2.4)	2 (2.4)	2 (2.4)
Azathioprine	1 (1.2)	1 (1.2)	0 (0.0)	0 (0.0)
Methotrexate + OC	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)

AA: alopecia areata; IS: immunosuppressant; OC: oral corticosteroid.

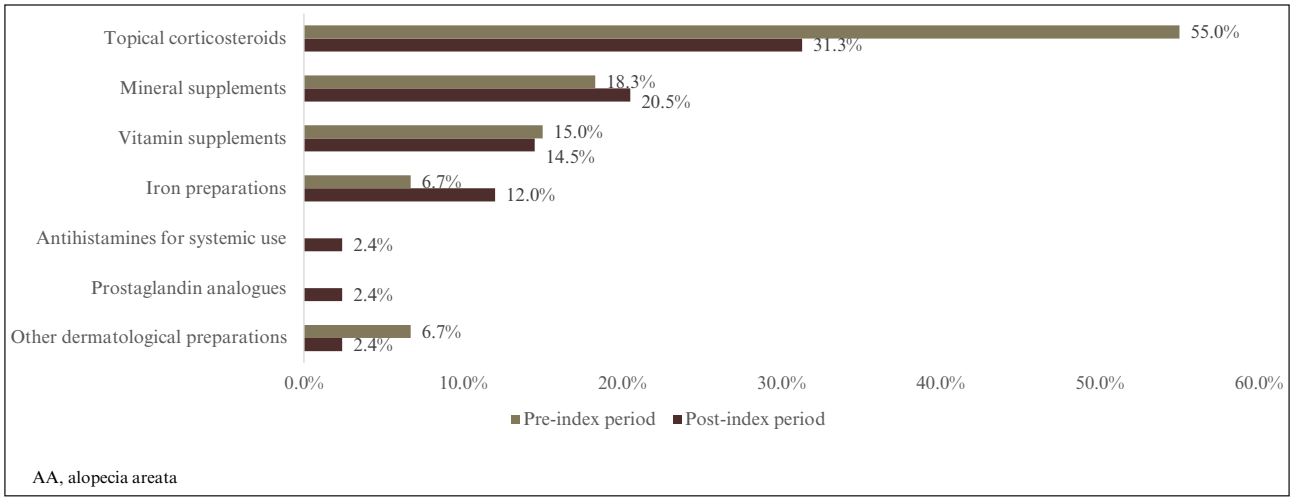


Figure 7. Non-systemic treatment for AA during the pre-index and post-index period among adults treated with systemic therapy for AA.

Table 6. Prescription of non-systemic treatments for AA among adult patients who received systemic treatment (pre- and post-index).

Variable	Adult AA patients with systemic treatment N=83
Pre-index period (from diagnosis to first prescription of an IS or OC)	
Number of non-systemic treatments prescribed for AA, per patient, mean (SD) Min-Max	1.4 (1.5) 0–8
Number of patients who received a prescription of non-systemic treatments, n (%)	46 (76.7)
Post-index period (from first prescription of an IS or OC to end of follow-up)	
Number of non-systemic treatments prescribed for AA, per patient, mean (SD) Min-Max	1.7 (2.9) 0–20
Number of patients who received a prescription of non-systemic treatments, n (%)	52 (62.7)

AA: alopecia areata; IS: immunosuppressant; OC: oral corticosteroid; SD: standard deviation.

prevalence of 0.44% and an incidence rate of 0.52 per 1,000 patient-years in 2021. While no differences by gender were detected, the prevalence and incidence of AA increased with age. These findings are consistent with the limited number of reports from other countries [7, 34, 35].

In the period of 2014-2018, our analysis revealed that 53.5% of AA adult patients were prescribed non-systemic treatments for AA, while only 2.7% underwent systemic treatment. These findings are consistent with the existing literature, which suggests that only around half of patients receive pharmacological treatment for AA within the initial year post-diagnosis [1, 7]. The cohort not receiving treatment for AA may include individuals with mild disease presentations, for whom a "watch-and-wait" strategy is clinically indicated [36–38]. Additionally, this group may encompass patients who experience spontaneous remission or those who elect self-management approaches. Self-management in these instances may involve the use of over-the-counter medications, or cosmetic solutions such as wigs or make-up [36–38].

Of particular interest were the characteristics of the subgroup of patients who received systemic therapy for AA with OC or IS; agents that are generally reserved for the treatment of more severe AA [2, 4, 24]. Given the small number of patients <18 years of age who received systemic therapy for AA (five patients), our analysis focused only on those patients aged ≥18 years. This population could be considered the population with more severe AA not responding to, or not well managed with, non-systemic treatments because 76.7% had received non-systemic therapies prior to their first prescription for systemic treatment of AA. Indeed, these adults demonstrated a higher frequency of GP consultations and received a greater number of non-systemic AA treatments. Additionally, they were more frequently prescribed treatments for comorbid conditions compared to adults who did not receive systemic therapy for AA. These differences were reflected in the numerically higher per-patient costs accrued by those who received systemic treatment for AA compared with those who did not. Also of note was the pattern of referral for dermatology assessment. Overall, the mean interval between diagnosis and first dermatology referral was 129.6 days. However, a marked difference in interval duration was noted between those patients receiving systemic therapy (192.8 days) and those not receiving systemic therapy (283.8 days). This observation is concerning, as it suggests that patients with seemingly less severe AA may experience a delay of a year or more in receiving effective treatment, prior to a referral for specialist assessment.

The analysis of systemic treatment patterns for AA demonstrated that the majority of adults received OC as firstline treatment (89.2%) and that a considerable proportion of patients received systemic treatment for AA for more than one and two years (25.3% and 20.5%,

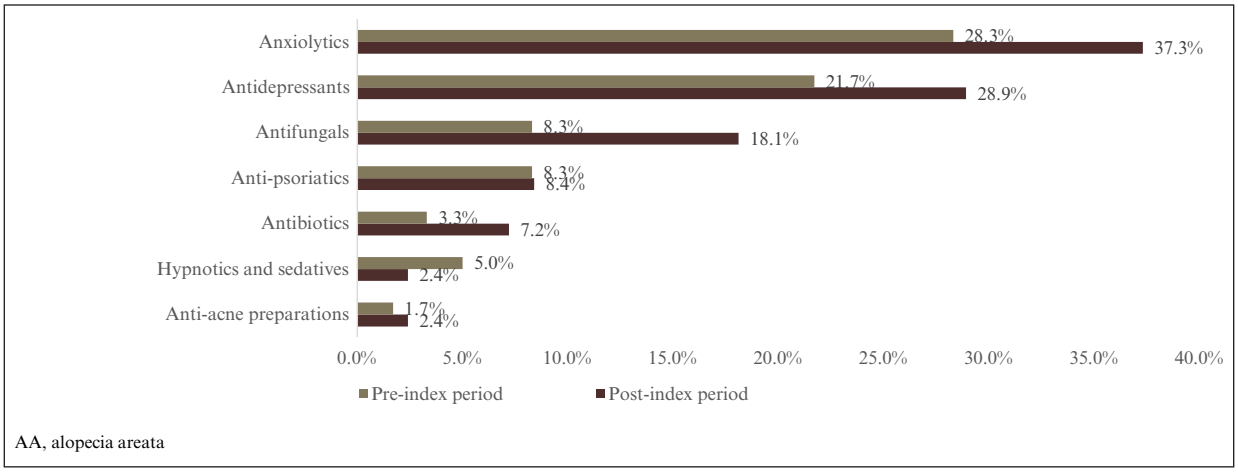


Figure 8. Concomitant treatments during the pre-index and post-index period among adults treated with systemic therapy for AA.

Table 7. Prescription of concomitant treatments for AA among adult patients who received systemic treatment (pre- and post-index).

Variable	Adult AA patients with systemic treatment N=83
Pre-index period (before first prescription of an IS or OC)	
Number of concomitant treatments prescribed, per patient, mean (SD) Min-Max	1.5 (2.8), 0–15
Number of patients who received a prescription of a concomitant treatment, n (%)	30 (50.0)
Psychiatric treatments (anxiolytics, hypnotics and sedatives, antidepressants)	26 (43.3)
Other concomitant treatments (antifungals, antibiotics, anti-psoriatic, antiacne preparations)	13 (21.7)
Post-index period (after first prescription of an IS or OC)	
Number of concomitant treatments prescribed, per patient, mean (SD) Min-Max	4.4 (8.6) 0–45
Number of patients who received a prescription of a concomitant treatment, n (%)	46 (55.4)
Psychiatric treatments (anxiolytics, hypnotics and sedatives, antidepressants)	35 (42.2)
Other concomitant treatments (antifungals, antibiotics, anti-psoriatic, antiacne preparations)	25 (30.1)

AA: alopecia areata; IS: immunosuppressant; OC: oral corticosteroid; SD: standard deviation.

Table 8. Healthcare resource utilization for the first post-index year among adults with and without systemic treatment for AA.

Healthcare resource, mean number per patient (SD)	Patients without systemic treatment N=3,042	Patients with systemic treatment N=83
General practitioner visits	7.0 (6.2)	7.3 (6.5)
Specialist visits	0.4 (1.7)	0.8 (3.0)
Systemic treatment prescribed for AA	NA	1.7 (1.2)
Non-systemic treatments prescribed for AA	0.7 (0.9)	1.0 (1.3)
Concomitant treatments for comorbidities	1.0 (2.0)	1.4 (2.6)
Laboratory tests	6.8 (16.2)	6.7 (19.9)

SD: standard deviation.
Note: For patients without systemic treatment, the index date was defined as the date of first record of AA between 1st January 2014 and 31st December 2018. For patients with systemic treatment, the index date was defined as the date of the first prescription between 1st January 2014 and 31st December 2018.

respectively). Dexamethasone was used with the same frequency as prednisolone for combination regimens with non-systemic therapies (10.8%), reflecting that both corticosteroids may offer similar efficacies. In addition, cyclosporine appeared to be the preferred IS therapy as compared with methotrexate (6.0% *vs* 3.6%, respectively), although methotrexate use is reported. The less frequent use of methotrexate reported in this study could be due to its limited efficacy for severe AA patients, with response rates reported to be as low as 38–64% [39–42]. Given the established side effects associated with long-term OC therapy [43, 44], our findings highlight a need for alternative treatment options for AA patients not responding to or not adequately managed with non-systemic treatments.

Our results indicate that the subgroup of adults with AA who received systemic therapy had a numerically higher incidence of dermatological immune-mediated systemic inflammatory disease than those not treated with systemic therapy for AA (4.8% *vs* 3.2%, respectively), contact dermatitis and other eczema (15.7% *vs* 11.1%), cardiometabolic disease (14.5% *vs* 10.2%) and psychiatric disease (8.4% *vs* 7.1%). These observations are consistent with previous reports of higher rates of

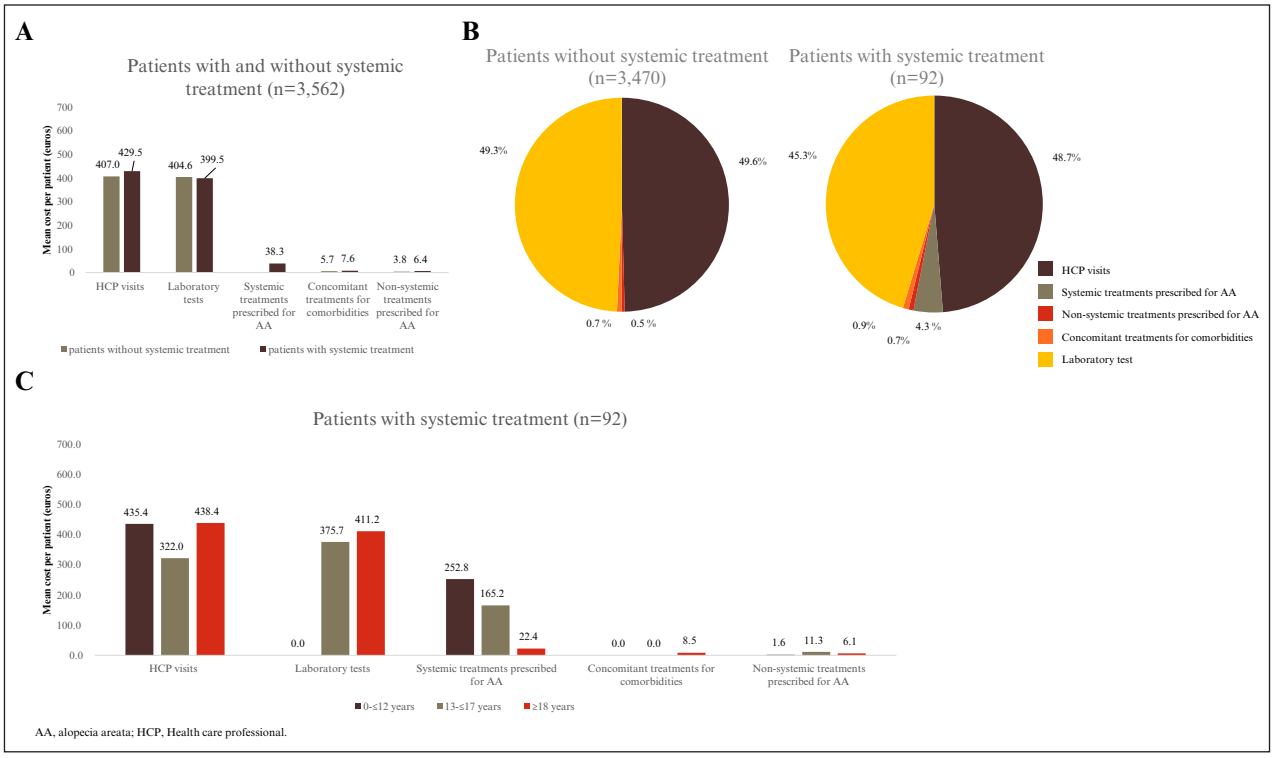


Figure 9. Mean cost of healthcare resource utilization for one year from index date in patients with and without systemic treatment **(A)** and their cost distribution **(B)**. Mean cost of healthcare resource utilization for one year from index date in patients with systemic treatment by age group **(C)**.

psychiatric conditions, including anxiety and depression, among people with AA, as compared with healthy control populations [45, 46]. In line with this, around half of this subgroup received prescriptions for medications for comorbid conditions both prior to the index date and during the post-index follow-up period after the first prescription of a systemic agent for AA. These observations suggest that the clinical picture for adults prescribed systemic therapy for AA is more complex than for those not prescribed systemic therapy.

In accordance with previous reports in other countries, our study has demonstrated the financial burden on healthcare systems caring for patients with AA [1, 7, 11–14]. The data analysed demonstrate that the average annual cost per patient in the first year after index date was €821.2 (SD: 1,065.6) for those who did not receive systemic treatment and €881.4 (SD 1,371.0) for those who received systemic treatment for their AA. These costs are double those reported in a previous study, which found that in the 12 months after an AA diagnosis, mean (SD) total AA-related healthcare costs were $419.12 [1]. However, there are no previous studies analysing costs in Spain with which our data can be compared. Annual costs associated with the treatment of other dermatological conditions include $4,411 for atopic dermatitis [47], $2,077 to $13,132 for psoriasis [48] and $900 to $2,400 for chronic urticaria [49].

The strengths of our study design include the use of a large, Spanish population-representative, outpatient cohort representing approximately 4% of the Spanish population, including almost 1.9 million patients with a longitudinal history of data since 2014. The THIN® database is fit for the purposes of this study since it provides anonymized patient data on demographics, clinical diagnoses, clinical measurements, laboratory test results and prescribed medicines, all of them recorded in clinical practice. On the other hand, the exclusion criteria of potentially confounding conditions (*i.e.*, alternative causes of hair loss) increases the accuracy of the study.

Limitations of our analysis include the use of retrospective data limited to that captured in the THIN® database from its inception in 2014 (the database captures patient encounters with the public health system). Therefore, it is expected that patients not active during the study period or exclusively treated in private clinics were not captured in this analysis. Furthermore, non-systemic treatments administered in the dermatologist's office, such as intralesional corticosteroid injections or contact immunotherapy, are not registered in the database, and were therefore not captured in our analysis. In addition, information regarding family history of AA, treatments not captured (such as phototherapy) and HCRU variables (such as telephone/remote consultations), emergency room visits and hospitalisations, were not available. Only data routinely documented in clinical practice were available. Consequently, other common variables used in clinical trials (*i.e.*, Severity of Alopecia Tool [SALT] score, % of total scalp hair loss, nail changes) were not available. The classification of diagnoses used in the clinical records from healthcare centres included in the THIN® database is the ICD9. Thus, the true incidence and prevalence of AA may be underestimated

as some cases will have been coded using other terms, including non-specific alopecia.

In summary, the prevalence and incidence of AA in Spain is comparable with that reported in the literature from other countries. Our data showed that AA is more prevalent among adults as compared with children and adolescents, with no difference between males and females. Patients with AA present a high comorbidity burden with limited use of systemic treatments for AA, mainly OC. Laboratory tests and visits to healthcare providers were the main drivers of healthcare-related costs.

These observations highlight a need for alternative systemic treatment options other than OC for those patients not responding to, or not adequately managed with, non-systemic treatments. The evolving landscape of AA treatments, including those emerging during and after the pandemic, presents a valuable area for further exploration. Future research is necessary to consider and incorporate data on these newer systemic treatments, providing a more comprehensive assessment of therapeutic choices for patients with AA. ■

Acknowledgements: *we thank Antonio Valente from Cegedim Health Data Spain and Maria Ruart from Adelphi Targis, SL for their contribution to the study design, data collection, analysis and interpretation of data as well as the preparation of this manuscript. We also thank Noelia Castellana for statistical analysis and Tracey Lonergan for supporting medical writing.*

Funding: *this work was supported by Eli Lilly Spain, 30 Avenida de la Industria, Alcobendas 28108, Madrid (Spain), including all publication fees.*

Conflicts of interests: *SV has received honoraria from Lilly to supervise study design, analysis, results and the manuscript. IF declares no conflicts of interest. EA, SDC, MN and TH are full-time employees and minor shareholders at Lilly, España. CI is Medical Director at Cegedim Health Data Spain. MA is a full-time employee at Adelphi Targis SL.*

References

1. Senna M, Ko J, Tosti A, *et al.* Alopecia areata treatment patterns, healthcare resource utilization, and comorbidities in the us population using insurance claims. *Adv Ther* 2021 ; 38 : 4646-58.

2. Alkhalifah A. Alopecia areata update. *Dermatol Clin* 2013 ; 31 : 93-108.

3. Vano-Galvan S, Saceda-Corralo D, Blume-Peytavi U, *et al.* Frequency of the types of alopecia at twenty-two specialist hair clinics: a multicenter study. *Ski Appendage Disord* 2019 ; 5 : 309-15.

4. Sterkens A, Lambert J, Bervoets A. Alopecia areata: a review on diagnosis, immunological etiopathogenesis and treatment options. *Clin Exp Med* 2021 ; 21 : 215-30.

5. Mirzoyev SA, Schrum AG, Davis MDP, Torgerson RR. Lifetime incidence risk of alopecia areata estimated at 2.1% by rochester epidemiology project, 1990-2009. *J Invest Dermatol* 2014 ; 134 : 1141-2.

6. Sobel MY, Zhou Xi, Napatalung L, E R Abstract 538 Incidence and prevalence of alopecia Areata in the US and UK. *Pharmacoepidemiol Drug Saf* 2019 ; 28 : 585-6.

7. Harries M, Macbeth AE, Holmes S, *et al.* The epidemiology of alopecia areata: a population-based cohort study in UK primary care. *Br J Dermatol* 2022 ; 186 : 257-65.

8. Li J, Sinclair R. Clinical observations in alopecia areata: implications and hypotheses. *Australas J Dermatol* 2016 ; 57 : e29-31.

9. Garcia Hernandez MJ, Camacho F. Epidemiología clínica de la alopecia areata. *Actas Dermosifiliogr* 2002 ; 93 : 223-8.

10. Sanchez-Diaz M, Diaz-Calvillo P, Soto-Moreno A, Molina-Leyva A, Arias-Santiago S. The impact of sleep quality on mood status and quality of life in patients with alopecia areata: a comparative study. *Int J Environ Res Public Health* 2022 ; 19 : 13126.

11. Vallerand IA, Lewinson RT, Parsons LMN, *et al.* Assessment of a bidirectional association between major depressive disorder and alopecia areata. *JAMA Dermatol* 2019 ; 155, 475-9.

12. Saceda-Corralo D, Grimalt R, Fernandez-Crehuet P, *et al.* Beard alopecia areata: a multicentre review of 55 patients. *J Eur Acad Dermatol Venereol* 2017 ; 31 : 187-92.

13. Titeca G, Goudetsidis L, Francq B, *et al.* 'The psychosocial burden of alopecia areata and androgenetica': a cross-sectional multicentre study among dermatological out-patients in 13 European countries. *J Eur Acad Dermatol Venereol* 34 2020 ; 406-11.

14. Goh C, Finkel M, Christos PJ, Sinha A. Profile of 513 patients with alopecia areata: associations of disease subtypes with atopy, autoimmune disease and positive family history. *J Eur Acad Dermatol Venereol* 2006 ; 20 : 1055-60.

15. Gilhar A, Paus R, Kalish R. Lymphocytes, neuropeptides, and genes involved in alopecia areata. *J Clin Investig* 2007 ; 117 : 2019-27.

16. Biran R, Zlotogorski A, Ramot Y. The genetics of alopecia areata: new approaches, new findings, new treatments. *J Dermatol Sci* 2015 ; 78 : 11-20.

17. Prie BE, Voiculescu VM, Ionescu-Bozdog OB, *et al.* Oxidative stress and alopecia areata. *J Med Life* 8 Spec Iss 2015 ; 43-6.

18. Manolache L, Benea V. Stress in patients with alopecia areata and vitiligo. *J Eur Acad Dermatol Venereol* 2007 ; 21 : 921-8.

19. You HR, Kim S. Factors associated with severity of alopecia areata. *Ann Dermatol* 2017 ; 29 : 565-70.

20. Rodrigo Sanchez MC, Pacheo L. Alopecia areata. *Med Fam Semergen* 2002 ; 28 : 212-5.

21. Seyrafi H, Akhiani M, Abbasi H, Mirpour S, Gholamreznanezhad A. Evaluation of the profile of alopecia areata and the prevalence of thyroid function test abnormalities and serum autoantibodies in Iranian patients. *BMC Dermatol* 2005 ; 5, 11.

22. Meah N, Wall D, York K, *et al.* The Alopecia Areata Consensus of Experts (ACE) study: results of an international expert opinion on treatments for alopecia areata. *J Am Acad Dermatol* 2020 ; 83, 123-30.

23. Vano-Galvan S, Fernandez-Crehut P, Grimalt R, *et al.* Alopecia areata totalis and universalis: a multicenter review of 132 patients in Spain. *J Eur Acad Dermatol Venereol* 2017 ; 31, 550-6.

24. Cranwell WC, Wy Lai V, Photiou L, *et al.* Treatment of alopecia areata: an Australian expert consensus statement. *Australas J Dermatol* 60 2019 ; 163-70.

25. Delamere FM, Sladden MJ, Dobbins HM, L.-B. J. Interventions for alopecia areata. *Cochrane Database Syst Rev* 2008 ; 16 : CD004413.

26. El-Zawahry BM, Bassiouny DA, Khella A, Zaki N. Five-year experience in the treatment of alopecia areata with DPC. *J Eur Acad Dermatol Venereol* 2010 ; 24, 264-9.

27. Lai VWY, Sinclair R. Utility of azathioprine, methotrexate and cyclosporine as steroid-sparing agents in chronic alopecia areata: a retrospective study of continuation rates in 138 patients. *J Eur Acad Dermatol Venereol* 2020 ; 34 : 2606-12.

28. Tosti A, Bellavista S, Iorizzo M. Alopecia areata: a long term follow-up study of 191 patients. *J Am Acad Dermatol* 2006 ; 55 : 438-41.

29. Vañó-Galván S., Fernández-Crehuet P, Grimalt R, *et al.* Alopecia areata totalis and universalis: a multicenter review of 132 patients in Spain. *J Eur Acad Dermatology Venereol* 2017 ; 31 : 550-6.

30. Network THI. Resources HUB.

31. Cegedim Health Data. Cegedim Health Data Website.

32. Linkedin profile. Cegedim Health Data.

33. Instituto Nacional de Estadística (INE). INEbase. Resultados encuesta europea de salud en España. 2020.

34. Beningo M, Anastassopoulos KP, Mostaghimi A, *et al.* A large cross-sectional survey study of the prevalence of Alopecia Areata in the United States. *Clin Cosmet Investig Dermatol* 2020 ; 13 : 259-66.

35. Richard MA, Corgibet F, Beylot-Barry M, *et al.* Sex- and age-adjusted prevalence estimates of five chronic inflammatory skin diseases in France: results of the « OBJECTIFS PEAU » study. *J Eur Acad Dermatol Venereol* 2018 ; 32 : 1967-71.

36. Aldhouse NVJ, Kitchen H, Knight S, *et al.* '"You lose your hair, what's the big deal?" I was so embarrassed, I was so self-conscious, I was so depressed:' a qualitative interview study to understand the psychosocial burden of alopecia areata. *J Patient Rep Outcomes* 2020 ; 4 : 76.

37. Messenger AG, McKillop J, Farrant P, McDonagh AJ, Sladden M. British Association of Dermatologists' guidelines for the management of alopecia areata 2012. *Br J Dermatol* 2012 ; 166 : 916-26.

38. Strazzulla LC, Chun Wang EH, Avila L, Lo Sicco K, Brinster N, Christiano AM, Shapiro J. Alopecia areata: an appraisal of new treatment approaches and overview of current therapies. *J Am Acad Dermatol* 2018 ; 78, 15-24.

39. Cranwell WC, Lai VW, Photiou L, *et al.* Treatment of alopecia areata: an Australian expert consensus statement. *Australas J Dermatol* 2019 ; 60 : 163-70.

40. Sterkens A, Lambert J, Bervoets A. Alopecia areata: a review on diagnosis, immunological etiopathogenesis and treatment options. *Clin Exp Med* 2021 ; 21, 215-30.

41. Alkhalifah A, Alopecia Areata Update. *Dermatol Clin* 2013 ; 31, 93-108.

42. Lintzeri DA, Constantinou A, Hillmann K, *et al.* Alopecia areata - Current understanding and management. *J Dtsch Dermatol Ges* 2022 ; 20 : 59-90.

43. Manson SC, Brown RE, Cerulli A, Fernandez Vidaurre C. The cumulative burden of oral corticosteroid side effects and the economic implications of steroid use. *Respir Med* 2009 ; 103 : 975-94.

44. Sarnes E, Crofford L, Watson M, Dennis G, Kan H, Bass D. Incidence and US costs of corticosteroid-associated adverse events: a systematic literature review. *Clin Ther* 2011 ; 33 : 1413-32.

45. van Dalen M, Muller KS, Kasperkovitz-Oosterloo JM, Okkerse JME, Pasmans S. Anxiety, depression, and quality of life in children and adults with alopecia areata: a systematic review and meta-analysis. *Front Med (Lausanne)* 2022 ; 9 : 1054898.

46. Okhovat JP, Marks DH, Manatis-Lornell, A, Hagigeorges D, Locascio JJ, Senna M. Association between alopecia areata, anxiety, and depression: a systematic review and meta-analysis. *J Am Acad Dermatol* 2023 ; 88 : 1040-50.

47. Fasseeh AN, Elzbawy B, Korra N, *et al.* Burden of Atopic dermatitis in adults and adolescents: a systematic literature review. *Dermatol Ther* 2022 ; 12 : 2653-68.

48. Burgos-Pol R, Martinez-Sesmero JM, Ventura-Cerda JM, Elias I, Caloto MT, Casado M. The cost of psoriasis and psoriatic arthritis in 5 European Countries: a systematic review. *Actas Dermosifiliogr* 2016 ; 107 : 577-90.

49. Goncalo M, Gimenez-Arnau A, Al-Ahmad M, *et al.* The global burden of chronic urticaria for the patient and society. *Br J Dermatol* 2021 ; 184 : 226-36.