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# Patient characteristics associated with all-cause healthcare costs of alopecia areata in the United States

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**Code availability:** Code used for the present analyses can be made upon reasonable request.

**Keywords:** alopecia areata; cost determinants; claims data; all-cause medical cost

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**Plain Language Summary**

Evidence on the factors of medical costs involved in the care of people with alopecia areata (AA) is limited, but mounting evidence points to significant variation in financial impact for patients with AA in the absence of effective treatments. This study explored drivers of medical costs among privately insured adults and adolescents with AA in the United States. The study found that patients of middle age (45-64 years), located in the Northeast region, with comprehensive health insurance, with greater extent of hair loss, or with other health disorders face greater all-cause medical costs. Adult females of young (18-44 years) and older (65+ years) age also faced greater costs on average. This research confirms high variability in the burden of AA, pointing to population subgroups that may be more affected by the disease and its commonly associated disorders.



**Abbreviations:**

AA (alopecia areata), AME, average marginal effect, AT (alopecia totalis), AU (alopecia universalis), CCI (Charlson Comorbidity Index), CI (confidence interval), CR (cost ratio), GLM (generalized linear model), ICD-10-CM (International Classification of Diseases, Tenth Revision, Clinical Modification), SD (standard deviation)

Alopecia areata (AA) is an autoimmune disease characterized by non-scarring hair loss on the scalp and potentially other areas of the body [1,2]. The disease affects approximately 1.14% of individuals in the United States, based on a recent population-based survey with clinician confirmation of diagnosis [3]. Estimates from the Global Burden of Disease study placed AA as the 10$^{th}$ most prevalent skin disease in the US in 2017, with an age-adjusted prevalence of 0.51% among females and 0.20% among males, and wide variation across states [4]. Its manifestations range from small patches of hair loss to complete loss of scalp hair (alopecia totalis [AT]), or complete loss of scalp, facial, and body hair (alopecia universalis [AU]) [5]. AA may be accompanied by various inflammatory, autoimmune, metabolic, cardiovascular, and psychiatric comorbidities [6-8], that may lead to additional disease burden.

Although previous studies have demonstrated that AA is associated with considerable economic burden [9], there is little evidence on the association of patient characteristics with costs. This prompted us to assess the potential drivers of healthcare costs, including patient characteristics, among patients with AA in the United States.

We conducted a retrospective, observational cohort study using the de-identified, nationally representative IBM/Truven MarketScan® Commercial Claims and Encounters and Medicare Supplemental databases (October 1, 2014 - March 31, 2019). We defined patients with AA as those with ≥2 claims with diagnosis codes for AA/AT/AU (International Classification of Diseases, Tenth Revision, Clinical Modification [ICD-10-CM]: L63.x). Institutional review board approval was not required to conduct this study.

Patients were required to be aged ≥12 years old on the index date and have continuous enrollment in a health insurance plan for ≥12 months before the index date (defined as the baseline period) and for ≥12 months after the index date (defined as the follow-up period). Patients in the AA

cohort were required to have ≥2 claims with a diagnosis of AA (International Classification of Diseases, Tenth Revision, Clinical Modification [ICD-10-CM]: L63.x) from October 1, 2015 to March 31, 2018. The AT (ICD-10-CM L63.0) and AU (ICD-10-CM L63.1) were grouped together as AT/AU. The index date was defined as the earliest AA diagnosis date for patients with AA. Patient characteristics were assessed during the baseline period.

Total payer health care costs were calculated as the amount reimbursed by the commercial plan and coordination of benefits (i.e., supplemental insurance and Medicare-paid amounts) during the follow-up period and inflated to 2018 US dollars using the medical care component of the Consumer Price Index.

Power coefficients, representing the relationship between the sample mean and variance, were assessed using a modified Park Test. For example, in the gamma distribution, the variance is the square of the mean. The Park test was conducted by first running a generalized linear model with the specified distribution to compute expected values and squared errors for each observation, conditional on covariates. The natural log of the expected values and errors were then calculated, and a second regression was used to fit the variance model. A power estimate of 0 (no relationship between mean and variance) would suggest that a Gaussian distribution is appropriate. Power estimates of 1, 2, and 3 would suggest the appropriateness of Poisson, Gamma, and inverse-Gaussian distributions, respectively. Based on the power coefficients estimated from each of these models (Supplemental Material), a Gamma distribution was selected as the most appropriate distribution to model healthcare costs.

A total of 16,207 patients with AA met the inclusion criteria for analysis. Descriptive statistics for variables used in the regression model in the sample of patients with AA are summarized in **Table 1**. The mean age of patients was 41.3 years, 64.5% were female and 8.5% had the AT/AU subtype. The most

common comorbidities were atopic (19.2%) and mental health disorders (18.3%), and 15.6% of patients had at least one of the comorbidities included in the Charlson Comorbidity Index (CCI) at baseline.

The mean all-cause payer costs in 2018 US dollars for the overall sample were $13,644 (standard deviation, SD $46,232). Predictors of costs were assessed using a generalized linear model (GLM) regression with a gamma distribution and a log link. Exponentiated coefficients (cost ratios [CR]) and incremental costs (expressed as average marginal effects), along with associated 95% confidence intervals (CIs) and p-values, are shown in **Table 2**. The reference group is composed of male patients aged 12-17 years without AT/AU, residing in the Northeast, enrolled in comprehensive health plans, with a CCI of 0 and no comorbidities. Compared to this group, only males aged 45-64 had 51.0% higher costs (CR 1.510, 95% CI [1.335, 1.707], $p < 0.001$), equivalent to $6,303 higher costs on average. Elderly females (aged >65 years) had the highest incremental cost, 113.1% higher on average compared to adolescent females (CR for female × age 65+: 2.131, 95% CI [1.406, 3.229], $p < 0.001$), followed by younger females with 52.9% higher costs (CR for female × age 18-44: 1.529, 95% CI [1.309, 1.785], $p < 0.001$).

AT/AU disease was associated with a slightly higher (15.8%) cost compared to non-AT/AU (CR 1.158, 95% CI [1.016, 1.319], $p = 0.028$), equivalent to an incremental cost of $2,183; the incremental cost of AT/AU did not differ significantly for females vs. males. There were also regional differences: the highest costs were observed in the Northeast, with costs in the other regions between 23.7% and 31.2% lower (all $p < 0.001$, range of incremental costs: -$4,263 to -$5,614).

Having at least one CCI comorbidity resulted in 104.4% higher costs than no CCI comorbidities (CR 2.044, 95% CI [1.927, 2.167], $p < 0.001$, incremental cost $12,113). Significantly higher costs were also associated with having any autoimmune, mental health, or cardiovascular disorder (all $p < 0.001$).

The findings of this study are consistent with existing literature showing high variability in healthcare costs among patients with AA [9]. In particular, this study found the highest costs among elderly women, followed by younger women and middle-aged men. Previous studies have shown comparable AA-related psychosocial impacts both sexes [10]. However, the current sample is composed of nearly two thirds women, perhaps reflecting the higher willingness of women to seek medical care [11]. The current study also found that AT/AU subtype is a modest driver of higher costs among both men and women. Finally, the highest cost was in the Northeast region, which may be related to a higher density of dermatologists [12].

The novel contribution of the current study consists of elucidating important associations between all-cause health care costs and patient demographic and clinical characteristics among adults and adolescents with AA in the US, using a multivariate regression analysis. While prior studies have described medical and pharmacy costs among adolescents and adults with AA [9,13-15] and the relationship between out-of-pocket costs and total financial burden [16], this study provides a clearer picture of the variation in costs across key subgroups of interest while also adjusting for other patient characteristics.

Limitations of this study include the retrospective nature of the analysis, the self-selected sample of patients seeking healthcare, and the identification of patients using the ICD-10-CM codes, which are intended primarily for billing purposes. Codes for AT/AU subtype may be less utilized in insurance claims databases [17], which may limit the ability to quantify differential costs in that population. The lack of information on patients' disease characteristics such as hair loss extent, treatment response, and psychosocial impacts may influence AA severity [18] , which precludes estimating a more granular association between AA and costs. Cost calculations also do not account for over-the-counter medications or off-label treatments used for AA and not captured in claims.

The Food and Drug Administration (FDA)'s recent approval of an oral medication for severe alopecia areata will impact the overall and distribution of costs among patients with AA. Confirmation of these findings in additional patient populations is needed, and additional analysis is critical for understanding trends over time. Overall, this study found that age, sex, and comorbidities are important drivers of cost differences in patients with AA, while AT/AU subtype is a modest driver. Additional research is needed to understand the impacts of more granular measures of disease severity on costs.

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**Tables and Figures**

**Table 1**. Baseline characteristics for patients with AA

| | AA patients<br>N = 16,207 |
|---|---|
| **Demographic and clinical characteristics** | |
| Age (years), mean ± SD | 41.3 ± 15.1 |
| Female | 10,446 (64.5%) |
| Region | |
| South | 6,383 (39.4%) |
| Northeast | 4,276 (26.4%) |
| Midwest | 2,837 (17.5%) |
| West | 2,711 (16.7%) |
| Insurance Plan Type | |
| Managed care[1] | 12,426 (76.7%) |
| Consumer-driven[2] | 3,277 (20.2%) |
| Comprehensive | 504 (3.1%) |
| Type of Alopecia Areata | |
| AT/AU | 1,380 (8.5%) |
| Non-AT/AU | 14,827 (91.5%) |
| **Comorbidities** | |
| Anemia | 525 (3.2%) |
| Any atopic disorder[3] | 3,106 (19.2%) |
| Any autoimmune disorder[4] | 2,194 (13.5%) |
| Any cardiovascular disorder[5] | 2,114 (13.0%) |
| Any mental health disorder[6] | 2,971 (18.3%) |
| Any other disorder[7] | 2,932 (18.1%) |
| Charlson Comorbidity Index, mean ± SD | 0.2 ± 0.6 |
| 0 | 13,674 (84.4%) |
| 1+ | 2,533 (15.6%) |

**Abbreviations:** AA: alopecia areata; AT: alopecia totalis; AU: alopecia universalis; CCI: Charlson Comorbidity Index; SD: standard deviation

**Notes:** Values are n (%) unless otherwise noted.
[1] Composite of health maintenance organization (HMO), preferred provider organization (PPO), point of service (POS), and exclusive provider organization (EPO) plans.
[2] Composite of consumer-driven health plans (CDHPs) and high-deductible health plans (HDHPs).
[3] Atopic comorbidities included: allergic rhinitis, asthma, atopic dermatitis, celiac disease, chronic urticaria, and conjunctivitis.
[4] Autoimmune comorbidities included: ankylosing spondylitis, Crohn's disease, diabetes mellitus, Hashimoto's disease, lupus erythematosus, psoriasis, rheumatoid arthritis, Sjogren's syndrome, ulcerative colitis, and vitiligo.
[5] Cardiovascular comorbidities included: atherosclerosis, chest pain, dyspnea, heart palpitations, and shortness of breath.
[6] Mental health comorbidities included: attention deficit hyperactivity disorder, anxiety disorders, depression, obsessive-compulsive disorder, and substance abuse.
[7] Other comorbidities included: hearing loss, thyroid disorder, and visual loss.

**Table 2.** Generalized regression model estimates for total payer costs by demographics, clinical characteristics, and comorbidities of AA patients

| | Cost ratio[1] | (95% CI) | p-value | Incremental cost,[2] 2018 USD (95% CI) |
|---|---|---|---|---|
| **Intercept (mean cost in reference group)[3]** | 7,767 | (6,582, 9,166) | <0.001 | - |
| **Demographics and clinical characteristics** | | | | |
| Female (vs male ref.) | 0.971 | (0.840, 1.121) | 0.685 | 3,268 (1,366, 5,169) |
| Age | | | | |
| 12-17 | (Ref.) | (Ref.) | (Ref.) | (Ref.) |
| 18-44 | 0.904 | (0.806, 1.014) | 0.085 | 2,337 (32, 4,642) |
| 45-64 | 1.510 | (1.335, 1.707) | <0.001 | 6,303 (3,823, 8,782) |
| 65+ | 1.284 | (0.868, 1.899) | 0.210 | 12,698 (5,537, 19,859) |
| AT/AU disease (vs non-AT/AU ref.) | 1.158 | (1.016, 1.319) | 0.028 | 2,183 (-1,061, 5,426) |
| Region | | | | |
| Northeast | (Ref.) | (Ref.) | (Ref.) | (Ref.) |
| Midwest | 0.763 | (0.717, 0.813) | <0.001 | -4,263 (-6,967, -1,558) |
| South | 0.688 | (0.654, 0.724) | <0.001 | -5,614 (-7,854, -3,374) |
| West | 0.761 | (0.715, 0.810) | <0.001 | -4,304 (-6,995, -1,613) |
| Insurance type | | | | |
| Comprehensive | (Ref.) | (Ref.) | (Ref.) | (Ref.) |
| Consumer-driven | 0.752 | (0.665, 0.852) | <0.001 | -3,698 (-8,778, 1,382) |
| Managed care | 1.010 | (0.898, 1.136) | 0.873 | 144 (-4,836, 5,125) |
| *Interaction terms* | | | | |
| Female × AT/AU disease | 0.995 | (0.851, 1.162) | 0.947 | - |
| Female × Age | | | | |
| Female × Age 12-17 | (Ref.) | (Ref.) | (Ref.) | - |
| Female × Age 18-44 | 1.529 | (1.309, 1.785) | <0.001 | - |
| Female × Age 45-64 | 1.130 | (0.962, 1.327) | 0.137 | - |
| Female × Age 65+ | 2.131 | (1.406, | <0.00 | - |

| | | | | |
|---|---|---|---|---|
| | | 3.229) | 1 | |
| **Comorbidities** | | | | |
| CCI 1+ (vs. CCI=0 ref.) | 2.044 | (1.927, 2.167) | <0.001 | 12,113 (8,474, 15,752) |
| Anemia | 1.245 | (1.112, 1.393) | <0.001 | 3,167 (-1,378, 7,713) |
| Atopic (any considered)[4] | 1.004 | (0.952, 1.058) | 0.883 | 57 (-2,107, 2,222) |
| Autoimmune (any considered)[5] | 1.826 | (1.722, 1.938) | <0.001 | 8,714 (6,010, 11,418) |
| Cardiovascular (any considered)[6] | 1.455 | (1.369, 1.546) | <0.001 | 5,422 (2,896, 7,948) |
| Mental health (any considered)[7] | 1.537 | (1.460, 1.619) | <0.001 | 6,223 (4,026, 8,420) |
| Other (any considered)[8] | 1.058 | (1.002, 1.117) | 0.041 | 817 (-1,381, 3,015) |

**Abbreviations:** AA: alopecia areata; AME: average marginal effect; AT: alopecia totalis; AU: alopecia universalis; CCI: Charlson Comorbidity Index; CI: confidence interval; Ref.: reference category; USD: United States dollar.

**Notes:**

[1] Coefficients, confidence intervals, and p-values were estimated using generalized linear models with a gamma distribution and log-link function. Model coefficients and confidence intervals were exponentiated.

[2] Incremental costs are expressed as average marginal effects. Marginal effects represent partial derivatives of the regression equation with respect to each variable for each unit (i.e., AA patient) in the data. Average marginal effects (AMEs) are the mean of these marginal effects over the sample.

[3] The reference group is composed of male patients aged 12-17 years without AT/AU disease, residing in the Northeast region, covered by comprehensive health plans, with a CCI of 0 and none of the considered comorbidities.

[4] Atopic comorbidities included: allergic rhinitis, asthma, atopic dermatitis, celiac disease, chronic urticaria, and conjunctivitis.

[5] Autoimmune comorbidities included: ankylosing spondylitis, Crohn's disease, diabetes mellitus, Hashimoto's disease, lupus erythematosus, psoriasis, rheumatoid arthritis, Sjogren's syndrome, ulcerative colitis, and vitiligo.

[6] Cardiovascular comorbidities included: atherosclerosis, chest pain, dyspnea, heart palpitations, and shortness of breath.

[7] Mental health comorbidities included: attention deficit hyperactivity disorder, anxiety disorders, depression, obsessive-compulsive disorder, and substance abuse.

[8] Other comorbidities included: hearing loss, thyroid disorder, and visual loss.