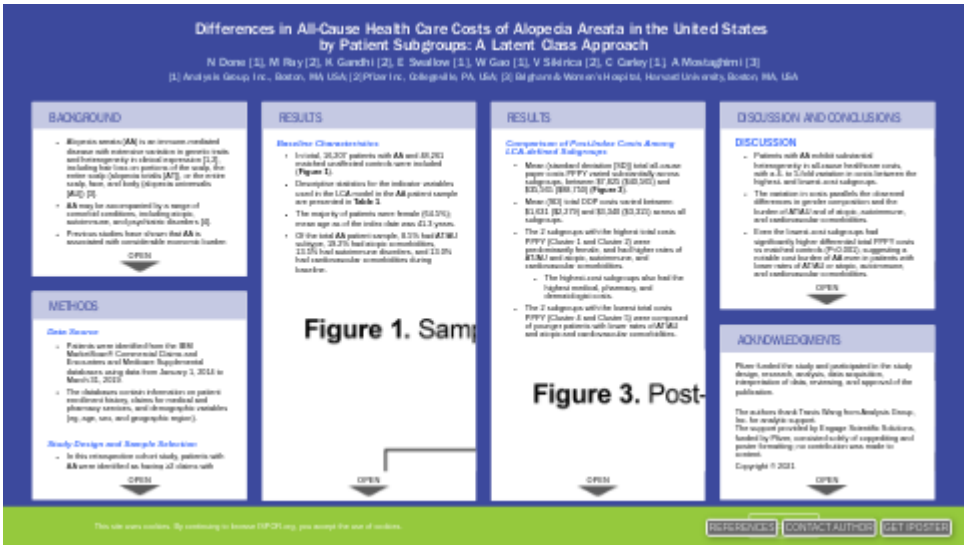
Differences in All-Cause Health Care Costs of Alopecia Areata in the United States by Patient Subgroups: A Latent Class Approach



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BACKGROUND

- Alopecia areata (AA) is an immune-mediated disease with extensive variation in genetic traits and heterogeneity in clinical expression [1,2], including hair loss on portions of the scalp, the entire scalp (alopecia totalis [AT]), or the entire scalp, face, and body (alopecia universalis [AU]) [3].

- AA may be accompanied by a range of comorbid conditions, including atopic, autoimmune, and psychiatric disorders [4].

- Previous studies have shown that AA is associated with considerable economic burden [5,6], but the heterogeneity in healthcare costs across the patient population is not well understood.

STUDY OBJECTIVES

- To identify subgroups of patients with AA in the US with distinct profiles and to characterize their corresponding healthcare costs.

- To evaluate the differences in healthcare costs between AA patients in each subgroup vs matched controls.

METHODS

Data Source

- Patients were identified from the IBM MarketScan® Commercial Claims and Encounters and Medicare Supplemental databases using data from January 1, 2014 to March 31, 2019.
- The databases contain information on patient enrollment history, claims for medical and pharmacy services, and demographic variables (eg, age, sex, and geographic region).

Study Design and Sample Selection

- In this retrospective cohort study, patients with AA were identified as having ≥2 claims with diagnosis codes for AA (International Classification of Diseases, Tenth Revision, Clinical Modification [ICD-10-CM]: L63.x).
- The **index date** was defined as the earliest AA diagnosis date for AA patients, and as the date of a randomly assigned medical claim for control patients.
- The **baseline period** was defined as the 12 months before the index date; the **follow-up period** was defined as the 12 months following the index date.
- Patients in the control cohort were required to have no diagnoses for AA at any point during the data period.
- Patients in both the AA and control cohorts were:
  - Aged ≥12 years old on the index date.
  - Had continuous enrollment in a health insurance plan for ≥12 months before and after the index date.
- Control patients without AA were matched to all AA patients on age, sex, index year, region, health plan type, and Charlson Comorbidity Index (CCI) score.

Subgroup Identification

- Latent class analysis (LCA) was used to segment the heterogeneous AA patient population into distinct unobserved patient clusters (ie, latent classes) based on multivariate patterns among observed demographic and clinical characteristics [7].
- Matched controls (3:1 to cases) previously assigned to AA patients were maintained in order to allow for an exposure-control comparison for each LCA-identified cluster.
- The following variables were included in the LCA model:
  - Demographics: age group (12–17, 18–44, 45–64, 65+ years), sex.
  - AA type: AT/AU vs other.
  - AT/AU patients were identified by ≥1 diagnosis of AT (ICD-10-CM: L63.0) or AU (ICD-10-CM: L63.1) on index date or at any point thereafter [8].

- Comorbidities:
  - Anemia.
  - Atopic disorders.
  - Autoimmune disorders.
  - Cardiovascular disorders.
  - Mental health disorders.
  - Other disorders (hearing loss, visual loss, or thyroid disorders).
  - CCI group (0 vs. 1+).

Statistical Analysis

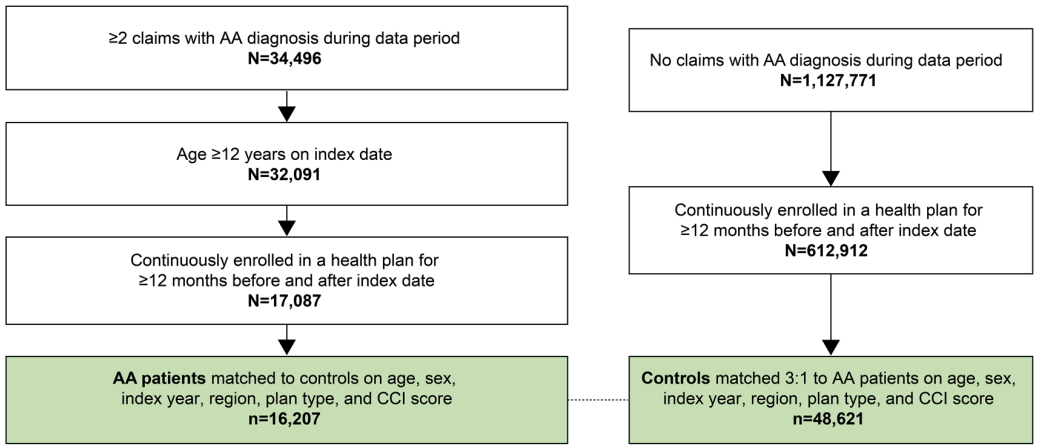
- The LCA model was estimated for a varying number of latent classes from 2 to 10. The Bayesian Information Criterion (BIC) was calculated for each number of classes.
- The optimal number of LCA-defined subgroups was selected based on the model with the lowest BIC (ie, best fit). Significant differences in model fit were tested using the Bayes Factor test.
- Baseline characteristics were described for the overall patient population and for each of the LCA-defined subgroups and their matched controls.
- Post-index per-patient-per-year (PPPY) healthcare costs and differences in costs vs matched controls were summarized for each of the LCA-defined subgroups, including: total health payer costs, comprised of costs for medical services and pharmacy, dermatologist costs (a subset of medical costs), and enrollee out-of-pocket (OOP) costs.

RESULTS

Baseline Characteristics

- In total, 16,207 patients with AA and 48,261 matched unaffected controls were included (**Figure 1**).
- Descriptive statistics for the indicator variables used in the LCA model in the AA patient sample are presented in **Table 1**.
- The majority of patients were female (64.5%); mean age as of the index date was 41.3 years.
- Of the total AA patient sample, 8.5% had AT/AU subtype, 19.2% had atopic comorbidities, 13.5% had autoimmune disorders, and 13.0% had cardiovascular comorbidities during baseline.

Figure 1. Sample selection



AA=alopecia areata; CCI=Charlson Comorbidity Index

Table 1: Baseline patient characteristics

	AA Patients N=16,207	Controls N=48,621	*P*-value
Demographic and clinical characteristics			
Age, mean ± SD, years	41.3 ± 15.1	41.3 ± 15.1	1.00
Female	10,446 (64.5%)	31,338 (64.5%)	1.00
Region			1.00
South	6,383 (39.4%)	19,149 (39.4%)	
Northeast	4,276 (26.4%)	12,828 (26.4%)	
Midwest	2,837 (17.5%)	8,511 (17.5%)	
West	2,711 (16.7%)	8,133 (16.7%)	
Insurance plan type			1.00
Managed care[a]	12,426 (76.7%)	37,278 (76.7%)	
Consumer-driven[b]	3,277 (20.2%)	9,831 (20.2%)	
Comprehensive	504 (3.1%)	1,512 (3.1%)	
Type of AA			-
AT/AU	1,380 (8.5%)	-	
Non-AT/AU	14,827 (91.5%)	-	
Comorbidities			
Anemia	525 (3.2%)	1,055 (2.2%)	< 0.001
Any atopic disorder[c]	3,106 (19.2%)	7,349 (15.1%)	< 0.001
Any autoimmune disorder[d]	2,194 (13.5%)	5,603 (11.5%)	< 0.001
Any cardiovascular disorder	2,114 (13.0%)	6,242 (12.8%)	0.507
Any mental health disorder	2,971 (18.3%)	9,467 (19.5%)	< 0.001
Any other disorder	2,932 (18.1%)	6,959 (14.3%)	< 0.001
CCI, mean ± SD	0.2 ± 0.6	0.2 ± 0.6	1.00
0	13,674 (84.4%)	41,022 (84.4%)	1.00
1+	2,533 (15.6%)	7,599 (15.6%)	1.00

Notes: Shaded rows and *P*-values equal to 1.00 indicate variables used to match AA patients to unaffected controls. Values are n (%) unless otherwise noted.
[a] Composite of health maintenance organization (HMO), preferred provider organization (PPO), point of service (POS), and exclusive provider organization (EPO) plans.
[b] Composite of consumer-driven health plans (CDHPs) and high-deductible health plans (HDHPs).
[c] Composite of allergic rhinitis, asthma, atopic dermatitis, celiac disease, chronic urticaria, and conjunctivitis.
[d] Composite of ankylosing spondylitis, Crohn's disease, diabetes mellitus, Hashimoto's disease, psoriasis, rheumatoid arthritis, Sjögren's syndrome, systematic lupus erythematosus, ulcerative colitis, and vitiligo.
AA=alopecia areata; AT=alopecia totalis; AU=alopecia universalis; CCI=Charlson Comorbidity Index; SD=standard deviation

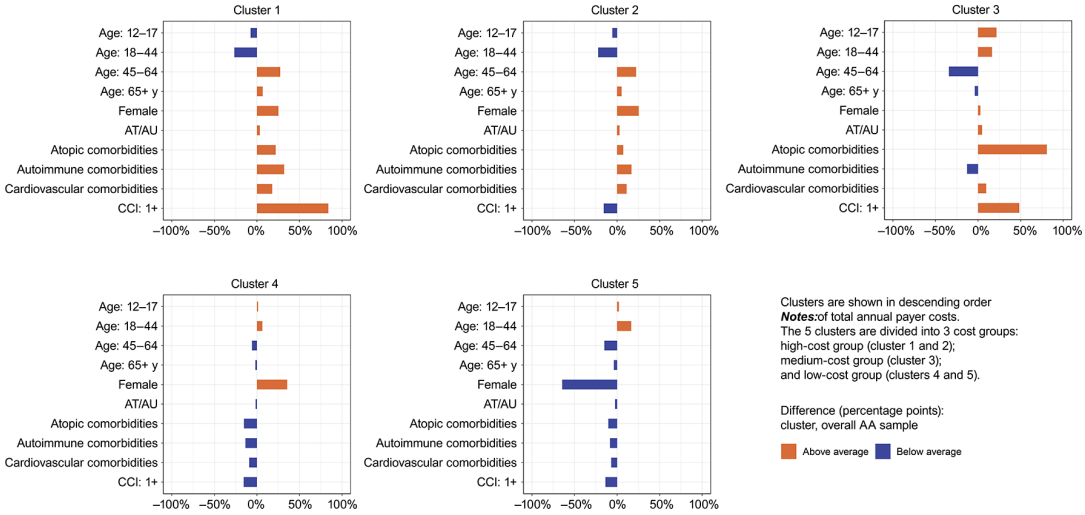
Comparison of Baseline Characteristics Among AA Patient Subgroups

- The LCA model identified 5 distinct subgroup characteristics, ranked by post-index total annual payer costs as follows (**Figure 2**).
  - **High-cost clusters**
    - **Cluster 1** (n=1,956)
      - Predominantly female (89.7%).
      - Mostly middle-aged (68.1% aged 45–64 years).
      - High rates of AT/AU (11.9%).
      - Very high rates of atopic (41.2%), autoimmune (45.6%), cardiovascular (31.0%), and CCI comorbidities (99.5%).
    - **Cluster 2** (n=3,409)
      - Predominantly female (89.9%).
      - Mostly middle-aged (63.2% aged 45–64 years).
      - High rates of AT/AU (11.4%).
      - High rates of atopic (26.3%), autoimmune (30.4%), and cardiovascular comorbidities.
      - No CCI comorbidities (0.0%).
  - **Medium-cost cluster**
    - **Cluster 3** (n=760)
      - Predominantly female (67.2%).
      - Largely younger adults (64.1% aged 18–44 years) and adolescents (29.3% aged 12–17 years).
      - Highest rate of AT/AU (13.3%) and atopic comorbidities (100.0%) of all clusters.
      - Low rate of autoimmune comorbidities (0.7%).
      - High rates of cardiovascular (22.6%) and CCI comorbidities (64.1%).
  - **Low-cost clusters**
    - **Cluster 4** (n=5,115)
      - Exclusively female (100%).

- Similar in age structure to the overall AA population.
- Low rates of AT/AU (7.0%).
- Very low rates of atopic (4.0%), autoimmune (0.0%), and cardiovascular (4.0%) comorbidities.
- Very low rates of CCI comorbidities (0.1%).

- **Cluster 5** (n=4,967)
  - Exclusively male (100.0%).
  - Predominantly younger (64.4% aged 18–44 years) and middle-aged (25.9% aged 45–64 years).
  - Lower rates of AT/AU (6.1%), atopic (8.8%), autoimmune (5.2%), and cardiovascular (6.2%) comorbidities.
  - Very low rates of CCI comorbidities (2.0%).

Figure 2. Baseline characteristics of AA patient subgroups relative to the overall sample



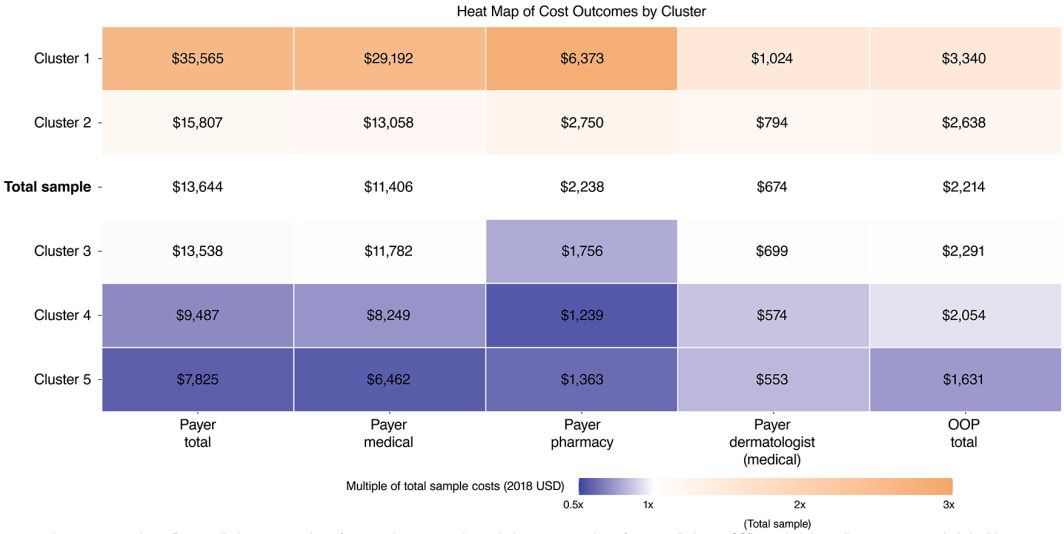
AA=alopecia areata; AT=alopecia totalis; AU=alopecia universalis; CCI=Charlson Comorbidity Index

RESULTS

Comparison of Post-Index Costs Among LCA-defined Subgroups

- Mean (standard deviation [SD]) total all-cause payer costs PPPY varied substantially across subgroups, between $7,825 ($40,565) and $35,565 ($88,750) (**Figure 3**).
- Mean (SD) total OOP costs varied between $1,631 ($2,279) and $3,340 ($3,315) across all subgroups.
- The 2 subgroups with the highest total costs PPPY (Cluster 1 and Cluster 2) were predominantly female, and had higher rates of AT/AU and atopic, autoimmune, and cardiovascular comorbidities.
  - The highest-cost subgroups also had the highest medical, pharmacy, and dermatologist costs.
- The 2 subgroups with the lowest total costs PPPY (Cluster 4 and Cluster 5) were composed of younger patients with lower rates of AT/AU and atopic and cardiovascular comorbidities.

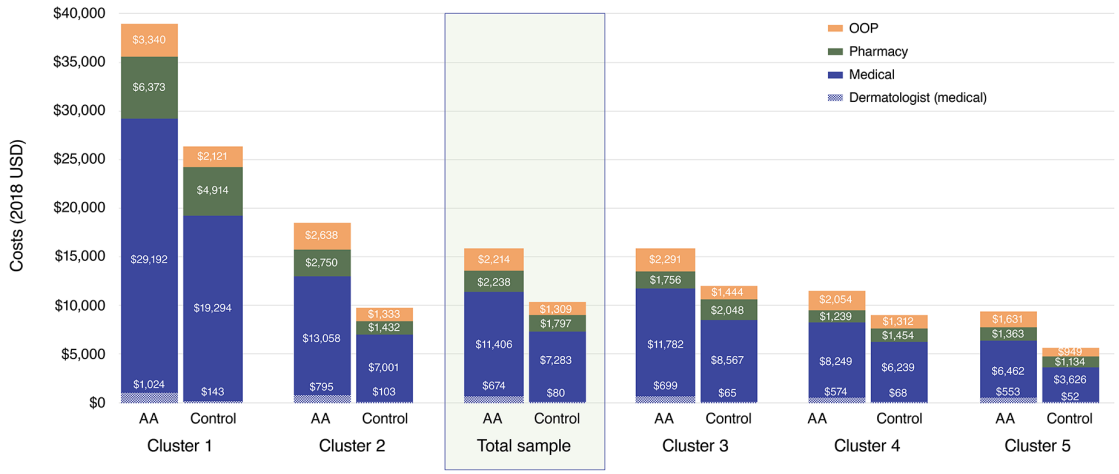
Figure 3. Post-index all-cause healthcare costs for the LCA-defined AA patient subgroups (2018 USD)



Mean costs per-patient-per-year are shown. Payer medical costs are a subset of payer total costs; payer dermatologist costs are a subset of payer medical costs; OOP costs include enrollee payments towards deductible, copays, and coinsurance.
Cell colors are based on costs of each cluster as multiples in reference to the costs in the total sample.
AA=alopecia areata; LCA=latent class analysis; OOP=out-of-pocket

Comparison of Post-Index Costs vs Matched Controls Among LCA-defined Subgroups (Figure 4)

Figure 4. All-cause healthcare costs for the LCA-defined patient subgroups and for the total sample compared with respective matched controls (2018 USD)



Note: Mean per-patient-per-year costs of AA patients vs respective matched controls are shown. Payer medical and payer pharmacy costs are subsets of payer total costs; payer dermatologist costs are a subset of payer medical costs; OOP costs include enrollee payments towards deductible, copays, and coinsurance.
AA=alopecia areata; LCA=latent class analysis; OOP=out-of-pocket

- Mean (SD) differential total payer costs vs matched controls ranged from $11,356 ($2,193) in Cluster 1 to $1,794 ($493) in Cluster 4.

- The 2 highest-cost subgroups (Cluster 1 and Cluster 2) also had the highest differential total medical, pharmacy, and OOP costs vs matched controls.
  - Cluster 1 costs vs controls:
    - Mean total medical ($29,192 vs $19,294) and pharmacy costs ($6,373 vs $4,914), (all P<0.001).
    - Mean enrollee OOP costs ($3,340 vs $2,121), ($P$<0.001).
  - Cluster 2 costs vs controls:
    - Mean total medical ($13,058 vs $7,001) and pharmacy costs ($2,750 vs $1,432), (all P<0.001).
    - Mean total enrollee OOP costs ($2,638 vs $1,333), ($P$<0.001).

- Cluster 4 had the smallest differential total medical costs vs matched controls:
  - Mean total medical costs ($9,487 vs $7,693), ($P$<0.001).

- Cluster 5 had the lowest difference in enrollee OOP costs:
  - Mean enrollee OOP costs ($1,631 vs $949), ($P$<0.001).

DISCUSSION AND CONCLUSIONS

DISCUSSION

- Patients with AA exhibit substantial heterogeneity in all-cause healthcare costs, with a 4- to 5-fold variation in costs between the highest- and lowest-cost subgroups.
- The variation in costs parallels the observed differences in gender composition and the burden of AT/AU and of atopic, autoimmune, and cardiovascular comorbidities.
- Even the lowest-cost subgroups had significantly higher differential total PPPY costs vs matched controls ($P<0.001$), suggesting a notable cost burden of AA even in patients with lower rates of AT/AU or atopic, autoimmune, and cardiovascular comorbidities.

Limitations

- The limitations of this study include those inherent to retrospective cohort studies utilizing administrative claims data, such as:
  - Coding inaccuracies in the claims data may have led to misidentification of AA/AT/AU patients or inaccurate calculation of costs.
  - Although this study used matched comparisons between AA patients and controls to adjust for several key characteristics, the results may be confounded by unmeasured covariates.
  - The generalizability of the study findings beyond patients with commercial or Medicare supplemental insurance coverage may be limited.
  - OOP costs in this study are those borne by the patients according to their insurance billing data and do not represent overall OOP costs patients may incur for any AA treatment not covered.
- The patient allocation to subgroups using the LCA method may change if other patient characteristics were added to the clustering model.

CONCLUSIONS

- This study identified distinct AA patient subgroups with substantial differences in healthcare costs.
- Notably, high-cost subgroups were predominantly female, had higher rates of AT/AU, and had a much higher comorbidity burden compared with the overall patient population.
- Future studies should further investigate the association of heterogeneity in patient characteristics with healthcare costs.

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