# Clinical and economic burden of patients with and without light chain (AL) amyloidosis: A matched case-control analysis of insurance claims

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## BACKGROUND & OBJECTIVE

- Amyloid light chain (AL) amyloidosis is among the most severe forms of systemic amyloidosis.[1,2]
  - Prognosis depends on the level of organ involvement, particularly cardiac involvement.
- Healthcare resource utilization (HCRU) and costs are expected to be higher in persons with AL amyloidosis than those without; however, real-world estimates of HCRU and costs are limited.[3]
  - Many older studies used the International Classification of Diseases, Ninth Edition, Clinical Modification (ICD-9-CM) diagnosis codes 277.30 or 277.39 to identify patients, and these codes are not specific to AL amyloidosis subtype.[4–8]
  - ICD-10-CM code E85.81, specific to AL amyloidosis, was introduced in 2017 enabling claims-based research specific to this patient population.
- Objective: To compare real-world HCRU, including hospitalizations and emergency department (ED) visits, and costs between persons with and without AL amyloidosis.

## METHODS

### Study design and data source

- Retrospective case-control analysis using 2018-2020 data from the Merative® MarketScan® Commercial and Medicare Supplemental and the IQVIA Pharmetrics Plus® databases.

### Patient population

- Adult persons with ≥1 inpatient or ≥2 outpatient claims for AL amyloidosis (ICD-10-CM code E85.81) in any diagnosis field during the calendar year of the study period (1/1/2018-12/31/2020) in the US (existing or newly diagnosed).
- Continuous enrollment in a health plan in each calendar year was required.
- AL amyloidosis-free persons (non-AL matched controls) were drawn from a 5% random sample from the respective database and exactly matched 2:1 to persons with AL amyloidosis on: age, sex, US geographic region, and type of insurance.
  - Non-AL matched controls met the same age and continuous enrollment criteria as persons with AL amyloidosis.
- Cases/controls were identified separately from each database, then combined for the final study cohorts.
  - To avoid possible duplicates, one person was randomly excluded among persons with the same gender, region, year of birth, and dates of AL amyloidosis claims.

### Study measures

- Demographic and clinical characteristics, all-cause HCRU, and costs for the calendar year.

### Statistical analysis

- Means, standard deviations (SD), and relative frequencies and percentages were reported for continuous and categorical data, respectively.
- Cost estimates were adjusted to 2020 USD using the Consumer Price Index to adjust for inflation.
- Data transformations and statistical analyses were performed using SAS® version 9.4 (SAS Institute, Cary, NC).

## RESULTS

### Demographic and clinical characteristics **(Table 1)**

- We identified 574 persons with AL amyloidosis and 1,148 non-AL matched controls (2018), 588 persons with AL amyloidosis and 1,176 non-AL matched controls (2019), and 667 persons with AL amyloidosis and 1,334 non-AL matched controls (2020).
- Persons with AL amyloidosis had a higher comorbidity burden than non-AL matched controls (P<0.001 for all years) – Mean (SD) Charlson Comorbidity Index score: 4.2 (2.8) vs. 1.0 (1.8); 4.0 (2.7) vs. 1.0 (1.9); 4.1 (2.8) vs. 1.0 (1.7).

**Table 1.** Demographic and clinical characteristics of persons with AL amyloidosis and non-AL matched controls

| | 2018 | | 2019 | | 2020 | |
|---|---|---|---|---|---|---|
| | Persons with AL Amyloidosis N = 574 | Non-AL Matched Controls[a] N = 1,148 | Persons with AL Amyloidosis N = 588 | Non-AL Matched Controls[a] N = 1,176 | Persons with AL Amyloidosis N = 667 | Non-AL Matched Controls[a] N = 1,334 |
| **Age, mean (SD) [median]** | 61.5 (10.2) [61] | 61.5 (10.2) [61] | 60.8 (9.9) [60] | 60.8 (9.9) [60] | 62.5 (10.2) [62] | 62.5 (10.2) [62] |
| 18-34, n (%) | 6 (1.0) | 12 (1.0) | 5 (0.9) | 10 (0.9) | 4 (0.6) | 8 (0.6) |
| 35-54 | 117 (20.4) | 234 (20.4) | 130 (22.1) | 260 (22.1) | 135 (20.2) | 270 (20.2) |
| 55-64 | 280 (48.8) | 560 (48.8) | 309 (52.6) | 618 (52.6) | 311 (46.6) | 622 (46.6) |
| 65+ | 171 (29.8) | 342 (29.8) | 144 (24.5) | 288 (24.5) | 217 (32.5) | 434 (32.5) |
| **Female, n (%)** | 259 (45.1) | 518 (45.1) | 251 (42.7) | 502 (42.7) | 299 (44.8) | 598 (44.8) |
| **Region, n (%)** | | | | | | |
| Midwest | 153 (26.7) | 306 (26.7) | 189 (32.1) | 378 (32.1) | 231 (34.6) | 462 (34.6) |
| Northeast | 159 (27.7) | 318 (27.7) | 122 (20.7) | 244 (20.7) | 121 (18.1) | 242 (18.1) |
| South | 182 (31.7) | 364 (31.7) | 204 (34.7) | 408 (34.7) | 227 (34.0) | 454 (34.0) |
| West | 80 (13.9) | 160 (13.9) | 73 (12.4) | 146 (12.4) | 88 (13.2) | 176 (13.2) |
| **Insurance type, n (%)** | | | | | | |
| Commercial | 346 (60.3) | 692 (60.3) | 384 (65.3) | 768 (65.3) | 380 (57.0) | 760 (57.0) |
| Medicare | 140 (24.4) | 280 (24.4) | 110 (18.7) | 220 (18.7) | 175 (26.2) | 350 (26.2) |
| Other | 88 (15.3) | 176 (15.3) | 94 (16.0) | 188 (16.0) | 112 (16.8) | 224 (16.8) |
| **CCI, mean (SD) [median][b]** | 4.2 (2.8) [4] | 1.0 (1.8) [0] | 4.0 (2.7) [4] | 1.0 (1.9) [0] | 4.1 (2.8) [4] | 1.0 (1.7) [0] |
| CHF, n (%)[b] | 287 (50.0) | 53 (4.6) | 287 (48.8) | 44 (3.7) | 360 (54.0) | 60 (4.5) |
| Renal disease[b] | 263 (45.8) | 56 (4.9) | 250 (42.5) | 67 (5.7) | 315 (47.2) | 75 (5.6) |
| Multiple myeloma[b] | 333 (58.0) | 2 (0.2) | 336 (57.1) | 1 (0.1) | 374 (56.1) | 2 (0.1) |

CCI: Charlson Comorbidity Index; CHF: congestive heart failure.
[a] Matched by database, age, sex, U.S. geographic region, and type of insurance. [b] P<0.001 for every year.

### Healthcare utilization and costs

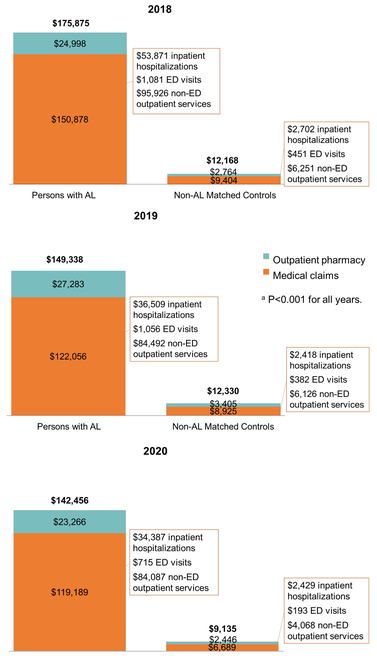
- Compared to non-AL matched controls, persons with AL amyloidosis had:
  - More frequent hospitalizations and ED visits (P<0.001 for all years):
    - 37.6% of persons with AL amyloidosis had hospitalizations (mean [SD] number of hospitalizations: 0.80 [1.42]) and 36.1% had ED visits vs. 6.5% of non-AL matched controls had hospitalizations (mean [SD] number of hospitalizations: 0.09 [0.42]) and 17.1% had ED visits (2018); 39.1% (0.83 [1.50]) and 36.7% vs. 6.0% (0.11 [0.58]) and 15.1% (2019); 39.0% (0.73 [1.30]) and 33.0% vs. 7.3% (0.11 [0.49]) and 14.3% (2020) **(Table 2)**.
  - Significantly greater total healthcare costs (P<0.001 for all years):
    - $175,875 vs. $12,168 (2018, adjusted to 2020 USD); $149,338 vs. $12,330 (2019, adjusted to 2020 USD); $142,456 vs. $9,135 (2020) **(Figure 1)**.

**Table 2.** Healthcare utilization[a] among persons with AL amyloidosis and non-AL matched controls

| | 2018 | | 2019 | | 2020 | |
|---|---|---|---|---|---|---|
| | Persons with AL Amyloidosis N = 574 | Non-AL Matched Controls[b] N = 1,148 | Persons with AL Amyloidosis N = 588 | Non-AL Matched Controls[b] N = 1,176 | Persons with AL Amyloidosis N = 667 | Non-AL Matched Controls[b] N = 1,334 |
| **Any inpatient hospitalizations, n (%)** | 216 (37.6) | 75 (6.5) | 230 (39.1) | 71 (6.0) | 260 (39.0) | 98 (7.3) |
| **No. of inpatient hospitalizations, mean (SD)** | 0.80 (1.42) | 0.09 (0.42) | 0.83 (1.50) | 0.11 (0.58) | 0.73 (1.30) | 0.11 (0.49) |
| Days of stay among utilizers,[c] mean (SD) [median] | 18.0 (30.1) [9] | 5.3 (6.7) [3] | 17.3 (26.1) [9] | 11.7 (24.4) [5] | 15.6 (18.2) [8] | 12.9 (41.5) [4] |
| **Any cardiac-related inpatient hospitalizations, n (%)** | 53 (9.2) | 7 (0.6) | 57 (9.7) | 10 (0.9) | 60 (9.0) | 12 (0.9) |
| **No. of cardiac-related inpatient hospitalizations, mean (SD)** | 0.12 (0.42) | 0.02 (0.14) | 0.14 (0.54) | 0.05 (0.34) | 0.14 (0.55) | 0.03 (0.17) |
| **Any ED visits, n (%)** | 207 (36.1) | 196 (17.1) | 216 (36.7) | 178 (15.1) | 220 (33.0) | 191 (14.3) |
| **No. of non-ED outpatient services, mean (SD) [median]** | 50.9 (43.9) [41] | 13.0 (16.1) [8] | 49.1 (43.2) [39] | 11.9 (14.7) [7] | 48.3 (39.1) [39] | 11.9 (15.3) [7] |
| No. of physician office visits, mean (SD) [median] | 22.3 (19.3) [17] | 9.3 (11.1) [6] | 20.9 (16.7) [16] | 8.1 (10.0) [5] | 19.4 (16.8) [15] | 7.4 (9.1) [4] |

[a] P<0.001 for each variable and every year unless noted. [b] Matched by database, age, sex, U.S. geographic region, and type of insurance.
[c] P=0.108 for 2019; P=0.529 for 2020.

**Figure 1.** Healthcare costs[a] among persons with AL amyloidosis and non-AL matched controls




## LIMITATIONS

- Limitations include possible miscoding, a common limitation of claims data research, leading some persons to possibly have been misidentified; however, our methodology for identifying individuals with AL amyloidosis is consistent with previously published work using claims data.[4,5,8-10]
- This study presents the measures of individuals with varied disease severity; however, we are unable to identify where they are in their AL amyloidosis journey.
- Some persons with AL amyloidosis were included in multiple years, however, each person with AL amyloidosis had a unique matched control in each calendar year. Outcomes (HCRU and costs) were limited to one calendar year even if the patient appeared in multiple years.
- Results may not be generalizable to other populations not covered by commercial and Medicare supplemental insurance.

## CONCLUSIONS

- Persons with AL amyloidosis had significantly greater HCRU and costs than matched controls without AL amyloidosis.
- Increased disease awareness, earlier diagnosis, and better treatment options could impact disease prognosis and decrease HCRU/costs.

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**AUTHOR DISCLOSURES**

This analysis was supported by Prothena Biosciences Ltd (Dublin, Ireland), a member of the Prothena Corporation plc group. A Conrad and I Sprinz are employees of Prothena Biosciences Inc and hold stock in Prothena Corporation plc. TP Quock is a former employee of Prothena Biosciences Inc. A D'Souza is an employee of the Medical College of Wisconsin, was paid by Prothena to consult as a subject matter expert. E Chang, AK Das, MS Broder and MH Tarbox are employees of PHAR, LLC, which received funding from Prothena to conduct the research described.

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