Economic Burden and Treatment Patterns Among Individuals With Hereditary Angioedema: a U.S. Closed Claims Analysis

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Key takeaways

This real-world, retrospective cohort study provides evidence of the substantial economic burden and healthcare resource utilization associated with hereditary angioedema (HAE) in the United States.

- Despite the use of available HAE therapies, substantial acute-care utilization, high treatment-related costs, and use of multiple or additional therapies persisted in this study population, highlighting an ongoing need for effective, convenient treatment options that can improve disease control and reduce treatment burden.

HAE-related acute care burden	HAE-related costs[a]	Gaps in treatment landscape
During follow-up[b] of ~2.4 years, 20-25% of pwHAE had ≥1 HAE-related inpatient stay or ER visit, despite being on HAE treatment	Median HAE-related medical and pharmacy costs PPPY[c] increased from baseline[d] to follow-up, accounting for ~96% of total healthcare spending	~40% of pwHAE on a single treatment strategy (ODT or LTP) added the other treatment option during follow-up

ER, emergency room; LTP, long-term prophylaxis; ODT, on-demand treatment; PPPY, per patient per year; pwHAE, people with HAE. [a]Costs were inflation-adjusted to 2025 (or most recent year) United States Dollars using the Consumer Price Index. [b]Follow-up period: variable, minimum 12 months post-index (days 0 to 365+). [c]Costs were reported as PPPY to account for variable follow-up. [d]Baseline period: fixed at 12 months pre-index (days −365 to −1).

Background

- **Hereditary angioedema (HAE):** a bradykinin-mediated condition characterized by recurrent, unpredictable, and potentially life-threatening angioedema attacks.[1,2]
- **Treatment strategies:** current management of HAE relies on two complementary therapeutic strategies: on-demand treatment (ODT) to resolve acute attacks and long-term prophylaxis (LTP) for prevention of attacks.[1]
  - Although treatment options for HAE have expanded in recent years, substantial limitations, including breakthrough attacks, treatment access, and adherence challenges, remain and potentially impact overall healthcare costs.[2-5]
- **Research gap:** in the United States, there are limited data on HAE-related healthcare costs.[6]

Objective

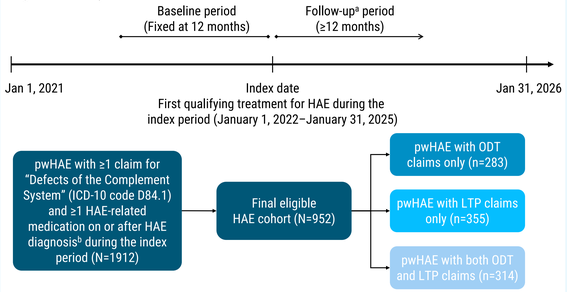
To examine healthcare resource utilization (HCRU), medical/pharmacy costs, and HAE treatment patterns among individuals with HAE receiving LTP and/or ODT in U.S. healthcare settings.

Methods

- **NorstellaLinQ database:** Using the NorstellaLinQ closed claims database, this retrospective cohort study analyzed de-identified administrative claims from January 1, 2021 through January 31, 2026 (**Figure 1**).
- **Eligibility:** U.S. individuals ≥12 years of age with claims-identified HAE with:
  - ≥12 continuous months of medical/pharmacy data (during both the baseline period [fixed at 12 months pre-index] and the follow-up period [post-index with ≥12 months continuous enrollment]).
  - ≥1 claim for "Defects in the Complement System" (*International Classification of Diseases, 10th Revision [ICD-10]* code D84.1) and ≥1 claim for HAE-related medication on or after HAE diagnosis during the index period.
  - People with HAE (pwHAE) with evidence of drug-induced angioedema (adverse effect of angiotensin-converting-enzyme inhibitors) were excluded.
- **Study cohorts:** pwHAE were stratified into the following cohorts at index:
  - pwHAE with ODT claims only; pwHAE with LTP claims only; pwHAE with both ODT and LTP claims.
- **Outcomes:** All-cause (regardless of diagnosis) and HAE-related HCRU, total all-cause and HAE-related costs, and HAE-related treatment patterns were assessed.
  - HCRU and cost outcomes included non–pharmacy-related (inpatient stays, emergency room [ER], office, urgent care, and other outpatient visits) and pharmacy-related (pharmacy fills) outcomes.
- **Statistical analysis:** All analyses were conducted using Panalgo's Instant Health Data platform and were descriptive.

Methods

Figure 1. Study timeline and treatment cohorts



HAE, hereditary angioedema; ICD-10, *International Classification of Diseases, 10th Revision*; LTP, long-term prophylaxis; ODT, on-demand treatment; pwHAE, people with HAE. [a]pwHAE were censored at the earliest of either lost to follow-up (end of continuous enrollment), death, or end of study period. [b]HAE was identified using a claims-based algorithm and was not clinically confirmed.

Results

- The overall median (interquartile range [IQR]) total follow-up time was 2.4 (1.7–3.5) years (**Table 1**).
- During the baseline period, 60.1% of pwHAE in the overall cohort had a Charlson Comorbidity Index score of 0, indicating a relatively healthy population outside of their HAE diagnosis (HAE identified using a claims-based algorithm and not clinically confirmed).
  - Angioedema, the most prevalent HAE-specific comorbidity, was highest in the ODT-only cohort (48.1%) compared with the LTP-only cohort (38.6%), which may be consistent with higher acute attack frequency in pwHAE with ODT claims only.

Table 1. Baseline demographics and clinical characteristics

Characteristics	Total cohort (N=952)	ODT only (n=283)	LTP only (n=355)	ODT and LTP (n=314)
Age at index, median (IQR), years	40.0 (27.0–53.0)	38.0 (25.5–53.0)	41.0 (27.0–52.0)	42.0 (28.0–54.0)
Sex, female, n (%)	688 (72.3)	208 (73.5)	238 (67.0)	242 (77.1)
Race or ethnicity, n (%)				
White	626 (65.8)	191 (67.5)	223 (62.8)	212 (67.5)
Hispanic or Latino	152 (16.0)	40 (14.1)	72 (20.3)	40 (12.7)
Black or African American	82 (8.6)	25 (8.8)	28 (7.9)	29 (9.2)
Asian	24 (2.5)	7 (2.5)	11 (3.1)	6 (1.9)
Other or unknown	68 (7.1)	20 (7.1)	21 (5.9)	27 (8.6)
Charlson Comorbidity Index, median (IQR)	0 (0-1)	0 (0-1)	0 (0-1)	0 (0-1)
Insurance type at index, n (%)				
Commercial	556 (58.4)	170 (60.1)	214 (60.3)	172 (54.8)
Managed Medicaid	342 (35.9)	102 (36.0)	117 (33.0)	123 (39.2)
Medicare Advantage	54 (5.7)	11 (3.9)	24 (6.8)	19 (6.1)
Total follow-up time, median (IQR), years	2.4 (1.7–3.5)	2.2 (1.5–3.2)	2.4 (1.6–3.4)	2.8 (1.8–3.8)
HAE attacks during baseline, median (IQR)	2 (1–5)	2 (1–6)	1 (0–3)	4 (2–8)

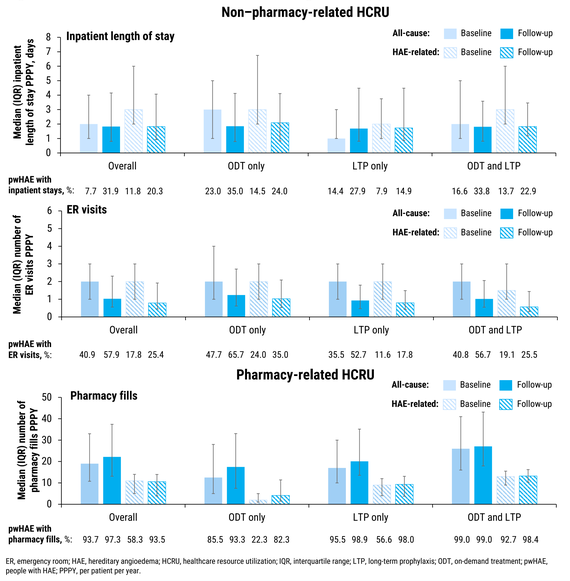
HAE, hereditary angioedema; IQR, interquartile range; LTP, long-term prophylaxis; ODT, on-demand treatment.

Results

HCRU

- HAE-related HCRU followed a similar trend to all-cause HCRU (**Figure 2**). For non–pharmacy-related HCRU (inpatient length of stay and ER visits), all-cause HCRU was mostly driven by HAE-related HCRU.
- The proportion of pwHAE in the overall cohort with ≥1 HAE-related inpatient stay increased from 11.8% during baseline to 20.3% during follow-up, and the proportion of pwHAE with ≥1 HAE-related ER visit increased from 17.8% to 25.4%, which may reflect residual disease burden despite the availability of different treatment options.
  - The ODT-only cohort had the highest all-cause ER utilization during follow-up (65.7%) versus the LTP-only (52.7%) and ODT+LTP cohorts (56.7%), which may indicate that pwHAE managed with ODT alone experience more unplanned acute care visits in the absence of prophylactic therapy.
- Despite an increasing proportion of pwHAE experiencing HAE-related inpatient stays and ER visits in the overall cohort during follow-up, more available treatment options may improve disease management, resulting in shorter HAE-related inpatient length of stay and fewer ER visits:
  - The median (IQR) HAE-related inpatient length of stay per patient per year (PPPY) decreased to 1.8 (0.9–4.1) days from 3.0 (2.0–6.0) days during baseline, and the median (IQR) HAE-related number of ER visits PPPY decreased to 0.8 (0.5–1.9) from 2.0 (1.0–3.0).
  - The median (IQR) HAE-related number of pharmacy fills PPPY was 10.6 (3.9–14.0) during follow-up versus 11.0 (5.0–14.0) during baseline.

Figure 2. All-cause and HAE-related HCRU during the study period



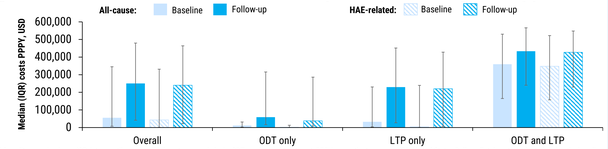
ER, emergency room; HAE, hereditary angioedema; HCRU, healthcare resource utilization; IQR, interquartile range; LTP, long-term prophylaxis; ODT, on-demand treatment; pwHAE, people with HAE; PPPY, per patient per year.

Results

Total costs

- HAE-related total medical and pharmacy costs in the overall cohort increased from median (IQR) $43,271 ($711–$331,330) during baseline to $240,064 ($22,233–$464,075) during follow-up (**Figure 3**).
  - A similar trend was observed when costs were analyzed by treatment cohort.
- Overall HAE-related costs closely approximated all-cause costs during follow-up, suggesting that HAE management accounted for a majority (~96%) of total healthcare costs (medical and pharmacy) in this population (**Figure 3**).

Figure 3. All-cause and HAE-related total medical and pharmacy costs during the study period

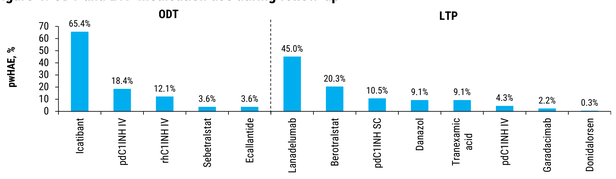


HAE, hereditary angioedema; IQR, interquartile range; LTP, long-term prophylaxis; ODT, on-demand treatment; PPPY, per patient per year; USD, United States Dollars. Total costs evaluated during the baseline and follow-up periods were inflation adjusted to 2025 (or most recent year) USD using the Consumer Price Index. Median (IQR) costs were reported as PPPY to account for variable follow-up time.

Treatment-related costs and treatment patterns

- During follow-up, the median (IQR) cost PPPY for all HAE-related medications in the overall cohort was $238,162 ($20,020–$462,247) versus $12,823 ($3878–$43,538) for ODT and $267,572 ($105,524–$447,552) for LTP.
- Overall, 730/952 (76.7%) pwHAE and 781/952 (82.0%) pwHAE, respectively, had any ODT and any LTP use during follow-up.
  - During follow-up, 39.9% of pwHAE with ODT claims only at index added LTP and 41.1% of pwHAE with LTP claims only at index added ODT.
  - Treatment switching was infrequent: 1.1% of pwHAE switched from ODT to LTP, and 0.3% switched from LTP to ODT.
  - Icatibant was the most used ODT (65.4%) and lanadelumab was the most used LTP option (45.0%) (**Figure 4**).

Figure 4. ODT and LTP medication use during follow-up



C1INH, C1 inhibitor; HAE, hereditary angioedema; IV, intravenous; LTP, long-term prophylaxis; ODT, on-demand treatment; pdC1INH, plasma-derived C1INH; pwHAE, people with HAE; rhC1INH, recombinant human C1INH; SC, subcutaneous.

Study limitations

- Limitations included: lack of an ICD-10 code specific to HAE; HAE subtype not identifiable through claims coding; cohorts reflecting medication claims at index and not representing all treatments prescribed or available to pwHAE; investigational therapies without a National Drug Code not captured; reported costs based on the Medicare Fee-for-Service fee schedule; costs not adjusted for refill non-adherence (yielding lower-than-expected median cost values); and residual confounding owing to the observational nature of the observational nature of the study.

References

1. Maurer M, et al. *Allergy.* 2022;77:1961-90. **2.** Bork K, et al. *Allergy Asthma Clin Immunol.* 2021;17:40. **3.** McDougall CF, et al. *J Allergy Clin Immunol Global.* 2026;5:1-6. **4.** Nicola S, et al. *Drugs Context.* 2019;8:212605. **5.** Lumry W, et al. *Orphanet J Rare Dis.* 2026;21:247. **6.** Guan X, et al. *Orphanet J Rare Dis.* 2024;19:256.

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Acknowledgments: Medical writing support was provided by MJ Hovenden, PhD, and Vanessa Ducas, PhD, of Envision Medical Communications, and funded by Pharvaris.