Disease Burden of Hereditary Transthyretin Amyloidosis (hATTR): Analysis of Real-World Data

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Background

- hATTR is a genetic, progressive, and fatal form of amyloidosis caused by extracellular deposition of transthyretin amyloid fibrils.[1]
- Diagnosis of hATTR remains a challenge, and there are no FDA approved therapies for the treatment of hATTR.[2]
- Liver transplantation is sometimes used with or without accompanying heart transplant, but this treatment is limited to few patients.[2]
- Current literature on the economic burden of amyloidosis is limited, and there is no current estimate of the cost of hATTR.[3]

Objective

To estimate hATTR-related healthcare utilization and costs.

Methods

- Retrospective study using Truven Health Analytics MarketScan® Commercial and Medicare Supplemental databases and the IQVIA Real-World Data Adjudicated Claims - US databases from 1/1/2012-12/31/2016.
- Patient identification
  - Patients ≥18 years at index (defined below) who were newly diagnosed with hATTR.
  - Diagnosis of hATTR defined as: ≥1 medical claim with a relevant diagnosis code for amyloidosis (ICD-9-CM 277.30-31, 277.39; ICD-10-CM E85.0-4, E85.82-.89, E85.9) between 7/1/2012-9/30/2016 (ID period) PLUS ≥1 additional qualifier occurring at any time during the study period (2012-2016):
    - ≥15 days diflunisal use without >30-day gap; liver transplant; or claim with ICD-10-CM codes E85.1 or E85.2.
  - Date of first claim with diagnosis code for amyloidosis was defined as the index date.
  - Patients had continuous enrollment in the 6 months prior to index diagnosis (baseline period) and during ≥3 months post-index.
  - Patients having a diagnosis code for amyloidosis during baseline were excluded to ensure new diagnosis.
- Observation period
  - Newly diagnosed patients were followed ≥3 months post-index to enrollment or study end, whichever came first.
- Study measures
  - First-year healthcare utilization and costs reported by quarter among patients still enrolled:
    - Hospitalization, outpatient services (e.g., ED and physician office visits), therapeutic procedures and devices, and pharmacy utilization.
    - Total, inpatient, outpatient medical (ED and non-ED services), organ transplant-related, and outpatient pharmacy costs.
  - Baseline characteristics (e.g., age, gender, comorbidities) and year of diagnosis.
- Statistical analysis
  - Descriptive statistics, including means, standard deviations (SD), and relative frequencies and percentages for continuous and categorical data, respectively, were reported.
  - All data transformations and statistical analyses were performed using SAS© version 9.4.

Results

Baseline Characteristics

- We identified 432 patients newly diagnosed with hATTR (52% from MarketScan®, 48% from IQVIA) **(Table 1; Table 2)**.

Table 1. Patient Identification

Criteria		Database: MarketScan	Database: IQVIA
A.	Any claim for amyloidosis (ICD-9CM 277.30-.31, 277.39; ICD10-CM E85.0-4, E85.82-.89, E85.9) between 7/1/2012-9/30/2016 (date of first such claim set as index date)	12,822	12,572
B.	Of A. did not have amyloidosis claim any time prior to index date	11,449	11,620
C.	Of B. who qualified for hATTR (had ICD-10-CM E85.1 or E85.2, ≥15 days of use of diflunisal, OR had liver transplant)[a]	299 E85.1 or E85.2: 225 Liver transplant: 46 Diflunisal use: 53	333 E85.1 or E85.2: 268 Liver transplant: 53 Diflunisal use: 40
D.	Of C. who had ≥6 months continuous enrollment prior to index	253	242
E.	Of D. who were ≥18 years old at index	249	234
F.	Of E. who were continuously enrolled for a ≥90 days after index	231	211
G.	Of. F, 10 patients were possible duplicates and removed (selected 5 from each database randomly)	226	206
H.	Combine G	N = 432	

[a] Among those identified, we identified hATTR patients based on criteria C.

Table 2. Patient Characteristics

N	432
Age, mean (SD)	57.5 (14.1)
Sex (Female), n (%)	227 (52.5)
Year of diagnosis, n (%)	
2012	24 (5.6)
2013	33 (7.6)
2014	41 (9.5)
2015	129 (29.9)
2016	205 (47.5)
Charlson comorbidity index[a], mean (SD)	1.9 (2.5)

[a] Charlson comorbidity index was calculated during the 6 months prior to the hATTR diagnosis (baseline period).

  - Mean (SD) age was 57.5 (14.1), 52.5% were female, and mean (SD) baseline Charlson comorbidity index was 1.9 (2.5).
  - The most common year of diagnosis was 2016 (47.5%) vs 5.6% in 2012.
  - By one year after index, enrollment dropped to 179 patients.
- Selected baseline comorbidities are reported in **Figure 1.** Conditions observed in ≥10% of patients are as follows:
  - Cardiovascular-related: dyspnea (27.3%), edema (17.1%), congestive heart failure (15.7%), ventricular hypertrophy (11.6%), and restrictive cardiomyopathy (10.0%).
  - Gastrointestinal-related: 11.1% diarrhea; 10.4% constipation.
  - Metabolic: diabetes (24.5%).
  - Nervous system-related: 15.0% neuropathy.
  - <10% experienced musculoskeletal and ocular-related comorbidities.

Healthcare Utilization

- Proportion of patients hospitalized in each quarter after index was 19.4%, 12.3%, 11.8%, and 12.3% **(Figure 2)**.
  - Mean (SD) length of stay was 10.6 (13.7), 16.1 (24.0), 13.5 (18.8) and 16.1 (17.1) days.
- Occurrence of ED visits was 19.9%, 14.9%, 10.7%, and 12.8% **(Figure 2)**, while mean (SD) number of physician office visits was 3.9 (3.8), 2.9 (3.4), 2.9 (3.5), and 3.2 (3.6) (results not displayed).
- Proportions of therapeutic procedures and devices received in each quarter after index are displayed in **Figure 3.**
  - Liver transplant, dialysis, walker/wheelchair, and defibrillator/pacemaker decreased from 1st to 4th quarter (6.9%-0.6%, 5.1-2.2%%, 4.4%-1.1%, 3.2%-0.6%, respectively).

Figure 1. Baseline Comorbidities

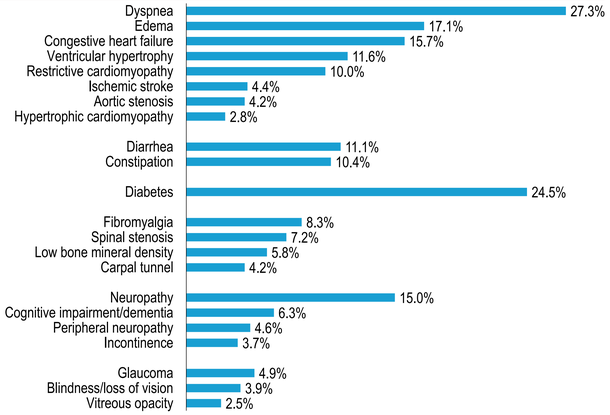


Figure 2. Healthcare Utilization in the First-Year after hATTR Diagnosis

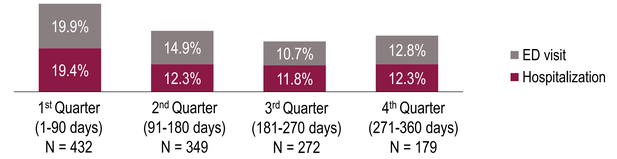
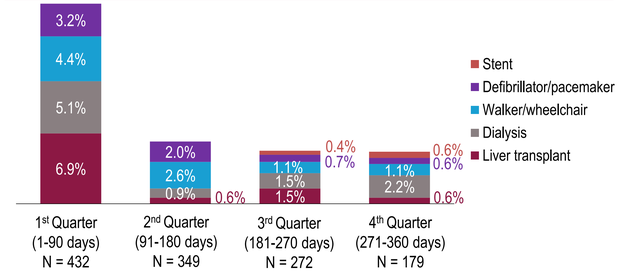
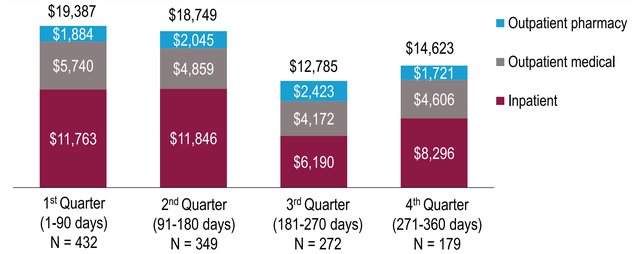


Figure 3. Therapeutic Procedures and Devices in the First-Year after hATTR Diagnosis



- Mean (SD) number of prescription fills in each period was: 10.6 (9.6), 10.3 (10.5), 9.8 (9.6), and 9.6 (9.8) (results not shown).

Figure 4. Healthcare Costs in the First-Year after hATTR Diagnosis



Costs **(Figure 4)**

- Mean total costs in each quarter ranged from $19,387 to $14,623.
- Mean medical costs varied by quarter and were highest in the first 2 months, while pharmacy costs were highest in the third quarter ($2,423).
- Mean costs related to solid organ transplant ranged from $1,487 (third quarter) to $4,750 (fourth quarter) (results not displayed).

Conclusion

- Patients with hATTR use significant healthcare resources and costs over time, even in the first year after diagnosis.
- This study adds to the limited understanding about the burden faced by patients with hATTR. However, further research over a longer time period with a larger sample is warranted to assess whether costs increase with disease progression, including near the end of life, similar to other fatal diseases.
- Limitations
  - Quarterly outcomes could not be compared directly due to changing samples based on enrollment; however, we found that the quarterly samples had similar demographics and comorbidities and believe utilization and costs in each quarter would likely be representative of the full sample of 432 patients.
  - Claims are meant for reimbursement, not research, so misclassification of patients with hATTR is possible.
  - This study examines only direct healthcare costs and does not include indirect costs such as decreased quality of life or productivity, which add to the picture of burden.

References

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2. Gertz M. Am J Manag Care. 2017;23:S107-S112.
3. Lin HM, Gao X, Cooke CE, et al. CMRO. 2017;33(6):1017-1031.

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