Factors associated with increased healthcare resource utilisation in individuals with transthyretin amyloid cardiomyopathy: results from a Japanese electronic health record database

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Aim

To identify patient characteristics associated with high healthcare resource utilisation among individuals with ATTR-CM in Japan

Introduction

- Transthyretin amyloid cardiomyopathy (**ATTR-CM**) is a progressive and under-recognised cause of heart failure, particularly in older adults[1,2].
- Diagnosis can be challenging because ATTR-CM presents with symptoms and comorbidities that overlap with more common cardiovascular conditions. Consequently, patients may undergo repeated clinical assessments, investigations and hospitalisations before ATTR-CM is identified[3].
- Following diagnosis, patients may require further diagnostic investigations, initiation or optimisation of ATTR-CM and cardiovascular treatments, and ongoing monitoring for disease progression and complications.
- Previous research has shown a considerable healthcare resource utilisation (HCRU) burden among people with ATTR-CM.[4] However, HCRU varies between individuals, and the patient characteristics associated with particularly high utilisation are not well understood, particularly in Japan.
  - Identifying factors associated with high HCRU in patients with ATTR-CM may help to identify patients with complex healthcare needs and support targeted monitoring, care planning and management.

Methods

Study design and data source

- This was a retrospective, open-cohort study using the June 2025 release of the Medical Data Vision (MDV) database in Japan[5,6].
- MDV is a large hospital-based database, derived from institutions operating under Japan's Diagnosis Procedure Combination payment system, and contains linked inpatient and outpatient claims and electronic health record data.
- Available data included diagnoses, procedures, prescriptions, selected laboratory records and healthcare utilisation information.
- The analysis included records collected between 1 January 2008 and 31 March 2025.

Study population and follow-up

- Adults aged ≥18 years were eligible if they had:
  - an amyloidosis diagnosis code or a tafamidis prescription; and
  - a recorded diagnosis of heart failure, cardiomyopathy or cardiac arrhythmia.
- Individuals were excluded if they had:
  - missing age or sex information
  - <6 months of observable data before index
  - had a diagnosis of amyloid light-chain amyloidosis or multiple myeloma before index
- The **index date** was defined as the date at which patients first fulfilled both ATTR-CM identification criteria, irrespective of the order in which the criteria occurred.
- Index dates were required to occur before **1 July 2024**, to ensure sufficient follow-up time was available.
- Patients were followed until the earliest of data collection end, death, exit from the MDV database, or diagnosis of light-chain amyloidosis or multiple myeloma.

Outcomes

- HCRU was evaluated across the following care settings:
  - inpatient admissions;
  - outpatient visits;
  - laboratory or diagnostic imaging visits;
  - emergency department visits; and
  - home-care service visits.
- **Total HCRU** was calculated as the sum of these healthcare events.

Analytical approach

- HCRU was assessed across eight predefined periods spanning the three years before and after the index date:
  - 2–3 years pre-index → 1–2 years pre-index → 7–12 months pre-index → 0–6 months pre-index → 0–6 months post-index → 7–12 months post-index → 1–2 years post-index → 2–3 years post-index
- HCRU and prescription outcomes were summarised as mean events **per person per year (PPPY)**.
- Descriptive analyses examined HCRU by demographic and clinical characteristics recorded at index to identify high-burden subgroups.
- Multivariable negative binomial regression was used to estimate independent associations between patient characteristics and total non-prescription HCRU.
  - Candidate covariates included age, sex, year of diagnosis, comorbidities, selected biomarker categories, New York Heart Association (NYHA) functional class, selected procedures and pharmacological treatments recorded at index.
  - Results are presented as incidence rate ratios (IRRs) with 95% confidence intervals (CIs).
  - Regression analyses were restricted to individuals with non-zero HCRU and complete data for continuous covariates.
- Baseline demographic and clinical characteristics were described using counts and percentages, or means with standard deviations and medians with IQRs, as appropriate.

Results

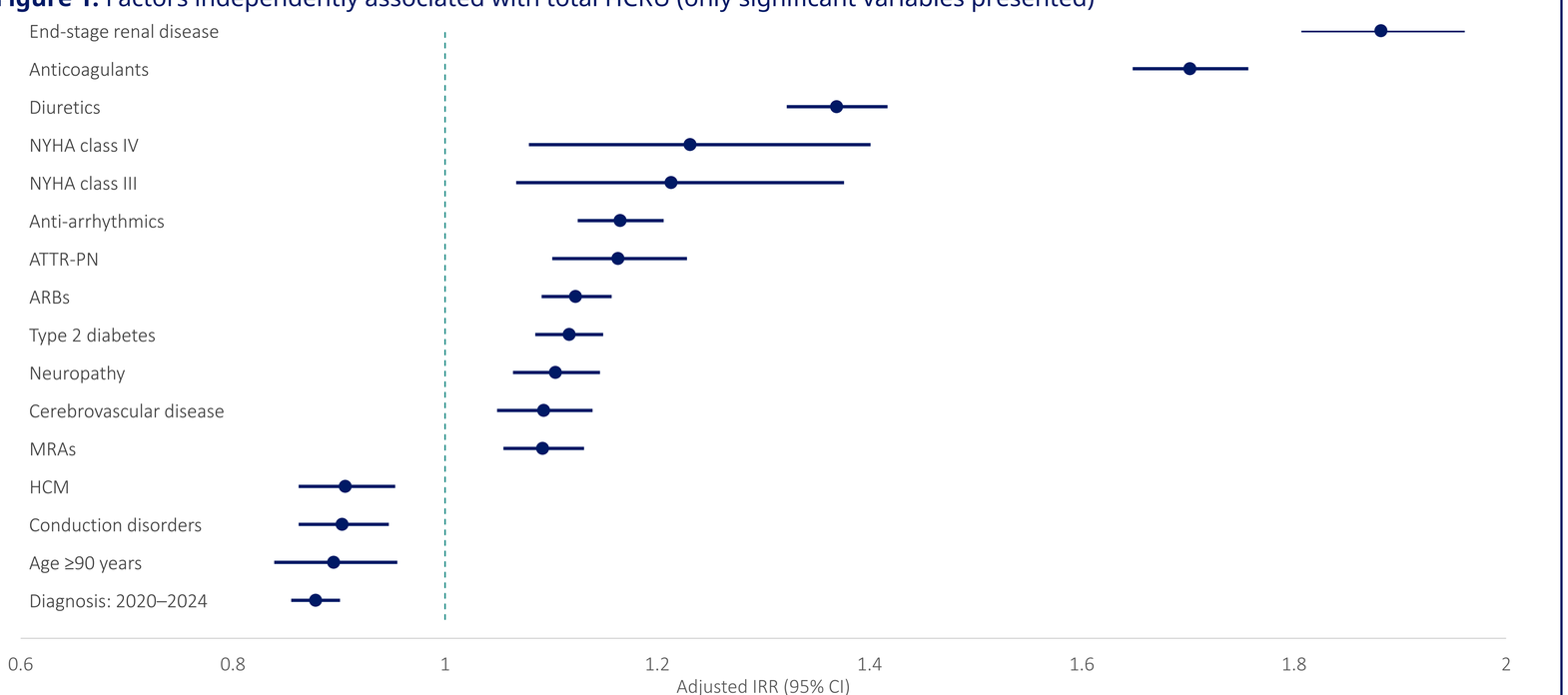
- **17,595 patients** met the study definition for ATTR-CM (Table 1).
  - Mean (SD) age at diagnosis was **71.3 (14.8) years**; median (IQR) age was **74 (64 - 82) years**.
  - **60.5%** of patients were male.
  - At index, heart failure was recorded in **64.9%** of patients, hypertension in **62.7%**, and arrhythmia in **38.8%**.
  - The multivariable analysis included **15,677 patients** with non-zero HCRU and complete covariate data.
- In the adjusted negative binomial regression model, ESRD was the strongest independent factor associated with total HCRU (Figure 1).
  - ESRD: IRR 1.88; 95% CI: 1.81–1.96
  - Anticoagulant use: IRR 1.70; 95% CI: 1.65–1.76
  - NYHA class IV: IRR 1.23; 95% CI: 1.08–1.40
  - NYHA class III: IRR 1.21; 95% CI: 1.07–1.38
  - Additional factors associated with higher HCRU included diuretics, anti-arrhythmic therapy, ATTR polyneuropathy, diabetes, angiotensin receptor blocker use, neuropathy, mineralocorticoid receptor antagonist use and cerebrovascular disease.

Table 1: Baseline cohort characteristics for the complete cohort

Characteristic	n (%)
Sex	
Female	6,955 (39.5%)
Male	10,640 (60.5%)
Age	
Mean (SD)	71.26 (14.8)
Median (IQR)	74 (64 - 82)
Age group	
<50	1,735 (9.9%)
50-59	1,697 (9.6%)
60-69	2,954 (16.8%)
70-79	5,350 (30.4%)
80-89	5,129 (29.2%)
90+	730 (4.2%)
Year of diagnosis	
2008-2010	62 (0.4%)
2011-2013	479 (2.7%)
2014-2016	1,812 (10.3%)
2017-2019	3,738 (21.2%)
2020-2022	6,796 (38.6%)
2023-2024	4,708 (26.8%)

Characteristic	n (%)
Comorbidity prevalence	
Aortic stenosis	778 (4.4%)
Arrhythmia	6,832 (38.8%)
Atrial fibrillation/flutter	4,752 (27.0%)
ATTR-PN broad	1,151 (6.5%)
ATTR-PN narrow	63 (0.4%)
Carpal tunnel syndrome	860 (4.9%)
Cerebrovascular disease	1,665 (9.5%)
Conduction disorders	1,236 (7.0%)
Dyslipidaemia	6,582 (37.4%)
End-stage renal disease	1,906 (10.8%)
Heart failure	11,425 (64.9%)
Hypertension	11,028 (62.7%)
Hypertrophic cardiomyopathy	1,114 (6.3%)
Ischaemic heart disease	1,639 (9.3%)
Liver failure	69 (0.4%)
Lumbar spinal stenosis	1,539 (8.8%)
Neuropathy	2,905 (16.5%)
Tendon injury	214 (1.2%)
Type 2 diabetes mellitus	4,976 (28.3%)

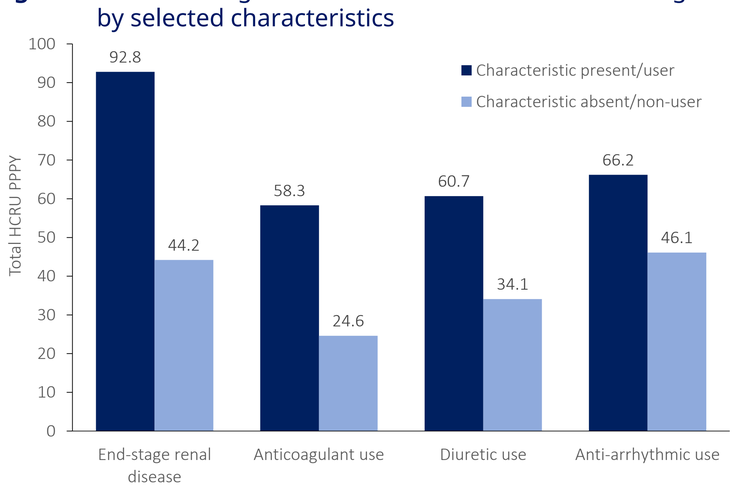
Figure 1: Factors independently associated with total HCRU (only significant variables presented)



ARB, angiotensin II receptor blocker; ATTR-PN, transthyretin amyloid polyneuropathy; CI, confidence interval; ESRD, end-stage renal disease; HCRU, healthcare resource utilisation; IRR, incidence rate ratio; HCM, Hypertrophic cardiomyopathy; MRA, mineralocorticoid receptor antagonist; NYHA, New York Heart Association.

- In the descriptive analysis, patients with **ESRD** had substantially greater HCRU than those without ESRD in the first six months after ATTR-CM identification (**92.8 vs 44.2 events PPPY;** Figure 2). This difference persisted during follow-up:
  - **7–12 months post-index:** 60.0 vs 18.4 events PPPY
  - **1–2 years post-index:** 54.5 vs 14.8 events PPPY
  - **2–3 years post-index:** 45.3 vs 12.4 events PPPY
- A similar pattern was observed across laboratory-derived renal function categories. Patients with estimated glomerular filtration rate (eGFR) values consistent with chronic kidney disease stage 5 had 118.3 events PPPY in the first six months after diagnosis, compared with 44.6 events PPPY among those with eGFR values consistent with stage 1 disease.
- Several indicators of cardiovascular complexity were associated with higher HCRU in the first six months after diagnosis:
  - **Anticoagulant users:** 58.3 vs 24.6 events PPPY among non-users
  - **Diuretic users:** 60.7 vs 34.1 events PPPY among non-users
  - **Anti-arrhythmic users:** 66.2 vs 46.1 events PPPY among non-users

Figure 2: HCRU during the first 6 months after ATTR-CM diagnosis by selected characteristics



Discussion

- This study identified substantial variation in HCRU among individuals with ATTR-CM in Japan. The highest utilisation was observed among patients with ESRD, markers of cardiovascular treatment intensity and advanced heart-failure functional limitation.
- End-stage renal disease was consistently associated with high HCRU in both descriptive and adjusted analyses. The persistent difference during follow-up suggests that renal disease may identify a subgroup with sustained and complex healthcare needs after ATTR-CM recognition.
- Anticoagulant, diuretic and anti-arrhythmic use were also associated with high HCRU. These treatments may act as surrogates of greater cardiovascular complexity, including atrial arrhythmia, congestion and intensive heart-failure management, rather than directly causing increased utilisation.
- Higher NYHA class was associated with increased early post-diagnosis HCRU, supporting the importance of functional limitation as an indicator of healthcare burden.

Strengths

- Large real-world cohort of 17,595 patients with ATTR-CM identified from a longitudinal Japanese hospital-based database.
- Assessment of HCRU across multiple settings, including inpatient, outpatient, diagnostic, emergency and home-care services.
- Combined descriptive subgroup analyses with adjusted negative binomial regression.

Limitations

- ATTR-CM was identified using diagnosis codes and/or tafamidis prescriptions; misclassification or incomplete capture of cases is possible.
- The MDV database is hospital based and does not link patients across institutions; care received elsewhere may not be captured completely, and some patients may have fragmented records.
- Several clinical measures, including biomarkers and NYHA class, had substantial missingness; results involving these variables should therefore be interpreted cautiously.

Conclusion

- High HCRU in ATTR-CM was concentrated among patients with ESRD, cardiovascular treatment complexity and more advanced heart-failure functional limitation.
- ESRD was the strongest independent factor associated with high HCRU, with an 88% higher adjusted encounter rate versus patients without ESRD in the first six months after ATTR-CM identification.
- **Identifying these high-risk patient profiles may help to target monitoring, multidisciplinary management and healthcare service planning towards those most likely to require higher-intensity care.**

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