Healthcare resource utilisation for individuals with transthyretin amyloid cardiomyopathy: results from a Japanese electronic health record database

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Silvia Capucci[1], René Lindholm Cordtz[1], Masaya Otsu[2], Ben Bray[3], Alistair Marsland[3], Andrew Thompson[3], Hideo Yasunaga[4]

Aim

To characterise healthcare resource utilisation before and after diagnosis of 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, including heart failure with preserved ejection fraction, hypertension, and atrial fibrillation[3,4].
  - Consequently, patients may undergo repeated clinical assessments, investigations and hospitalisations before ATTR-CM is identified.
- Previous real-world studies have reported considerable healthcare burden among people living with ATTR-CM[4]; however, evidence describing how healthcare resource utilisation (HCRU) changes in the years immediately before and after diagnosis is limited, particularly in Japan.
  - Characterising these longitudinal patterns may help to identify the period of greatest healthcare burden and inform efforts to support earlier recognition and management of ATTR-CM.

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; or
  - 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.

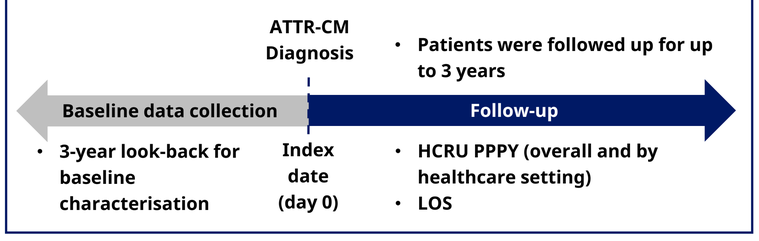
Outcomes

- 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 non-prescription HCRU** was calculated as the sum of these healthcare events.
- The number of **unique prescription drugs** was assessed separately.
- Hospital **length of stay (LOS)** was evaluated among admissions.

Analytical approach

- Outcomes were 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)**.
- LOS was summarised as **median days** with **interquartile range (IQR)**.
- Baseline demographic and clinical characteristics were described using counts and percentages, or means with standard deviations and medians with IQRs, as appropriate.

Figure 1: Study design overview



Results

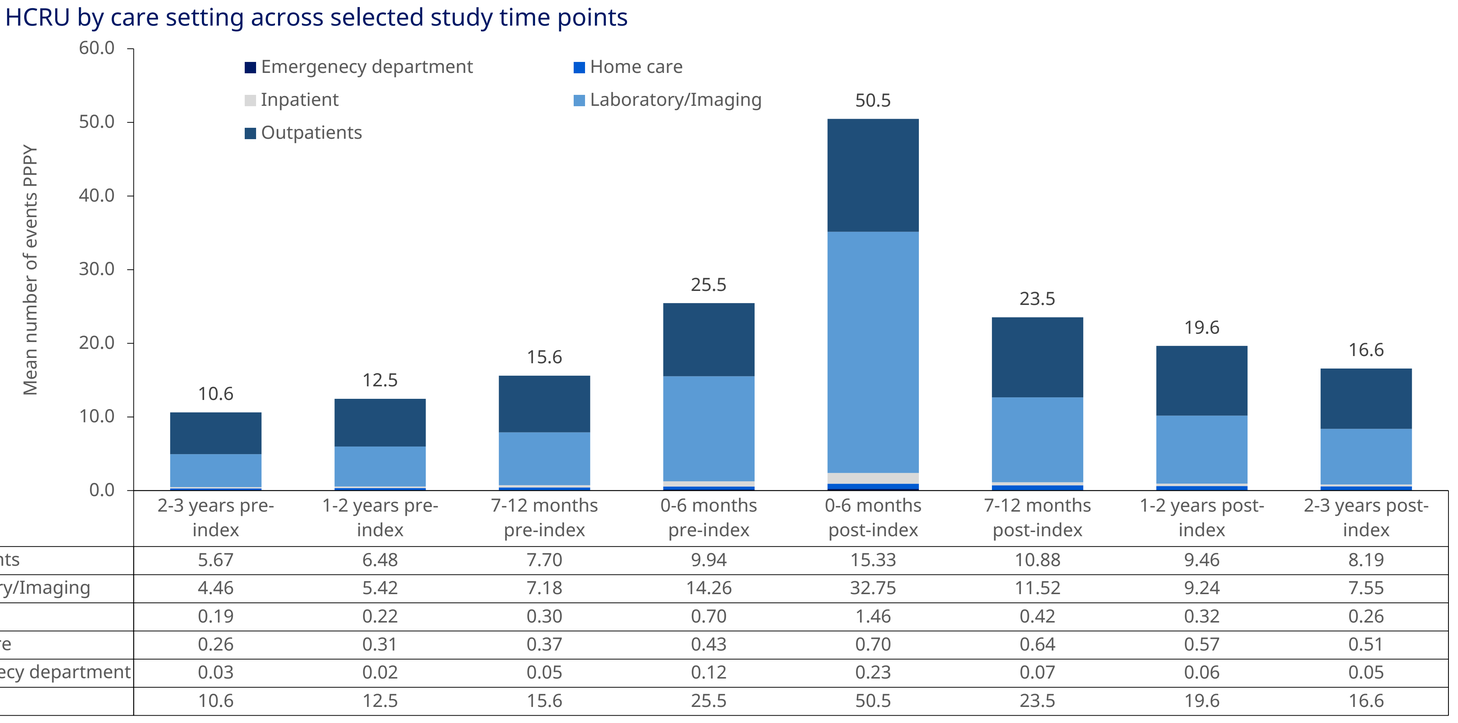
- **17,595 patients** met the study definition for ATTR-CM (Table 1).
  - Mean (SD) age at diagnosis was **71.3 years (14.8)**; median age (IQR) was **74 (64 - 82) years**.
  - **60.5%** of patients were male.
  - At index, heart failure was recorded in **64.9%** of patients, hypertension in **62.7%**, and arrhythmia in **38.8%**.
- Total non-prescription HCRU increased progressively in the three years before diagnosis, rising from **10.6 events PPPY** at 2–3 years pre-index to **25.5 events PPPY** in the final six months before index (Figure 2).
- HCRU peaked at **50.5 events PPPY** in the first six months after diagnosis. Although utilisation declined during subsequent follow-up, it remained above the earliest pre-diagnosis level.
- The increase around diagnosis was principally driven by greater use of **inpatient care, laboratory/diagnostic imaging and outpatient visits**.
- The number of unique prescriptions progressively increased before diagnosis and peaked in the first six months after diagnosis, consistent with intensification of medical management immediately after ATTR-CM recognition (Figure 3).
- Prescription utilisation subsequently declined but remained elevated relative to earlier pre-diagnosis periods.

Table 1: Baseline cohort characteristics

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%)

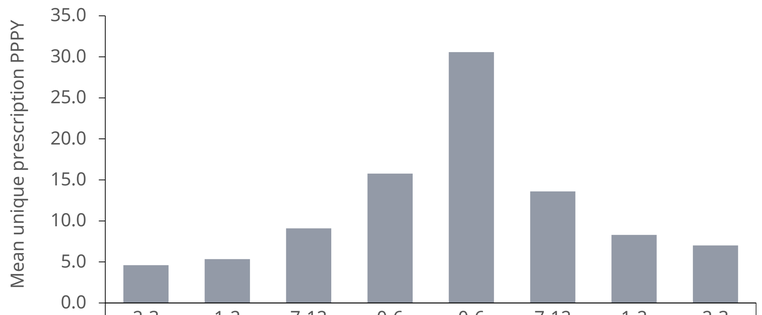
Characteristic	n (%)
Comorbidity prevalence	
Aortic stenosis	778 (4.4%)
Arrhythmia	6,832 (38.8%)
Atrial fibrillation/flutter	4,752 (27.0%)
ATTR-PN broad	1,151 (6.5%)
ATTR-PN narrow	63 (0.4%)
Carpal tunnel syndrome	860 (4.9%)
Cerebrovascular disease	1,665 (9.5%)
Conduction disorders	1,236 (7.0%)
Dyslipidaemia	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 2: HCRU by care setting across selected study time points



	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
Outpatients	5.67	6.48	7.70	9.94	15.33	10.88	9.46	8.19
Laboratory/Imaging	4.46	5.42	7.18	14.26	32.75	11.52	9.24	7.55
Inpatient	0.19	0.22	0.30	0.70	1.46	0.42	0.32	0.26
Home care	0.26	0.31	0.37	0.43	0.70	0.64	0.57	0.51
Emergenecy department	0.03	0.02	0.05	0.12	0.23	0.07	0.06	0.05
Total	10.6	12.5	15.6	25.5	50.5	23.5	19.6	16.6

Figure 3: Unique prescriptions across selected study time points



	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
Prescription	4.6	5.3	9.1	15.8	30.6	13.6	8.3	7.0

- Median hospital LOS increased from **13.0 days** *(IQR: 3.0–19.0)* at 2–3 years pre-index to **21.0 days** *(IQR: 5.0–26.0)* in the final six months before diagnosis (Figure 4).
- Following ATTR-CM identification, median LOS declined modestly but remained prolonged, at **18.0 days** *(IQR: 4.0–25.0)* in the first six months post-index and **16.0 days** *(IQR: 4.0–23.0)* at 2–3 years post-index.

Figure 4: LOS across selected study time points



	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
LOS (days)	13.0	15.0	18.0	21.0	18.0	17.0	17.0	16.0

Discussion

- In this retrospective Japanese cohort, HCRU increased progressively in the years preceding ATTR-CM identification, with a marked peak during the first six months after the index date.
- The rise in utilisation around ATTR-CM diagnosis was primarily driven by inpatient admissions, laboratory/diagnostic imaging and outpatient visits. This pattern may reflect increasing disease severity before diagnosis, diagnostic investigations, management of cardiovascular complications and/or treatment optimisation following diagnosis.
- HCRU remained elevated in subsequent post-index periods, although it was substantially lower than during the first six months after diagnosis.
- Increasing prescription use and prolonged hospital length of stay further indicate increasing clinical complexity before diagnosis and ongoing management needs afterwards.

Strengths

- Large real-world cohort of 17,595 patients with ATTR-CM identified from a longitudinal Japanese hospital-based database.
- Assessment of multiple types of HCRU over a six-year observation window, spanning three years before and after ATTR-CM identification.
- Evaluation of utilisation trajectories provides insight into the changing burden surrounding diagnosis, rather than describing HCRU at a single time point.

Limitations

- ATTR-CM was identified using diagnosis codes and/or tafamidis prescriptions; misclassification or incomplete capture of cases is possible.
- The MDV database primarily captures care delivered at participating acute-care hospitals; healthcare encounters occurring elsewhere may not have been observed, including on going prescriptions.
- The index date reflects the first date at which study identification criteria were met, rather than the true date of clinical diagnosis.

Conclusion

- **HCRU increased progressively before ATTR-CM diagnosis and peaked immediately afterwards, before declining substantially but remaining above the earliest pre-diagnosis level.**
- Earlier recognition and appropriate management of ATTR-CM may offer an opportunity to address rising healthcare needs before they reach their highest levels

[1]Novo Nordisk A/S, Søborg, Denmark; [2]Novo Nordisk Pharma Ltd., Tokyo, Japan; [3]Lane Clark & Peacock LLP, London, UK; [4]University of Tokyo, Tokyo, Japan

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References:

(**1**) Ruberg et al. *J Am Coll Cardiol* 2019;73:2872–2891; (**2**) Brito et al. *Glob Heart* 2023;18:59; (**3**) Minamisawa et al. *Circ J* 2025;89:432–441; (**4**) Lauppe et al. *ESC Heart Fail* 2022;9:1636–1642; (**5**) Fujinaga and Fukuoka. *Drugs Real World Outcomes* 2022;9:543–550; (**6**) Hayashida et al. *J Epidemiol* 2021;31:1–11;