Direct healthcare costs for individuals with transthyretin amyloid cardiomyopathy: results from a Japanese electronic health record database

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Aim

To characterise direct healthcare costs 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].
  - Consequently, patients may undergo repeated clinical assessments, investigations and hospitalisations before ATTR-CM is identified.
  - Such care needs may result in substantial direct medical costs; however, evidence describing how costs evolve before and after ATTR-CM diagnosis remains limited in Japan[4,5].
- Understanding when costs accumulate, and which components of care drive expenditure, may help to inform healthcare planning and disease 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[6,7].
- 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 cost 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.

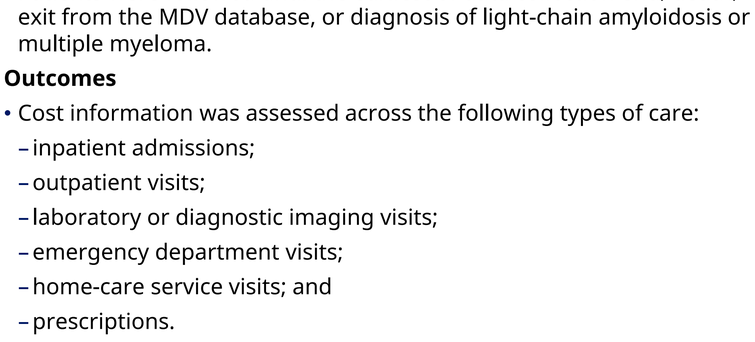
Outcomes

- Cost information was assessed across the following types of care:
  - inpatient admissions;
  - outpatient visits;
  - laboratory or diagnostic imaging visits;
  - emergency department visits;
  - home-care service visits; and
  - prescriptions.
- **Total direct healthcare costs** were defined as the sum of all cost components.

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
- Costs are presented as **mean per person per year (PPPY)**.
- Costs were standardised to **2024 Japanese Yen** (JPY) using the Japanese Consumer Price Index and converted to **US dollars** (USD) using the Bank of Japan exchange rate: **USD 1 = JPY 156.35**.
- 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

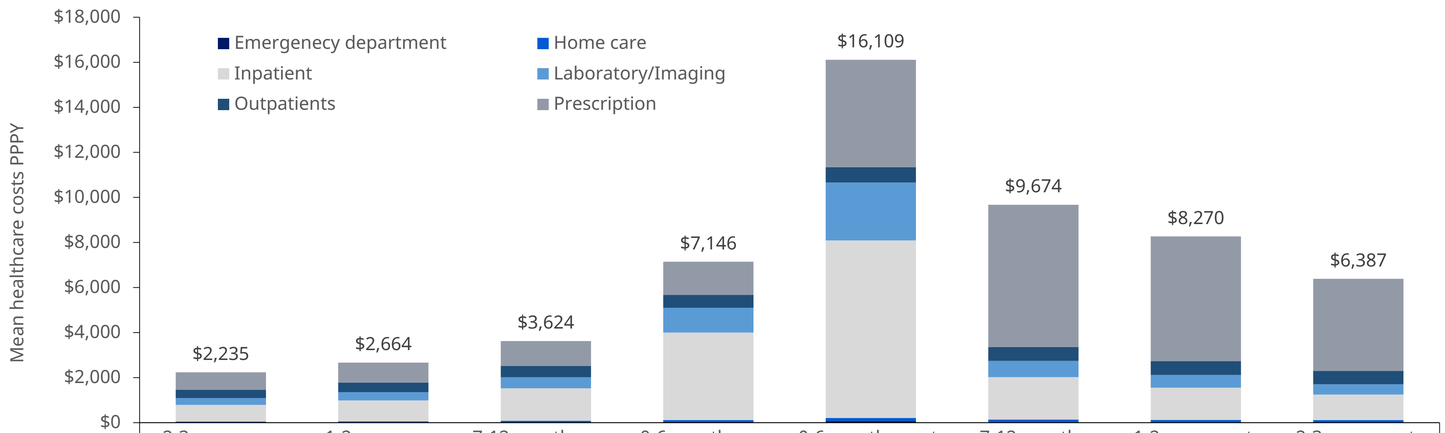
- **17,595 patients** met the study definition for ATTR-CM (Table 1).
  - Mean (SD) age at diagnosis was **71.3 (14.8) years**; median (IQR) age was **74 (64 - 82) years**.
  - **60.5%** of patients were male.
  - At index, heart failure was recorded in **64.9%** of patients, hypertension in **62.7%**, and arrhythmia in **38.8%**.
- Direct healthcare costs increased before diagnosis and peaked in the first six months after diagnosis (Figure 2).
  - Mean total direct healthcare costs increased progressively before ATTR-CM diagnosis, from **USD 2,235 PPPY** at 2–3 years pre-index to **USD 7,146 PPPY** in the final six months before index.
  - Costs peaked at **USD 16,109 PPPY** during the first six months after diagnosis. Although costs declined during later follow-up, expenditure generally remained above early pre-diagnosis levels.
  - Mean total direct costs were approximately **7.2-fold higher** in the first six months after diagnosis than at 2–3 years before diagnosis.
- Cost burden remained elevated following diagnosis
  - Following the peak in the first six months after index, total direct costs decreased but remained higher than the earliest pre-index period.

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: Healthcare costs by care setting across selected study time points

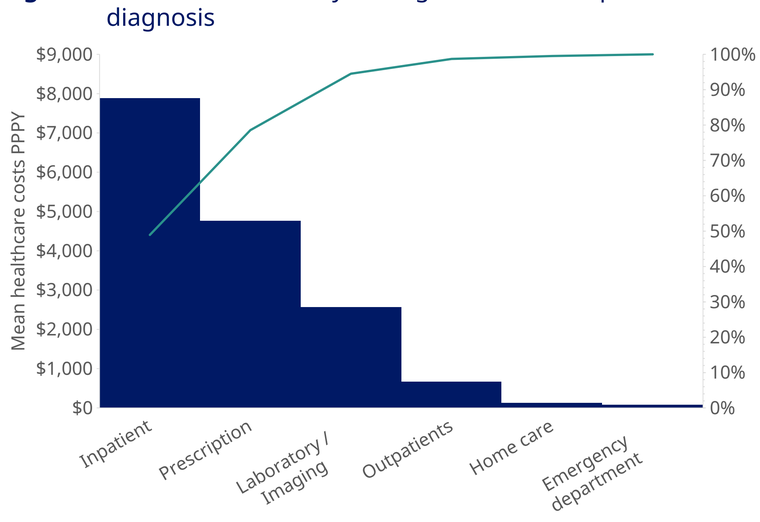


	2-3 years pre-index	1-2 years pre-index	7-12 months pre-index	0-6 months pre-index	0-6 months post-index	7-12 months post-index	1-2 years post-index	2-3 years post-index
Prescription	775.5	882.8	1105.6	1471.3	4769.3	6313.9	5536.4	4092.7
Outpatients	369.3	428.2	504.7	573.9	674.1	617.8	616.6	589.1
Laboratory/Imaging	300.3	364.8	489.2	1099.0	2571.1	720.3	561.3	458.1
Inpatient	737.4	927.4	1438.2	3882.1	7885.3	1880.9	1434.1	1134.9
Home care	43.9	55.2	73.8	83.2	132.4	120.8	107.2	99.5
Emergeney department	8.6	6.1	12.6	36.2	76.5	20.4	14.7	12.5
Total	$2,235	$2,664	$3,624	$7,146	$16,109	$9,674	$8,270	$6,387

Costs were standardised to 2024 Japanese Yen and converted to US dollars. Values are mean direct healthcare costs per person per year

- Inpatient care was the largest contributor to direct healthcare costs throughout the study period and was the principal driver of the marked increase in total expenditure around ATTR-CM diagnosis (Figure 3).
  - In the first six months after diagnosis, mean inpatient costs reached **USD 7,885 PPPY**, accounting for **48.9%** of total direct costs (**USD 16,109 PPPY**).
- Pharmacy costs were the second-largest component during this period (**USD 4,769 PPPY**; 29.6% of total costs), followed by laboratory/diagnostic imaging costs (**USD 2,571 PPPY**; 16.0%).
  - By comparison, outpatient (**USD 674 PPPY**), home-care (**USD 132 PPPY**) and emergency department costs (**USD 77 PPPY**) made relatively small contributions to overall expenditure.
- The predominance of inpatient costs indicates that the economic burden of ATTR-CM in Japan is largely associated with high-intensity hospital-based management rather than ambulatory care alone.

Figure 3: Cost contribution by setting in 0-6 months post-ATTR-CM diagnosis



Discussion

- In this retrospective Japanese cohort, direct healthcare costs increased progressively in the years before ATTR-CM diagnosis, with a marked peak during the first six months after the index date.
- The increase in expenditure around diagnosis was driven principally by inpatient care, suggesting that acute hospital-based management is a major component of the economic burden associated with ATTR-CM.
- Prescription and laboratory/diagnostic imaging costs were also substantial during the early post-diagnosis period, potentially reflecting treatment initiation, optimisation of cardiovascular management and diagnostic assessment.
- Costs remained elevated after the initial post-index peak, indicating that the economic burden of ATTR-CM extends beyond the diagnostic period.

Strengths

- Large real-world cohort of 17,595 patients with ATTR-CM identified from a longitudinal Japanese hospital-based database.
- Assessment of direct healthcare costs across a six-year patient journey, spanning three years before and after ATTR-CM identification.
- Granular breakdown of expenditure by inpatient, outpatient, diagnostic, emergency, home-care and prescription components.

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 hospital-based activity; primary care, community care and healthcare received outside participating institutions may not be fully captured.
  - Furthermore, indirect costs, patient out-of-pocket spending, unpaid care or wider societal burden are not captured.
- The index date reflects the first date at which study identification criteria were met, rather than the true date of clinical diagnosis.

Conclusion

- **ATTR-CM was associated with a progressive rise in direct healthcare costs before diagnosis, a marked peak immediately afterwards, and a sustained economic burden during follow-up.**
- Inpatient care was the principal contributor to direct healthcare costs immediately after ATTR-CM diagnosis, highlighting the importance of hospital-based management in the overall economic burden of ATTR-CM.
- Earlier recognition and appropriate management of ATTR-CM may offer an opportunity to address escalating healthcare costs before they reach their highest levels, reducing the overall cost burden to healthcare systems.

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(**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**) Ahmad et al. *Am J Med Sci* 2023;366:347–354; (**5**) Lauppe et al. *ESC Heart Fail* 2022;9:1636–1642; (**6**) Fujinaga and Fukuoka. *Drugs Real World Outcomes* 2022;9:543–550; (**7**) Hayashida et al. *J Epidemiol* 2021;31:1–11