Costs and Healthcare Resource Utilization in Patients With Transthyretin Amyloid Cardiomyopathy: A Systematic Literature Review

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OBJECTIVE

- **To conduct a systematic literature review (SLR) of available literature on costs and healthcare resource utilization (HCRU) related to disease severity in patients with transthyretin amyloid cardiomyopathy (ATTR-CM)**

INTRODUCTION

- ATTR-CM is a progressive and fatal disease caused by the destabilization of transthyretin and aggregation of amyloid fibrils in the heart that leads to heart failure (HF), with a higher prevalence in patients aged > 60 years[1–4]
- Given the recent approval of treatments for ATTR-CM, the latest publications concerning the disease have focused on clinical outcomes and treatment efficacy[5]
- The paucity of data regarding costs and HCRU in patients with ATTR-CM hinders informed decision-making by healthcare providers and policymakers about resource allocation and cost-effective strategies
- Comprehensive analyses of the financial implications and HCRU needs of patients at varying stages of ATTR-CM are required to better understand the impact of the disease on healthcare systems and to improve patient care

METHODS

- This SLR followed the standards set out in the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement,[6] the Cochrane Handbook for Systematic Reviews of Interventions, and rigorous standards required by the National Institute for Health and Care Excellence[7]
- Systematic literature searches were conducted on November 23, 2023, in Embase, MEDLINE, CENTRAL, and EconLit databases for peer-reviewed articles (published in 2013–2023)
- Gray literature hand searches for conference abstracts were conducted for conferences not already indexed and captured (published in 2021–2023)
- Publications were evaluated against predetermined population, intervention, comparator, outcomes, and study design criteria to establish which studies were eligible for inclusion in the SLR (**Table 1**)
- Only full-text articles underwent a quality assessment, owing to the lack of details available for conference abstracts

TABLE 1: Population, Intervention, Comparator, Outcomes, and Study Design Inclusion and Exclusion Criteria

Domain	Inclusion Criteria	Exclusion Criteria
Population	• Adult (aged ≥ 18 years) patients with ATTR-CM with wild-type or variant genotype, or their caregivers • Subgroups based on NYHA class or NAC stage	Patients without ATTR-CM
Intervention	None required	NA
Comparator	None required	NA
Outcomes	Costs • Total costs • Direct costs • Indirect costs (including caregiver burden) HCRU • Hospital admissions and readmissions (HF- or CV-related and overall or all-cause) • Length of stay • Emergency room visits • Outpatient visits • Specialist visits • Electrocardiogram • Cardiac imaging (CMR, PET scan, or echocardiogram) • Cardiac or bone scintigraphy • Phlebotomy • Treatments and procedures (eg, ultrasound, blood work, liver transplantation) • Drugs • Primary care • Missed days of work	No outcomes of interest
Study design	• Observational studies (prospective or retrospective, including surveys and questionnaires, national registries) • Clinical trials • SLRs or meta-analyses	Narrative reviews; study protocols; case reports; editorials; letters; and animal, cellular, molecular, genetic, or pharmacokinetic studies

CONCLUSIONS

- **This SLR suggests that hospitalization costs are the main driver of healthcare costs in the ATTR-CM population**
- **The economic impact of ATTR-CM may be underestimated owing to insufficient literature describing indirect costs**
- **Early diagnosis and treatment may reduce hospitalizations and lower the burden on healthcare systems**

RESULTS

- 35 publications, including one clinical trial and 32 observational studies, were included (**Figure 1, Table 2**)
  - Healthcare cost evidence mainly described direct costs

FIGURE 1: PRISMA Flow Diagram – Costs and HCRU SLR

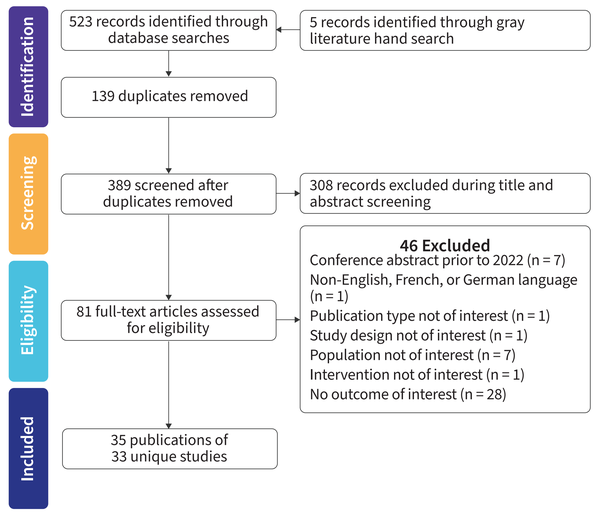
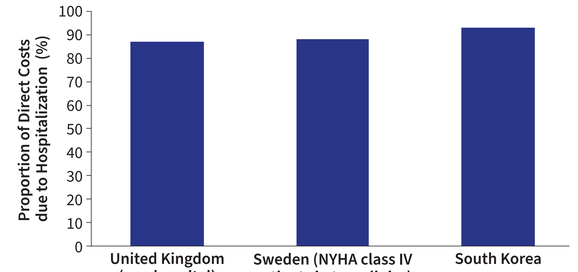


TABLE 2: Study Characteristics

Variable	n (%)
Total studies	33 (100)
Minimum sample size, patients	17
Maximum sample size, patients	16 955
Study location	
Europe (Bulgaria, Denmark, Finland, Germany, Greece, Ireland, Norway, Spain, Sweden, and the United Kingdom)	13 (39)
North America (United States)	13 (39)
Asia & Pacific (Australia, Japan, Korea)	4 (12)
South America (Argentina, Brazil)	2 (6)
Global	1 (3)
Study design	
Observational	32 (97)
Prospective	4 (12)
Retrospective	24 (73)
Cross-sectional	4 (12)
Post-hoc analysis of a randomized controlled trial	1 (3)

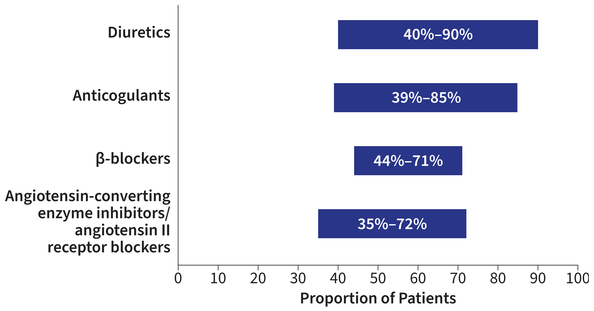
- Total direct costs (2022 United States dollars) to public healthcare systems reported per patient per year (PPPY) were $136–$22 600 (depending on disease severity) in the United Kingdom and $25 371 in South Korea[8,9]
- In the United States, out-of-pocket costs for ATTR-CM were estimated at $16 488 PPPY in 2021–2022[10]
- Two studies showed that direct costs increased with New York Heart Association (NYHA) class disease severity[8,11]
- All-cause hospitalization rates were 1.5 (Brazil) to 4.6 (South Korea) PPPY, and length of stay was 3.1 (United States) to 5.7 (South Korea) days[9,12,13]
- Hospitalization was the main driver of direct costs, accounting for 87% in patients from one hospital in the United Kingdom; 47% and 88% in patients with NYHA class II (not shown in **Figure 2**) and IV ATTR-CM, respectively, from two clinics in Sweden; and 93% of costs in patients in South Korea[8,9,11] (**Figure 2**)

FIGURE 2: Proportion of Direct Costs Attributable to Hospitalization



- The most common procedures across the 33 studies at baseline or during follow-up (1.5–3.5 years) were echocardiograms (100%), bone scintigraphy (47%–99%), magnetic resonance imaging (48%–50%), cardiac biopsy (14%–29%), pacemaker implantation (4%–30%), heart transplantation (0%–29%), and cardioverter-defibrillator implantation (0%–14%)[9,12,14–19]
- The most used drugs across the 33 studies at baseline or during follow-up (7.8–39 months) were diuretics, anticoagulants, β-blockers, and angiotensin-converting enzyme inhibitors/ angiotensin II receptor blockers[12,15–17,20–24] (**Figure 3**)

FIGURE 3: Concomitant Medications Across Studies



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ABBREVIATIONS: ATTR-CM, transthyretin amyloid cardiomyopathy; CMR, cardiovascular magnetic resonance; CV, cardiovascular; HCRU, healthcare resource utilization; HF, heart failure; NA, not applicable; NAC, National Amyloidosis Centre; NYHA, New York Heart Association; PET, positron emission tomography; PPPY, per patient per year; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; SLR, systematic literature review.

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