Epidemiology and Future Burden of Transthyretin Amyloid Cardiomyopathy (ATTR-CM) among Adults in the United States: A Systematic Review

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Authors: Shaw PD[1], Xavier S[1], Prasad J[1*], Ulahannan U[1]

[1]Evalueserve, Bengaluru, India *Presenting Author: Jagriti Prasad

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INTRODUCTION

- Transthyretin cardiac amyloidosis (ATTR-CM) is an increasingly recognized, yet still underdiagnosed, cardiomyopathy in the United States, with contemporary real-world data demonstrating burden, particularly among older adults and males. [1,2]
- The disease is associated with advanced age, male sex, progressive heart failure, and increased mortality risk, underscoring its growing public health relevance in aging populations.
- Diagnostic and outcome disparities persist across patient subgroups, contributing to delayed identification and variation in disease burden and prognosis, despite growing clinical awareness of ATTR-CM. [2]
- ATTR-CM is highly prevalent in specific high-risk clinical populations, including patients with heart failure with preserved ejection fraction (HFpEF) and individuals undergoing carpal tunnel release, indicating that population-level estimates likely underestimate the true burden. [3,4]
- As recognition of ATTR-CM expands beyond traditional heart failure cohorts, consolidated epidemiologic evidence and forward-looking projections are needed to support targeted screening, healthcare planning, and health economic decision-making.

OBJECTIVES

To synthesize epidemiology of ATTR-CM among adults in the United States (US) and project incidence and prevalence through 2030 to inform screening strategies, service capacity, and budget planning.

METHODS

- **Data source:**
  - PubMed, Medline, EMBASE, and DOAJ
  - Supplementary open search on Google Scholar and Google
- **Search Period:** Inception till December 2025
- **Screening and Data Extraction:** Conducted by four reviewers independently
- **Inclusion criteria:** US studies reporting adult ATTR CM incidence/prevalence; sub-cohort screening yields (e.g., HFpEF, carpal tunnel syndrome) were eligible.
- **Geographic scope:** US
- **Population:** Adults (age 18+)
- **Case definition:** ATTR-CM cases were identified using ICD-9 and ICD-10 diagnostic codes reported in the literature.
- **Projections:** Annual age and gender adjusted incident and prevalent case estimates from 2025 to 2030.
  - Based on historical data, a logarithmic trendline was derived to model the observed near-linear growth while allowing for gradual attenuation consistent with improving case ascertainment and diagnosed incidence and prevalence rates for projected years were estimated using the derived equation.
- **Population baseline**: Diagnosed incidence and prevalence rates were applied to UN adult population projections for US to derive the respective case counts.

RESULTS

- Four studies met the inclusion criteria.
- A diagnosed incidence of 12.7 per 1,000,000 (95% CI: 7.8-16.6) and diagnosed prevalence of 41.1 per 1,000,000 (95% CI: 31.0-49.1) was reported in 2022.
- The burden was higher in males (75%) and individuals aged ≥65 years (85%), consistent with established demographic risk factors for ATTR-CM.
- The comorbidity proportions were 69% for hypertension, 27% for diabetes, 30% for coronary artery disease, and 65% for hyperlipidemia.
- In clinical subgroups, ATTR-CM is observed in 10.2% of HFpEF patients, while it occurs in 7.1% individuals with carpal tunnel syndrome.
- The proportion of ATTR-CM patients who received pharmacologic treatment in 2025 was 81%.
- Forecasts indicated rising disease burden, with incidence increasing from 16.2 per 1,000,000 (case count: 4,445) in 2025 to 22.2 per 1,000,000 (case count: 6,325) in 2030. and prevalence increasing from 60.9 per 1,000,000 (case count: 16,709) in 2025 to 99.3 per 1,000,000 (case count: 28,317) in 2030.

Fig 1: Diagnosed Incidence of ATTR-CM

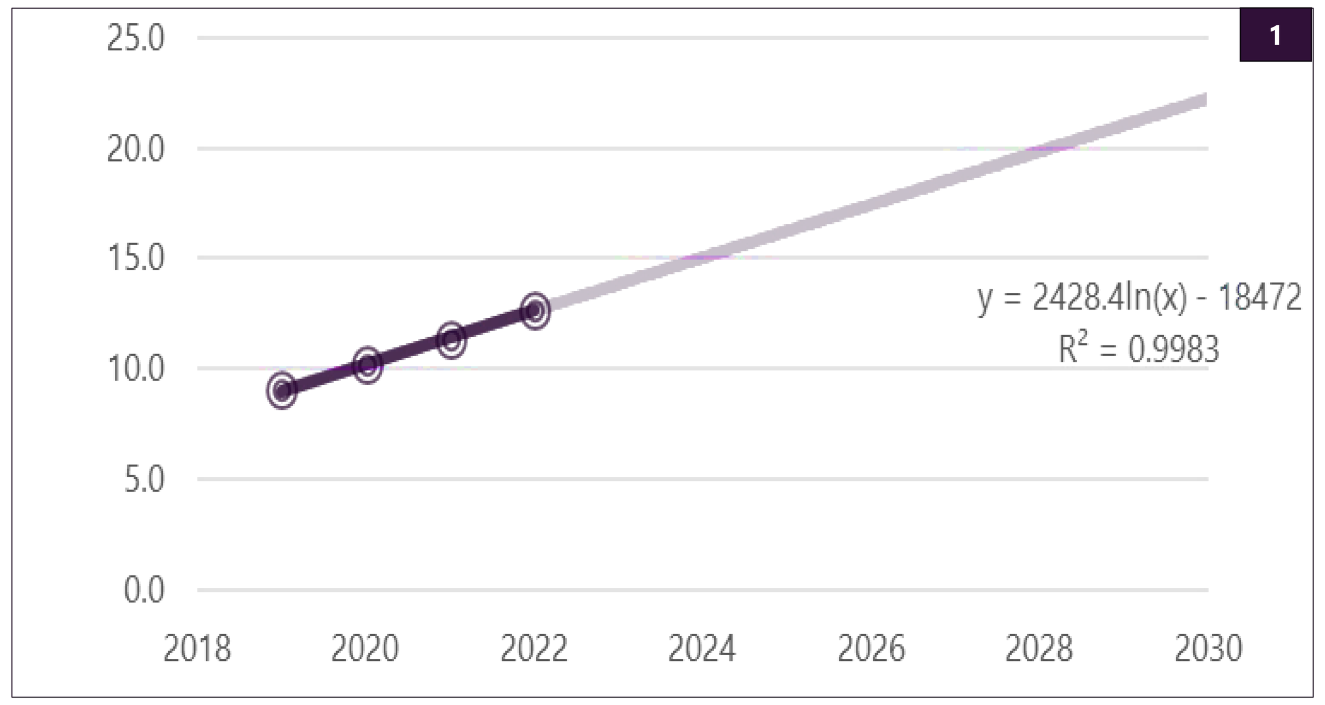


Fig 2: Diagnosed Prevalence of ATTR-CM

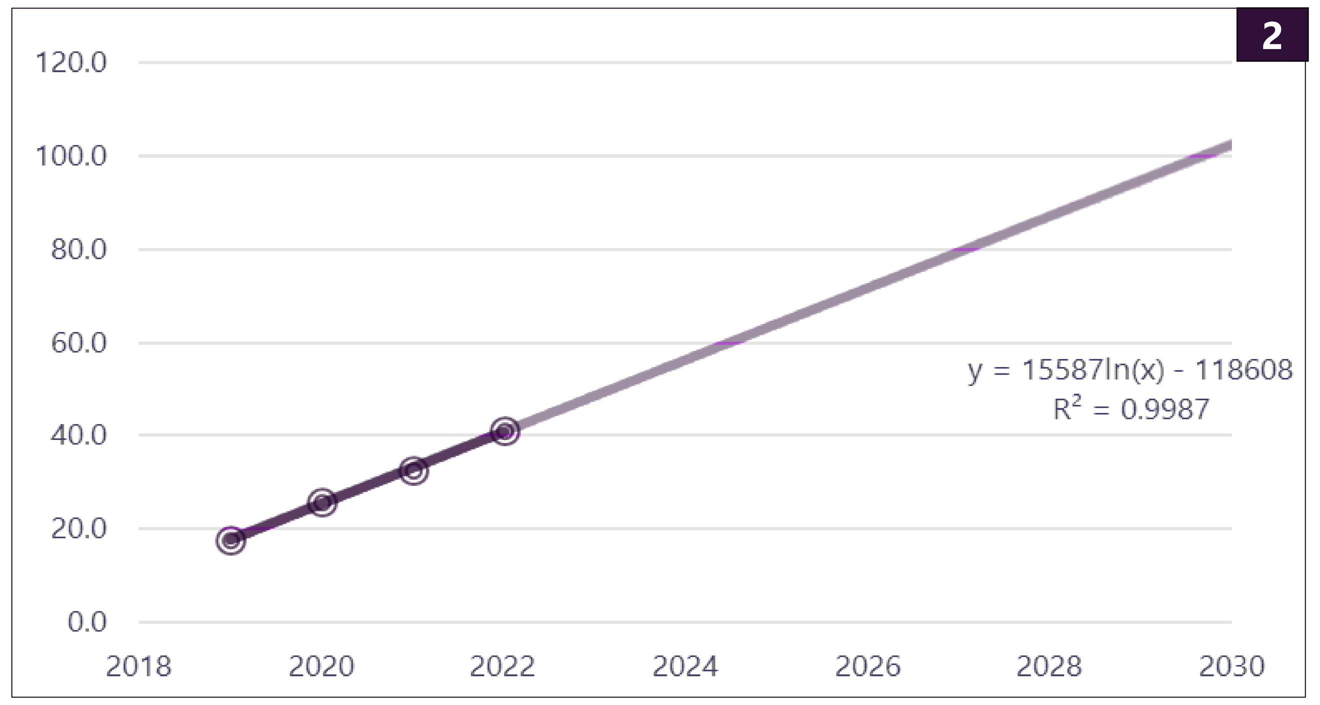


Fig 3: (A) Gender and (B) Age Distribution of ATTR-CM Cases in 2025

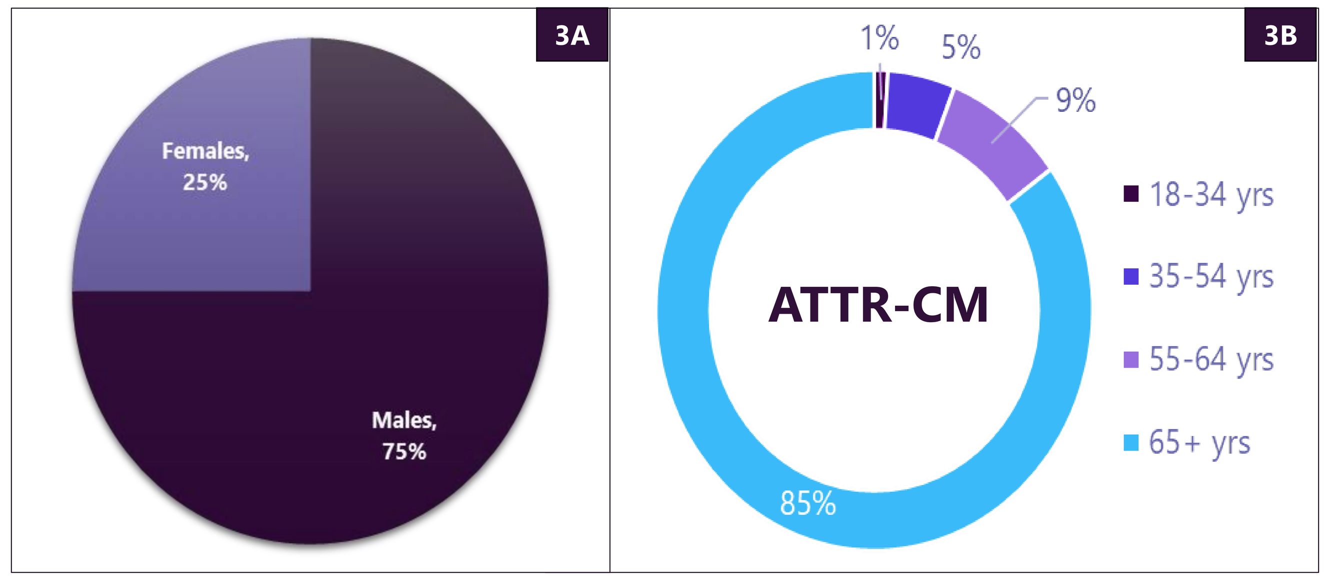
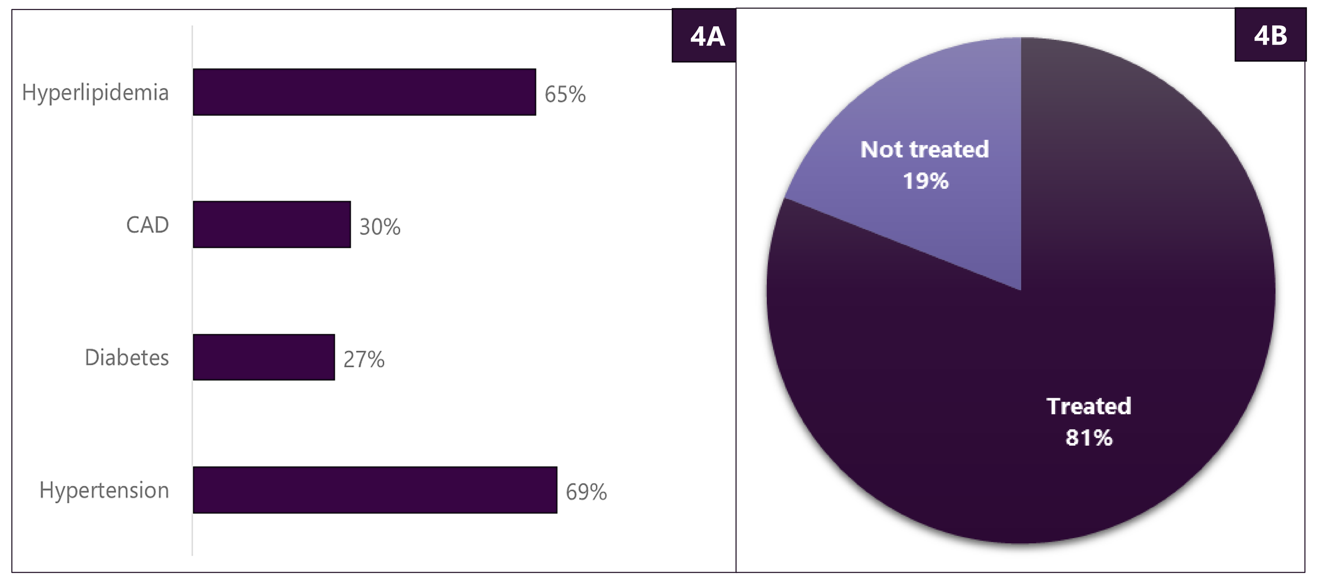
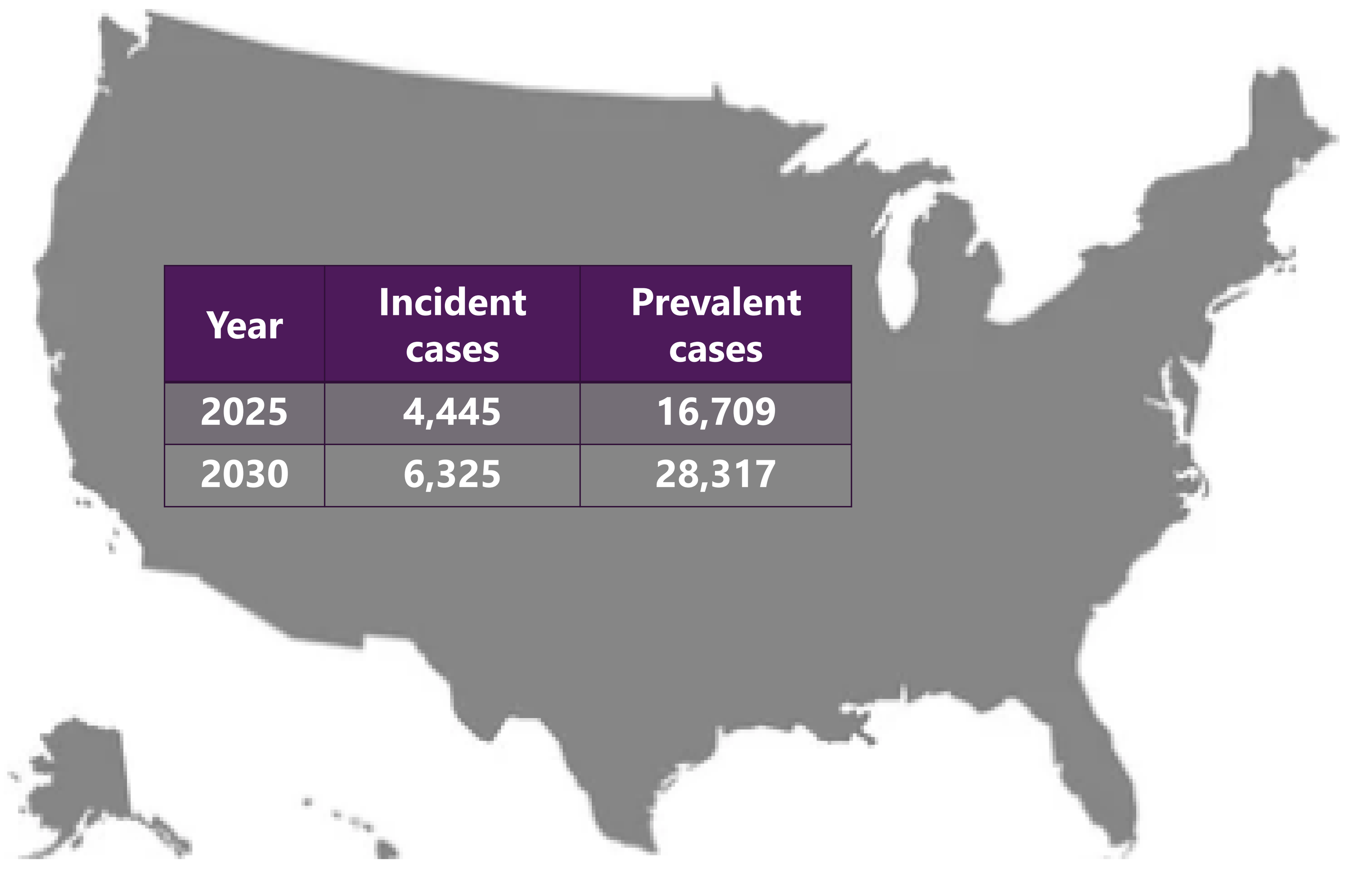


Fig 4: Proportion of (A) Comorbidity and (B) Treatment Observed among ATTR-CM Patients



KEY TAKEAWAY

Projected US ATTR-CM burden is **expected to rise substantially** through 2030, driven by aging populations and concentrated in **older, male, and high-risk clinical subgroups**, underscoring the need for targeted screening and healthcare planning.



Year	Incident cases	Prevalent cases
2025	4,445	16,709
2030	6,325	28,317

Image source: Shutterstock: myprecious

DISCUSSION AND CONCLUSION

- This synthesis demonstrates a substantial and increasing ATTR-CM burden in the United States, with strong age dependence, male predominance, and high prevalence of cardiometabolic comorbidities, reinforcing the clinical complexity and healthcare needs of this population.
- High observed prevalence of ATTR-CM within HFpEF and carpal tunnel syndrome subgroups underscores the value of targeted case-finding approaches, suggesting that focused screening in selected high-risk populations may improve timely diagnosis.
- Projected growth in incidence and prevalence through 2030 highlights important HEOR and policy implications, including the need for expanded service capacity, forward-looking budget impact planning, and improved epidemiologic infrastructure to capture costs, outcomes, and quality-of-life burden associated with ATTR-CM.

ABBREVIATIONS

- ATTR-CM - Transthyretin cardiac amyloidosis
- CAD - Coronary artery disease
- HFpEF - Heart failure with preserved ejection fraction
- ICD – International Classification of Diseases
- US – United States
- UN – United Nations

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