

Amylo'ExTTRa: Exploring Extra-Cardiac Manifestations in Patients With ATTR-CM Using a French National Health Data System

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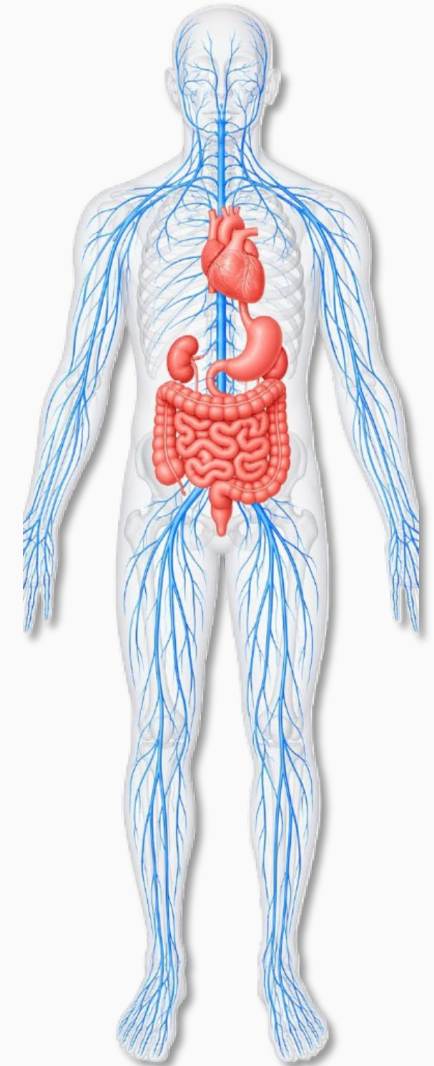
Extra-Cardiac Burden in ATTR-CM

Background

- **Misfolded TTR accumulating** as amyloid deposits in multiple systems in patients with ATTR-CM¹ results in extra-cardiac manifestations that can be associated with **frailty** and impairment of **QoL, in an already ageing population**^{2,3}
- Assessment of extra-cardiac manifestations in patients with ATTR-CM is important for providing a **multisystemic and multidisciplinary approach** for patient management and **treatment selection**

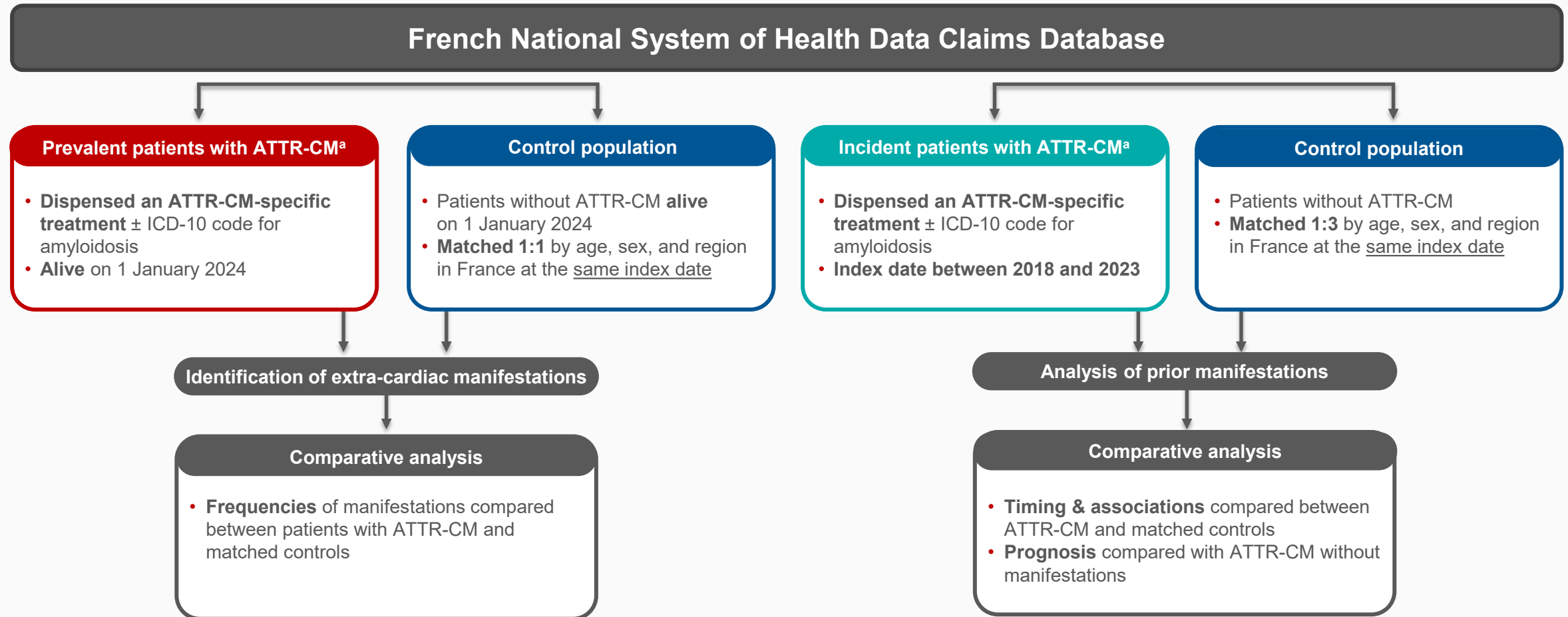
Objective

- **To characterise the multisystem extra-cardiac burden** in patients with ATTR-CM vs matched controls in a real-world setting and explore its **clinical implications**



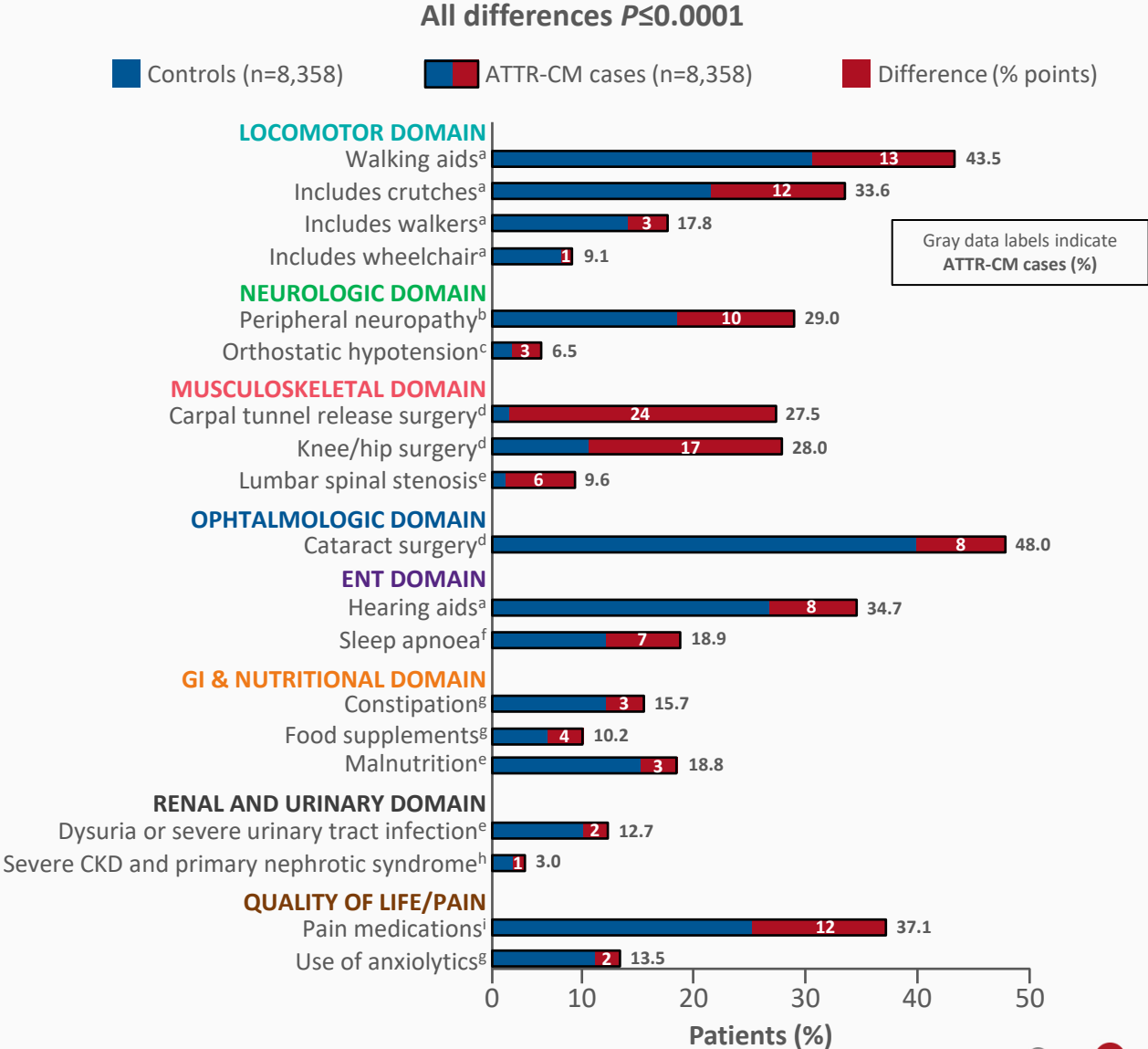
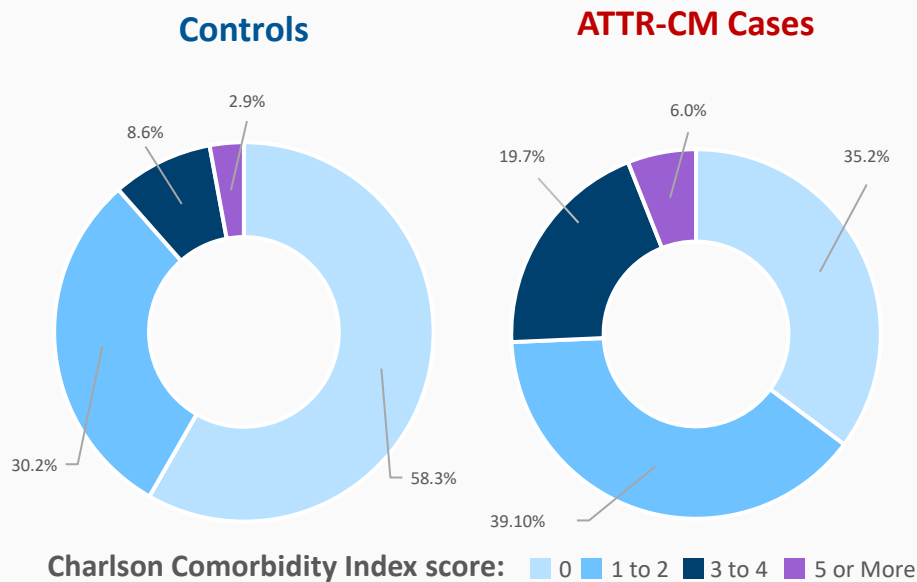
Study Design and Data Source

- Identification based on healthcare utilisation parameters (ICD codes, treatments, procedures)
 - **Index date**: 1st occurrence of ICD code identification or specific treatment



Marked Increase in Prevalence of Multisystem Extra-Cardiac Burden in ATTR-CM vs Matched Controls

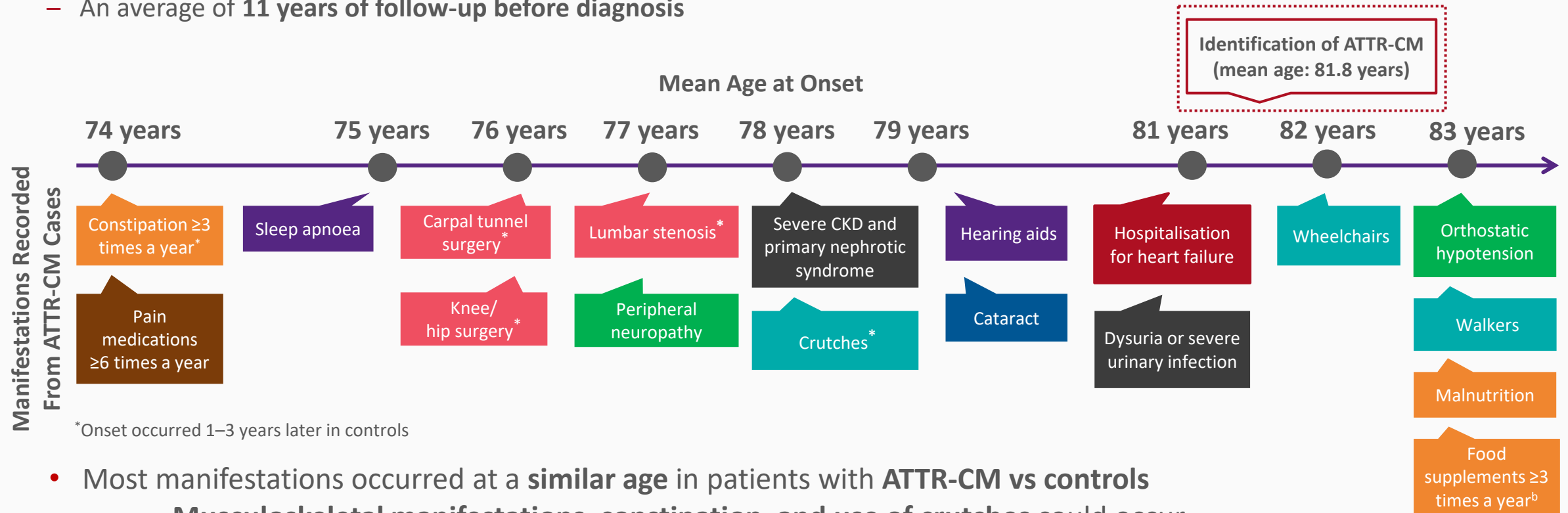
- Data from 8,358 prevalent patients with ATTR-CM with 1:1 matched controls were included in the analysis (as of 1 January 2024)
 - Mean age 82.7 years; 78% male
- Patients with ATTR-CM present with higher Charlson Comorbidity Index scores than controls



^aLPP code; ^bHospitalisation for peripheral neuropathy (ICD-10) or prescription of midodrine, gabapentin, or pregabalin, or use of a foot lifter; ^cHospitalisation for orthostatic hypotension (ICD-10) or administration of midodrine; ^dHospitalisation with a specific ICD-10 code; ^eHospitalisation with a specific ICD-10 code or LPP code; ^fMedications or LPP for the event prescribed ≥3 times in 2023; ^gALD 19 effective in 2023; ^hMedications for an event occurring ≥6 times in 2023; ⁱAbbreviations: ALD, active long-term disease; ATTR-CM, transthyretin amyloidosis with cardiomyopathy; CKD, chronic kidney disease; ENT, ear, nose and throat; GHM, Groupes homogènes de malades; GI, gastrointestinal; ICD-10, ICD-10, International Statistical Classification of Diseases and Related Health Problems 10th Revision; LPP, Liste des Produits et Prestations.

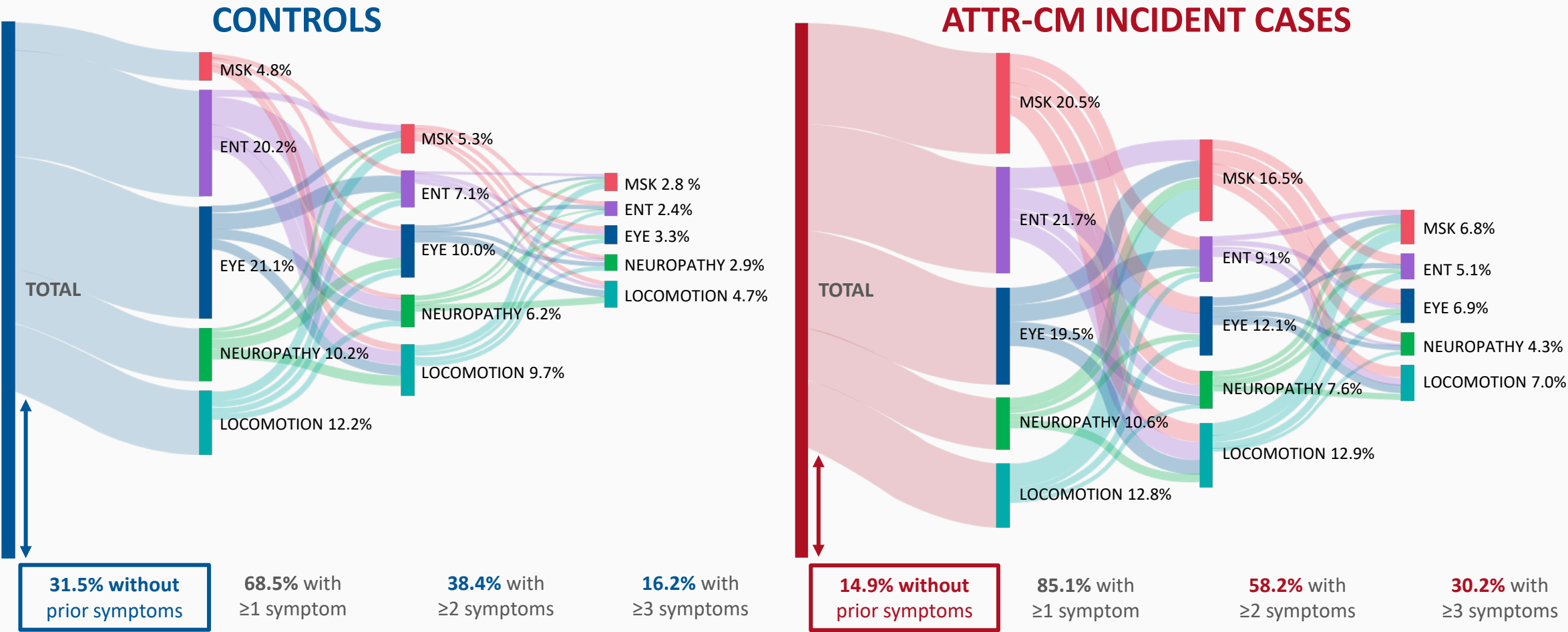
Extra-Cardiac Manifestations Are Recorded Years Before ATTR-CM Identification^a

- Data from **8,767 incident ATTR-CM cases** vs **26,301 matched controls** (1:3) were identified between 2018 and 2023
 - Mean age: 81.8 years; 78% were male
 - An average of **11 years of follow-up** before diagnosis



- Most manifestations occurred at a **similar age** in patients with **ATTR-CM vs controls**
 - **Musculoskeletal manifestations, constipation, and use of crutches** could occur 1–3 years earlier in ATTR-CM cases
- Suggests a **prolonged pre-diagnostic phase** with **evolving multisystem involvement**

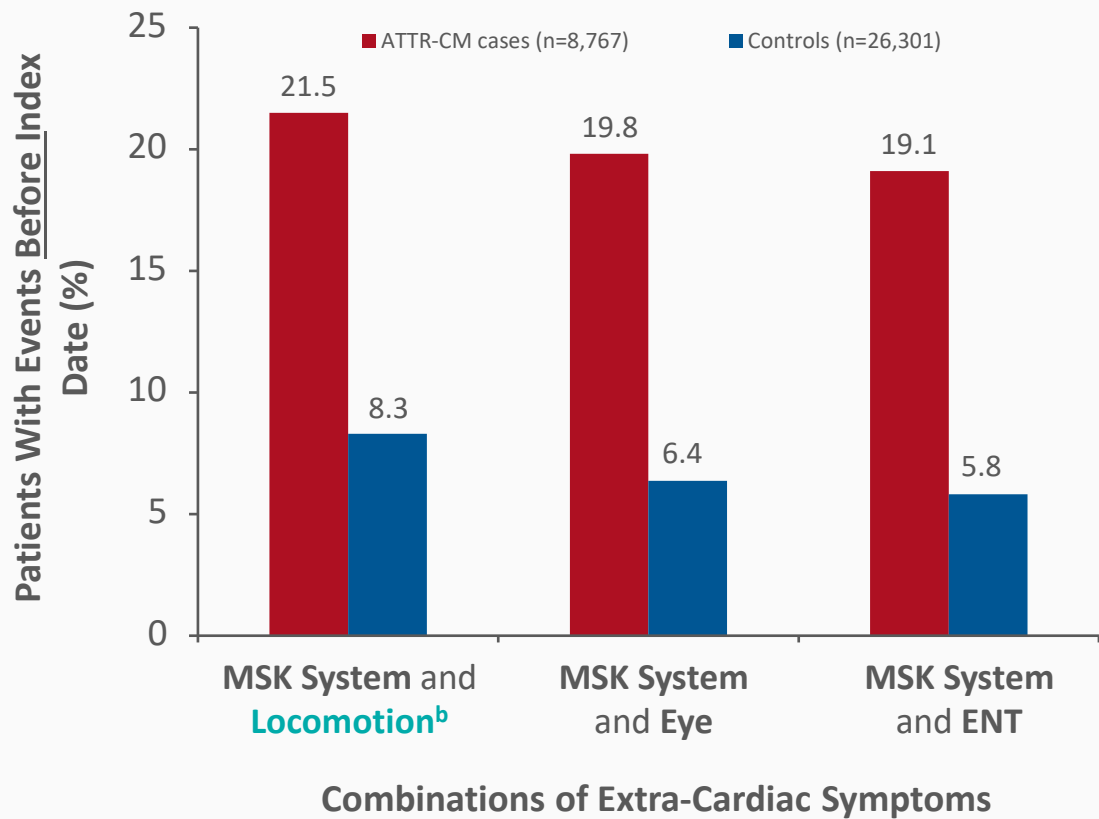
Accumulation of Extra-Cardiac Manifestations Is More Frequent in ATTR-CM Versus Matched Controls^{a,b}



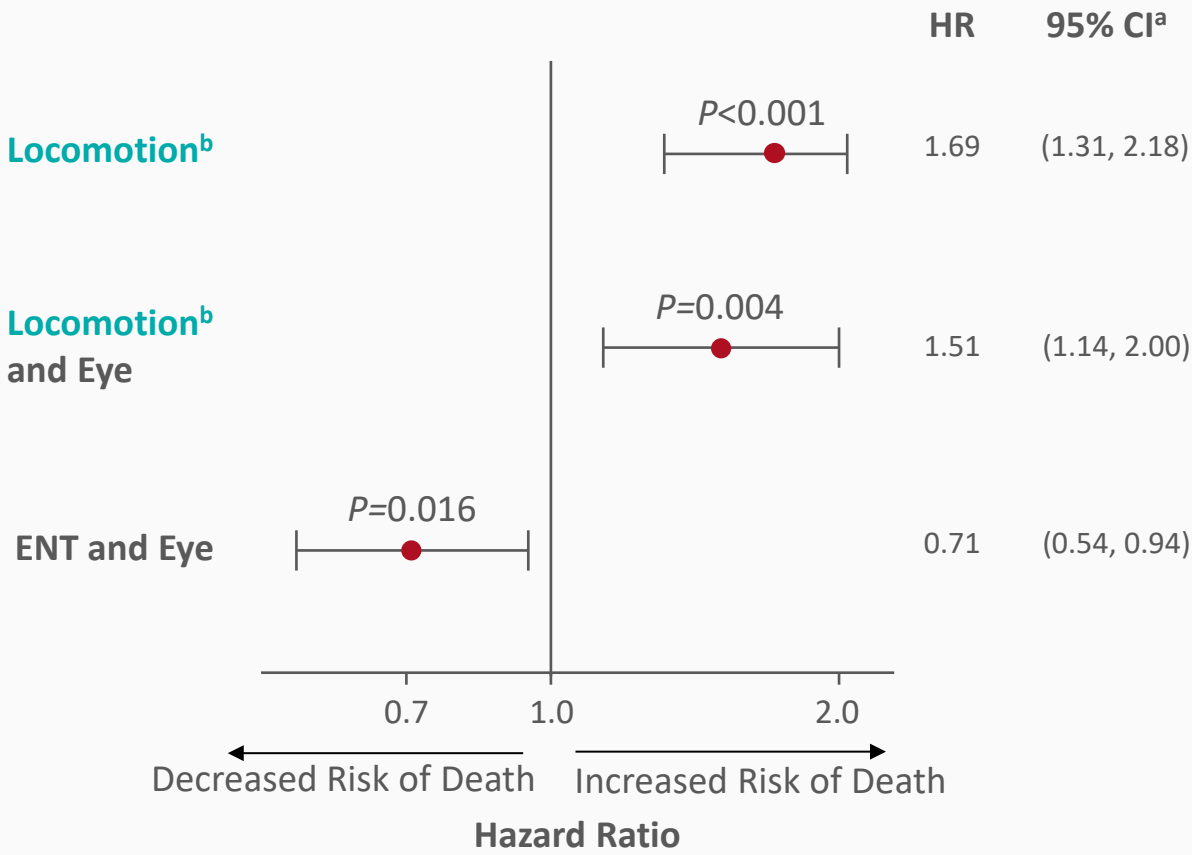
P < 0.001 for all differences between controls and patients with ATTR-CM

Locomotion Impairment: A Key Driver of Increased Mortality Risk in ATTR-CM

Combinations of Extra-Cardiac Symptoms With the Largest Differences Between ATTR-CM Incident Patients and Controls



Extra-Cardiac Symptoms Significantly Associated With Risk of Death



Conclusions

- Patients with ATTR-CM exhibited a **significantly higher burden of extra-cardiac manifestations** across multiple organ systems compared with matched controls
 - Multiple manifestations were **recorded years before ATTR-CM identification** and tended to **accumulate**, suggesting a long pre-diagnostic phase
 - **Multisystem patterns of manifestations may serve as clinical red flags, particularly when combined with MSK manifestations**
 - **Markers of locomotion impairment were associated with worse outcomes**
- These data confirm the multisystemic nature of ATTR-CM and support the need for a **holistic approach** when managing patients with ATTR-CM
- Findings should be interpreted in the context of claims-based data, reflecting healthcare patterns rather than direct clinical phenotyping

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