



# Screening Recognition and Barriers to Diagnosis of ATTR

MED-US-DZSTATE-2400017



## ATTR Disease State Slide Deck

- This resource provides information about ATTR.
- This resource is intended to be viewed in its entirety to support scientific exchange and is not intended as recommendations for clinical practice.
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| | Screening, Recognition, and  
Barriers to Diagnosis

# Increasing Clinical Suspicion

## Improving recognition of overlapping conditions, misdiagnosis and multiorgan presentation<sup>1</sup>

- Diversity of diagnostic clues can manifest in a patient across many years
- Non-cardiac red flags often precede the diagnosis of ATTR

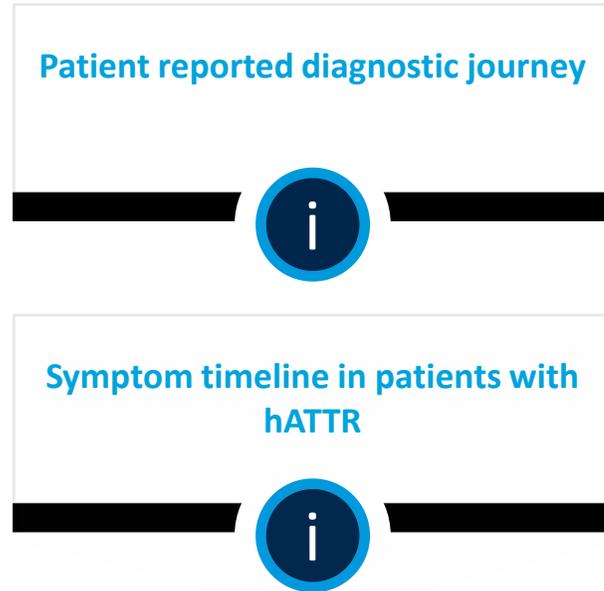
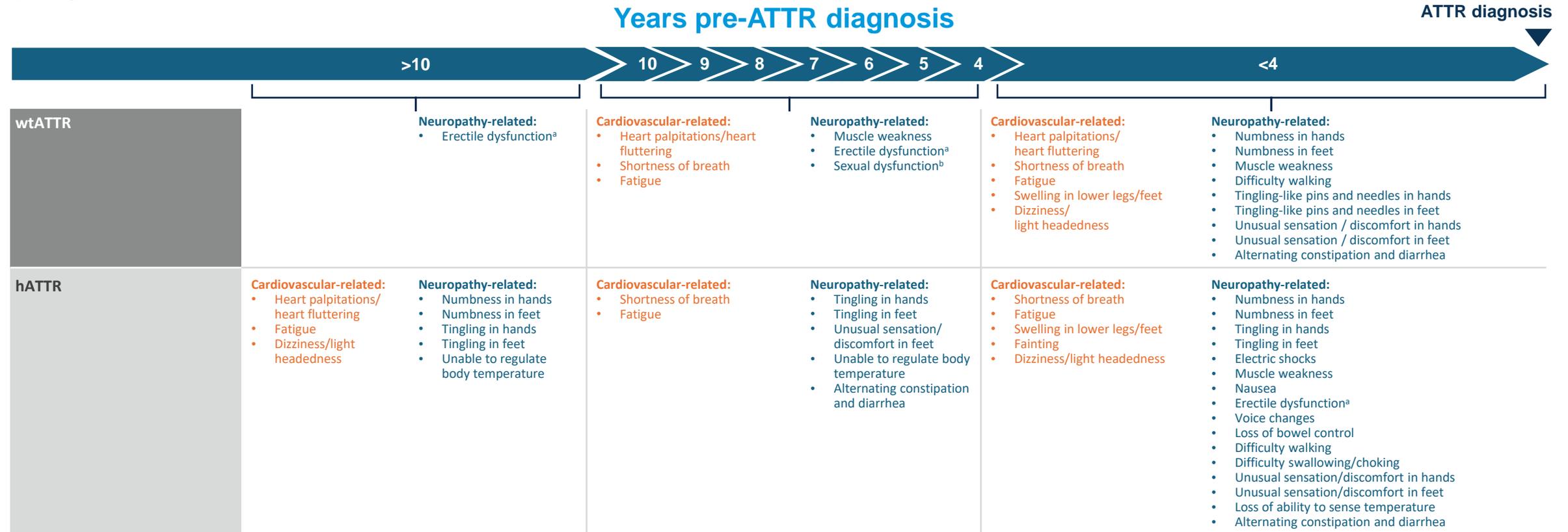


Figure taken from Nativi-Nicolau et al. 2022<sup>1</sup>

# Patient-reported Diagnostic Journey



Symptoms may start more than 10 years before diagnosis and appear to accumulate over time



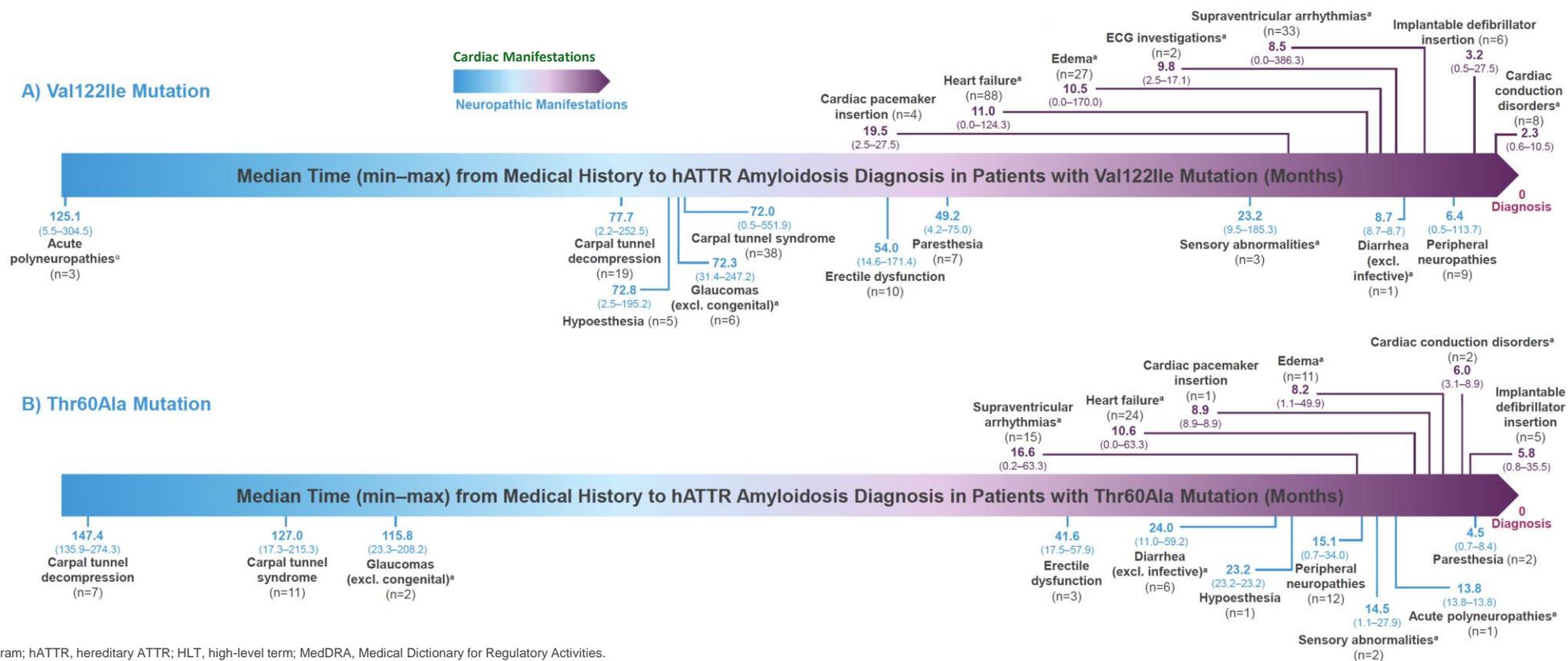
<sup>a</sup>Male only. <sup>b</sup>Female only.  
Figure taken from Karam et al. 2022<sup>1</sup>

1. Karam et al. Meeting of the International Society of Amyloidosis. 2022; Poster P192.

# Symptom Timeline in Patients with V122I and T60A hATTR



## Median time from medical history to hATTR diagnosis for common clinical manifestations



• <sup>a</sup>MedDRA HLT  
 • ECG, electrocardiogram; hATTR, hereditary ATTR; HLT, high-level term; MedDRA, Medical Dictionary for Regulatory Activities.  
 • 1. Grogan et al. *J Card Fail.* 2019;25(8)(Supp):S9-10.

# || Misdiagnosis of ATTR

## Overlapping neurologic conditions and misdiagnoses of ATTR<sup>1</sup>

Idiopathic (small-fiber) neuropathy
Diabetic neuropathy
Alcohol neuropathy
Chronic inflammatory demyelinating polyneuropathy
Motor neuron disease/ALS
Fibromyalgia
Occupational carpal tunnel syndrome
Malignancy or autoimmune disease

## Overlapping cardiac conditions and misdiagnoses of ATTR<sup>2</sup>

Heart failure with preserved ejection fraction
Hypertensive cardiomyopathy
Aortic stenosis
Hypertrophic cardiomyopathy
Light chain amyloidosis with cardiac involvement
Idiopathic restrictive cardiomyopathy
Iron overload
Other infiltrative cardiomyopathies (eg, Fabry disease)

# Awareness of High-Risk Populations Serves as a Key to an Early Diagnosis of ATTR-CM

High-risk population	Prevalence of ATTR-CM
<b>Atrial fibrillation</b> 	<ul style="list-style-type: none"> <li>Studies have reported variable AF prevalence rates of 15-70% in patients with ATTR-CM<sup>1</sup></li> </ul>
<b>HFpEF</b> 	<ul style="list-style-type: none"> <li>Cardiac amyloidosis, predominantly ATTR, is suspected to account for 6-30% of HFpEF cases<sup>2</sup></li> <li>A cross-sectional analysis found ~13% of patients admitted for HFpEF, ≥60 years old and LV wall thickness ≥12 mm, were found to have wtATTR<sup>3,4</sup></li> </ul>
<b>Left ventricular hypertrophy</b> 	<ul style="list-style-type: none"> <li>A cross-sectional study revealed that 5.7% of patients with unexplained LVH and an initial diagnosis of hypertrophic cardiomyopathy had hATTR<sup>5</sup></li> </ul>
<b>Aortic stenosis</b> 	<ul style="list-style-type: none"> <li>Approximately 16% of patients admitted with severe calcific AS undergoing percutaneous TAVR screened positive for ATTR-CM<sup>6</sup></li> </ul>
<b>Extracardiac musculoskeletal manifestations</b> 	<ul style="list-style-type: none"> <li>Carpal tunnel syndrome, spinal stenosis, or spontaneous biceps tendon rupture may present as “red flags” for ATTR-CM<sup>2</sup> <ul style="list-style-type: none"> <li>CTS, primarily affecting those ≥50 years is found in 15-60% of patients with ATTR-CM</li> <li>CTS may manifest prior to cardiac symptoms, serving as an early sign of disease</li> </ul> </li> </ul>

AF, atrial fibrillation; AS, aortic stenosis; ATTR, transthyretin amyloidosis; ATTR-CM, ATTR with cardiomyopathy; wtATTR, wild-type ATTR; CTS, carpal tunnel syndrome; CV, cardiovascular; HFpEF, heart failure with preserved ejection fraction; LV, left ventricle; LVH, left ventricular hypertrophy; TAVR, transcatheter aortic valve replacement.

1. Griffin et al. *JACC*. 2021;3(4):488–505; 2. Brito et al. *Glob Heart*. 2023;18(1):59; 3. Gonzalez-Lopez et al. *Eur Heart J*. 2015;36:2585–94; 4. Castano et al. *Curr Cardiovasc Risk Rep*. 2017;11:17; 5. Damy et al. *Eur Heart J*. 2016;37(23):1826-1834; 6. Castano et al. *Eur Heart J*. 2017;38(38):2879–87.

# Diagnostic Challenges

ATTR is often underdiagnosed or misdiagnosed, leading to a delay in treatment and/or initiation of potentially detrimental treatments<sup>1</sup>

Barriers to diagnosis identified in a global online patient survey conducted by the ARC<sup>2</sup>

hATTR



Average physicians seen prior to correct diagnosis

32%

Reported misdiagnosis

26%

Reported trouble getting tested

19%

Reported trouble finding a specialist

wtATTR



Average physicians seen prior to correct diagnosis

18%

Reported misdiagnosis

7%

Reported trouble getting tested

14%

Reported trouble finding a specialist

• ARC, Amyloidosis Research Consortium; ATTR, transthyretin amyloidosis; hATTR, hereditary ATTR; wtATTR, wild-type ATTR.  
1. Nativi-Nicolau et al. *Heart Fail Rev.* 2022;27(3):785–93; 2. Amyloidosis Research Consortium. ARC 2022 Community Survey Results. Published 2022. Accessed November 6, 2023. <https://arci.org/arc-2022-community-survey/#wild>.

# Summary

- ATTR is a multisystemic, rapidly progressive, debilitating, and fatal disease caused by misfolded TTR accumulating as amyloid deposits in multiple organs and tissues including nerves, heart, and GI tract<sup>1-4</sup>
  - Patients diagnosed with hATTR and wtATTR have a median survival of 4.7<sup>5</sup> and 2.5-5.5 years,<sup>6-8</sup> respectively
- ATTR remains underdiagnosed or misdiagnosed<sup>4,9,10</sup>
- Patients with ATTR experience substantial burden, including reduced QoL<sup>11-14</sup> and functional impairment<sup>6,15</sup>

There remains a need for health care professionals to:

1

Recognize the constellation of red-flag symptoms of ATTR<sup>16,17</sup>

2

Collaborate with a multidisciplinary team for a potential diagnosis<sup>16,17</sup>

3

Employ the diagnostic algorithm and confirmatory diagnostic tools to verify diagnosis<sup>17-19</sup>

4

Assess progression of disease following treatment and provide patient with holistic care (mental, physical, and social support)<sup>20,21</sup>

ATTR, transthyretin amyloidosis; hATTR, hereditary ATTR; wtATTR, wild-type ATTR; GI, gastrointestinal; QoL, quality of life; TTR, transthyretin.

1. Hanna. *Curr Heart Fail Rep.* 2014;11:50–7; 2. Mohty et al. *Arch Cardiovasc Dis.* 2013;106:528–40; 3. Adams et al. *Neurology.* 2015;85:675–82; 4. Maurer et al. *Circ Heart Fail.* 2019;12:e006075; 5. Swiecicki et al. *Amyloid.* 2015;22:123–31; 6. Lane et al. *Circulation.* 2019;140:16–26; 7. Aus dem Siepen et al. *Clin Res Cardiol.* 2018;107(2):158–69; 8. Givens et al. *Aging health.* 2013;9(2):229–35; 9. Hawkins et al. *Ann Med.* 2015;47:625–38; 10. Castano et al. *Heart Fail Rev.* 2015;20:163–78; 11. Coelho et al. *Muscle Nerve.* 2017;55:323–32; 12. Vinik et al. *J Peripher Nerv Syst.* 2014;19:104–14; 13. Ines et al. *ISPOR Congress 2015.* Poster N21; 14. Obici et al. *Amyloid.* 2020;27:153–62; 15. Bolte et al. *Orphanet J Rare Dis* 2020;15:287; 16. Nativi-Nicolau et al. *Heart Fail Rev.* 2022;27(3):785–93; 17. Kittleson et al. *JACC.* 2023; 81(11):1076–176; 18. Namiranian and Geisler. *Am J Med.* 2022;135 Suppl 1:S13–19; 19. Ando et al. *Orphanet J Rare Dis.* 2013;8:31; 20. Adams et al. *Orphanet J Rare Dis.* 2021;16:411; 21. Obici et al. *BMJ Open.* 2023;13:e073130.