EARLY DIAGNOSIS IS KEY:
UNDERSTANDING AND IDENTIFYING ATTR-CM

What is ATTR-CM?

ATTR-CM (transthyretin-mediated amyloidosis) is a life-threatening progressive heart disease that negatively impacts patients.[1,2] There are 2 subtypes of ATTR-CM[1,3]:

Wild-type ATTR-CM (ATTRwt-CM)[2,3]:

- Caused by TTR destabilization due to aging
- Typically presents later in life; often remains undiagnosed for years

Variant ATTR-CM (ATTRv-CM)[3]:

- Caused by TTR gene mutations
- May present earlier; associated with faster disease progression and more aggressive cardiac disease

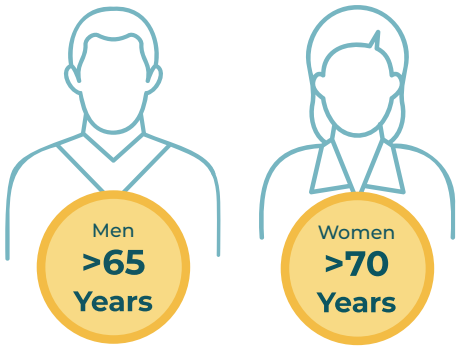
Who may be at risk for ATTR-CM?

Although predominantly diagnosed in men, ATTR-CM is becoming increasingly recognized in women[4]

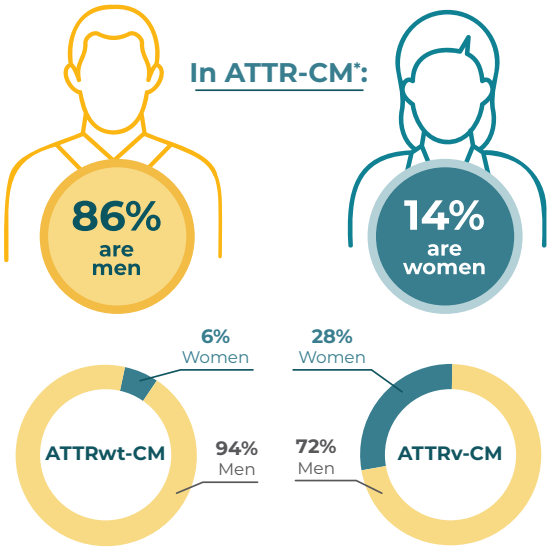
Patients at risk for ATTR-CM[4]

Heart failure OR presence of red flag symptoms **AND** Increased myocardial wall thickness of >12 mm

Typical age at onset:



Sex differences in ATTR-CM subtype[4]



ATTR-CM can be challenging to recognize and diagnose, as symptoms can mirror other serious conditions or appear unrelated to a heart condition.[2]

*In a study of 1732 consecutive patients, comprising 1095 with ATTRwt-CM and 637 with ATTRv-CM.[4]

ATTR-CM=transthyretin amyloid cardiomyopathy; ATTRv=variant transthyretin-mediated amyloidosis; ATTRwt=wild-type transthyretin-mediated amyloidosis; TTR=transthyretin.

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DON'T MISS THE SIGNS AND SYMPTOMS: IDENTIFYING RED FLAGS OF ATTR-CM

Cardiac

Cardiac[1,5]

- [ ] HFpEF
- [ ] Atrial fibrillation
- [ ] Increased left ventricular wall thickness without obvious cause
- [ ] Pacemaker requirement
- [ ] Orthostatic hypotension

Heterogeneous symptoms resemble and/or overlap with more common cardiac diseases[1,2]

- Hypertrophic cardiomyopathy
- Hypertensive heart disease
- Aortic stenosis
- HFpEF

If clinical findings raise suspicion for ATTR-CM—regardless of family history of heart failure or polyneuropathy—consider EKG, laboratory and/or imaging evaluation, or referral to a cardiac amyloidosis specialist.[1,5]

Refer to the 2023 ACC Expert Consensus for more information on diagnosing ATTR-CM.

Extracardiac

Musculoskeletal[5,6]

- [ ] Back pain/lumbar spinal stenosis
- [ ] Bilateral carpal tunnel syndrome
- [ ] Spontaneous biceps tendon rupture
- [ ] Shoulder, hip, or knee surgery

Gastrointestinal[7]

- [ ] Early satiety
- [ ] Weight loss
- [ ] Abdominal pain
- [ ] Nausea
- [ ] Constipation
- [ ] Diarrhea

Neurological[5]

- [ ] Sensorimotor polyneuropathy (paresthesias and weakness)
- [ ] Autonomic dysfunction (orthostatic hypotension, postprandial diarrhea alternating with constipation, gastroparesis, urinary retention, and incontinence)

ATTR-CM=transthyretin amyloid cardiomyopathy; EKG=electrocardiogram; HFpEF=heart failure with preserved ejection fraction.

References: 1. Witteles RM, Bokhari S, Damy T, et al. Screening for transthyretin amyloid cardiomyopathy in everyday practice. *JACC Heart Fail*. 2019;7(8):709-716. doi:10.1016/j.jchf.2019.04.010 **2.** Greve AM, Christoffersen M, Frikke-Schmidt R, Nordestgaard BG, Tybjærg-Hansen A. Association of low plasma transthyretin concentration with risk of heart failure in the general population. *JAMA Cardiol*. 2021;6(3):258-266. doi:10.1001/jamacardio.2020.5969 **3.** Hornstrup LS, Frikke-Schmidt R, Nordestgaard BG, Tybjærg-Hansen A. Genetic stabilization of transthyretin, cerebrovascular disease, and life expectancy. *Arterioscler Thromb Vasc Biol*. 2013;33(6):1441-1447. doi:10.1161/ATVBAHA.113.301273 **4.** Patel RK, Ioannou A, Razvi Y, et al. Sex differences among patients with transthyretin amyloid cardiomyopathy – from diagnosis to prognosis. *Eur J Heart Fail*. 2022;24(12):2355-2363. doi:10.1002/ejhf.2646 **5.** Kittleson MM, Maurer MS, Ambardekar AV, et al. Cardiac amyloidosis: evolving diagnosis and management: a scientific statement from the American Heart Association. *Circulation*. 2020;142(1):e7-e22. doi:10.1161/CIR.0000000000000792 **6.** Nativi-Nicolau J, Judge DP, Hoffman JE, et al. Natural history and progression of transthyretin amyloid cardiomyopathy: insights from ATTR-ACT. *ESC Heart Fail*. 2021;8(5):3875-3884. doi:10.1002/ehf2.13541 **7.** Kittleson MM, Ruberg FL, Ambardekar AV, et al. 2023 ACC expert consensus decision pathway on comprehensive multidisciplinary care for the patient with cardiac amyloidosis: a report of the American College of Cardiology Solution Set Oversight Committee. *J Am Coll Cardiol*. 2023;81(11):1076-1126. doi:10.1016/j.jacc.2022.11.022

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