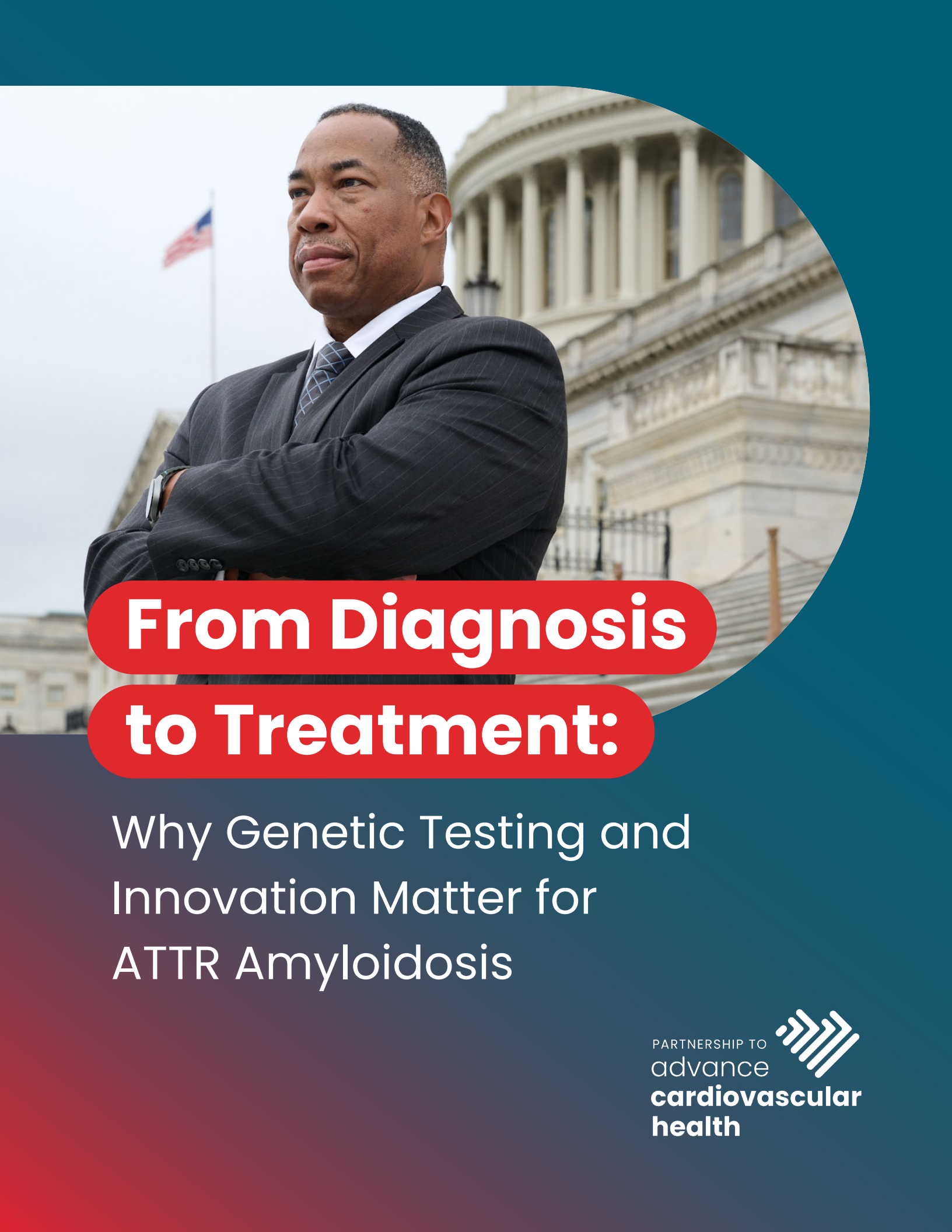


A photograph of a Black man in a dark pinstripe suit, white shirt, and patterned tie, standing with his arms crossed. He is looking off to the side with a thoughtful expression. In the background, the US Capitol building is visible, along with an American flag on a pole. The image is framed within a circular cutout on a teal background.

From Diagnosis to Treatment:

Why Genetic Testing and
Innovation Matter for
ATTR Amyloidosis



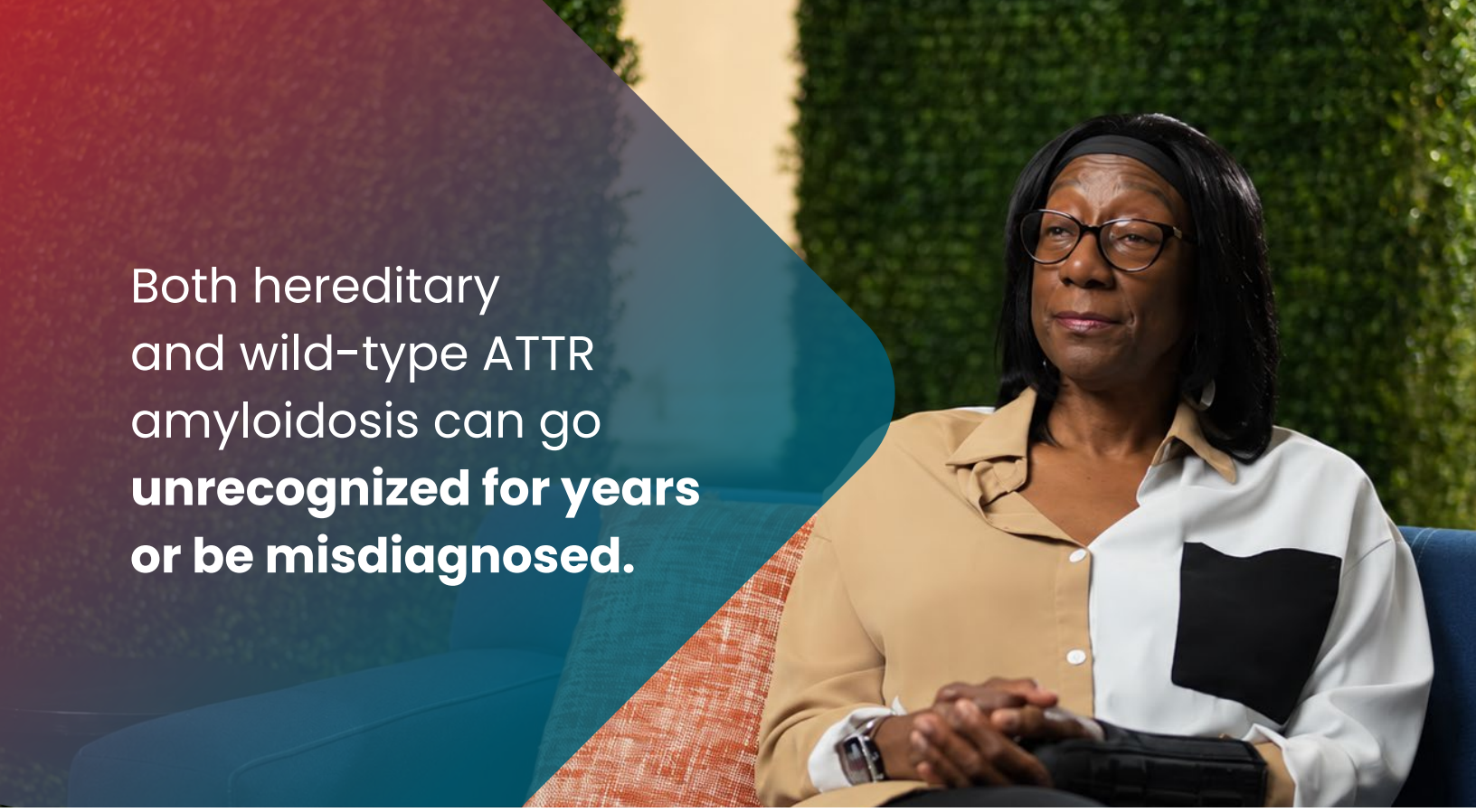
Introduction

Amyloidosis is a serious, rare disease caused by misfolded proteins that form amyloid deposits in tissues and organs. Over time, these deposits can cause irreversible damage and become life-threatening if left untreated. It is a devastating disease, which is now being diagnosed with increased frequency.

Transthyretin amyloidosis, or ATTR, is the most common form of amyloidosis in the United States and often affects the heart. Delays in diagnosis can be fatal, as individuals living with ATTR amyloidosis can have an [average life expectancy](#) between 3 and 5 years after symptom onset without appropriate treatment.

Most people living with ATTR have one of two main forms: wild-type (wtATTR), which is linked to aging, or hereditary (hATTR), caused by an inherited genetic mutation. Family history can suggest hATTR amyloidosis, and genetic testing can identify individuals who carry the mutation, helping guide treatment planning.

Greater awareness, early genetic testing and proactive screening can help shorten the diagnostic journey for individuals and families affected by ATTR amyloidosis.



Both hereditary
and wild-type ATTR
amyloidosis can go
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Hereditary vs. Wild-Type ATTR Amyloidosis

ATTR amyloidosis commonly occurs in two forms: hereditary and wild-type.

Hereditary ATTR amyloidosis, also called variant transthyretin amyloidosis, is caused by a genetic mutation passed down through families. More than 150 different gene variants have been [associated](#) with the disease, which affects an estimated [50,000](#) people across the world. A parent carrying an ATTR genetic mutation has a 50% chance of passing the mutation to their child. However, inheriting the mutation does not necessarily mean an individual will develop the disease. Among those who develop the disease, the clinical presentation and age of onset vary even within the same family.

Wild-type ATTR amyloidosis is the most prevalent form. The disease [affects](#) an

estimated 200,000 to 500,000 people worldwide. Clinicians often diagnose wATTR amyloidosis in male adults [aged](#) 65 and older. Wild-type ATTR amyloidosis symptoms can [resemble](#) age-related heart conditions like heart failure or other cardiac diseases such as hypertrophic cardiomyopathy, which can delay diagnosis. It also can coexist with other more common forms of disease.

Both hereditary and wild-type ATTR amyloidosis can go unrecognized for years or be misdiagnosed, which can lead to irreversible disease progression. Understanding the differences between the two forms can help clinicians and individuals recognize the warning signs earlier to reduce diagnostic delays.

How ATTR Affects the Body:

Early Warning Signs and Symptoms

Among the most serious manifestations of amyloidosis are those that occur when amyloid deposits build up in the cardiovascular system. When protein deposits build up in the heart, they can thicken and stiffen the heart muscle, increasing the risk of cardiovascular complications such as irregular heartbeats and heart failure. An estimated 50,000 to 150,000 Americans have heart failure due to ATTR amyloidosis. Patients have about a five-year life expectancy after a heart failure episode without proper care.

Symptoms can vary widely and often affect multiple organs at once, leading to overlapping complications across the body. Early warning signs of ATTR amyloidosis include numbness or tingling in the feet, dizziness and balance problems, shortness of breath, irregular heartbeat, swollen feet, digestive issues and unintentional weight loss.

Many individuals with ATTR symptoms present with common heart and neurologic issues which can be overlooked when they should be treated as early warning signs. For instance, carpal tunnel syndrome can be mistaken

for a simple wrist problem, though it may signal ATTR amyloidosis before the onset of cardiac symptoms. Ten percent of patients with carpal tunnel syndrome go on to develop ATTR, especially if it is bilateral. For clinicians, combinations of these signs or a family history of similar symptoms should prompt evaluation for ATTR amyloidosis.



Gaps in Diagnosis

Early diagnosis is critical for ATTR amyloidosis—the earlier the diagnosis, the better the outcome is for patients.

Yet ATTR amyloidosis is frequently misdiagnosed or underdiagnosed. One review of published studies [found](#) that the average diagnostic delay for those with hereditary ATTR cardiomyopathy was 5.7 years, and misdiagnosis occurred in 34% to 57% of patients with ATTR cardiomyopathy, or ATTR-CM, across the analyzed studies. A separate Veterans Health Administration study [determined](#) that the median time from heart failure to diagnosis of ATTR-CM was 490 days.

Accurate recognition of ATTR amyloidosis can help individuals access appropriate treatment earlier and preserve quality of life. Expanding access to diagnostic tools, improving clinical awareness of early disease indicators and educating patients on when to seek care can help reduce misdiagnosis. Disease-modifying therapies are most effective when started early in the disease.

Diagnostic challenges are not experienced equally across all populations. Gaps are especially pronounced among Black Americans. The Val122Ile, or V142I, genetic variant, which primarily affects the heart, is more [common](#) in this population and often mistaken for more common heart conditions, such as hypertensive heart disease. About 3% to 4% of Black Americans, including those of Caribbean descent, carry the V122I variant. As a result, misdiagnoses may leave families unaware of the potential inherited risk of a life-threatening disease.

Addressing diagnosis disparities requires improving clinician awareness of ATTR amyloidosis in high-risk populations and expanding access to appropriate diagnostic testing.

A man with short grey hair, wearing a light blue button-down shirt and a grey checkered blazer, is sitting on a red couch. He has his hands clasped in his lap and is looking off to the side with a thoughtful expression. The background is a blurred indoor setting with a plant and a window.

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Why Genetic Testing Matters: Earlier Genetic Testing, Earlier Diagnosis

Early diagnosis of ATTR amyloidosis can help patients access appropriate therapies and reduce the risk of irreversible disease progression. ATTR symptoms can vary and may begin as early as age 30 in patients with some hereditary forms. Recognizing early signs and considering genetic testing are appropriate steps toward a timely diagnosis.

Genetic testing helps [distinguish](#) hereditary ATTR amyloidosis from wild-type ATTR amyloidosis, as the two conditions can look similar in signs and symptoms. That distinction matters: It affects which treatments a patient may be eligible for, and whether family members are at risk. Testing identifies the specific TTR genetic mutation, helping clinicians better understand how the disease may progress. Different genetic mutations affect the body uniquely, and understanding the variant offers valuable insight into disease progression and aids targeted treatment.

A study found that only 32% of patients with a genetic TTR variant [reported](#) a known family history of ATTR amyloidosis. This finding suggests that many individuals may carry a life-threatening variant without realizing it. Expanding access to genetic testing can support earlier diagnosis and improve understanding of inherited disease risk.

Genetic testing also strengthens shared decision-making between clinicians and patients by providing crucial information to guide follow-up for changes in symptoms and determine whether specialized care is needed. Identifying an ATTR genetic mutation can improve patient understanding of their disease and support more personalized treatment planning.



Cascade Testing: Protecting Families

Genetic testing is recommended for all patients with ATTR amyloidosis; if a pathogenic TTR variant is identified, cascade testing of first-degree relatives is recommended. Cascade testing involves targeted genetic testing of blood relatives after a disease-causing variant is identified in one family member, allowing clinicians to identify and monitor at-risk relatives before symptoms develop.

For individuals who have family members with hATTR amyloidosis, genetic testing can be done between five and ten years before the predicted onset of symptoms as a way of early monitoring and diagnosis. Evidence shows that cascade testing makes a difference: A 2026 study of more than 1,200 relatives of hATTR patients [found](#) that family members identified through genetic screening were diagnosed earlier and had significantly better survival than the first person diagnosed in their family, likely because they could begin treatment sooner.

Despite the critical role of genetic testing in identifying hATTR amyloidosis, significant barriers to access remain. Patients can face insurance coverage restrictions, prior authorization requirements and denials that limit access to testing. Medicaid coverage of genetic testing varies by state, creating gaps in access. Insurers should cover this life-changing tool for diagnosing a complex and progressive disease.

Family members identified through genetic screening were **diagnosed earlier and had significantly better survival.**



Treating ATTR Amyloidosis: What GTTs Are and Why They Matter

New therapies have transformed the outlook for people with ATTR amyloidosis. These include silencers, which reduce the body's production of TTR, and stabilizers, which prevent the TTR protein from misfolding. New treatments have been found to reduce deaths in clinical trials of patients with ATTR cardiomyopathy and allow patients to manage their chronic condition.

Genetically targeted technologies, or GTTs, are among the most important treatment advances for people specifically with ATTR amyloidosis. Rather than merely treating symptoms, these technologies target the disease at its source: they act on the genetic instructions the body uses to make transthyretin, so the body produces less protein, and fewer deposits form.

There are two types of GTTs used to treat ATTR amyloidosis. Antisense oligonucleotides, or ASOs, attach directly to the genetic message that tells the body to make transthyretin and cause it to break down. Small interfering RNA, or siRNA, therapies use RNA interference (RNAi) to find and destroy that same message.

The two approaches work slightly differently, but both aim to lower the amount of transthyretin the body makes.

These technologies have altered the treatment landscape for ATTR amyloidosis. GTTs reduce production of both the faulty and normal forms of the protein, slowing disease progression and helping protect the nerves and heart from further harm. Because they also lower normal transthyretin, one GTT, vutrisiran, is now approved to treat ATTR cardiomyopathy, including the wild-type form. GTTs were the first treatments approved in the U.S. for nerve damage caused by ATTR amyloidosis, and they remain the only class of drugs approved for that use.

How GTTs Differ From Gene Therapy

Genetically targeted technology is not the same as gene therapy.

Gene therapy changes a person's genetic material—either by adding a new gene, replacing a faulty one or editing DNA directly—and is often intended as a one-time treatment. GTTs leave the DNA untouched. Instead, they intercept the genetic message after it is copied from the gene, preventing it from being used to make transthyretin.

Since the underlying gene is never altered, the effect of a GTT wears off over time. Patients

can receive regular doses by injection or infusion every few weeks to every few months, depending on the medication. The U.S. Food and Drug Administration reviews and approves GTTs as drugs, not as gene therapies or biologics, a distinction that matters for federal drug pricing policy. Gene-editing approaches for ATTR amyloidosis are being studied in clinical trials, but they are a separate category of treatment from the GTTs available today.

Policy Opportunities

Awareness, Access and Innovation

A medical breakthrough, however, is only valuable if patients are diagnosed in time to benefit from it and can access it.



1 Improve Awareness Among Providers

Because ATTR amyloidosis is relatively rare and its symptoms span many specialties, the clinicians who are most likely to see early signs—primary care physicians, cardiologists, neurologists, hand surgeons and gastroenterologists—may not recognize them. Policymakers and health systems can support continuing medical education on ATTR warning signs, encourage electronic health record tools that flag combinations of symptoms and strengthen referral pathways to amyloidosis specialists.



2 Close Gaps in Genetic Testing and Counseling

Genetic testing plays a critical role in early identification of ATTR amyloidosis, helping confirm whether an individual has wild-type or hereditary amyloidosis and identifying the presence of specific variants. Genetic testing can guide personalized treatment that best addresses a patient's symptoms. Genetic counseling can help individuals and family members interpret results and support treatment planning. Public and private insurers should cover genetic testing for people with signs or symptoms of ATTR amyloidosis and for at-risk relatives through cascade testing.



3 Raise Awareness Among Policymakers and Protect Continued Innovation

Congressional briefings, engagement with rare disease caucuses and state rare disease

advisory councils and awareness campaigns can help ensure policymakers understand ATTR amyloidosis and the value of early genetic testing.

Continued progress in GTTs depends, in part, on federal policy that will ensure patient access. The Inflation Reduction Act allows Medicare to negotiate the prices of certain drugs after they have been on the market for a set number of years. Under the law, small-molecule drugs become eligible for selection seven years after approval, with negotiated prices taking effect about two years later, while biologics become eligible after 11 years. Although GTTs are complex medicines that require years of research and an intricate manufacturing process, much like biologics, they are approved as drugs rather than biologics, which gives them the shorter seven-year window. This leaves manufacturers with less time to recover the large investments needed to create these therapies, which could discourage research into new treatments for rare diseases like ATTR amyloidosis.

The bipartisan Maintaining Investments in New Innovation, or MINI, Act (H.R. 1672) would address this gap.

It would require genetically targeted drugs, including the ASO and siRNA medicines used to treat ATTR amyloidosis, to be on the market for at least 11 years before they qualify for Medicare price negotiation, placing them on the same timeline as biologics. By preserving incentives for investment, the MINI Act would help ensure that the next generation of GTTs continues to move from the lab to patients.

A photograph of a middle-aged Black man with short hair, wearing a dark blue suit jacket over a light blue button-down shirt. He is smiling and speaking into a microphone. The background is blurred, showing other people in a social setting.

**Educational resources
and reliable support**
help patients make
informed decisions.

Resources for Patients and Caregivers

ATTR amyloidosis can create challenges that extend beyond managing symptoms. Because the disease can cause complex and changing symptoms, patients need access to ongoing information and support beyond clinical appointments. Educational resources and reliable support help patients make informed decisions about symptom management and maintaining quality of life.

Peer mentor programs give patients an opportunity to connect with others who share the experience of living with ATTR amyloidosis. These connections can provide reassurance, strengthen patients' confidence in navigating their care and offer practical insights into managing daily life with the disease. Because ATTR amyloidosis is rare, community building can help patients develop a support system and feel less alone. State and local support groups can be especially helpful.

Caregivers play an active role in managing a loved one's ATTR amyloidosis experience by helping coordinate medical care and support

daily living. Caregiving responsibilities can be highly demanding and affect caregivers' emotional, financial and physical well-being when adequate support systems are unavailable.

Respite care can give caregivers time to rest and attend to personal responsibilities, reducing the risk of physical and emotional burnout. Programs such as the National Family Caregiver Support Program can [connect](#) caregivers with support and respite services. In addition, the Family and Medical Leave Act can [help](#) eligible caregivers take time off work while keeping employer-sponsored health insurance.



Conclusion

Amyloidosis was once considered a fatal disease. Before effective treatments, the disease progressed relentlessly, often leading to death and debility within a decade of symptoms beginning. Now, thanks to scientific advancements, investments and medical breakthroughs, amyloidosis is a treatable condition, and therapies can slow or halt its progression, especially when started early.

But there is still work to be done. Amyloidosis is rare and complex; it places a heavy burden on patients and the families who care for them, and it is often misdiagnosed, which delays treatment while the disease causes lasting damage. Genetic testing is critical to closing the diagnostic gap. A diagnosis can alert family members to their own risk and enable cascade testing to identify relatives who may have the inherited form of amyloidosis. Greater awareness among clinicians, along with attention to family history, is the foundation for earlier and more accurate diagnosis.

Policy can accelerate this progress. Policymakers should support provider education on the warning signs of ATTR and prioritize reducing the financial and administrative barriers that delay genetic testing, diagnosis and treatment. Policies such as the bipartisan MINI Act can help protect access to GTTs while supporting the development of the next generation of targeted therapies.

The progress made against ATTR amyloidosis is a story of hope. By working together, policymakers, clinicians and patient advocates can make this disease history.



The **Partnership to Advance Cardiovascular Health** works to advance public policies and practices that result in accelerated innovation and improved cardiovascular health for heart patients around the world. This work requires patient advocates who know how to advocate for themselves and a better health system.

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