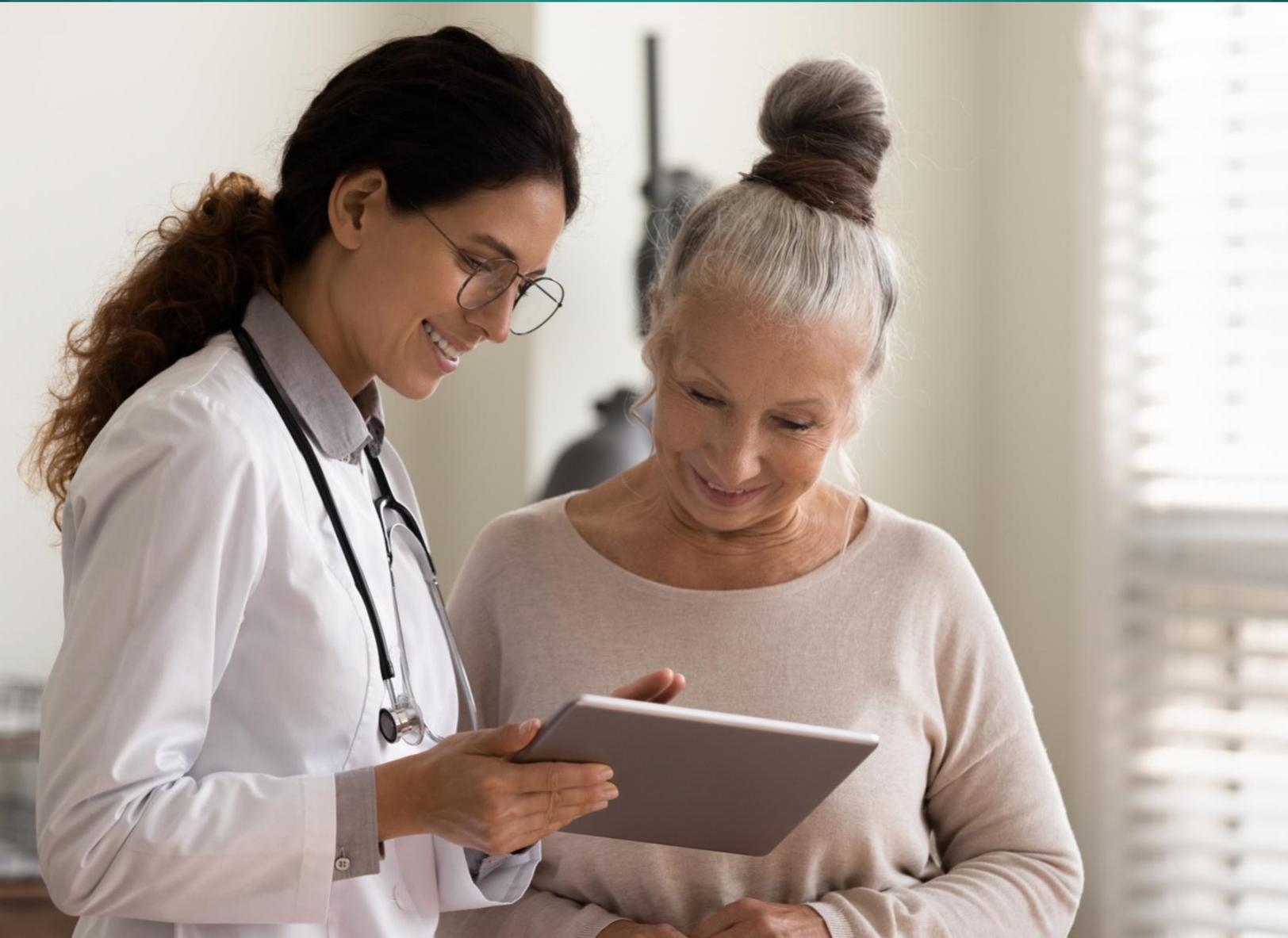




UNIVERSITY OF OTTAWA
HEART INSTITUTE
INSTITUT DE CARDIOLOGIE
DE L'UNIVERSITÉ D'OTTAWA

Cardiac Amyloidosis Clinic



A GUIDE FOR PATIENTS AND CAREGIVERS

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This document is also available in French under the title: | *Cette publication est aussi disponible en français sous le titre : Clinique d'amylose cardiaque*

UOHI 254

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Referral to the Cardiac Amyloidosis Clinic

Your doctors have referred you to the University of Ottawa Heart Institute Cardiac Amyloidosis Clinic because they have a high suspicion you may have cardiac amyloidosis. The purpose of this guide is to help you and your family to better understand the condition.

Clinic number: 613-696-7000 ext. 17000



If you have any questions or concerns, you can call the nursing coordinator at 613-696-7000 and then press 0. There is a nurse available 24 hours a day, 7 days a week. The nurse will return your call as soon as they are able (within the same day you called).

What is amyloidosis?

Amyloidosis is an uncommon condition that develops over a period of months to years. *Amyloid* is the name given to the tangles of protein substance that characterize the disease and cause many of the disease symptoms. Amyloid deposits can be found in the heart, nerves, digestive system, kidneys and other organs. Their presence stops these organs from working properly. As a result, amyloid patients can develop breathing difficulties and experience sensation loss, constipation, and fluid retention.

What is cardiac amyloidosis?

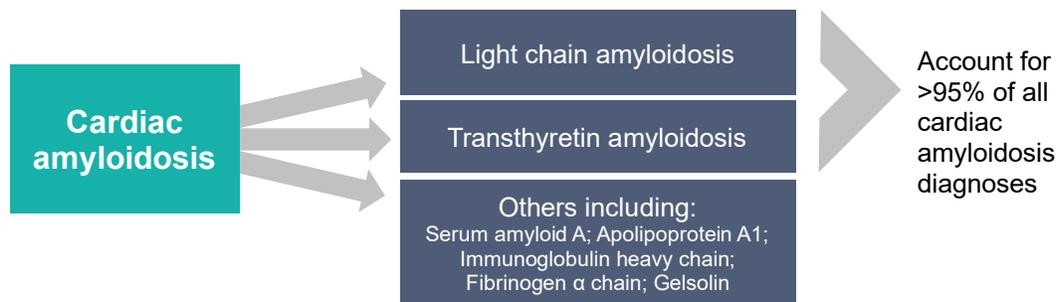
Cardiac amyloidosis occurs when amyloid protein tangles are found in the heart muscle. The extra protein deposits prevent the heart from squeezing or contracting properly. They also interfere with how the heart relaxes between beats. Amyloid protein is not overly elastic, so its presence makes the heart stiff and difficult to fill.

It is the heart stiffness that initially presents as shortness of breath during exercise. During exercise, the heart must fill rapidly and empty efficiently to enable blood to reach the body's muscles. If it cannot fill due to a loss of elasticity, then the muscles do not receive the blood they need. As a result, patients with this condition may experience breathlessness.

In response to the lack of blood reaching the tissues, the body responds by retaining water. The retained water causes ankle swelling and swelling within the lungs, which can make breathing difficult.

Types of amyloidosis

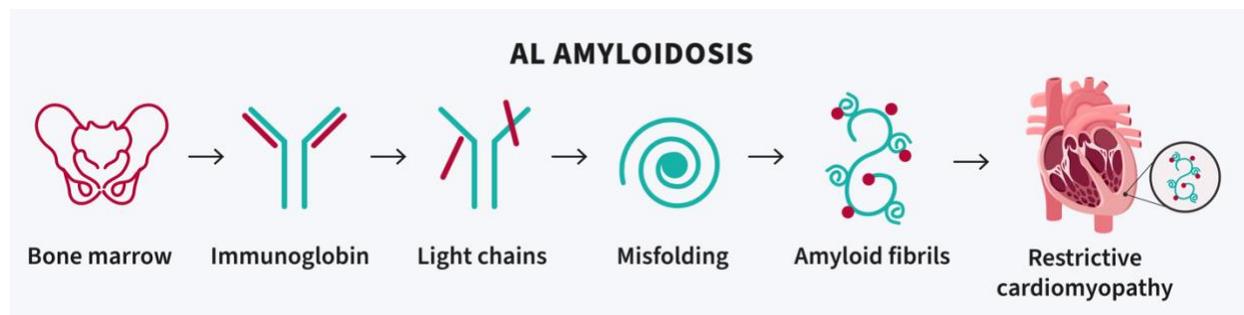
Amyloidosis can affect many different organ systems within the body. The protein at the centre of the tangles determines which organs are affected. Different proteins have specific organs that they target. Your cardiologist will order multiple tests to determine your type of cardiac amyloidosis. It is important to identify the type of amyloidosis you have as this will determine your treatment. The two most common forms of amyloidosis observed in the Cardiac Amyloidosis Clinic are light chain amyloidosis (AL) and transthyretin amyloidosis (ATTR).



Light chain amyloidosis (AL)

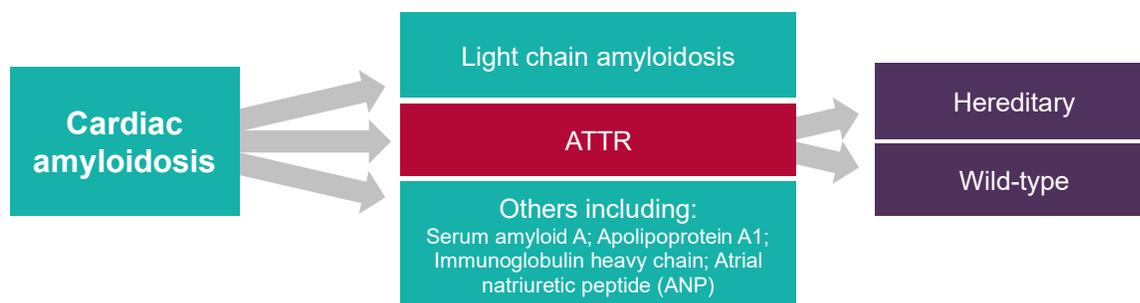
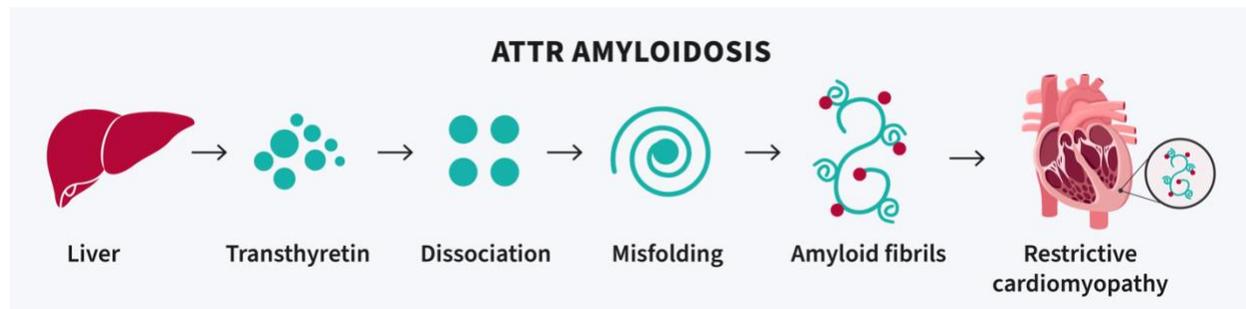
The protein at the centre of the tangles in AL amyloidosis is the light chain component of an antibody protein. Antibodies are usually a part of the body's defence against infections. In AL amyloidosis, however, plasma cells in your bone marrow make mutated or “misfolded” (folded in an incorrect shape) light chain proteins instead of functional antibodies. These abnormal light chain proteins can gather in your heart, kidneys and other organs, causing organ dysfunction.

If you have been diagnosed with AL amyloidosis, you will be referred to a hematologist/oncologist who will discuss chemoimmunotherapy directed at the underlying plasma cell responsible for dysfunctional light chain proteins.



Transthyretin amyloidosis (ATTR)

The most common form of cardiac amyloidosis is caused by abnormal tangles made from transthyretin (TTR) protein. This protein is made in the liver and is involved with transporting thyroid hormone and retinol (vitamin A) in our bodies. Amyloidosis occurs when there is a misfolding of the TTR protein that then produces amyloid fibrils. There are two forms of ATTR amyloidosis: hereditary and wild-type.



Hereditary

This type is caused by a change (known as a mutation) in the TTR gene. This change can be passed down from parent to child and is diagnosed by genetic testing. The two most common places for these deposits to build are in the heart and the nervous system. Deposits in the heart can lead to heart failure or abnormal heart rhythms. Deposits in the nervous system can lead to neurological symptoms, including numbness and tingling in the arms and legs.

Wild-type

This type develops for unknown reasons as people get older. Just as joints become stiff and inflexible as we age, protein molecules also become less flexible. If the TTR protein becomes less flexible, it accumulates as amyloid tangles. It is more common than hereditary transthyretin amyloidosis. It most often develops in people over 65 years of age and is more common in men.

Both the hereditary and wild subtypes of ATTR amyloidosis have an unknown prevalence and incidence and are a slowly progressing disorder.

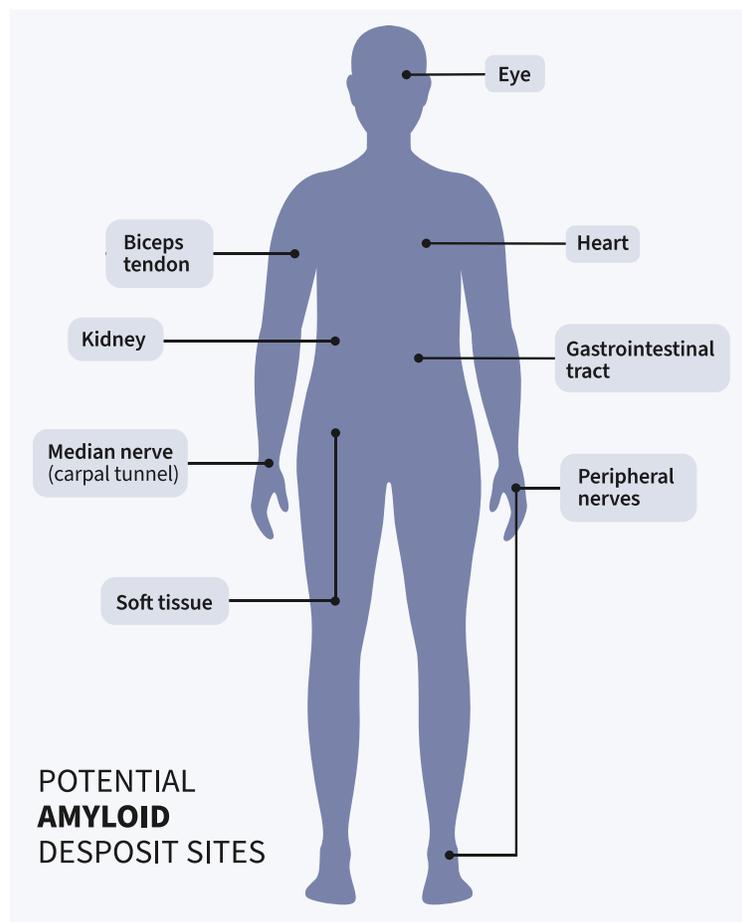
Causes of amyloidosis

Some people have hereditary transthyretin amyloidosis, which is caused by a change (known as a mutation) in a person's genes. Otherwise, there is no known cause to explain why some people develop amyloidosis.

Symptoms of cardiac amyloidosis

- Shortness of breath with exertion
- Fatigue
- Rapid/irregular heartbeat
- Swelling/water retention

Non-heart-related symptoms, such as carpal tunnel syndrome or problems in the joints, nerves and spine, can develop before heart problems in patients with cardiac amyloidosis. Other symptoms can include problems with digestion, bowel or bladder function, and vision changes.



How is cardiac amyloidosis diagnosed?

Cardiac amyloidosis can be difficult to diagnose. The diagnosis may be suspected because of typical symptoms and the results of the following routine cardiac tests.

- **Blood work:** Blood tests to assess various organ involvement, including heart, liver and kidneys, given the systemic nature of the disease. Also used to screen for plasma cell disorders.
- **Electrocardiogram (ECG):** A simple and painless test that measures and records the electrical activity of the heart.
- **Echocardiogram (Echo):** An imaging technology that uses ultrasound to create images of your heart. It is a diagnostic test used to examine the heart and its blood supply, determine how large the heart is, how well it contracts, and how the valves function.
- **Cardiac magnetic resonance imaging (MRI):** A test performed to visualize the structure and function of the heart, valves and major arteries and veins.

Once suspected, other specialized tests are needed to confirm a diagnosis, including those mentioned below.

- **Tissue biopsy:** This test determines the presence of amyloid protein. This is done by taking a small tissue sample.
- **Pyrophosphate scan:** A nuclear imaging technique used to determine whether a patient has AL or ATTR amyloidosis.
- **Nuclear imaging:** PET (positron emission tomography) myocardial perfusion imaging is an imaging process that shows how well blood flows to the muscle of the heart.
- **Genetic testing:** Performed using a sample of blood a cardiologist has ordered. The blood sample is then examined by specialists. Only the TTR gene will be analyzed. None of the other 22,000 genes are analyzed.

How is cardiac amyloidosis treated?

Treatment for cardiac amyloidosis is based on the specific type of condition present.

Symptoms

Symptoms are usually treated with medications that reduce swelling, support blood pressure, control heart rate and reduce stroke risk. Typical heart failure medications are usually used, including ACE (angiotensin-converting enzyme) inhibitors, ARBs (angiotensin II receptor blockers), beta blockers, diuretics, and aldosterone antagonists.

Some patients may not tolerate these medications due to amyloid tangles in the nerves that control blood pressure response. Your medication will therefore be individualized and titrated by your cardiologist.

AL amyloidosis treatment

Treatment includes chemotherapy and sometimes stem cell transplant. This will be prescribed by your hematologist or oncologist.

ATTR amyloidosis treatment

There are many treatment options for managing ATTR amyloidosis. The earlier the diagnosis, the sooner treatment begins, symptoms are managed, and overall amyloid deposition is reduced.

Vyndaqel® (tafamidis meglumine) or Vyndamax® (tafamidis) are oral medications and are the standard of care for those with either hereditary or wild ATTR amyloidosis. These medications work by stabilizing the TTR protein to prevent it from breaking down, misfolding and infiltrating the heart.

Onpattro® (patisaran) and Tegsedi® (inotersen) are gene silencers. They work by switching off the production of the TTR protein. The gene silencers have been shown to help with neurological symptoms of ATTR. Gene silencer prescriptions in Ontario require proof that amyloidosis is present in the neurological system. This is typically determined through electromyography (EMG), a test used to detect neuromuscular abnormalities.

A note about funding

Both Vyndaqel® and Vyndamax® require either private insurance or approval from the Ontario Ministry of Health Exceptional Access Program. The Cardiac Amyloidosis Clinic nurse will collect your test results to apply for funding. **Please rest assured you will not experience a gap in your coverage.**

The Heart Institute Cardiac Amyloidosis Clinic

The Cardiac Amyloidosis Clinic is a specialized outpatient clinic for patients diagnosed with or who have suspected amyloidosis in the heart. The goal of the clinic is to optimize cardiac amyloidosis care, coordinate between multidisciplinary teams, and provide clinical expertise to help patients manage complex pathways and improve access to treatment.

Our clinic is a shared model of care, meaning you will see any of the physicians within the program. Your constant point of contact, however, will be the clinic nurse. The clinic nurse can address any questions or concerns you may have.

Do I need to change my lifestyle?

Incorporating heart-healthy habits is of benefit to all individuals with heart conditions. Eating well, exercising regularly, and managing stress in your life can help support your heart and keep it healthy over the long term.

We recommend you cook at home more often, eat regular meals, enjoy a variety of vegetables and fruit, choose whole grains, and use plant-based fats (that is, olive or canola oil) in your cooking more often. You can check out the top 10 tips for healthy eating and the nutrition 101 videos on the UOHI's website (ottawaheart.ca/healthy-eating) to learn more.

A brisk walk of 20 to 30 minutes each day is excellent exercise and can be done in all weather (and even in the mall, if necessary). It is important to remember to listen to your body.

A note on genetics

What test is needed to find out if I have hereditary ATTR amyloidosis?

Genetic testing can determine whether you have a variant in the TTR gene. Genetic testing is done through a blood test that your cardiologist will order. The blood sample is sent to the Children's Hospital of Eastern Ontario (CHEO) Genetic Diagnostic Laboratory to be examined by specialists. Only the TTR gene will be analyzed; none of your other genes will be analyzed. The cost of this clinical test is covered under the Ontario Health Insurance Plan for all Ontario residents, and by RAMQ (Régie de l'assurance maladie du Québec) for residents of Québec. If you are not covered by OHIP or RAMQ, please speak with your cardiologist, as other arrangements may be needed.

What are the possible results of the test?

There are three possible results of the genetic test.

1. **Positive:** A mutation is found in the TTR gene that is associated with amyloidosis. This would mean that you have hereditary ATTR amyloidosis.
2. **Negative:** No mutations were found in the TTR gene. This would mean that it is most likely that you have wild ATTR amyloidosis. However, it does not rule out rare types of amyloidosis or other types of hereditary cardiomyopathies.
3. **Variant of uncertain clinical significance:** A change is found in the TTR gene, but we are not able to determine if it is a variant that may cause amyloidosis. This type of result is uncommon, and it would mean that we would not be able to determine if you have wild ATTR amyloidosis or hereditary ATTR amyloidosis.

If your genetic test is positive or detects a variant of uncertain clinical significance, you will be referred to a genetic counsellor to discuss the implications for you and your family members.

It is important for you to tell your cardiologist if you have a biological relative (parent, grandparent, sibling, child, aunt, uncle, or cousin) with a medical history of any of the conditions listed below.

- Cardiomyopathy (heart muscle disease), particularly thickening of the heart muscle
- Sensorimotor neuropathy (progressive numbness and/or a decreased ability to feel pain or temperature) with cardiomyopathy or kidney disease
- A known variant in the TTR gene

How is hereditary ATTR amyloidosis inherited?

Hereditary ATTR amyloidosis is an autosomal dominant condition. This means that each of your siblings and children, of either sex, has a 50% risk of having the TTR variant. Not everyone with the TTR variant will develop hereditary ATTR amyloidosis. However, those with the TTR variant are at increased risk of developing amyloidosis and should consult a cardiologist to be assessed. If you have a TTR variant, you and your family members can meet with a genetic counsellor to further discuss recommendations.

Genetic testing for family members: If you have hereditary ATTR amyloidosis, this could have implications for your close biological relatives because they may have the same TTR gene variant. If you do not have hereditary ATTR amyloidosis, your family members are not at increased risk for developing amyloidosis.

Who has access to my genetic results?

Your genetic results will be given only to you and your healthcare team. Your cardiologist will use the results to complete the Ontario Ministry of Health Exceptional Access Program application.

Thanks to the *Genetic Non-Discrimination Act*, individuals are protected from discrimination based on genetic results. This means that insurance companies, employers, etc., cannot request genetic test results. Your healthcare provider can also redact this information when sending reports.

Additional resources

TTR Amyloidosis Canada

The focus of this organization is to help support and advocate for patients and families living with ATTR amyloidosis. This group can help connect you and your family with local, regional, and national amyloid community support. Their website is a comprehensive trusted resource for the latest information about treatments, clinical trials, and advocacy. Visit madhatr.ca/ or call 905-580-2802.

Physical activity

ottawaheart.ca/physical-activity-heart-health

Nutrition

ottawaheart.ca/healthy-eating

Mental health

Read the sections about stress, anxiety and depression, and find additional mental health resources in the Heart Institute's Heart-Healthy Living Guide.

ottawaheart.ca/document/heart-healthy-living-guide

Cardiac rehabilitation | Top 10 Tips series

ottawaheart.ca/rehab-top-10-tips

Smoking Cessation Program

ottawaheart.ca/quit-smoking-program

University of Ottawa Heart Institute Patient Alumni Association

ottawaheartalumni.ca

Women@Heart Program

cwhhc.ottawaheart.ca/womenheart-program

What you need to know about advance care planning

Advance care planning is the process of thinking about and planning for future medical care. Early advance care planning reduces hospitalizations and visits to the emergency room and improves quality of life and decision-making at the end of life.

There is no pressure to make a final decision today, or all at once. Rather, the advance care planning process is designed to help patients and their families express their values and preferences for medical treatments needed in the future.

The six steps to advance care planning

1. **Think.** Prepare to make decisions as situations arise. This is decisional readiness. While you are healthy and well, think about what you might want if you were to become unwell. Understand your preferences may change over time.
2. **Learn.** Consider your individual and overall health, as well as your preferences regarding major decisions, such as cardiopulmonary resuscitation and intensive care admission.
3. **Identify.** Designate a substitute decision-maker or power of attorney and involve this person early and often throughout the advance care planning process.
4. **Talk.** Although you may find these conversations difficult, the earlier and more often you have them, the better your substitute decision-maker or power of attorney is positioned to help you when you need it. You can start these conversations any time. You should also tell your health care team about your goal of care decisions.
5. **Document.** Record your goals of care, the name and contact information of your substitute decision-maker or power of attorney, and your wishes for major health decisions. Refer to the Speak Up campaign (advancecareplanning.ca) or the Plan Well Guide (planwellguide.com) for help.
6. **Review.** You may change your mind about your advance care plans at any time. Review your decisions to ensure they align with your goals of care.

