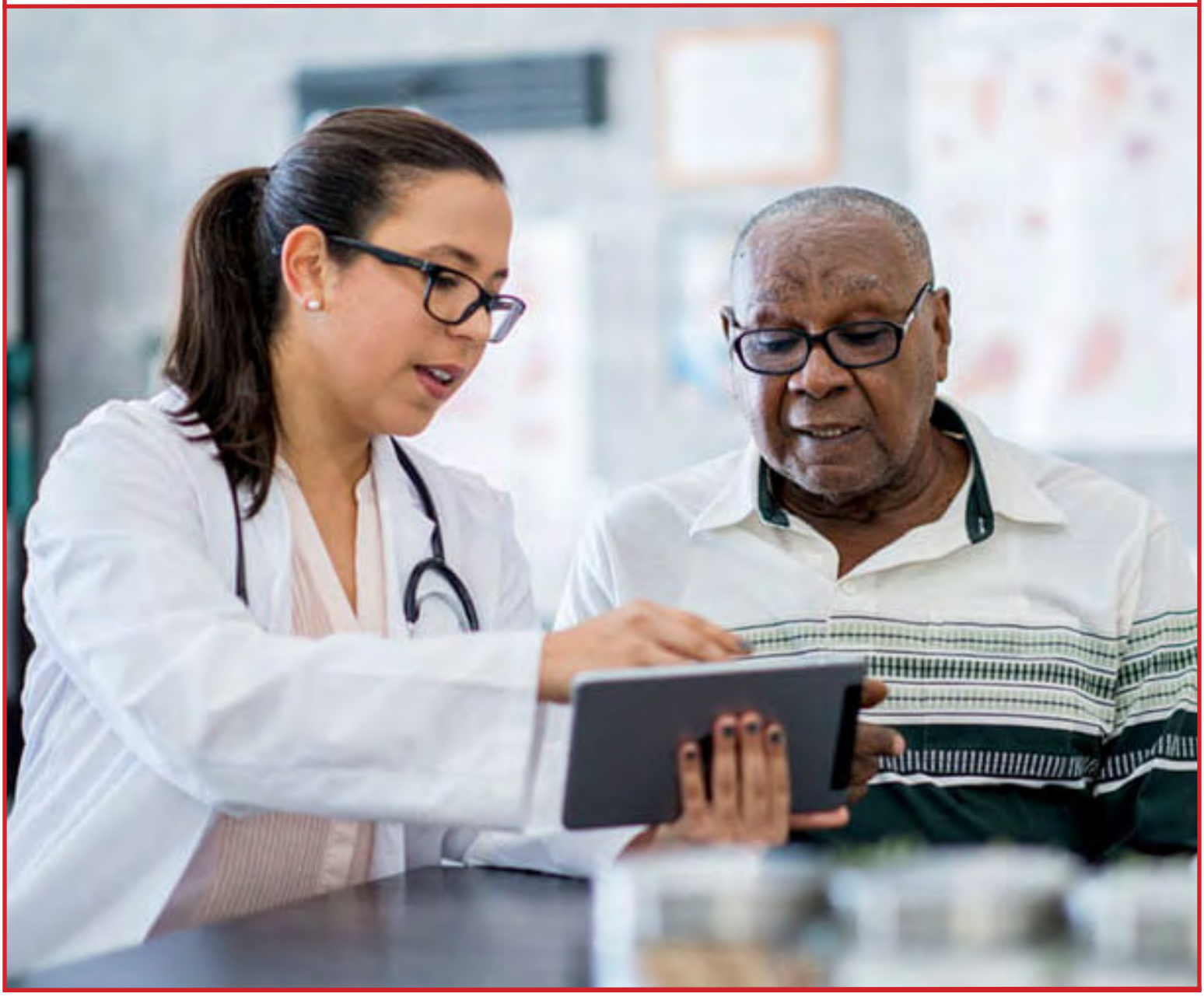
American Heart Association®

Talking to Patients About Gene Editing and Clinical Trials: A Guide for Clinicians



1. Resource Guide for Engaging Your Patients

Tips for discussing gene editing and gene therapy with your patients

This guide provides you with some talking points about gene editing and gene therapy. This may be useful when discussing the intricacies of each treatment with your patients who have genetic conditions that affect the heart, like transthyretin amyloid cardiomyopathy (ATTR-CM), who may be eligible for clinical trials.

Your patients may need to discuss the differences between gene editing and gene therapy.

Gene editing vs. gene therapy: Clinical overview[1-4]

Gene Editing

Gene editing is a precise technique that directly modifies the DNA sequence within a patient's cells to correct or eliminate genetic variants. It uses molecular tools to target specific regions of the genome for alteration. Unlike gene therapy, gene editing aims to permanently change the genetic code at its root.

Gene editing is often considered as a treatment for hereditary diseases, which can be passed down from one or more parents to their children. But gene editing can also treat health conditions that are not hereditary.

Gene Therapy

Gene therapy is a medical approach designed to treat or prevent diseases by introducing or replacing genetic material within a patient's cells. The goal is to address the underlying genetic cause of a condition by either supplementing a missing or defective gene or silencing a harmful one. Gene therapy often uses vectors, such as modified viruses (e.g., adeno-associated viruses [AAVs]), to deliver therapeutic genes into target cells.

Comparison framework

Aspect	Gene Editing	Gene Therapy
Purpose	Directly modifies the DNA sequence to correct or eliminate variants.[1]	Introduces or replaces genetic material to compensate for defective genes.[1]
Precision	Highly precise; targets specific DNA sequences for modification.[2,3]	Less precise; relies on gene delivery to target cells but may affect non-target cells.[1]
Mechanism	Uses molecular tools (e.g., CRISPR-Cas9) to edit the genome.[1]	Uses vectors (e.g., AAVs) to deliver therapeutic genes.[1]
Duration of Effect	Permanent changes to the genome; effects are typically long-lasting.[1]	May require repeated treatments depending on the condition.[5]
Current Status	Investigational; clinical trials are ongoing for various genetic diseases.[2,3]	Approved for certain conditions (e.g., spinal muscular atrophy, inherited retinal diseases).[6,7]
Risks	Off-target edits, ethical concerns, long-term safety unknown.[1,2]	Immune response to vectors, off-target effects, limited efficacy in some cases.[1]
Applications	Explored for conditions like ATTR-CM, sickle cell anemia, and Huntington's disease.[2,8,9]	Can treat conditions like ATTR-CM, hemophilia, and inherited retinal diseases.[2,7,10]

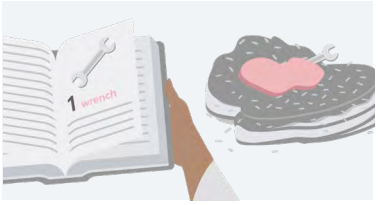
Both gene therapy and gene editing represent transformative approaches to treating genetic conditions that affect the heart like ATTR-CM. Discuss the investigational status, risks, and benefits of each approach with your patients.[2]

2. Tips for Discussion With Your Patients

Introducing the concept: The recipe book metaphor[1,2]

Gene editing and gene therapy can be explained using the metaphor of a recipe book.

Imagine the human genome as a recipe book containing instructions for how the body functions. Each recipe (gene) contributes to the body's health. Sometimes, a recipe has a mistake that leads to problems.



Gene editing is like fixing the recipe directly in the book. It removes or corrects the faulty instruction so future batches (cell replications) are made correctly.

Gene therapy is like adding a missing ingredient or replacing a faulty recipe with a new one. It doesn't change the recipe book itself but supplements it to restore balance.

Tips for addressing patient concerns

Your patients are likely to be nervous or concerned when considering these types of treatments. You can anticipate common worries and respond with clarity and compassion:

"This feels overwhelming."
That's totally natural. We're here to help you understand every step.

"Will this change all my genes?"
No—it only targets the specific gene causing the issue. It's like fixing one recipe, not the whole book.[2,3]

"I don't trust clinical trials."
We understand your concerns. Today's trials follow strict ethical guidelines with informed consent and safety checks.[11-13]

"How does this affect my family or future children?"
These treatments affect only the targeted cells, not reproductive cells, so they won't pass on changes to children.[3]

"Will I be treated differently because of my race, gender, or religion?"
This treatment is available to all eligible patients, and we're committed to ensuring everyone has equal access to care.[11-13]

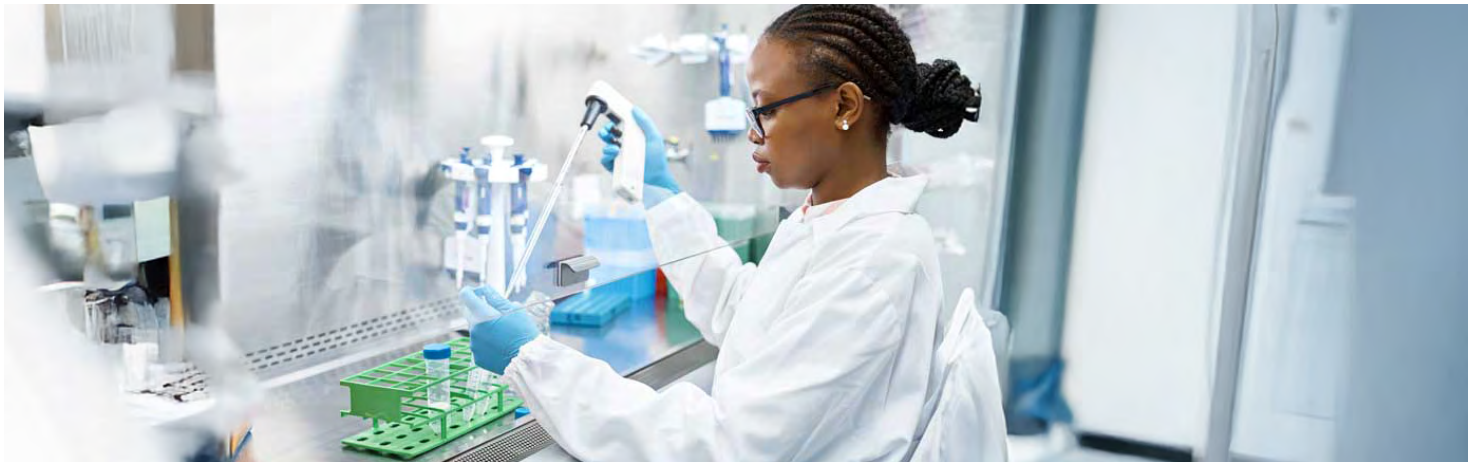
Reinforce transparency and shared decision-making:
Let's talk through the risks and benefits together.
You can opt out of participation at any time. This is your decision.[14]

Whether at diagnosis, during genetic counseling, or at the time of choosing a path forward, balancing optimism with realism fosters trust. This encourages informed decision-making and ensures your patients feel supported throughout their care journey.

3. Explaining Clinical Trial Participation Clearly and Transparently

Demystifying clinical trial participation

Clinical trials are a vital part of advancing medical research, and discussing them with your patients and their caregivers requires clarity, empathy, and transparency. Below are some tips to help you guide these conversations effectively.[14]



Clinical trials are an important part of scientific research.

Key aspects of clinical trials

Purpose
Trials aim to test new treatments, improve existing ones, or explore innovative approaches to care. Participation contributes to medical advancements while prioritizing patient safety.[11,14]

Process Overview
Trial participation involves a sequence of screening, doctor visits, procedures, and follow-ups. They are highly structured and include ongoing support throughout the process.[12,14]

Patient Protections
Safety measures include informed consent, ethical oversight, and patient monitoring. Patient privacy and well-being are top priorities.[11-14]

Benefits and Risks
There are potential benefits (e.g., access to cutting-edge treatments) and risks (e.g., side effects or uncertainty of outcomes), and both must be considered on balance.[11,13,14]

Values-Based Decision-Making
Patients should be encouraged to reflect on their personal values, goals, and preferences when considering trial participation.

Prompts to encourage patient engagement

Consider talking through these topics with your patients:

"Let's assess the pros and cons of this treatment."

"Let me explain how your safety will be monitored during the trial."

"Here's what will happen if you decide to leave the trial early."

"Let's discuss how this trial will impact your daily life (e.g., time commitment, travel)."

"Let's review any potential costs involved, and whether they will be covered."

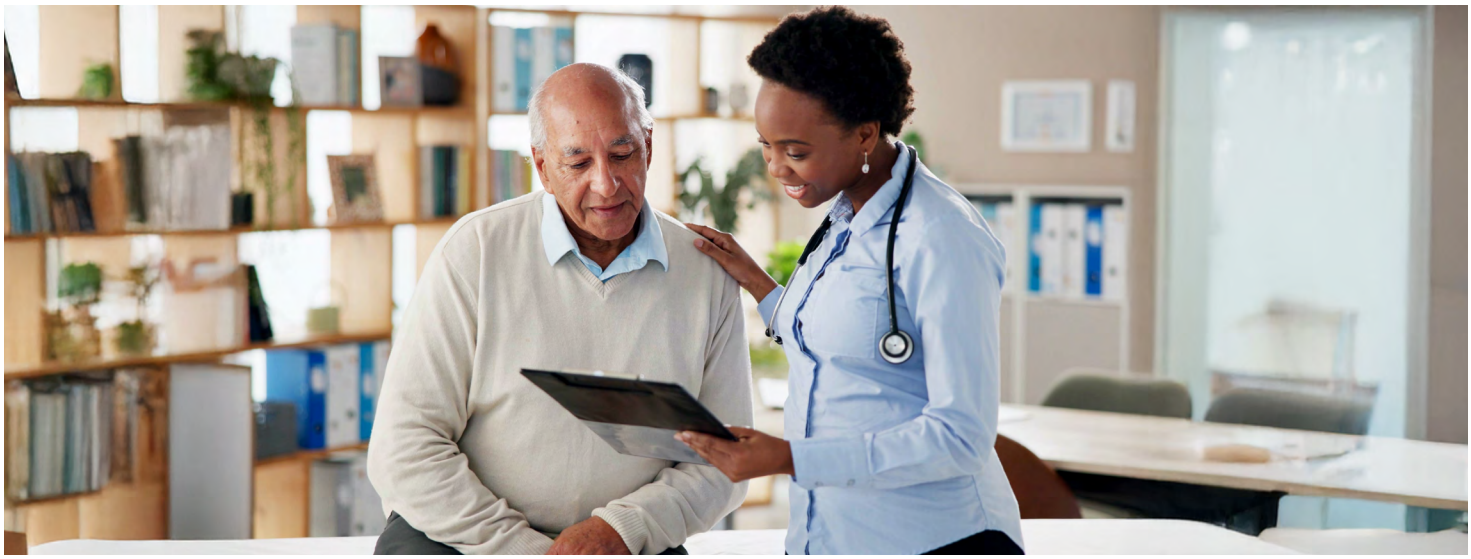
"If you are interested, I can try and connect you with someone who has participated in a similar trial."

Patients often want information on these topics

Trial Logistics
The number of visits and procedures and time commitment involved.[12,14]

Support Systems
The availability of study team members, research nurses, or study coordinators to guide them through the process.[12]

Realistic Expectations
The trials aim to test treatments, not guarantee cures, and outcomes may vary.[14]



Encourage your patients to ask questions about clinical trial participation.

By addressing these points, you can foster trust, empower your patients to make informed decisions, and position trial participation as a partnership rather than a solitary decision.

4. Trusted Tools for Supporting Informed Decision-Making

Resources to share with your patients and their caregivers

You play a critical role in guiding your patients and their caregivers through the complex process of understanding clinical trials, genetic conditions, and emerging therapies like gene editing. Below are some trusted tools designed to support informed decision-making and foster clear, confident conversations.

Key resources

American Heart Association Your Guide to Gene Editing and Clinical Trials for Heart Health

- A comprehensive, plain-language guide to genetic conditions that affect the heart like ATTR-CM, gene editing, gene therapy, and clinical trial participation
- Builds foundational understanding, answers key questions, and empowers patients and caregivers to make informed decisions
- Includes a values-based decision-making tool that encourages patients to reflect on their personal values, time commitments, and preferences
- Extensive FAQ section for answering patient concerns
- Available for download at www.heart.org/ATTR-CM

American Heart Association Clinical Trial Infographic

- One-page explanation of what patients and their caregivers can expect in a clinical trial
- Anchored to easy-to-understand visuals
- Available for download at www.heart.org/ATTR-CM

ClinicalTrials.gov Website

- A general resource to find relevant trials, understand eligibility criteria, and review trial phases
- Simplifies the process of finding trials and provides transparency about trial logistics
- For more information visit https://clinicaltrials.gov/

NSGC Directory for Genetic Counselors

- A directory from the National Society of Genetic Counselors (NSGC) to help patients connect with certified genetic counselors
- Provides access to professionals who can explain genetic conditions, assess risks, and discuss trial participation in detail
- Visit https://findageneticcounselor.nsgc.org/

By leveraging these trusted tools, you can direct your patients and their caregivers to information about their care and participation in clinical trials.

5. Gene Therapy in Cardiovascular Disease: Recent Advances and Future Directions in Science

A science advisory from the American Heart Association

Top things to know:

1. Many cardiovascular diseases, the leading cause of morbidity and mortality worldwide, are caused by damaging DNA variants and require lifelong treatments that mitigate but do not cure disease.
2. Clinical genetic testing can precisely define disease-causing variants and enable the application of emerging genetic therapies to halt or cure disease.
3. Gene therapies deliver exogenous genes to supplement insufficient protein levels or use gene editors to correct, delete, or modify sequences that cause monogenic disorders.
4. Gene therapies do not currently aim to alter multiple common variants that cause polygenic disorders.
5. Significant challenges remain for the effective delivery of gene therapies to specified cells.
6. Non-infectious adeno-associated viruses are effective delivery agents for gene therapies, but with distinct limitations. Non-viral delivery vectors overcome many issues, but uptake by cardiomyocytes remains limited.
7. Many first-in-human gene therapy trials are in progress and anticipate important clinical risks, including tissue-specific targeting, vector-associated adverse events, off-target effects, and treatment durability.
8. Ongoing trials offer transient treatments by supplementing protein-coding sequences for insufficient proteins such as LAMP2 and MYBPC3 in genetic cardiomyopathies and DNA therapies, which will cause permanent effects in recipient cells—providing a potential one-and-done intervention.
9. Gene therapies raise societal and regulatory issues, including long-term monitoring, high cost, equitable access, and ethical concerns.
10. Educating clinicians, patients, and society is critical to understanding genetic concepts, appropriately interpreting genetic test results, and advancing gene therapies to benefit patients and reduce the burden of cardiovascular disease.

Scan this QR code to read the full American Heart Association journal article

Intellia Therapeutics is proud to support the American Heart Association's Gene Therapy Awareness and Education resources.

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