

SUPPLEMENTAL MATERIAL

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Supplemental Methods

This qualitative, cross-sectional study involved in-depth, semi-structured interviews conducted between March and August 2023. Qualitative research enabled the investigation of open-ended questions, providing nuanced and contextualized insights.¹ This study was methodologically grounded in abductive analysis. Abductive analysis is an iterative approach to qualitative research which integrates awareness of existing theoretical frameworks and research evidence with inductive approaches, such as open coding, to maximize detection of anomalous findings.² This approach was well-suited to address our research questions given our goal of understanding perspectives of people with cardiogenetic conditions on gene therapy within the context of broader literature from other disease groups.

Inclusion criteria for this study were similar to those proposed for ARVC gene therapy clinical trials: (1) age ≥ 18 years, (2) meets 2010 Task Force Criteria for ARVC,³ (3) pathogenic or likely pathogenic variant identified in a desmosomal gene, and (4) currently has an ICD.³ 2010 Task Force Criteria for ARVC³ are the standard for establishing a diagnosis of ARVC based on integrating findings from imaging, electrocardiography, genetic testing, clinical history and family history. Clinical and genetic data were drawn from the Johns Hopkins ARVC Registry, a prospective, observational longitudinal cohort study.⁴

Participants were recruited by email from the Johns Hopkins ARVC Registry. Purposive sampling techniques were utilized to maximize variation in terms of gender, age at diagnosis, length of time lived with disease, race, and education.⁵ Participants provided oral consent and participated in a semi-structured interview lasting approximately 90 minutes conducted by ES. The study was approved by the Johns Hopkins Medicine institutional review board.

Interviews included the following topics: 1) the impact of ARVC on one's life, 2) prior research experiences, 3) perceptions of gene therapy, including risks and burdens associated with research, and 4) projected personal decision making if asked to participate in a gene therapy clinical trial. The interview guide is available in the supplemental material. Basic educational content about the mechanisms of gene therapy and the clinical trials process was provided partway through the interview, after eliciting current gene therapy knowledge. The educational content was piloted and optimized to suit individuals with varying science literacy and included content from the American Society of Cell and Gene Therapy's patient education site.⁶ The educational script and slides are available in supplemental material. Information about the potential risks and burdens of gene therapies was also incorporated into questions during the latter part of the interview. Discussion of gene therapy risks included information about uncertainty of benefit, medical procedure risks (including immune reaction to viral vector), immunosuppression, long term unknowns, and future ineligibility for other gene therapies. Discussion of burdens included the significant time and travel commitments likely required by clinical trial participation.

Interviews were conducted and audiorecorded via Zoom. After transcription, interviews were double coded utilizing MAXQDA software. Preliminary codes were developed based on prior literature, and the codebook was iteratively refined and adjusted throughout the process. Following independent coding of each transcript, the two coders (ES and LO) came to agreement on definitions and applications of final codes. Abductive analysis of the interviews was conducted to identify major themes and ranges of responses discussed in the interviews.

Limited statistical analyses were conducted based on demographic and clinical characteristics of participants. Participants were divided into two groups based on whether they

stated they would be willing to consider participation in a Phase I clinical trial or not (Table 2). Using a Fisher exact test, the differences between the two groups were compared in terms of genetic variant causative of ARVC (PKP2 vs other), age at diagnosis (under 30 years old or 30 and over), history of ICD shock, history of sustained ventricular tachycardia, history of ablation, qualitative right ventricular ejection fraction (normal or low normal vs reduced), and quantitatively grouped left ventricular ejection fraction (60% or greater vs lower). The mean left ventricular ejection fraction between the groups was also compared using an unpaired t-test.

Supplemental Tables

Table S1. Supplemental Quotations: Awareness, attitudes, and interest in participation

Topic	Quotations from Participants
Awareness of gene therapy	<p data-bbox="500 365 1416 569">“I don’t know if I’ve heard about anything specific to ARVC. But just general gene therapy, you know, like you hear about it in the news, you – I’m interested in that kind of stuff, so I would like read an article on it. I feel like there’ve been a number of things in the last couple of years about gene therapy that have been intriguing.” -115</p> <p data-bbox="500 617 1406 772">“Only loosely [aware]. I knew that there were some advancements and some research going into it recently from the last appointment that I had with my doctor, and he was excited about the prospects of it but I don’t know that much about it.” – 117</p> <p data-bbox="500 827 1416 1108">“I’m aware that [gene therapy] that’s certainly a focus right now...I know that’s kind of where we’re going with this. I know there are some challenges to it. You have to treat specific mutations, individually. I think the delivery method is always probably one of the biggest challenges on how to provide this type of genetic treatment, or if they’re going to fix anything. I think another challenge would be any adverse reaction to it by getting the body to accept that change.” -102</p>
Attitudes toward gene therapy	<p data-bbox="500 1121 1409 1276">“I’d say like, you know, I feel pretty optimistic about it. It sounds like you know this could eventually be a really good therapy for those of us with ARVC. I don’t know what the right word is—I think the right word is impatient.”-111</p> <p data-bbox="500 1331 1416 1444">“It still seems kind of amazing that we’re at a place in this world where we can actually direct treatments using these viruses in gene therapy. It just still kind of blows my mind.” -105</p> <p data-bbox="500 1499 1367 1612">“If I was looking to be one of the subjects of the trial, I’d be very apprehensive to that [research participation], because, yeah, I mean, you can kill people with that.” -102</p> <p data-bbox="500 1667 1399 1864">“She’s [my mom] is like ‘There’s a cure,’ and I’m like, ‘What are you talking about?’ And then she was just saying that people have been going crazy [on Facebook] saying that this is a very favorable treatment at the moment, and that they’re looking for human participants, and that’s all she said, because then she started crying...I</p>

	<p>cried, and we were in the [restaurant], so we didn't talk about it anymore." -104</p>
<p>Interest in participating in phase I gene therapy clinical trials</p>	<p>"Well of course, I would definitely—my husband and I have already talked about it a little bit, but we would talk about that, but yeah, I still feel that I would be super excited to start, and yes I pray that it will happen soon and would be available [<i>So do you think you would intend to participate if it was available?</i>] Yes, absolutely, yes." -103</p> <p>"I don't know what my decision would be, and I thought before this interview that I would. I thought it would be an instant yes, and now I'm just like, oh, I don't know, because there's a lot more to consider...I honestly don't know what I would decide." -116</p> <p>"It would be a hard no just because of the whole unknown...and then where I'm at with my condition right now." -108</p>

Table S2. Supplemental Quotations: Characteristics of the patient and hypothetical decision making

Theme	Quotations from Participants
Perceived disease severity	<p data-bbox="521 340 1377 457">“I’m hoping it [gene therapy clinical trials] would start right away because time is of essence. Time with this progression it’s a killer, true killer.” -114</p> <p data-bbox="521 508 1414 625">“Yeah I mean, I would definitely consider it, I would definitely look more at the later stages of things. I don’t think my situation warrants getting into the early stage of any of this, it just isn’t necessary.” -117</p> <p data-bbox="521 676 1409 835">“I’m not in a state of desperation or worry. I know I’m very healthy...but if it was a different case where this was as severe, like I was having a problem almost every day and this was a hopeful way, then it would more lean towards yes.” -104</p> <p data-bbox="521 886 1409 961">“I mean, at the end of the day, I’m relatively healthy and now to go and intentionally get yourself sick...that’s the dilemma for me.” -110</p>
Adaptation to disease	<p data-bbox="521 970 1414 1297">“I think it would be something that I might obsess over again, like is it really worth it? Is it going to be beneficial? Is it going to help me at all? Where I kind of know the risks that I’m dealing with now...[right after I was diagnosed] I probably would have been all for it [participating in gene therapy research] cause it was just such a radical upset in my life that I would have done anything to get rid of it. And now I’m like okay, well, it’s been 10 years. I’m fine for the most part, like I’ve adjusted.” -116</p> <p data-bbox="521 1348 1401 1507">“When I just got diagnosed, I would have thought of it in one of two ways. I would have either been much more exuberant to try it right away or I would have said, ‘Well, I don’t know how this is affecting me, it hasn’t really affected me’.”-107</p> <p data-bbox="521 1558 1419 1839">“At the beginning, it was, you know, and I had no fear...it’s not like I’m not determined to find a cure. I was, like, I want to be that reason. I was all about, like, if I could be that cure or that person to get that shot to do whatever, sign me up...you know, life changes and my life changed over time. I mean, I think I was at that point of depression and having that need to get back at it [exercise]. And I don’t think I have that need in over 10 years.” -108</p>

<p>Involvement with ARVC community</p>	<p>“The studies are very much—I’m not just helping myself. It helps a big group of people who deal with similar things.”-107</p> <p>“While I am me, I care more about, you know, like any child of mine, and how they would be affected. So I would say that would be a huge factor for me...future generations.” -106</p> <p>“I would prefer to be in Phase III or later, honestly, I’d rather not be one of the very first people. But at the same time, you know again, someone has to be.” -118</p>
<p>Coping styles</p>	<p>“That [previous research participation] was a really hard point for me, because it reminded me again like ‘Oh, you have this chronic disease that you can’t necessarily reverse.’” -104</p> <p>“I guess I figuratively stuck my head in the sand...Part of me, I just haven’t gotten too informed because I just didn’t want more things to make me stressed out. The genetic treatment, it’s kind of sparked my interest.”-105</p>
<p>Life stage</p>	<p>“I think that’s [having kids] probably a big difference from me five years ago even is there’s a lot more right now. Like my life is big right now. So, there’s a lot more to lose.” -115</p> <p>“The fact that I’m a mom, and I’m not just thinking for myself...Doing it comes with a risk, because there’s no guarantee, like there could be long term effects that we don’t know, and there could be negative things that happen that we just can’t anticipate right now, and they need me. They need their mom, and they can’t have a mom that isn’t fully there, or present, or whatever. So, that’s a negative. But at the same time, they can’t not have their mom, and I want what’s best for them. So, it also feels like not participating would be hindering that too [advancing treatments that would potentially prolong their mom’s life].”-113</p> <p>“I’m almost 60 years old, and so most of my life has been lived as far as I know. And I think maybe I’d be more inclined to give gene therapy a try, be part of a study at this point in my life than I would have been shortly after diagnosis just because of a 15-year interval, and not even knowing a lot about ARVC and living with ARVC at that point. Now, I do. I know how to manage it. I think I would be</p>

	more willing to consider participating in gene therapy trials and studies.” -112
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Table S3. Supplemental Quotations: Perceived characteristics of the trial important to decision-making

Theme	Quotations from Participants
Perceived trial benefits	<p>“Maybe it could freeze it where it’s at, so that I could not have further deterioration. Or maybe even better, give me a healthy heart, and I can kind of go back and be a normal person and just be done with this...I really am hopeful maybe someday I could be told, ‘Do whatever you want.’ Sorry [crying]. ‘You can do whatever you want. You don’t have to worry about this.’” -105</p> <p>“Even just if it’s not a cure then it’s something that sort of stalls it or stops it or—I don’t expect a rollback of my heart condition [laughs] frankly or anything.” – 107</p> <p><i>[If you were to undergo a gene therapy treatment, what specific aspects of your life would you hope would change?]</i> “Remove the ICD. Stop the beta blockers. That’s it. I mean, that solves the whole problem.” -101</p> <p>“I think if it would help me at all, that would be great. That’s really it, like the potential that it could be some great cure that those in the trial could benefit from in their lifetime, cause I know oftentimes trials take years, so the pipedream is that it could be something instantly beneficial.” -116</p>
Perceived trial risks	<p>“Definitely no concerns about the kind of discrete parts of the immune suppression and all that, more concerns about unknowns and then the potential of being excluded from a future treatment that’s better.” -117</p> <p>“I know how vaccines work and so it [using viral vectors] doesn’t really scare me that much.” -106</p> <p>“I guess it could go to the wrong place, or it could possibly cause tumors or something, but, I mean, I still feel that overall, there would always be some risk anytime you try something new, and I still feel that the benefits would outweigh any risks that there would be.” -103</p>

	<p>“I think the whole world has unknown side effects. So again, it’s a risk that you are agreeing to take when you do anything. So that doesn’t really faze me either.” -118</p> <p>“And that [unknown long term side effects] is my understanding also with some medications I take, right? Some of them are relatively new, some have been around a long time. Have they been used in combination? In my specific case, the combination that they’re being administered and what’s the long-term effect of that going to be? One of these years, oh sorry, you have a hole in your heart, because we didn’t know that one of these medications caused something bad. So I’m going on blind faith that there’s not going to be long-term effects of the medications that I’m on, but I don’t know, so I’m willing to take that risk. So yeah, here I am, a walking contradiction. I’m willing to take that risk. So the more I would think about gene therapy, the more I would understand about it, and specifically risk/benefit in a couple different categories that we’ve talked about, I might start to open up more to it, if that makes sense.” -112</p> <p>“Just overall looming fear of potential, you know, death from the situation that could occur, I also just would fear any financial strain from participating, any additional strain on, you know, loved one, family, current work, you know, career, et cetera. Anything basically that would, like, disrupt current life.” -106</p> <p>“Especially because this specific chronic illness hits so many targets, you know, along the checklist, if you will, of what chronic illness involves, I am—I very much so see the risks being equivalent from living with ARVC to living post-research operation. I weigh the risks equally.”-106</p>
<p>Trial stage and data availability</p>	<p>“Honestly, that would really be the only question to me is how far down the road---and again, you’re assuming that as time goes on that people believe the therapy is safer or whatever the treatment is, is safer because you have more data points and that’s your reasoning, you know, behind it. But, you know, I would think if it was available at some point I would undoubtedly do it. It’s just a matter of how far down that line I would go before I decided like, oh yeah, I deem this safe.” -109</p>

	<p>“Like would I be willing to sign up for a gene therapy trial not understanding, you know, all the risks and benefits? Probably not, but like, if you tell me, hey, we’ve tested it, and like, you do this, you have side effects for, I don’t know, the time that it takes for you to kind of get the treatment, and I don’t know, a month after, 30 days after. I’ll be like, okay, I’m willing to kind of go through with that, and you know, nothing is guaranteed, but with a high likelihood of me, you know, like this being a cure, then you kind of have my full attention.” -120</p>
<p>Perceived burden of trial participation</p>	<p>“Well, it seems like a large commitment...at this time I would have to say no. I can't make that commitment at this point...In the future, right—again, I think it depends on employment, right? It depends on family obligations, what I have going on here, wife, kids, all that, so that’s what I would take into consideration as to whether or not to commit to that type of time.” -102</p> <p>“I mean, if my family and I get to a place where we say, ‘Yes, we definitely want to do this,’ then the logistics become less of an issue and the time factor becomes less of an issue because I'm invested.” -110</p>
<p>Trust in clinicians and researchers</p>	<p>“For me and my experience with my medical kind of life, having trust in the service providers, in anybody, is huge. So, if the more I know somebody and kind of not just their technical qualifications, but how they feel about people, and how they feel about patients, and why I think they’re motivated to be involved, that makes a big difference to me...When you’re doing a clinical trial, I guess you want to be part of the team, not just a patient...I would want the information. I wouldn’t want to be left out of anything...I wouldn’t want to ever feel like something was being kept from me, because that would cause me not to trust the people that I was depending on for treatment, and I think that’s a really risky relationship to have occur, so I think trust and transparency and inclusion are really important.” -105</p> <p>“I would probably do my own research first. I would investigate the company. I’d probably get the opinions of [my doctors].” -102</p>
<p>Anticipated cost of gene therapy</p>	<p>“So I have heard about other therapies that have been a couple million dollars for treatment. I hope that this doesn’t cost that much, and I do worry about an insurance company saying ‘We’re not gonna pay for your treatment,’ ...It’s a pretty big concern actually</p>

	<p>that this gene therapy would be produced and I couldn't get it...if for whatever reason I do research and I figure out kind of how insurance companies make their decisions, and I don't think I'd be eligible then I would probably want to participate more in research, because then it can get paid for through that, because I would definitely would want access to it, and I would probably be willing to take more risks for the benefit if I felt like that was the only avenue to getting treatment.”-105</p> <p>“If at the end of the day I felt that this treatment would be inaccessible to a large group of people who couldn't afford it, then I was wasting my time...I wouldn't want to be a part of it.” -110</p> <p>“Any technology is very expensive very early on and generally it doesn't work...Then it gets better and better and then it is accessible to everybody...Am I worried it's not going to be available to everybody? No. I think all wonderful things in the world that I've discovered is, like, you know kind of like, given to a select few for only a few years at the most.”-101</p> <p>“I think that there should be ways to apply for the gene therapy if you're unable to pay for it or something. I think there should be options, I guess is what I'm trying to get at, for anybody who has ARVC. I don't think that the cost of it should be escalated just because it's a gene therapy. I think it should be treated like any other procedure that we would have to endure because of our diagnosis.” -106</p>
Gene specificity	<p>“I feel like that's kind of how things are right now anyway. Some things seem to be more known with different variants. So, I think I expect that.”-113</p> <p>“Even if it's like for a gene that I don't have and therefore it's like not available to me, I still think it's fantastic to people who will benefit from it.”-115</p> <p>“Good for those people if they're not me. Yeah. I mean progression in terms of treatment and things like that is good. Progress in one subset probably means that it gives people more funding, more drive to find it in other places.”-109</p>

	<p>“It would be like your brother or your sister, right? Getting a really awesome opportunity. And maybe you’re a little jealous, but really you want them to succeed and to be healthy. And, you know, I think in general that’s how this community is. I think less jealousy, more happiness for others. So I don’t think it’s going to hurt the community at all.” -118</p>
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Interview Guide

Before we start the interview, I have a few questions about your demographic information and ARVC history. You can refuse to answer any of the following questions if you prefer.

- What is your age?
- What is your gender?
- How would you describe your race or ethnicity?
- What is the highest level of education you have completed?
- What state do you live in?
- Do you live in an urban, suburban, or rural area?
- Have you been clinically diagnosed with ARVC?
- Do you know the genetic cause of your/your family's ARVC?
- How many years ago were you diagnosed/did you learn about the results of your genetic test?
- Do you have an ICD?
- Have you ever received a shock from your ICD?
 - How many times?

We will get started with the interview. To be clear, the purpose of these interviews is to understand what you and other people with ARVC think about gene therapy and what your major priorities and concerns are. We will start with talking about what your experience has been like with ARVC, and then move to talking about gene therapy. I will also present some information about gene therapy partway through the interview to facilitate our discussion. There are no right or wrong answers, and we are hoping to collect input from people with a variety of levels of familiarity with gene therapy. What you say during these interviews will not affect the clinical care you receive from your care team. Please feel free to be transparent about how you feel. Also, feel free to share any questions you have about the topics that come up, and but to maintain the integrity of the research I may not be able to answer all of your questions during the interview. If needed, I will direct you to further resources or people who can answer your questions after the interview. So now we can get started with the questions.

- I wanted to start off with hearing about what your life is like living with ARVC. How would you say having ARVC impacts your life right now?
 - Tell me about how ARVC affects your life on a daily, weekly or monthly basis.
- How does this [the impact of ARVC on your life] differ from when you were first diagnosed?
 - Were there any big turning points that changed the way you think about your ARVC? (life events, changes in your health)
 - How has your diagnosis impacted the rest of your family?

- To what extent do you have other people in your life who have ARVC? Are there other people in your family that have ARVC or at risk for the disease? Do you think your story is different from theirs?
 - Do you know others who have ARVC? Do you feel connected to the ARVC community?
- How severe would you describe your ARVC as being?
 - What worries do you have related to your ARVC?
 - What hopes do you have related to your ARVC?
 - What hopes do you have related to future treatments for ARVC?
 - Thinking about potential future treatments, what specific aspects of your life would you hope could change?
- How do you feel about the current medical options for managing your ARVC?
 - How do you feel about the care you're currently receiving from your doctor or care team?

Next, before we get into talking about gene therapy, I wanted to talk about research in general. There are many different types of research that require different levels of effort and risk on the part of participants. There is registry research, which usually just involves using a form that allows researchers to use your information to learn more about a condition. There is observational research, like taking surveys or participating in an interview like you are today. Finally, there is some medical research, usually known as a clinical trial, which tests a new drug or procedure to be used for treatment. These projects are usually trying to learn whether a treatment is safe in humans and effective at treating a disease.

- Apart from this study, have you participated in research in the past?
 - Can you tell me about your experiences?
 - What type of research was it (of the ones I mentioned)
 - Was it related to ARVC or something else? Have you participated in any research unrelated to ARVC?
 - How comfortable do you feel about participating in research in general? Do you feel differently about the types of research I mentioned at the beginning?
 - Can you tell me why you feel that way?
 - What are the major reasons that you might want or not want to participate in research?
 - Would it make a difference to you who was in charge of the research? (if the research is run by a group you're not familiar with or by a company?)

Now we will talk about gene therapy. First, I'd like to hear about what you've heard about gene therapy in the past. It's ok if you're not confident that all of the information is accurate, we're just trying to understand what kind of information people are hearing about these treatments.

- Prior to hearing about this interview study, what had you heard about gene therapy before?
 - o Where did you get this information?
 - o Where have you heard people in talk about gene therapy for ARVC specifically?

Next, I'm going to share some information about gene therapy. You may have heard some of this information in the past, but I'm sharing it to make sure that everyone is on the same page.

[Share gene therapy educational content parts 1 & 2]

Now, I want to hear what you think about gene therapies.

- Do you have any clarifying questions about the information that I just shared?
- Do you have any initial reactions, thoughts, or feelings about the information I just shared?
 - o Did anything about that information surprise you?
- What are your concerns about gene therapy?
 - o Do you have any concerns about gene therapy that you think you wouldn't have about other types of new treatments?
 - o What aspects of gene therapy do you want more information about?

Now I'm going to give some more information about clinical trial research to help guide our conversation about gene therapy trials.

[Share gene therapy educational content part 3]

- What are your thoughts and feelings about participating in gene therapy research?
 - What are some reasons you might want to participate?
 - What are some reasons you might not want to participate?
- What are your feelings toward participating in an early-stage clinical trial compared to a later stage clinical trial?

Next, I want to learn about your reactions to the potential risks of participating in gene therapy clinical trial research. I'll talk about some specific considerations or risks that could be possible to see what you think about each of them. And then we can discuss overall how this impacts what you think about these trials afterward.

- One consideration is that the benefits of gene therapy are not guaranteed. Since these therapies are still being studied, participating in a clinical trial means there would be a chance the treatment might not work. How do you feel about the uncertainty of the potential benefits of the treatment?
- There are risks associated with any medical procedure, and those specific to gene therapy include an infection, an intense immune reaction, and possibly other risks. How do you feel about the potential risks of having a medical procedure?
- Some aspects of these trials might require suppression of the immune system leading up to receiving the gene therapy to temporarily prevent the immune system from reacting to

the treatment. Having your immune system suppressed can make someone more vulnerable to infection or getting very sick from an infection.

- o How would you feel about undergoing treatments to temporarily compromise your immune system prior to receiving the therapy?
- Since gene therapy is intended to create changes in your gene that can last a lifetime, it's possible there could be other side effects in the long term that we don't know about yet. How do you feel about the possibility of unknown long term side effects?
- Once a person received one type of gene therapy, it's possible they might not be eligible to get another type of gene therapy in the future because of concerns about their body reacting poorly to a second dose. How do you feel about the possibility of being excluded from participation in future gene-therapy-based treatments?
- How does the information about the risks I just went through factor into your thoughts about gene therapy research?
 - o Of the potential risks we've talked about so far, which ones are weighing most on your mind, make you feel the most worried, or would be the most important to your decision?
 - o What would need to be in place to make you feel comfortable participating in a trial?

Next, I'd like to get your thoughts about some of the logistics associated with participating in a clinical trial.

- Depending on the clinical trial, participation can require a lot of time and energy. For example, sometimes people may be required to travel to a hospital far from home to receive the treatment and might have stay there for days to weeks afterward for monitoring.
 - o How long at a time do you think you could conceivably be away from home to participate in this kind of trial?
 - o How would you feel if you were asked to spend a week in the hospital?
 - o How would you feel about travelling to a different city? To a different state?
 - o If you are working, would your job allow you to take time off or work remotely multiple times a year if you needed to come back to the hospital to be monitored?
 - o Would it matter to you whether you were working with center/care team that you already receive regular care from versus a new care team that you had never met before? What about if that new care team was located closer to your home?
- It's possible that clinical trial participants could be asked to get a variety of tests to make sure they are healthy and to check whether the treatment is harming them in any way. Some of these tests could be invasive, like having a biopsy of the heart. How would you feel about having those tests conducted?
 - o Would it make a difference to you if there are some invasive procedures, like heart biopsy, included in the study?

- How do the time and resources possibly required to participate factor into your thoughts about gene therapy research?

Next, I have a few final questions about your overall thoughts about participating in gene therapy clinical trial research given everything we've talked about today.

- How do you weigh the risks of living with your condition against the risks of participating in a gene therapy clinical trial?
 - Can you say more about how you think about weighing the risks you face every day against the risks of a potential trial?
 - Do you see any important differences between these types of risks?
- How does your current life stage or things that are happening in your life right now factor into how you think about gene therapy?
 - Is there a certain time in your life that you think you would be most willing to participate?
- How much do you expect gene therapy should cost or will cost if it is approved? Does that affect your willingness to participate in this research?
 - If gene therapy is approved, do you think gene therapy would be easily available to anyone who wanted to participate?
- Some of these gene therapies may only work for individuals who have a specific genetic change, like the PKP2 genetic change that you have. In other words, only some of the people with ARVC might be eligible for some of these treatments. What are your thoughts or feelings about this?
 - What do you think the impact of this will be on the ARVC community at large?
- Given everything that we talked about today, and acknowledging the fact that you don't have all the details here, if you were asked to participate in a gene therapy clinical trial, how might you approach making that decision?
 - Do you have any idea what that decision would be, and why?
- What other thoughts do you have about gene therapy that we haven't talked about today, or is there anything you were hoping or expecting me to ask about that we didn't talk about?

Educational Module

Part 1:

Gene therapy is the use of genetic material to treat or prevent diseases. Gene therapies are currently being developed to treat many different genetic diseases.

Genetic diseases typically happen when someone has a harmful genetic change, also known as a pathogenic variant or mutation. This harmful genetic change means that something in the body isn't working the way it normally does and can result in a variety of symptoms. As you probably know, in the case of ARVC, changes in a gene can cause the breakdown of the proteins that hold the heart muscle together, causing the heart to malfunction and putting someone at higher risk for arrhythmias.

Part 2:

Gene therapies work to treat genetic diseases by providing a copy of the gene that does not have this harmful genetic change. The idea is that when a working copy of the gene is inserted into the cells, then it can compensate for the copy of the gene that wasn't working and allow the cells to function more normally moving forward.

The packaging used to deliver the working copy of the gene into the cells is known as a vector. Most vectors are derived from viruses, which are naturally effective at delivering information to cells. The part of the virus that causes illness is removed, and the working copy of the gene is put in its place. Then the vector with the working gene is delivered to a targeted part of the body, typically the affected part, like the heart in ARVC.

Part 3:

Extensive research must be done to test the safety, effectiveness, and side effects of medications before they are available for treatment, and this is also true of gene therapies. If early research in laboratory studies and/or animals shows that a gene therapy is promising and appears to be safe, the research will progress to clinical trials in humans. Early phase trials, known as Phase I or Phase II, include a very small number of participants. These early trials are intended to check whether a treatment is safe, whether it has any side effects, and what the dosage of the medication is safe. Later trials, usually known as Phase III, include a larger number of participants and are intended to determine if the medication produces effects that are better than currently available treatments, and how much better they are.

There are not any currently approved gene therapies to treat ARVC. There are not yet any clinical trials to test gene therapy for ARVC. Gene therapies for ARVC, and clinical trials to treat them, may be available in the coming years.